Supplement to

Blood Cell Therapy
The official journal of APBMT

ABSTRACTS

from
the 27th Annual Congress of APBMT

October 6 – 9, 2022

Kochi, India

Hybrid

Contents

ABSTRACTS

The tables and figures attached at the time of submission have been deleted due to space limitations.

PLENARY TALKS

Plenary Talks

CD7-targeted CAR-T cellular therapy for R/R CD7+ T cell acute lymphoblastic leukemia

He Huang

The First Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou, China

Chimeric antigen receptor-T cell (CAR-T) therapy in T cell malignancies faces fratricide, T cell aplasia, and product contamination. So CAR-T cell studies for T-ALL are limited. In China, CAR-T targets for T-ALL were focused on CD5 and CD7. As reported, 4 out of 5 patients achieved deep remission and 1 relapsed quickly after infusing CD7-targeted universal CAR-T product, although all 5 patients developed severe CRS. In another trial enrolling 20 patients with R/R T-ALL, donor-derived CD7 CAR T cells obtained a CR rate of 90%. In a case report, CD4 cCAR was also able to eradicate leukemia blasts and successfully reverse refractory Sezary syndrome. We successfully developed a universal anti-CD7 CAR-T product (RD13-01). RD13-01 contains a bbzg-CAR comprising an anti-CD7 single-chain variable fragment, a 4-1BB costimulatory domain, a CD3ζ signaling domain, the intracellular domain of the common γ chain, and a natural killer cell inhibitory molecule (E-cadherin). TRAC, CD7 and HLA-II were disrupted to avoid graft versus host disease (GvHD), fratricide and rejection. Bbzg-CAR-T exerted antitumor effects superior to those of conventional CAR-T, while exhibiting reduced cytokine production. Among 11 evaluable relapsed/refractory (r/r) patients, no dose-limiting toxicity, GvHD, immune effector cell-associated neurotoxicity or severe cytokine release syndrome (grade≥3) occurred. Nine (82%) showed objective response. For r/r leukemia and NHL, complete response rates were 75% and 33.3% respectively.

Plenary Talks

TIM-3 marks residual leukemic stem cells responsible for relapse in allogeneic hematopoietic stem cell transplantation

Yoshikane Kikushige[1,2]

[1]Department of Medicine and Biosystemic Sciences, Kyushu University Graduate School of Medicine, Fukuoka, Japan
[2]Center for Cellular and Molecular Medicine, Kyushu University Hospital, Fukuoka, Japan

Acute myeloid leukemia (AML) is one of the most common hematological malignancies. AML is derived from a fraction of stem cells that have self-renewal and high propagation activities, which are called leukemic stem cells (LSCs). LSCs remain quiescent and are resistant to conventional chemotherapy. Residual LSCs after chemotherapy eventually drive leukemia regrowth, leading to AML relapse. Therefore, eradicating LSCs is critical for achieving a cure for AML. We previously identified T-cell immunoglobulin mucin-3 (TIM-3) as an LSC-specific surface molecule by comparing the gene expression of LSCs with that of hematopoietic stem cells (HSCs). TIM-3 expression clearly discriminated LSCs from HSCs within the $CD34^+CD38^-$ stem cell fraction. Furthermore, AML cells secrete galectin-9 (gal-9), a TIM-3 ligand, in an autocrine manner, leading to constitutive TIM-3 signaling that maintains the self-renewal capacity of LSCs through the induction of β-catenin accumulation. Thus, TIM-3 is an indispensable functional molecule for human LSCs.

In this symposium, we would like to give a presentation on the functional aspects of the TIM-3 molecule in AML and present the data on the evaluation of minimal/measurable residual disease focusing on $CD34^+CD38^-$ $TIM\text{-}3^+$ LSCs. $CD34^+CD38^-TIM\text{-}3^+$ cells in the complete remission (CR) phase after allo-SCT represent the LSCs responsible for relapse using sequential genomic analysis in identical patients. We retrospectively evaluated the incidence of $TIM\text{-}3^+$ residual LSCs at our institute. All analyzed patients achieved CR and complete donor chimerism (CC) at the engraftment phase; however, the higher frequency of residual $TIM\text{-}3^+$ LSCs within the $CD34^+CD38^-$ fraction at engraftment was a significant and independent risk factor for relapse. The levels of residual $TIM\text{-}3^+$ LSCs in the engraftment phase had a stronger impact on relapse than pre-SCT disease status. Thus, evaluation of residual $TIM\text{-}3^+$ LSCs is a promising approach for predicting leukemia relapse after allogeneic stem cell transplantation (allo-SCT).

PRESIDENTIAL SYMPOSIUM

Presidential Symposium

Activity and Regulation of Cellular therapies in Europe

Anna Sureda

Clinical Hematology Department. Institut Català d'Oncologia-Hospitalet, Barcelona, Spain

CAR-T therapies have revolutionized the management of both pediatric and adult relapsed/refractory B-cell lymphoproliferative disorders. The acceptance of phase II trial data for marketing authorization by the FDA and EMA, however, also raised efficacy and safety concerns. The European Society for Blood and Marrow Transplantation (EBMT) took the lead in different tasks and activities in order to contribute to the development of a comprehensive structure and legal framework that did not exist before; the EBMT registry was upgraded to allow data to capture in more detail on other cellular therapy interventions and nowadays contains more than 3,000 patients treated with autologous CART cells, the post-authorization studies (PAS) were developed in order to capture long-term follow-up data of CAR-T cells mostly in safety but also in efficacy and in 2020 the EBMT launched multi-stakeholder GrOup for immune effector cells such as Chimeric Antigen Receptor T cells (GoCART), a CAR-T-cell community platform. With the primary aim to create a public private/multistakeholder collaboration to maximize the potential of CAR-T cells.

Presidential Symposium

Global Trends in Cellular Therapy and its integration with Hematopoietic Stem Cell Transplantation (HSCT) - Worldwide Network for Blood & Marrow Transplantation (WBMT) Perspective

Dietger Niederwieser[1,2,3], Helen Baldomero[4], Wael Saber[5], Daniel Neumann[6], Sebastian Galeano[7], Yoshiko Atsuta[8], Mahmoud Aljurf[9]

[1]University of Leipzig, Germany; [2]Aichi Medical University School of Medicine, Nagakute, Japan; [3]Lithuanian University of Health Sciences, Kaunas, Lithuania; [4]The Worldwide Network of Blood and Marrow Transplantation (WBMT) Transplant Activity Survey Office, University Hospital, Basel, Switzerland; [5]CIBMTR, Medical College of Wisconsin, Milwaukee, WI, USA; IMISE, [6]University of Leipzig, Germany; [7]Hospital Británico, Montevideo, Uruguay; [8]Japanese Data Center for Hematopoietic Cell Transplantation (JDCHCT), Nagoya, Japan; [9]King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia

In the year 1957, engraftment of allogeneic hematopoietic cells was shown in humans opening new exciting treatment opportunities. After progresses in understanding immune alloreactivity, drug development and supportive care, outcome of hematopoietic stem cell transplantation (HSCT) continuously improved and worldwide activity progressively increased. Today, HSCT is the only curative treatment option for several hematologic disorders and what was learned from HSCT paved the way for cellular therapy with advanced therapy medicinal products (ATMP). WBMT, a worldwide network of scientific societies and NGO in official relations with the World Health Organization, plays an important role in this process by promoting excellence and access to cellular therapy. To reach his mission, WBMT publishes a survey collating information from EBMT, CIBMTR, APBMT, EMBMT, ABMTRR, CTTC, LABMT, EMBMT and transplantation centers.

In 2016, 1662 centers reported more than 82.000 HSCT procedures corresponding to an increase of 77.6% from 2006. Preliminary analyses revealed increases to 92812 HSCT in 2018 and estimates of 100.000/year after 2020. HSCT/10 million inhabitants showed regional differences ranging from 561 and 439 in North America and Europe to 77, 54, 36 and 9 in Latin America, SEAR/WPR, EMRO and Africa regions, respectively. The relative increase in HSCT was higher in low as compared to high/intermediated income countries. The leading indications for autologous HSCT (53.5% of all) were lymphoproliferative diseases (+45.7% from 2006) and for allogeneic leukemias and non-neoplastic disorders (+74.5% and +139.4% from 2006, respectively). In comparison to previous years, we observed a notable increase in haploidentical HSCT. Non-HSCT cellular therapies included donor lymphocyte infusion, CAR-T cells, selected/expanded T-cells, T-REGS, NK cells, dendritic cells, mesenchymal cells and genetically modified CD34 cells.

In conclusion, a persistent increase in HSCT activity is observed worldwide with some variability in indications. Of note is the increase in haploidentical HSCT and in cellular therapies outside HSCT.

Presidential Symposium

Activity and Regulation of Cellular Therapies in North America

Miguel-Angel Perales

[1] Adult Bone Marrow Transplantation Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, 10065, USA
[2] Department of Medicine, Weill Cornell Medical College, New York, NY, 10065, USA

Since 2017, several chimeric antigen receptor (CAR T-cell) therapies have been approved for patients with hematologic malignances in the US. Current approved CAR T cells target either CD19, present on most B cell malignancies or B cell maturation antigen (BCMA), present on myeloma cells. Tisagenlecleucel (tisa-cel, Novartis) was 1st approved in pediatric and young adult patients (< 26 years) with relapsed/refractory acute lymphoblastic leukemia. Three products are approved for relapsed/refractory aggressive large B cell lymphomas after two lines of therapy: axicabtagene ciloleucel (axi-cel, Kite/Gilead), tisa-cel and lisocabtagene maraleucel (liso-cel, Bristol Myers Squibb). In addition, axi-cel and liso-cel were recently approved in second line following the results of large prospective phase 3 randomized clinical trials. Axi-cel is also approved in advanced follicular lymphoma. Brexucabtagene autoleucel (brexu-cel, Kite/Gilead) is approved for relapsed/refractory mantle cell lymphoma (MCL) and adult patients with relapsed/refractory B-ALL. Idecabtagene vicleucel (ide-cel, Bristol Myers Squibb) and ciltacabtagene autoleucel (cilta-cel, Janssen) are both BCMA-targeted CAR T-cell approved for the treatment of patients with advanced myeloma. In addition to these commercially available CAR T-cells, several CAR T-cell products with different targets are under investigation in other blood cancers, such as chronic lymphocytic leukemia, Hodgkin lymphoma, and T-cell lymphoma. CAR T-cells can cause several unique adverse events including cytokine release syndrome (CRS), immune effector cell associated neurotoxicity syndrome (ICANS), hypogammaglobulinemia and prolonged cytopenia. As part of their approval, the US FDA has required that manufacturers collect data on efficacy, safety and long-term follow-up on a large number of patients (1,000 to 1,500) treated post-approval. Most US centers have reported the outcomes of patients treated with CAR T-cells to the CIBMTR Cellular Immunotherapy Data Resource (CIDR). In this presentation, we will review the current US treatment landscape of CAR T-cells, including data reported to the CIDR and real-world data.

Presidential Symposium

Activity and regulation of cellular therapy in Asia-Pacific region

Shinichiro Okamoto

Keio University School of Medicine, Tokyo, Japan

As of April 2022, twenty-two countries/regions are participating in APBMT. Among those countries/regions hematopoietic cell transplantation (HCT) and other cellular therapies are actively performed, however, their activities vary significantly. Regarding HCT, the access rate exceeds 75% in one quarter of countries/regions, but the rate is 25%> in 9 countries, and 10% in 2 countries/regions. The activity/access rate to CAR T-cell therapy also varies significantly. Our recent survey demonstrated that CAR T-cell therapy is available in 9 countries/regions, and the therapy is available as clinical trial/clinical practice in 5 countries/regions, and as clinical trial only in 4 countries/regions. The major sites performing CAR T-cell therapy are HCT centers in all countries/regions, but in about 20% of countries/regions the therapy is also available in hematology or medical oncology service. The factors that impede the access to CAR T-cell therapy include financial constrain of patients, inadequate funding from government, inadequate number of sites performing the therapy, inadequate laboratory infrastructure support, and poor public awareness. Those factors also impede the access to HCT.

Regulation for cellular therapies also differ significantly among Asia-Pacific countries/regions. In Korea, Singapore, and Taiwan cellular therapies are regulated as a drug similar to the US and EU. New regulation (not by drug law) has been introduced for cellular therapy which require manufacturing license and registration for cellular products in China and Japan. There are no cellular therapy specific regulations yet in some countries. In Japan, Cellular therapies such as CAR T-cell therapy are categorized into regenerative medicine, and the regulatory agency planned to capture the data of CAR T-cell therapy in the regenerative medicine registry. However, it is very important to use our transplant outcome registries to assess the best positioning of CAR T-cell therapy and other cellular immunotherapies for a variety of hematological malignancies. Japanese data center for HCT was able to take the clinical data of CAR T-cells into our registry with the generous support of CIBMTR. This experience emphasizes the importance of global collaboration in the rapidly expanding field of cellular therapies in our field.

SESSION 01 –
ACUTE LEUKEMIA

Session 01 - Acute Leukemia

Prophylactic/Pre-emptive Strategies in AML post Allo transplant. What's relevant in 2022?

Auro Viswabandya

Division of Medical Oncology and Hematology, Princess Margaret Cancer Centre, Toronto, Canada

Allogeneic hematopoietic stem cell transplantation (Allo-HSCT) offers a potential cure to high-risk acute Myeloid Leukemia (AML). However, high relapse rate post Allo-SCT remains the major barrier to a long-term remission. Outcome of patients with AML relapsing after Allo-HSCT is dismal and a 2-year survival remains less than 20%. Preventive strategies to reduce relapse ideally should be considered as part of a comprehensive treatment algorithm post Allo HSCT in high-risk AML patients. Introduction of Minimal Residual disease (MRD) based treatment algorithm is changing the paradigm of both pre-and post-transplant management in AML. However, this has not been widely adopted yet because of cost, differences in detection methods, standardization and appropriate understanding and intervention strategies. Post-transplant intervention can be prophylactic (without any evidence of disease relapse with 100% donor chimerism) or pre-emptive (with disease detected at MRD level or a mixed chimerism or at molecular relapse). Maintenance therapy using FLT3 inhibitor (sorafenib) has been shown to reduce relapse rate and improve survival in randomized trials in patients with AML who are FLT3 mutated. The result of a large phase III randomized trial using another FLT3 inhibitor (Gilteritinib) in post-transplant setting is eagerly awaited. However, the optimal dose, duration of therapy and risk-based stratification while using FLT3 inhibitor are some open questions. Use of hypomethylating agents is another strategy to reduce relapse rate and to prolong survival. It can be used in both prophylactic and pre-emptive settings. Despite published phase II and multiple retrospective studies, the randomized trial using Azacytidine as a maintenance therapy post-Allo-HSCT was not found to statistically reduce relapse rate or improve survival (the caveats being very long duration of trials, less patient enrollment, and appropriate risk stratification). Decitabine with G-CSF has been found to improve survival and reduce relapse rate in phase II trial post Allo-HSCT in high-risk AML. Other modalities to reduce relapse rate post Allo-HSCT in high-risk AML is reduction of immunosuppression early post transplantation, use of Donor Lymphocyte Infusion (DLI) or a combination of DLI and hypomethylating agents. This presentation in conference will briefly describe about these modalities and talk of prophylactic and pre-emptive strategies to reduce relapse rate post Allo-HSCT in high-risk AML.

Session 01 - Acute Leukemia

ALL-CR1 Allo-HSCT in 2022: Who should get it?

David Marks

University Hospitals Bristol NHS Trust, Bristol, UK

Allogeneic HSCT has a major role in curing adults with ALL and has the greatest anti-leukaemic effect, however its positive effects are reduced by a high transplant-related-mortality and significant late effects such as chronic GVHD and second cancers.

Selecting the right patients in CR1 has become more controversial with the upfront use of targeted therapy and the use of later generation tyrosine kinase inhibitors in Ph- positive ALL.

All patients with high risk Ph-negative ALL should be considered for a CR1 allograft if they are fit and have a sibling or well-matched unrelated donor. The use of double cord units or haploidentical donor will depend on the TRM of the transplanting BMT Unit. In particular patients with high-risk genetic lesions should be allografted, irrespective of MRD status.

Patients failing to achieve MRD-negativity after 2 courses of chemotherapy should be given blinatumomab then allografted (Gokbuget N, Blast trial, Blood).

Furthermore, patients >40 years should be offered a well-matched sibling or unrelated transplant using reduced-intensity-conditioning. Recent published data from UKALL14 showed 55% 4-year survival in 249 patients (median age 50), half of whom had high-risk genetics (Marks DI et al. Lancet Haem 2022). Severe acute GVHD was infrequent, 37% had chronic GVHD and quality-of-life was preserved.

Patients with Ph-positive ALL can now be treated with blinatumomab and dasatinib (Foa R, NEJM) or dasatinib (Short N, MD Anderson) and achieve high rates of MRD-negativity. On trial it may be reasonable to not allograft molecular responders, however all other patients should be offered an allograft with post-transplant TKI as a standard-of-care.

Older patients treated with upfront inotuzumab (Kantarjian H, Lancet Oncology) with hyperCVD had good medium-term survival without an allograft but these results require confirmation. The use of upfront blinatumomab with intensive chemotherapy is being examined by the US Intergroup and the outcome of non-transplanted patients will be of interest.

Efforts should be made to reduce mortality and the future upfront use of CAR-T cells in very high-risk patients is likely.

Session 01 - Acute Leukemia

Consolidation Allogeneic HSCT in ALL Patients post CAR-T

Peihua Lu

Lu Daopei Hospital, Beijing Lu Daopei Institute of Hematology, Beijing, China

CD19-targeted chimeric antigen receptor (CAR) T-cell therapy has demonstrated striking responses among B-cell acute lymphoblastic leukemia (B-ALL), however, some 40% relapse. Allogeneic hematopoietic stem cell transplantation (allo-HSCT) as an approach could improve the long-term remission after CAR-T cell therapy in patients with B-ALL, although the data have been mixed, and the practice remains controversial.

We have summarized the long-term follow up results of 254 B-ALL treated with CD19 CAR-T cells from 5 clinical trials. Patients with consolidative allo-HSCT after CAR-T therapy had a superior OS and LFS compared to those who did not. This benefit was also observed in both pediatric and adult patients as well as in patients either in high or low risk groups.

Another study at our center demonstrates that even for R/R B-ALL patients who relapsed after first allo-HSCT, MRD-negative CR can still be achieved through CAR-T cell therapy. To improve duration of remission, CAR T-cell therapy followed by consolidation second allo-HSCT may be considered for selected young and fit patients.

However, a recent study enrolled 74 patients showed that humanized CD19 CAR-T cells showed high response rates, and durable remissions without further therapy in children and young adults with relapsed or refractory B-ALL.

In May 2022, we just published the first-in-human study on naturally selected CD7 CAR-T(NS7CAR) cell therapy in T-cell malignancies on *Blood*. In our phase 1 trial (NCT04572308), 20 patients with relapsed/refractory T-cell acute lymphoblastic leukemia (T-ALL, n=14) and lymphoblastic lymphoma (T-LBL, n=6) were treated with NS7CAR. With a median follow-up of 142.5 days (32 to 311 days) post infusion, 14 patients subsequently received allo-HSCT (10 consolidative, 4 salvage) following NS7CAR infusion with no relapses to date. Of the six patients who did not receive a transplant, four remained in CR at a median time of 54 days (32 to 180 days).

In summary, a consolidative allo-HSCT after CAR-T for patients with high-risk features, either pediatric or adult patients is recommended. The role of consolidation allo-HSCT should be continuously redefined with the development of novel CAR-Ts and combination therapies.

Session 01 - Acute Leukemia

AML CR1 Allo-HSCT in the era of genomics

Yasuhito Nannya

Division of Hematopoietic Disease Control
Institute of Medical Science, The University of Tokyo, Tokyo, Japan

Whether allogeneic transplantation should be used for post-remission therapy in AML CR1 has been the subject of debate for many years and a meta-analysis of studies addressing this issue concluded that transplantation can be spared for low-risk cases but confers better prognosis for intermediate- and high-risk cases. However, this conclusion is not unchangeable, and indeed would be affected by novel study results and insights. Substantial decrease in non-recurrent mortality in the last decades due to improved transplantation techniques represents an example that moves watershed of decision toward allo-SCT. Another factor includes introduction of novel parameters that allows us to evaluate minimal residual disease (MRD) at molecular level. Refinement of prognostic systems by incorporating mutational profile and other genetic alterations also contribute to identify the cases for which a novel system recommends distinct indication of allo-SCT from conventional prognostic systems such as European LeukemiaNet (ELN). These evolutions are being achieved in clinical practice with the introduction of genomic analysis. Indeed, a line of evidence suggest that ELN low risk cases benefit from post-consolidation allo-SCT when MRD remains positive after 2nd consolidation. Similarly, ELN intermediate-risk cases who showed favorable response to induction and consolidation treatment to undetectable level of MRD have almost identical outcomes irrespective of allo-SCT, and upfront SCT would not be justified for this group of patients. In addition, integration of large-scale data including mutational profile would provide more sophisticated prognostic systems compared with conventional ones. Detection of *TP53* one-hit mutation and germline *DDX41*-mutations would identify a group of cases who can spare upfront allo-SCT among ELN high-risk cases. Allelic status of *TP53* can only be evaluated by integrating copy number alterations and allelic imbalances into genomic analysis and genome tests that enables such multimodal measurements are required to achieve standard of care in the era of genomics.

SESSION 02 –
PEDIATRIC SESSION 1

Session 02 - Pediatric Session 1

A Report on The Outcome of Hematopoietic Stem Cell Transplantation in Pediatric Patients with Hemophagocytic Lymphohistiocytosis at The Largest Children's Medical Hospital in Iran

Amir Ali Hamidieh[1], Leila Jafari [1], Maryam Behfar [1], Rashin Mohseni[1], Yalda Karamlou[1]

[1]Pediatric Cell and Gene Therapy Research Center, Gene, Cell and Tissue Research Institute, Tehran University of Medical Science, Tehran, Iran

Aims
Primary Hemophagocytic Lymphohistiocytosis (HLH) is a severe hyper-inflammatory syndrome which consists of two major subgroups; one is Familial Hemophagocytic Lymphohistiocytosis (FHLH) and the other is comprised of a group of immunodeficiencies including Chediak–Higashisyndrome (CHS), Griscelli syndrome type II (GS-II), and X-linked lymphoproliferative (XLP) syndrome. These patients have poor prognosis and lose their lives early in life without sufficient treatment. Hematopoietic stem cell transplantation (HSCT) is an imperative treatment modality for these patients and it aims to downregulate their hyperactive immune system. The use of reduced intensity conditioning (RIC) regimen decreases transplant-related morbidity and mortality; however, it is associated with the occurrence of mixed chimerism and heightened risk of relapse. In this unprecedented study, we report the outcomes of HSCT in HLH pediatric patients using RIC regimen at the Children's Medical Center.

Methods:
In this prospective study, we analyzed the outcome of 14 pediatric patients afflicted with PHLH who had received HSCT from 2017 to 2021, with a male to female ratio of 11 to 3. Whole Genome Sequencing was performed to confirm the diagnosis in all patients. From 14 patients, 8 were familial HLH (median age: 4.5 years) and 6 had other forms of HLH (median age: 7 years) including GS-II (n=3), CHS (n=2) and XLP (n=1). All of the patients received the same RIC regimen based on fludarabine in combination with melphalan and rabbite antithymocyte globulin (ATG).
Cyclosporine and short course methylprednisolone were also used as a Graft-vs.-host-disease prophylaxis.The graft source in 13 patients was peripheral blood stem cells, whereas only one patient received bone marrow stem cells. All patients were transplanted with full match donor except one patient. The median doses of CD34+ and CD3+ cells were 6.6×10^6/kg and 269×10^6/kg, respectively.

Results:
On average, neutrophils and platelet engraftment transpired in all patients 12 and 15 days after transplantation, respectively. Amongst all 14 HLH patients, 85% (n=12) of patients had full chimerism and only two patients presented mixed chimerism. 3-year and 4-year overall survival (OS) rate of our patients was 81% and 65%, respectively.
8 patients (57.1%) experienced acute GvHD; which included 4 cases of grade I-II and the rest had grade III-IV. Additionally, 3 patients (21.4%) manifested symptoms of chronic GVHD. The leading cause of death in HLH cases were acute GVHD.

Conclusion:
Even though utilizing RIC regimen is often associated with mixed chimerism and graft failure, our study demonstrated that the use of less toxic reduced intensity conditioning regimen based on Fludarabin and Melphalan was seemingly associated with acceptable engraftment and HSCT outcome for PHLH patients.

Conflict of interest
Nothing to declare

Session 02 - Pediatric Session 1

Upfront Haplo Transplant for Aplastic Anemia in Children - Are We Justified?

Carmem Bonfim

Director Pediatric Blood and Marrow Transplantation Program at Hospital Pequeno Príncipe
Professor at the Pele Pequeno Principe Research Institute and Federal University of Parana
Curitiba-PR-Brazil

Acquired severe aplastic anemia(SAA) in children is a rare, life-threatening disease, and allogeneic hematopoietic cell transplantation(HCT) from a matched related or unrelated donor(MUD) is currently the treatment of choice. Immune suppression treatment (IST) with horse-ATG and cyclosporine is recommended for children without matched donors. However, it may take 3-6 months to achieve a hematological response; up to 30% of patients eventually relapse, and an average of 20% develop clonal evolution. Adding Eltrombopag to the IST improved response rate and outcomes in adults but there is limited data regarding efficacy and safety in pediatric patients. If a patient fails to respond to IST, alternative donor transplantation using haploidentical donors is usually considered. More recently, haploidentical HCT using pos-transplantation cyclophosphamide(Haplo-PTCy) has improved access to transplantation worldwide and is associated with low rates of GvHD and rejection. Haplo-PTCy does not require graft manipulation resulting in a low graft acquisition cost and rapid expansion of this method, especially in low- and middle-income countries. Many studies have demonstrated the safety and efficacy of using the Haplo-PTCy platform for refractory/relapsed and treatment naïve SAA. If an HCT can rapidly restore hematopoiesis and decrease the risk of relapse or clonal evolution, and outcomes are excellent across all donor types, why should we offer a haplo-PTCy only after IST failure? This option is especially relevant for ethnical minorities where a MUD is not easily found or for countries that cannot afford the cost and logistics of searching for an unrelated donor. Although we need prospective studies comparing front-line IST to a MUD or a haploidentical donor in SAA, these studies will be hard to accrual patients and may take too long to accomplish. Implementing HCT as a curative approach with the best available donor will provide children with acquired SAA the best chance of long-term disease-free survival.

Session 02 - Pediatric Session 1

Haplo-identical transplant in Thalassemia Major: Current Status

Usanarat Anurathapan

Department of Pediatrics, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Krung Thep Maha Nakhon (Bangkok), Thailand.

Thalassemia, a hemoglobinopathy, is common in Asian descendants. In early life, patients with Thalassemia Major (TM) need a regular transfusion with an iron chelator. Hematopoietic stem cell transplantation is one of the curative treatments for patients with TM. However, the chance of finding matched donors, related or unrelated, for those patients is slim. Haplo-identical donors, a parent of the affected patients, are attractive. Recently, we published outcomes of TM patients receiving haplo-identical transplantation with a reduced toxicity conditioning regimen (RTC) and post-transplant cyclophosphamide (PTCY). Eighty-three patients, the median age of 12, either received pre-transplant immunosuppression (PTIS), comprised of fludarabine and dexamethasone, or fortified PTIS, adding rituximab and bortezomib, for patients with high donor-specific antibody. The RTC, containing anti-thymocyte globulin, fludarabine, and busulfan, was administered to all patients before stem cell infusion. The PTCY, followed by a calcineurin inhibitor and mycophenolate, were given to prevent graft-versus-host disease (GVHD). The median follow-up time was 15 months (range, 7-53). The 3-year overall and event-free survival rates were 96%. Adverse events included severe GVHD (7.2%), grade 3 mucositis (12.0%), cytomegalovirus diseases (2.4%), BK virus hemorrhagic cystitis (27.7%), adenovirus hemorrhagic cystitis (3.6%) and gram-negative septicemia (6.0%). Four patients died from pneumonia, GVHD complications, and bacterial sepsis. Moreover, we analyzed immune reconstitution of haplo-identical transplants compared with matched transplants. We found that patients receiving haplo-identical stem cells had significantly higher acute GVHD than those performing matched transplants. Patients with matched transplants had significantly higher helper T cell and NK cell numbers at one-month post-transplant than those with haplo-identical transplants. However, NK cell numbers at three- and six-month post-transplant were higher in patients receiving haplo-identical transplants. Whereas B cell numbers of matched-transplant patients were higher than haplo-identical transplant patients at one-, three-, and six-month timepoints, resulting in lower immunoglobulin G levels at six-month in haplo-identical transplant patients.

SESSION 03 –
LYMPHOMA / MYELOMA

Session 03 – Lymphoma / Myeloma

Managing post-transplant relapses in multiple myeloma - APBMT Oct 2022

Chandramouli Nagarajan

SingHealth Duke-NUS Blood Cancer Center, Singapore General Hospital, Singapore

Multiple myeloma is an incurable plasma cell neoplasm despite the huge advances in therapeutics over the last 3 decades. The natural history of Myeloma is characterised by relapsing and remitting course typically with decreasing duration of remission and increasing number patients being lost to refractory disease or unsuitability to salvage therapies with each relapse. Given the myriad treatment options available, treatment choices used to salvage early relapses have become crucial since they present the best opportunity to give patients a better overall survival.

Most centres in Asia-Pacific still employ high dose therapy with Autologous stem-cell transplant (ASCT) as a part of induction treatment strategy in fit eligible newly diagnosed multiple myeloma patients. Despite recent data from the west suggesting no difference in the overall survival between early and deferred ASCT approaches, in our region this should be taken with much caution as down-the line treatment options available for salvaging 1st and subsequent relapses in our patients are very different to those in western countries and ASCT should, as such, remain a cornerstone of therapy in patients in our region due to its well-proven efficacy and relatively low mortality. The cost of salvage therapies in myeloma affects our patients disproportionately compared to the west.

In the post ASCT relapse, multiple factors dictate the choice of salvage therapy. Type of relapse (biochemical Vs clinical; bone marrow Vs extra-medullary), patient fitness, prior therapies used and their duration of remission, use and timing of relapse after any maintenance therapies used, any remaining toxicities from prior treatments, feasibility of 2nd ASCT, access to clinical trials or newer generation novel agents are all crucially important considerations in managing such relapses. These factors and the different regimens, their choice, usefulness, and limitations will be discussed in detail at the presentation.

Finally, a group of myeloma patients will continue to relapse despite all salvage therapies and fit to the description of late relapse/refractory myeloma. Managing these patients is particularly challenging as they often have disease refractory to proteasome inhibitors / immunomodulatory drugs and CD38 monoclonal antibodies, often have multiple co-morbidities that are either age related or from recurrent relapses or from prior therapies. Access to and use of newer novel agents for this group of patients is particularly important as conventional therapies might produce little benefit in these patients. Finally, avoiding toxic or higher intensity treatment options in inappropriate situations and choosing palliative care approach in joint discussions with patient and family can serve to improve the quality of life in this as yet incurable malignancy.

Session 03 – Lymphoma / Myeloma

Autologous or Allogeneic Transplantation in Peripheral T-Cell Lymphoma

Jong Ho Won

Dept. of Hematology & Oncology, Blood and Marrow Transplantation Center, Soonchunhyang University College of Medicine, Seoul, Korea

Autologous hematopoietic stem cell transplantation (auto-HCT) is recommended for patients either with relapsed non-Hodgkin's lymphoma (NHL) or in first remission. Because of the high relapse rate even after chemotherapy with auto-HCT and effect of graft versus lymphoma (GVL) after allogeneic (allo) HCT, patients with NHL are considered for allo-HCT. Because of the lack of outcome in large-scale prospective studies, current recommendations and timing of selection of auto- or allo-HCT are affected by patient- or disease-related factors, physicians' preferences, and institutional practices.

Several nonrandomized prospective and retrospective studies have reported favorable outcomes in patients with peripheral T-cell lymphoma (PTCL) undergoing first-line consolidation with high-dose therapy (HDT) followed by auto-HCT. Some studies have reported that achieving complete remission before HDT and auto-HCT is an independent prognostic factor of improved survival in patients receiving first-line consolidation.

In sensitive relapse, auto-HCT is recommended in patients with PTCL who have not undergone front-line consolidation. Allo-HCT is recommended for PTCL, even in patients with failed auto-HCT. In the case of angioimmunoblastic T-cell lymphoma (AITL), EBMT data showed a 3-year overall survival (OS) of 81% in patients with chemotherapy-sensitive cases compared with 37% in chemotherapy-refractory cases (P=0.002).

Allo-HCT is recommended (weakly) for primary refractory or relapsed refractory PTCL. Data supporting allo-HCT are scarce, and the available results are disappointing. In other histologies, the use of allo-HCT appears more promising. For instance, the aforementioned EBMT study showed a 3-year OS of 37% in patients with AITL treated with allo-HCT in refractory disease, suggesting a promising GVL effect in this histology.

Owing to the relatively low incidence and lack of well-designed randomized controlled trials, international cooperation is needed to better understand the role of HCT. Moreover, the incorporation of novel agents and genomic understanding of T-cell lymphomas will improve transplant outcomes.

Session 03 – Lymphoma / Myeloma

Checkpoint Inhibitors in refractory HD

Young Rok Do

Dongsan Medical Center, Keimyung University, Korea

Hodgkin lymphoma is a malignancy characterized by low-abundant tumor cells surrounded by variable mixture of non-neoplastic inflammatory cells. Treatment options are limited in patients with relapsed or refractory classical Hodgkin lymphoma(cHL) after brentuximab vedotin and autologous stem cell transplantation. Recently, immune checkpoint inhibitors that targeting the PD-1/PD-L1 pathway has achieved great success in relapsed and refractory Hodgkin lymphoma patients. Reed-Sternberg cells(RSCs) are large, abnormal lymphocytes and the hallmark cells of Hodgkin lymphoma. PD-L1 is commonly overexpressed in Hodgkin lymphoma and recent studies have demonstrated impressive response rates with the PD-1 inhibitors nivolumab and pembrolizumab in relapsed or refractory Hodgkin lymphoma. Further studies have shown that the RSCs overexpressed PD-L1 and PD-L2 due to genetic amplification of the 9p24.1 locus. The overexpression of the PD-L1 causes a T-cell-exhausted tumor microenvironment. The RSCs with copy number alterations of 9p24.1/CD274(PD-L1)/PDCD1LG2(PD-L2) are surrounded by PD-L1-positive tumor-associated macrophages. This is often described as a “castle and moat” model as the RSCs are surrounded by inactivated immune cells to protect them from the immune system. Alterations of PD-L1 and PD-L2 are closely related to reduced progression-free survival (PFS) when treated with standard chemotherapy regimens. Therefore, anti-PD-1/PD-L1 immune checkpoint inhibitors therapy is a well-founded treatment of cHL. The overall and complete response rates to PD-1 inhibitors in patients with relapsed or refractory HL are 70% and 20%, respectively, with a long median duration of response of 16 months. We review the immune micro-environment and mechanisms of immune evasion in Hodgkin lymphoma. We also provide the evidence of using the PD-1 inhibitors in relapsed or refractory Hodgkin lymphoma and highlight the response in patients treated with this immunotherapy. And we discuss primary or acquired resistance to immune checkpoint blockade in Hodgkin lymphoma.

SESSION 04 –
PEDIATRIC SESSION 2

Session 04 – Pediatric Session 2

Allogeneic HSCT for High-Risk ALL: Optimising Conditioning for Children

Christina Peters

St. Anna Children's Hospital, Vienna, Austria

Children and adolescents with ALL have an excellent chance of cure. Only patients with high relapse risk are nowadays candidates for allogeneic HSCT. The preparative conditioning regimen has a crucial role for acute and long-term sequel and disease control by the graft-versus-leukemia-effect.

In a multicenter, international, randomized, phase 3 clinical Trial (FORUM study), we showed that pediatric ALL-pts who received total body irradiation (TBI) in combination with etoposide (eto) had a significantly superior probability of 2-year overall (OS) and event-free survival (EFS) in comparison to patients given either of two myeloablative chemo-conditioning regimens (fludarabine/thiotepa/busulfan (flu/thio/bu) or flu/thio/treo (treosulfan)). Overall survival (OS) was the primary endpoint with an aim to demonstrate non-inferiority in the chemo-conditioning arm. 413 eligible patients were randomized. Due to significantly inferior outcome with chemo-therapy-based conditioning, the randomization was prematurely stopped. The 2-year-overall survival was 75%±4% for the chemoconditioning and 91%±2% for TBI/etoposide (intention to treat p< 0.001). In per-protocol analysis OS after flu/thio/bu, flu/thio/treo and TBI/eto was 77%±5%, 77%±5% and 91%, respectively (p=0.003). Two-year-treatment-related-mortality was 6%±3%, 12%±4% and 3%±1% (n.s.). Two-year-cumulative-relapse-incidence was 30%±5%, 31%±5% and 12%±4% (p=0.004) after flu/thio/bu, flu/thio/treo and TBI/eto, respectively. In Cox-model-analysis only time of relapse in CR2-patients and conditioning (TBI/eto vs. flu/thio/bu or flu/thio/treo: p< 0.001, HR 3.37) significantly influenced EFS. After the randomisation stop, most centers apply TBI/eto for patients above four years of age with similar results compared to the randomized cohort. Younger patients receive chemo-conditioning according to FORUM-protocol. The most common treatment failure is relapse (44% ± 4%) while non-relapse mortality is 5% ± 2%. TBI/etoposide is recommended as standard conditioning regimen with prospective monitoring of late complications, endocrine functions and incidence of secondary malignancies.

Session 04 – Pediatric Session 2

Cellular therapies in Neuroblastoma

Giuseppe Barone

Great Ormond Street Hospital, London, UK

Neuroblastoma is the most common solid tumour in children after brain tumour and it accounts for the highest childhood mortality for cancer amongst non-brain tumour.

Cellular therapies in neuroblastoma encompass the use of peripheral blood stem cells as a rescue after high dose chemotherapy as well as the use of CAR-T cell anti-GD2 in the relapse settings.

Despite recent controversies, the use of high dose chemotherapy is currently standard of care for children with high-risk neuroblastomas in COG and SIOPEN. Interestingly, the COG has explored the use of double high dose treatment showing improved EFS and OS, thus a large phase III randomised study is now assessing whether double High Dose can be rolled out as standard of care and how this compares to the use of MIBG and one high dose chemotherapy. Similarly, in the SIOPEN group the new high risk neuroblastoma trial is exploring the use of one high dose versus two sequential high dose treatments. In addition, the VERITAS trial for refractory and poor responders is evaluating the use of MIBG and high dose chemotherapy versus double high dose chemotherapy.

CART cells have been developed with some encouraging results showing proof of principles. However published results have not confirmed sustained responses. Studies are currently ongoing to identify how to improve the persistence as well as reduce the exhaustion of CAR-T cells.

In addition, novel approach of combining chemotherapy to antibody anti-GD2 together with NK cells and the use of mismatched haploidentical bone marrow transplant have been explored with encouraging results. In a St Jude's clinical trial antibody anti-GD2 and NK cells added to chemotherapy in induction resulted in a 40% increase in response rate. The German group has shown that haploidentical transplantation with mismatched NK cells could be used as consolidation therapy in the context of relapsed disease.

Session 04 – Pediatric Session 2

Late effects of HSCT and its management

Revathi Raj

Apollo Hospitals, Chennai, India

In HSCT, it is essential to consider Day 100 as an important landmark when immune reconstitution occurs and families return to their homes. The initial follow-up of HSCT patient revolves around the underlying condition for which the child is transplanted and the effects of HSCT such as relapse of leukemia, graft rejection, graft failure and reactivation of viruses.

Vaccination after HSCT is an integral part of follow up and all primary vaccines need to be repeated to boost the new immune system. Annual influenza vaccination and review of infections in children with chronic graft versus host disease is recommended. All infections need to be treated promptly with antibiotics.

Cardiac evaluation and a healthy lifestyle should be encouraged to avoid metabolic syndrome. Recording blood pressure and adequate control of hypertension is essential to prevent long term renal damage. Radiation and busulfan affect the lung and annual pulmonary function tests are mandatory. Patients with chronic graft versus host disease should be encouraged to follow up with the transplant physician to prevent poor quality of life and late morbidity. Renal function needs to be monitored with annual creatinine, urine routine, and blood pressure.

High-doses of chemotherapy and radiotherapy used during conditioning necessitates the need for vigilant annual follow-up, especially during puberty. The most significant side effect that can be prevented with adequate calcium and vitamin D replacement is a bone disease, including avascular necrosis of the femoral head. Tanner staging and puberty follow-up with an early endocrine referral can prevent delayed or precocious puberty resulting in short stature in these children. TSH, Free T4 screening every two years helps prevent morbidity due to hypothyroidism. Premarital counseling forms another unique aspect and patients may need assisted fertility options.

Psychosocial integration of the child and family back into routine life remains an unmet need in resource poor settings.

SESSION 05 – IMMUNOLOGY OF TRANSPLANTATION GVHD

Session 05 – Immunology of Transplantation GVHD

Towards Predictable Immune Reconstitution after Transplantation

Jaap Jan BOELENS

Memorial Sloan Kettering Cancer Center, New York, USA

Hematopoietic cell transplantation (HCT) is a curative treatment option for specific 'hard-to-tread' malignant and non-malignant diseases. Success of the procedure mainly depends on disease control and treatment-related complications. Pharmacotherapy plays a major role in HCT, and significantly impacts the outcomes, in particular because of the unpredictable impact on immune reconstitution.

Increasing evidence suggests individualized dosing, will improve outcomes after HCT; higher efficacy and lower toxicity, mainly driven by better predictable immune reconstitution. Pharmacokinetics (PK) is found to be highly variable and these highly variable drug exposures are found to have huge impact on outcomes. For agents like Busulfan, Thymoglobuline (ATG) and Fludarabine the highly variable drug exposures found after standard weight or BSA-based dosing resulted in significant impact on survival. For example, transplantation-related mortality (TRM) was found to be related to over-exposure of Thymoglobuline and/or Fludarabine. Overexposure impacted immune reconstitution dramatically, resulting in more difficult to treat infections and subsequently higher TRM. Dose individualization of these drugs, using population PK models will result in a better predictable drug exposure and subsequently in better predictable immune reconstitution. This was also recently shown in a prospective clinical trial (PARACHUTE; Admiraal et al, Lancet Hematology 2022). Further individualizing, considering PK of agents used in HCT, will make HCT significantly safer and more effective and will result in higher survival chances.

Session 05 – Immunology of Transplantation GVHD

Novel insights in biology and treatment of chronic GVHD

Ken-ichi Matsuoka

Department of Hematology and Oncology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan;

Allogeneic hematopoietic stem cell transplantation (HSCT) represents a curative treatment for otherwise incurable hematological diseases, including malignancies and bone marrow failure syndromes. With improvements in immune suppressive therapy and supportive care, fewer patients develop acute graft-versus-host disease (GVHD) and more patients survive beyond the first year after transplant. However, chronic GVHD, exhibiting clinical manifestations resembling those of autoimmune disease still remains to be a major complication after allogeneic HSCT that could cause morbidity and non-relapse mortality for long-term survivors after HSCT. Similar to autoimmune diseases, both T and B cell responses appear to play a role in the pathogenesis of chronic GVHD, suggesting that this reflects a general loss of immune tolerance including abnormalities in the function of Tregs. We previously demonstrated that the administration of low-dose IL-2 restored Treg homeostasis and ameliorated the clinical symptoms in patients with active chronic GVHD. In addition to Treg, recent studies have accumulated evidence showing that altered B-cell homeostasis plays an important role in chronic GVHD pathogenesis. The delayed reconstitution of naïve B cell subsets including IL-10 producing regulatory B cells and the compensatory increase of soluble B cell-activating factor (BAFF) were associated with the expansion of activated B cells in patients with chronic GVHD. Our murine model study recently found that post-transplant Treg reconstitution is essential for the favorable restoration of B cell tolerance which prevents chronic GVHD. Based on the understanding of the pathogenesis of chronic GVHD, novel therapies for chronic GVHD have been developed. In this session, I would like to introduce the recent advances of basic and clinical studies for chronic GVHD and discuss the future landscape of this field.

Session 05 – Immunology of Transplantation GVHD

GVHD-Prophylaxis: Options and Current Clinical Use with a Focus on Non-CNI based Strategies

Olaf Penack

Charité Universitätsmedizin Berlin, Berlin, Germany

Acute graft-versus-host disease (aGVHD) and chronic (cGVHD) remain the most important treatment-related side effects of allogeneic hematopoietic stem cell transplantation (alloSCT). The optimal use of prophylactic regimens potentially could improve patient outcome.

Olaf Penack is currently the chairperson of the GVHD subcommittee in the transplant-complications working party of the European Society for Blood and Marrow Transplantation (EBMT) and he is an expert in the pathophysiology of GVHD. In this presentation, he will explain the current standard GVHD prophylaxis approach that is supported by the EBMT. Dr. Penack has coordinated the current EBMT recommendations on prophylaxis of GVHD. He will specifically highlight the difficulty of calcineurin inhibitor (CNI)-related toxicity. A focus of the presentation are clinical results of CNI-free GVHD prophylaxis regimens in alloSCT. He will summarize recent advances in CNI-free regimens in haploidentical alloSCT and will give also an overview of the use of CNI-free GVHD prophylaxis in matched-related as well as matched-unrelated alloSCT.

Finally, this presentation will give a future perspective on our field and will give up to date information on prophylactic agents in the late pre-clinical pipeline and clinical stage development.

Session 05 – Immunology of Transplantation GVHD

Novel insights in biology and treatment of acute GVHD

Takanori Teshima

Department of Hematology, Hokkaido University Faculty of Medicine, Sapporo, Japan

Acute graft-versus-host disease (GVHD) is alloreactive T-cell mediated inflammatory disease after allogeneic hematopoietic stem cell transplantation (alloSCT). Studies on GVHD pathophysiology have been primarily focusing on the induction phase of GVHD. Recent studies on the mechanisms of the target tissue injury uncovered that tissue stem cells are targets of GVHD, leading to impaired tissue homeostasis. Thus, GVHD is a disorder of tissue regeneration and repair. Impairment of intestinal homeostasis also disrupts intestinal microbial ecology, which further accelerate GVHD. These novel insights suggests that immunosuppression alone is not sufficient and novel concept of GVHD control should integrate both immunomodulation and tissue modulation. Strategies to increase capacity to recover when immune insult is arrested could facilitate tissue repair and restoration of tissue homeostasis. Based on this concept, several strategies to modulate intestinal homeostasis have been tested in preclinical models and clinical trials as an adjunct to immunosuppressive GVHD prophylaxis. As our understanding of the contribution of tissue injury to GVHD deepens, novel strategies to optimize prophylaxis and treatment for GVHD may emerge.

SESSION 06 – INFECTIONS

Session 06 – Infections

Does Gut Microbiome Predict Infections Post Transplant

Florent Malard

Saint Antoine Hospital, Paris, France

Over the last decade, a growing number of studies established a link between bacterial gut microbiota and patients' outcomes after allogeneic hematopoietic cell transplantation (allo-HCT). In particular, loss of bacterial diversity at engraftment of allo-HCT is associated with a lower overall survival. Furthermore, intestinal domination, defined as occupation of at least 30% of the microbiota by a single predominating bacterial taxon, occurred frequently after allo-HCT and is associated with an increased risk of bacteremia in those patients. On the contrary intestinal colonization with bacteria such as Barnesiella confers resistance to intestinal domination and bloodstream infection with vancomycin-resistant Enterococcus after allo-HCT. In addition, gut microbiota has also been associated with pulmonary complication after alloHCT. Finally, fungal gut microbiota has also been associated infection post-transplant since intestinal expansion of pathogenetic *Candida* species precede *Candida* bloodstream infections. Based on this gut microbiota manipulation are being developed in the setting of hematological malignancies, in particular fecal microbiota transplantation (FMT), in order to prevent dysbiosis and infectious complication. In particular it was shown that FMT after intensive chemotherapy for acute myeloid leukemia is associated with gut microbiota diversity restoration and reduction of multidrug resistant bacteria. Data available will be presented and discussed during the conference.

.

Session 06 – Infections

PTLD - Risk Factors, Preventive Strategies and Treatment

Hsiu-Hao Chang

National Taiwan University, Taipei, Taiwan

Post-transplant lymphoproliferative disorder (PTLD) refers to lymphoid and/or plasmacytic proliferations that develop after solid organ or allogeneic hematopoietic cell transplantation (HCT). The majority of PTLD cases are associated with the Epstein–Barr virus (EBV), a common pathogen, for which more 90% of adults in the general population show serological evidence of infection. After primary EBV infection, a subpopulation of the infected B cells downregulates viral antigen expression and escapes immune surveillance. These infected latent B cells may later reactivate with the suppression of T cell-mediated immunity subsequent to some HCT conditioning regimens, giving rise to lymphoproliferative diseases such as PTLD. PTLD following HCT is a rare, yet often lethal complication. The reported incidence varies among transplant centers because of their different populations and transplant practices. The cumulative incidence is approximately 1.0% at 10 years, typically occurring within 1–5 months after transplant. Historically, mortality rates of HCT-related PTLD were as high as 80%–90%, but recent studies suggested that outcomes have significantly improved through therapeutic approaches such as reduced-intensity conditioning, rituximab, adoptive immunotherapy, and cytokine treatment. Although EBV seropositivity can be a major risk factor, it cannot predict all occurrences of PTLD. Several other risk factors for the development of PTLD following HCT have been well established, most of which are generally controllable and depend on the degree of T cell immunosuppression, such as the use of antithymocyte globulin as a conditioning regimen, a T cell–depleted allograft, and the use of grafts from HLA-mismatched or unrelated donors. Preventive measures including tapering immunosuppressive therapy and pre-emptive treatment of viral reactivation with rituximab have shown to decrease the incidence of PTLD. Therefore, early prediction of PTLD risk is important. The risk factors, preventive strategies and treatment for PTLD after allogeneic HCT will be discussed in this presentation.

Session 06 – Infections

Treatment of multi drug resistant (MDR) gram negative infections in patients undergoing bone marrow transplantation

Parikshit Prayag

Deenanath Mangeshkar Hospital, Pune

Gram negative infections remain an important cause of morbidity and mortality in patients undergoing hematopoietic stem cell transplantation (HSCT). These bacteria can develop resistance to beta lactam antibiotics by production of beta lactamase enzymes, efflux pumps, mutations in penicillin binding proteins or by modification of porin channels. Various clinically important enzymes will be discussed along with the modalities to detect these enzymes in clinical practice. The spectra of beta lactamase inhibitors and their limitations will be highlighted. Interpreting minimum inhibitory concentrations (MICs) and extracting relevant data from the microbiology laboratory will be discussed. Management strategies have to take into account numerous factors; including the host status, resistance mechanisms, pharmacodynamic parameters, drug toxicities and cost of therapy. Therapeutic options for specific enzymes and bacteria will be discussed using real case scenarios. Through these cases the challenges of dealing with these infections in patients undergoing bone marrow transplantation will become evident. Limitations of polymyxin based therapy, including pharmacodynamic pitfalls and difficulties in obtaining accurate minimum inhibitory concentrations (MICs) will be highlighted. Use of combination therapies will be discussed. Also special problems in this population will be highlighted, including the utility of pre-transplant screening for detecting colonization with MDR gram negative bacteria. Newer therapies on the horizon will also be included, including their likely limitations.

SESSION 07 –
CELLULAR THERAPIES BEYOND TRANSPLANTATION

Session 07 – Cellular Therapies Beyond Transplantation

Cellular therapy for post-transplant infections

David J Gottlieb

University of Sydney, Westmead Hospital

There is growing awareness that allogeneic stem cell transplantation represents a platform technology that itself is likely to require modification along with post-transplant interventions to optimally deal with issues of infection, graft versus host disease (GVHD) and recurrent malignancy. Post-transplant therapies may include pharmacological and biological treatments as well as active and passive immunological approaches. Over the last 20 years much information has been obtained about the use of cellular therapies for treatment of post-transplant viral infections. Most attention has focused on reactivations of herpes viruses, particularly cytomegalovirus and Epstein-Barr virus but other viral infections targeted have included adenovirus and HHV-6 and recent attention has also turned to treatment of BK virus cystitis and nephropathy using specific T-cells. There is also evidence that T-cells can be generated to herpes simplex and varicella zoster viruses as well as to influenza and SARS-CoV2. T-cells targeting fungal infections are now also in clinical trial. Several major questions arise in the application of infection directed adoptive immunotherapy after transplant. While T-cells from the patient's stem cell donor can be generated if the donor has prior exposure to the pathogen, third party partially HLA matched T-cells from cryopreserved banks offer not only greater speed and convenience but access to therapy at much lower cost. The model of how banks might be created and maintained will depend on how a country's underlying health system is organized. The clinical place of infection directed adoptive immunotherapy remains unclear. Most treatment to date has focused on patients who have exhausted traditional options and have refractory and/or resistant disease. Whether T-cell directed therapy should be limited to this clinical context or utilized as prophylactic or pre-emptive therapy is unclear but is the subject of current trials. Finally, treatment of infection represents only one indication for post-transplant cellular therapies. Donor lymphocyte infusions, and peptide stimulated and CAR T-cell and NK cell infusions for prevention and treatment of disease relapse are all likely to be part of future cell therapy approaches to post-transplant treatment.

Session 07 – Cellular Therapies Beyond Transplantation

Indigenous CAR-T product for B Cell Malignancies

Gaurav Narula

Oncology & Health Sciences, Tata Memorial Center, Homi Bhabha National Institute, Mumbai, India

B- Acute Lymphoblastic Leukemia (B-ALL) in children, adolescents and young adults has been a highly curable malignancy for several decades now, with continued improvement, but challenges remain in adults. These are amplified in India and Low-Middle Income Countries (LMICs) especially with relapsed/ refractory disease (r/r B-ALL), where large numbers of patients and inadequate health-care coverage for advanced treatments become restrictive. This underlines the need to adopt newer technologies like Chimeric Antigen Receptor (CAR) T-cells rapidly, indigenously and in a cost-effective manner, as their prohibitive cost in developed countries makes them inaccessible. With this aim, we designed and developed novel humanized CD19-directed CAR T-construct-HCAR19, completed pre-clinical development, efficacy and safety testing, translated production to clinical-grade in cGMP (Good Manufacturing Practise) setting, participated in the making of regulatory norms for cell therapies in India, and then met regulatory requirements to commence the first Phase 1 CAR T Trials in the country, which are now completed, in an Investigator-initiated academic center publicly funded project. The product met Phase 1 Trial objectives for safety and showed good responses and correlation with pre-clinical characteristics providing the platform to pursue Phase 2 trials that now await approvals. At the same time, the need for similar therapies in India and similar LMICs is huge and requires a country-wide effort from multiple centers and academic-industry partnerships for novel products, and scale-up of production to meet the demand. This is happening through multiple approaches with collaborations with entities abroad resulting in another Phase 2 trial opening in India, and other academic centers and established Pharmaceutical companies now venturing into Cell Therapies through innovations and collaborations, with a coordinated and well-intentioned push from the Government through its Scientific and Funding agencies.

Session 07 – Cellular Therapies Beyond Transplantation

Various DLI Strategies Post-Transplant to Prevent and Treat Relapse in Haematological Malignancies

Sarita Rani

Department Of Blood And Marrow Transplantation
Dharamshila Narayana Hospital And Research Centre, New Delhi, India

The most important cause of treatment failure after a hematopoietic cell transplantation (HCT) is relapse (30-40%) and in absence of some post-transplant intervention the disease progression is probably in-evitable in high risk hematological malignancies. The hypothesis of graft vs leukemia(GVL) effect is based on the fact that there is more of relapse after an autologous or syngeneic HCT, compared to an allogeneic HCT and the observation that patients who had Graft Vs Host disease(GVHD) develop less relapse. Furthermore, patients who received T cell depleted transplant experienced higher incidence of relapse compared to T Cell replete HCT. Donor lymphocyte infusion (DLI) was first used by Kolb and Slavin in 1990 in patients with relapsed CML. However, its use has always been debated as to when to use (preemptively/ prophylactically /therapeutically) and what to use- GCSF-mobilised (G-DLI) or just conventional DLI (cDLI). Most importantly, which are the actual effector components in a given disease (T cells/NK +/- NKT/ gamma-delta cells) to achieve maximum GVL effects without GVHD. Should we use DLI alone or with other targeted novel or immunomodulatory agents to enhance the GVL effect? Amongst the several pathways of immune escape mechanisms of cancer cells post-HCT, DLI might benefit in certain situation and not in others. Most importantly DLI can be manipulated as per required cell of interest. Selection of the cells of interest can be carried out ex-in vivo or even in-vivo. We have used sequential T-cell co-stimulation blockade (CTLA4Ig) followed by G-mobilised DLI early post-transplant in patients with advanced leukemia with impressive results in terms of relapse free survival without increased GVHD. Further exploration of mechanistic pathways demonstrated a unique pathway of augmented NK cell cytotoxicity unveiled by this approach. We are going to discuss different aspects of all of these burning questions as jury is still out for selection of “perfect DLI” in the era of CARs.

SESSION 08 –
POST TRANSPLANT COMPLICATIONS

Session 08 – Post Transplant complications

TA-TMA- diagnosis, risk factors and treatment

Eleni Gavriilaki

Hematology Department, G Papanicolaou Hospital, Thessaloniki; Greece

Complement is an elaborate system of the innate immunity. Genetic variants and autoantibodies leading to excessive complement activation are implicated in a variety of human diseases. Among them, the hematologic disease paroxysmal nocturnal hemoglobinuria (PNH) remains the prototype model of complement activation and inhibition. Eculizumab, the first-in-class complement inhibitor, was approved for PNH in 2007. Addressing some of the unmet needs, a long-acting C5 inhibitor, ravulizumab, and a C3 inhibitor, pegcetacoplan have been also now approved with PNH. Novel agents, such as factor B and factor D inhibitors, are under study with very promising results. In this era of several approved targeted complement therapeutics, selection of the proper drug needs to be based on a personalized approach. C5 inhibition with eculizumab and ravulizumab, as well as inhibition of the lectin pathway with narsoplimab, are investigated in transplant-associated thrombotic microangiopathy (TA-TMA). TA-TMA is a potentially life-threatening complication, mostly of allogeneic hematopoietic cell transplantation (HCT). Better understanding of its pathophysiology has led to improved patient outcomes over the last decade.

Session 08 – Post Transplant complications

Diagnosis and management of poor graft function

Khalid Halahleh

Bone Marrow Transplantation Program and Cell Therapy,
King Hussein Cancer Center, Amman, Jordan

Poor graft function (PGF) is a serious, potentially life-threatening complication of allogeneic hematopoietic cell transplantation(alloHCT). It is characterized by persistent cytopenias despite evidence of full donor chimerism. This is in contrast to graft failure because of retained recipient immune-effector cells manifested by loss of donor chimerism and late failure of platelet recovery due to platelets decrease after blood count recovery. The true incidence is difficult to calculate and the clinical course is variable. The quoted incidence is reported in 5% to 27%. The course varies from spontaneous recovery to death due to complications of cytopenias.
The diagnosis is based on the presence of cytopenia in at least 2 lineages (PLT < 20 ×109/L, ANC < 0.5 × 10E9 /L, Hb < 7.0 g/dL), and/or with transfusion requirement beyond day +28 post-alloHCT, and full donor chimerism and without evidence of relapse or severe graft versus host disease (GvHD).
The pathogenesis of PGF remains elusive and clinical management is challenging. Bone marrow microenvironment plays an important role and dysfunctional endothelial and mesenchymal stem cells, elevated reactive oxygen species (ROS) levels, and immune abnormalities are believed to contribute to PGF. Risk factors are variable, including low infused CD34 dose; HLA disparity between the donor and recipient; conditioning intensity; post-allo-HCT immunosuppression intensity, donor-specific antibody, cytomegalovirus infection, GvHD, iron overload and splenomegaly, ABO mismatch.
There are currently no consensus guidelines for the management of PGF. Treatment strategies focused on improving HSC number and function and microenvironment support of hematopoiesis have been employed with variable success. The use of immune manipulation has been limited, but emerging therapies hold promise. Treatment approaches are based on pathogentic drivers of PGF including HSC support (CD34 boost), TPO agonists, antioxidant therapy with N-acetyl cysteine, immune manipulations (ATG, anti-IFN-g McA) cellular immune modulators, HSC, marrow microenvironment, and stromal cell directed therapies.

Session 08 – Post Transplant complications

Novel Conditioning Regimens for Allogeneic Stem Cell Transplantation (HSCT) focusing on Acute Leukemia

Arnon Nagler

Chaim Sheba Medical Center,Tel-Hashomer, Israel

Allogeneic transplantation (HSCT) is an effective curative therapy for high-risk acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL) which are the two most frequent indications for HSCT in Europe accounting for 38% and 16% of the transplants, respectively. Before HSCT, a conditioning or preparative regimen is administered. The conditioning regimen has 2 components; one target the myeloid system aiming to eradicate the leukemic clones but also to provide space in the bone marrow (although controversial), while the other target the immune/lymphoid system to ensure engraftment and to prevent rejection. The conditioning is one of the few aspects that can be modified and controlled in the treatment paradigm of acute leukemia and is thus of major importance. Some of the compounds used in the conditioning are more myeloablative for example melphalan while some are more lymphodepletion like fludarabine or Cytoxan. The pre-transplant conditioning may include total body irradiation (TBI) which is beneficial in ALL or be radiation-free and includes only chemotherapy. In recent years, serotherapy, specific targeted novel compounds, as well as monoclonal antibodies and radiolabeled antibodies, started to be incorporated into specific disease-oriented conditioning regimens. Not just the individual drugs and doses but also the type of combination and formulations as well as the schedule and order of administration may differ in the various conditioning regimen protocols dictating their efficacy but also the toxicity profile. Traditionally, TBI was used as the primary cytoreduction in combination with cyclophosphamide (CY) for its immunosuppressive properties. Modern preparative regimens include reduced doses of TBI and targeted administration. As an alternative, high-dose busulfan (Bu) is the most commonly used TBI-free-based conditioning regimen. However, high-dose chemo-radiotherapy with HSCT is associated with significant morbidity and mortality due to the toxicity of the preparative regimen, graft-versus-host disease (GVHD), and the immune-deficient state that accompanies the procedure. Extensive research, including pharmacokinetics and pharmacodynamics studies, has been directed towards the development of safer and less toxic conditioning regimens for HSCT, optimizing the conditioning and allowing its applications to elderly patients and patients with comorbidities. These modern conditioning regimens which are based in part on the immune-mediated graft versus leukemia (GVL) effect are in principle low-dose, less toxic, and tolerable conditioning regimens termed reduced intensity (RIC) with different immunosuppressive and myelosuppressive properties. These regimens combine immunosuppressive agents (such as fludarabine with or without serotherapy with ATG or Campath) with agents with moderate myelosuppressive effects. However, they typically result in a higher relapse rate. The optimal regimen is thus the one with intensive anti-leukemic activity, but with limited toxicity-the so-called reduced toxicity regiments (RTC). These novel regimens are mostly fludarabine based and incorporate drugs like melphalan; thiotepa; treosulfan and clofarabine. Other protocols that will be discussed are the so-called TBF protocol which includes two alkylating agents like busulfan and thiotepa- and the FLAMSA protocol which includes fludarabine, cytarabine, and amsacrine. The modern conditioning regimens enable HSCT in elderly patients and those with comorbidities reducing drastically transplant-related mortality and organ toxicities in combination with improved anti-leukemic effects.

Session 08 – Post Transplant complications

Management of non-infective pulmonary Complications: What is new?

Yasuyuki Arai

Kyoto University, Kyoto, Japan

Allogeneic hematopoietic stem cell transplantation (HSCT) can be a curative treatment option for hematologic malignancies. Patient prognosis has been improved, however, late complications involving several organ systems still remains unsolved. One of these complications can appear in the respiratory system and this is called “non-infectious pulmonary complications (NIPCs)”.
The etiology in this wide spectrum of complications includes pre-transplant chemotherapies and irradiation, infection, and graft-versus-host disease (GVHD). Clinically, NIPCs are often experienced by patients who previously have the signs and symptoms of pneumonia, as well as evidence of widespread alveolar injury in the absence of lower respiratory tract infection and cardiac, renal, or iatrogenic etiology.
NIPCs include idiopathic pneumonia syndrome (IPS) and late-onset non-infectious pulmonary complications (LONIPCs). IPS is characterized by acute lung dysfunction of noninfectious etiology with a median time of onset of 2-3 weeks. LONIPCs are also recognized as major pulmonary events after HSCT encompassing a range of different events occurring later than 3 months after transplantation, including interstitial pneumonia (IP), bronchiolitis obliterans with organizing pneumonia (BOOP), bronchiolitis obliterans syndrome (BOS), and lung fibrosis.
The pathophysiology of NIPCs remains unknown and effective treatments have not been established. Moreover, since HSCT procedures are complicated, the risk factors and prognosis of NIPCs remain unclear. The impact of stem cell source (bone marrow, peripheral blood, or umbilical cord blood) and HLA disparity (matched, mismatched, or haploidentical) has not been fully evaluated. Effectiveness of the newly developed treatment options for GVHD on NIPCs has yet to be known. In my talk, most updated etiology, diagnosis and treatment strategies for NIPCs will be discussed.

SESSION 09 – ALTERNATE DONOR TRANSPLANTATION

Session 09 – Alternate Donor Transplantation

Haplo vs MUD vs Cord in acute leukemia - current status

Ming Yao

National Taiwan University Hospital, Taipei, Taiwan

Allogeneic hematopoietic stem cell transplantation remained the only curative modality in the treatment of some patients with acute leukemia. Transplant using alternative donor became more and more popular in recent decade. There are three options for choosing alternative donor: mismatched related donor (including haploidentical related donor) or matched unrelated donor (or even mismatched unrelated donor) or cord blood. The choice of alternative donor had changed time to time and the order remained variable. Haploidentical related donor had been investigated for decades. Owing to its readily accessibility and improvement of conditioning regimen and adjustment of anti-graft versus host disease strategy, more and more cases had been reported and the result was nearly equal to that using matched sibling donor in some experienced centers. Unrelated donor had been established for more than three decades, a well-organized donor registry and interregional collaboration remained a core for donor recruitment, searching and donation. Cord blood had also been an ideal source for allogeneic stem cell transplantation, the result was comparable with other modality and even better in some countries. Because cell number was limited by its nature, cord blood transplantation was executed mainly in pediatric patients. Because the advance of immunology and microbiology, the dream of crossing the HLA-barrier and overcome the post transplantation complication had come true. The choice of alternative donors was variable according to interinstitutional difference. In this COVID-19 pandemic era, we faced a big challenge in many aspects of stem cell processing and may further change our thought for choosing alternative donor for treating patient with acute leukemia.

Session 09 – Alternate Donor Transplantation

Bone Marrow Or PBSC: Does It Really Matter In T-replete Haploidentical Transplantation

Navneet S Majhail

Transplant and Cellular Therapy Network, Sarah Cannon, Nashville, TN

Post-transplant cyclophosphamide (PTCy) platform for graft-versus-host-disease (GVHD) prevention has become standard of care for T-cell replete haploidentical hematopoietic cell transplantation (HCT). Although initial reports using this approach used bone marrow (BM) as the preferred donor source, several studies have since shown the efficacy of peripheral blood stem cells (PBSC) with comparable outcomes. Similar to other donor sources, there are advantages and disadvantages to the use of PBSC and BM as a graft source in haploidentical HCT. PBSC recipients have been observed to experience shorter time to neutrophil engraftment and lower rates of graft failure but higher risks of acute and chronic GVHD compared to BM recipients. The majority of available literature indicates no difference in overall survival, progression free survival, graft-versus-host disease free relapse free survival, and non-relapse mortality between the two graft sources among haploidentical HCT recipients. An important consideration in graft source selection is the experience, expertise, and set up to perform BM harvests whereas PBSC collection using apheresis is more universally available. BM and PBSC are acceptable graft sources for T-cell replete haploidentical HCT using PTCy based GVHD prophylaxis. The decision to use a specific graft source needs to be tailored towards patient characteristics and transplant center experience.

Session 09 – Alternate Donor Transplantation

Donor Selection for Haploidentical Hematopoietic Stem Cell Transplantation

Piyanuch Kongtim

University of California Irvine, California, USA

The field of haploidentical hematopoietic cell transplantation has grown significantly over the past decades making a one HLA haplotype match relative a preferred alternative donor choice with several studies have shown improved transplant outcomes comparable to HLA matched donor transplants. The utility of HLA-haploidentical related donor provides several benefits including increase donor availability for almost all patients in need. Additionally, having an immediately available related donor can help accelerate a shorter time to transplantation for patients with more advanced diseases and increase donor accessibility for post-transplant donor-derived cellular therapy to help prevent disease relapse and improve treatment-related complications associated with this procedure. When donor availability is now not a limitation because the great majority of patients have more than one potential haploidentical donor available for donation and not all these donors can provide equivalent transplant outcomes, making donor considerations becoming increasingly complex. Carefully select a donor who can provide the best outcomes is one of the most important elements for successful haploidentical stem cell transplantation.
In an effort to optimize donor selection strategies, several groups of researchers have studied the impacts of donor characteristics on outcomes including the presence of donor specific anti-HLA antibodies in the recipient's serum, donor age, sex, degree and characteristics of donor-recipient HLA mismatches, ABO compatibility, donor-recipient CMV serology as well as NK cell alloreactivity.
In this session, we will discuss the emerging data of impact of different donor characteristics on outcomes of a haploidentical hematopoietic stem cell transplantation using various platforms.

Session 09 – Alternate Donor Transplantation

Is it the end of the road for cord transplant?

William YK Hwang[1,2,3]

[1]National Cancer Centre Singapore
[2]Singapore General Hospital
[3]Duke-NUS Medical School

Both umbilical cord blood (UCB) and haploidentical transplantation can be carried out despite significant HLA mismatches between patients and donors. This significantly extends the availability of donors for allogeneic hematopoietic stem cell transplantation, especially in the Asia Pacific, where full-matched unrelated donors are harder to find due to smaller donor registries and diverse ethnicities. Studies of UCB transplantation showed that 1 to 2 antigen mismatched cord blood transplantation could have equivalent results compared to fully matched unrelated bone marrow donors. Studies of transplants carried out with half-matched (haploidentical) donors have also shown equivalent outcomes to full matched donor transplantation with either extensive cell selection methods or novel peri-transplant conditioning and prophylaxis protocols including the widely used post-transplant cyclophosphamide (PTCy) regimen. A prospective multicenter comparison of double-unit UCB and haploidentical transplantation with reduced-intensity conditioning did not show a statistically significant difference in 2-year PFS between the donor sources, albeit higher transplant-related mortality (TRM) with UCB transplantation. Studies using a uniform myeloablative regimen revealed similar results. Interestingly, a comparison between UCB and fully matched donor transplantation revealed that mismatched UCB grafts had reduced relapse rates and superior leukemia-free survival versus fully-matched adult donor stem cells, suggesting revealed superior leukemia control with UCB grafts despite more manageable graft versus host disease (GVHD). A prospective multicenter study of ex-vivo hematopoietic stem cell expanded versus conventional UCB transplantation revealed superior engraftment, reduced TRM, and superior survival in patients who received expanded grafts. Haploidentical transplantation has replaced UCB due to similar outcomes and reduced cost. However, UCB is more rapidly available as a source of cells for transplantation, and continued improvements in UCB technology could result in a resurgence in usage if costs could be controlled.

MULTIDISCIPLINARY TRACK

Multidisciplinary Track

Technical Issues in Transplantation

Advances in T cells depletion techniques

Godfrey Chi-Fung Chan[1, 2]

[1]Department of Paediatrics & Adolescent Medicine, The University of Hong Kong
[2]Department of Paediatrics, Hong Kong Children's Hospital and HKU-Shenzhen Hospital

One of the major morbidities and mortalities in allogeneic HSCT is GvHD. Even under fully HLA matched setting, GvHD can still occur. The use of matched unrelated or haploidentical donors further intensifies this problem. The mechanism of GvHD is complex and involves the activation or suppression of different immune cells with respective cytokines release. The final effector cells for GvHD are T cells, therefore experts developed different T cells depletion strategies to prevent the occurrence of GvHD. The earliest method involved positive selection of CD34 cells and depleting all other cell types from the donor graft. This approach is associated with delayed engraftment, higher graft rejection and increase infection for this also removed most supportive cells for engraftment and anti-infection. Then the approach shifted to the depletion of T cells, both via *ex-vivo* technique to remove CD3+ve T cells or *in-vivo* using ATG or post-HSCT addition of cyclophosphamide. The retained unopposed B cells can lead to EBV activation with increase PTLD, therefore, B cells removal with either anti-CD19 *ex-vivo* or *in-vivo* was adopted by most HSCT teams. Subsequently, reports showed that T cells subset known as α/β-T cells, are the main mediator of GvHD, whereas γ/δ-T cells are important for infection control and tumour surveillance. Therefore, selective depletion of α/β-T cells was used by several HSCT teams, but it was found that γ/δ-T cells can also mediate GvHD indirectly by recruiting activated donor T cells. Since in acute GvHD, the antigen presenting cells with allogeneic response specifically activate naïve T cells (CD45RA+ve), then the latest approach is to selectively deplete CD45RA+ve T cells. The advantage is that it leaves behind many important immune cells that can promote engraftment, enhance graft versus tumour effect, and against infection. Future direction is to identify even more specific GvHD related cell subsets for depletion.

Multidisciplinary Track

Technical Issues in Transplantation

Optimising Red Cell Depletion

Halvard Bonig

Goethe University, Frankfurt a.M., Germany; German Red Cross Blood Service Baden-Württemberg-Hessen, Frankfurt a.M., Germany; University of Washington, Seattle, WA, USA.

Transplantation of ABO major- or minor-mismatched red-cell (RBC)-replete bone marrow (BM) is often associated with severe hemolysis, due to the presence of isoagglutins of frequently meaningful titer strength. To prevent this, RBCs and plasms can be depleted from the graft using a variety of ex-vivo manipulation techniques. RBC depletion is also required prior to cryopreservation of a BM graft. The greatest risk of ex vivo RBC depletion is loss of stem cells. When it first became available, we identified Spectra Optia BMC as the preferred method for RBC depletion, based on a favorable comparability exercise with several density gradient-based technologies. Between 2014 and 2021, we thus performed 120 RBC depletions of allogeneic BM transplants; the indication was in approximately equal part ABO major and minor mismatch. Spectra Optia BMC was employed throughout, using the BMC accessory kit and an IDL consumable with the appropriate filler. The initial virtual collection preference was set to 50; maintenance of an apparent hematocrit of approximately 5% typically required adjustment of the collection preference to 30-35. 8-9 BM volumes were processed with an inlet flow velocity of 120 mL/min for a packing factor of approximately 10. The specification of achieving >70% recovery of CD34+ cells in 90% (108/120) procedures was exceeded (mean, 89%; specification reached in 114/120 procedures) and depletion of RBC to <0.5 ml RBCs/kg in 90% of procedures was achieved in 100% (mean residual RBC volume, 6.5 ml). Product volume, and hence isoagglutin content, was reduced by 90%, from a mean of 1147 to 119 mL. BM products thus processed were tolerated without adverse events related to hemolysis and provided timely engraftment. In experienced hands, RBC (and plasma) depletion with Spectra Optia is a robust and efficient technique. Given the paucity of BM transplants performed, establishment of central processing sites might be considered.

Multidisciplinary Track

Technical Issues in Transplantation

CAR-T Cell Manufacturing using Automated Cell Processing Platforms

Parameswaran Hari

Medical College of Wisconsin, Milwaukee, USA

With current approvals of commercial CAR-T cells, engineered T cell therapies are starting to impact the natural history of lymphoma and myeloma in developed countries. For the vast majority of patients worldwide though, access remains a major issue limited by manufacturing costs, logistical and capacity limitations inherent to commercial GMP manufacturing. The ability of manufacture CAR-T cells in nearby patient environment (local hospital) can solve some of the logistical limitations but this is limited to a few specialized centers with infrastructure and expertise. Simplified, reproducible CAR-T-cell manufacturing with reduced labor intensity semi-automated CAR-T production platforms within a closed-system is highly desirable to overcome the challenges of infrastructure and expertise. Decentralizing this process to near patient in-hospital settings promises to solve many logistical and cost issues while raising questions of standardization. Standardization in starting materials and process automation through closed-manufacturing solutions are promising in this regard. Ultimately for these innovations to be successful, they have to be balanced by internationally agreed upon standards for establishing CAR-T functionality, criteria for release and comparability of products made at various centers. The talk will focus on the design and production of dual targeted CD19-20 CAR-T cells using a closed system manufacturing with serial innovation.

Multidisciplinary Track

Technical Issues in Transplantation

Development of an affordable, semi-automated, functionally closed and scalable manufacturing platform for CAR-T Cell therapy: an experience from India

Atharva Karulkar[1,2], Ankesh Kumar Jaiswal[1], Shreshtha Shah[2], Aalia Khan[1], Afrin Firfiray[2], Sweety Asija[1], Prashant Suvasia[1], Priyanshi Suvasia[1], Juber Pendhari[1], Smrithi Ravikumar[2], Ambalika Chowdury[1], Neha Sharma[3], Minal Poojary[3], Sumathi Hiregoudar[3], Albeena Nisar[3], Preeti Desai[3], Anisha Navkudkar[3], Sunil Rajadhyaksha[3], Prashant Tembhare[3], Jaya Thorat[3], Navin Khattry[3], Manju Sengar[3], Hasmukh Jain[3], Gaurav Narula[3], and Rahul Purwar[1,2]

[1]Indian Institute of Technology Bombay (IIT Bombay), Mumbai, India, [2]Immunoadoptive Cell Therapy Private Limited (ImmunoACT) Mumbai, India, [3]Tata Memorial Centre, Mumbai, India

Objective

Chimeric Antigen Receptor (CAR) T cells therapy has shown remarkable success in hematological malignancies. However, complexity of the manufacturing platform and exorbitant costs of the available therapy are the major barriers for the CAR-T cell therapy access in countries with limited resources including India. Here, we will share our experience in developing semi-automated, integrated and scalable CAR-T cell manufacturing platform.

Methodologies

Lymphocytes were collected from 10 patients of r/r B cell malignancies (DLBCL and PMBCL) through apheresis and transported to the manufacturing site at room temperature (15-25°C) upon receiving the regulatory approvals from central agencies (CDSCO, DBT/RCGM, ICMR) and local agencies (ethics and biosafety committees). CD3+ T cells were isolated and activated using CTS™Dynabeads™ CD3/CD28 for 36-48 hours followed by consecutive double transduction with lentivirus vector containing CD19 targeted CAR gene. After incubation, cells were washed and expanded for 3-4 days before harvesting. Final product was cryopreserved and stored in ultra-low temperature until further use. All steps were carried out in closed gas permeable bags designed for T-cell activation and expansion. Final product quality control (QC) assays were performed by flowcytometry, ELISA, analytical and cell-based assays.

Results-

To develop the infrastructure, process and CAR-T cell therapy platform, we designed and developed an integrated cGMP facility at IIT-B and recently at ImmunoACT, a spin off company of IIT Bombay. The end-to-end CAR-T cell manufacturing (including the lentiviral vector manufacturing and QC) was performed in semi-automatic, closed, scalable platform to examine the feasibility and functionality of the manufacturing process and platform. Total 100-200 million CD3+ T cells from patient (n=10) were enriched, activated and expanded. Final CAR-T product (transduction efficiency; 31.9 ± 4.86%) showed robust expansion, achieving the required dose within 8 days. Functionally, final CAR-T cell product was robust and effective in killing tumor cells. All the batches of CAR-T cells qualified the QC release criteria for safety, identity, purity and potency as per regulatory guidelines. The estimated cost of CAR-T cell manufacturing in our setting was approximately $30,000 including logistics, lentiviral vector cost and quality control.

Conclusion

Overall, we established an affordable, functionally closed and scalable model for end-to-end CAR-T cell manufacturing to improve the CAR-T cell therapy access in countries with limited resources including India.

Multidisciplinary Track

Challenges in Data Management

Number of autologous hematopoietic stem cell transplantation registered in Asian countries/regions is smaller than that in Europe and the United States

Koichi Miyamura

Department of Hematology, Inuyama Chuo General Hospital, Inuyama, Japan

Japan has fewer registered autologous hematopoietic stem cell transplants (HSCTs) than allogeneic HSCTs (2174 vs. 3900 in 2020). The number of autologous HSCTs in Europe and the United States is almost twice as high as allogeneic HSCTs. According to Asia-Pacific Blood and Marrow Transplantation Group (APBMT) registry data, a similar trend is observed. A ratio of >1.5 was reported in China, India, Iran, Pakistan, and Sri Lanka in 2016, while a ratio of <0.67 was reported in Australia, New Zealand, and Thailand.

To determine factors contributing to these discrepancies, we conducted a questionnaire on the registration of autologous HSCT in each country/region, obtaining the following outcomes. “The main reason for this is the low rate of autologous HSCT for malignant lymphoma and myeloma compared to that in Western countries.” “The number of registrations from oncology societies or academic societies other than hematopoietic cell transplantation society may be small.” “Registration of HSCT for myeloma patients may not be strictly performed.” It is also assumed that registration is done by busy clinicians, and allogeneic HSCT must be prioritized for registration during the limited time.

A lump-sum payment system based on diagnosis procedure combinations (DPCs) was introduced in acute care hospitals throughout Japan in 2003. DPC data are accurate because they are based on the insurance claim for transplant costs. Using DPC data, it is expected that almost 20% of autologous HSCTs were not recorded Japan.

These analyses may improve compliance with registrations. Consequently, patients in Asia would receive transplants when needed. Improved registration compliance will also lead to enhanced medical safety.

Multidisciplinary Track

Challenges in Data Management

Bangladesh Experience

Mafruha Akter[1*], Mohiuddin Ahmed Khan[1], Abu Jafor Mohammad Saleh [2], Mohammed Mosleh Uddin[3]

[1*] Assistant Professor,BMT unit, Department of Hematology, Dhaka Medical College & Hospital.
[1]Ex-Head of Department of Hematology, BMT Unit, Dhaka Medical College & Hospital.
[2]Senior consultant and Coordinator, Hematology and Stem cell transplant division, Evercare Hospital Dhaka.
[3]Department of Hematology, Combined Military Hospital (CMH) Dhaka.
*Corresponding and presenting author

HSCT databases are the backbone of any quality transplant program. Since 1960's HSCT has evolved from a clinical concept to an amazing clinical result for several blood diseases with the tremendous development and progress in this field. Statistical data analysis is a fundamental to assess the effectiveness of treatment and it provides valuable information on clinical approach and outcome.

Since 2014 total 168 HSCT have been done in Bangladesh in five centres. Among them 129 were autotransplant for multiple myeloma (52), NHL (39), Hodgkin lymphoma (27) and for others (11). Total 39 allogeneic transplants were done for acute leukemia (30), aplastic anemia (5), thalassemia (2) and Lymphoma (2).

But the country is lacking national transplant registry which is yet to be developed. There is no professional data manager to keep the medical records in most centres in Bangladesh. Each centre is responsible for keeping medical records on their own format which done by physicians who actively participate in the transplant program. The data is usually kept using microsoft excel sheets with the basic data set including demographic, clinical and laboratory data.
Every year data centre of APBMT sends data sheets of activity survey that are filled up by registry committee member of Bangladesh part. Bangladesh also share the data in redcap data entry system sent by data centre of APBMT and tries to give the updated follow up of each patient.
HSCT centres in Bangladesh are requested to share the transplant related data in January and July each year so that we can compile the data and update those in APBMT system.
Transplant registries depends on effective database and data management, that would identify and describe the quantity and quality of transplants and outcomes. Registries outcomes encompass time trends in stage, treatment patterns and survival outcomes.
The major challenges in collecting data in Bangladesh is lack of proper training and exposure on data management. Regular analysis of demographic, clinical and
outcome data is indispensable for ensuring and maintaining quality in a hematopoietic stem cell transplant (HSCT) centre. We need to establish an adequately staffed data management team with a team supervisor, implement formal data management training.
In addition to trained personnel for data management, other challenges are lack of funding, lack of national collaboration between centres and lack of national registry.

Transplant databases are the systematic approach at monitoring the natural history of the disease, demographics, therapeutic interventions, toxicity/safety, treatment effectiveness, quality assessment, and sustainability of this high-stake tertiary care service in a HSCT centre. To observe short- and long-term complications of HSCT it requires long term follow-up data of patients.

Multidisciplinary Track

Challenges in Data Management

Introduction to APBMT Registry - Successes and Challenges

Minako Iida

Department of Promotion for Blood and Marrow Transplantation
Aichi Medical University, School of Medicine, Nagakute, Japan

APBMT established the Asian Blood and Marrow Transplant Registry and Data Center in 2006 and performed the first activity survey in 2007. In the beginning, only seven countries/regions from China, Hong Kong, Iran, Japan, Malaysia, Singapore, and Vietnam participated in the survey, and the total number of annual transplants was around 4,600. The number of participating countries/regions increased to 21 in the past decade, and the annual number of transplants exceeded 27,000 in 2019. The activity survey that has continued for more than 15 years has revealed the evolution of hematopoietic stem cell transplantation in the Asia-Pacific region and the diversity among countries/regions within this region. On the other hand, collecting and analyzing the detailed information of each patient is essential for the community to improve transplant outcomes and develop new strategies. APBMT Registry Committee established the least minimum dataset to collect patients' outcome data in 2009. Data Center and Registry Committee made efforts to collect outcome data through the National Registries and the data transplant agreement with CIBMTR (launched in 2014). In addition, Data Center developed the electronic data capture system in 2017. The number of outcome data submissions increased gradually; however, the rate of outcome data collection in proportion to total transplants is still low, at less than 40%. The main reasons for this low capture rate are 1) insufficient human resources and funding and 2) little understanding of the importance of outcome data collection. APBMT Data Center and Registry Committee will strive to overcome all difficulties.

Multidisciplinary Track

Challenges in Data Management

HCT Outcome Registry in Japan: Achievements and Future Goals

Yoshiko Atsuta

Japanese Data Center for Hematopoietic Cell Transplantation
Department of Registry Science for Transplant and Cellular Therapy,
Aichi Medical University School of Medicine, Nagakute, Japan

The annual number of HCTs in Japan has exceeded 5,500 in recent years, and a steady increase in the number HCTs has been seen globally. Collection and analysis of information on diseases and the post-transplant course of HCT recipients have played important roles in improving therapeutic outcomes. A centralized registry of HCT designed by the Japanese Society for Transplant and Cellular Therapy (JSTCT) using Transplant Registry Unified Management Program (TRUMP®) was started in 2006. Based on the "Act on Promotion of Appropriate Provision of Hematopoietic Stem Cells Used for Transplantation" passed in 2014, surveys with a high supplement rate are conducted by the JSTCT and the Japanese Data Center for Hematopoietic Cell Transplantation (JDCHCT), which are responsible for data collection and management. The database includes the data of more than 120,000 cases of HCT. The collected data are actively utilized for research, and more than 400 academic papers have been published to date. The construction of an accessible data utilization system for adequate data utilization by researchers would promote greater research activity. Study approval and management processes and authorship guidelines also need to be organized within this context. Quality control of processes for data manipulation and analysis will also affect study outcomes. Shared scripts have been introduced to define variables according to standard definitions for quality control and improving efficiency of registry studies. A registry system that can continuously meet society and community needs can only be established if the system includes measures to deal with the expectations and burdens placed on the central data management site, as well as incentives to deal with expectations for and the burden of data registration at treatment sites.

Multidisciplinary Track

Clinical Trial Designs and Outcome Assessment in HSCT

Survival analysis endpoints including competing risks in transplant studies

Yoshinobu Kanda

Jichi Medical University, Tochigi, Japan

Time-to-event analysis, often called survival analysis, is the mainstay of outcome analyses in studies on hematopoietic stem cell transplantation (HSCT). It analyzes the length of time until the occurrence of a well-defined endpoint of interest. The simplest endpoint is death, but in HSCT analysis, more complex endpoints are often used. For example, composite endpoints such as disease-free survival or graft-versus-host disease (GVHD)-free, relapse-free survival are frequently analyzed. However, a significant drawback of these endpoints is that death, a terminal event, is combined with non-terminal events including relapse or GVHD. The conventional time-to-event analysis for composite endpoints treats these events to have the same importance, but non-terminal events could be recovered by treatments whereas death can never be recovered. An approach to avoid this drawback is competing risk analysis. The effect of covariates on each event can be estimated using two different methods: the conventional Cox proportional hazard model by treating competing events as censoring or Fine-Gray model that reports subdistribution hazard ratio of each event. Another approach for the composite endpoint analysis is a current event-free survival analysis, that estimates the probability that a patient is alive without an occurrence of any events or in subsequent event-free status after treatment for an event. It can also be calculated using two different methods: a multistate modelling approach or a linear combination of Kaplan-Meier estimates. These analyses are complex but can be performed by point-and-click access using a free statistical software, EZR (easy R), except for the multistate modeling. I will show the examples of these analyses, as well as their advantages and disadvantages.

ORAL PRESENTATION

Oral Presentation

LEUKEMIAS (197)

IMPROVED SURVIVAL WITH ALLO-HSCT FOR RELAPSED/REFRACTORY B-ALL IN NON-REMISSION OR MRD+ AFTER CART

Yanzhi Song*[1], Erhui Yuan[1], Zhihui Li[1], Yongqiang Zhao[1], Qishu Qin[1], Qi Wang[1], Tong Wu[1]
[1]Bone Marrow Transplantation, Beijing Boren Hospital, Beijing, China

Aims & Objectives: Relapsed/refractory (r/r) B-cell acute lymphoblastic leukemia (B-ALL) patients who can not get complete remission after chimeric antigen receptor T-cell (CART) therapy have very poor prognosis. We evaluated the efficacy and safety of allogeneic hematopoietic stem cell transplantation (allo-HSCT) for r/r B-ALL patients who were still in non-remission (NR) or minimal residual disease (MRD) positive (+) after CART therapy.
Patients / Materials & Methods: Between January 2018 and June 2022, 38 consecutive patients with r/r B-ALL who were in NR (12) or MRD+ (26) after CART and received allo-HSCT in our hospital were included. Table 1 and 2 showed the clinical characteristics of included patients. Before allo-HSCT, 22 patients (57.9%) received at least two kinds of CART. Myeloablative conditioning regimens were used. Some patients received maintenance regimens with targeted medicine up to 2 years post-transplant.
Results: 37 patients achieved durable engraftment. One patient in MRD+ occurred graft rejection on the +30 days post-HSCT and his self-hematopoiesis recovered. There was no difference in two-year OS (overall survival, Figure 1) and LFS (leukemia free survival, Figure 2) between NR and MRD+ groups. For patients in NR before transplantation, the median follow-up time was 150 (39-1127) days. Four of them had been alive free of leukemia and MRD negative, 8 patients died of relapse. Two-year OS and LFS were 32.7% and 25.4%. No patient died of transplant-related events. 3 patients developed grade III~IV acute GVHD (aGVHD) and 2 patients had extensive chronic GVHD (cGVHD). One patient died of grade IV aGVHD and the others were resolved with immune- suppressants. CMV and EBV reactivation was detected in 7 and 1 patients. There was one patient had severe lung fungal infection and bacteremia, respectively. 2 cases developed severe hemorrhagic cystitis. For the patients with MRD+, the median follow-up time was 258 (39-1389) days and two-year OS and LFS were 41.4% and 30.5%. 15 patients relapsed. 6 and 3 patients developed grade III~IV aGVHD and extensive cGVHD. All of them were resolved except 2 died from grade IV aGVHD. CMV and EBV reactivation was found in 11 and 4 patients. 4 patients had bacteremia. 12 and 1 patients had mild and severe hemorrhagic cystitis. The one-factor regression analysis showed age, sex, CART courses, first or sencond HSCT did not influence the outcomes.
Discussion and Conclusion: Our results indicate that salvaged allo-HSCT has improved survival remarkably in r/r B-ALL patients who failed both chemotherapy and CART therapy. Under our protocol, transplant-related mortality is quite low (3/38), and for so heavily treated patients, allo-HSCT is also safe and effective for r/r B-ALL who are still in NR or MRD+ with CART therapy.
No conflict of interest to disclose.

Disclosure of Interest: None Declared

Keywords: CART, HSCT, non-remission, salvaged

Oral Presentation

LEUKEMIAS (237)

OUTCOME OF HEMATOPOIETIC STEM CELL TRANSPLANTATION IN ACUTE LYMPHOBLASTIC LEUKEMIA

Jhansi J*[1], Ashish Dixit[1], Mallikarjun Kalashetty[1], Amit Rauthan[2], Poonam Patil[2], Giri Punja[1]
[1]Clinical Hematology, [2]Medical Oncology, Manipal Hospitals, Bangalore, India

Aims & Objectives: Hematopoietic stem cell transplantation (HSCT) is one of the most promising consolidation therapies for Acute Lymphoblastic Leukemia (ALL), which has been proven to improve cure rates. This study aims at reviewing outcome variables including overall survival (OS), progression-free survival (PFS), and identifying long term complications like graft-versus-host disease (GVHD), transplant-related mortality (TRM) and relapse amongst patients with ALL who underwent HSCT.
Patients / Materials & Methods: A retrospective cohort study was performed using the hospital registry at our centre. We included patients with ALL (both B ALL and T ALL) who underwent hematopoietic stem cell transplantation between January 2009 and December 2021. Data on baseline disease characteristics like response to initial therapy and MRD assessment, various conditioning regimens used, types of transplantation offered, and post-transplant follow-up were collected. Chi-square tests were used to compare the proportions of categorical variables in various subgroups. Survival curves were assessed using the Kaplan-Meier method, and survival estimates were compared with the log-rank test.
Results: A total of 39 patients diagnosed with ALL who underwent HSCT between January 2009 and December 2021 were included. Median age of the group was 16 years. Pediatric patients (age<18 years) comprised 56% of the population. Amongst the patients with initial treatment records available, 10 were prednisolone responders, 15 had post-induction remission, and 4 had post-induction MRD positivity. HSCT was done in first remission (CR1) for 30.7% of the cases. Matched allogeneic transplantation was performed in 50% of the cases and the other 50% had haplo-identical transplantation. Cyclophosphamide with Total Body Irradiation (TBI) was the most commonly used conditioning regimen. TRM was seen in 4 cases, where all the subjects belonged to the adult age group (p=0.042). Post-HSCT GVHD was seen in 53.8% of the patients (35.9% had acute GVHD and 17.9% had chronic GVHD), most of whom presented with skin GVHD. On follow-up, 25% of the cases had died (excluding TRM), and 28% of the cases had relapsed. Median overall survival of the patients post-HSCT was 56.04 months, which was observed to be significantly higher in patients who had remission post-induction therapy (p=0.0254). Median PFS post-HSCT was 55.87 months.
Discussion and Conclusion: Although HSCT is one of the most potent therapies with curative intent in ALL, efforts to reduce long-term complications need to be addressed. Since the advent of HSCT, there has been significant improvement in the safety of the procedure. Attention to supportive care for transplant patients, use of alternative donors and focus on GvHD prevention may further expand the use and efficacy of transplantation in ALL.

Disclosure of Interest: None Declared

Keywords: Acute lymphoblastic leukemia, BMT BONE MARROW TRANSPLANT, OUTCOME

Oral Presentation

LEUKEMIAS (285)

EFFECT OF STEM CELL DOSE ON TRANSPLANT OUTCOMES IN HAPLO-SCT

Shouriyo Ghosh[*1], Arijit Nag[1], Reghu K.S.[1], Vivek S. Radhakrishnan[1], Niharendu Ghara[1], Saurabh Bhave[1], Jeevan Kumar[1], Reena Nair[1], Rizwan Javed[1], Mammen Chandy[1]
[1]TMC , Kolkata, India

Aims & Objectives: The ideal stem cell dose in haploidentical transplants is debatable. Higher cell doses are associated with an increased risk of GVHD, while lower doses may lead to graft failure and relapses. In this study, we divided the patients into 2 cohorts: those receiving a stem cell dose of ≤ 4 x 106/kg and those receiving > 4 x 106 cells/kg and analyzed the transplant outcomes in the above cohorts.
Patients / Materials & Methods: This retrospective study was done on all haploidentical transplants performed at our center from 2012-2021. Analysis of incidence of acute Grade III/grade IV GVHD, relapse and graft failure rates, GRFS at 100 days post-transplant was done. Event-free survival, overall survival was compared between the 2 cohorts with respect to stem cell dose. Statistical analysis was done using SPSS, v.23. Mean and median were calculated for continuous variables. EFS and OS of the 2 cohorts were calculated using Cox proportional regression and Kaplan-Meier survival analysis.
Results: Total of 103 patients underwent haplo-identical transplant during the period 2012- 2021. Mean age of the entire population was 29.43 +/- 14.06 years (range 4-60 years). Males and females constituted 70/103 (68%) and 33/103 (32%) respectively. Indications for transplant were acute leukaemia, CML, JMML, HL and NHL relapse post ASCT, plasma cell leukaemia, WAS and MDS. Most patients received myeloablative conditioning (99/103, 96.1%) and GVHD prophylaxis was mostly PTCY + tacrolimus + MMF. Of the study population, 39/103 (37.86%) patients received cell dose ≤ 4 x 106/kg (cohort 1) while the rest were in cohort 2 (>4 x 106/kg). Acute GVHD was seen in 45/103 (43.68%) patients. Grade III/IV acute GVHD was seen in 21/103, (20.4%) of all patients. Acute Gr III/GrIV GVHD was higher with high cell dose; 17/64 (16.5% of total) vs 4/39 (3.9% of total); p=0.038. Chronic GVHD was seen in 25/103 (24.3%) patients. Relapse rate was 12/102 (11.7%) while graft failure was seen in 10/103(9.7%) patients. There was no difference in relapse or graft failure rates: 3/39 vs 9/64, p = 0.259 and 2/39 vs 8/64, p=0.191 respectively. At 100 days, 64/103 patients (62.1%) were alive. GRFS at 100 days: better with lower cell dose – 21/39 vs 21/64, p=0.041. Median EFS not reached in cohort 1 while it was 107 days (95%CI 55.25 to 158.74 days) in cohort 2. Median OS was better in cohort 1 as compared to cohort 2. Neither EFS, nor OS were statistically different between the cohorts. In multivariate analysis, there was no association of EFS or OS with age, sex, diagnosis, CMV status at transplant or CMV reactivation
Discussion and Conclusion: Stem cell dose of less than or equal to 4 x 106/kg in the haplo-SCT setting, is a reasonable approach, associated with lower acute GVHD rates, better EFS and OS, and without a significant increase in relapse or graft failure rates.

Disclosure of Interest: None Declared

Keywords: CD 34 cell dose, GRFS, Haploidentical transplants

Oral Presentation

LEUKEMIAS (288)

THE ROLE OF ALLO-HSCT IN ACUTE LEUKEMIA PATIENTS WITH KMT2A REARRANGEMENT

Bingqian Jiang*[1], Yanmin Zhao[1], Yi Luo[1], Jian Yu[1], Huarui Fu[1], Xiaoyu Lai[1], Lizhen Liu[1], Weiyan Zheng[1], Jie Sun[1], Jingsong He[1], Yi Zhao[1], Guoqing Wei[1], Zhen Cai[1], He Huang[1], Jimin Shi[1]
[1]the First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, China

Aims & Objectives: Acute leukemia with KMT2A rearrangements (KMT2A-r AL) is associated with a poor prognosis. The role of allogeneic hematopoietic stem cell transplantation (allo-HSCT) in KMT2A-r AL is at issue.
Patients / Materials & Methods: 666 AL patients who underwent allo-HSCT at our institution from April 2016 to August 2021 were analyzed and 37 out of them were identified with KMT2A rearrangement.
Results: In KMT2A-r AL group, the median age at HSCT was 39 (range, 20-67) years and the median white blood cell count at first diagnosis was 31.5 (range, 1.1-497.4) ×109/L. The 5-year overall survival (OS), relapse-free survival (RFS) rates were 62.7% and 57.3%, respectively, whereas the 5-year cumulative incidences of relapse and non-relapse mortality (NRM) were 25.6% and 17.1%, respectively. The most common translocation partner gene was AF4 (10 cases, 28.6%). 8 cases (21.6%) harbored AF9, 6 cases (17.1%) harbored AF6 and 13 cases (35.1%) harbored other gene partners. No differences in OS (overall P=0.64), RFS (overall P=0.45), relapse (overall P=0.49) and NRM (overall P=0.49) were observed among KMT2A-r AL patients with different gene partners. Compared with those without KMT2A rearrangements, the 5-year OS and RFS rates of KMT2A-r AL patients were lower (62.7% v 72.0%, P=0.013; 57.3% v 66.7%, P=0.023; respectively). In multivariable analysis for OS, KMT2A rearrangements (HR=2.192, 95% confidence interval [CI] 1.161-4.140, P=0.016) and poor disease status before HSCT (HR=1.712, 95%CI 1.338-2.191, P<0.001) were significantly associated with decreased OS. Parallel results were observed that KMT2A rearrangements (HR=1.801, 95%CI 1.007-3.220, P=0.047) and poor disease status before HSCT (HR=1.675, 95%CI 1.355-2.070, P<0.001) were risk factors of RFS. In order to eliminate the impact of disease status before HSCT, KMT2A-r AL patients offered allo-HSCT in first complete remission (CR1) (n=27) were selected for further exploration. Those undergoing HSCT in CR1 and at intermediate risk for AML or at good risk for ALL evaluated by NCCN risk stratification (n=233) were selected as control. The survival analysis between the two groups revealed the similar outcomes in terms of 5-year OS rate (70.6% v 74.8%, P=0.36) and 5-year RFS rate (65.4% v 69.3%, P=0.32), which suggested that compared to those patients without KMT2A rearrangement at lower risk, KMT2A-r AL patients receiving allo-HSCT in CR1 obtained a comparable prognosis.
Discussion and Conclusion: The poor prognosis of KMT2A-r AL patients is irrelevant to the gene partner involved. KMT2A-r AL patients can benefit from allo-HSCT in first remission.

Disclosure of Interest: None Declared

Keywords: acute leukemia, KMT2A, stem cell transplantation

Oral Presentation

LEUKEMIAS (379)

LONG TERM OUTCOME OF HLA MATCHED ALLOGENEIC TRANSPLANT IN AML: A SINGLE CENTRE EXPERIENCE FROM INDIA

Nishant Jindal*[1], Kaumil Patel[1], Muralidaran C[1], Malini Garg[1], Libin Mathew[1], Komal Kumbhalwar[1], Sadhana Kannan[1], Sumeet Mirgh[1], Akanksha Chichra[1], Lingaraj Nayak[1], Avinash Bonda[1], Anant Gokarn[1], Sachin Punatar[1], Bhausaheb Bagal[1], Navin Khattry[1]
[1]Advanced Centre for Treatment, Research and Education in Cancer (ACTREC), Tata Memorial Centre, Navi Mumbai, India

Aims & Objectives: Allogeneic transplant remains the standard of care for a majority of patients with Acute Myeloid Leukemia (AML). We report outcomes of patients with AML who underwent matched related (MRD) or unrelated transplant (MUD) at our centre and analyze possible prognostic factors.
Patients / Materials & Methods: This is a single centre retrospective study. All patients of AML who underwent 10/10 or 9/10 MRD or MUD transplants between July 2008 and July 2021 were included. Full intensity (FI) conditioning regimens used were FluBu or BuCy (16 mg/kg oral busulfan or equivalent IV dose) [4], CyTBI (TBI > 8 Gy) [11] or FluTreo (42 g/m2) [7]. Reduced intensity (RI) regimens included FluMel (140 mg/m2) [49], FluTreo (30 or 36 mg/m2) [6], FluBu (<16 mg/kg) [6] and FluCyTBI (2 Gy) [3]. Peripheral blood stem cells and standard GVHD prophylaxis (calcineurin inhibitors and methotrexate/MMF) were used. Rabbit ATG was added for MUD or 9/10 MRD transplants. CMV reactivation was defined as more than 1000 CMV copies/mL. Acute GVHD (aGVHD) and chronic GVHD (cGVHD) were graded according to standard criteria. Cumulative incidence of relapse (CIR) was computed with transplant related mortality (TRM) as competing risk. Leukemia free survival (LFS) and overall survival (OS) were estimated using the Kaplan Meier method. Prognostic factors analysed for survival were age, gender, disease status at transplant, EBMT score, HCT CI, DRI, conditioning intensity, CMV reactivation and presence of acute or cGVHD. Univariate analysis was done using log rank test and Cox regression was used for multivariate analysis.
Results: Eighty six patients were included. Median age at transplant was 34 years and 70.9% were males (table 1). CMV reactivation was seen in 41.9% patients and was higher in those with aGVHD (60.5% vs 27.1%, p=0.002) and extensive cGVHD (68.2% vs 37%, p=0.008). Incidence of grade 2-4 aGVHD was 27.9% and was higher in patients who received FI conditioning (61.5% vs 36.7%, p=0.033). Forty-one patients developed cGVHD with FI conditioning (73.1% vs 37.9%, p=0.003) and female to male transplants (65.6% vs 38.5%, p=0.016) being significant risk factors. 2 year CIR was 31.47%. It was lower in females (42.5% vs 14.1%, p=0.018) and in those with cGvHD (59% vs 10.2%, p=0.000). TRM was 16.3%. Five year LFS and OS were 42.9% and 49.2% respectively. On multivariate analysis, female gender and presence of cGVHD were associated with better OS while CMV reactivation was associated with inferior outcome (table 2)(figure).
Discussion and Conclusion: Approximately half of our patients who underwent transplant for AML are long term survivors. Female gender and presence of cGVHD were associated with better OS while CMV reactivation resulted in inferior outcomes. Harnessing the graft versus leukemia effect is possibly the key to improving AML transplant outcomes.

Disclosure of Interest: None Declared

Keywords: Acute Myeloid Leukaemia (AML), ALLOGENEIC HAEMATOPOIETIC STEM CELL TRANSPLANTATION, PROGNOSTIC FACTORS

Oral Presentation

LEUKEMIAS (395)

LONG TERM OUTCOME OF HLA MATCHED ALLOGENEIC TRANSPLANT IN ALL: A SINGLE CENTRE EXPERIENCE FROM INDIA

Kaumil Patel*[1], Nishant Jindal[1], Libin J. Mathew[1], Komal Kumbhalwar[1], Sadhana Kannan[1], Muralidaran C[1], Malini Garg[1], Sumeet Mirgh[1], Akanksha Chichra[1], Lingaraj Nayak[1], Avinash Bonda[1], Anant Gokarn[1], Sachin Punatar[1], Bhausaheb Bagal[1], Navin Khattry[1]
[1]MEDICAL ONCOLOGY, ACTREC, TATA MEMORIAL CENTRE, NAVI MUMBAI, India

Aims & Objectives: Allogeneic stem cell transplant (ASCT) is the most curative treatment for acute lymphoblastic leukemia (ALL). There is paucity of data from India regarding long term outcome of ALL patients undergoing HLA matched ASCT. We report long term outcome of our patients and analyze possible prognostic factors.
Patients / Materials & Methods: This is a single center retrospective study of ALL patients who underwent full or 9/10 matched related (MRD) or unrelated (MUD) transplant from November 2007 and July 2021. Patients with t(4; 11), t(9; 22) and t(1; 19) were considered high risk (HR). Full intensity (FI) conditioning regimen was Cy-TBI (TBI ≥12Gy) [n=49]; reduced intensity (RI) regimens were Flu-Mel (140 mg/m2) [n=25], Flu-Treosulfan (≤36mg/m2) [n=4], Flu-TBI (7.2-8Gy) [n=3], and Flu-AraC-Mel [n=1]. Peripheral blood stem cell graft and standard GvHD prophylaxis (CNI and MTX/MMF) were used. Rabbit ATG (2.5-5 mg/kg) was added for MUD or 9/10 MRD transplants. Pre transplant flow minimal residual disease (MiRD) was available for 56 (68.3%) – 42 (75%) and 14 (25%) were negative and positive respectively. Acute GVHD (aGVHD) and chronic GVHD (cGVHD) were graded as per standard criteria. Cumulative incidence of relapse (CIR) was computed with transplant related mortality (TRM) as competing risk. Leukemia free survival (LFS) and overall survival (OS) were estimated using the Kaplan Meier method. Prognostic factors analysed for LFS and OS were age, gender, cytogenetic risk, disease status at transplant, female to male transplant, CMV reactivation, EBMT score, HCT Comorbidity Index (HCT-CI), Disease Risk Index (DRI), intensity of conditioning regimen and presence of acute or cGVHD. Univariate analysis was done using log rank test. Cox regression method was used for multivariate analysis
Results: Eighty-two patients (median age 27 years, 78% males) were included (table 1). CMV reactivation was seen in 40 (49%) and was higher with aGVHD (p=0.007). Grade 2-4 aGVHD was seen in 40%. Thirty nine (48%) developed cGVHD with female to male transplants (p=0.04) being only significant risk factor. Two years CIR was 33.0 %(95%CI, 23.1%-43.3%) with cGvHD being protective (16.3 vs. 64.6%, p=0.001). TRM was seen in 22%. Median LFS and OS of whole cohort were 20 and 48 months. On univariate analysis, Philadelphia (ph) positive ALL, low EBMT score (0-2), cGVHD and negative pre-SCT flow MiRD in patient with intermediate DRI had significantly better LFS and/or OS (table 2). On multivariate analysis, cGVHD (HR=0.165, 95% CI 0.083-0.33, p=0.000) and EBMT score ≤2 (HR=3.65, 95% CI 1.40-9.51, p=0.008) were associated with better OS.
Discussion and Conclusion: Low EBMT score and cGVHD were associated with better LFS and OS. Adding pre-transplant MRD to refine the DRI for intermediate risk patients may lead to better prognostication.

Disclosure of Interest: None Declared

Keywords: DRI, EBMT, Pre SCT Flow MRD

Oral Presentation

LEUKEMIAS (397)

THE IMPACT OF KIR MISMATCH IN HAPLOIDENTICAL STEM CELL TRANSPLANTATION

Sujith Karumathil*[1], Uday Kulkarni[1], Mathumithra Thangaraju[1], Anu Korula[1], Fouzia NA[1], Sharon Lionel[1], Sushil Selvarajan[1], Kavitha Lakshmi[1], Alok Srivastava[1], Aby Abraham[1], Biju George[1]
[1]Clinical Hematology, CMC , Vellore, India

Aims & Objectives: There is conflicting data on the impact of KIR mismatch using the ligand-ligand model on the outcomes of haploidentical transplantation (HaploSCT) using the post-transplant cyclophosphamide (PTCy) approach. We analyzed the impact of KIR mismatch in patients undergoing HaploSCT for hematological malignancies using PTCy
Patients / Materials & Methods: This was a retrospective analysis of patients with various hematological malignancies who underwent haplo SCT using PTCy, at our center between June 2010 and November, 2019. KIR mismatch using the ligand-ligand model (https://www.ebi.ac.uk/ipd/kir/matching/ligand/) and PIRCHE scoring was calculated with online software. Disease Risk Index was calculated using CIBMTR software. Univariate and multivariate Cox regression analysis was performed for predictors of overall survival
Results: A total of 119 patients underwent HaploSCT for malignant diseases out of which 75 (63%) were males. Median age at HCT was 24 (Range:4-58) years. Graft failure was noted in 7 (5 primary and 2 secondary) while neutrophil engraftment occurred at a median of 16 (11-44 days). Forty-four (37%) patients developed acute GvHD of any grade (34 had grade II-IV), while 25 (21%) developed chronic GvHD (11%-extensive). Relapse occurred in 24 (20.2%) at a median of 6.5 months (range :1-45.6 months). Based on the KIR status the entire cohort was classified into KIR matched group (KIR 0), KIR mismatch in host versus graft [HvG] direction (KIR 1) and KIR mismatch in graft versus host [GvH] direction (KIR 2). Baseline characteristics were similar between the 3 groups (Table 1). Relapse rates were not different among the three KIR groups. The 2-year OS in KIR 0, 1 and 2 group were 39.7% ± 7%, 26.3% ± 8.1%, and 52.3 ± 8.4% at 24 months (log rank p 0.07). The 2 year overall survival for the entire cohort was 39.9% ± 4.6%. On multivariate Cox regression analysis, independent predictors of worse overall survival include older age, KIR mismatch in HvG direction, use of non-myeloablative conditioning, higher disease risk index and presence of acute GVHD (table 2).
Discussion and Conclusion: KIR mismatch in the HvG direction using the ligand-ligand model seems to be associated with worse overall survival in our cohort, probably due to increased deaths related to infections. KIR mismatch is not associated with increased relapse rate in HaploSCT using the PTCy GVHD prophylaxis approach. This needs to be evaluated further in larger studies.

Disclosure of Interest: None Declared

Keywords: Haploidentical stem cell transplantation, KIR, PTCy

Oral Presentation

PEDIATRIC TRANSPLANTATION (292)

OUTCOME OF TCR ALPHA BETA AND CD19 DEPLETED HAPLOIDENTICAL HAEMATOPOIETIC STEM CELL TRANSPLANTS

Sohini Chakraborty*[1], Kavitha Ganesan[1], Suresh R Duraisamy[1], Satish K. Meena[1], Vigneswar Venkatesan[1], Venkateswaran V. Swaminathan[1], Ramya Uppuluri[1], Revathi Raj[1]
[1]Paediatric Haematolog y, oncology and Blood and Marrow Transplantation, Apollo Cancer Centre, chennai, India

Aims & Objectives: Haploidentical Haematopoietic stem cell transplants (HSCT) are now being increasingly performed in patients with no available fully matched donors. Ex vivo T cell depletion in the form of TCR alpha beta (αβ) and CD19 depletion have demonstrated high rates of engraftment and low rates of graft versus host disease (GVHD) leading to significant improvement in outcomes. The aim of this study was to analyse the outcome of children undergoing TCR αβ and CD19 depleted haploidentical HSCT at our center and to study the relation of gamma delta (γδ) T cell dose with transplant outcome.
Patients / Materials & Methods: We performed a retrospective study in children up to 18 years of age with nonmalignant disorders who underwent TCR αβ and CD19 depleted haploidentical HSCT between February 2014 to February 2022 at our center. Data was collected through retrospective review of patient charts and medical records.
Results: A total of 51 patients were included in the study group comprising of 37 males and 14 females (M:F ratio 2.6:1) with a median age of 1.5 years (1 month to 14 years). The indications of transplant were inborn errors of immunity in 37, inborn errors of metabolism in 10 and other causes in 4 patients. The median infused γδ T cell dose was 5.115 x 106/ kg (1.27 to 42) and median CD34 dose was 7 x 106/kg (2.01 to 15.46). Forty four (86.2%) patients engrafted neutrophils with median time of engraftment being 10.5 days (9-14 days). Secondary graft failure occurred in 4 (7.8%) patients. CMV reactivation was observed in 33 (64.7%) patients. Out of 44 patients who engrafted neutrophils 18 had acute (40.9%) and 10 patients had chronic GVHD (22.7%). There was no difference in incidence of GVHD between those who received or did not receive additional calcineurin inhibitors as GVHD prophylaxis. The mortality was 29.4% and the overall survival at 2 years was 73.6%. The mean TCR γδ cell dose was 11.63x106/kg in those who engrafted vs 9.03x106/kg among those with primary graft rejection. Drawing an ROC curve, we derived a TCR γδ dose cut-off of 7.3x10*6/kg to distinguish between those who engrafted and those with primary graft failure with a sensitivity of 64% and specificity of 62%. The mean absolute lymphocyte counts at 1 month post HSCT was 1006 in those alive vs 545 in those who died.
Discussion and Conclusion: An overall survival of 73.6% can be achieved with haploidentical transplants using TCR alpha beta and CD19 depletion technique. Primary graft failure remains a significant problem and we need to focus on the TCR γδ cell dose for preventing primary graft failure. Maintaining a minimum TCR γδ cell dose of 7.3x10*6/kg would enable further sustained engraftment and the ALC at one month should prompt the need for stem cell top up to enable immune reconstitution.

Disclosure of Interest: None Declared

Keywords: CHILDREN, Haploidentical transplants, T CELL DEPLETION

Oral Presentation

PEDIATRIC TRANSPLANTATION (316)

HSCT OFFERS SUPERIOR SURVIVAL IN CHILDREN WITH SEVERE APLASTIC ANEMIA IN A TERTIARY REFERRAL CENTRE

Venkateswaran V S*[1], Sohini C[1], SATISH K. M[1], KAVITHA G[1], SURESH R D[1], VIGNESHWAR V[1], INDIRA J[1], RAMYA U[1], REVATHI RAJ[1]
[1]PEDIATRIC HEMATOLOGY ONCOLOGY AND BLOOD AND MARROW TRANSPLANTATION, APOLLO CANCER CENTRE, CHENNAI, India

Aims & Objectives: Hematopoietic stem cell transplantation offers the best chance of survival in children with acquired aplastic anemia.Fluarabine and cyclophosphamide were used in all children with the addition of 2Gy TBI in alternate donor HSCT. Antithymocyte globulin was added to unrelated HSCT but only included in our conditioning in haploidentical HSCT since 2019. We present our data on children treated at our centre who underwent HSCT for severe aplastic anemia and to analyze the impact of improved supportive care and serotherapy on matched family and alternate donor HSCT
Patients / Materials & Methods: We conducted a retrospective analysis from January 2004 to April 2022 and included children who underwent HSCT for acquired aplastic anemia.. The impact of serotherapy was analyzed with the study period before and after January 2019 when rabbit ATG was added to the conditioning.
Results: A total of 1170 children underwent HSCT in our center of which 35 had acquired aplastic anemia (2.9%)with a male : female ratio of 1.3. A fully matched family donor was available in 25/35(71%)children. Failed immunosuppression in8/35(22%) and life threatening infection in 2/35 (6%) warranted an upfront haploidentical HSCT in 9 children and a matched unrelated HSCT in one child.We used peripheral blood stem cells in 27/35 (77%) children and documented engraftment in31/35 (89%). During HSCT 10/35 (29%) had bacterial infection during the neutropenic phase and 4/35 (11%)died before engraftment.Viral reactivation with CMV was seen in 6/35 (17%), BK virus in 1/35(3%) and adenoviral reactivation in 1/35 (3%) and HHV8 encephalitis which resulted in the death of 1/35 (3%) one child. Acute graft versus host disease (GVHD) was seen in 2/35 (6%) of which one child died of grade 4 gut GVHD. Limited chronic GVHDinvolving mouth was seen in 2/35 (6%) andextensive in 3/35 (9%) resulting in the death of one child with lung GVHD.The overallsurvival in our cohort was 80% with GVHD resulting in significantly poorer survival with a p value of 0.03. The survival prior to 2019 was 22/30 (73%) and with the addition of serotherapy in 2019 has improved to 5/5 (100%) survival with no significant graft versus host disease
Discussion and Conclusion: With improved supportive care, HSCT with the addition of serotherapy offers close to 100% event free survival in children with acquired aplastic anemia since 2019. The outcomes of matched family donor and alternate donor are now equally optimal and HSCT should be placed upfront in the treatment algorithm for all children with severe aplastic anemia

Disclosure of Interest: None Declared

Keywords: Alternate donor, aplastic anemia, HSCT

Oral Presentation

PEDIATRIC TRANSPLANTATION (358)

PRETRANSPLANT IMMUNOSUPPRESSION PRECEDING HEMATOPOIETIC STEM CELL TRANSPLANTATION IN THALASSEMIA

Shweta Pathak*[1], Ravi joshi[1], Shobha Bediger[1], Pooja Mallya[1], SANTOSHKUMAR ASANGI[1], Swathi M[1], Monika Bhukar[1], Manojit Chakraborty[1], Gayathri S[1], Lakshmi T[1], Kamini S[1], Sunil Bhat[1]
[1]Pediatric hemato-oncology and Bone marrow transplant unit, Mazumdar shaw hospital, Banglore, India

Aims & Objectives: Pretransplant immunosuppression (PTIS) prior to conditioning chemotherapy in patients with thalassemia suppresses recipient T cell function hence facilitating engraftment and reducing the risk of Graft versus host disease (GVHD). This study aimed to assess the clinical profile and outcome of patients who received pre-transplant immunosuppression before conditioning chemotherapy.
Patients / Materials & Methods: This is a retrospective study conducted at Mazumdar Shaw Medical Center, Bangalore. Data of One hundred sixteen patients who underwent hematopoietic stem cell transplants in our center from January 2017 to January 2022.
Results: A total of one hundred and sixteen patients received Pre-transplant immunosuppression preceding conditioning chemotherapy during the study period of 5 years. Patients undergoing haploidentical HSCT received 3 cycles of PTIS and those undergoing MSD/MUD received 2 cycles of PTIS. All the patients undergoing MSD HSCT in this cohort were Class II/III.
The median patient age was 6 years 10 months (ranging from 1.5 to 22 years). Male: female ratio was 1.5:1. The transplant characteristics are tabulated in Table 1.
The mean CD34 cell dose and MNC dose were 11.1 and 5.2 million cells per kg, respectively. The median day for neutrophil engraftment was 13 days (range 9-20) and platelets 14 days respectively. Acute graft versus host disease (GVHD) was seen in forty-two patients, out of which grade I-II GVHD was seen in 31.8 % and grade III-IV in 6% of patients. Veno occlusive disease (VOD) developed in forty-four patients with mild in 23%, moderate in 12%, and severe in 9% of patients respectively. CMV reactivation was seen in thirty-two patients.
Out of one hundred sixteen patients, 89.6 % achieved full donor chimerism on day+28. Six patients developed mixed chimerism post-transplant necessitating withdrawal of immunosuppressants to regain full chimerism. Five patients had primary graft rejection out of which one patient underwent a second transplant and survived, the remaining four patients died due to sepsis. Two patients developed secondary graft failure and died due to sepsis and secondary HLH. The transplant-related mortality was 16.3%, causes were Sepsis (42%), GVHD (26.3%) Primary graft failure (21%), secondary graft failure (10%), and Severe VOD (5.2%). The overall survival and thalassemia-free survivals were 83.6 % and 82.7 % respectively, with a median follow-up of 54 months. Haplo transplant with TCR alpha beta depletion showed a better survival probability (P=0.023) as compared to a MUD, MSD, and Haplo PTCY (Table2)
Discussion and Conclusion: We conclude that this novel sequential immunosuppression prior to conditioning chemotherapy is a safe and effective approach with improved overall survival and thalassemia-free survival

Disclosure of Interest: None Declared

Keywords: hematopoietic stem cell transplantation, Pretransplant immunosuppression, Thalassemia Major

Oral Presentation

LYMPHOMA/MYELOMA (203)

AUTOLOGOUS STEM CELL TRANSPLANTATION IN HODGKIN'S LYMPHOMA- A SINGLE CENTRE EXPERIENCE FROM INDIA

Mangai Suseela Murugesan*[1], Jayachandran Perumal Kalaiyarasi[1], Parathan Karunakaran[1], Nikita Mehra[1], Venkatraman Radhakrishnan[1], Gangothri Selvarajan[1], Sivasree Kesana[1], Carthikeyan Subramaniam Murali [1], Sagar Tenali Gnana [1], Krishnarathinam Kannan[1]
[1]Medical Oncology, Cancer Institute (WIA), Chennai, India

Aims & Objectives: Hodgkin Lymphoma is a type of lymphoid neoplasm which is considered as a curable malignancy. Relapsed Hodgkin's is treated with salvage chemotherapy followed by Autologous Stem Cell Transplant (ASCT). This Retrospective study is on Relapsed Hodgkin's lymphoma patients who underwent Autologous transplant from a single centre from South India
Patients / Materials & Methods: This study is collection of Retrospective data on ASCT in patients with Relapsed Hodgkin's lymphoma who underwent ASCT during the period of January 1997 to December 2021. Kaplan Meier method was used for survival analysis and Log Rank test was used for comparison of factors
Results: In this study which included 62 patients, the median age of the patients at diagnosis was 22.5 years (Range: 4-47 years) and Median age at Transplant was 24.5 years (Range: 4-50 years). Study compromised 63% Males (n=39) and 64.5% (n=40%) had Advanced disease at presentation. Most. Common regimen used upfront was ABVD/AVD (82%, n=51). In relapse setting 33.3%, 36.6% & 30% had Stage 2,3 and 4 respectively(n=60). Bone marrow involvement at the time of relapse was seen in 13.5% (n=59). Last salvage chemotherapy regimen used was GVD in 38 patients, DHAP in 13 patients and ICE/others in 11 patients. 63% had Complete remission of disease prior to transplant. 74% (n=46) patients underwent transplant after 1st line salvage regimen (CR2). LACE, BEAM/BEAC, CBV was used as conditioning regimen in 33.8% (n=21), 45% (n=28) and 19.3% (n=12) respectively. Out of 62 patients, dose of stem cell collected was available for 55 patients and median was 5.3x106 cells/kg (Range: 1.5x106 – 14.8x106 cells/kg). Febrile neutropenia (FN) was seen in 93.5%. It took a median duration of 11 days and 14 days for neutrophil and platelet recovery. Treatment related mortality was 4.8% (n=3). The median duration of follow up was 30 months. Three out of 62 patients underwent chemomobilization for stem cell collection followed by ASCT. The median relapse free survival (RFS) and overall survival (OS) was not reached in the study. The 3- year RFS and OS were 67.1% and 78% respectively. The factors adversely influencing OS and RFS were type of salvage regimen used and disease remission occurring after 2nd or 3rd line salvage regimen. Advanced stage of disease at diagnosis had poor outcome in terms of OS
Discussion and Conclusion: ASCT in Hodgkin's lymphoma shows improvement in overall survival in relapsed setting with more than 2/3rd of patients surviving without relapse after 3 years. Factors that predict risk of relapse post-transplant, methods to sustain remission post-transplant with use of newer agents needs further studies

Disclosure of Interest: None Declared

Keywords: ASCT in Hodgkin's Lymphoma, Relapse free survival after transplant in Hodgkin's Lymphoma, Relapsed Hodgkin's lymphoma

Oral Presentation

LYMPHOMA/MYELOMA (333)

FERTILITY OUTCOMES POST AUTOLOGOUS STEM CELL TRANSPLANTATION FOR HODGKIN LYMPHOMA WITH LACE REGIMEN

Muralidaran C*[1], Nishant Jindal[1], Libin J. Mathew [1], Komal Kumbhalwar[1], Kaumil Patel[1], Malini Garg[1], Sumeet Mirgh[1], Akanksha Chichra[1], Lingaraj Nayak[1], Avinash Bonda[1], Bhausaheb Bagal[1], Anant Gokarn[1], Sachin Punatar[1], Navin Khattry [1]
[1]BMT, ACTREC, Kharghar , India

Aims & Objectives: Autologous stem cell transplant (ASCT) remains the standard of care for relapsed Hodgkin lymphoma (HL). Infertility is an important long-term concern following ASCT after high dose therapy. At our center, LACE (lomustine, cytarabine, cyclophosphamide and etoposide) is the most commonly used conditioning regimen for lymphoma transplants. In this study, we determine the incidence of pregnancy and factors affecting fertility in young adults with HL undergoing ASCT using LACE as the conditioning regimen.
Patients / Materials & Methods: This is a single center retrospective analysis of patients of HL who underwent ASCT between 2007 and 2019 using LACE regimen. For fertility analysis, patients whose current age is more than 21 years were included. Those who were more than 45 years at the time of transplant were excluded. All patients eligible for this analysis were contacted telephonically. The incidence of pregnancy among patients who desired conception was determined.
Results: Hundred and one patients of HL underwent ASCT using LACE regimen between 2007 and 2019. Of these, 64 patients fulfilled the inclusion criteria. Sixteen patients could not be contacted. Among the remaining 48 patients, 17 patients desired conception and 31 did not desire conception. Nine of these 17 patients who desired conception (52.9%) conceived at a median of 6 years post-transplant (1-15 years). The other 8 patients were not able to conceive (figure 1). Patients who failed conception were older at the time of transplant although this difference was not statistically significant. There was no difference in the gender of patients and number of lines of chemotherapy received prior to ASCT between those who conceived and those who failed to conceive following ASCT (table 1).
Discussion and Conclusion: Half of the patients who desired conception were able to conceive following ASCT using LACE regimen. We could not identify factors affecting fertility post ASCT. Fertility rates following LACE conditioning appear to be better than those reported with other conditioning regimens including BEAM and TBI based regimens. Large multi-center dataset is needed to corroborate the findings from this study.

Disclosure of Interest: None Declared

Keywords: Fertility outcomes, Hodgkin lymphoma, LACE regimen

Oral Presentation

LYMPHOMA/MYELOMA (373)

AUTOLOGOUS STEM CELL TRANSPLANTATION FOR MULTIPLE MYELOMA – A SINGLE CENTER EXPERIENCE FROM INDIA

Nihar Desai*[1], Gopinathan M[1], Archit P[1], Ashish Mishra[1], Manoj Singh[1], Madhuri Smith[1], Priyanka Chauhan[1], Manish Singh[1], Sanjeev Yadav[1], Dinesh Chandra[1], Anshul Gupta[1], Naresh Tripathy[1], K Rahman[1], Ruchi Gupta[1], Rajesh Kashyap[1], Soniya Nityanand[1]
[1]Hematology, SGPGIMS, Lucknow, India

Aims & Objectives: Autologous stem cell transplantation (ASCT) remains the standard of care for patients with newly diagnosed multiple myeloma (MM) despite the approval of novel agents. Numerous trials have demonstrated a progression-free survival (PFS) advantage with ASCT.
To study the demographics, clinical profile, and outcomes of patients with MM undergoing ASCT at a tertiary care center in northern India.
Patients / Materials & Methods: This is a medical records review of 29 patients with MM who underwent ASCT between 2007 and 2021. The demographics, clinical profile, induction regimen, details of ASCT, and outcomes were retrieved. Descriptive analysis, Progression Free Survival (PFS), and Overall Survival (OS) were determined. Data are expressed as median and interquartile range (IQR).
Results: The median age of the cohort was 56 years (50-61) and 21 (72%) were males. The follow-up duration from diagnosis was 60 months (18-74). The most common immunoglobulin isotype was IgG kappa (28%) followed by IgG lambda (24%) and IgA kappa (21%). R-ISS staging was available for 26 patients and 21 of 26 (72%) had stage III disease. High-risk cytogenetics were identified in 19 patients (66%). Nine patients (47%) had t(4;14) and four (21%) had deletion 17p. Triplet induction consisting of Bortezomib, dexamethasone, and IMiD was the most common induction regimen (18, 62%). Two patients received quadruplet induction consisting of daratumumab, bortezomib, lenalidomide, and dexamethasone. The median time from diagnosis to transplant was 12 months (8-22). Most patients (24, 79%) were transplanted in first complete remission (CR1). The most common conditioning regimen was high dose melphalan, dosed at 200mg/m2. Nine patients (31%) received a reduced dose of melphalan (140mg/m2) in view of reduced GFR, poor ECOG performance status, secondary amyloidosis, and other co-morbidities. The median stem cell dose was 5.44 x106/kg (4.98-6.01 x 106/kg). The median time to engraftment was 9 days (8-10). Mucositis was the most common complication post ASCT (26, 90%), and grade 3/4 mucositis complicated seven transplants (24%). Three patients (10.3%) died during the post-ASCT neutropenic period secondary to sepsis. Eleven patients (42%) relapsed, and the median duration of remission (PFS) post-ASCT was 34 months (30.5-40.5) (Figure 1). Of those who relapsed, five (45.5%) died of disease progression, one died (9%) of myocardial infarction and five patients (45.5%) were alive at the time of the last follow-up. The OS was 89.7% with the median survival time post-ASCT being 39 months (7-60) (Figure 2).
Discussion and Conclusion: ASCT remains the standard of care for patients with multiple myeloma, especially in lower-middle-income countries where access to second-line therapies is limited.

Disclosure of Interest: None Declared

Keywords: india, Melphalan, Mucositis, Progression-Free Survival, Transplantation, Autologous

Oral Presentation

LYMPHOMA/MYELOMA (386)

OUTCOME OF AUTOLOGOUS STEM CELL TRANSPLANT FOR MULTIPLE MYELOMA -A RETROPROSPECTIVE STUDY.

Mohmad Hussain Mir* [1]
[1]Medical Oncology and HSCT Unit, SKIMS, Srinagar, India

Aims & Objectives: Study the clinical profile and outcome of autologiou stem cell transplant in multiple myeloma patients at our Center.
Patients / Materials & Methods: Hospital based retro-prospective observational study. We analyzed the data of 57 patients of MM who underwent autologious stem cell transplant at SKIMS from December 1st, 2010 up to December 31, 2021.Their clinicalprofile and autologous stem cell transplant outcomes were analysed in a prespeicified proforma.
Results: A total of 57 patients underwent autologious stem cell transplant for multiple myeloma (MM). There were 33 males (57.9 %) and 24 females (42.1 %). Median age was 49.5 years (Range 19-65 years). Majority of patients (n=47;82.4%) had ECOG performance score of 0-2. The IgG type of MM was most common (n=34,59.6%), followed by Ig A type (n=11;19.3%). Half of our patients were in ISS stage III at presentation (n=29; 50.8%) followed by satge II (n=20;35.15) and Stage I (N=8;14.5%). Mean time from induction chemotherapy to autologous stem cell transplant (ASCT) at our Center was 9.9 months (range 4-12 months). CyBorD (Cyclophosphamide,Bortezomib and Dexamethasone) was the commonest induction regimen used in 36 patients (63.15%) followed by VRd (Bortezomib,Lenalidomide and Dexamethasone) regimen in 21 patients (36.75%). Stem cell mobilisation with single agent G-CSF was done in 22 patients and combination of G-CSF and Plerexifor in 35 patients. The median CD34+ cell count infused was 4.90x106/kg body weight (2.5-5.4 x106/kg). Post transplant complete response rates (CR) were 71.92% compared to 49.12% in pretransplant (p value <0.05). There was no transplant related mortality on day +30 and day +100 post transplant. Post transplant Lenalidomide mainatance was used in 94.73% (n=54) and Bortezomib mainatance in 5.27% only (n=3). Median duration of follow up was 81.3 months (range 2.1-121 months). Twenty three patients (40.35%) had progressive disease on last assessment and amongt them sixteen patients (28.1%) had died at last assessment. Most common cause of death was progressive disease (81.5 %{n=13}). Serum albumin (>3.5 g/dl), and ISS Stage I & II were predictors of improved overall survival. However achievement of CR post transplant were predictors of improved PFS and overall survival in this study on multivariate analysis. Median PFS and OS from date of transplant was 68.4 months [95% CI, 56.31-80.51] and 81.3 months [95% CI, 65.8-97.72] with estimated 5 year overall survival rate of 65.5% (figure 1 and figure 2).
Discussion and Conclusion: One of the most important advantages of ASCT in MM is better and deeper response which was reflected in our study. Transplant related mortality was nil in our study.Treatment with novel agents and achievement of complete remission post-transplant, were predictors of long-term survival for patients with Multiple myeloma.

Disclosure of Interest: None Declared

Keywords: Autologous,, Multiple Myeloma,, Novel agents, Stem Cell Transplant,

Oral Presentation

LYMPHOMA/MYELOMA (400)

ESTABLISHING THE FIRST STEM CELL TRANSPLANT PROGRAM IN EAST AFRICA

Sachin Jadhav*[1], Amey Panchal[1]
[1]Haematology, Healthcare global enterprises limited , Bengaluru, India

Aims & Objectives: Due to the significant resources involved in creating an HSCT Programs there is significant disparity in the availability of this treatment modality between the developed and developing countries. This manuscript details the process and the outcomes of the first HSCT Program in East Africa which was started at Muhimbili National Hospital (MNH) in Dar-es-Salaam, Tanzania.
Patients / Materials & Methods: Information and data were collected on the processes which had been implemented for starting the HSCT Program at MNH. The details of the collaborations, training, infrastructure development, acquisition of the biomedical equipment, as well as the actual process for HSCT, as well as the outcomes of treatment are described.
Results: The project has been detailed in 4 stages for ease of description:
Stage 1: Preparatory work which was performed by the Government of Tanzania, as well as the administrators and clinicians from MNH (July 2017-September 2021). Stage 2: Exploratory Gap Analysis by the teams from MNH and International Hematology Consortium of HCG Hospital, India (HCG-IHC) in October 2021. Stage 3: Activities for closure of gaps (November 2021). Stage 4: Stem Cell Transplantation Camps (November 2021 to March 2022).
11 peripheral blood stem cell transplants were done in two camps, November 2021 (5 patients), and February 2022 (6 patients). 10 patients underwent autologous peripheral blood stem cell transplantation for multiple myeloma and 1 for lymphoma. The median duration of hospital stay was 19±6 days. Median time to neutrophil engraftment was on 8.8± 0.8 days and for platelet engraftment was 9.6±2.4 days. Median observation period for survivors was 75.45 days post-transplant (126 days – 33 days). Progression free survival was 100%, and there was no mortality.
Discussion and Conclusion: Commonalities in the socio-economic challenges in developing countries can be leveraged to create robust HSCT Programs in other developing countries.

Disclosure of Interest: None Declared

Keywords: Low socio economic countries, Myeloma, stem cell transplantation

Oral Presentation

GVHD (170)

WITHAFERIN-A PREVENTS ONSET OF ACUTE GRAFT VERSUS HOST DISEASE BY INHIBITING JAK2-STAT3 SIGNALING

Vikram Gota[*1,2], Saurabh K. Gupta[1,2], Dievya Gohil[1,2], Girish C. Panigrahi[1,2], Subhash Yadav[2,3], Rajiv K. Kaushal[2,3], Navin Khattry[2,4]

[1]Clinical Pharmacology, ACTREC-TATA MEMORIAL CENTRE, Navi-Mumbai, [2]Homi Bhabha National Institute, [3]Department of Pathology, TATA MEMORIAL HOSPITAL, Mumbai, [4]Department of Medical Oncology, ACTREC-TATA MEMORIAL CENTRE, Navi-Mumbai, India

Aims & Objectives: Aim: To evaluate the acute GvHD prophylactic potential of oral Withaferi-A (WA) in murine model of alloHSCT and to understand its mechanism of action

Patients / Materials & Methods: A complete mismatch animal model of aGvHD was developed to evaluate the aGvHD prophylactic potential of WA. Recipient BALB/c (H-2Kd) mice were given a myeloablative 6.5 Gy of total body radiation. The irradiated mice were transplanted with 5x106 bone marrow cells and 15x106 spleen cells from donor C57BL/6 (H-2Kb) mice which would result in aGvHD. Following transplantation, the recipient mice were divided into (1) control and (2) WA treatment groups (N=6 each). WA treatment was administered orally for 21 days following transplantation. Furthermore, in a different set of experiment we compared the efficacy of WA with standard prophylactic regimens comprising of cyclosporine and methotrexate (CSA+MTX). Outcomes of GvHD and alloHSCT such as clinical signs/symptoms, survival and donor cell engraftment was monitored periodically. Further, on day +7, +14 and +21 cytokines of the T-cell subset and histopathology of GvHD target organs were evaluated. Next, we evaluated the GvHD prophylactic mechanism of WA by exposing splenic lymphocytes of C57BL/6 mice to WA and quantifying the JAK2-STAT3 signaling using western blot

Results: Oral administration of WA significantly decreased aGvHD associated morbidity including weight loss, diarrhoea, ruffed hair, denuding of skin, lack of activity and hunch back. Survival improved significantly compared to the control [HR=0.07 (0.01-0.35); p=0.013]. Additionally, WA treatment to recipient mice did not compromise donor cell engraftment. Furthermore, WA arm had better overall survival compared to standard prophylactic regimen of CSA+MTX [HR=0.19 (0.03-1.13), p=0.09]. Addition of WA to low dose CSA+MTX had better outcomes in terms of survival and morbidity compared to standard CSA+MTX regimen. WA also decreased the pro-inflammatory cytokine secretion from Th1 (IL-2, IL-6, TNF-α, IFN-γ), Th2 (IL-4, IL-10) and Th17 (IL17A) cells. Histopathological examination of GvHD target organs showed marked protection against GvHD in WA treated animals compared to control. Further, the lymphocyte infilteration to GvHD target organ were found to be decreased in WA group. In-vitro, WA treatment of splenic lymphocytes decreased the protein levels of pJAK2 and pSTAT3 significantly, indicating that WA suppresses JAK2-STAT3 mediated immune cell response and therefore prevents the onset of GvHD.

Discussion and Conclusion: Oral administration of WA prevents aGvHD by inhibiting JAK2-STAT3 signalling. WA as a single agent was superior to CSA+MTX. The efficacy of WA for the prophylaxis of aGvHD should be tested in a prospective clinical trial.

Disclosure of Interest: None Declared

Keywords: acute Graft versus Host Disease, JAK2-STAT3, Trnaplant related mortality, Withaferin-A

Oral Presentation

GVHD (171)

EFFICACY OF ALLOGENIC CORD BLOOD PLATELET GEL ON WOUNDS OF CHRONIC SKIN GVHD PATIENTS AFTER HSCT

Rashin Mohseni[*1], Maryam Behfar[1], Leila Jafari[1], Zahra Karimizadeh[1], Yalda Karamlou[1], Amir Ali Hamidieh[1]
[1]Pediatric Cell and Gene Therapy Research Center, Gene, Cell and Tissue Research Institute, Tehran, Iran

Aims & Objectives: Graft versus host disease (GVHD) is the most common complication following HSCT. The most prevalent form of GVHD, skin GVHD is treated by topical corticosteroids and calcineurin inhibitors (e.g. tacrolimus). Platelet Gel consists of platelet-rich plasma, which has been previously utilized for a variety of purposes especially for ameliorating burns, diabetic foot ulcer, and Epidermolysis bullosa. In this unprecedented study, we aim to assess the efficacy of umbilical cord blood-derived platelet gel on healing wounds resulting from chronic skin GVHD.
Patients / Materials & Methods: In the current prospective study, 6 pediatric patients were enrolled in this experiment with the limited chronic skin GVHD. Each patient had wounds with a surface area between 2-5 cm2, which had lasted for more than 6 weeks. On each patient, the wound on one side was considered as the control, whereas the other was treated. Platelet rich plasma (PRP) was initially procured from human cord blood, then thrombin and calcium were added to form a gel. Prior to intervention, the surface area of each wound- control and treatment- was calculated. Subsequently, PG was applied only on one side, whereas the control wound was only covered with sterile gauze. This process was repeated 6 times every 5 days.
Results: After 6 sessions of treatment, PG-treated wounds had a significantly lower surface area, comparatively. Prior to the first session of the treatment, the experiment and control wounds had an average surface area of 9.319 mm2 (sd=5.956) and 8.059 mm2 (sd=5.931), respectively. The surface area of PG-treated wounds decreased by approximately 2.56 mm2 and 7.819 mm2, on average, after the first and the sixth sessions of treatment, respectively. Notably, in the first and second sessions, the surface area of the PG-treated and control wounds didn't have a marked difference; however, in the following sessions, the PG-treated wounds had significantly lower surface area than the control group (the P-values for the third, fourth, fifth and sixth sessions were 0.023, 0.005, 0.004, and 0.02, respectively). The surface area of the control group decreased by roughly 0.197 mm2 subsequent to the first session; however, an increase in the surface area of the wound occurred in the fifth session (8.787 mm2) and after the final sixth session, the surface area of the wound had an overall increase of about 0.197 mm2, from the first session to the sixth.
Discussion and Conclusion: In this pilot study, application of cord blood- derived platelet gel on chronic skin GVHD wounds, which is one of the major complications following allogeneic HSCT in pediatric patients presented auspicious results by expediting wound-repair, as evident by the comparison between the control and treatment wounds.

Disclosure of Interest: None Declared

Keywords: Chronic Skin GvHD, Cord Blood, Pediatrics, platelet gel, Wound healing

Oral Presentation

GVHD (245)

A PROSPECTIVE STUDY OF ITOLIZUMAB IN INDIAN PATIENTS WITH CHRONIC GRAFT VS HOST DISEASE-AN UPDAT.E

Aditi Shah*[1], Bharath Ram[1], Sharat Damodar[1]
[1]Haematology, Narayana Hrudayalaya, Bangalore, India

Aims & Objectives: Primary objective: To assess the safety profile of Itolizumab in the treatment of chronic GVHD.
Secondary objective: To assess the efficacy of Itolizumab in the treatment of steroid dependent, moderate to severe chronic GVHD.
Patients / Materials & Methods: Nine adult patients with steroid dependant moderate to severe chronic GVHD have been recruited from May 2020 after taking the institutional ethics committee's approval.
The schedule of Itolizumab given is 1.6 mg/kg every 2 weeks for 6 doses followed by every 4 weeks upto 1 year or till resolution of symptoms of GVHD, whichever is sooner.
Response assessment is done before every dose as per the 2014 NIH Consensus Updated Response Criteria.
Results: Nine patients (7 males and 2 females) have received Itolizumab to date. The mean age of the study group is 41.11 years (ranging from 20 to 57 years). Baseline characteristics of the patients are shown in Table: 1.
All patients have responded to Itolizumab after 2 or 3 doses (100% response).
There is a marked improvement in symptoms of GVHD as evaluated by the mean overall patient's self-assessment score which improved from a baseline value of 6.11/10 to a value of 3/10 at the end of last dose and the mean overall clinician's assessment score which improved from a value of 6.22/10 to 3.11/10 respectively. There is objective improvement in the extend and severity of GVHD lesions as assessed based on the NIH GVHD grading, especially evident in patients with oral mucosal GVHD.
Steroid taper was possible in 6 out of 9 patients (66.66%) and it was discontinued in 3 of them (33.33%)
One patient developed cytomegalovirus (CMV) infection, 1 developed bacterial pneumonia, and 1 had an upper respiratory tract infection. Three patients developed transaminitis which resolved after increasing the dosing interval.
GVHD grading, response assessment and adverse events are depicted in table 2:
Discussion and Conclusion: Steroid dependent chronic GVHD leads to long-term morbidity and often the patient is on multiple lines of immunosuppressive therapy.
Itolizumab is a humanized anti-CD6 monoclonal antibody and has shown efficacy in early trials of acute GVHD.
In our prospective study of 9 patients, we have seen 100% response with use of Itolizumab. There was marked symptomatic improvement in all the patients and also these was objective improvement in the GVHD grade especially in patients with oral mucosal GVHD. Steroid taper was possible in 2/3rd of the cases and sustained discontinuation in 1/3rd,
Infections and transaminitis were frequently noted adverse events however, overall, the drug was well tolerated.
According to our study, Itolizumab is both effective and well tolerated in the treatment of chronic GVHD, however larger studies and long term data are required.

Disclosure of Interest: None Declared

Keywords: chronic gvhd, Itolizumab, steroid dependant

Oral Presentation

GVHD (277)

UTILITY OF EGVHD APP FOR BEDSIDE GVHD ASSESSMENT

Deepesh P. Lad*[1], Kripa S. Kasudhan[1], Prashant Chhabra[1], Niranjan Khaire[1], Shaweta Kaundal[1], Madhu Chopra[1], Arihant Jain[1], Gaurav Prakash[1], Alka Khadwal[1], Pankaj Malhotra[1]
[1]Clinical Hematology and Medical Oncology, Postgraduate Institute of Medical Education and Research, Chandigarh, India

Aims & Objectives: In clinical practice, scoring acute and chronic graft versus host disease (GVHD) after allogeneic hematopoietic cell transplantation (allo-HCT) remains challenging and confusing. The EBMT-NIH-CIBMTR task force recommends using the validated eGVHD app to score acute GVHD as per the Mount Sinai Acute GvHD International Consortium (MAGIC) criteria and chronic GvHD as per the NIH 2014 criteria. This study aimed to prospectively score GVHD using the eGVHD app and evaluate discrepancies in scoring without app use.
Patients / Materials & Methods: In this single-center study, the eGVHD app was used prospectively at the bedside to score the severity of GVHD in allo-HCT recipients from 2016-2021. The discrepancy in GVHD scoring without using the app was evaluated retrospectively. We also used the standard terminology for the onset of GVHD and response to therapy.
Results: 100 consecutive allo-HCT recipients were included (male- 70, female-30) with a median age of 23 years (17-39 Years). The median follow-up was 295 days (109-981 days). Underlying diagnoses included hematological malignancies (n=81) and aplastic anemia (n=19). Conditioning was myeloablative in 54, reduced intensity in 46 patients. The source of stem cells was peripheral blood in all recipients. The type of HCT was matched related donor in 57 patients, matched unrelated donor in 9, and haploidentical in 34 patients. Acute GVHD occurred in 43 patients (43%) with onset at a median of 38 days (25-67 days). Onset was classic in 33 (77%), late-onset in 6 (14%) and recurrent in 4 (9%) patients. The GVHD severity using the eGVHD app was MAGIC grade I in 9 (21%), grade II in 10 (23%), grade III in 8 (19%), and grade IV in 16 (37%) patients. There was a discrepancy in scoring the severity in 5 (12%) patients without using the app, with severity being downgraded in 1 and upgraded in 2. Acute GVHD was steroid-responsive in 28 (65%) and steroid-refractory in 15 (35%). Chronic GVHD occurred in 45 patients (45%) with onset at a median of 168 days (117-212 days). The onset was denovo in 20 (44%), quiescent in 21 (47%), and progressive in 4 (9%). The severity was mild in 9 (20%), moderate in 21 (47%), and severe in 15 (33%) patients. There was a discrepancy in scoring chronic GVHD in 17 (38%) patients without the use of the app, with severity being downgraded in 13 (29%) and upgraded in 4 (9%) patients. All patients were steroid-responsive, but 11 (25%) were steroid-dependent.
Discussion and Conclusion: There is more discrepancy in the scoring of chronic GVHD (28%) than acute GVHD (12%) without using the app. The eGVHD app can assist in documenting the GVHD severity at the bedside and improve the quality of data submitted to registry studies. Adding the onset and response definitions to the eGVHD app will be helpful as a single source for all-in-one GVHD assessment.

Disclosure of Interest: None Declared

Keywords: app, GVHD, score

Oral Presentation

GVHD (293)

MICRO-VASCULOPATHY RESULTING FROM ENDOTHELIAL DAMAGE &GVHD IN RECIPIENTS OF ALLOGENEIC TRANSPLANT

Sayan S. Roy[*1], Raghuraman Soundararajan[2], Manphool Singhal[3], Ashok K. Yadav[4], Shefali Sharma[5], Arihant jain[1], Deepesh Lad[1], Alka Khadwal[1], Pankaj Malhotra[1], Gaurav Prakash[1]
[1]Clinical Hematology and Medical Oncology, [2]Radiodiagniosis, [3]Radiodiagnosis, [4]Experimental Medicine, [5]Internal Medicine, PGIMER, Chandigarh, India

Aims & Objectives: Micro-vasculopathy plays an important role in steroid resistant GVHD. To date, the means of assessing endothelial dysfunction are limited. The aim of this study is to investigate non-invasive, real-time assessment of endothelial dysfunction & vasculopathy by using nail fold video capillaroscopy (NFVC), and flow mediated dilation (FMD)
Patients / Materials & Methods: Thirty-five post alloSCT recipients and 24 controls were included. NFVC was performed using Optilia video capillaroscope under 200X magnification. In total 16 images for each participant were analysed according to EULAR criteria for capillary density, diameter, neoangiogenesis, microhaemorrhages, & morphology. Flow-mediated dilatation of the brachial artery was observed using high-resolution ultrasound using the principle of postocclusive reactive hyperaemia and analysed using edge detecting software
Results: AlloSCT recipients had significantly higher mean capillary apical diameter (Mean=20.56 micron) compared to controls (Mean=14.33micron)($p<0.001$). The number of fingers showing dilated capillary was significantly higher in the alloSCT recipients (Mean=3.06) vs. controls (Mean=0.63) $p<0.001$.
Number of fingers showing neoangiogenesis and microhemorrhages were significantly higher in the alloSCT group (Mean=4.09) compared to controls (Mean=0.29)($p<0.001$) and (Mean=1.51) vs. (Mean=0.13)($p=0.02$), respectively.
The median capillary density was significantly lower in the allo SCT recipients (Mean=6.63)compared to controls (Mean=8.38)($p<0.001$).
A higher number of fingers with dilated capillary (Mean=3.83 vs 2.90), neoangiogenesis (Mean=5 vs 3.9) & microhemorrhages (Mean=3 vs 1.21) were found in patients with acute GVHD.
Similarly, compared to patients without cGVHD, patients with cGVHD had higher median capillary diameter (Mean=21.4 vs 19.9 micron) & neoangiogenesis (Mean=4.59 vs 3.53,). Capillary density was less in patients with cGVHD (Mean=6.53 vs 6.65,) compared to patients without cGVHD
(FMD)
The alloSCT cohort had lower values of FMD (Mean=13.98, SD±12.92) than the healthy controls (Mean=17.18, SD=8.8) but this difference was not significantly different ($p=0.2$). Patients with cGVHD had lower FMD (Mean=10.83,SD,Median=10.58) compared to patients without cGVHD (Mean=17.49,SD=,Median=11.81,Range).($p=0.16$)
Discussion and Conclusion: Our observation that micro-vascular structural abnormalities noted via nail-fold capillaroscopy were significantly altered in alloSCT recipients with GVHD in comparison to patients without GVHD & healthy controls.
These microvascular structural abnormalities can be assessed in-vivo, in real time, non-invasively by NFVC. Result from our study indicates presence of structural micro vasculopathy in the post alloSCT setting, and NFVC holds promise as research as well as clinical tool in this setting.

Disclosure of Interest: None Declared

Keywords: Dysfunction, Endothelial, GVHD, vasculopathy

Oral Presentation

GVHD (303)

GENITAL GRAFT VERSUS HOST DISEASE IN CHILDREN – AN UNDERDIAGNOSED AND UNDERTREATED ENTITY.

Sohini Chakraborty*[1], Kavitha Ganesan[1], Suresh R Duraisamy[1], Satish K. Meena[1], Vigneswar Venkatesan[1], Venkateswaran V. Swaminathan[1], Ramya Uppuluri[1], Revathi Raj[1]
[1]Paediatric Haematolog y, oncology and Blood and Marrow Transplantation, Apollo Cancer Centre, chennai, India

Aims & Objectives: Chronic graft versus host disease (GVHD) causes significant morbidity and mortality in children undergoing hematopoietic stem cell transplantation (HSCT). Genital graft-versus-host disease (GVHD) is an underdiagnosed and poorly recognized complication, especially in the paediatric population. We describe here, our case series of children with genital manifestations of GVHD and their unique clinical features.
Patients / Materials & Methods: The study included children up to 18 years of age who underwent HSCT. Data was collected retrospectively from review of patient charts over a twenty-year period from February 2002 to February 2022. The presence of chronic oral GVHD served as a marker to the presence of genital GVHD. Genital GVHD presented as phimosis in male children and urethritis in female children. The number of children needing circumcision was documented. We collected data on the impact of the age of the child at HSCT, the indication including malignant or non-malignant disorder, the source of stem cells the presence of HY mismatch and association with mouth GVHD.
Results: A total of 1035 children underwent HSCT in the study period. Genital GVHD was documented in 164 (15.8%) children. Among the 164 children, 23 (14%) belonged to age group < 2 years, 98 (59.8%) to 2-10 years and 43 (26.2%) children were more than 10 years of age. One hundred three (62.8%) were male children, while female children were 61 (37.2%). The underlying diagnosis was hemoglobinopathies in 72 (43.9%), malignancies in 42 (25.6%), inborn error of immunity 16 (9.8%), 12 (7.3%) had inherited bone marrow failure syndromes, and 22 (13.4%) had other diagnoses. Conditioning regimen was myeloablative in 122 (74.4%) and 42 (25.6%) children received RIC regimen. Donor type was matched family donor 62 (37.8%), matched unrelated donor in 44 (26.8%) and 34 (20.7%) underwent haploidentical HSCT. Peripheral blood stem cells were used in 129 (78.7%) children. HY mismatch was noted in 51 children (31.1%). Chronic mouth GVHD was noted in all the 164 children. On further analysis, overall incidence of chronic mouth GVHD was 342 (33%), and 47.9% of these had genital GVHD. Twenty-two (21.5%) male children underwent circumcision for phimosis secondary to GVHD. One female child had haematocolpos requiring surgical management.
Discussion and Conclusion: Our case series highlights the significant association between chronic oral and genital GVHD. It is imperative to examine the genital area in all children on follow up for chronic GVHD as the association between mouth and genital GVHD rate is high and undertreated in children. HY mismatch and the use of PBSC as a stem cell source predispose to chronic genital GVHD. Early interventions in the form of topical steroids and tacrolimus helps prevent scarring and complications like phimosis.

Disclosure of Interest: None Declared

Keywords: CHILDREN, genital GVHD, HSCT

Oral Presentation

GVHD (347)

INCIDENCE, RISK FACTORS AND OUTCOME OF CHRONIC GVHD IN CHILDREN UNDERGOING HAPLO-HSCT WITH PTCY

Sunisha Arora*[1], Dhwanee Thakkar[1], Upasana K[1], Anjali Yadav[1], Neha Rastogi[1], Satya Prakash Yadav[1]
[1]Pediatric Hematology Oncology and BMT, Medanta Hospital, Gurgaon, India

Aims & Objectives: Chronic graft vs host disease (cGVHD) is a major cause of morbidity and sometimes mortality post haploidentical hematopoietic stem cell transplant (HSCT). However, there is paucity of literature describing cGVHD in children. Here, we describe the incidence, risk factors, characteristics and effects on outcome of cGVHD in children post Haploidentical HSCT using post-transplant cyclophosphamide (PTCy).
Patients / Materials & Methods: Total of 51 pediatric patients who underwent 1st Haplo-HSCT with PTCy between January 2016-December 2021 at our centre and survived beyond 100 days post-transplant were included in this retrospective study. Conditioning regimens used were: Thiotepa-Fludarabine-Cyclophosphamide with 2Gy single fraction TBI, Thiotepa-Busulfan-Fludarabine, Fludarabine-TBI and Fludarabine-Melphalan. Peripheral blood was used as stem cell source in all patients. GVHD prophylaxis was PTCy 50mg/kg on day +3 and +4, Mycophenolate mofetil (MMF) and Calcineurin inhibitors (CNI). Impact of various patient, donor and transplant related factors on development of cGVHD were analysed. Incidence of relapse, Event Free Survival (EFS) and Overall Survival (OS) were calculated and compared between cGVHD and no cGVHD groups.
Results: Median age of transplant of our cohort was 7.5 years with M:F = 1.6:1. Forty three out of 51 patients (84.3%) engrafted. Incidence of total cGVHD and mild, moderate & severe cGVHD were 44.2%, 20.9%, 13.9% and 9.3% respectively. Of the patients diagnosed with cGVHD, 10/19 (52.6%) had history of aGVHD. Skin was the most common organ involved (100%) followed by gastrointestinal tract (GIT) (47.4%), liver (36.8%), eyes (21%), lungs (21%), mouth (15.7%) and joints (5.2%). None of the patients had involvement of genitals. Advanced donor age (>30 years) and previous aGVHD were found to be significantly associated with increased risk of developing cGVHD. At last follow up with us, complete and partial remission of cGVHD was seen in 31.5% and 21.1% patients respectively. EFS and OS of full cohort was 58.6% and 70.6% respectively. Compared to patients without cGVHD, patients with cGVHD demonstrated a lower relapse (18.2% vs 40%, p=0.2333), better EFS (68.4% vs 53.1%, p=0.283) and OS (73.7% vs 68.8%, p=0.708). However, these differences were not found to be statistically significant.
Discussion and Conclusion: Incidence of cGVHD post PTCy based Haplo-HSCT is higher in our cohort when compared to other similar studies possibly due to use of peripheral blood as stem cell source and early withdrawal of immunosuppression in malignant conditions. Donor age and previous aGVHD are the risks factors for development of cGVHD. Children with cGVHD have lower incidence of relapse translating into better survival outcomes but this difference was found to be statistically non-significant.

Disclosure of Interest: None Declared

Keywords: chronic gvhd, Haploidentical transplants, pediatrics, PTCy

Oral Presentation

GVHD (359)

FECAL SHORT-CHAIN FATTY ACIDS AS BIOMARKER OF ACUTE GRAFT VERSUS HOST DISEASE

Shaweta Kaundal[*1], Lekshmon K S[1], Amol Patil[2], Amit Arora[3], Ashwin Nair[1], Kripa Kasudhan[1], Madhu Chopra[1], Charanpreet Singh[1], Aditya Jandial[1], Arijant Jain[1], Gaurav Prakash[1], Alka Khadwal[1], Pankaj Malhotra[1], Deepesh Lad[1]
[1]Department of Clinical Hematology and Medical Oncology, [2]Department of Clinical Pharmacology, [3]Medical Microbiology, Postgraduate Institute of Medical Education and Research, Chandigarh, India

Aims & Objectives: The gut microbiome (GM) plays an important role in Hematopoietic cell Transplant (HCT) outcomes specifically graft versus host disease (GVHD) and overall survival. There is data to show that GM is influenced by broad-spectrum antibiotics and dietary fibers and resistant starch which are food for colonic bacteria. Short-Chain Fatty Acids (SCFAs) which are a byproduct of GM metabolism, are involved in gut mucosal homeostasis. There is evolving data that SCFA are biomarkers of GM diversity and GVHD outcomes. In this study, we explored the association of dietary fiber and resistant starch with fecal SCFA levels and acute GVHD outcomes.
Patients / Materials & Methods: In this single-center prospective study, consecutive allo-HCT recipients aged ≥ 12 years were included from July 2020- June 2022. Baseline demographic, disease and HCT details were recorded along with a detailed diet diary and antibiotic exposures. Serial (pre-HCT, week 2, and week 4 post-HCT) fecal SCFAs (Acetate, Propionate, and Butyrate) were measured using Liquid-chromatography Mass Spectrometry/Mass spectrometry (LC-MS/MS). Dietary fiber and resistant starch were calculated using the ICMR Nutrify India app. Acute GVHD was graded as per the MAGIC criteria. The baseline characteristics and dietary and fecal SCFA were compared among patients who had Grade II-IV acute GVHD and those without, using chi-square and t-tests.
Results: A total of 25 patient data is included in this analysis. Grade II-IV acute GVHD occurred in 12 (48%) of patients at a median of 33 days (20-100). Patients with and without Grade II-IV acute GVHD were matched for age, gender, diagnosis, type of HCT, conditioning regimen, and GVHD prophylaxis (Table 1). The two groups were also matched for dietary fiber and resistant starch intake, total parenteral nutrition, and carbapenem/ colistin exposures. Both groups also had matched fecal acetate, propionate, and butyrate levels pre-HCT (Table 1). However, patients who had acute GVHD had significantly lower butyrate levels at week 2 (0.19± 0.23 vs. 0.71± 0.70, p = 0.026) and week 4 (0.30± 0.3 vs. 1.2± 0.8, p=0.003) post-HCT, respectively. The week 4 fecal propionate levels were also significantly lower in patients with acute GVHD (p = 0.01).
Discussion and Conclusion: Fecal butyrate levels are associated with the occurrence of grade II-IV acute GVHD. Week 2 and 4 butyrate levels can be used as biomarkers to predict acute GVHD. This may be used for planning dietary intervention studies to ameliorate GVHD. This study is ongoing to look at the association of dietary fiber and resistant starch with GM diversity and SCFA levels in HCT outcomes in a larger sample size.

Disclosure of Interest: None Declared

Keywords: GVHD, HCT, LC-MS/MS, SCFAs

Oral Presentation

GVHD (396)

OUTCOMES OF RUXOLITINIB USE IN STEROID REFRACTORY ACUTE GVHD: A SINGLE CENTRE EXPERIENCE FROM INDIA

Urmimala Bhattacharjee[*1,2], Ketan Modak[2], Poojitha Byreddy[2], Pavitra DS[2], Manasi Gupta[2], Vijay Chaudhary[2], M Joseph John[2]
[1]Department of Clinical Haematology, Haemato-oncology, Bone marrow (stem cell) transplantation, [2]Clinical Haematology, Haemato-oncology and Bone marrow (stem cell) transplantation, CMC Ludhiana, Ludhiana, India

Aims & Objectives: To analyse and compare the clinical profile, complications and outcomes of steroid-refractory acute GVHD patients before and after the introduction of ruxolitinib use as second line option (year 2018) in our institution.
Patients / Materials & Methods: This retrospective analysis included all allogeneic hematopoietic stem cell transplant (allo-HSCT) patients from our center between January 2009 till June 2022. The treatment records of all eligible patients were reviewed. Acute GVHD, SR-aGVHD and response evaluations were defined as per previously published criteria. Complete response (CR) was defined as the resolution of all symptoms and manifestations of acute GVHD. Partial response (PR) was defined as an improvement of one or more organs without deterioration in other organs. No response (NR) was defined as no improvement, mixed response or disease deterioration.
Results: One hundred and sixty eight allogeneic HSCTs were conducted in our center in the study period. The median age of the patients was 17 years (range 1-64 years). The basic disease for undergoing transplant was β thalassemia major in 90 (53.6 %) patients. Total 63 (37.5 %) patients had aGVHD- of which 44 patients (26.1 %) had classic aGVHD, 5 (2.9 %) patients had late onset and 11 patients (6.5 %) had persistent aGVHD. Nineteen (30.2 %) patients had SR-aGVHD. The median overall survival of SR-aGVHD patients was 13 months (95% CI=8-17 months), whereas it was not reached in non-steroid refractory group (p=0.010) (Figure 1). Table 1 highlights the baseline characteristics of all allo-transplant patients from our center.
The clinical features, treatment, complications and outcomes of SR-aGVHD patients are mentioned in table 2. In the pre-ruxolitinib era, etanercept (8 patients, 72.7%) and cyclophosphamide (3 patients, 27.2%) were the main second line options used. Day 28 overall response rate (ORR) in pre-ruxolitinib era (before 2018) was 36.4 % (CR 18.2 % and PR 18.2 %), whereas with ruxolitinib the day 28 ORR was 62.5 % (all CR), p=0.124. The median time to best response (CR/PR) in pre-ruxolitinib era was 55 days (range 35-223 days) while it was 19 days (range 5-64 days) for ruxolitinib. Majority of deaths in pre-ruxolitinib era (72.7 %) were due to refractory aGVHD, the one death in ruxolitinib cohort was due to baseline disease relapse. Figure 2 shows the survival curves of SR-aGVHD patients with and without the use of ruxolitinib as second line option.
Discussion and Conclusion: Use of ruxolitinib as second line option in SR-GVHD has been associated with greater day 28 CR rates and trend towards better overall survival.

Disclosure of Interest: None Declared

Keywords: Acute graft versus host disease, Ruxolitinib, Steroid refractory acute graft versus host disease

Oral Presentation

INFECTIONS (302)

CYTOMEGALOVIRUS REACTIVATION AS A RISK FACTOR FOR MORTALITY IN HEMATOPOIETIC STEM CELL TRANSPLANT

Sohini Chakraborty*[1], Kavitha Ganesan[1], Suresh R Duraisamy[1], Satish K. Meena[1], Vigneswar Venkatesan[1], Venkateswaran V. Swaminathan[1], Ramya Uppuluri[1], Revathi Raj[1]
[1]Paediatric Haematolog y, oncology and Blood and Marrow Transplantation, Apollo Cancer Centre, chennai, India

Aims & Objectives: Cytomegalovirus (CMV) reactivation predisposes to an increased risk of morbidity and mortality post haematopoietic stem cell transplant (HSCT). The aim of the study was to analyse the burden of CMV reactivation in children undergoing HSCT at our centre and its correlation with all cause mortality.
Patients / Materials & Methods: We performed a retrospective study in children who underwent allogeneic HSCT between February 2002 to December 2021 in our center. Data was analysed on the incidence of CMV reactivation and its impact on all cause mortality and overall survival.
Results: A total of 1035 patients were included in the study group comprising of 647 males and 388 females (M:F ratio 1.66:1) with a median age of 6 years. Five hundred forty-three (52.4%) patients underwent MFD HSCT, 213 (20.5%) underwent MUD HSCT while remaining 279 (26.9%) underwent haploidentical HSCT (T cell replete in 213 and T cell depleted in 66 patients). CMV reactivation was documented in 258 (24.9% patients). CMV was seen in 39 (7.2%) MFD, 77 (36.1%) MUD, 106 T cell replete (49.7%) and 36 T cell depleted (54.5%) transplants (p value = 0.0001).
There was a total of 255 deaths in the study group (24.6%). However, the overall mortality rate was significantly higher in the CMV positive group (103/258), as compared to the CMV negative group (152/777) (39.9% versus 19.6%, p value = 0.0001). CMV was the direct cause of death in 13/1035 children (1.2%). Among the 13 children who died of CMV, underlying diagnosis was inborn errors of immunity (IEIs) in 9 (69%) children, and two each with malignancies and aplastic anaemia. GVHD as a cause of death was found to be significantly higher among those with CMV (n=32) as compared to those without CMV (n=14) (35.6% versus 9%, p value = 0.0001). The mean survival time was 13.7 years (range 13.1 – 14.4) in the CMV negative group, versus 9.2 years (range 7.5 – 11) in the CMV positive group (p value = 0.0001).
Discussion and Conclusion: Although 95% of the Indian population is known to be positive for CMV, we documented CMV reactivation only in 25% of HSCT recipients with a high proportion of haploidentical HSCT recipients. CMV was the direct cause of death in only 1.2% of the cohort, with IEIs being the predominant underlying disorder. CMV reactivation was shown to significantly impact all cause mortality and there was a significantly increased risk of mortality due to GVHD among those with CMV reactivation. Data from our study highlights the importance of regular surveillance and early initiation of pre-emptive therapy for CMV and possibly consider prophylaxis especially in children undergoing haploidentical HSCT

Disclosure of Interest: None Declared

Keywords: CMV, HSCT, mortality

Oral Presentation

INFECTIONS (336)

IMPROVED ALLOGENIC TRANSPLANT OUTCOMES FOLLOWING IMPLEMENTATION OF ANTIMICROBIAL STEWARDSHIP PROGRAM

Rashmi Yawalkar*[1], Merlin Moni[2], Rema G[1], Chitresh Yadav[1], Anjusha C[1], Somasundharam K[1], Manoj Unni[1], Nikhil Krishna Haridas[1], Neeraj Sidharthan[1]
[1]Clinical Haematology, [2]Infectious Diseases, Amrita Institute of Medical Sciences, Kochi, India

Aims & Objectives:
Aim
To determine impact of implementation of multidisciplinary antimicrobial stewardship program on the clinical outcomes of patients undergoing HSCT from our tertiary care centre
Objectives
1. To determine the mean 100 days overall survival of pre and post Antimicrobial Stewardship Program
2. To compare incidence of febrile neutropenia, documented infection, use of reserve antibiotics and duration of hospital stay in both cohorts
Patients / Materials & Methods: A retrospectively collected clinical and microbiological data of the 5 bedded blood and marrow transplant unit obtained from electronic medical records was analysed. Institutional multidisciplinary ASP program tailored to HSCT was implemented in January 2020. A comparison of outcomes between patients transplanted during January 2013 to December 2018 (Cohort 1) and during January 2020 to May 2022 (Cohort 2) was performed. Patients who underwent autologous transplant were excluded from the study. The difference in supportive care between the two cohorts was the introduction of antibiotic prophylaxis, ASPs and early granulocyte transfusion during neutropenia along with exclusion of neutropenic diet in Cohort 2. Prospective audit and feedback of all reserve antimicrobial prescriptions as per WHO AWaRe classification was done and appropriateness of prescriptions were assessed by clinical pharmacist driven stewardship team and in relevant cases bedside Infectious disease consultations were initiated.
Results: Out of 92 enrolled patients, 57 belonged to cohort 1and 35 patients to cohort 2. The demographics of both cohorts were comparable across most variables (table 1). There was statistically significant reduction in incidence of febrile neutropenia (100% to 82.9%, p=0.005) and documented infections (71.9% to 45.7% p=0.012) in the post ASP intervention cohort. The reduction in cohort 2 of blood stream infections (BSI) (36.8% to 31.4%, p-0.597), use of reserve antibiotics (91.2% to 82.9%;p-0.230) as well as Carbapenem (93% to 88.6%,p-0.47) did not reach statistical significance. However, there was statistical reduction in duration of hospital stay (Median 39 to 51,p-0.010). The mean 100 day overall survival was better in cohort 2 (94±4 % vs 88.03±3 %; p-0.019) and is demonstrated in the Kaplan Meier curve in figure 1.
Discussion and Conclusion: Retrospective pre post analysis of implementation of multidisciplinary ASPs revealed significant improvement in outcomes which includes incidence of febrile neutropenia, duration of hospital stay and mean 100 days survival. Additional predictive factors for 100 days survival included Fludarabine and Treosulphan based conditioning regimen.

Disclosure of Interest: None Declared

Keywords: Antimicrobial stewardship programs, Blood stream infections, Haematopoietic stem cell transplant

Oral Presentation

INFECTIONS (405)

SAFETY AND EFFICACY OF GRANULOCYTE TRANSFUSIONS DURING HEMATOPOIETIC STEM CELL TRANSPLANT

Rasmi Palassery*[1], Parikshit Jayaprakash[1], Deepa D[2], Santhosh K. Devadas[1]
[1]Medical Oncology, [2]Transfusion Medicine, Ramaiah Medical College, Bengaluru, India

Aims & Objectives: Bacterial infections are a major cause of mortality in hematopoietic stem cell transplant (HSCT) recipients, especially in areas with a high Carbapenem-resistant Enterobacteriaceae (CRE) carriage rate among the patient population. Granulocyte transfusions (GTX) have been used to treat infections during febrile neutropenia with mixed results. Our aim was to study the safety and efficacy of GTX in the patients who underwent HSCT in our center.
Patients / Materials & Methods: The details of patients who underwent HSCT from April 2017 to May 2022 and received GTX during the HSCT were collected retrospectively. The changes in the absolute neutrophil count (ANC) and C-reactive protein (CRP) before the 1st GTX to 24, 48 and 72 hours after the last GTX were compared using SPSS v18 software. Repeated measures of ANC and CRP were compared using Friedman test and combinations of repeated measures using Wilcoxon signed rank test.
Results: A total of 37 GTX were administered to 19 patients during the study period (table 1). All patients were on >/= 3 parenteral antibiotics and >/= 1 antifungal agents prior to GTX. The mean GTX dose was 2.97 (±1.47)x108/kg. There were no infusion reactions. Fifteen (78.94%) patients responded to GTX with resolution of the index infection and survived for >30 days post-HSCT. Out of the 4 (21.05%) who didn't survive, 3 died of progressive infection and septic shock while the fourth patient engrafted, but succumbed to hemophagocytic lymphohistiocytosis (HLH). The average number of days to fever resolution, first negative blood culture and stopping of therapeutic antimicrobials were 3.5 (±3.5), 6.1 (±2.2) and 8.5 (±3.1) days. The rise in ANC (p=0.00) and the fall in CRP (p=0.034) from pre-GTX to 24, 48 and 72 hours post-GTX were statistically significant in the data sets available from 17 patients. The median values, comparisons between the combinations of repeated measures and the statistical significance are shown in table 2. The rise in ANC was significant when compared between pre- and 24, 48 and 72 hours post GTX values. The fall in CRP was delayed in comparison and was significant starting from 48 hours after the GTX.
Discussion and Conclusion: GTX transfusions are safe, increase the ANC and reduce the inflammatory markers in HSCT patients with infections during febrile neutropenia. They can be useful especially in resource limited settings where multidrug resistant gram negative bacterial infections are prevalent.

Disclosure of Interest: None Declared

Keywords: Bacterial infection, Granulocyte transfusion, Neutropenia

Oral Presentation

CONDITIONING REGIMENS (142)

TREOSULPHAN IMPROVES THE OUTCOMES IN ALLOGENIC STEM CELL TRANSPLANTAION FOR AML AND MDS PATIENTS

Chitresh Yadav*[1], Nikhil K. Haridas[1], Mobin Paul[2], Manoj Unni[1], Rema Ganapathy[1], Rashmi Yawalkar[1], Priyadarshini V[3], Renjitha Bhaskaran[3], Neeraj Sidharthan[1]
[1]Clinical Haematology, Amrita institute of Medical Sciences, [2]Clinical Haematology, Rajagiri Hospital, [3]Amrita institute of Medical Sciences, kochi, India

Aims & Objectives: AIM: To evaluate the safety and efficacy of conditioning with Treosulfan plus Fludarabine based regimen compared with Busulfan plus Fludarabine based regimen in AML and MDS patient.
Objective: To Compare immediate the immediate and long-term outcomes between the two-conditioning regimens post allogenic HSCT
Patients / Materials & Methods: A retrospective analysis of data collected from two centers between May 2014 to May 2022 of 43 patients with AML or MDS which underwent Allogenic HSCT, 22 cases received I.V Busulfan from 2014 till 2019 and 21 cases received I.V Treosulphan (10-14g/m2) from 2019 till 2022, Both groups received 30 mg/m2 I.V fludarabine for 5 days, Stem cell source was peripheral blood in all cases, Prophylaxis for Graft vs host disease (GVHD) consisted of calcineurin inhibitor (CNI) plus Methotrexate or mycophenolate mofetil (MMF) in Matched sibling donor. ATG (2.5-5 mg/kg)/ post-transplant cyclophosphamide (PTCy) was used for Matched unrelated donor. Haplo transplant patients received PTCy/ATG with CNI and MMF. Comorbidities were scored according to the HCT-CI. Neutrophil and platelet engraftment were defined as per standard criteria. Early toxicity after HSCT was graded according to CTCAE version 5. Acute GVHD and chronic GVHD were recorded according to standard criteria. Between the two cohort's toxicities in various arms were compared by Chi-square test or Fisher exact test, while OS was calculated by Kaplan Meier method and the survival probabilities were compared using log-rank test.
Results: Patients characteristic's and demographic variables as enumerated in table 1 were comparable across both the groups. FluTreo group had significant reduction in documented infections (28.6% compared to 63.7%, p=0.03), Reduced blood stream infections (28.6% compared to 54.5%, p=0.02), decrease incidences acute GVHD all grades (28.6% compared to 68.2%, p-0.01), as well as acute GVHD grade 2 and above (28% compared to 68.1 %, p=0.01), decrease all-cause proportional mortality (14.3% compared to 59%, p=0.004), the mean hospital stay was only 29 days as compared to FluBu group of 50 days (P=0.02)(table 2), The mean overall survival is 581±60 days with survival probability of 70±7% Vs 50%± 10% in FluBu group, p-0.14 (Figure 1)
Discussion and Conclusion: Treosulphan based regimen showed improved outcomes in terms of infection rates, decreased mortality, acute GVHD and hospital stay however study being limited by Retrospective design, small sample size, conditioning regimens being tried in two different time periods with availiabity of better supportive care in recent years, with shorter follow up in Treosulphan group. Since the Treosulphan based conditioning outcome results are still emerging in southeast asian countries this guiding the development of larger future prospective studies for confirming the findings.

Disclosure of Interest: None Declared

Keywords: Acute Myeloid Leukaemia (AML), Allogeneic hematopoietic stem cell transplantation (HSCT), Fludrabine+ Treosulphan (FluTreo), Fludrabine+Busulphan (FluBu), Myelodysplastic Syndrome (MDS)

Oral Presentation

CONDITIONING REGIMENS (174)

THE OUTCOME OF HSCT IN PEDIATRIC PATIENTS WITH NON-SCID PID USING RIC REGIMENS

Leila Jafari*[1], Maryam Behfar[1], Rashin Mohseni[1], Yalda Karamlou[1], Azam Rahmani[1], Fahimeh Jafari[1], Elahe Maki[1], Zeinab Nikfetrat[1], Amir Ali Hamidieh[1]
[1]Pediatric Cell and Gene Therapy Research Center, Gene, Cell and Tissue Research Institute, Tehran, Iran

Aims & Objectives: Primary immunodeficiencies (PIDs) are a diverse group of inherited immune disorders characterized by impaired immunity system, resulting in high susceptibility to infection and lethal complications in the first years of the patient's life. Hematopoietic stem cell transplantation (HSCT) is the only curative treatment for the majority of PIDs.
Reduced-intensity conditioning (RIC) is an alternative choice for PID patients; however, as a drawback, mixed chimerism (MC) and graft failure occur comparatively higher while using this regimen. In this study, we aimed to report the results of RIC regimen before HSCT in pediatric patients with non-SCID PIDs at the largest Children's Medical Hospital in Iran.
Patients / Materials & Methods: In this retrospective study, 82 pediatric patients (50 males, 32 female), who underwent HSCT between 2017 and 2021 were enrolled. The median age of patients was 7 years old (range: 2-16 years).
Whole Genome Sequencing and immunological tests were performed to corroborate the diagnosis of all patients.
47 (57.3%) of donors were identical siblings, 20 (24.4%) were other related and the rest (n=15, 18.2%) were unrelated donors.
The graft source of 80 patients (97%) was peripheral blood stem cells. Most patients (n=62,75.6%) received transplant from a full-match donor and the others had one-locus-mismatch donors.All patients received the same RIC regimen based on fludarabine, in combination with melphalan and rabbit antithymocyte globulin (ATG). Cyclosporine and methylprednisolone were used as a Graft-vs.-host-disease prophylaxis. The median doses of CD34+ and CD3+ cells were 5.9×106/kg and 245×106/kg, respectively.
Results: On average, day 15 and 17 post-transplantation was when neutrophil and platelet engraftment ensued, respectively. Amongst all patients, only 22% (n=18) had mixed chimerism and two patients experienced graft failure. 17 patients (21%) experienced acute GvHD; which consisted of 7 cases of grade I-II GVHD and 10 cases of grade III-IV GVHD. Additionally, 8 patients (10%) manifested symptoms of limited chronic GVHD. The 3-year overall survival (OS) and disease free survival (DFS) rate was 70% and 65%, respectively. The leading cause of death in all cases were acute GVHD and infection, respectively.
Discussion and Conclusion: The results of this study delineate that Fludarabine-based RIC regimen, despite being notorious for low chimerism rates and graft failure, is associated with acceptable chimerism rate, lower toxicity and higher OS in comparison to myeloablative conditioning regimen, making it an ideal choice for treating PID patients especially in developing countries, patients are not only referred late for HSCT or have a history of multiple infections prior to HSCT.

Disclosure of Interest: None Declared

Keywords: HSCT, Peditric, PID, RIC

Oral Presentation

CONDITIONING REGIMENS (409)

EXPERIENCE WITH CYTOKINE-BASED REGIMENS IN THE SETTING OF AUTOLOGOUS STEM CELL TRANSPLANTATION

Sushil Selvarajan*[1], Uday Kulkarni[1], Sharon Lionel[1], Fouzia Aboobacker[1], Anu Korula[1], Aby Abraham[1], Alok Srivastava[1], Vikram Mathews[1], Biju George[1]
[1]Department of Clinical Haematology, Christian Medical College, Vellore, Vellore, India

Aims & Objectives: Since early 2020 due to the COVID-19 pandemic, transplant units across the globe have had to rethink treatment protocols in view of a crisis in critical care backup, blood bank shortages and COVID-19 itself complicating the course of transplants. In light of these constraints, the department of Haematology, Christian Medical College, Vellore made many adjustments of which one of the important measures was to modify autologous stem cell transplantation(ASCT) protocols to include a cytokine-based regimen, targeting rapid engraftment and decreased transfusion requirements.
Patients / Materials & Methods: Based on various seminal publications in this field we designed a regimen containing erythropoiesis stimulating agents(ESA) + Parenteral Iron, Granulocyte-Colony Stimulating Factor(G-CSF) and Thrombopoietin analogues (See Figure). We describe our experience with this regimen and compare it with a large set of ASCT controls from immediately prior to the pandemic.
Results: From April 2020 till December 2021, 131 consecutive patients underwent ASCTs – all incorporating the cytokine-based regimen. 131 consecutive controls from the preceding months were chosen. Important baseline characteristics of these 2 groups are listed below(Table 1).
Importantly, transplant related mortality(TRM) appeared no different between the 2 groups; 7 Vs 6 deaths in those receiving cytokine-based regimens and control patients respectively, despite the raging pandemic ongoing. Improvements in time to neutrophil engraftment and packed cell transfusions required were noted in those receiving the cytokine-based regimen.
There was no documented increase in ICU admissions, or any life-threatening toxicity attributable to the use of aforementioned regimen. However, significantly higher rates of peri-engraftment diarrhoeal symptoms were noted in those given cytokines[72(67%) Vs 35(33%), p<0.001].
Transplant costs for ASCT at our institution in these two periods showed no meaningful difference - mean transplant admission cost with cytokine-based regimen was INR 791,864/- while mean cost in the control group was INR 753,630/-.
Discussion and Conclusion: Despite the extenuating circumstances brought about by the pandemic no significant increase in TRM was noted in ASCT setting. The use of a cytokine-based regimen in the post-transplant management of ASCT, was well tolerated and showed improvements in time to engraftment and transfusions required. The only significant treatment related toxicity appeared to be an increase in peri-transplant diarrhoeal symptoms, in comparison to controls. Cost differences between the two groups were not striking.
Overall, this large retrospective case-control study, describes our experience using cytokine-based regimens and highlights its role in our successful continuation of safe & cost-effective ASCT.

Disclosure of Interest: None Declared

Keywords: Autologous Stem Cell Transplantation(ASCT), COVID-19, Cytokines, Engraftment

Oral Presentation

BONE MARROW FAILURE SYNDROMES INCLUDING MDS. (162)

BONE MARROW TRANSPLANTATION IN PEDIATRIC INHERITED BONE MARROW FAILURE SYNDROMES: OUR EXPERIENCE

Gayathri S*[1], Shobha Badiger[2], Pooja Mallya[3], Ravi Joshi[4], Santosh Asangi[3], Shweta Pathak[3], Swathi P M[3], Monika Bhukar[5], Manojit Chakraborthy[3], Lakshmi T[5], Ritu Lamichhane[5], Kamini Kanagasabesan[3], Sunil Bhat[3]
[1]Pediatric Hemato- Oncology And Bone Marrow Transplant Unit, [2]Pediatric Hemato-Oncology And Oncology And Bone Marrow Transplant Unit, [3]Pediatric Hemato-Oncology And Bone Marrow Transplant Unit, [4]Pediatric Hemato-Oncology And Bone Marrow Transplant Unit, [5]Pediatric Hemato- Oncology And Bone Marrow Transplant Unit, Mazumdar Shaw Medical Centre, Bangalore, India

Aims & Objectives: Inherited bone marrow failure syndromes (IBMFS) are a relatively rare disorders characterized by abnormal haematopoiesis presenting with significant cytopenia usually in association with one or more somatic abnormality. Hematopoietic Stem Cell Transplantation (HSCT) remains the only curative option for haematological complications among these patients. This study was aimed to assess the outcome of Allogeneic HSCT in IBMFS at our center.
Patients / Materials & Methods: We retrospectively analysed the data of 34 children with IBMFS who underwent HSCT at our centre between Jan 2013 to October 2021.
Results: Out of the 34 IBMFS cases majority of cases were Fanconi Anaemia(FA) with 55.8% followed by Congenital Neutropenia(SCN) with 12%(table 1)Majority of the patients were male (61.7%) . Mean age at transplant was 79.29 months (7-235). Donor was Matched Sibling (MSD) in 23.5%, Matched Related (MRD) in 20.8% , Matched unrelated (MUD) in 11.7% and Haploidentical in 50% of cases. Fanconi anemia(FA) , congenital amegakarycytic thrombocytopenia (CAMT)and Dyskeratosis Congenita(DKC) patient subgroups received reduced intensity conditioning regimen, while others received a myeloablative conditioning regimen. Peripheral blood was used as stem cells source in majority(73.5%) . Mean CD 34 cell dose in bone marrow was 11.26 million cells/kg and in PBSC it was 5.48 million cells/kg. Neutrophil engraftment was seen in 31 (91%). Median neutrophil and platelet engraftment noted at day +12 (range day7-16) and day +13 (range day 8-23) respectively. Acute Graft versus Host Disease was seen in 29.4% ,CMV reactivation seen in 39% and Veno occlusive disease of liver in 9% of cases . Median follow up among our patient was 34 months (4months to 92 months). 71 % had full donor chimerism at 1 month post transplant . Mixed chimerism was seen in 5% and got improved by stopping immunosuppression and donor lymphocyte infusions. Primary graft rejection was seen in 11.7% and secondary rejection seen in 8%. Transplant related mortality was 26.4 %. Major cause for mortality was sepsis secondary to graft failure .Overall Survival (OS) was 67.6 % [68.7% in Haplo depletion, 75% in MRD, 80 % in MSD and 60% in MUD].(Table 2)
Discussion and Conclusion: HSCT using alternative donor, disease and patient specific tailoring of conditioning regimen shows promising survival and reduced toxicities among IBMFS patients

Disclosure of Interest: None Declared

Keywords: BONE MARROW FAILURE SYNDROME, BONE MARROW TRANSPLANT, OUTCOME

Oral Presentation

BONE MARROW FAILURE SYNDROMES INCLUDING MDS. (280)

COMPARABLE OUTCOMES OF DIFFERENT DONOR TYPES IN PATIENTS WITH MDS SYNDROME FOLLOWING ALLOGENEIC HSCT

Tingting Yang*[1], Bingqian Jiang[1], Mingming Zhang[1], Yi Luo[1], Yanmin Zhao[1], Jian Yu[1], Xiaoyu Lai[1], Lizhen Liu[1], Huirui Fu[1], Yamin Tan[1], Yuanyuan Zhu[1], Yongxian Hu[1], Jingsong He[1], Jie Sun[1], Weiyan Zheng[1], Yi Zhao[1], Guoqing Wei[1], Zhen Cai[1], He Huang[1], Jimin Shi[1]
[1]The First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, China

Aims & Objectives: Outcomes of hematopoietic stem cell transplantation (HSCT) from haploidentical donors (HIDs) have made notable progress, but the role of HID-HSCT in myelodysplastic syndrome (MDS) has not been fully defined. Data of HID-HSCT in MDS and the comparisons of transplant outcomes from HIDs with those from identical sibling donors (ISDs) and unrelated donors (URDs) are urgently needed.
Patients / Materials & Methods: We compared outcomes of 117 MDS patients who received allogeneic HSCT from different donor types between 2016 and 2021. Survival outcomes among three groups were analyzed.
Results: The cumulative incidences of acute and chronic graft versus host disease were not different among three donor types (P>0.05). With a median follow-up of 28.6 (range, 7-65.5) months, the 3-year cumulative incidences of non-relapse mortality were 12.9%, 15.0% and 11.5% in ISD, URD, and HID cohorts, respectively (overall P=0.624), of relapse were 22.6%, 25.0% and 18.0%, respectively (overall P=0.834). The 3-year probabilities of overall survival were 69.2%, 75.0% and 78.1%, respectively (overall P=0.9), and of disease-free survival were 64.5%, 60.0% and 70.5%, respectively (overall P=0.8). Multivariate analysis for OS revealed that positive-MRD at HSCT (HR=10.26, 95%CI=1.37-77.15, P=0.024), long interval from diagnosis to HSCT(≥8.56 months) (HR=2.79, 95%CI=1.08-7.16, P=0.033) were risk factors, and higher dose of CD34(≥6.1106/kg) was associated with superior OS(HR=0.396, 95%CI=0.16-0.95, P=0.039).
Discussion and Conclusion: Our data elucidated comparable transplant outcomes of different donor type among MDS patients receiving allo-HSCT.

Disclosure of Interest: None Declared

Keywords: donor type, MDS, stem cell transplantation

Oral Presentation

BONE MARROW FAILURE SYNDROMES INCLUDING MDS. (363)

ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN APLASTIC ANEMIA - LONG TERM OUTCOME

Giri Punja*[1], Ashish Dixit[1], Mallikarjun Kalashetty[2], Amit Rauthan[1], Poonam Patil[1], Nitin Yashas Murthy[1], Jhansi Jayachandran[1], Santhosh Subramanian[1]
[1]Department of Medical Oncology and Hematology, [2]Hematology, Manipal Hospital, Bangalore, India

Aims & Objectives: Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) can cure Aplastic Anemia (AA), but transplantation is associated with substantial short- and long – term adverse events. Outcomes and adverse events are influenced by the age of the recipient. Survival after allogeneic HSCT in adults has not changed significantly for decades.
Objectives : To estimate overall survival of patients undergoing HSCT for AA.To estimate the incidence of acute and chronic graft versus host disease.
Patients / Materials & Methods: A total of 32 patients with AA who underwent 35 allogeneic HSCT in our tertiary care institute were retrospectively analyzed between May 2004 and May 2021.This included 4 patients of Inherited AA (3 with Fanconi anemia and 1 with Dyskeratosiscongenita). Three patients underwent a second transplant.
Results: A total of 35 allogeneic transplants for AA were included in the study which included 26 HLA matched related donor, 8haploidenical and 1 matched unrelated donor transplants. Pediatric patients comprised 53% of the study group. The median age of patients was 15 years (age range 1 year – 59 years). Majority were males (62.5%). Four patients had very severe AA, one had non-severe AA and rest all had severe AA. A small PNH clone was found in 3 patients and 2 patients had Hepatitis associated AA. Fly-Cy (n=19), Cy-TLI (n=8), Cy-ATG(n=7) were the commonly used non-myeloablative and reduced intensity conditioning regimens. Acute GVHD was seen in 20% cases (grade III to grade IV in 11.5%) and chronic GVHD in 11.4% of total cases. Only one patient had primary graft failure and 2 patients had secondary graft failure. Day 100 transplant related mortality was 31.4% (including 17.1% of day 30 mortality). Sepsis was the leading cause of death for TRM followed by acute GVHD.
On Kaplan Meier survival analysis, the median overall survival (OS) was not reached for both adult as well as pediatric patients. There was no difference in OS between pediatric and adult patients (p=0.628) (Figure 1). No difference in OS between matched related donor and haploidentical donors in our study (p=0.526).At a median follow up of 5 years, median OS was not reached. The Kaplan meier estimate for 1year and 5 years for the entire cohort was 65.7% and 62% respectively. Higher mortality in first 30 days could be attributed to recurrent infections as seen in Indian setting due to prolonged persistent neutropenia before initiating transplantation.
Discussion and Conclusion: Allogeneic HSCT is a curative therapy for AA. Neutropenic sepsis is the main cause of mortality. Less incidence of chronic GVHD can be attributed to predominant use of bone marrow harvest based stem cells.Early referral before major infections holds the key for longtermsuccess of transplant.

Disclosure of Interest: None Declared

Keywords: Allogeneic HSCT, Aplastic anemia, Transplantation

Oral Presentation

BONE MARROW FAILURE SYNDROMES INCLUDING MDS. (401)

ALLOGENEIC STEM CELL TRANSPLANTATION FOR APLASTIC ANEMIA AT A TERTIARY CARE CENTER IN INDIA

Vinay Anand Guntiboina[1], Satarupa Mahapatra[*2], Dibakar Podder[1], Rizwan Javed[1], Arijit Nag[1], Mita Roy Chowdhury[1], Jeevan Kumar[1], Saurabh Bhave[1], Reena Nair[1], Mammen Chandy[1]
[1]Clinical Hematology & HCT, Tata Medical Center, Kolkata, [2]Clinical Hematology, All India Institute of Medical Sciences, Bhubaneswar, India

Aims & Objectives: Aplastic anemia (AA) is an acquired disorder leading to bone marrow failure. Allogeneic hematopoietic cell transplantation (allo HCT) is the only curative treatment. This study aims to analyze patients undergoing allo HCT at a tertiary care cancer center in Eastern India, with a focus on transplant type and conditioning used, donor characteristics, transplant related morbidity and overall survival.
Patients / Materials & Methods: This was a single center, retrospective study and patient data was collected from the electronic medical records of the hospital. We included all patients with AA registered to undergo allo HCT at Tata Medical Center, Kolkata between 2012 to 2022. Data analysis was done using Microsoft Excel and GraphPad Prism version 9.0.
Results: The total number of patients with AA that underwent allo HCT at our center was 33, of which 2 expired prior to the date of transplant and were excluded from the analysis. Ten patients in our study were less than 18 years of age. Of the analyzed patients (Table 1), majority (61.3%) underwent a matched sibling donor (MSD) transplant with a Fludarabine based non myeloablative conditioning regimen used in 96.7% patients. Anti-thymocyte globulin and total body irradiation (TBI) was utilized in the conditioning regimen in 45.1% and 19.3% of patients, respectively. Peripheral blood was the preferred graft source for all patients. Median CD34 cell dose administered was 7.65 x 106 cells/kg (range: 3-19.08 x 106), with a median graft volume of 273 ml (range: 80-581). The most common regimen related toxicity was mucositis (83.9%) followed by diarrhea (16.1%) (Table 2). Grade II-IV acute GVHD was seen in 29% of patients with skin and gut commonly involved. Moderate to severe chronic GVHD was seen in 13% of our patients. Documented bacterial infections were noted in 58% of the patients during the post-transplant period. Viral infections were noted in 41.9% (13/31) patients, of which CMV reactivation remained the most common entity. Uncontrolled sepsis was the most common (75%) cause of death. In the patients with sepsis related mortality beyond day 60, steroid administration was observed as a precipitating factor. Overall survival (OS) at 100 days was 70.5% (95% CI:50.9-83.4%) while at 1 and 2 years was 56.1% (95% CI: 36.5 – 71.8.). Most of the deaths occurred in the first 3 months of transplant (75%). 33.3% of patients died within the first 28 days of transplant.
Discussion and Conclusion: With a majority of deaths being attributable to sepsis, infection remains the major challenge faced by us during transplant. Infections remains the major challenge faced by us during transplant. With better infection prevention and control measures we can aspire to see an improvement in transplant related mortality as well as morbidity in the future.

Disclosure of Interest: None Declared

Keywords: Allogeneic Hematopoietic Cell Transplantation, Aplastic Anemia, Bone Marrow Failure

Oral Presentation

CELL AND GENE THERAPY (181)

A NOVEL RISK MODEL FOR PREDICTING EARLY RELAPSE IN PATIENTS WITH AML RECEIVING ALLO-HSCT

Xiao-Lin Yuan[*1,2,3], Xiao-Yu Lai[1,2,3], Yi-Bo Wu[1,2,3], Lu-Xin Yang[1,2,3], Ji-Min Shi[1,2,3], Li-Zhen Liu[1,2,3], Yan-Min Zhao[1,2,3], Jian Yu[1,2,3], He Huang[1,2,3], Yi Luo[1,2,3]
[1]Bone Marrow Transplantation Center, the First Affiliated Hospital, Zhejiang University School of Medicine, [2]Liangzhu Laboratory, Zhejiang University Medical Center, [3]Institute of Hematology, Zhejiang University, hangzhou, China

Aims & Objectives: Relapse remains the main cause of death in acute myeloid leukemia (AML) patients after allogeneic hematopoietic stem cell transplantation (allo-HSCT), which limits the success of allo-HSCT for the treatment of AML patients. Identifying the high-risk group of patients who will relapse after allo-HSCT could facilitate early intervention, thereby improving survival.The objective of this study was to identify prognostic factors associated with post-transplantation early relapse of patients with de novo AML.
Patients / Materials & Methods: We enrolled patients aged 14-60 years with AML and received their first allo-HSCT from September 2014 to April 2020 in our center. The primary endpoint was early relapse (relapse within 1 year) after allo-HSCT. The factors associated with early relapse were investigated, and a prognostic model was developed based on multivariate analysis.
Results: Between September 2014 and April 2020, a total of 414 AML patients were enrolled. The overall cumulative incidence of relapse (CIR) after allo-HSCT at 1 year and 4 years were 11.1% (95%CI, 8.1% -14.1%) and 21.1% (95%CI, 17.0%-25.2%), respectively. The 3-year overall survival (OS) of the patients who relapsed within 1-year was 6.2%. The 1-year CIR of patients with the primary resistance was significantly higher than that with non-primary resistance (22.7% vs. 10.3%; P=0.015). The CIR for the patients with DNMT3A mutation group and without DNMT3A mutation group at 1 year was 22.7% (95%CI, 10.9-34.5%) and 10.3% (95%CI, 7.2%-13.4%) (P=0.012). The CIR at 1 year was 7.5% for patients without pre-MRD, 18.6% for patients with pre-MRD, and 18.2% for no remission (NR) patients(P=0.005). The 1-year CIR of patients with WBC ≤20 ×109/L and WBC >20 ×109/L were 10.3% and 22.7% (P= 0.015). For patients who achieved first complete remission (CR1) or second complete remission (CR2) prior to allo-HSCT, the early relapse rate and 4-year CIR were similar between CR1 and CR2. Patients with pre-MRD had a higher relapse rate compared without pre-MRD, no matter in CR1 or in CR2. After multivariable adjustment, primary resistance, pre-MRD, DNMT3A mutation, and white blood cell (WBC) at diagnosis remained statistically significantly associated with early relapse. The predictive model for early relapse based on these features performed well for the early identification of at-risk patients and the AUC was 0.73. The early relapse rate in high-risk and low-risk patients were 23.7% and 7.1%(P<0.001).
Discussion and Conclusion: Primary resistance, pre-MRD, DNMT3A, and WBC count at diagnosis were independent risk factors for early relapse after allo-HSCT. The model might be applied to help identify patients at relapse risk.

Disclosure of Interest: None Declared

Keywords: acute myeloid leukemia, Allogeneic hematopoietic stem cell transplantation, Relapse

Oral Presentation

CELL AND GENE THERAPY (204)

PROPHYLACTIC VERSUS PREEMPTIVE DLI FOR PATIENTS WITH HIGH-RISK ACUTE LEUKEMIA AFTER ALLO-HSCT

Luxin Yang[*1,2,3], Xiaoyu Lai[1,2,4], Lizhen Liu[1,2,4], Jimin Shi[1,2,4], Yamin Zhao[1,2,4], Jian Yu[1,2,4], Yongxian Hu[1,2,4], Yibo Wu[1,2,4], Huang He[1,2,4], Yi Luo[1,2,4]
[1]Bone Marrow Transplantation Center, the First Affiliated Hospital, Zhejiang University School of Medicine, [2]Liangzhu Laboratory, Zhejiang University Medical Center, [3] Institute of Hematology, Zhejiang University, [4]Institute of Hematology, Zhejiang University, Hangzhou, China

Aims & Objectives: To compare the efficacy and safety of prophylactic modified DLI (pro-DLI) and preemptive modified DLI (pre-DLI) after allogeneic hematopoietic stem cell transplantation (allo-HSCT) in patients with high-risk acute leukemia
Patients / Materials & Methods: Patients with high-risk acute leukemia who received myeloablative conditioning and allo-HSCT during August 1, 2014 to August 30, 2020 were eligible for this study. Pro-DLI was scheduled at three months after HSCT for patients in pro-DLI cohort. In the pre-DLI cohort, patients would stop immunosuppressive drugs and receive pre-DLI immediately after MRD turning positive with morphology remission.
Results: Pro-DLI was performed in ninty-five patients while two hundred and six patients were included in the pre-DLI cohort. Thirty-eight patients in the pre-DLI cohort became positive MRD and received pre-DLI. Patients in the pro-DLI cohort achieved a lower cumulative incidence of relapse (CIR) (27.6% versus 37.1%, p=0.027) and comparable overall survival (OS) (65.2% versus 59.3%, p=0.303) comparing with patients in the pre-DLI cohort. The 100-days cumulative incidence of grade III-IV acute graft-versus-host-disease (aGVHD) and chronic graft-versus-host-disease (cGVHD) were comparable between cohorts. Further subgroup analysis of patients who received allo-HSCT at CR1, pro-DLI achieved lower 3-year cumulative incidence of relapse (CIR) (27.6% versus 37.1%, p=0.027) while no benefit in OS (72.2% versus 69.2%, p=0.864) comparing with pre-DLI cohort. On the other hand, pro-DLI significantly decreased the CIR (13.25% versus 28.77%, p=0.044) and increased OS (60.7% versus 42.3%, p=0.022) when compared with pre-DLI in patients who received HSCT beyond CR1. Multivariate analysis demonstrated the strong protective effect of pro-DLI on long-term OS and PFS in patients who received HSCT beyond CR1.
Discussion and Conclusion: From these date, pro-DLI was highly recommended for patients with high-risk features who received allo-HSCT beyond CR1 with significantly decreased incidence of relapse and increased survival rates. Pre-DLI could be chosen by those who received allo-HSCT in CR1 in view of comparable survival rates regardless of higher relapse rates compared with pro-DLI.

Disclosure of Interest: None Declared

Keywords: acute leukemia, preemptive modified DLI, prophylactic modified DLI

Oral Presentation

ALLIED (NURSING, TECHNICAL ASPECTS SUCH AS GRAFT PROCESSING, CRYOPRESERVATION, ETC) (180)

APPLICATION OF MULTIMEDIA DIGITAL PLATFORMS TO DELIVER PRE-HSCT PATIENT EDUCATION DURING COVID-19

Xiaoxia Wang[*1]
[1]Beijign Gobroad Boren Hospital, Beijign, China

Aims & Objectives: Pre-HSCT patient education (PE) was usually delivered by face-to-face interaction, thereby enhancing patient/provider relationships and relieving anxiety in patients and their families. During COVID-19, recorded video lessons played a role but lacked efficient real-time feedbacks and interactions between patients and health providers. Therefore, the purpose of the study was to describe methods and implementation of delivering pre-HSCT PE via multimedia digital platforms as a more interactive and effective way.
Patients / Materials & Methods: 400 HSCT patients at Gobroad Boren Hospital received PE via multimedia digital platforms from Dec 2019 to Jun 2022. Disease types included leukemia, lymphoma, and aplastic anemia, etc. A major proportion of the patients received secondary transplantation or refractory salvage transplantation. Patients' age ranged from 1 to 72 years. The participated patients received treatments such as allo-HSCT, auto-HSCT, HLA-haploidentical HSCT, HLA-matched HSCT and CAR-T bridging HSCT, etc. Patients would receive standard one-by-one conversation between patients and nurse-in-duty when patients were transferred to HSCT ward and the following PE: 1. Distributing PE handouts both in paper and on WeChat; 2. Publishing written and video PE materials on our Official WeChat Account; 3. Playing PE video on the TV of the HSCT ward; 4. Playing video PE on TV in room; 5. Setting up podcast channel and published voice PE content on Himalaya FM APP; 6. live-streaming on WeChat Channels and TikTok to offer seminar and answer questions. The PE contents introduced information from pre-HSCT to post-HSCT in detail, including personal items preparation, environment walkthrough, caregiving instructions, meal, medication, safety and prevention of all kinds of mucositis and other complications. The layouts of the handouts, displays and videos were well designed with detailed explanations, making sure population from different education backgrounds could benefit.
Results: 400 patients and their families were satisfied with the PE materials provided. They were able to receive HSCT with better cooperation and showed very well understanding. The incidence of oral and perianal mucositis was 30% and 10% accordingly. No infection in the central venous catheter was found. The patients did not develop any mental disorder such as emotional turmoil due to anxiety, and we encountered harmonious nurse-patient relationship.
Discussion and Conclusion: Good PE and patient adherence promotes outcome of HSCT. All the PE materials were reusable and co-published on different platforms, reducing workload and being sustainable. Patients were able to communicate with the medical team on social medica platforms in a timely manner, building closer relationship despite of social distancing during COVID-19.

Disclosure of Interest: None Declared

Keywords: COVID-19, PE, PRE-HSCT PATIENT EDUCATION

Oral Presentation

ALLIED (NURSING, TECHNICAL ASPECTS SUCH AS GRAFT PROCESSING, CRYOPRESERVATION, ETC) (290)

ASSESSING COMPASSION FATIGUE AMONG NURSES IN A TERTIARY CANCER CARE CENTRE

Rynel D. Quadras*[1], Rosy Pinto[1], Meera Achrekar[1], Anjali Rawat[1]
[1]ACTREC, Tata Memorial Centre, Navi Mumbai, India

Aims & Objectives: To assess compassion fatigue among HSCT nurses and oncology nurses in a tertiary cancer care center.
Patients / Materials & Methods: A survey was conducted in a tertiary cancer care center in July 2022 amongst HSCT nurses and nurses working in other departments. The data were collected using a demographic proforma prepared by the researcher and PROQOL version 5. PROQOL is a 5-point Likert scale consisting of 30 items. 10 items measure compassion satisfaction, 10 measure burnout and the other 10 measure secondary traumatic stress. Burnout and secondary traumatic stress together measure compassion fatigue. Across all three domains, When the score is 22 or less it is rated low, between 23 and 41 it is rated as moderate and scores greater than 42 are rated as high. The data were analysed using descriptive and inferential statistics.
Results: A total of 143 nurses, 44 from HSCT unit and 99 from other departments participated in the study. Majority (83%) of the nurses were females, almost 40% of the nurses were in the age group of 30- 34 years. More than half (60%) of the nurses had pursued B.Sc. nursing. 78% of the nurses had 3- 5 years of professional experience.
Almost 40% of the participants reported to have difficulty in sleeping at night, approximately 34% of the participants exercise regularly. 38% of the nurses partake in relaxing activities such as writing a journal or dairy, reading etc. Approximately 18% of the participants practice yoga and meditation.
High level of compassion satisfaction was found among nurses working in the HSCT unit (45%) compared to the nurses working in other departments (37%), but the difference was not statistically significant, p value 0.362. High levels of burnout and secondary traumatic stress were found among nurses working in the HSCT unit (9%) compared to the others (1%), the difference was statistically significant, p value 0.015. Moderate levels of burnout and secondary traumatic stress were found among 61% of the nurses working in the HSCT unit and 70% of nurses working in other units, but the difference was not statistically significant, p value 0.54.
Discussion and Conclusion: Though most of the nurses partake in activities to relieve stress at a personal level, a significant number of nurses had moderate levels of compassion fatigue and some had high levels of compassion fatigue. More number of nurses from the HSCT unit had high levels of compassion fatigue. Raising awareness and employing strategies to relieve stress at departmental and organisational level is of utmost importance.

Disclosure of Interest: None Declared

Keywords: burnout, compassion fatigue, Nursing Care

Oral Presentation

ALLIED (NURSING, TECHNICAL ASPECTS SUCH AS GRAFT PROCESSING, CRYOPRESERVATION, ETC) (296)

ASSESSMENT OF BURDEN AMONG PRIMARY CAREGIVER OF POST HSCT PATIENTS

Lalita Bhoir[*1], Deepti Wairkar[1], ROSY PINTO[1], Meera Achrekar[2]
[1]BMT- NURSING, [2]NURSING, ACTREC, NAVI MUMBAI, India

Aims & Objectives: The aim of the study was to determine the caregiver burden among the primary caregivers of cancer patients who had undergone HSCT and to analyze the association between the caregiver burden and demographic variables.
Patients / Materials & Methods: The cross-sectional descriptive study was conducted in a tertiary care cancer hospital from May 2022 to June 2022. The study included 30 caregivers of cancer patients who were willing to be part of the study. They were given Zarit burden interview (ZBI) questionnaire containing 22 questions, each answer being measured on 5 point likert scale (0 – 5) which included never, rarely, sometimes, frequently, always. Scores for 5 domains were obtained from 22 questions, (1) burden in the relationship (6 items), (2) emotional well-being (7 items), (3) social and family life (4 items), (4) finances (1 item), and (5) loss of control over one's life (4 items). As per ZBI scoring total burden score ranges from 0-88, 0-20 mild, 21-40 moderate, 41-60 moderate severe , and 60-88 severe.The SPSS version 22.0 was used for data analysis.
Results: There were no relatives without any burden. Among 30 relatives, 17 (56.7%) had moderate to severe burden, 11(36.7%) had mild to moderate burden and 2(6.6%) had severe burden as per categorization of total burden scores. Total burden was higher among relatives aged between 31 and 45 years. Total burden scores in different age groups showed significant difference (p value of 0.013). Similarly, it was higher with significant differences in relationship burden scores and emotional wellbeing scores with p value 0.010 and 0.036
Financial burden was higher in relatives earning <5000 Rs/month. There was significant differences in financial problems scores between different income group of relatives with p value of 0.046. Burden was higher in relatives who cooked food for patients. There was significant differences in emotional wellbeing scores between relatives cooking food compared to those not cooking (p= 0.028).
Discussion and Conclusion: Caregiver burden is common among primary caregivers of cancer patients undergoing HSCT. From this study, we conclude that majority of caregivers had moderate to severe burden with age group 31-45 affected most. Caregivers with income <5000 INR/ month and who cooked food for their patients had higher burden.

Disclosure of Interest: None Declared

Keywords: caregiver burden, financial burden, Zarit burden interview (ZBI)

Oral Presentation

ALLIED (NURSING, TECHNICAL ASPECTS SUCH AS GRAFT PROCESSING, CRYOPRESERVATION, ETC) (331)

NEXT GENERATION STRATEGY TO REDUCE MORTALITY DUE TO DRUG RESISTANT BACTERIA IN PAEDIATRIC HSCT UNIT

Deepa Karmegam*[1], Jerlyn Robin[1], Sharmila D[1]
[1]Blood and Marrow transplantation Unit, Apollo Speciality Hospital, chennai, India

Aims & Objectives: Bacterial infections during the neutropenic phase are the biggest challenge in supportive care during haematopoietic stem cell transplantation. There is an escalating trend in infections due to multidrug-resistant bacteria and polymicrobial therapy is employed to reduce mortality and improved clinical outcome. This increases the cost of care which is the biggest challenge in resource constrained settings. We aimed to analyse the impact of placement of temporary central lines combined with prompt line change within 24 hours of the onset of fever in our unit with emphasis on sepsis related mortality.
Patients / Materials & Methods: We included all children undergoing HSCT from 2016 and divided them into two groups from Group 1 from January 2016 to December 2018 (48 months) and Group 2 from January 2019 to June 2022 (30 months). From January 2020, we instituted a policy of early replacement of central lines in the HSCT unit by the anaesthetic team and all children had a new line within 24 hours of the onset of febrile neutropenia. Data regarding culture positive sepsis, the number of days of central line and mortality were collected in a retrospective manner from case records and the was analysed using SPSS software. The study was approved by our Institutional Ethics Committee.
Results: A total of 480 children in Group 1 and 256 children in Group 2 were included in the study. The age group ranged from new born to 18 years and the male: female ratio was 1.3:1. The median time to removal of central line from the onset of neutropenia was 7 days. The incidence of culture positive sepsis was 76/480 (15.8%) in Group 1. The organism was sensitive to antibiotics in 35/76 (46%) and resistant in 41/76 (54%) of children. The mortality due to sepsis in this group was 7/76 (9.2%) and all children had a resistant organism on blood culture. In Group 2, the culture positive sepsis rate was 25/256 (9.7%) and the organism was sensitive to antibiotics in 16/25 (64%) and resistant in 9/25 (36%) children. The mortality due to sepsis was 1/25 (4%). Central line placement in critically ill children with low counts resulted in procedure related complications in 7/736 (1%). Sepsis related mortality reduced from 9.2% to 4% and this was statistically significant.
Discussion and Conclusion: Nursing interventions in supportive care is the key to optimal outcomes in HSCT units. With increasing incidence of resistant bacterial infections, the placement of tunnelled lines and long-term catheters during the neutropenic phase can increase mortality. A simple strategy to use temporary central venous access may be the smartest next generation solution to prevent mortality due to sepsis in resource restrained setting.

Disclosure of Interest: None Declared

Keywords: central line, Nursing, sepsis related mortality

Oral Presentation

ALLIED (NURSING, TECHNICAL ASPECTS SUCH AS GRAFT PROCESSING, CRYOPRESERVATION, ETC) (332)

VITAMIN K DEFICIENCY IN CHILDREN UNDERGOING HSCT – A STITCH IN TIME SAVES NINE

Viveka Veeramani*[1], Thilagavathi G[1], ANSIL SABO[1]
[1]Blood and Marrow Transplantation Unit, Apollo speciality hospitals, Chennai, India

Aims & Objectives: Micronutrient deficiency is common in children undergoing hematopoietic stem cell transplantation due to mucositis following high dose chemotherapy. The role of Vitamin K is especially undervalued as the combination of poor oral intake, mucositis and the use of broad-spectrum antibiotics post HSCT results in universal Vitamin K deficiency. The aim of our study was to analyse the incidence of prolonged PT and APTT due to vitamin K deficiency in children undergoing HSCT and the benefit of replacement of Vitamin K.
Patients / Materials & Methods: We performed a retrospective study from January 2019 to June 2022 and included all children undergoing HSCT for beta thalassaemia major in our unit. Prolongation of Prothrombin time PT and Activated Partial Thromboplastin Time APTT were used as a screening tool to detect Vitamin K deficiency. All children had PT and APTT test on Day 5 post stem cell infusion. We initiated a policy of intravenous replacement of Vitamin K at a dose of 2 mg in less than 2 years of age, 5 mg in 2 to 8 years and 10 mg in age above 8 years in January 2019 on Day 5 post HSCT. All children had the same myeloablative conditioning with thiotepa, treosulfan and fludarabine and this resulted in grade 2 to 4 mucositis. The platelet count was less than 10,000 and they required transfusion support and the incidence of mucosal bleeding was documented in all these children. The data was analysed using SPSS software and the Institutional Ethics Committee had approved the study.
Results: A total of 54 children underwent HSCT for thalassaemia major with age from 1 year to 16 years and a male: female ratio of 1:1.2. All children had severe mucositis and remained on parenteral nutrition for the previous 5 days. All children had been exposed to broad spectrum antibiotics for febrile neutropenia including 13/54 (24%) on oral vancomycin. The mean PT on Day 5 was 20.6 seconds with a control of 13 seconds. The mean APTT was 40.5 seconds with a control of 30 seconds. All patients needed platelet support and 7/54 (13%) had significant mucosal bleed including one child with an intracerebral bleed. There was no mortality related to bleeding in our study cohort.
Discussion and Conclusion: Nursing interventions in supportive care helps reduce morbidity and mortality in children undergoing HSCT. Our study clearly highlights the universal lack of Vitamin K, an essential micronutrient to prevent bleeding in children undergoing myeloablative conditioning that results in severe mucositis. Prompt recognition and replacement of Vitamin K helps prevent mortality due to bleeding. We recommend all paediatric HSCT units follow the policy of universal Vitamin K prophylaxis especially in resource constrained setting where children are not on total parenteral nutrition that helps replace micronutrients

Disclosure of Interest: None Declared

Keywords: HSCT, Nursing, Vitamin K

Oral Presentation

ALLIED (NURSING, TECHNICAL ASPECTS SUCH AS GRAFT PROCESSING, CRYOPRESERVATION, ETC) (355)

CENTRAL LINE ASSOCIATED BLOOD STREAM INFECTION (CLABSI) ZERO TARGET

Kavitha S. Nair* [1, 1, 2]
[1]NURSING, [2]BMT, AIMS, ERNAKULAM, India

Aims & Objectives: AIM:
1. To reduce the incidence of CLABSI among BMT patients.
2. To improve the compliance of RNs with the standards of care related to caring of central lines

Patients / Materials & Methods: METHODS:
A quality improvement study conducted by Guerin et al (2010) identified that routine quality assessment of central catheter on different aspects has a crucial role in reducing the incidence of CLABSI among patients. Also he states that regular staff training & reinforcement on care and maintenance of central catheters by the experts can also positively influence there deduction of CLABSI among patients.
The data were collected from January 2016 to December 2021 with Infection Control Report (HH compliance report, room culture report and internal audit report) & microbiological report (Blood culture report, Room culture reports). This quantifies the rate of CLABSI among BMT patients. In 2016, the numbers of incidences of CLABSI were 7 and in 2017 two incidences were reported in the months of February and March respectively. Then, we started to practice the standard interventions that were supported by strong evidence were chosen to prevent CLABSI.
These interventions consist of the following:
Hand hygiene
Use of full barrier precautions
Chlorhexidine (CHG) skin preparation such as CHG bath and cleaning with chlorhexidine tincture
Avoiding insertion of tunnelled catheter...Hickman
Q-syte instead of three way stopcock with closures
Reduced intensity conditioning regimen
Terminal cleaning
Pre transplant work up as op basis
Restricted entry of portable machines inside the unit
Stool surveillance culture just prior to admission
Prompt removal of CVCs
Line insertion inside the unit
Minimal disconnection of lines
Infection control link nurse

Results: BMT patients are a high-risk population for CLABSIs due to chemotherapy, severe neutropenia and immunosuppressive therapy. It increases the patient co-morbidities and length of hospital stay which also increases the cost of care. This need collaborative joint team to control and prevent CLABSI; it is not limited to nurses but to physicians, patients, and their bystanders.

Discussion and Conclusion: By having a system with clear guidelines and continuous audits by the infection control department helps in the dramatic reduction in CLABSI rate.

Disclosure of Interest: None Declared

Keywords: Blood stream infections, central line, CLABSI

POSTER PRESENTATION

Poster Presentation

LEUKEMIAS (113)

DETECTION OF EARLY RELAPSE OF B-ALL AFTER ALLOGENEIC HSCT BY FISH-XY CHIMERISM

Mintu A. Joy[*1], Gurpreet Kaur Bains[1], Ketan Modak[2], Preethi A. M. Paul[1], M J. John[2]
[1]Pathology, [2]Clinical Hematology, Hemato-Oncology and Bone Marrow (Stem Cell) Transplantation, Christian Medical College and Hospital, Ludhiana, India

Aims & Objectives: Fluorescence in-situ hybridization (FISH) is a powerful tool for chimerism analysis & monitoring engraftment after sex-mismatched allogeneic hematopoietic stem cell transplantation (Allo-HSCT). The finding of host hematopoietic cells after HSCT is indicative of graft rejection or disease relapse. We present a case of early relapse of B-lymphoblastic leukemia (B-ALL) detected by FISH-XY chimerism analysis.
Patients / Materials & Methods: A 19-year-old gentleman, who was diagnosed to have B-ALL 18 months back & treated with Berlin-Frankfurt-Munich-95 (BFM) protocol elsewhere, presented to our hospital with relapsed disease while on the maintenance phase of BFM protocol. Bone marrow (BM) & flow cytometry (FCM) confirmed B-ALL relapse, & he was started on BFM-85 relapse protocol. Subsequently, he achieved remission & underwent matched sibling Allo-HSCT with his younger sister as the donor (Table 1). Following HSCT, FISH-XY chimerism analysis was performed using Interphase FISH between Days +27 & +444. Heparinized PB sample was collected & processed in the Pathology lab. Dual colour X (spectrum orange)/ Y(spectrum green) 3µL probe mix (Vysis, Abbott Molecular Inc, USA) was hybridized with the PB at 75°C for 5 minutes and 37°C for 16 hours in the hybridizer, followed by post-hybridization washes and DAPI counterstaining.
Results: Patient underwent serial FISH-XY chimerism analyses on Days +27, +45, +64, +90, +226, +403, +409 and +444. A total of 7500 interphase cells from the PB were analyzed. Initial chimerism analysis showed male recipient cells (XY) ranging from 0-0.7%, while the remaining were female donor cells (XX) ranging from 99.3-100%. On Day +403, FISH-XY chimerism analysis showed 2.2% abnormal cells (XXY), while the remaining were 0.8% male (XY) recipient and 97% female (XX) donor cells. A suspicion of early relapse of B-ALL post-HSCT was raised & BM was performed on Day +410. Though BM aspirate was a dry tap, touch smears showed 40% blasts. BM trephine biopsy was solidly cellular with sheets of blasts. He was confirmed to have relapse of B-ALL post-HSCT. Subsequently, he developed fever, lymphadenopathy, and splenomegaly. He was started on palliative therapy with prednisolone and methotrexate, and was on regular follow-up for 7 months. Thereafter, the patient was lost to follow-up. Cytogenetics could not be performed due to very low PB counts.
Discussion and Conclusion: FISH-XY chimerism is a very useful tool in the detection of early relapse of disease after Allo-HSCT, especially in cases with cytogenetic abnormalities like ALL. The presence of abnormal populations of cells, like XXY in our case, should raise the suspicion of relapse.
Conclusion: Abnormal cell population in FISH-XY chimerism must raise the flag for early relapse of disease, which can help initiate early treatment and may improve the prognosis.

Disclosure of Interest: None Declared

Keywords: B-ALL, Chimerism, Fluorescence in situ hybridization, Hematopoietic stem cell transplantation, Relapse

Poster Presentation

LEUKEMIAS (156)

CARE OF PAIN IN PATIENTS WITH AML AFTER ADMINISTRATION OF FLT3 INHIBITOR INVESTIGATIONAL NEW DRUG

Mingyue Xu[*1], Yan Cui[1]
[1]GCP, Institute of Hematology and Blood Diseases Hospital, Tianjin, China

Aims & Objectives: To analyze the clinical data and nursing measures of pain after oral administration of FLT3 inhibitor investigational new drug in patients with acute myeloid leukemia and to improve nurses' care for special types of pain.
Patients / Materials & Methods: A series of personalized nursing measures were implemented for different patients in addition to conventional nursing care in terms of pain site, pain score, pain tolerance, and psychology. After oral drug administration, the patient's blood counts decreased, immune function declined, and pain, in bones and joints, was observed at different sites (both lower extremities and posterior back) and in different degrees. Pain assessment was performed and exclusive pain care sheets were designed for individual patients, and the assessment was based on a numerical scale. Patients are encouraged to report their pain proactively, and the nursing staff can notify the physician in a timely manner based on the pain that patients report. Patients can be given the correct and timely pain medication according to the specific pain to reduce their level of suffering. After patients take pain medication, nurses conduct secondary pain assessment to achieve continuous assessment. When patients have pain symptoms, we need to pay more attention to the psychological changes of patients, informing them that pain is a common pathological state and that irritability and anxiety will only aggravate the pain. Through psychological guidance, we can help patients to be emotionally stable and help to reduce the pain. Through psychological implication, we can enhance patients' confidence to overcome the disease by telling them how to cooperate with the treatment and be explaining to them the previous successful cases and the role and side effects of the investigational new drug, so as to achieve the purpose of pain relief. In our routine nursing care, we also incorporated methods of pain relief through distraction, relaxation, music, and family support system to help reduce patients' symptoms of pain in an all multifaceted fashion.
Results: Patients' pain level after oral administration of FLT3 inhibitor drugs was reduced, and patients' confidence in overcoming the disease was enhanced.
Discussion and Conclusion: Our patients have relapsed refractory Acute myeloid leukemia, and the participation in clinical trials is their last hope. However, the new drug has a more obvious side effect of pain, which generates more negative and could aggravate the patient's condition. We implement quality nursing and psychological care for patients, which can improve their quality of life. Therefore, we should focus on our clinical care and psychological care in future patients with acute leukemia, who takes the investigational new drug, to improve the quality of life of patients and reduce their suffering.

Disclosure of Interest: None Declared

Keywords: acute myeloid leukemia, Nursing, oral FLT3 investigational new drug, pain

Poster Presentation

LEUKEMIAS (184)

EXCELLENT RESULTS OF ALLO-HSCT FOR MLL GENE-ASSOCIATED HEMATOLOGIC MALIGNANCIES

Zhihui Li*[1], Fan Wu[1], Teng Xu[1], Jing Li[1], Xiaopei Wen[1], Xianxuan Wang[1], Tong Wu[1]
[1]Beijing Gobroad Boren Hospital, Beijing , China

Aims & Objectives: The abnormality of MLL is a unique form of acute leukemia and About 10% of leukemias have MLL1 translocations. The 5-year EFS of infants was 20-40% with MLL-rearrangement ALL and was 60% with wild-type MLL. In our study, we evaluated the safety and efficacy of allo-HSCT in patients with MLL gene.
Patients / Materials & Methods: Between January 2018 to December 2021, 37 patients (21 males and 16 females) with MLL1 gene-associated hematologic malignancies bridge to allo-HSCT in our hospital were evaluated. AML was found in 19 (51.4%), B-ALL in 13 (35.1%), T-ALL in 1 (2.7%),B-LBL in 2 (5.4%), and T-LBL in 2 (5.4%). There were 10 (27%) MLL-AF4 fusion gene positive cases, 10 (27%) MLL-AF6 fusion gene positive cases, 8 (21.6%) MLL-AF9 fusion gene positive cases, 6 (16.2%) MLL-PTD fusion gene positive cases, 2 (5.4%) MLL-ENL fusion gene positive cases. MLL-AF10 fusion gene was positive in 1 case (2.7%). The median age was 15(1-62) years and the median course was 16.5(5-128) months. There were 23 (62.1%) MRD positive patients before HSCT. 9 cases (24.3%) had extramedullary lesion involvement before transplantation. Six patients (16.2%) received a second transplantation. There were 30 (81.1%) haploidentical donors, 5 (13.5%) unrelated donors (HLA 10/10 or 9/10 matched), and 2 (5.4%) sibling matched donors with full HLA matching. Myeloablative reduced-toxicity conditioning (RTC) with either total body irradiation (TBI)/fludarabine-based (11, 29.8%) or busulfan (BU) /fludarabine-based (26, 70.2%) were applied. Cyclosporine, mycophenolate mofetil and short-term methotrexate were employed for graft-versus-host disease (GVHD) prophylaxis.
Results: Full donor engraftment was achieved in all patients. The median time for neutrophil and platelet engraftment was 14 (9-21) days and 15 (5-23) days. With a median follow-up of 857 (363-1162) days, one-year OS was 67.59% and one-year LFS was 62.38% ; two-year OS was 54.53% and two-year LFS was 50.13%. The non-relapse mortality (NRM) was 8.1% (3/37). At present, 24 patients (64.9%) survived and 13 patients (35.1%) died(B-ALL in 9, AML in 4). 10 patients died of disease recurrence(B- ALL in 7, AML in 3), two died of severe infection (B-ALL in 2) and one AML patient died of chronic GVHD. 7 patients (18.9%) developed grade III to IV aGVHD and 3 patients (8.1%) developed generalized cGVHD. There were 14 patients happened viremia, 10with CMV, 2with EBV and 2with both cytomegalovirus and EPstein-Barr virus activation. The incidences of CMV and EBV viremia were 27.0%, 10.8%. Hemorrhagic cystitis was found in 10 (27.0%) cases.
Discussion and Conclusion: Our results suggest that allo-HSCT is a good treatment for MLL gene-associated hematologic malignancies. The 2-year OS and LFS were 54.53%, 50.13%, respectively. In addition, transplant-related mortality was quite low (3/37).

Disclosure of Interest: None Declared

Keywords: Allogeneic hematopoietic stem cell transplantation, leukemia-free survival, MLL gene, MLL gene-associated hematologic malignancies, overall survival

Poster Presentation

LEUKEMIAS (187)

ALLO-HSCT IMPROVES THE POOR PROGNOSIS IN MLL-AF6 POSITIVE ACUTE MYELOID LEUKEMIA

Rui Wang*[1], Yongqiang Zhao[1], Zhihui Li[1], Fan Yang[1], Yanzhi Song[1], Feifei Li[1], Dongfang Yang[1], Tong Wu[1]
[1]GoBroad Boren Hospital, Beijing, China

Aims & Objectives: The prognosis of the patients with MLL-AF6 positive acute myeloid leukemia (AML) is extremely poor due to low complete remission (CR) and high relapse rate by chemotherapy. In present study, whether the prognosis of MLL-AF6 positive AML could be improved by allogeneic hematopoietic stem cell transplantation (allo-HSCT) was investigated.
Patients / Materials & Methods: Between May 2018 and May 2022, nine patients with MLL-AF6 positive AML who underwent allo-HSCT in our center were included and analyzed retrospectively. The median age was 27 (6-50) years old. One patient was diagnosed as t-AML and 1 case received the second allo-HSCT. Donor types were either haploidentical (n=8) or matched related (n=1). Before transplantation, 6 (66.7%) patients were in CR and 3 (33.3%) cases were in non-remission (NR). In CR patients, only 1/6 case was minimal residual disease (MRD) positive at 0.19% measured by flow cytometry. In NR patients, the blasts in bone marrow were 8.5%, 14.5%, 30% respectively. MLL-AF6 were still positive in 8/9 patients before conditioning with the median level at 3.1 (0.006-36.54) %. Eight of 9 patients received BU/FLU-based conditioning and 1 case who underwent the second allo-HSCT received TBI/FLU-based regimen due to the conditioning for the first allo-HSCT was BU/CY/FLU regimen. In 8/9 patients with MLL-AF6 positive before transplant, some anti-leukemia medicines were added into conditioning with either cytarabine/etoposide (cytarabine 1g/m2, 3days; etoposide 150-200g/m2, 3days) or cytarabine/decitabine (cytarabine 1g/m2, 5days; decitabine 20mg/m2, 5days). Cyclosporine, mycophenolate mofetil and short-term methotrexate were employed for graft-versus-host disease (GVHD) prophylaxis. ATG was applied in haploidentical transplant.
Results: All patients achieved durable engraftment. Two patients developed acute GVHD and 6 cases had chronic GVHD. Virus reactivation was found in 5 patients (CMV only in 4; CMV and BKV in 1; EBV in 1). With the median follow-up 18.5 (6.5-42.5) months, the overall survival (OS) and disease-free survival (DFS) were all 66.7%. Three patients died (relapse in 2; GVHD and infection in 1). The transplant-related mortality (TRM) was 11.1%. One patient MLL-AF6 fusion gene became positive at 4 months post-transplant and turned to negative after treatment with azacitidine and venetoclax.
Discussion and Conclusion: With current protocol, allo-HSCT has remarkably improved the prognosis of MLL-AF6 positive AML with 66.7% DFS even majority of the patients (8/9) with fusion gene positive before transplant.

Disclosure of Interest: None Declared

Keywords: acute myeloid leukemia, Allogeneic hematopoietic stem cell transplantation, MLL-AF6

Poster Presentation

LEUKEMIAS (188)

OUTCOMES OF MATCHED SIBLING DONOR AND HAPLOIDENTICAL TRANSPLANT IN ACUTE MYELOID LEUKEMIA

Shilpa Prabhu[*1], Bharath Ram[2], Sharat Damodar[2], Nataraj K S[3], Akshatha Nayak[2]
[1]Bone marrow transplant and CART therapy, University Hospital Bristol and Weston, Bristol, United Kingdom, [2]Bone marrow transplant, Mazumdar Shaw Medical Centre, [3]Haematology and bone marrow transplant, Shankara Cancer Institue, Bangalore, India

Aims & Objectives: To compare the outcomes of matched sibling donor (MSD) versus haploidentical donor (HID) HSCT with respect to the survival, the incidence of graft-versus-host disease (GVHD), and infections
Patients / Materials & Methods: We retrospectively analyzed 75 AML patients who underwent HSCT with either MSD or HID at our center from January 2010 to June 2019. Fludarabine (35 mg/m2 from day -7 to day-3) plus Busulfan (3.2 mg/kg for day -7 to day -4) or melphalan (140 mg/m2 on day -2) conditioning regimen was used in MSD transplant based on patient's co-morbidity index and pre-transplant performance status, while modified John Hopkins protocol (fludarabine 30 mg/m2 from day -6 to -2, cyclophosphamide 14 mg/kg on day -6, melphalan 90 mg/m2 on day -2, and TBI on day -1) was followed in HID transplant. Cyclosporine and methotrexate were used as post-transplant GVHD prophylaxis in MSD, whereas cyclophosphamide (50 mg/kg for 2 days; on days +3, and +4), tacrolimus, and mycophenolate were used for HID transplants.
Results: Out of 75 patients, 42 (56%) were males, and the median age was 39 (IQR; 18, 69) years. Fifty (66.6%), and 25 (33.3%) patients underwent MSD and HID transplants respectively. Peripheral blood stem cell (99.2%) was the major graft source. Mean-time to neutrophil (12.7 vs 16.4 days) and platelet engraftment (12.8 vs 19.3 days) was significantly earlier in MSD than in HID group (P<.001). At the last follow-up, 90% were in remission in MSD compared to 96% in HID with relapse rates of 10% in MSD compared to 4% in HID (P=0.65). The day-100 survival was significantly higher in MSD than in HID transplantation (74% vs. 48%; P= .03). The OS was not different at 1-year and 3-year time points between the groups (MSD, 57.8%, 54.6%, and HID 52%, 44%, P=0.141)fig1. The incidence of acute GVHD grade 2 to 4 (46% vs. 24%; P = 0.08) and chronic GVHD (18% vs. 4%; P = 0.15) were also similar between both groups. The rate of infections in MSD transplant was comparatively lower (18.3%) than in HID transplant (30%) though was not statistically significant (P=0.209).
Discussion and Conclusion: Our study showed comparable outcomes in MSD and HID transplants with respect to the incidence of GVHD, mortality rate, OS, and RFS. HID transplant is a feasible option with comparable results to MSD in AML transplants.

Disclosure of Interest: S. Prabhu But No Conflict with: None, B. Ram But No Conflict with: None, S. Damodar But No Conflict with: None, N. K S But No Conflict with: None, A. Nayak But No Conflict with: None

Keywords: Acute myelogenous leukemia, Haploidentical donor, hematopoietic stem cell transplantation, Matched sibling donor

Poster Presentation

LEUKEMIAS (211)

HAPLOIDENTICAL STEM CELL TRANSPLANT IN BANGLADESH - REPORTS OF FIRST 5 CASES FROM A SINGLE CENTRE

Masba U. Chowdhury[*1], Quazi S. Haq[1], Zannatun Nesa[1], Kaniz F. Rahman[1], Menoti P. Mukti [1], Tangia Muquith [1], Muhammad Shahidul Islam S. Rumi[1], Md Sazzad Z. Chowdhury[1], Shamim A. Begum[1], Abu Jafar M. Saleh[1]
[1]Hematology & SCT , Evercare Hospital, Dhaka, Bangladesh

Aims & Objectives: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) remains a curative therapy for patients with various hematological malignancy. Wthout matched sibling donors, haploidentical hematopoietic stem cell transplantation (haplo-HSCT) using post-transplant cyclophosphamide (PTCy) for graft versus host disease (GvHD) prophylaxis has emerged as an alternative transplant strategy. Aim of the study is to analyze transplant outcomes of first five haplo-HSCT transplants in a single private centre of Bangladesh.
Patients / Materials & Methods: We retrospectively analyzed patients with hematological malignancy who underwent haplo-HSCT from August 2020 to April 2022 at Evercare Hospital Dhaka, Bangladesh in their first or second complete remission (CR) from a T cell replete G-CSF mobilised PBSC donor.
Results: The analysis included 5 patients (all males): Acute Myeloid Leukemia (AML, n=2), Acute Lymphoblastic Leukemia (ALL, n= 1), Acute Undiffentiated Leukemia (AUL, n = 1), Relapsed/Refractory Hodgkin Disease (R/R HD, n = 1). Median age was 20 years (range 8-37). Disease status at the beginning of pre-transplant conditioning was CR1 in 3 patients, CR2 in 2 patients. Pre-transplant conditioning regimen: RIC in 1 patient (FLU/MEL/THIOTEPA/ATG), MAC in 4 patients (FLU/TBI 2, CY/TBI 1, THIOTEPA/BU/FLU/ATG 1). All patient received immunosuppressive therapy with CSA/MMF/PTCy. The mean CD34+ cells dose was 10 x 106/kg (range, 6.2-12.5). The median time to white blood cells recovery was +14 days(range 12-19). Median follow-up was 13 months. There was no transplant related mortality. Primary engraftment was observed in all patients. One year overall and progression free survival was 75%. One patient relapsed within 3 month of transplant & eventually died of sepsis. Four (80%) patients developed grade I-II acute GvHD (2 skin & 2 gut), all responded completely with first line immunosuppressive. One patient developed chronic gut GvHD. Among non-classical infectious: CMV reactivation in found in 4 patients, hemorrhagic cystitis in 2 patients, HHV6 and C. Diff in 1 patient respectively. Immunological event (Pure red cell aplasia) not associated with GvHD was observed in 1 patient.
Discussion and Conclusion: Due to lack of matched siblings, in many cases haplo-HSCT is the only HSCT option for patients with high risk disease. Advances in transplantation techniques, such as donor selection, modifications of conditioning regimen and GvHD prophylaxis have successfully improved the outcomes of haplo-HSCT. These advancements also extended the haploidentical transplant indications for hematological malignancy. Though limited by small number of patients and short time follow up, our analysis shows encouraging results of haplo-HSCT in various hematological malignancy.

Disclosure of Interest: None Declared

Keywords: Graft versus Host Disease, Haploidentical donor, Hematologic malignancy

Poster Presentation

LEUKEMIAS (216)

OUTCOME OF MATCHED SIBLING VERSUS HAPLOIDENTICAL DONOR TRANSPLANT FROM A SINGLE CENTRE IN BANGLADESH

Masba U. Chowdhury*[1], Quazi S. Haq[1], Zannatun Nesa[1], Kaniz F. Rahman[1], Menoti P. Mukti[1], Dilshad Jahan[1], Tangia Muquith[1], Muhammad Shahidul Islam S. Rumi[1], Shamim A. Begum[1], Maruf A. Hasan[1], Md Sazzad Z. Chowdhury[1], Abu Jafar M. Saleh[1]
[1]Hematology & SCT , Evercare Hospital, Dhaka, Bangladesh

Aims & Objectives: HLA identical or matched sibling donor (MSD) is the optimal and first choice for allogeneic hematopoietic stem cell transplantation (allo-HSCT). Haploidentical hematopoietic stem cell transplantation (haplo-HSCT) is an important treatment option when a matched sibling donor is unavailable. With the increasing experiences with haplo-HSCT, specially with T-cell replete & post transplantation cyclophosphamide (PTCy) approach, outcome of haplo-HSCT found to be comparable to allo-HSCT from MSD which are historically considered as the optimal source of donor stem cell graft. Aim of this study is to compare clinical outcomes between haplo-HSCT and MSD-HSCT in patients with hematological malignancy.
Patients / Materials & Methods: We retrospectively analyzed patients who underwent their first allo-HSCT at Evercare Hospital Dhaka, Bangladesh between 2019 and 2022, either from a T-cell replete haplo or MSD donor. Chi squared test were used to compare between categorical variable, whereas unpaired t test were used to compare mean between groups. Hazzard Ratio (HR) for overall survival (OS) and progression free survival (PFS) were estimated using the Cox Regression analysis. For all statistical analysis p value <0.05 considered as statistically significant.
Results: The analysis comprised 20 patients: haplo-HSCT-5 (AML 2, ALL 1, AUL 1, R/R HD 1); MSD-15 (AML 11, ALL 2, MDS 1, R/R Lymphoma 1). Median follow-up was 12 months. Median age was 20 (range 8-37) and 40 (rang 7-53) years in haplo-HSCT and MSD-HSCT respectively. Similar conditioning regimen were used (MAC 80% & RIC 20% in both group respectively). Measurable residual disease (MRD) positivity was higher in Haplo group (60% vs 33.3%, p value 0.282). All patients received PTCy along with CSA & MMF for graft versus host disease (GvHD) prophylaxis in the haplo-HSCT setting, while majority (93%) patients received CSA/MTX in MSD group. Median neutrophil engraftment was earlier in MSD transplants compared to haplo-HSCT (13 vs 14 days, p = 0.4). Incidence of acute GvHD was higher in haplo-HSCT than MSD (80% vs 40% respectively). Main causes of death were relapsed (20% in both group). Transplant related mortality (TRM) was observed 13% in MSD group, whereas no TRM in haplo-HSCT group. OS and PFS did not differ significantly between the 2 transplant groups, HR = 0.70 (95% CI 0.20–2.4, p = 0.57) and HR = 0.79 (95% CI 0.24–2.66, p = 0.71) respectively.
Discussion and Conclusion: Haplo-HSCT offers an attractive and feasible curative therapy for high risk patients with hematological malignancy as almost everyone has a donor. With the advances in transplantation techniques and better understanding, outcomes of haplo-HSCT improved significantly in last two decades. Our analysis shows outcome of haplo-HSCT is comparable and acceptable to MSD-HSCT in terms of OS, PFS.

Disclosure of Interest: None Declared

Keywords: Graft versus Host Disease, Haploidentical donor, Hematopoietic stem cell transplantation, Matched sibling donor

Poster Presentation

LEUKEMIAS (217)

COST EFFECTIVENESS OF BMT AT PRIVATE SET UP IN BANGLADESH

Kaniz F. Rahman*[1], Quazi S. Haq[1], Masba U. Chowdhury[1], Zannatun Nesa[1], Menoti P. Mukti[1], Abu Jafar M. Saleh[1]
[1]Hematology, Evercare Hospital, Dhaka, Bangladesh

Aims & Objectives:
Introduction: Bone marrow transplantation is a costly procedure worldwide. Starting from 2016, we did 60 bone marrow transplantation and we tried to analyze cost effectiveness in a private sector for both allogenic and autologous set up.
Patients / Materials & Methods: Method: We evaluated retrospectively total 60 bone marrow transplant patients, done from March,2016 to June,2022. We used a single longitudinal administrative data base to establish a cohort of autologous and allogeneic HSCT recipients. Inpatient and outpatient direct medical costs from transplant hospitalization through first 30 days post-transplantation were analyzed.
Results: Result: We identified 60 patients who had received their first transplant during this study period (autologous-40, allogeneic-20). The median 30-days total costs for autologous HCT were TK7.6 lac (±2lac) and for allogeneic HCT were TK14.88 lac (±4.9lac). Among the total costs, the major cost areas were IPD Bed charge-TK2.29 lac (±1.02 lac), physicians' consultation fees- TK88 thousand (±51thousand), laboratory tests- TK1.90lac (±1.12lac) and medicines- TK1.82lac (±1.41lac) for all BMT patients during this study period.
These cost areas vary significantly between auto SCT and allo SCT. In case of auto SCT, IPD Bed charge- TK1.64 lac (±54.6thousand), physicians' consultation fees-TK67thousand (±35thousand), laboratory tests- TK1.22lac (±55thousand) and medicines- TK1.39lac (±76thousand) where as for allo SCT, IPD Bed charge- TK3.34 lac (±73thousand), physicians' consultation fees- TK1.28lac (±48thousand), laboratory tests- TK3.01lac (±80thousand) and medicines- TK2.38lac (±1.74lac)
Discussion and Conclusion: Conclusion: Autologous stem cell transplant costs far less than allogenic stem cell transplant because of less hospital stay and less complications. Major costs occurred during the initial period of hospitalization for both autologous and allogeneic HCT recipients. The major cost areas for BMT are IPD bed charges, physician's' consultation fees, laboratory tests and medicines.

Disclosure of Interest: None Declared

Keywords: allo transplant, cost effectiveness, stem cell transplantation

Poster Presentation

LEUKEMIAS (218)

A QUALITATIVE STUDY ON THE REAL EXPERIENCE OF SPLENOMEGALY IN PATIENTS WITH PRIMARY MYELOFIBROSIS

Qianqian Zhang[*1], Wenjun Xie[1], Junjie Li[1]
[1]Institute of Hematology & Blood Diseases Hospital, Tianjin, China

Aims & Objectives: To understand the real experience of Splenomegaly in patients with Primary Myelofibrosis, and to provide evidence for the implementation of targeted interventions.
Patients / Materials & Methods: According to the phenomenological research method in qualitative research, 10 patients with Primary Myelofibrosis were conducted one-by-one in-depth personal interviews through semi-structured interviews. Interview outline was based on the literature, clinical experience and consulting experts; During the interview, the recording were made after the patient's consent. Then Listen to the recordings repeatedly, sort the recordings into words. The data were analyzed with the Colaizzi 7 step analysis method by the Nvivo 11.0 software: read the interview data repeatedly, analyze, reflect, code, classify and extract the themes.
Results: 4 themes are extracted :①Perception of splenomegaly symptoms: splenomegaly causes pain, early satiety and abdominal discomfort; ②Cognition of splenomegaly: the patients thought that splenomegaly is the symptom of disease; ③Influence on patients: it has great influence on patients' emotional-social communication and quality of life (more obvious for women); ④ Coping strategies: patients took varied measures to deal with splenomegaly-including positive coping and negative coping.
Discussion and Conclusion: Patients with Primary Myelofibrosis has obvious symptoms cluster of splenomegaly and the coping strategies are in high demand. The nursing staff should pay attention to explore the development and response of splenomegaly, targeted formulate corresponding management measures to cope with the situation in order to improve the patients quality of life.

Disclosure of Interest: None Declared

Keywords: Primary Myelofibrosis, Qualitative research, Splenomegaly, Symptom Cluster

Poster Presentation

LEUKEMIAS (222)

35 BMT FROM A SINGLE CENTER DURING COVID PANDEMIC IN BANGLADESH

Quazi S. Haq[*1], Masba U. Chowdhury[1], Zannatun Nesa[1], Kaniz F. Rahman[1], Menoty P. Mukti[1], Tangia Muquith[1], Muhammad S. I. Rumi[1], Md. Sazzad Z. Chowdhury[1], Shamim A. Begum[1], Abu Jafar M. Saleh[1]
[1]Hematology & SCT, Evercare Hospital , Dhaka, Bangladesh

Aims & Objectives: : Severe acute respiratory syndrome coronavirus (SARS-CoV-2) named novel corona virus is the causative agent of covid -19. It was first identified in December 2019 and in March 2020, the World Health Organization (WHO) declared the covid-19 outbreak, a pandemic. Widespread community transmission puts serious threat on health care system. As majority health care resources directed to covid care, non-covid patients care became challenging. Particularly hematology patients who are mostly immunocompromised, thought to be at higher risk of infection with covid -19. Initial recommendations in many centers were to delay bone marrow /hematopoietic stem cell transplantation for standard risk group. But postponing an effective therapeutic approach might result in irreversible relapse or progression of hematologic malignancies.
Patients / Materials & Methods: We developed a practical approach at hematology department of Evercare hospital Dhaka, which included isolation, social distancing, and patient and donor education for prevention of infection. Patient entered in hematology and BMT ward only with negative PCR test result. Single attendee was allowed as care giver during whole hospital stay, with negative PCR report prior to entry. They were advised using masks while health care provider enters the room. Absolute isolation by putting a biometric access which only opened to hematology identification. All health care stuffs maintained barrier precautions like, masks, double gloves, and fluid resistant gowns separately for each patient. If any patient became PCR positive after admission, immediately shifted to designated covid ward to avoid transmission.
Results: In Bangladesh which is a densely populated country with lower-middle economy, preventive measure like social distancing was much challenging. Here first covid case was detected in March 2020. And after that number of covid patients were rising exponentially. In this crisis period, transplant activities were continuing at our center. From June 2020 to December 2021 total 35 hemopoietic stem cell transplant procedures were done including both autologous and allogeneic transplantation. Only one autologous patient infected with covid infection after engraftment during hospital stay and he recovered completely with supportive treatment. Among 35 patients, 19 patients underwent autologous SCT, and 16 patients received allogeneic SCT, including haplo-identical related donor transplants.
Discussion and Conclusion: During long lasting covid pandemic, it was not practically feasible to postpone hemopoietic SCT in patients with hematologic malignancy. Our overall data showed that by applying strict preventive and supportive measures, hemopoietic stem cell transplantations can be carried out with safety even in a lower-middle income country like ours.

Disclosure of Interest: None Declared

Keywords: COVID-19 pandemic, Hematopoietic stem cell transplantation, SARS-CoV-2

Poster Presentation

LEUKEMIAS (223)

OUTCOME OF BONE MARROW TRANSPLANT FROM THE LARGEST CENTER IN BANGLADESH

Zannatun Nesa*[1], Quazi Haq[1], Masba Chowdhury[1], Kaniz F. Rahman[1], Menoti P. Mukti[1], Dilshad Jahan[1], Tangia Muquith[1], Muhammad S. I. Rumi[1], Md.Sazzad Z. Chowdhury[1], Maruf A. Hasan[1], Shamim A. Begum[1], Abu Jafar M. Saleh[1]
[1]Haematology and Stem Cell Transplant, Evercare Hospital Dhaka, Dhaka, Bangladesh

Aims & Objectives: Hematopoietic stem cell transplant (HSCT) is an integral part of the management of patients with hematologic disorders. HSCT program at Evercare Hospital Dhaka (EHD) commenced in March 2016 and till now 60 stem cell transplant procedures have been carried out, which is the largest number of transplants performed in a single center in our country.
Patients / Materials & Methods: Data were analyzed retrospectively for all patients who underwent HSCT over a period of around 6 years,from March 2016 to June 2022.
Results: Out of the total of 60 patients, autologous and allogeneic were 40 and 20 respectively with a male-female ratio, of 2:1. Median age for auto-HSCT and allo-HSCT were 49 years (range13-71) and 29 years (range 7-53) respectively. Indications for auto-HSCT were: myeloma 21 (52.5%), lymphoma 18(45.5%) and AML 1(2.5%) while for allo-HSCT: AML 65% (13),ALL 15% (3), R/R Lymphoma 10% (2), MDS 5% (1), Acute Undifferentiated Leukaemia 5%(1). For all patients, peripheral blood stem cells were used. Conditioning for auto HSCT was mainly melphalan and BEAM. For an allogeneic transplant, both myeloablative and reduced intensity conditioning was used with a selection of standard protocol and total body irradiation (TBI). The median time of neutrophil engraftment for auto-HSCT was 11 days (range 8-14) and for allo-HSCT was 14 days (range 8-19). Transplant-related mortality (TRM) for allo-HSCT was 10% (2) but no TRM was observed in auto-HSCT. Primary graft failure for auto-HSCT was not observed whereas for allo-HSCT in only one patient (5%). During a median follow-up of 13 months for auto-HSCT overall survival (OS) was 85% and the cumulative incidence of relapse was 27.5%. For allo-HSCT, the median follow-up period was 1 year with an OS of 70%, and the cumulative incidence of relapse was seen at 20%. In auto-HSCT, the complication mainly was infection documented in 5 cases (Clostridium difficile 4, E. coli 1, COVID 1).For allo-transplant complications include acute graft-versus-host disease (GvHD) 55.5% (mostly limited),Chronic GvHD in 22.2% cases, cytomegalovirus (CMV) infection 50%, documented bacterial infection 25%, haemorrhagic cystitis 15% and VOD of liver 5%.
Discussion and Conclusion: Our overall result as a new center is encouraging but longer follow-up and a larger number of cases will give us a more realistic picture.

Disclosure of Interest: None Declared

Keywords: BONE MARROW TRANSPLANT, LARGEST CENTRE, OUTCOME

Poster Presentation

LEUKEMIAS (225)

OUTCOME OF ALLO-SCT FROM A PRIVATE CENTER IN BANGLADESH

Quazi S. Haq[*1], Masba U. Chowdhury[1], Zannatun Nesa[1], Kaniz F. Rahman[1], Menoty P. Mukti[1], Dilshad Jahan[1], Tangia Muquith[1], Muhammad S. I. Rumi[1], Md. Sazzad Z. Chowdhury[1], Md.Maruf A. Hasan[1], Shamim A. Begum[1], Abu Jafar M. Saleh[1]
[1]Hematology & SCT, Evercare Hospital , Dhaka, Bangladesh

Aims & Objectives: Allogeneic hematopoietic stem cell transplantation offers a potentially curative treatment option for a number of otherwise fatal hematological diseases. This study reports the initial data on first 20 allogeneic SCT for hematological malignancies at Evercare hospital Dhaka from Bangladesh.
Patients / Materials & Methods: Patients with hematological malignancies were evaluated who have received allogeneic PBSC transplantation of Filgrastim (G-CSF) mobilized peripheral blood stem cells. Donors include HLA-identical siblings as well as haplo-identical. Indication for SCT were, AML –13, ALL - 3 MDS – 1, Acute undifferentiated leukemia-1, Refractory HD-1 and one for refractory DLBCL. Pre-transplant workup done as per standard protocol. Stem cell source was peripheral and mobilized with G-CSF at a dose of 10µg/kg daily for five days. Different conditioning regimen used for most of them.
Results: Total 20 allogeneic transplants were carried out from Aug 2019 to April 2022 including 5 haplo-identical related transplants. Among them 15 were males and 5 were females. Eighteen patients achieved successful engraftment. Median time to engraftment (ANC > 0.5 x 10^9 /L) was 13 days. Six patients died, three of them before 100 days (post-transplant). Four patients died from disease relapse. Post-transplant complications included acute graft versus host disease (GvHD) 55.5 % (mostly limited), Chronic GvHD 27.7 %, hemorrhagic cystitis 15 %, VOD liver 5 %, documented bacterial infections 25 %, cytomegalovirus (CMV) infection 50 %, among the evaluable patients. An unexpected and rare post-transplant complication found in two patients, which is cyclosporine induced neurotoxicity. Transplant related mortality was 10 %. Two patients died before engraftment and in both cases cause of death was protracted neutropenia with septic shock, and one of them had primary graft failure. Four more patients died during follow up period due to disease relapse. Overall survival at a median follows up of 1 year was 70 %.
Discussion and Conclusion: Allogeneic stem cell transplantation is a pertinent treatment option in patients with hematological malignancies. Our outcomes are comparable with results from neighboring countries as well as the western world.

Disclosure of Interest: None Declared

Keywords: Allogeneic transplantation, hematopoietic stem cell transplantation, Treatment outcome

Poster Presentation

LEUKEMIAS (229)

REPORT OF POST BMT INFECTIOUS COMPLICATIONS FROM A PRIVATE SETUP IN BANGLADESH

Dr. Menoti P. Mukti*[1], Quazi S. Haq[1], Masba U. Chowdhury[1], Zannatun Nesa[1], Kazin F. Rahman[1], Dilshad Jahan[1], Tangia Muquith[1], Muhammad S. I. Sikder Rumi[1], Md.Sazzad Z. Chowdhury[1], Maruf A. Hasan[1], Shamim A. Begum[1], Abu Jafar M. Saleh[1]
[1]Haematology & SCT, Evercare Hospital Dhaka, Dhaka, Bangladesh

Aims & Objectives: Hematopoietic cell transplant (HCT) patients are at risk of infectious diseases resulting from bacterial, viral, fungal, and parasitic infections which account for most of the morbidity and mortality after Hematopoietic stem cell transplantation (HSCT). Pattern and risk of developing infections vary according to the stem cell source, donor type, conditioning intensity, region, prophylaxis strategy and co morbidities, such as graft versus host disease and invasive fungal infection. The aim of this study is to present an overview of infections following HSCT
Patients / Materials & Methods: Total of 60 patients from March, 2016 to May, 2022 were reviewed retrospectively. The number of Allogeneic HSCT (Allo SCT) was 20 and autologous HSCT (ASCT) was 40. We reviewed medical records of our patients that describes microbiologically confirmed incidence rates of infections and deaths during the transplant period.
Results: In case of Allo SCT, during pre-engraftment period, bacterial infection was predominant. Documented bacterial infection was 25% of which E. coli and Clostridium difficile were the most common. After engraftment predominant is viral, caused by cytomegalovirus, was developed in 50% of patients. Although there was no documented fungal infection in our center except for a single case of esophageal candidiasis. In Auto SCT, Clostridium difficile was most common bacterial infection documented in 15%. The overall mortality 20 % (12/60) and infection related mortality rates in allogeneic was 10 % (2/20) and in autologous all patients died due to disease relapse
Discussion and Conclusion: Autologous HSCT leads to more rapid recovery of immune function than allogenic HSCT, thus infections are less in Autologous than allogenic. As infection was one of the main post- HSCT complication, more attention should be given to the management of infections in HSCT recipients.

Disclosure of Interest: None Declared

Keywords: Disease relapse, Graft versus Host Disease, Haemopoietic stem cell transplantation, Invasive fungal infection

Poster Presentation

LEUKEMIAS (231)

EXPERIENCE OF TBI CONDITIONING- FIRST TIME IN BANGLADESH IN EVERCARE HOSPITAL, DHAKA

Dr. Menoti P. Mukti[*1], Quazi S. Haq[1], Masba U. Chowdhury[1], Zannatun Nesa[1], Kazin F. Rahman[1], Dilshad Jahan[1], Tangia Muquith[1], Muhammad S. I. Sikder Rumi[1], Md.Sazzad Z. Chowdhury[1], Maruf A. Hasan[1], Shamim A. Begum[1], Abu Jafar M. Saleh[1]
[1]Haematology & SCT, Evercare Hospital Dhaka, Dhaka, Bangladesh

Aims & Objectives: Total body irradiation (TBI) is an established part of conditioning regimens prior to stem cell transplantation in lymphoid malignancy with high risk of CNS relapse. But it is associated with long term toxicity. Having dual role of cytotoxic and immunosuppressive it allows to eliminate disease and create space in marrow for engraftment. It also impairs the immune system from rejecting the foreign donor cells being transplanted. It has greater tumor cytotoxicity and better tissue penetration. The aim is to analyze survival, immediate and long-term toxicity associated with TBI as a conditioning regimen.
Patients / Materials & Methods: Total 6 patients were analyzed between September, 2020 and April, 2022. Conditioning treatment as per protocol consisted of chemotherapy (CT) and TBI with 3 Gy o.d on 3 consecutive days to 2 Gy b.i.d with total dose of 12 Gy. One patient received 2 Gy o.d as an immunosuppressive regimen.
Results: Out of 6 patients, 2 patients died due to early relapse after 3 and 2 months respectively. The rest of the 4 patients are in remission till now with follow-up up to 2 and 1 year respectively. Almost all patients developed TBI induced severe nausea, vomiting, mucositis, loose motion and generalized weakness. One patient developed TBI induced dermatitis, one TBI induced Gastrointestinal (GI) toxicity.
Discussion and Conclusion: TBI containing conditioning regimens in stem cell transplantation (SCT) are highly effective. In low resource setting like Bangladesh TBI is first introduced in our hospital. Comparing other patients who received other myeloablative regimen, TBI groups experienced less toxicity and mortality. Efforts should be undertaken to optimize TBI techniques and accompany the treatment with systematic follow-up programs.

Disclosure of Interest: None Declared

Keywords: graft rejection, stem cell transplantation, TBI related toxicty, Total Body Irradiation

Poster Presentation

LEUKEMIAS (233)

PROGNOSTIC FACTORS IN PATIENTS WITH RELAPSED ACUTE LEUKEMIA AFTER STEM CELL TRANSPLANTATION

Yang Gao*[1], Zhuoyue Shi[1], Hengwei Wu[1], Fei Gao[1], Jimin Shi[1], Yi Luo[1], Jian Yu[1], Xiaoyu Lai[1], Lizhen Liu[1], Huarui Fu[1], He Huang[1], Yanmin Zhao[1]
[1]Bone Marrow Transplantation Center, the First Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou, Zhejiang, P. R. China, Hangzhou , China

Aims & Objectives: This study aimed to clarify the survival and prognostic factors of acute leukemia (AL) patients with relapse after allogeneic hematopoietic stem cell transplantation (HSCT) and to establish a simple risk stratification system for post-relapse overall survival (prOS).
Patients / Materials & Methods: The 178 AL patients relapsing after transplantation who were transplanted in the Institute of Bone Marrow Transplantation Center, The First Affiliated Hospital, Zhejiang University School, China, between January 2013 and December 2018 were used to establish the prOS risk stratification system. The 54 AL patients relapsing after transplantation who were transplanted in our center between January 2019 and December 2020 were grouped according to this prOS risk stratification system to further verify its feasibility.
Results: This retrospective study included 178 patients with acute leukemia who relapsed after transplantation, with a median age of 29.6 (12.0-64.6) years. The median follow-up time after relapse was 185 (3-2633) days. The median disease-free survival (DFS) and median prOS were 174 days and 204 days, respectively; the 1-, 3-, and 5-year cumulative prOS were 31.6%, 18.0%, and 10.7%, respectively.
Cox proportional hazards regression model analysis showed that patients with grade 3-4 acute graft-versus-host disease (aGVHD) after transplantation and >20% blasts at relapse had worse prOS; patients with chronic graft-versus-host disease (cGVHD) after transplantation, recurrence later than 1 year after transplantation and with no bone marrow involvement had better prOS. The results of the multivariate analysis were summarized in Table 1.
The 178 AL patients were divided into three groups according to the number of independent risk factors affecting prOS (0-2 risk factors, 3 risk factors, 4-5 risk factors, defined as low risk, intermediate risk, and high risk, respectively). The 1-year prOS of the three groups were 61.7%, 29.4%, and 11.8%; the median prOS were 871 days, 230 days, and 97 days, respectively, with statistical significance (P<0.001). (Figure 1) To verify this risk stratification system, 54 AL patients who relapsed after transplantation from 2019 to 2020 were also divided into three groups according to the number of risk factors. The 1-year prOS of the three groups were 70.1%, 43.0%, and 6.7%; the median prOS were 479 days, 322 days, and 115 days, which were statistically significant (P<0.001). (Figure 2)
Discussion and Conclusion: In general, tumor burden at relapse, time and site of relapse, and the occurrence of GVHD are closely related to the prognosis in patients with relapsed AL after HSCT. Identifying prognostic factors for relapsed patients after transplantation and individualizing treatment for patients with poor prognosis so that they can achieve longer survival are critical.

Disclosure of Interest: None Declared

Keywords: acute leukemia, allogeneic hematopoietic stem cell transplantation, prognosis, relapse

Poster Presentation

LEUKEMIAS (235)

ACUTE MYELOID LEUKAEMIA WITH PULMONARY INVOLVEMENT MANAGED WITH EXTRA CORPOREAL MEMBRANE OXYGENATION

Shilpa Prabhu[*1], Richard Dillon[2], Caroline Besley[1]
[1]Bone marrow transplant and CART, University Hospital Bristol and Weston, Bristol, [2]Haematology , King's College London, London , United Kingdom

Aims & Objectives: Role of Extracorporeal Membrane oxygenation in managing patients with acute myeloid leukemia with pulmonary involvement
Patients / Materials & Methods: An 18 year old female presented to the Emergency department with respiratory distress in March 2021. CT chest showed extensive ground glass nodules bilaterally. In view of worsening breathlessness she was mechanically ventilated, despite prone ventilation, oxygenation could not be adequately maintained. Hence she was transferred urgently to a tertiary centre where she was initiated on veno –venous ECMO was started on chemotherapy while on ECMO . Following clinical improvement, she was de-cannulated after 5 days and then underwent tracheostomy. Broncho alveolar lavage (BAL) fluid isolated acute myeloid leukaemia (AML) blasts, along with medullary disease. Genetics confirmed KMT2A rearranged AML. She underwent induction with Daunorubicin, Cytarabine and Gemtuzumab Ozagamycin. Post induction bone marrow was in remission, BAL had persistent blasts.She received re-induction with Fludarabine,Cytarabine , Filgrastim , Idarubicin (FLAG-IDA) . Post FLAG-Ida bone marrow was in molecular remission with reduction in blasts in BAL fluid to 2%, further therapy was escalated to FLAG-Ida with Venetoclax ;after which she maintained molecular remission in the bone marrow with no evidence of AML on BAL. This response was consolidated by a myeloablative haplo-identical transplant with Thiotepa, Busulfan and Fludarabine conditioning followed by Ciclosporine , Mycophenolate mofetil and post-transplant Cyclophosphamide as immunosuppression. She developed grade 2 skin GVHD after stopping the immunosuppression, this required initiation of oral steroids .She is now one year post-transplant, with bone marrow in molecular remission and full donor chimerism.
Results: After initiation of the chemotherapy , her lung shadows improved significantly, as shown in the image . The images displayed in the bottom line are after 2 cycles of chemotherapy.
Discussion and Conclusion: Leukaemia related lung injury can occur due to high blast counts causing poor tissue perfusion; pulmonary leukemic infiltration or acute lysis pneumopathy, a cell mediated process following chemotherapy [7]. VV ECMO is treatment option in patients with HM presenting in ARF. The general consensus is that in patients with ARF and HMs, ECMO is not offered routinely. However, with the advent of newer chemotherapy and targeted chemotherapy, improvements in management of acute respiratory distress syndrome and careful patient selection, ECMO can be used as an artificial lung in providing extra corporeal gas exchange and minimising trauma to the lungs due to mechanical ventilation.In this way , ECMO can ‘buy time’ for the action of chemotherapy and reduce the early mortality from ARF, with successful long term outcomes.

Disclosure of Interest: S. Prabhu But No Conflict with: None, R. Dillon But No Conflict with: None, C. Besley But No Conflict with: None

Keywords: acute myeloid leukemia, acute respiratory distress syndrome, extra corporeal membrane oxygenarator, pulmonary involvement

Poster Presentation

LEUKEMIAS (250)

EXTRAMEDULLARY RELAPSE POST HAPLO-TRANSPLANT IN CBF AML (T8;21) WITH FLT3-ITD & NUP98-NSD2 MUTATION

Nitin Chaudhary[*1], Anshul Gupta[1]
[1]Hematology, SGPGI, Lucknow, Lucknow, India

Aims & Objectives: .
Patients / Materials & Methods: .
Results: .
Discussion and Conclusion: A 15 year male presented with right eye proptosis, lower limb paraplegia and leucocytosis. On evaluation was found to have AML with translocation t(8;21). Molecular analysis revealed FLT3-ITD (allelic ratio <0.5) and NSD2 mutation. He received radiotherapy, 3+7 Induction therapy followed by 3 cycles of high dose cytarabine. Post BM showed morphological remission. He was then taken for transplant with sister having 7/10 match. Flu Bu Cy myeloablative conditioning was given. GVHD prophylaxis given with PTCy, MMF and Cyclosporine. He achieved and maintained 100% donor chimerism. After 9 months post transplant he presented with decreased oral intake and vomiting. PET-CT showed pararectal soft tissue lesion with extension to left ischiorectal fossa. Biopsy was suggestive of Myeloid Sarcoma while BM examination showed no excess of Blasts. Radiotherapy and DLI was attempted but PET CT showed residual disease. Presence of NSD2 mutation confers a very high risk and is associated with very poor prognosis. It is seen in a subset of patients carrying FLT3 mutation.

Disclosure of Interest: None Declared

Keywords: AML, FLT3, haplo-identical, NUP98-NSD2

Poster Presentation

LEUKEMIAS (260)

GOOD OUTCOMES OF CAR-T BRIDGING TO ALLO-HSCT FOR RELAPSED/REFRACTORY PH-POSITIVE B-ALL

Zhanxiang Liu*[1], Kong Gao[1], Fan Wu[1], Zhihui Li[1], Yongqiang Zhao[1], Yanzhi Song[1], Tong Wu[1]
[1]Bone Marrow Transplantation, Beijing Boren Hospital, Beijing, China

Aims & Objectives: Chimeric antigen receptor T-cell (CAR-T) therapy bridging to allogeneic hematopoietic stem cell transplantation (HSCT) is the most effective therapy for relapsed/refractory (r/r) B cell acute lymphoblastic leukemia (B-ALL). We evaluated the efficacy and safety of CAR-T bridging to HSCT for patients with relapsed/refractory (r/r) Ph+ B-ALL.
Patients / Materials & Methods: Between November 2018 and June 2022, 25 consecutive patients with r/r Ph+ B-ALL who received CAR-T bridging to HSCT in our hospital were included. The median age was 30(3-59) years old. The median disease course was 50 (15-129) months. Twelve patients (48%) were BCR-ABL1 positive and 13 patients (52%) were in relapse before CAR-T. Fifteen (60%) got remission by CART therapy, 10 remained BCR-ABL1 + (9) and relapse (1) state before HSCT. 10 patients (40%) had T315I mutation. 8 patents (32%) underwent the second transplantation. Patients received HSCT from sibling matched 4(16%), haploidentical 17(68%) and unrelated (4, 16%, HLA 10/10 or 9/10 matched) donors, respectively. Myeloablative conditioning regimens with total body irradiation (fractionated, total 10 Gy) /etoposide (200mg/m2 x 3) /fludarabine (30mg/m2 x 5) or cyclophosphamide (1.8g/m2 x 2) /rabbit anti-T-cell globulin were used. Cyclosporine, mycophenolate mofetil and methotrexate were employed for graft-versus-host disease (GVHD) prophylaxis. All patients received sensitive TKIs based on their ABL1 gene mutations up to 2 years post-transplantation.
Results: All patients achieved durable engraftment. the median follow-up time was 8 (1-36) months and two-year overall survival (OS) and leukemia free survival (LFS) was 84% and 76%. 5 patients remained BCR-ABL1+ after HSCT, 1 of them get remission at later follow-up, 2 still positive and alive up to date, 1 died due to relapse. 1 patient developed grade III~IV aGVHD. All of them were resolved with immune-suppressants except 1 died from grade IV aGVHD. One died of alveolar hemorrhage and one died of severe pulmonary infection six and eight months after HSCT, respectively. Ten patients had CMV reactivation and no EBV reactivation reported. Two patients had mild hemorrhagic cystitis. The non-relapse mortality (NRM) was 12% (3/25). For the ten patients with T315I mutation, one died of relapse and one died of aGVHD. The two years OS and LFS were both 80%. For the 10 patients with BCR-ABL1+ before HSCT, 6 got continually MRD-remission and alive, 2 remained MRD+ and alive, one patient died of alveolar hemorrhage and one died of severe GVHD.
Discussion and Conclusion: Our results indicate that CAR-T bridging to allo-HSCT is an excellent therapeutic method with very low NRM for r/r Ph+ B-ALL. The two years OS and LFS can respectively reach to 84% and 76%. Even for patients with T315I mutation or MRD positive before HSCT, survival was also remarkedly good.

Disclosure of Interest: None Declared

Keywords: Allo-HSCT, CAR-T, Ph-positive B-Cell Acute Lymphoblastic Leukemia

Poster Presentation

LEUKEMIAS (267)

AUTOIMM HEMOLYTIC ANEMIA AFTER HAPLOIDENTICAL TRANSPL IN ACCELERA PHASE OF CML

Mehrdad Payandeh*[1], Mehrak payandeh[1]
[1]Kums , Kermanshah , Iran

Aims & Objectives: A 28 years old women in accelerated phase of cml with poor tolerated of TKI therapy in cml refer for haploientical AlLogenic transplant of his brother .
6 days after transplant with decreased abruptly of Hb and hyperbilirubin with positive direct Coombs , treated with plasmapheresis , Methylprednisolone , IVIG.
Patients / Materials & Methods: After conditioning regimen of busulfan cyclophosphamide combined with dasatinib ,in Peripheral blood stem cell
Results: Despite of good conditioning processing and toleration in patient she complicated with catastrophic hemolytic anemia that caused cardiac arrest.
Discussion and Conclusion: Catastrophic hemolysis is an life threatening event after haploientical transplant in high risk cml that need close evaluation of patient for this complication and sooner of doing plasmapheresis and low dose cotton therapy can be live saving for patient.

Disclosure of Interest: None Declared

Keywords: Cml, Haploientical, Hemolysis, Plasmapheresis

Poster Presentation

LEUKEMIAS (301)

MOLECULAR EVALUATION OF GENE MUTATION PROFILES AND COPY NUMBER VARIATIONS IN ACUTE MYELOID LEUKEMIA

Jagdish P. Meena[*1], Nivedita Pathak[1], Aditya K. Gupta[1], Sameer Bakhshi[2], Ritu Gupta[3], Harshita Makkar[1], Rachna Seth[1]
[1]Division of Pediatric Oncology, Department of Pediatrics, [2]Department of Medical Oncology, Dr. B.R.A. IRCH, [3]Laboratory Oncology Unit, Dr. B.R.A. IRCH, All India Institute of Medical Sciences, New Delhi, India

Aims & Objectives: Cytogenetically normal acute myeloid leukemia (AML) is currently categorized as intermediate-risk, yet this group is quite heterogeneous. The objectives of this study were to investigate the mutation profile of targeted genes and copy number variations (CNVs) in normal karyotype and normal cytogenetics (NKC) AML and correlate it with treatment response
Patients / Materials & Methods: This prospective study was conducted from October 2018 to December 2020. The next-generation sequencing (NGS) (30 gene panel) and chromosomal microarray analysis (CMA) using Affymetrix Cytoscan 750 K GeneChip were performed in NKC-AML.
Results: A total of 94 patients aged ≤18 years were screened. After excluding 24 patients, 70 patients with AML underwent conventional karyotyping/cytogenetic analysis. Forty-five (64.3%) had abnormal karyotype/cytogenetics (AKC) and 25 (35.7%) had NKC. Twenty-three out of 25 NKC-AML were further processed for gene mutation profiles and CNVs using NGS and CMA, respectively. Twenty-two out of 23 (95.7%) patients were detected to have mutations in various genes. The common mutations were: NRAS, NPM1, CEBPA, KRAS, KIT, RUNX1, NOTCH1, WT1, GATA1, GATA2, FLT3, KMT2D, FLT3-TKD, and PHF6. Copy number variations (CNVs) were detected in nine patients (39%), and the four (17%) had a loss of heterozygosity (LOH). A long contiguous stretch of homozygosity was detected on ch5, ch7, ch11, and ch19. The gains were more common than losses. The gains were observed on ch 8, 9, 14, 19, 21, and 22, and the losses were detected on ch 7 and 10. Monosomy was observed in three patients. Three patients (monosomy 7, n=2 and FLT-ITD, n=1)] were reclassified to the high-risk category. Post-induction, complete remission was achieved in all evaluable patients.
Discussion and Conclusion: NKC-AML patients have genetic abnormalities that can be detected by more advanced techniques like NGS and CMA. These genetic abnormalities play a role in risk stratification that may remain hidden in otherwise NKC-AML.

Disclosure of Interest: None Declared

Keywords: Acute myeloid leukemia, Chromosomal microarray analysis, Gene copy number variations, Mutation profiles, Next-generation sequencing

Poster Presentation

LEUKEMIAS (306)

A COMPREHENSIVE OUTCOME ANALYSIS OF CYTOGENETICS, MOLECULAR, AND SURVIVAL IN ACUTE MYELOID LEUKEMIA

Jagdish P. Meena* [1], Harshita Makkar[1], Aditya K. Gupta[1], Sameer Bakhshi[2], Ritu Gupta[3], Deepshi Thakral[3], Nivedita Pathak[1], Rachna Seth[1]
[1]Division of Pediatric Oncology, Department of Pediatrics, [2]Department of Medical Oncology, Dr. B.R.A. IRCH, [3]Laboratory Oncology Unit, Dr. B.R.A. IRCH, All India Institute of Medical Sciences, New Delhi, India

Aims & Objectives: Despite the advancements in diagnostic techniques and the discovery of newer chemotherapeutic agents, the outcome of acute myeloid leukemia (AML) remains dismal. The objectives of this study were to investigate the cyto-molecular analyses and survival outcomes of pediatric acute myeloid leukemia (AML).
Patients / Materials & Methods: This prospective study was carried out in a tertiary care hospital from October 2018 to December 2020. Karyotype and cytogenetics analyses were done to identify chromosomal aberrations, and PCR, RT-PCR, and fragment analysis were utilized for the targeted molecular panel.
Results: A total of 70 patients of AML aged ≤18 years were enrolled in this study. The cytogenetic analyses revealed abnormal karyotype/cytogenetics (AKC) in 64.3% of patients and normal karyotype/cytogenetics (NKC) in 35.7%. FAB M2 subtype showed frequent aberrant expression of CD19 marker. CD7, CD11b, and CD36a were significantly present in the absence of molecular markers. Common chromosomal abnormalities were t(8;21) translocation (55%), monosomy/deletion 7 (13%), monosomal karyotype (5%) and complex karyotype (3%). The fusion transcripts RUNX1-RUNX1T1 [t(8;21)](41%) and CBFB-MYH11 [(16;16)](3%) were detected by RT-PCR and FLT3-TKD D835 mutation (1.5%) by allele-specific oligo PCR. Fragment analysis revealed NPM1 (8%) mutation and FLT-ITD (9.5%) mutations. Complete remission was achieved in all evaluable patients. The median follow-up period of our patients was 225 days (IQR 28;426 days). The median event-free survival (EFS) in all patients was 11.9 months (95% CI, 5-12.6). The forty months overall survival probability (pOS) was 58% in all patients.
Discussion and Conclusion: The majority of patients had abnormal karyotype/cytogenetics. FAB M2 subtype showed frequent aberrant expression of CD19. The absence of molecular markers may suggest the presence of CD7, CD11b, and CD36a expression. The overall survival has increased considerably in LMIC.

Disclosure of Interest: None Declared

Keywords: Acute myeloid leukemia, Cytogenetics, Karyotype, Molecular, Survival

Poster Presentation

LEUKEMIAS (325)

VALIDATION OF ELN 2022 RISK STRATIFICATION FOR AML- COMPARISON WITH ELN 2017 & 2010

Ramesh Balasubramanian*[1], Vandana Arya[2], Nitin Gupta[1], Jyoti Kotwal[2]
[1]Clinical Hematology, [2]Hematology, Sir Ganga Ram Hospital, New Delhi, India

Aims & Objectives: The major change in ELN 2017 was addition of FLT3-ITD allelic ratio(AR). NPM1 and FLT3-ITD mutated with low allelic burden(AR<0.5) was assigned favourable risk group, whereas with AR>0.5 to Intermediate group. ELN 2022 has removed AR and assigned all FLT3-ITD mutated to intermediate risk. NGS plays a crucial role in establishing the risk categories in ELN 2022.
AIM:
To validate ELN 2022 risk stratification in AML patients with cytogenetics and molecular mutations and comparing it with ELN 2017 & 2010.
Patients / Materials & Methods: All AML patients presented to our hospital in past 3 years were diagnosed by bone marrow aspiration, biopsy and flowcytometry. Karyotyping and AML-PCR panel for NPM1, FLT3 ITD, AML::ETO, Inv(16)were done in all patients. FLT3-ITD allelic ratio was calculated by fragment analysis. NGS was done in selected patients due to financial constraints.
Results: A total of 113 AML patients with median age 54 years (30-83) were included. The study group comprises 55.3% males and 44.7% females. Normal karyotype (NK) was found in 60% (60/100). Amongst NK, mutations were present in 56.7% (34/60). Overall, clinically significant mutations were detected in 56.7% (64/113) [Figure 1]. Of total, 21.2% (24/113) were only NPM1 mutated (Table 1). 3.5% (4/113) cases with NPM1 and low AR FLT3-ITD mutation were shifted from Intermediate to Favourable risk group of ELN 2017. According to ELN 2022, they were shifted back to Intermediate risk group as in ELN 2010. The shift of patients in risk groups amongst ELN 2022, 2017 & 2010 is depicted in Figure 2. All patients were treated with standard-of-care chemotherapy with 7+3 induction or Azacytidine, according to their fitness. AlloHSCT was done in intermediate and adverse risk patients who are fit. The response to therapy is shown in Table 2. Kaplan-Meir survival analysis was done in patients followed upto 2 years. OS and DFS at 2 years were not statistically significant amongst different ELN 2017 risk groups.
Discussion and Conclusion: In our study, the patients having FLT3-ITD low AR shifted from intermediate to favourable risk in ELN 2017 are shifted back to intermediate risk of ELN 2022 similar to ELN 2010. The 2year OS & DFS were not statistically improved in patients having low AR designated to favourable group in ELN 2017 as shown in our study. The survival of all FLT3-ITD patients were low, irrespective of AR. Thus, elimination of AR by ELN 2022 seems to be valid, though large scale study is required to conclude this. NGS for all patients, as emphasized by ELN 2022 is practically impossible in resource constrained countries like India. Assigning age-related mutations like only ASXL1 mutated to adverse risk also needs to be validated with large study population.

Disclosure of Interest: None Declared

Keywords: AML, ELN 2022, RISK STRATIFICATION, VALIDATION

Poster Presentation

LEUKEMIAS (335)

COMBINATION THERAPY VS MONOTHERAPY OF HMAS IN ACCELERATED OR BLAST PHASE MYELOPROLIFERATIVE NEOPLASM

Jia Chen*[1], kefei Wang[1], Zhijian Xiao[1], Zefeng Xu[1]
[1]Institute of Hematology and Blood Diseases Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, tianjin, China

Aims & Objectives: There is a lack of evidence regarding whether combination therapy of hypomethylating agents (HMAs) is associated with improved outcomes than HMAs alone in patients with MPN-AP/BP.
Patients / Materials & Methods: Pubmed, Embase, Web of Science, and Cochrance library databases were searched for studies from inception of each database until December 31, 2021. Data extraction and synthesis were conducted following the PRISMA reporting guideline
Results: The pooled ORR was higher with HMAs plus venetoclax (47%, 95%CI: 37-57%; I2=18%) than HMAs monotherapy (32%, 95%CI: 23-42%; I2=73%), but there was not statistically significantly different in meta-regression analysis (p=0.1716). CR/CRi rates were reported by 6 studies of HMAs plus venetoclax. The pooled CR/CRi rate was 36% (95%CI: 27-46%; I2=0%) for HMAs plus venetoclax and 19% (95%CI: 12-27%; I2=61%) for monotherapy, which reached statistically significant difference in meta-regression analysis (p=0.0204). PR rates were reported by 4 studies of HMAs plus venetoclax. The pooled PR rate was 12% (95%CI: 6-20%; I2=0%) for HMAs plus venetoclax and 13% (95%CI: 9-19%; I2=26%) for monotherapy, which did not reach statistically significant difference in meta-regression analysis (p=0.8577).
The ORR of pooled studies was 41% (95%CI: 33-50%; I2=0%) for HMAs plus Ruxolitinib and 32% (95%CI: 23-42%; I2=73%) for HMAs alone, which was not statistically significantly different in meta-regression analysis (p=0.2981). The pooled CR/CRi rate was 31% (95%CI: 22-40%; I2=0%) for HMAs plus Ruxolitinib and 19% (95%CI: 12-27%; I2=61%) for monotherapy, but there was not statistically significant different in meta-regression analysis (p=0.1020). The pooled PR rate was 18% (95%CI: 8-32%; I2=65%) for HMAs plus ruxolitinib and 13% (95%CI: 9-19%; I2=26%) for monotherapy, which did not reach statistically significant difference in meta-regression analysis (p=0.4113).
We summarized the proportion of patients with CR/CRi underwent Allogeneic hematopoietic stem cell transplantation (allo-HSCT) in each treatment group. The rates of received allo-HSCT were 70% (95%CI: 34-95%; I2=62%), 25% (95%CI: 8-48%; I2=0%) and 54% (95%CI: 19-87%; I2=54%) for patients who received HMAs plus venetoclax, HMAs plus ruxolitinib and HMAs alone, respectively, with no statistically significant difference in meta-regression analysis.
Discussion and Conclusion: We confirmed that the use of HMAs plus venetoclax was associated with better outcomes for unfit MPN-AP/BP patients and may offers more opportunity of allo-HSCT.

Disclosure of Interest: None Declared

Keywords: Accelerated / blast phase, Hypomethylating agents, Myeloproliferative neoplasms, post-MPN AML, Venetoclax

Poster Presentation

LEUKEMIAS (369)

A SUCCESSFUL CASE OF ALLOGENIC-HSCT FOR AML-M4 PATIENT WITH FLUDARABIN MELPHALAN CONDITIONING

Damai Santosa[*1,2], Budi Setiawan[1], Eko Adi Pangarsa[1], Daniel Rizky[1], Muji Rahayu[3], Like Rahayu[3], Christina Hari Nawangsih Prihharsanti[4], Catharina Suharti[2]
[1]Division of Hematology Medical Oncology, Department of Internal Medicine, Dr. Kariadi Hospital, [2]Division of Hematology Medical Oncology, Department of Internal Medicine, Diponegoro University, [3]Clinical Pathology, Dr. Kariadi Hospital, [4]Radiology, Diponegoro University, Semarang, Indonesia

Aims & Objectives: The clonal growth and ensuing rise in malignant myeloid precursors in the bone marrow and peripheral blood are hallmarks of acute myeloid leukemia (AML), a hematologic malignancy. Allogeneic hematopoietic stem cell transplantation is the consolidation treatment with the best possibility of sustained complete remission (CR) in AML patients (allo-HSCT), especially for high risk patients. We reported a case report with diagnosed as AML.
Patients / Materials & Methods: A 36-year-old man was diagnosed with AML-M4 by the FAB classification in January 2021. His chromosome analysis showed a 46, XY karyotype without any cytogenetic abnormalities. He was treated with induction chemotherapy (cytarabine and daunorubicine). On day 21, from bone marrow aspiration examination, he achieved a complete remission, and underwent consolidation chemotherapy with high dose cytarabine 3 cycles. He had a matched HLA donor from one out of his three siblings. His donor was his older sister with CMV seropositive status. His conditioning included fludarabine 25 mg/m2 (D-6 until D-2) and melphalane 120 mg/m2 (D-1). Because of the limited supply, we used combination of melphalan injection for 80% dosage and oral preparation for the rest. Because of his CMV seropositive also positive, he received valgancyclovir 450 mg b.i.d for 21 days before transplant. The product was given as a fresh infusion.
Results: The patient had grade 1-2 skin and liver GVHD. He had neufrophyl engraftment on day 17th, methotrexate and tacrolimus were used for GVHD prophylaxis. Patient currently is still survive in good quality of live with durable response.
Discussion and Conclusion: In recent years, efforts to treat newly diagnosed AML have mostly been directed at enhancing induction chemotherapy. However, the development of algorithms intended to identify individuals likely to benefit from allo-SCT in CR1 has been emphasized due to the growing accessibility of allo-SCT.This is the longest durable response known after allogenic-HSCT procedure in Indonesia. Allogenic-HSCT for AML patients is consolidation especially for high risk AML. With this success experience, we hope to increase the proportion of AML patients consolidated with allogenic-HSCT.

Disclosure of Interest: None Declared

Keywords: Allo HCT, AML, FLu-Mel, Survival

Poster Presentation

LEUKEMIAS (383)

G-CSF MOBILIZED STEM CELL COLLECTION AND OUTCOME OF 40 CASES OF AUTO SCT

Kaniz F. Rahman*[1], Abu Jafar Mohammed Saleh[1], Quazi Smita Haq[1], Masba Uddin Chowdhury[1]
[1]Hematology, Evercare Hospital, Dhaka, Bangladesh

Aims & Objectives: Introduction: Stem cell is collected for autologous stem cell transplant using G-CSF alone or by Chemo- GCSF. At Evercare Hospital Dhaka we used GCSF only mobilization for 40 cases of auto SCT.
The objective of our study is to analyse 40 cases of auto SCT mobilized with GCSF and compare with other cpublished data.
Patients / Materials & Methods: Methods: Total 40 patients with different hematological malignancies were evaluated from March 2016 to June 2022 who received auto SCT. Mobilization was done with GCSF at a dose of 10µg/kg daily for 5days. Stem cells were collected by apheresis using both spectra Optia (Version 11) and Cobe Spectra (Version 7.0). CD34 Cell dose was calculated from collected stem cell using BD stem cell enumeration (SCE) kit and then infused as per protocol. Cryopreservation was also done as needed.
Results: Result: Among 40 patients, male 25 (62.5%) and female 15 (37.5%), Median age was 49 years (13-71yrs). Indications for transplantation were Multiple Myeloma 21 (52.5%), Lymphoma 18 (45%), AML 1 (2.5%). Conditioning of these patients were done by Melphalan 28 (70%), BEAM 11 (27.5%), BEAM plus Thiotepa 1 (2.5%), BU-CY 1 (2.5%). Number of fresh and cryopreserved Stem cell were 24 (60%) and 16 (40%) respectively.
Median CD 34 dose was 5.8X106/kg body weight. All 40 patients achieved successful engraftment and median time of neutrophil engraftment was 11 days (8-14 days).
During transplant, there were no major complications except infection. Total documented infection was 5, among them Clostridium difficile 4, E. coli 1, Covid 1. Overall survival at a median follow up of 13 months was 85% and cumulative incidence of relapse was 27.5%.
Discussion and Conclusion: Conclusion: Stem cell collection with GCSF for auto SCT is feasible. Collection with optia or cobe spectra didn't show significant difference and overall outcome is satisfactory.
"No conflict of interest to disclose".

Disclosure of Interest: None Declared

Keywords: BUSULPHAN THIOTEPA, Granulocyte colony stimulating factor, stem cell transplantation

Poster Presentation

PEDIATRIC TRANSPLANTATION (110)

SOLUBLE HEMOJUVELIN MAY POSE A RISK FACTOR FOR DEATH AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION

Artur Slomka[*1], Monika Lecka[2], Katarzyna Albrecht[3], Michal Romiszewski[3], Ewa Zekanowska[1], Jan Styczynski[2]
[1]Department of Pathophysiology, [2]Department of Pediatric Hematology and Oncology, Nicolaus Copernicus University in Torun, Ludwik Rydygier Collegium Medicum, Bydgoszcz, [3]Department of Oncology, Hematology, Bone Marrow Transplantation and Pediatrics, Medical University of Warsaw, Warsaw, Poland

Aims & Objectives: Iron overload is a common and severe complication of hematopoietic stem cell transplantation (HSCT), with state-of-the-art data demonstrating prognostic implications. Although findings from preliminary studies have implicated a potential association between proteins that control iron metabolism and HSCT patients' outcomes, the precise mechanism beyond iron overload remains far from being understood. Soluble hemojuvelin (sHJV) is the critical protein that can lead to iron overload via suppression of hepcidin expression. Therefore, this pilot study was designed to investigate the relationship between sHJV levels and death in HSCT patients.
Patients / Materials & Methods: This study examined 21 pediatric patients who underwent allogeneic (n = 18) or autologous (n = 3) HSCT for malignancies at two medical university centers in Poland (Bydgoszcz, Warsaw) between February, 2019, and June, 2020. The main reasons for HSCT were acute myeloblastic leukemia (AML, n = 8) and acute lymphoblastic leukemia (ALL, n = 6). Blood samples for serum sHJV measurement by enzyme-linked immunosorbent assay (Cloud-Clone Corp., Katy, TX, USA) were collected one month after HSCT. Each patient was followed until their death or the end of the study period (early May 2022). We used a Student's t-test to compare post-transplant sHJV levels between survivors and non-survivors and performed a receiver operating characteristic (ROC) curve analysis to determine the availability and optimal cutoff value of sHJV levels for predicting the death of HSCT patients. Statistical significance was defined as $p < 0.05$.
Results: Of 21 HSCT patients, 12 were male (57.1 %), and the mean age was 8.5 ± 5.9 years. A total of six (28.6 %) patients died during the follow-up period. Post-transplant sHJV levels in non-survivors were almost 1.5 times lower than in survivors, however, the difference did not reach statistical significance (34.4 ± 12.5 ng/mL vs 49.2 ± 18.2 ng/mL, $p = 0.08$). The ROC curve analysis for post-transplant sHJV showed an area under the curve (AUC) of 0.789 (95% confidence interval (CI): 0.57 - 1.00, $p = 0.01$) for the prediction of death in HSCT patients. Post-transplant sHJV levels of 35.9 ng/mL were determined as the optimal cutoff value, with resulting sensitivity and specificity of 83.3% and 80.0%, respectively, for the prognosis of death.
Discussion and Conclusion: Decreased sHJV levels may increase risk of death for pediatric patients that underwent HSCT.

Disclosure of Interest: None Declared

Keywords: hematopoietic stem cell transplantation, hemojuvelin, iron, leukemia

Poster Presentation

PEDIATRIC TRANSPLANTATION (122)

PLERIXAFOR USE IN PERIPHERAL BLOOD HEMATOPOIETIC STEM CELL DONORS IN PEDIATRIC ALLOGENEIC HSCT.

Aditya Kumar Gupta[*1], Jagdish Meena[1], Rachna Seth[1,2], Pranay Tanwar[3], Poonam Coshic[4]
[1]Pediatrics, [2]AIIMS, New Delhi, India, [3]Laboratory Oncology, IRCH, [4]Transfusion Medicine, AIIMS, New Delhi, India

Aims & Objectives: The use of plerixafor for normal healthy allogeneic donors in pediatric HSCT is less reported. It is very important to have a good peripheral blood(PB) circulating hematopoietic stem cell(HSC) count if there is a constrain on the amount of blood volumes that can be processed for harvest e.g. if the donor's weight is significantly lighter compared to the recipient or the donor is considerably younger. A good PB-HSC count, yeilds adequate stem cell harvest and can prevent a second apheresis procedure for the donor.
Patients / Materials & Methods: In this retrospective analysis , we report the efficacy and safety of the use of plerixafor in five healthy allogeneic HSC donors and compare the outcomes with five others allogeneic HSCT's in which plerixafor was not used. Plerixafor was used at a dose of 0.24mg/kg, subcutaneously approximately 11 hrs prior to harvest. All donors were on granulocyte colony stimulating factor (GCSF) at a dose of 5 mcg twice a day for 4 days before getting plerixafor.
Donors were given plerixafor if it was essential to have a higher CD-34 stem cell to be given to the recipient e.g., for the haploidentical transplants or if the donor was of a lighter weight than the recipient.
In one case where there was a minor blood group incompatibility between the donor and the recipient and the isoagglutinin titres in the recipient were high, it was imperative that we gave as less donor plasma as possible and, plerixafor was used to increase the PB HSC count of the donor before harvest.
Results: Ten allogeneic HSCT were included in the analysis, 5 in which the donor received plerixafor and in the other five the donor did not get it. In all the HSCT, PB HSC were the product(table 1) . No significant difference in terms of recipients age and weight; donors age and weight and the CD 34 count in PB before plerixafor were there between the two groups. However, the CD-34 HSC count in the harvested product was significantly higher in the group that received plerixafor (p=0.032). The stem cell dose transfused to the patient was also higher when the donor got plerixafor, although the difference was not significant. None of the donors suffered any side effects and underwent the subsequent apheresis uneventfully.
Discussion and Conclusion: The use of plerixafor in healthy stem cell donors for allogeneic stem cell transplant allowed a better yield of stem cells . Such a strategy can be used when the donor is of a significantly lighter weight compared to the recipient, if the stem cell dose needs to be good (e.g. for haploidentical HSCT), if the plasma volume in the product needs to be less (e.g. in ABO mismatched HSCT) or if a second apheresis procedure is to be avoided for the donor (in view of poor stem cell yield of the first apheresis). In our experience the use of plerixafor was safe for the donors.

Disclosure of Interest: None Declared

Keywords: HSCT, pediatrics, plerixafor

Poster Presentation

PEDIATRIC TRANSPLANTATION (123)

USE OF PLERIXAFOR IN PEDIATRIC AUTOLOGOUS HSCT

Aditya Kumar Gupta[*1], Jagdish Meena[1], Rachna Seth[1], Pranay Tanwar[2], Poonam Coshic[3]
[1]Pediatrics, [2]Laboratory Oncology,IRCH, [3]Transfusion Medicine, AIIMS, New Delhi, India

Aims & Objectives: Pleraxifor for peripheral blood stem cell (PBSC) mobilization in children undergoing autologous hematopoietic stem cell transplantation is mainly used when there is a failure of initial attempt to mobilise . Data on Pleraxifor being used upfront is limited in literature.
Patients / Materials & Methods: In this retrospective study done from a single tertiary care center in India we report the efficacy and safety of the use of prelixafor in 10 children with relapsed/refractory solid tumors or lymphomas. All children apart from the HR NB were heavily pre-treated with chemotherapy (two or more than two lines of chemotherapy). The HR NB underwent autologous HSCT as a part of their consolidation. Prelixafor was used at a dose of 0.24mg/kg , subcutaneously approximately 11 hrs prior to harvest and if the CD 34 count the following day was not adequate a repeat dose was given .
Results: Ten patients (8 males) , with a median age of 8 years (range 2-18 years) received prelixafor before the planned peripheral blood stem cell harvest. All patients were on GCSF before administration of prelixafor for meidan of 4-7 days (dose of GCSF used was 5 mcg/kg twice a day of 10 mcg per kg once a day SC) . Median dose of GCSF pre prelixafor was 47.5mcg/kg (30-75) .All patients received a dose of GCSF immediately prior to the peripheral blood stem cell harvest.
The median CD 34 count (per cumm)/total leucocyte count (TLC) (per cumm) for all patients pre prelixafor was 29(3-95)/TLC 40991 (17400-65830) and in all patients except one there was a rise in the CD 34 post prelixafor to a median of CD34 of 148 (26-458)/ TLC 53195 (31390-95690) . In the 9 patients in whom there was a rise the percentage change in CD 34 was 225 (13-9467) . In 9 patients we had the values of the CD 34 count and TLC of the harvested product available and in all cases we could achieve a good yield.
Discussion and Conclusion: The use of perlixafor in the pediatric age group is being explored. In our cohort of heavily chemotherapy pretreated patients the use of prelixafor resulted in a satisfactory yield of peripheral blood stem cells . The youngest patients in
whome we used prelixafor was 2 years. None of the patients had any side effects and underwent the harvest procedure uneventfully.

Disclosure of Interest: None Declared

Keywords: autologous HSCT, pediatrics, plerixafor

Poster Presentation

PEDIATRIC TRANSPLANTATION (124)

MATCHED UNRELATED DONOR HSCT FOR IL-10 R B DEFECT

Aditya Kumar Gupta[*1], Rohan Malik[1], Jagdish Meena[1], K Padma Sagarika[1], Rachna Seth[1], Sushil Kabra[1]
[1]Pediatrics, AIIMS, New Delhi, India

Aims & Objectives: A female child born to a non-consanguineously married couple had presented with recurrent infections, foul smelling discharge through the introitus and erythematous skin lesions in the groin folds since early infancy. She had persistent diarrhoea. There were multiple perineal fissures and the colonic biopsy revealed severe cryptitis with mucosal depletion.
On investigating for a very early onset IBD she was diagnosed on the clinical exome sequencing with a likely pathogenic homozygous IL 10 Receptor B mutation resulting in IBD-12. This was a novel mutation on chromosome 21 that alters the ATG start codon and consequently affects its translation. Diversion ileostomy was performed, in view of the rectovaginal fistula.
Patients / Materials & Methods: The child was planned for a matched unrelated donor HSCT.
Results: She was admitted at 25 m of age for the HSCT. Conditioning regimen used consisted of busulfan, fludarabine and ATG. The child received a 10/10 HLA matched from a matched unrelated adult female donor with bone marrow stem cell product at a dose of 5.6 M CD34+/kg . Neutropjil and platelet engraftment occurred on day +15. Cyclosporine was used for GVHD prophylaxis. Post-transplant she had complications of a Staphococcus aureus Hickmann tunnel infection and CMV reactivation, which were successfully managed . She was discharged on day+46 after HSCT with the day+30 chimerism showing 100 % donor cells.
Discussion and Conclusion: Presently she is more than 3 months post HSCT, with resolution of the fistulae and erythematous skin lesions over the groin. She is being transitioned to a normal diet with no further diarrhoea.

Disclosure of Interest: None Declared

Keywords: HSCT, IL 10 receptor defect, MUD HSCT

Poster Presentation

PEDIATRIC TRANSPLANTATION (161)

HEMATOPOIETIC STEM CELL TRANSPLANTATION IN LYSOSOMAL STORAGE DISORDERS : A SINGLE CENTRE EXPERIENCE

Swathi P M* [1], Shobha Badiger[1], Pooja Mallya[1], Ravi Joshi[1], Shweta Pathak[1], Santosh Asangi[1], Monika Bhukar[1], Gayathri S[1], Manojit Chakarborty[1], Lakshmi T[1], Ritu Lamichhane[1], Kamini Kanagasabesan[1], Ruchira Misra[2], Sunil Bhat[1]
[1]Paediatric Hemato Oncology and BMT, Mazumdar Shaw Medical Center, Bangalore, [2]Paediatric Hemato Oncology and BMT, NH SRCC Children's Hospital, Mumbai, India

Aims & Objectives: Lysosomal storage disorders (LSD) comprise a heterogeneous group of disorders characterized by tissue substrate deposits caused by a deficiency of the enzyme. The affected individuals have visceral, skeletal, and neurological abnormalities and a limited life expectancy. The principle of Hematopoietic Stem Cell transplantation (HSCT) in LSDs is in cross-correction, where donor-derived myeloid cells produce enzymes, which are then taken up by enzyme-deficient host cells. Furthermore, the superiority of HSCT to enzyme replacement therapy (ERT) lies in its exploitation of donor-derived cells to migrate across the blood brain barrier and differentiate into tissue macrophages, known as microglia, which secrete the deficient enzyme to the central nervous system, improving neurocognitive outcomes.
Present study was aimed to study the clinical profile and outcome in patients with LSD post Allogeneic HSCT.
Patients / Materials & Methods: We retrospectively analyzed the data of 23 children with Lysosomal storage disorders who underwent HSCT at our center from Feb 2016 to Feb 2022.
Results: Out of the 23 cases, 15 were of Mucopolysaccharidosis, 2 Gauchers, 2 Niemann Pick, 1 each of Alpha- Mannosidosis, Krabbe disease, Metachromatic Leukodystrophy and Farber's Disease. (Disease and Transplant type details mentioned in Table 1 &2)
Majority were males 82 % (19/23). Mean age at transplant was 41 months (12-93 months). Graft source was peripheral blood stem cells (PBSC) in 70 % (16/23). Myeloablative Conditioning regimen was used in all cases. Median cell dose was 12.7 million/kg of recipient body weight. Engraftment was seen in 95.6 % (22/23) patients. Mean neutrophil engraftment was at 12 days (10-22 days) and mean platelet engraftment was seen at 13 days (7-20 days). Acute Graft vs Host Disease (GvHD) developed in 10 patients (5 haplo, 4 MUD, 1 MSD). Of these 5 had skin, 5 had gut GvHD. CMV reactivation was seen in 7 and Adenoviremia in 1 patient. Transplant related mortality was 13 %. Overall Survival (OS) was 87 % (20/23). Post Transplant evaluation revealed sustained increase in linear growth, regression of organomegaly, improvement in skeletal deformities and developmental milestones. Enzyme assay revealed normal levels in 20 alive patients, which was low before and subnormal in 1 patient which was undetectable before (2 patient's enzyme levels have been sent, report awaited).
Discussion and Conclusion: Multidisciplinary management beyond the period of transplantation is fundamental in the care of patients with LSD. Advances in HSCT, particularly those aimed at reducing GvHD, may lead to a reduction in procedure-related risks and improve the outcomes. Haploidentical HSCT can serve as a potential alternative when MSD/MUD is not available.

Disclosure of Interest: None Declared

Keywords: Allogeneic HSCT, Lysosomal Storage Disorder, Survival

Poster Presentation

PEDIATRIC TRANSPLANTATION (163)

HEMORRHAGIC CYSTITIS PROFILE POST HEMATOPOIETIC STEM CELL TRANSPLANT: A SINGLE CENTRE EXPERIENCE

Monika Bhukar*[1], Pooja Mallya[1], Shobha Badiger[1], Ravi Joshi[1], Santosh Asangi[1], Shweta Pathak[1], Swathi P M[1], Gayathri S[1], Manojit Chakarborty[1], Lakshmi T[1], Ritu Lamichhane[1], Kamini Kanagasabesan[1], Sunil Bhat[1]
[1]Paediatric Hemato-oncology, Mazumdar Shaw Medical Center, Bangalore, India

Aims & Objectives: Hemorrhagic cystitis (HC) is one of the important complication of allogeneic hematopoietic stem cell transplant (HSCT) in children with incidence ranging from 10% to 70% worldwide, with high morbidity by prolonging hospital stay and worsening quality of life. This study was aimed to describe the incidence, clinical profile and treatment modalities in pediatric patients with hemorrhagic cystitis following HSCT.
Patients / Materials & Methods: This is a retrospective study conducted at Mazumdar Shaw Medical Center, Bangalore. Data of all patients with HC following HSCT from January 2020 to February 2022 were analyzed.
Results: Twenty one patient (11.8%) out of 182 transplants during study period had HC with male predominance (n=14, 67.7%). Median age at transplant was 109 months (54-180month). The transplant characteristics are tabulated in Table 1.
Mean neutrophil and platelet engraftment was at 13 days & 17 days, respectively. Incidence of HC in Haploidentical HSCT, MSD and MUD was 14.7%, 6% and 5.8%, respectively. According to HC classification, one patient had grade 2 (4.8%), 10 had grade 3 (47.6%) and the remaining 10 had grade 4 HC (47.6%). The median time of HC onset was 27days (0-135 days) post-transplant, with a median duration of symptoms 32 days (10-108 days). The incidence of HC was significantly high with Haplo HSCT. The median onset of HC was similar in both group of Haplo HSCT, but duration was longer in Haplo HSCT with T cell replete as compared with Haplo HSCT with T cell depletion (74 versus 34.5 days, respectively).
In HC patients, BK viremia was detected in 19 (90%) patients, CMV in 5 (23.8%), adenovirus in 3 (14.2%), EBV in 2 (9%) and HSV in 1 (4.7%) patient. Graft versus host disease (GVHD) and HC developed simultaneously in 10 patients. Supportive measures with oral hydration, quinolones for BK virus prophylaxis and analgesics were given to all patients. Specific treatment modalities included Intravenous fluids with forced diuresis (n=18, 85.7%), bladder irrigation (n=10, 47.6%), cystoscopic clot evacuation with suprapubic catheterization (n=4, 19%), Inj. cidofovir (n=12, 57%),and hyperbaric oxygen therapy (n=7, 33.3%). Mortality rate among HC & non HC group was 38% and 19.2%, respectively. Cause of mortality in HC group was sepsis in 5, gut GVHD in 2 and primary graft failure in 1 patient.
Discussion and Conclusion: HC remains frequent and troublesome complication post-transplant causing prolonged hospitalization and morbidity. Early detection and aggressive supportive care is of prime importance in managing such cases.

Disclosure of Interest: None Declared

Keywords: Allogeneic HSCT, Clinical Profile, Hemorrhagic Cystitis

Poster Presentation

PEDIATRIC TRANSPLANTATION (198)

ALLOHCT FOR CHILDREN WITH NON-MALIGNANT DISEASES AT A GOVERNMENT HOSPITAL IN M P, INDIA

Prachi Chaudhary[1], Preeti Malpani[*1], Amrita Chouhan[1], Dharmanshu Chaube[1], Prachiti Karode[1], Ashok Yadav[2], Amrita Tripathi[2], Manish Purohit[3], Sachin Sharma[2], Anita Mootha[3], Preety Jain[4], Om prakash Gurjar[4], Ramesh Arya[4], Prakash Satwani[5]
[1]Pediatrics, [2]Transfusion Medicine, [3]Microbiology, [4]Radiation Oncology, MGM Medical College , Indore, India, [5]Prediatric Stem Cell transplant, Columbia University, New York, United States

Aims & Objectives: In India, majority of AlloHCT are conducted at private centers which is out of reach for families with limited financial resources. Our BMT unit was established with the aim of reaching out to the financially challenged families and making AlloHCT accessible to all strata of society, especially the poorest one.
Patients / Materials & Methods: Unit: 5 bed BMT unit was constructed at Mahraja Yaswantrao Hospital in Indore, India. Two pediatricians were trained for 6 months at Columbia University, NY, where they developed SOP and protocols.
Financial support: Physician and nursing services, basic drugs and consumables are not charged for. For the additional expenses, Ayushman Yojna, Chief/Prime Minister funds, and CSR funds are arranged by medical team.
Conditioning regimen: Patients with hemoglobinopathies received r-ATG-6mg/kg, FLU-150mg/m2, IV BU 12.8-16mg/kg and Cyclophosphamide-200mg/kg. For SAA patients, most received an r-ATG free regime consisting of FLU 200mg/m2, Cyclophosphamide 200mg/kg and 4 Gray TBI.
Prophylaxis: For aGVHD prophylaxis, Cyclosporine ± Methotrexate was used. Acyclovir, Bactrim Azoles/Micafungin were utilized for anti-infection prophylaxis.
Follow up: Patients are regularly followed up as per protocol
Results: First Allo HCT was done in 2018. 97 % of families were below poverty line, only one family was able to arrange for chemotherapy on their own. 35 children with hemoglobinopathies and 10 with SAA have been transplanted in last 4 years. The patient and donor characteristics have been summarized in table 1. The incidence of grade I-III mucositis & grade I-III aGVHD was 62% and 8%respectively. One patient developed moderate VOD requiring defibrotide. One patient developed limited chronic GVHD. The incidence of bacterial, fungal, protozoal infections and CMV reactivation was 58%, 13%, 16% and 24%, respectively. The median additional cost of AlloHCT was rupees 6 lakhs (4 – 14 lakhs), which was not paid by the families.
The overall survival of the patients has been 86%. The cause of death in 5/6 patients was infection (4-bacterial, 1- fungal infection), and one patient died of graft failure.
Discussion and Conclusion: With dedicated pediatricians and nursing staff and adequate remote supervision, it is feasible to conduct AlloHCT in a limited resource settings and provide reasonable outcomes to children who would have otherwise ultimately succumbed due to their illness and social/demographic challenges. Despite living in remote villages, poverty and socio-economic challenges, families with minimal education can be trained to provide appropriate care at home. Blood stream and water borne gastrointestinal infections remain a major concern. Due to encouraging early experience, MP Government is planning to open few other BMT units in the state.

Disclosure of Interest: None Declared

Keywords: Allo HCT, government hospital, non-malignant diseases

Poster Presentation

PEDIATRIC TRANSPLANTATION (252)

HSCT: A SINE QUA NON FOR CHILDREN WITH TRANSFUSION-DEPENDENT ANEMIA (TDA)

Ruchira Misra*[1], Sunil Bhat[1], Sujata Mushrif[1], Priyank Rajan[1], Purna Kurkure[1]
[1]Pedatric Hematology Oncology and BMT, SRCC Children's Hospital, managed by Narayana health , Mumbai, India

Aims & Objectives: HSCT is the only curative option for children with TDA with alternative donor transplants now available for those who do not find a match. Matched sibling donor transplants(MSD) are considered standard of care, while reservations exist for mismatched donor transplants.
Patients / Materials & Methods: We did a retrospective analysis of the children treated at our centre, from August 2018 to June 2022, to analyze the differences in outcomes of those transplanted with matched donors versus mismatched donors.
Results: 30 children underwent HSCT,with 17 children receiving stem cells from 10/10 matched donors (Group A) & 13 from mismatched donors (Group B)(Table 1). 27 children had Thalassemia major(TM),2 had Pyruvate kinase deficiency (PKD) &1 patient had pure red cell aplasia(PRCA). M: F ratio was3: 1 for Group A and1.3:1 for Group B. Median age was 87 months in Gp. A(range 24-188) & 72 months in Gp. B(Range 33-144). Class 1 patients received ATG-Cy-Flu-Bu conditioning while the remaining received ATG-Thiotepa-Treo-Flu conditioning. Median cell dose was7 x10^6 CD34 cells/kg (range 3-17.6) & 14 x10^6 CD34 cells/kg(range 3.85-22) in Gp. A & B respectively. Median time to engraftment for neutrophils was 20 days & 21 days for platelets in Gp. A; & 16 days & 22 days in Gp. B. Primary Graft failure (PGF) was seen in 1 MUD transplant & 2 Haploidentical T-cell replete transplants. Acute GVHD was seen in 3 patients in Gp. A &4 in Gp. B. The GVHD was usually skin GVHD & was controlled with steroids. Gut GVHD was seen in 4 patients; Grade 4 Gut GVHD was seen in 1 MUD transplant & 1 haploidentical T-cell replete transplant; & Grade 2 Gut GVHD in 1 haploidentical T-cell deplete transplant & 1 antigen mismatched MSD each. Both the PKD patients died due to complications (PGF and Grade 4 Gut GVHD). There was 1 death in the MSD cohort (infective cause), 1 in MUD (Grade IV GVHD Gut), & 1 in the Haploidentical T-cell replete cohort (PGF) before Day 100. Between 3 months to 1 yr. post-transplant, there were 3 deaths in Group B (infection 2, GVHD 1) but none in Group A (12 patients). Mixed chimerism was seen in 1 MSD and 1 Haploidentical T-cell deplete transplant - however, they have not required any transfusions. TRM at 100 days was 11% for the study group - 13% in Group A & 8.3% in Group B; OS at 1 year was 71% for the study group (15/ 21 evaluable) - 83% in Group A (10 /12 evaluable) & 56% in Group B (5/9 evaluable). Of the mismatched transplants – all the deaths have been in the T-Cell replete group & none in the T-Cell deplete cohort.
Discussion and Conclusion: HSCT in TDA is a safe & effective treatment. PKD patients should be transplanted early as delayed transplants lead to higher complications and mortality. MUD transplants had more complications. T-Cell Deplete transplants are safer than T-cell replete transplants & as safe as MSD

Disclosure of Interest: None Declared

Keywords: Haploidentical transplants, Survival, Transfusion dependent anemia

Poster Presentation

PEDIATRIC TRANSPLANTATION (259)

ALLOGENEIC HSCT IN CHILDREN WITH THALASSEMIA MAJOR AND HUMAN IMMUNODEFICIENCY VIRUS INFECTION

Ravi Joshi[*1], Pooja P. Mallya[2], Shobha Badiger[2], Santosh kumar Asangi[2], Shweta Pathak[2], Swathi P M[2], Monika Bhukar[2], Gayathri S[2], Manojit Chakraborty[2], Ritu L[2], Lakshmi T[2], Kamini K[2], Sunil Bhat[2]
[1]Mazumdar shaw medical center Narayana health city Bangalore, [2]Pediatric hematology ,oncology and bone marrow transplant, Mazumdar shaw medical center , Bangalore, India

Aims & Objectives: Allogeneic stem cell transplantation is curative in patients with Thalassemia major. In most of the blood banks and transfusion centers in India ,specially in peripheral areas ,nucleic acid testing (NAT) for Human immunodeficiency /Hepatitis B/ Hepatitis C viral screening of blood products is not done. Bone marrow transplant in children with Thalassemia major and HIV infection is challenging. Here we present 3 such cases ,who underwent hematopoietic stem cell transplant (HSCT) at our center.
Patients / Materials & Methods: We collected retrospective data of 3 children with Thalassemia major and HIV infection ,who underwent HSCT at our center.
Results: We analyzed data regarding patient characteristics ,response to pre transplant immunosuppression ,conditioning regimen and other parameters (Mentioned in table 1). All 3 patients had received anti retroviral therapy (ART)prior to transplant. HIV viral load was negative before transplant. 2 patients underwent matched sibling donor HSCT and one patient had matched unrelated donor HSCT. Peripheral blood was source of stem cells in all 3 transplants. Median CD 34 cell dose was 5.6 X 10*6 cells/kg. All patients engrafted neutrophils from day+11 to day+14. Platelets engrafted from day+14 to day +23. One patient had stage II gut graft vs host disease and 2 patients had stage I skin GVHD. All responded well to short course of steroids. All 3 patients had full donor chimerism by day +28. There was good immune reconstitution post transplant. HIV viral loads were monitored regularly and remained undetectable for all 3 patients. ART was continued through out PTIS, during conditioning regimen and post transplant.
There was no toxicity attributable to ART. One patient died of septic shock 6 months after transplant at a peripheral hospital where there were no facilities to treat such patients. One patient has completed 2 years post transplant and ART has been stopped since 3 months. He is doing well and plan to monitor viral titers on regular basis.One patient is 4 months post transplant and is still on ART and viral titers are negative.
Discussion and Conclusion: With the introduction of highly active anti retroviral therapy (HAART) it has become easier to treat HIV infected patients.In our study we have shown that its possible to continue HAART and they can undergo allogeneic HSCT, without having any complications specifically related either to HIV infection or to HAART. HIV viral titers remained undetected post transplant in all 3 patients. It will be interesting to follow viral titers and long term outcome in such patients.

Disclosure of Interest: None Declared

Keywords: Anti retroviral therapy, HIV infection, Thalassemia major, Viral titers

Poster Presentation

PEDIATRIC TRANSPLANTATION (351)

AUTOIMMUNE CYTOPENIA'S POST HEMATOPOIETIC STEM CELL TRANSPLANTATION IN CHILDREN

Manojit Chakarborty[*1], Pooja P Mallya[2], Ravi Joshi[2], Shobha Badiger[2], Santosh Asangi[2], Shweta Pathak[1], SWATHI P M[1], Monika Bhukar[1], Gayathri sajeevan[1], Ritu Lamichhane[1], Lakshmi T[1], Sunil Bhat[1]
[1]Pediatric Hemato Oncology and BMT, [2]Pediatrics, Mazumdar Shaw Hospital, Bangalore, India

Aims & Objectives: Aim : To assess the incidence, contributing factors, and available treatment options for Autoimmune cytopenia post-HSCT.
Patients / Materials & Methods: METHODS: This was a retrospective study conducted at a tertiary care center in southern India. The medical records of all pediatric patients who underwent HSCT for benign and malignant diseases and developed Autoimmune cytopenia (AIC) were analyzed from January 2019 to May 2022.
Results: 286 pediatric patients underwent HSCT during this time frame. Among these 17 (5.9%) patients developed AIC. The mean age in this cohort was 86 months (12-204 months). The median time of onset of AIC was 6 months (2-12 months) post HSCT. Eight (47%) had isolated anemia, 6 (35%) had bicytopenia, and 3 (18%) had pancytopenia. Transplant associated thrombotic microangiopathy(TA- TAMA)was noted in 3 (17.6%) of the 17 patients.
The prevalence of AIC in benign disorders was higher than that of malignant diseases, which was 82% (with thalassemia as the primary diagnosis) and 18% respectively. The incidence was highest in haploidentical HSCT followed by matched sibling and unrelated donor HSCT which was 71%, 18%, and 12% respectively. Among the haploidentical transplants, the incidence was equal in T cell deplete and replete transplants.
AIC was seen in 71% of the patients who received peripheral blood, compared to 29% who received bone marrow as the stem cell source. Among this major ABO incompatibility was found in 53% of the patients. In this cohort, 59% of the patients had acute GVHD with the majority having gut GVHD.
All these patients received steroids as the 1st line of treatment (94%). Among these 10(59%) patients required the addition of Rituximab (anti-CD20 monoclonal antibody). Majority of the patients (82%) required blood component transfusion. The 3 patients with TA-TAMA received Eculizumab. All patients responded to above line of management except 2 patients who had TA- TAMA. In this study 3 patients died, 2 patients died of TA-TAMA and one due to sepsis.
Discussion and Conclusion: AIC is not a infrequent complication post HSCT, with higher incidence in benign conditions and those undergoing haplo-identical transplant. Outcomes of TA-TAMA are poor.

Disclosure of Interest: None Declared

Keywords: Autoimmune Cytopenia, Hematopoietic stem cell transplantation, Pediatric

Poster Presentation

PEDIATRIC TRANSPLANTATION (360)

EFFICACY OF HIGH DOSE PLERIXAFOR AND LARGE VOLUME LEUKAPHERESIS IN ABSOLUTE POOR MOBILIZERS

Sriraksha Ganiga*[1], Amit Jain[1], Rajesh Patil[1], Ratna Sharma[1], Pranoti Kini[1], Nidhi Mehta[1], Ashutosh Walawalkar[1], Mamta Manglani[1]
[1]MCGM-Comprehensive Thalassemia Care, Pediatric Hematology-Oncology and BMT Centre, CCI compound, Borivali East - 400066, Mumbai, India

Aims & Objectives: To study the efficacy of high dose plerixafor with LVL to achieve a stem cell dose of >3*10^6 in patients undergoing autologous HSCT with day 4 Peripheral blood CD34 count of <5 cells/ul.
Introduction: Peripheral blood stem cell (PBSC) collection is a challenge in patients undergoing autologous HSCT if their absolute peripheral blood (PB) CD34 count is <5 cells/ul after 7 doses of G-CSF at Day 4(absolute poor mobilizer). They have a high chance of requiring multiple apheresis procedures and are at risk of mobilization failure. Hence, additional strategies like use of high dose plerixafor and large volume leukapheresis (LVL) have been implemented to overcome this problem.
Patients / Materials & Methods: We reviewed the charts of all pediatric patients who underwent autologous stem cell transplant (ASCT) from July 2018 to June 2022 with a day 4 PB CD34+ ≤5 cells/ul after receiving 7 doses of GCSF (5 mcg/kg/dose). These children were administered high dose Plerixafor (0.48 mg/kg, maximum 24 mg) followed by LVL (4 TBV) 4 to 6 hours later. The outcome measure was CD34+ ≥ 3.0 x 106 cells/kg.
Results: Of the 89 patients who underwent ASCT, 13 patients (M:F::3.3:1) were included in the analysis (12 - Neuroblastoma, 1-Hodgkin Lymphoma). Mean age was 6.4 years (1 to 15 years), mean body weight was 18 kg (9.9 - 41.2 kg). 69.3% (9/13) required one apheresis and 30.7% (4/13) required 2nd apheresis. All patients successfully mobilized the desired stem cell dose. Mean stem cell dose was 6.8*106/kg (3.4 to 12.8*106/kg). No significant adverse events were observed.
Discussion and Conclusion: GCSF and high dose plerixafor with large volume leukapheresis achieves a desired stem cell dose in pediatric patients with absolute peripheral CD 34 <5 cells/ul. It is safe and feasible even in small children. Prospective randomized controlled trials are needed to establish this strategy as standard of care.

Disclosure of Interest: None Declared

Keywords: absolute poor mobilizer, high dose plerixafor, large volume leukapheresis

Poster Presentation

PEDIATRIC TRANSPLANTATION (367)

SINUSOIDAL OBSTRUCTION SYNDROME IN PEDIATRIC HSCT OUR EXPERIENCE

Poulami Das*[1], Ratna Sharma[1], Rajesh Patil[1], Amit Jain[1], Pranoti Kini[1], Ashutosh Walawalkar[1], Santosh Khude[1], Krisha Shah[1], Pranoti Chiwarkar[1], Muralidharan C[1], Mamta Manglani[1]
[1]Comprehensive Thalassemia Care, Pediatric Hematology Oncology and BMT Centre, Mumbai, India

Aims & Objectives: Sinusoidal obstruction syndrome (SOS) is a life-threatening endothelial complication following hematopoietic stem cell transplantation (HSCT). We present a retrospective analysis of SOS among children transplanted at our centre.
The aim of our study was to evaluate the incidence of SOS in a cohort of children transplanted at our centre on the basis of the new EBMT criteria, the risk factors contributing to it and the outcomes.
Patients / Materials & Methods: We reviewed the charts of all pediatric HSCTs performed between June 2018 to June 2022. The new pediatric EBMT criteria were applied for diagnosis of SOS, identifying the risk factors and grading of severity.
Results: During the study period, 216 children underwent 223 transplants (7 patients underwent second transplant). Sixteen children (7.4%) developed SOS– 7/77 (10%) among allogeneic matched, 3/50 (6%) among allogeneic haploidentical and 6/89 (6.7%) among autologous transplants, with a median age of 10 years (2-16 years) and a male to female ratio of 4.3:1.
Among those who developed SOS, the indication for transplant was malignancy in 9 (56.2%) and a benign disease in 7 (43.7%). Two (16%) were patients with aplastic anemia who underwent a second transplant in view of graft failure. Ten patients (62.5%) received myeloablative conditioning. TBI was a part of the conditioning regimen in 3 patients (18.7%) and busulfan in 8 patients (50%).
Refractory thrombocytopenia was seen in all patients, weight gain in 10 (62.5%) and elevated serum bilirubin (more than 2g/dL) in 11(69%). One (6.2%) patient had very severe, nine patients (56.2%) had severe, and 3 (18.7%) patients each had moderate and mild SOS. The median time of occurrence of SOS was 12 days after HSCT (range: 3-41 days). Fluids were restricted and furosemide infusions were given to all. Four patients (25%) 3 of mild and 1 of moderate SOS patients completely recovered with this approach. One patient with moderate SOS additionally required high dose steroids (Methylprednisolone 500mg/m2 Q12H). Eleven patients (69%) recovered following treatment with low dose defibrotide (25 mg/kg/day in 4 divided doses) with or without high-dose steroids given for a median time of 6 days (range 1 to 9 days). Of these, 1 patient had very severe, 9 patients had severe and 1 patient had moderate SOS. The time taken for complete resolution of SOS was 2 to 14 days (median duration: 6 days).There was no mortality due to SOS in our cohort with a median follow up of 27 months (4- 49 months).
Discussion and Conclusion: The overall incidence of SOS in our cohort was 7.6%. Even the severe and very severe SOS(4.6%) recovered completely with defibrotide. Identifying the risk factors associated with SOS helps in timely management and prevents mortality due to this potentially fatal complication.

Disclosure of Interest: None Declared

Keywords: Defibrotide, HSCT complication, SOS, VOD

Poster Presentation

LYMPHOMA/MYELOMA (108)

LESS THAN ONE MONTHS SECOND AUTO BMT IN MM COVID PATIENT

Mehrdad Payandeh*[1], Fateme Yari[2]
[1]Kums , [2]Kums , Kermanshah , Iran

Aims & Objectives: Cryopreserving Cell can save the life of MM patient with ARDS covid lung disease
Patients / Materials & Methods: We presented here a MM 45 years old case , that after 7 days of autologous BMT complicated with covid infection lung with respiratory failure .
After this event he suffer of prolonged pancytopenia in 18 days of transplant.
Due to suppressing effect of covid virus on graft in BM aspiration analysis .
we decide doing ret-transplantation for him with cryopreserved his cell .
Results: We treated his covid with remdisivir and dexamethasone and two courses of plasmapheresis .
After second cell transplantation he engraftment in + 24 of BMT.
Discussion and Conclusion: Cryopreserving is critical for autologous BMT cases and we need this support for maximal care for complicated covid life threatening cases .

Disclosure of Interest: None Declared

Keywords: Covid, Myeloma, Re transplant

Poster Presentation

LYMPHOMA/MYELOMA (118)

LONG TERM OUTCOME OF MULTIPLE MYELOMA PATIENTS POST AUTOLOGOUS STEM CELL TRANSPLANT IN KLANG VALLEY

Chin Sum Cheong[*1], Soo Chin Ng[2], Ping Chong Bee[1], Fui Min Edmund Chin[1], Shasha Khairullah[1], Chee Chiat Liong[1], Mohd Yazid Zamri[3], Kee Hean Alan Teh[2], Mohd Haris Fadzillah Abdul Rahman[2], Gin Gin Gan[1]
[1]Faculty of Medicine, University of Malaya, Kuala Lumpur, [2]Hematology, Subang Jaya Medical Centre, Subang Jaya, [3]Department of Medicine, University Malaya Medical Center, Kuala Lumpur, Malaysia

Aims & Objectives: Autologous stem cell transplant (ASCT) has consistently shown to improve outcome of multiple myeloma (MM) patients. However, the role of ASCT is being questioned recently with the introduction of novel agents. Unfortunately, these novel agents are not easily accessible in developing nations such as Malaysia. This study aims to report on the long-term outcome of MM patients post ASCT in this new era of novel agents.
Patients / Materials & Methods: MM patients who were diagnosed between June 2001 and June 2020, and underwent ASCT in two hospitals were retrospectively studied. Patients' demographic details and treatment details were included for analysis of progression free survival (PFS) and overall survival (OS).
Results: Eighty-five patients were included. The median age at presentation was 55 years old (ranged from 26 to 73 years old). More than half were Chinese (56.5%), followed by Malay (25.9%). Immunoglobulin (Ig) G was the most common subtype (60%), followed by light chain disease (24.7%). Cytogenetic risk was determined for 44 patients, 9.1% was found to have poor risk. 28.8% of 52 patients belonged to Stage III based on International Staging System (ISS). Only 24.7% of patients achieved complete remission (CR) and 37.6% had very good partial response (VGPR) before ASCT. 58.8% of patients received maintenance therapy post ASCT. Median OS and PFS of patients after ASCT were 147 months and 40 months, respectively. Multivariate analysis showed that those in CR prior to ASCT compared to those in VGPR had significant better PFS (median PFS 73 months versus 32 months, p=0.034). Poor cytogenetic risk adversely affected PFS (median PFS 10 months versus 42 months, p=0.004) and OS (median OS 33 months versus 147 months, p=0.029). Maintenance therapy post ASCT improved OS (median OS not reached versus 79 months without maintenance, p=0.041).
Discussion and Conclusion: This study demonstrated that ASCT has still a role in improving outcome of MM patients. However, patients with adverse cytogenetic risk may benefit from newer therapies with the aim of achieving CR prior to transplant. Maintenance therapy post ASCT should be practiced for better outcome.

Disclosure of Interest: C. S. Cheong But No Conflict with: No conflict of interest to disclose, S. C. Ng But No Conflict with: No conflict of interest to disclose, P. C. Bee But No Conflict with: No conflict of interest to disclose, F. M. E. Chin But No Conflict with: No conflict of interest to disclose, S. Khairullah But No Conflict with: No conflict of interest to disclose, C. C. Liong But No Conflict with: No conflict of interest to disclose, M. Y. Zamri But No Conflict with: No conflict of interest to disclose, K. H. A. Teh But No Conflict with: No conflict of interest to disclose, M. H. F. Abdul Rahman But No Conflict with: No conflict of interest to disclose, G. G. Gan But No Conflict with: No conflict of interest to disclose

Keywords: autologous stem cell transplantation, Malaysia, multiple myeloma, South East Asia, treatment outcome

Poster Presentation

LYMPHOMA/MYELOMA (158)

CARE OF A PATIENT WITH SEZARY SYNDROME COMBINED WITH MASSIVE GANGRENOUS HERPES ZOSTER

Yuhua Fan*[1], Yan Cui[1]
[1]GCP, Institute of Hematology and Blood Diseases Hospital, Tianjin, China

Aims & Objectives: To summarize the effective nursing experience of a patient with Sezary syndrome combined with massive gangrenous herpes zoster, in order to provide relevant guidance for the care of patients with Sezary syndrome and related complications.
Patients / Materials & Methods: The chemotherapy regimen was dynamically changed according to the changes of the patient's condition, and chemotherapy drugs were infused to treat the primary disease actively and reduce the tumor load. We also observed adverse drug effects and provided symptomatic treatment timely. For gangrenous herpes zoster, appropriate and strict drug changes are given through close cooperation between the dermatology, burns and testing departments. We also strengthened the care of the peripheral skin and applied neotype dressings to prevent the formation of pressure sores. In case of high fever, we provide the patient timely physical or pharmacological cooling methods and monitor pulse rate, blood pressure, consciousness and urine output to be on guard against the occurrence of infectious shock. We adjusted antibiotics timely to prevent the development of drug-resistant bacteria. We cautioned against contraindications and synergistic effects between different drugs to avoid aggravating hepatic and renal toxicity. We strengthened pain care and management of toxic anesthetics. Implement personalized psychological interventions to reduce patients' anxiety and improve their quality of life. We strengthed the implementation of the concept of asepsis, and take bedside isolation according to the bacterial culture results in a timely manner to avoid cross-infection.
Results: The patient was discharged with significant improvement in symptoms and no cross-infection occurred.
Discussion and Conclusion: By adjusting the treatment plan several times, multidisciplinary cooperation, and taking effective nursing measures, patients' symptoms could be improved and patients' quality of life could be enhanced.

Disclosure of Interest: None Declared

Keywords: Herpes Zoster, Nursing, Sezary Syndrome

Poster Presentation

LYMPHOMA/MYELOMA (167)

AUTOLOGOUS STEM CELL TRANSPLANTATION IN MULTIPLE MYELOMA: A RETROSPECTIVE SINGLE CENTER ANALYSIS

Sui Keat Tan[*1], Shu May Chong[1], Ai Sim Goh[1]
[1]Hematology Unit, Department of Medicine, Penang General Hospital, Penang, Malaysia

Aims & Objectives: Multiple Myeloma (MM) is the third commonest hematological malignancy. Induction with a triplet or quadruplet regimen followed by autologous stem cell transplantation (ASCT) has been the standard therapy for young patients (< 65 years). We would like to evaluate the demographic data, prognostic factors and long term outcome and survival for patient with MM who underwent ASCT in our centre.
Patients / Materials & Methods: We included a 13 years cohort of patients transplanted from 1st August 2008 to 31st July 2020. The variables assessed included demographics, MM subtypes, clinical presentation, induction regimen, remission status pre-transplant and maintenance therapy post-transplant. Analyses were generated using SPSS version 23.0. Prognostic factors for progression free survival (PFS) and overall survival (OS) were analysed using simple and multiple Cox proportional hazard regression analysis.
Results: A total of 50 patients (22 males, 28 females) were evaluated. The median age at transplant was 54.5 years (range 31.4 - 64.9 years). There were 23 Malay (46 %), 19 Chinese (38 %) and 8 Indian (16 %). 74% had IgG kappa subtype. 46% presented with ISS III, 36% ISS II and 10% ISS I. The commonest induction regimen received before ASCT was a combination of immunomodulatory agent (IMID) and bortezomib (n= 31, 62%). 58% of patients were transplanted with at least a very good partial response (VGPR) compared with 42% with partial response (PR). 62% of patients received maintenance post-ASCT. The median follow up was 55.3 months (range: 8.6 – 147.8 months). There was no transplant related mortality. The 5 years and 10 years overall survival (OS) were 65.4% and 37.6 % respectively whilst the 5 years and 10 years progression free survival (PFS) were 37.2% and 12.4% respectively. Adjusted for gender, subtypes and remission status, International Staging System (ISS) III (aHR 5.71; 95% CI 1.69 -19.25) and older age during transplant (aHR 1.09; 95% CI 1.01-1.18) were independent risk factors for increased mortality.
Similarly, both ISS III (aHR 2.54; 95% CI 1.04-6.22) and older age during transplant (aHR 1.09; 95% CI 1.01-1.17) were also significant predictors for post-ASCT relapse.
Discussion and Conclusion: ASCT improves survival in patients with multiple myeloma and is safe in patients below 65 years. ISS III and older age at transplant are independent risk factor of OS and PFS.

Disclosure of Interest: None Declared

Keywords: Autologous Stem Cell Transplantation(ASCT), International Staging System (ISS), Multiple Myeloma(MM)

Poster Presentation

LYMPHOMA/MYELOMA (172)

ORAL DOMICILIARY THERAPY OF MULTIPLE MYELOMA WITH CYCLOPOMDEXA -ALL ORAL REGIMEN IN COVID ERA

Goutham Kumar*[1], Sachin S. Jadhav[1]
[1]Hematology and BMT, HCG Cancer Hospital, Bangalore, India

Aims & Objectives: To use an all-oral treatment of CyPomDexa (Cyclophosphamide, Pomalidomide and Dexamethasone) for the treatment of myeloma both as a first-line regimen as well as for relapsed and refractory patients who had not been exposed to this regimen in the past, and to observe the feasibility and efficacy of domiciliary, oral treatment with cyclophosphamide, pomalidomide and dexamethasone (Cy-Pom-Dex) for myeloma patients during the COVID-19 pandemic.
Patients / Materials & Methods: A Prospective, observational, single-arm, pilot study was conducted from 1st March 2020 to 30th September 2020 in patients who were newly-diagnosed (NDMM) or relapsed multiple myeloma (RMM) at a tertiary care Centre in Bengaluru. The patients were started on oral treatment with CyPomDexa during lockdown mandated by the COVID-19 pandemic. This regimen was chosen as a replacement for cyclophosphamide, bortezomib, dexamethasone (CyBorD), which was the previous standard of care in our centre. Haematological and biochemical parameters of the patients were checked pre-treatment. Weekly complete blood counts and biochemistry was checked with home collection of blood samples. This was combined with weekly video consultations. Face-to-face visits were conducted monthly, and myeloma parameters were checked at the end of every 2 months.
Results: Conclusion: 6 patients underwent the planned treatment. Among these 4 had NDMM and 2 had RMM. 1 patient who received CyPomDexa from the first cycle was lost to follow-up (COVID 19 positive). Among the remaining 5 patients ,3 (50%) achieved VGPR (very good partial response) and 2 (33.33%) achieved sCR (stringent complete response) after 4 cycles of therapy.
Discussion and Conclusion: This regimen achieved good disease control in all the evaluable patients, within 4 cycles. A larger, prospective study is however required to draw definitive conclusions.

Disclosure of Interest: None Declared

Keywords: Covid-19, Cyclopomdexa, Multiple Myeloma(MM)

Poster Presentation

LYMPHOMA/MYELOMA (185)

DONOR-DERIVED CD7 CAR T CELLS FOR RELAPSE T-ALL AFTER ALLO-HSCT : PHASE I TRIAL

Hui Shi* [1], Kai Hu[1]
[1]Beijing Gobroad Boren Hos[ital, Beijing, China

Aims & Objectives: T-acute lymphoblastic leukemia (T-ALL) is an aggressive hematological malignancy. 25% T-ALL patients experienced relapse after allo-HSCT, which indicates a dismal prognosis, and represents a significant unmet clinical need.
Patients / Materials & Methods: We designed an open label, phase I clinical trial enrolled patients with a pathological confirmed CD7-positive T-ALL/LBL. When necessary, bridging chemotherapy was given to patients to control their disease progression. To minimize CD7 CAR T-cell–mediated fratricide, we used IntraBlock technology to prevent CD7 expression on CAR T cells surface.
Results: Seven eligible patients were enrolled between November 2020 and December 2021. Donor-derived CD7 CAR T cells were infused into all 7 patients. The median age of the 13 patients was 30 (28-38) years old. Patients were heavily pretreated with a median of 4 (3-8) lines of therapies before enrollment. At relapse, three patients had tumor cells infiltration of bone marrow, diagnosed with T-ALL. While 6 patients (2 T-ALL and 4 T-LBL) developed extramedullary disease, including diffuse involvement (n=1) or bulky mediastinal masses >7 cm in diameter (n=1), or central nervous system (CNS) involvement (n=3).
CAR T cells peaked between days 11 and 15 with a mean count of 51.1/uL (range 7.17-497) in blood by flow cytometry testing. The rate of CRS and ICANS was 85.7% and 14.3%, respectively. Only one patient had a grade 3 CRS and a serious grade 4 ICANS, resolved by dexamethasone and tocilizumab. Other five patients experienced CRS Grade 1. Only two patients (28.6%) develop GVHD. Hematologic CAR T cells related adverse events (AE) included leukopenia, thrombocytopenia and neutropenia were observed in 6 patients (85.7%). Infections occurred in 5 patients (71.4%).
On day 28, the patients who had bone marrow involvement achieved minimal residual disease (MRD) negative complete remission (CR, n=1) or CR with incomplete hematologic recovery (CRi, n=2). The patients who had CNS leukemia achieved CR on day 28. Five patients with their EMD encountered CR at day 90. The optimal ORR and CR were 100% and 100%, respectively. Th CR/CRi rate was 85.7% on month 3. The median followed-up time was 4 months (range 3-16 months). Two patients died of serious infection and one patient died of brain hemorrhage. Four patients were alive until the cut-off time.
Discussion and Conclusion: Among 7 patients with r/r T-ALL enrolled in this trial, donor-derived CD7 CAR T cells exhibited efficient expansion and achieved a high complete remission rate with manageable safety profile.

Disclosure of Interest: None Declared

Keywords: Allogeneic HSCT, DONOR-DERIVED CD7 CAR T CELLS, T-ALL

Poster Presentation

LYMPHOMA/MYELOMA (209)

CENTRAL NERVOUS SYSTEM RELAPSE AFTER CAR-T CELL THERAPY IN B-CELL LYMPHOMA

Tianning Gu[*1], Wenfa Huang[2], Lei Wang[2], Yuqi Lv[1], Lixin Wang[2], Yongxian Hu[1], He Huang[1]
[1]Bone Marrow Transplantation Center, the First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, [2]Department of Hematology and Oncology, International Cancer Center, Shenzhen University General Hospital, Shenzhen, China

Aims & Objectives: Chimeric antigen receptor T (CAR-T) cell therapy has revolutionized the landscape of cancer therapy, obtaining significant efficacy especially in relapsed and refractory (R/R) B cell malignancies. In clinical patients, CAR-T cells are able to migrate into various organs, including the central nervous system (CNS), which serves as an immunological privileged site protected from peripheral blood, and exert cytotoxicity on tumor cells. However, whether there is a possibility of the CNS relapse in patients with B-cell lymphoma who achieved complete remission (CR) after CAR-T cell therapy has not been reported yet. We aim to describe the features of the CNS relapse after CAR-T cell therapy in B-cell lymphoma, and try to identify correlated factors and propose potential management strategy in the upcoming research.
Patients / Materials & Methods: We preliminarily reviewed 6 patients (5 presented) who received CAR-T cell therapy for the treatment of B-cell lymphoma in our center and Shenzhen University General Hospital. We compared the baseline of patient characteristics before CAR-T cell therapy, described the clinical response and efficacy during the treatment, and reported the occurrence of CNS relapse after patients achieving CR.
Results: All 5 patients were heavily pre-treated with multiple lines of chemotherapy prior to CAR-T cell therapy, with 2 of them received additional autologous hematopoietic stem cell transplantation (HSCT) (Table 1). All patients suffered from previous relapse in multiple peripheral lymph nodes, with 2 of them involved in other organs like liver and breast, and 1 of them involved in the CNS. Three patients received CD19-22 bispecific CAR-T product, 1 patient received CD19-20 bispecific CAR-T product, and 1 patient received CD19 CAR-T product (Table 2). All patients responded well with tolerable toxicities by monitoring body temperature, inflammation markers, cytokines, and hemogram, and all achieved CR defined by PET/CT after CAR-T treatment (Figure 1). All patients eventually developed CNS relapse with different locations, respectfully, which was confirmed by imaging along with pathological diagnosis or targeted drug treatment (Figure 2).
Discussion and Conclusion: We first reported the CNS relapse after CAR-T cell therapy in patients with B-cell lymphoma, suggesting that routine monitory is required for patients who achieved remission after CAR-T treatment to manage the CNS involvement in time. If possible, additional application of PD-1 monoclonal antibody, BTK inhibitors or other immunomodulatory drugs that can function in the CNS might prevent the CNS relapse without affecting CAR-T cell function.

Disclosure of Interest: None Declared

Keywords: CAR-T cell therapy, CNS relapse, Lymphoma

Poster Presentation

LYMPHOMA/MYELOMA (214)

G-CSF MOBILIZED STEM CELL COLLECTION AND OUTCOME OF 40 CASES OF AUTO SCT FROM A SINGLE CENTRE

Kaniz Rahman*[1]
[1]Evercare Hospital Dhaka, Dhaka, Bangladesh

Aims & Objectives: Granulocyte colony-stimulating factor (G-CSF) is widely used to induce peripheral blood stem cell mobilization for bone marrow transplantation. This mobilized peripheral blood stem cell (PBSC) is the main source for auto SCT. Autologous hematopoietic stem cell transplantation is an important treatment option for hematologic malignancies like relapsed lymphoma or multiple myeloma which can improve progression free survival as well as overall survival. Poor collection of stem cell is a clinical problem in G-CSF-induced peripheral blood stem cell (PBSC) collection. It would be beneficial to be able to predict the PBSC count yield from recipient before mobilization or harvesting.
The objective of this study is to better characterize the outcomes of 40 auto SCT mobilized with G-CSF in our centre.
Patients / Materials & Methods: Patients with 40 hematological malignancies were evaluated from March 2016 to June 2022,who have received auto SCT with GCSF mobilized peripheral blood stem cells. Stem cell source was peripheral blood and mobilization was done with GCSF at a dose of 10µg/kg daily for 5days. Different conditioning regimens were used for these patients.
Results: Total 40 auto transplant were carried out from March,2016 to June 2022. Among them male 25 (62.5%), female 15 (37.5%), Median age was 49 years (13-71yrs). Indications for transplantation were Multiple Myeloma 21 (52.5%), Lymphoma 18 (45%), AML 1 (2.5%). Conditioning of these patients were done by Melphalan 28 (70%), BEAM 11 (27.5%), BEAM plus Thiotepa 1 (2.5%), BU-CY 1 (2.5%). Number of fresh and cryopreserved Stem cell were 24 (60%) and 16 (40%) respectively. Median CD 34 dose was 5.8X106 /kg body weight. All 40 patients achieved successful engraftment and median time of engraftment was 11 days (8-14 days). During transplant, the only complication was infection. Total documented infection was 5, among them Clostridium difficile 4, E. coli 1, Covid 1. Overall survival at a median follow up of 13 months was 34 (85%) and cumulative incidence of relapse was 11 (27.5%).
Discussion and Conclusion: Auto stem cell transplantation is a pertinent treatment option for patients with hematological malignancies. Our outcomes are comparable with results from neighboring countries as well as western world.

Disclosure of Interest: None Declared

Keywords: Autologous Stem Cell Transplantation(ASCT), Granulocyte colony stimulating factor, peripheral Blood Stem Cell

Poster Presentation

LYMPHOMA/MYELOMA (219)

TACKLING NLPHL AFTER AUTO-HSCT AND REFRACTORY TO IMMUNE CHECKPOINT INHIBITOR: A CASE REPORT

Zannatun Nesa*[1], Quazi S. Haq[1], Masba U. Chowdhury[1], Kaniz F. Rahman[1], Menoti P. Mukti[1], Tangia Muquith[1], Muhammad S. I. Rumi[1], Md.Sazzad Z. Chowdhury[1], Abu Jafar M. Saleh[1]
[1]Hematology and stem cell transplant, Evercare Hospital Dhaka, Dhaka, Bangladesh

Aims & Objectives: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) represents a potential curative strategy for patients with relapsed/refractory(R/R) Hodgkin lymphoma (HL), particularly after a prior autologous hematopoietic stem cell transplant (auto-HSCT). Haploidentical donor transplant (HIDT) is a promising treatment option, especially for minorities for whom suitably matched siblings or unrelated donors are not widely available. Patients achieving complete remission (CR) after HIDT show a significantly better progression-free survival (PFS) and lower relapse incidence (RI) compared to those allografted with HLA-Identical (HLA-id) donor.
Patients / Materials & Methods: Retrospective single case study
Results: Case presentation: To our knowledge, we report the first case of R/R nodular lymphocyte predominant Hodgkin lymphoma (NLPHL) in Bangladesh, who have had a prior auto-HSCT, treated by upfront and urgent haplo-HSCT after salvage therapy and reduced intensity conditioning (RIC). This case highlights the challenges involved in treating a patient with R/R disease after auto-HSCT, not achieving a response to immune checkpoint inhibitor (ICI) with nivolumab. We present a case of a 20-year-old young man with extensive relapse of NLPHL after 16 months of achieving a PET negative complete remission with auto-HSCT. At the time of relapse, this patient started treatment with ICI-nivolumab and remained refractory to it even after 12 cycles necessitating an urgent allo-HSCT.In the absence of a matched sibling's donor, HIDT was the only rapid alternative for this patient. So, he underwent a successful HIDT using Fludarabine/Melphalan/Thiotepa/ATG-based RIC regimen following two cycles of Obinutuzumab-GDP combination salvage therapy. Post-transplant immunosuppressive was given with cyclosporin/MMF/PTCy(post-transplant-cyclophosphamide) to prevent GvHD. During the transplant period, he experienced chemotherapy induced nausea vomiting (CINV), and mucositis. Also, cyclosporine induced raised blood pressure which improved with dose adjustment. On day+17 he developed gut acute GvHD requiring I/V methylprednisolone. He had repeated attacks of gut GvHD even after six months which improved with steroid and budesonide. During a follow-up period of 12 months, this patient is doing well in a state of complete remission.
Discussion and Conclusion: This report not only creates huge scope for haploidentical transplantation in difficult-to-treat R/R HL patients lacking HLA identical donors but also challenges the question of donor choice in terms of improved outcome. Moreover, the efficacy of allo-HSCT may be increased by prior use of anti-PD-1 nivolumab with increased incidence of acute gut GvHD. Thus, prior anti-PD-1 should not preclude a subsequent allo-HSCT.

Disclosure of Interest: None Declared

Keywords: Allo-HSCT, Immune check point inhibitor, Relapse/Refractory NLPHL

Poster Presentation

LYMPHOMA/MYELOMA (243)

PHARYNGEAL-CERVICAL-BRACHIAL VARIANT GBS IN MULTIPLE MYELOMA POST ASCT

Rajesh R. Nair*[1], Sanjeevan Sharma[2], Vadlamani S. Prakash[1], Shaman Gill[3], Rajeev Ranjan[3], Priyanka Mishra[4], Neerja Kushwaha[5]
[1]Medical oncology, [2]Hematology, [3]Neurology, [4]Hematopathology, [5]Transfusion medicine, Command Hospital central command, Lucknow, India

Aims & Objectives: To report a hitherto unreported complication of ASCT - PCB variant GBS.
Patients / Materials & Methods: We report a rare neurological complication in a patient with multiple myeloma after ASCT, hitherto unreported in post-transplant literature. We performed a systematic and extensive pubmed online search in which we searched terms like; variant GBS, PCB, multiple myeloma, transplantation. We have read the titles and abstract of every identified literature and critically appraised the full text of potentially eligible studies.
Results: 66 years old male, a case of multiple myeloma (IgA lambda subtype- RISS stage 3) was admitted for ASCT on 05/04/2022 in CR1 post Bortezomib – Lenalidomide – Dexamethasone induction. Stem cell mobilization was done with Inj GCSF + Plerixafor protocol for 5 days. PBSC harvest was done on day-1 with cell dose of 4.1 x 106 CD34+ cells/Kg. Inj Melphalan 200 mg/m2 was given the same evening, and the collected PBSC was infused on Day-0. Patient developed grade III mucositis and atrial fibrillation with rapid ventricular response on Day +6. He was managed with inj amiodarone and other supportive measures. Neutropenic period was managed with prophylactic antifungal therapy, TPN, and culture guided antibacterial therapy. Neutrophil engraftment and platelet engraftment was established on Day +10 and Day +12 respectively. As there was no focus of infection / mucositis / organ specific dysfunction, he was discharged from the transplant unit. On Day +21 he developed acute onset difficulty in swallowing associated with nasal regurgitation and nasal twang of voice. Clinically he was found to have complete bulbar weakness associated with neck muscle and weakness of both upper limbs along with areflexia sparing lower limbs. MRI brain was normal and CSF examination revealed albumin- cytological dissociation (acellular CSF with protein – 75 mg/dl). NCS revealed prolonged latency with delayed conduction velocity and reduced CMAP amplitudes in median and ulnar nerves and sensory NCS showed reduced SNAP amplitudes in upper limbs. In lower limbs sural SNAPs, peroneal and tibial CMAPs were also not recordable. IVIG 2g/Kg was started on Day +21 however the clinical course was complicated with aspiration pneumonia along with sepsis and multiorgan dysfunction syndrome and finally succumbed to his illness.
Discussion and Conclusion: GBS is a rare complication after ASCT. PCB is a rare variant of GBS which accounts for 3% of cases2. This case report illustrates the importance of considering rare causes of neurological dysfunction following engraftment after autologous stem cell transplantation. We emphasize that transplant patients require stringent observation and close follow up by transplant physicians in the early post-transplant period.

Disclosure of Interest: None Declared

Keywords: GBS, nerve conduction study, Myeloma, Complication, Transplantation, Variant, Neurological

Poster Presentation

LYMPHOMA/MYELOMA (246)

OUTCOMES OF CONSOLIDATION TRANSPLANT IN MULTIPLE MYELOMA:COMPARING DOUBLET AND TRIPLET INDUCTIONS

Kiran K. Satti*[1], Nikita Mehra[1], Jayachandran P. Kalaiyarasi[1], Parathan Karunakaran[1], Tenali G. Sagar[1], Krishna K. Rathinam[1]
[1]Medical Oncology, Cancer Institute(W.I.A), Chennai, India

Aims & Objectives: To analyse the outcomes of patients receiving novel agents: proteasome inhibitor-immunomodulatory drugs (PI-IMiD)-based triplet or doublet induction regimens followed by consolidation high-dose melphalan and autologous stem cell transplant (ASCT) for multiple myeloma (MM). The primary objectives of the study are Progression-free Survival and Over-all Survival

Patients / Materials & Methods: This is a single-centre retrospective analysis of patients diagnosed with MM who received doublet or triplet novel agent induction chemotherapy with either bortezomib, IMiD or both- followed by consolidation with ASCT. Data were retrieved from case files and electronic records from the tumour registry. Statistical analysis was done through SPSS version 20.

Results: Ninety-nine patients received induction with PI-IMiD-based triplet OR doublet regimens and were subsequently consolidated with ASCT for multiple myeloma.

Among 99 patients, the median age: 49.5 years (range:30-66) and males-61 (62%). ISS Stage: I-10 (10%), II- 20(20%), III-51 (52%), stage not available- 18 (18%) due to missing β2 microglobulin.

Induction regimen(s) prior to transplant: PI-IMiD-based triplet regimen-42 (42%): VTD-39 (39)%, VRd-3 (3%), IMiD-based doublet alone- 47 (48%): Thalidomide-Dexamethasone (Thal-Dexa)- 29 (29%), Lenalidomide-Dexamethasone (Len-Dexa)- 18 (18%). PI-based doublet: Borteozomib-Dexamethasone- 10 (10%). Pre-transplant disease status: ≥ very good partial response (VGPR)-82(83%); partial response (PR)- 17(17%).

Melphalan was used as a high-dose conditioning regimen in all patients: Mel200- 68 (69%), Mel<200- 31 (31%). The median CD34 count was 5.5×106 cells/kg (3.1-10×106), and plerixafor was used in 22 (29%) patients. All the patients received non-cryopreserved stem cells. Among the patients with PR prior to ASCT, 53% achieved VGPR or better after ASCT (9/17). Seventy-eight (78%) patients received maintenance therapy: thalidomide- 37 (48%) lenalidomide- 26 (34%), or bortezomib- 14 (18%).

The median follow-up of the study was 49 months. The median PFS of the entire study population was 46 months (95% CI: 30.6-61.3). The median PFS in the PI-IMiD based triplet arm was 46 months (95% CI: 31.7-58.2) whereas the PFS in doublet arms was 45 months (95% CI:36.1-55.8) (p=0.8).The median OS of the entire group was 109 months (95% CI: 69.8-148); the median OS in the triplet arm was not reached and the median OS in the doublet arm was 109 months(95% CI: 70-147) (p=0.3).

Discussion and Conclusion: To conclude, there was no statistically significant difference in the outcomes of patients receiving doublet or triplet novel agent induction chemotherapy followed by ASCT for multiple myeloma.

Disclosure of Interest: K. Satti But No Conflict with: No conflict of interest to disclose, N. Mehra But No Conflict with: No conflict of interest to disclose, J. Kalaiyarasi But No Conflict with: No conflict of interest to disclose, P. Karunakaran But No Conflict with: No conflict of interest to disclose, T. Sagar But No Conflict with: No conflict of interest to disclose, K. Rathinam But No Conflict with: No conflict of interest to disclose

Keywords: Autologous Stem Cell Transplantation(ASCT), Multiple Myeloma(MM), PI-IMiD based Triplet and Doublet

Poster Presentation

LYMPHOMA/MYELOMA (268)

ALLOGENIC AFTER FIRST CR IN ANGIOGENIC IMMUNOBLASTIC NHL IS BETTER AUTOLOGOUS OR NOT?

Mehrdad Payandeh[*1], Mehrak payandeh[1]
[1]Kums , Kermanshah , Iran

Aims & Objectives: When according to poor prognostic factor exists in a patient with malignancy it is better you do better selection for patient before that time that he/she been complicated and resistant to therapy.
Patients / Materials & Methods: Here we presented a known case of T cell NHL that presented with (high risk) presentation of resistant pancytopenia to routine treatment and is hard to classic management.
After intensive chemotherapy with R-CHOP pluse etoposide , we decide refer him to AlLogenic transplantation .
Due to poor results of autologous transplantation result in T cell NHL and sooner recurrence , this policy select for this 47 years old man.
Results: After six years he is alive without any sign of recurrence .
Discussion and Conclusion: First soon best decision is better choice for poor prognosis case that we had poor experience with it, then despite of toxic complication , clinical decision is choice especially as an clinical trial.

Disclosure of Interest: None Declared

Keywords: ALlogenic, AUTOLOGOUS FEMATOPOIETIC STEM CELL TRANSPLANTATION, T cell

Poster Presentation

LYMPHOMA/MYELOMA (271)

TOXICITY AS AN CHALL IN AUTOLOGOUS MULTIPLE MYELOM WITH RENAL FAILURE

Mehrdad Payandeh[*1], Fateme Yari[2]
[1]Kums , [2]Kums , Kermanshah , Iran

Aims & Objectives: Dose reduction in melohalan and on time hemodialysis are critical point in OS and PFS in MM with renal failure
Patients / Materials & Methods: 15 cases in MM. and renal failure with GFR 30-60 selected for autologous during 7 years 2015-2022 in KUMS BMT center in west of iran
Medium age between 34-65 years old
Results: More than 42 months without relapse .
Engraftment medium time positive 10 days after transplant.
There were significantly more high grade (grades 3–4) toxicities including high grade electrolyte abnormalities, mucositis.
Discussion and Conclusion: dose reduction of melphalan during conditioning may improve outcomes in this population. improvements in treatment regimens have resulted in reduced TRM and toxicities for patients with renal insufficiency undergoing ASCT.

Disclosure of Interest: None Declared

Keywords: AUTOLOGOUS FEMATOPOIETIC STEM CELL TRANSPLANTATION, Myeloma, Renal failure

Poster Presentation

LYMPHOMA/MYELOMA (276)

TIMING OF TRANSPLANT CAN BE INDIVIDUALIZED

Mehrdad Payandeh*[1], Mehrak payandeh[1]
[1]Kums , Kermanshah , Iran

Aims & Objectives: transplant prolongs PFS and transplant remains a viable and valuable component of therapy in eligible patients in multiple myeloma."
"Similar overall survival in multiple trials of early versus delayed [disease] means that the timing of transplant can be individualized based on a number of factors including age, patient preference, risk status, and feasibility,"
transplant comes with both short- and long-term toxicities that must be discussed with the patient and mitigated. "
Maintenance therapy until progression remains an important part of myeloma therapy,"
While ASCT remains very relevant and important in prolonging PFS in younger and eligible patients, "it may not be mandatory in all eligible patients upfront,"
Patients / Materials & Methods: We evaluate the Overall survival and progressive free survival of patients with diagnosis of myeloma that been autologous BMT in early and late transplant according to patient and physician decision .
Results: When the physician decide refer patients at first remission to autologous BMT the results of os and pfs been better than delayed BMT due to not classic approaches
Discussion and Conclusion: As for future directions, regimens are already moving beyond VRd/KRd triplets to quadruplets such as DARA-VRd, isatuximab-VRd, and both D-KRd and I-KRd."
We may no longer be immediately dividing patients into transplant eligible versus transplant ineligible.
We will likely incorporate more immunotherapy in frontline myeloma and early phase trials are already underway."

Disclosure of Interest: None Declared

Keywords: Deep of response, Early transplant, Myeloma, Relapse

Poster Presentation

LYMPHOMA/MYELOMA (282)

AUTOLOGOUS STEM CELL TRANSPLANTATION IN ADULT HODGKIN LYMPHOMA: A SINGLE CENTER EXPERIENCE

Sudhir Kumar[*1], Atul Sharma[1], Sameer Bakhshi[1], Ajay Gogia[1], Raja Pramanik[1], Deepam Pushpam[1], Akash Kumar[1], Mehar C. Sharma[2], Sanjay Thulkar[3], Ritu Gupta[1], Vinod Raina[4]
[1]Medical Oncology, [2]Pathology, [3]Radiodiagnosis, All India Institute of Medical Sciences, New Delhi, [4]Medical Oncology, Fortis Memorial Research Institute, Gurgaon, India

Aims & Objectives: The purpose of this study was to assess the long-term outcomes and prognostic factors of patients with relapsed/refractory (rrHL) who underwent under the care of our transplant team.
Patients / Materials & Methods: The data on adults (>16 years) with biopsy-confirmed rrHL who were autografted from 1 January 2000 to 31 December 2020 at Dr Bhim Rao Ambedkar Institute Rotary Cancer Hospital (DR BRA IRCH), All India Institute of Medical Sciences (AIIMS), New Delhi, were retrospectively reviewed and their long-term outcomes together with factors that predict them were analyzed.
Results: Overall, 134 patients with Hodgkin lymphoma underwent ASCT in this duration. The median age was 26 (IQR, 20-35) years and there were 85 (63.4%) males and 49 (36.6%) females. Nodular sclerosis (45.5%) was the most common histology followed by mixed cellularity Hodgkin lymphoma (41.0%). Majority of patients (70.4%) presented in an advanced stage with a median Hasenclever score of 3 (IQR, 1-5). ABVD regimen was the most used first-line combination chemotherapy in 120 (89.5%) patients. The median duration of remission in those who achieved CR was 7.5 months (IQR, 0-30) with 74 (55.2%) exhibiting early relapse. The median time from diagnosis to transplant was 25.8 (IQR, 17.1-51.4) months and the median lines of treatment received before ASCT was 2 (range, 2-5). The median times for neutrophil and platelet engraftment were 11 (IQR, 9-13) and 14 days (IQR, 12-18) respectively. After ASCT, 104 (77.6%) were in complete remission and 19 (14.1%) had persistent disease. At a median follow up of 38.2 (range, 0.1-240) months, 3- and 5- year progression-free survival (PFS) for our cohort was 48.4% (95% CI 38.7-57.3) and 45.3% (95% CI 35.4-54.6) respectively. Probability of overall survival (OS) at 3- and 5-year was 65.7% (95% CI 55.4-74.6) and 60.5% (95% CI 49.6-69.8) in our patients. Eleven (8.2%) patients suffered transplant-related mortality by 100 days. Post-transplant disease response, pre-transplant serum albumin and chemo-sensitivity of tumor at transplantation were independent prognostic factors determining PFS. Likewise in multivariate analysis, age ≥30 years, ECOG performance status ≥1 and residual disease after transplantation were correlated with inferior OS.
Discussion and Conclusion: This study reports one of the longest follow up data for rrHL patients who underwent ASCT in India. Long term outcomes of this cohort of patients are comparable to western literature in the era of peripheral blood stem cell transplantation. Those who achieved complete remission post-transplant fared much better. Pre-transplant performance status and serum albumin also determined survival in our cohort

Disclosure of Interest: None Declared

Keywords: autotransplantation, hodgkin lymphoma, refractory, relapsed

Poster Presentation

LYMPHOMA/MYELOMA (310)

ROMIPLOSTIM IN AUTOLOGOUS STEM CELL TRANSPLANT - A SINGLE CENTER EXPERIENCE

Monisha Harimadhavan*[1], Bharath Ram[1], Akshatha Nayak[1], Nataraj KS[1], Shilpa Prabhu[1], Karthick RG[1], Chaithanya GB[1], Sharat Damodar[1]
[1]Clinical Hematology, Mazumdar Shaw medical centre, Narayana Health , Bangalore, India

Aims & Objectives: Romiplostim has been investigated as an option for reducing the risk of thrombocytopenia in patients undergoing haematopoietic stem cell transplantation. Based on evidence from literature on its efficacy and safety an institutional policy change was made to incorporate Romiplostim into the transplant protocol from August 2021. We retrospectively compare the thrombocytopenia rates and transfusion requirement in patients before and after instituting Romiplostim in the transplant protocol.
Patients / Materials & Methods: Data from 17 consecutive patients admitted for Autologous stem cell transplant since adding Romiplostim to the treatment protocol were obtained from hospital records. These patients received injection Romiplostim in a dose approximately 4 to 5mcg/Kg subcutaneously on Day + 3 of stem cell infusion . Data from 17 consecutive patients preceding the policy change was obtained from hospital records for comparison. The criteria for platelet engraftment was taken as the first day to achieve a sustained PLT count of greater than 20 x 10^6/L in the absence of PLT transfusion support for at least 72 hours
Results: Overall we had 34 patients in the study including 24 males and 10 females. The Romiplostim group and control group were comparable with regard to the primary indication for autologous transplant and the remission status prior to transplant. The patients in the Romiplostim group had statistically significant reduction in the median volume of platelet transfusion compared to the control group (200ml vs.500ml , p = 0. 04). Similarly there was a statistically insignificant decrease in the median number of days of Grade III -IV thrombocytopenia in the Romiplostim group compared to the control group (6 days vs 7 days ,p = 0.12). Also , 4 patients in the Romiplostim group never dropped their platelet count less than 20000 compared to 1 patient in the control group. Only one patient in the Romiplostim group had bleeding of WHO grade more than or equal to 2, compared to four in the control group. The median day of platelet engraftment and the median days of hospitalization was approximately 12 days and 14.5 days respectively in both the groups
Discussion and Conclusion: Our study shows the efficacy of a single dose Romiplostim in reducing the platelet transfusion requirement in patients undergoing autologous stem cell transplant. Reduced transfusion requirement can translate to reduced costs and transfusion associated complications. Similarly the number of days of Grade III -IV thrombocytopenia and the incidence of bleeding complications were also reduced in the Romiplostim group though not statistically significant

Disclosure of Interest: None Declared

Keywords: Autologous Stem Cell Transplantation(ASCT), platelet transfusion, Romiplostim

Poster Presentation

LYMPHOMA/MYELOMA (340)

POST-SCT ANALYSIS IN MYELOMA: REVIEW AT A BMT UNIT IN INDIA WITH RESPECT TO OVERALL SURVIVAL

Madhura Tinaikar[*1], Aditi Joshi[1], Chandrakant Lahane[1], Abhijit Giram[1], Rajesh Phatale[1], Kannan Subramanian[1,2], Shashikant Apte[1]
[1]Hematology, sahyadri specialty hospital, [2]Hematology, KEM Hospital, Pune, India

Aims & Objectives: To analyze the success and survival of Multiple Myeloma patients, post autologous stem cell transplant at a BMT unit in India.
Patients / Materials & Methods: This is a retrospective observational study. We studied the post-autologous transplant course of 45 patients from 2013 to March 2022.
All 45 patients received high dose Melphalan conditioning. All the patients underwent GCSF mobilized peripheral blood stem cell collection. Post 3 to 4 months of the transplant, patients were offered maintenance treatment individualized as per the patient characteristics. These patients were reassessed at regular fixed intervals with guided interventions
Results: A total of 35 out of 45 patients (77%) are alive to date amounting to 23% mortality. Five patients died (11%) secondary to transplant-related mortality. The other four deaths were secondary to relapse-related causes one patient died of a secondary cause.
Of the 45 patients studied 16 were females (36.4%) and 28 were males (63.6%). The median age group was 56 years. Ig G kappa was seen in a maximum of 31.8% of patients followed by Ig G lambda (25%), Lambda light chain was seen in 16% of the patients, and 3 cases had primary amyloidosis.
At the time of transplant; 50% (n=22) of the patients were in CR1, 15.9% (n =7) were in sCR and 1 patient was in sCR3. 31.8% patients (n=14) were in VGPR.
All the patients received maintenance treatment after 3 months of their post-transplant period. Of the total 35 patients, 4 received Thalidomide alone as maintenance, 10 patients received Lenalidomide alone whereas 11 patients received Lenalidomide plus Dexamethasone as a combination therapy where lenalidomide dosage was adjusted to the patient's tolerability to the drug.
Of the total 45 patients, 13 cases had documented relapse of the disease. Out of these 4 patients had an early relapse (within 6 months of transplant) and 4 patients died secondary to relapse-related causes. The remaining patients were offered the best possible therapy and are following up with us. None of the patients underwent a second transplant.
Discussion and Conclusion: Autologous stem cell transplant has really changed the outlook of patients with Myeloma in India. Lenalidomide alone or in combination with dexamethasone and/or Bortezomib has improved the overall survival and quality of life (QoL) post SCT.
Induction chemotherapy with triplets from the generic source has met the need of the hour for myeloma patients with comparable results

Disclosure of Interest: None Declared

Keywords: Lenalidomide, Multiple myeloma (MM), stem cell transplantation

Poster Presentation

LYMPHOMA/MYELOMA (384)

OUTCOMES OF STEM CELL TRANSPLANTATION FOR LYMPHOMA : A SINGLE CENTER EXPERIENCE FROM NORTH INDIA

Archit S. Pandharipande*[1], Nihar Desai[1], Gopinathan Mathiyazgan[1], Ashish Mishra[1], Manoj Singh[1], Madhuri Smith[1], Priyanka Chauhan[1], Manish Singh[1], Sanjeev Yadav[1], Dinesh Chandra[1], Anshul Gupta[1], Naresh Tripathi[1], Khaliqur Rahman[1], Ruchi Gupta[1], Rajesh Kashyap[1], Soniya Nityanand[1]
[1]Clinical Hematology, SGPGIMS, Lucknow, India

Aims & Objectives: Introduction: Stem Cell Transplant (SCT) Is A Potentially Curative Option For Relapsed and Refractory Lymphomas.
We Report Outcomes For Relapsed Lymphomas Who Underwent Stem Cell Transplant For Lymphoma At Our Institution.
Patients / Materials & Methods: Retrospective analysis of 23(hodgkin+non hodgkin lymphoma)patients who underwent Autologous & allogenic SCT at our centre was done.The demographic profile ,disease characteristic,salvage therapies ,conditioning regimen and outcomes are presented below.
Results: 21 patients underwent Auto SCT, 2 patients underwent allo SCT(1 ALK+ALCL & 1 R/R Hodgkins lymphoma).
Median age of SCT for Hodgkins & NON Hodgkins lymphoma was 24 & 52 years respectively.
The number of patients were 12 & 11 for NHL & HL respectively.
Indications for SCT in hodgkins were refractory disease & Relapse in 20% & 80% respectively.
indications of SCT in Non hodgkins lymphoma were Relapse in 60 % & upfront in 40% (5 patients of mantle cell lymphoma).
80% were males , 20 % were females.
DHAP,GDP,ICE,BV+Benda were most commonly in 63%,27%,5%,5% respectively.
DHAP & DHAP/GDP were preferential salavage therapies in NHL & HL respectively.
Mobilisation regimens were GCSF+Plerixafor(70%),GCSF (26%),Chemomobilisation(4%)
BEAM was the most commonly used conditioning regimen.
The median stem cell dose was 5.85 *10^6 cells/kg.
The median day of engraftment was D10 for neutrophil & D15 for platelet transfusion.
Allogenic SCT were done in 2 patients with FLU-MEL Conditioning and Cyclosporine and methotrexate prophylaxis.
Patients engrafted on D+12 and D+15 respectively and 1 had mixed chimerism at D+365 and 1 had 100 % donor chimerism respectively .
1 patient in autologous SCT arm died due to Covid-19 pneumonia 3 years after SCT .
Rest 22 patients are alive and doing well at a median follow up of 2 years.
Discussion and Conclusion: The outcomes of SCT in lymphomas are very encouraging and should be implemented widely in relapsed setting as a standard of care so that maximum patients can be lymphoma free and have a good quality of life.
Allogenic SCT may also help in improving outcomes till further cellular therapies become widely available.

Disclosure of Interest: None Declared

Keywords: Allogenic HSCT, autologous HSCT, hodgkin lymphoma, non hodgkins lymphoma

Poster Presentation

LYMPHOMA/MYELOMA (390)

MYELOMA- A BEGINNER'S HOPE FOR SETTING UP A NEW TRANSPLANT CENTRE IN TIER-2 CITY IN INDIA

Subbaiah Ramanathan*[1], Prabakaran Sankaralingam[2], Thilagavahy Manoj Kumar[3], Senthilvel Murugan[4]
[1]Haematology, [2]Transfusion medicine, [3]Microbiology, [4]Radiology, Kauvery hospitals, Tiruchirapalli, India

Aims & Objectives: Most of the haemopoietic stem cell transplant (HSCT) centres are established in tier-1 cities (population of 1 million and above). Establishing a HSCT centre in a tier-2 city (0.5 to less than 1 million population) remains a challenge for a new transplant physician especially in a private sector health centre. Here we share our experience in establishing a new and the first HSCT in Tiruchirapalli (a tier-2 city in Tamil Nadu, South India). As usual Myeloma, remained the first disorder to be transplanted here, bringing hope for the physician, new HSCT team as well as patients in this part of the country.
Patients / Materials & Methods: We have established a 2 bedded HSCT unit with HEPA filter module. Patients with myeloma were managed with standard regimens. First line regimen was VRD (Bortezomib, Lenalidomide, Dexamethasone), CyBorD (Cyclophosphamide, Bortezomib, Dexamethasone) or Thalidomide Dexamathasone. Second line regimens (VDT PACE or KPD) were used if the first line regimen (minimum 4 cycles) failed to show at least a partial response as per IMWG criteria. Patients with at least a partial response and up to 65 years with a good physical performance were counselled for an autologous stem cell transplantation. Stem cell mobilization was done with G-CSF and Plerixafor. Peripheral blood stem cell harvest was done using haemonetics MCS+ or Spectra optia apheresis systems through a Jugular venous HD catheter. Conditioning regimen used was Melphalan (200mg/sq.m if normal renal function, 140mg/sq.m if renal failure). Supportive care (antibiotics, mucositis care, irradiated blood products) was given until engraftment and recovery of mucositis or defervescence.
Results: Amongst transplant eligible patients especially during Covid-19 pandemic, 10 patients (6 males, 4 females) have undergone autologous BMT procedure over last 2 years. Median age was 51.7 years (range 25-61 years). Bone lesions were present in all 10, anaemia was present in 9/10, renal failure in 4/10 and one had hypercalcemia at diagnosis. Two had diabetes mellitus, 3 had hypertension and 3 had peripheral neuropathy. Very good partial response was achieved in 5, complete response in 4 and one had only a partial response. Mean CD34 cell dose infused was 7.84 x 106/Kg (ranged from 4.54 x 106/Kg to 14.18 x 106/Kg). Nine patients engrafted neutrophils and platelets successfully (90%). Two patients grew microbes in blood culture (Pseudomonas aeruginosa and Acinetobacter baumanii). One patient expired on day +18 before engraftment in view of Acinetobacter sepsis.
Discussion and Conclusion: Myeloma still remains the most common disorder where a haematologist starting transplantation services at a new centre begins with. It brings hope for both the patient as well as the new stem cell transplantation team.

Disclosure of Interest: None Declared

Keywords: Myeloma, new HSCT centre, Tier-2

Poster Presentation

GVHD (134)

EVIDENCE-BASED NURSING CARE FOR SKIN ACUTE GRAFT VERSUS HOST DISEASE

Yen Ping Hung[* 1, 2, 3], Jui-Yi Chen[1], Ming Yao[2, 4]
[1]Department of Nursing, [2]Hematology, National Taiwan University Hospital, [3]Nursing, National Taipei University of Nursing and Health Sciences, [4]Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan, China

Aims & Objectives: Graft versus host disease (GVHD) often occurs after allogeneic hematopoietic stem cell transplantation, and mild immune rejection is thought to reduce the chance of relapse of hematological malignancies. Acute GVHD affects 40-60% of patients, typically affects major organs including intestinal, liver, and skin, usually occurs for a limited time but can be life-threatening, and is one of the leading causes of mortality. Skin manifestations are the most common sign of GVHD, especially in grade 3 or 4 cause severe infection, pain, impaired body image, and affect the quality of life.
Patients / Materials & Methods: Despite grades 3 to 4 acute skin GVHD causes burden or discomfort to patients, and limited information currently available on skin and wound care also challenges clinical caregivers. To improve the severity of patients with acute skin graft versus host disease, we searched PubMed, Cochrane, EMBASE, and nursing-related literature from 2000 to 2021 and compiled recommendations with evidence levels.
Depending on the degree of skin change, we reviewed the evidence of effective and feasibly to guide skin and wound care, including physical hygiene, topical and systemic treatment, infection prevention, pain relief, activities of daily living (ADL), and impact on body image. Skin and wound care focuses on the use of preventive pain medication (especially before wound dressing), cleaning and moisturizing (including appropriate product selection), maintaining skin integrity (especially bullae and integrity of wound bed), using contain soft silicone or foam dressings, supplementary absorbent dressing layers (e.g., Tubifast), use of pressure-relief mattresses, etc. The multidisciplinary team includes WOC nurses (wound and ostomy nurses), pharmacists, dermatologists, dietitians, infectious diseases physicians, anesthesiologists, and transplant teams to assess and improve patients' acute symptoms.
Results: These supportive intervention approaches to skin and wound care were applied to 6 patients with grade 3 to 4 GVHD, and whose grades of skin were downgraded to grade II or I within three weeks. This demonstrates the importance of evidence-based recommendations for skin and wound care and enables advances in the care of acute skin GVHD.
Discussion and Conclusion: Even with great progress in the skin and wound care but difficult wound with severe damage (adding more nursing hours, patients unable to afford dressings at their own expense, etc.) and deteriorating nutritional status are still problems, and what is more difficult is how balancing the treatment of infection with the pharmacological treatment of GVHD is a challenge. It is hoped that future research will integrate more appropriate care models to improve the acute GVHD.

Disclosure of Interest: None Declared

Keywords: Acute, Evidence, Graft versus Host Disease, Nursing, Skin

Poster Presentation

GVHD (135)

WITHAFERIN-A ALLEVIATES ACUTE GRAFT VERSUS HOST DISEASE THROUGH IMMUNE MODULATION

Saurabh K. Gupta[*1,2], Deepshikha Dutta[2,3], Kajal Dalvi[4], Twinkle Khanka [4], Prashant R. Tembhare[2,4], Syed K. Hasan[2,3], Lal Hingorani[5], Navin Khattry[2,6], Vikram Gota[1,2]
[1]Clinical Pharmacology, ACTREC-Tata Memorial Centre, Navi-Mumbai, [2]Homi Bhabha National Institute , Mumbai, [3]Cell and Tumor Biology Group, [4]Hematopathology Laboratory, ACTREC-Tata Memorial Centre, Navi-Mumbai, [5]Pharmanza Herbal Pvt. Ltd, Gujrat, [6] Department of Medical Oncology, ACTREC-Tata Memorial Centre, Navi-Mumbai, India

Aims & Objectives: To evaluate anti-GvHD efficacy and immunomodulatory effects of Withaferin-A (WA)
Patients / Materials & Methods: To evaluate the in-vivo anti-GvHD potential of WA, a complete mismatch model of GvHD was developed. Recipient BALB/c (H-2Kd) mice were expose to 6.5 Gy of total body radiation. The irradiated mice were transplanted with bone marrow cells of donor C57BL/6 (H-2Kb) mice resulting in aGvHD. Following transplantation, mice were randomised into [1] GvHD control, [2] Clinical score (CS) 1-3, [3] CS 4-6, [4] CS 7-9, [5] CS 9-11 groups. All mice were observed closely and their clinical score were monitored on daily basis. WA were administered orally (1mg/kg for 21 days) as and when mice developed the above clinical score. For mechanistic understanding, whole blood from healthy donors were collected and human peripheral blood mononuclear cells (hPBMCs) were isolated using ficoll gradient method. hPBMCs were ex-vivo treated with WA (1μM) or dimethyl sulfoxide (vehicle) for 2 hrs and cells were stimulated with PHA for the next 72 hrs. Media supernatant of all samples were collected for cytokine analysis and cells were processed for evaluation of proliferation and immune cell phenotyping by flow cytometry. JAK2-STAT3 signalling in hPBMCs was investigated using western blotting.
Results: WA treatment significantly improved the clinical score of aGvHD in terms of diarrhoea, weight loss, ruffling of skin and loss of movement. WA also significantly improved the overall survival irrespective of the severity of GvHD. Proportion of animals survived at day 40 was 0/8, 4/6. 3/6, 2/6 and 0/4 in GvHD control, CS 1-3, CS 4-6, CS 7-9 and CS 10-11 groups respectively. The hazard ratio in the four treatment groups were 0.19 (95% CI = 0.05-0.7), 0.29 (95% CI= 0.08-0.96), 0.25 (95% CI= 0.07-0.8), 0.23 (95% CI= 0.08-0.87) for CS1-3, CS4-6, CS7-9 and CS10-11 respectively in comparison with GvHD control. Ex-vivo treatment of hPBMCs with WA suppressed proliferation of T-cell subsets and modulated the immune cell phenotypes. The immune subset of absolute monocyte, classical monocyte, PD1-CD4 cells and Tim3-CD8 cells were found to be significantly decreased on treatment with WA. Moreover, the absolute non-classical monocytes and γδT-cells increased by WA treatment. Additionally, WA treatment also lead to significant inhibition of cytokine (IFN-γ, IL-6, TNF-α, IP-10, IFN-L1, GM-CSF, IL-1β and IL-10) secretion from hPBMC ($P<0.05$). It was also observed that WA treatment significantly inhibits the protein levels of pJAK2 and pSTAT3.
Discussion and Conclusion: WA abrogates GvHD manifestation and improves survival by regulating immune cell proliferation, differentiation and cytokine storm via inhibition of JAK2-STAT3 signalling. Survival data from mice supports further investigation of WA for GvHD in a prospective clinical trial.

Disclosure of Interest: None Declared

Keywords: Anti Graft versus Host Disease, Human periphearal blood mononuclear cells, Immunemodulation, Withaferin-A

Poster Presentation

GVHD (139)

STROMAL CELL-DERIVED EXOSOME- ENRICHED EXTRACELLULAR VESICLES FOR CHRONIC CUTANEOUS GVHD

Mehrdad payandeh[*] [1]
[1]Kums , Kermanshah , Iran

Aims & Objectives: Allogeneic peripheral blood stem cells transplantation (PBSCT) is now among the treatments for different haematological diseases and malignancies such as acute myeloid leukaemia (AML).
Although this treatment is very advanced, graft-versus-host disease (GVHD) is still the most common and severe side effect.
Human mesenchymal stromal cells (hMSC) have been used to treat many inflammatory diseases/disorders in the clinic. A recent systematic review and meta-analysis showed that treatment with these cells is not associated with any severe or notable side effects.
Exosomes are natural extracellular vesicles released by different cell types and contain proteins, lipids and RNA. These vesicles have been known to participate in intercellular interactions and communications. Depending on the origin and microenvironment of exosomes, they could play different roles, of which immune modulation is one of the most important ones.
Patients / Materials & Methods: The patient was a 39-year-old Caucasian male diagnosed with AML type M4 5 years ago (April 2016). Following routine treatments and after reaching complete remission, he underwent PBSCT (one ses- sion) from an identical donor (brother).
At his clinic visit, reticulated pink to violet papules and plaques admixed with post-inflammatory hyperpigmentation were noted on his face and other areas. vitiligo/amelanic patches with scarring alopecia were detected on his scalp.
The exosomes-enriched EVs were isolated from placental- derived human mesenchymal stromal cells as has been described, and the patient received four treatments at a weekly interval (June 2021; 5 years and 2 months after the transplantation). In each ses- sion, 0.5–0.8 mg (1.9–2.6 × 1011 particles) of exosome-enriched EVs were administrated in 50 ml saline (0.9%) through the right cubital vein access. patient well tolerated the treatment, and no side- effect was observed following the intervention.
Results: The changes began after the third injection, and on the 15th day following the last intervention, when he began to feel significant changes in his condition, the patient was evaluated more closely. (15 days following last injection), his skin has become less hyperpigmented. Also, the frequency and severeness of the mentioned ulcers, wounds and keratotic and atrophic lesions de- creased, healing of the wounds observed. the stiffening ,dryness of skin were significantly improved fol- lowing treatment.
Discussion and Conclusion: Although many studies have used mesenchymal stem cells in clin- ics, data on using MSCs exosome therapy for GVHD are extremely limited. The experience of our team with hPMSC exosome-enriched EVs therapy on the described cutaneous cGVHD patient was clini- cally successful, making it a potential treatment for this pathology. further complementary studies and trials are strongly suggested.

Disclosure of Interest: None Declared

Keywords: Corticosteroid, Exosome, Gvhd, Healing

Poster Presentation

GVHD (146)

REAL WORLD EXPERIENCE OF RUXOLITINIB IN STEROID REFRACTORY GRAFT VERSUS HOST DISEASE

Akanksha Garg*[1], Kamlesh Shah[1], KINNARI PATEL[2], Ambika Vacchani[1], HARDIK K. SOLANKI[1], RAJAN YADAV[1], Sandip Shah[1, 2]
[1]The Gujarat Cancer and Research Institute, [2]HOC Vedanta, Ahmedabad, India

Aims & Objectives: Graft-versus-host disease (GVHD), especially steroid-refractory GVHD, remains a life-threatening complication after hematopoietic stem cell transplantation (HSCT). Second line therapy for steroid refractory GVHD remains a challenge. Data from lower- middle income countries (LMICs) is scarce. We aimed to evaluate the experience of use of ruxolitinib at our centre.
Patients / Materials & Methods: We conducted a retrospective analysis of all patients who received ruxolitinib for steroid refractory GVHD between January 2015 to May 2022. Twenty patients were eligible for this study. Patient details were obtained from case files. Dose of ruxolitinib used was 5 mg BD started initially and if tolerated increased to 10 mg BD. In pediatric patients, dose used was 2.5 mg BD (<15 kg) and 5 mg BD (>15 kg.) The GVHD prophylaxis used was cyclosporine and methotrexate for matched sibling donor transplants and post-transplant Cyclophosphamide (PTCy) with Mycophenolate-mofetil and Cyclosporine/tacrolimus/sirolimus for haploidentical transplants. All patients were transfused peripheral blood stem cells from donors. Post transplant, patients continued regular follow up as per schedule. Supportive care was given as per unit protocol.
Results: Twenty patients received ruxolitinib for steroid refractory GVHD. Median age was 17 Years (range-2-50 years) and 70% were males. Eleven (55%) patients were <18 years age. Matched sibling donor transplants were done in 18 patients (90%), and haploidentical transplants in 2 patients (10%). Benign hematological disorders included thalassemia major (n=9) aplastic anemia (n=6), and paroxysmal nocturnal hemoglobinuria (n=1). Malignant disorders included relapsed acute lymphoblastic leukemia (n= 1), relapsed acute myeloid leukemia (n=1), therapy related acute myeloid leukemia (n=1) and chronic myeloid leukemia (n=1). Acute GVHD was seen in 11 patients (55%) and chronic GVHD in 9 patients (45%). Median number of previous lines of therapy were 3 (range-1-4). Grade 3 and 4 GVHD was seen 14 (70%) patients. Predominant sites were gut (60%), skin (30%) and liver (20%). Overall response rates were 65% (n=13). Main adverse events noted with ruxolitinib were cytopenia (n=5), CMV reactivation (n=4) and transaminitis in one patient. Tapering of steroids was possible in majority of the patients Overall survival for patients with acute GVHD at 6 months was 55% and for those with chronic GVHD at 1 year was 67%. GVHD relapse occurred in 3 patients after they reduced or continued their ruxolitinib doses.
Discussion and Conclusion: Ruxolitinib in the real life setting is an effective and safe treatment option for GVHD, with an ORR of 65% in heavily pretreated patients. However, CMV reactivation and underlying cytopenias are potential causes for mortality in LMICs.

Disclosure of Interest: None Declared

Keywords: GVHD, Ruxolitinib, Steroid refractory

Poster Presentation

GVHD (227)

PIRCHE ASSOCIATION WITH TRANSPLANT OUTCOMES IN HAPLOIDENTICAL/MISMATCHED HSCT.

Jyoti Rajak[*1], Selma D'Silva[1], Sachin Punater[2,3], Manisha Tambe[1], Andrea Pinto[1], Bansi Parsaniya[1], Anant Gokarn[2,3], Lingraj Nayak[2,3], Akanksha Chhabra[2,3], Sumeet Mirgh[2,3], Nishant Jindal[2,3], Navin Khattry[2,3], Meenakshi Singh[1,3]
[1]Transplant Immunology and Immunogenetics, [2]Bone Marrow Transplantation Unit, Advanced Centre for Treatment, Research and Education in Cancer (ACTREC), Tata Memorial Centre, Navi Mumbai, [3]Homi Bhabha National Institute, Mumbai, India

Aims & Objectives: The aim of the current study was to investigate the effect of PIRCHE (Predicted Indirectly recognizable HLA epitopes) on clinical outcomes of haploidentical/mismatched retrospective cases.
Patients / Materials & Methods: High-resolution NGS typing of 46 patient and donor pair was performed from stored DNA samples. The samples were analyzed using Gendx NGS engine v2.26. PIRCHE I and II scores were determined using PIRCHE model v3.3.50. Statistical analysis for the data was performed using SPSS software version 25 (SPSS, Chicago IL, USA).
Results: The study cohort included 46 patients who had undergone T-cell replete haploidentical/mismatched transplantation. The median age of the patients was 26 years (5-50 years) and that of donors were 35 years (9-56 years). Patient were divided into 2 groups of having PIRCHE score less than 10 and greater than 10. The median PIRCHE score was 12 (0-62) and 20 (0-75) for PIRCHE I and PIRCHE II respectively. The PIRCHE I score which corresponds to the HLA Class I presentation (to CD8+ T cells) showed no effect on engraftment (p-1.00), acute (p-0.708) or chronic (p-0.216) GVHD (Graft versus host disease) and overall survival (p-0.474). 78.3% patient (3 of 4) didn't engraft in group having PIRCHE II score greater than 10 (p-1.00). Similarly, 76.5% suffered acute (p-1.00) and 78.6% suffered chronic GVHD (p-1.00). Also the overall survival was affected in patients having the PIRCHE II score greater than 10 (p-0.297).
Discussion and Conclusion: PIRCHE I did not correlate with the clinical outcome of haploidentical/mismatched HSCT. PIRCHE II group having a greater than 10 score correlated with engraftment, acute, chronic GVHD, and overall survival but the effect was non-significant. Our study highlights the importance of PIRCHE score in transplant outcomes in haploidentical/ mismatched HSCT cases. However, since this was a pilot study, we aim to investigate the effect of PIRCHE in a larger cohort.

Disclosure of Interest: None Declared

Keywords: Haplo-identical/mismatched HSCT, PIRCHE, Transplant Outcome

Poster Presentation

GVHD (273)

INTNSE APPROACH IN ACUTE GVHD GI IN NEW CASE OF AML AFTER FIRST REMISSION

Mehrdad Payandeh[*1], Farzaneh Chardoli [1]
[1]Kums , Kermanshah , Iran

Aims & Objectives: A 35 years old women new case of high risk AML in CR1 consolidated with full match ALlogenic transplantation . After discharge she come back soon with grade 4 diarrhea , grade 3 skin Involved.
Poor intake tolerated the basic drugs especially cyclosporine .
After UGI endoscopy . With probability of A-GVHD treated with mehylprednisolone pulse and IV cyclosporine.
The diarrhea and poor vomiting lated for controlled .
The ibrutinib and three part of exsosme mSCT add TO THERAPY.
Patients / Materials & Methods: After one months of intensive mixing therapy GI sign controlled .
Results: An aggressive presentation of GVHD need to treat by multiple line of drugs because in this type of presentation in A-GVHD we can see more than 50% mortality if delayed the time and decide to step by step therapy protocol.
Discussion and Conclusion: Aggressive therapy for aggressive presentation of GVHD can prevent the progression and resolved the problem .

Disclosure of Interest: None Declared

Keywords: Exzosome, GVHD, Ibrutinib

Poster Presentation

GVHD (312)

CYTOTOXIC AND REGULATORY T LYMPHOCYTES EXPRESSION IN PREDICTING THE STEROID RESPONSE IN GI GVHD.

Karthick R G* [1], Rekha PR[2], Bharat Ram[1], Nataraj KS[1], Shilpa Prabhu[1], Akshatha Nayak[1], Monisha H[1], Chaitanya G B[1], Sharat Damodar[1]
[1]Hematology&BMT, [2]Pathology, Narayana hrudayalaya hospital, Bangalore, India

Aims & Objectives: To analyze the role of cytotoxic T lymphocytes and regulatory T lymphocytes in predicting the response to steroids in GI GVHD.
Patients / Materials & Methods: A retrospective and prospective observational study was conducted at Narayana Hrudayalaya hospital-Bangalore. 42 allogeneic transplant patients more than 18 years of age with GI GVHD were included in the study. Demographic, clinical, laboratory and response details of the patients in the study were recorded as per the proforma. H&E stained slides were assessed to know the histological grade of GI GVHD; Expression of CD 3, CD 8, FOXP 3 were assessed under 40X power for 10 high power fields. Sum total of each marker's expression was made for each patient. Histological grading of GI GVHD of these patients was done as per Lerner's grading and clinical staging of these patients was done as per Modified Glucksberg criteria. Analysis was done using Microsoft Excel and statistical analysis was performed by SPSS 23.0.
Results: The most common histological grade of GI GVHD in our study population is grade II-IV(25;59.52%).
The most common clinical staging of GI GVHD is Stage IV(21;50%).
12/42 patients responded to steroids within 3 to 5 days of onset of GI GVHD symptoms; 29/42 patients were started on second line of treatment.
There was a statistically significant association of CD 3 and CD 8 expression with histological grading of GVHD (p-value of <0.001- CD3 and 0.046 - CD8).
There was a statistically significant association of CD8 with clinical staging of GI GVHD(p value-0.020).
There was a statistically significant association between steroid response and CD 8 expression(p<0.001).
A cut off value of 263 cells/10 HPF for CD3 and 202 cells/10 HPF for CD8 was taken from ROC analysis to predict the steroid non responsiveness in the clinical setting of acute GI GVHD.
The CD3 cut off value of ≥ 263 cells/10 HPF has 80% sensitivity and 67% specificity and CD8 cut off value of ≥ 202 cells/10 HPF has 96% sensitivity and 67% specificity in predicting steroid non responsiveness.
Discussion and Conclusion: 1. Histological grading of GVHD does not correlate with clinical staging at all times which could be due to progression of GVHD in some patients and lack of follow up biopsies.
2. In addition to Lerner's grading, estimation of CD3, CD8 expression can serve as additional markers in biopsies to predict the severity of GI GVHD.
3. There was a statistically significant association of CD8+ T cells with steroid response in the absence of concomitant CMV infection.
4. Regulatory T cells (FOXP3) did not have a statistical correlation with histological grading, clinical staging and steroid responsiveness as claimed in other studies(Rieger et al).
5. GVHD is a dynamic process, hence repeat GI biopsies and assessment of markers may better predict the GVHD outcomes.

Disclosure of Interest: None Declared

Keywords: Cytotoxic T lymphocytes(CD8), GI GVHD, Regulatory T lymphocytes(FOXP3), Steroid response

Poster Presentation

GVHD (375)

LYMPHOCYTE RECONSTITUTION FOLLOWING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

Mohini Mendiratta[*1], Vineet Govinda Gupta[1], Sandeep Rai[2], Saroj Singh[2], Lalit Kumar[1], Ritu Gupta[2], Smeeta Gajendra[2], Ranjit Kumar Sahoo[1]
[1]Department of Medical Oncology, [2]Department of Laboratory Oncology, All India Institute of Medical Sciences, New Delhi, India

Aims & Objectives: Hematopoietic stem cell transplantation is a therapeutic modality used in the treatment of hematological and non-hematological malignancies. The current prospective study aims to identify cellular signatures of the patients responsible for the development of acute GVHD (aGVHD) in the allo-HSCT recipients.
Patients / Materials & Methods: Fifteen patients who underwent allogeneic hematopoietic stem cell transplantation were recruited prospectively from January 2021 onwards. Peripheral blood specimens were collected from the recipients of Allo-HSCT at different time points: Pre-conditioning, D+14, D+30, D+60, D+100, D+180 post-Allo-HSCT, and at the onset of aGVHD to determine the pattern of immune reconstitution and immune profile leads to the development of aGVHD in Allo-HSCT recipients. The immune cellular (B lymphocytes, T lymphocytes, regulatory T helper cells, Natural killer cells, Dendritic cells, and their subsets) profiles were assessed using fluorochrome-conjugated antibodies by flow cytometry.
Results: The pattern of reconstitution of lymphocyte subsets in Allo-HSCT recipients: Natural Killer (NK) cells, dendritic cells > helper T cells > Tregs > cytotoxic T cells > B lymphocytes. In Allo-HSCT recipients, the level of both immature (CD56+ CD16-) and mature (CD56dim CD16+) subset of NK cells was higher after D+60 which revealed reduction in GVHD severity. Similarly, dendritic cells (CD11c+ HLA-DR+) were reconstituted in majority of patients by D+30. Conventional dendritic cells (CD11c+CD123-) constitute vast majority of circulating dendritic cells than plasmacytoid dendritic cells (CD11c+CD123+). Helper T cells (CD3+ CD4+) started to appear early than cytotoxic T cells (CD3+ CD8+) in peripheral blood specimens after Allo-HSCT. Effector memory (CCR7- CD45RA-) and central memory (CCR7+ CD45RA-) subsets of helper T cells constituted a major proportion of helper T cells. There was a slight delay in reconstitution of cytotoxic cells as these appeared by D+60. Effector (CCR7- CD45RA+) and effector memory subsets of cytotoxic cells were more prominent in Allo-HSCT recipients and showed an immediate effect on cell cytotoxicity and might be related to aGVHD. The level of B cells (CD19+ CD20+) was much lower at D+180 and memory phenotype (CD27+ IgD+/-) of B lymphocytes was more than naïve B cells in peripheral blood of the Allo-HSCT recipients.
Discussion and Conclusion: Delayed immune recovery was associated with a higher risk of inhibition of Graft-versus-leukemia effects and the occurrence of GVHD in allogeneic settings. Conclusively, the current prospective study is the first from India to the best of our knowledge and would guide the clinicians to prevent aGVHD by employing strategies to enhance immune reconstitution together with preventing the development of aGVHD at an early stage.

Disclosure of Interest: None Declared

Keywords: Acute Graft-versus-host-disease, Allogeneic hematopoietic stem cell transplantation, Lymphocytes reconstitution

Poster Presentation

GVHD (415)

JAK INHIBITORS IN THE TREATMENT OF GRAFT-VERSUS-HOST DISEASE: FRIEND OR FOE?

Karthikeyan Gandhi*[1], Kalpana Rajesh[1], Prasanth Ganesan[1], Biswajit Dubashi[1], Smita Kayal[1]
[1]Medical Oncology, Jawaharlal Institute of Postgraduate Medical Education & Research, PONDICHERRY, India

Aims & Objectives: Corticosteroids is the first-line treatment for acute or chronic Graft-versus-host disease (GvHD). Second-line treatment in both the settings remains a challenge. Janus kinase (JAK) inhibitor, Ruxolitinib, has been shown as an effective and safe treatment option for patients with acute (aGvHD) and chronic (cGvHD) after failure of one or two lines of therapy. Preliminary results of phase1/2 study have shown safety and efficacy of another JAK inhibitor, Baricitinib, in GvHD. We hereby present real world experience of the use of these JAK inhibitors in the management of refractory GvHD.
Patients / Materials & Methods: We reviewed the medical records of all patients who underwent allogeneic HSCT in our centre from January 2019 to December 2021. Of the 31 patients who had an allogeneic HSCT over the past 3 years, 9 had received JAK inhibitors during the course of their GvHD management. Baseline patient characteristics, type of allogeneic HSCT, conditioning, GvHD prophylaxis, onset, course, treatment and outcomes of acute and chronic GvHD were studied.
Results: Nine patients of allogeneic transplant were included, 7 adults and 2 children. Summary of the baseline characteristics, GvHD course and final outcomes for all patients is shown in Table 1. Majority had HSCT with matched sibling donor (n=7), one had matched unrelated donor (MUD), and one had a haploidentical family donor. Acute GvHD was observed in 8/9 patients and cGvHD in 8/9. Ruxolitinib was used as second line therapy for aGvHD in 1 patient, as second and third line therapy for cGvHD in 5 and 1 patient respectively. Baricitinib was used as second or third line therapy in 2 patients with cGvHD, and as substitution therapy for ruxolitinib, in view of cost issues, in 2 patients. At 4 weeks, 5 patients had partial response, 2 had stable disease, one had no response, and one patient was un-evaluable due to very early discontinuation. For 7 patients JAK inhibitor had to be discontinued at different time points during the course, mostly due to uncontrolled infection in 6 patients, and inadequate response in 1. One or more episode of different infections were observed in all the patients (cytomegalovirus, BK virus, pneumocystis pneumonia, tuberculosis, COVID-19, hepatitis B); 4 died due to infection complications, 3 from severe COVID pneumonia and 1 from pneumocystis. Grade 3 /4 thrombocytopenia was seen in 4. At the last follow up, 4 patients were alive, all had their primary disease and GvHD in remission, two were off immunosuppressant, and the other 2 were on tapering steroids.
Discussion and Conclusion: JAK inhibitors shows good early response in second or third line therapy for GvHD. However, risk of infection is high which warrants careful monitoring, early identification and appropriate treatment for improved outcomes.

Disclosure of Interest: None Declared

Keywords: GvHD, Infection, JAK inhibitor

Poster Presentation

INFECTIONS (150)

EPIDEMIOLOGY OF CMV INFECTION AND DISEASE IN HSCT RECIPIENTS: A SYSTEMATIC REVIEW

Clarisse Martins Machado[1], Sung-Yeon Cho[2], Monica Slavin[*3], Inderjeet Singh[4], Anudeep Sandhu[5], Dirk Demuth[5], Depei Wu[6]
[1]Institute of Tropical Medicine, University of São Paulo (IMT-FMUSP), São Paulo, Brazil, [2]Seoul St. Mary's Hospital, Seoul, Korea, South, [3]Victorian Infectious Diseases Service, Royal Melbourne Hospital, Melbourne, Australia, [4]Takeda Pharmaceuticals India Pvt Ltd, Haryana, India, [5]Takeda Pharmaceuticals International AG – Singapore Branch, Singapore, Singapore, [6]Department of Hematology, the First Affiliated Hospital of Soochow University, Suzhou, China

Aims & Objectives: Cytomegalovirus (CMV) is a prevalent herpes virus with higher seroprevalence in South America, Africa, and Asia than in Europe and North America. In hematopoietic stem cell transplant recipients (HSCT), CMV infection is a common opportunistic infection and major cause of morbidity and mortality. A systematic review (PROSPERO; CRD42020205559) was conducted to better understand the epidemiology of CMV infection and disease post-HSCT in selected countries outside of Europe and North America.
Patients / Materials & Methods: Observational studies that included HSCT recipients (any age) from 15 selected countries in Asia-Pacific, Latin America, Russia and the Middle East were screened (search period: 01 Jan 2011–21 Jul 2021). Outcomes of interest were incidence, recurrence rates and risk factors of CMV infection and CMV disease, and CMV-related mortality at any time point. Indexed publications (Ovid® MEDLINE and Embase, Cochrane Database of Systematic Reviews and World Health Organization database Global Index Medicus) were searched, supplemented by pragmatic searches of the grey literature and snowballing of references lists.
Results: The review included 63 studies (range: 33 to 10,206 patients [pts]) that mostly enrolled adults (≥18 years [y]; n=49 studies, 77.8%) and allogeneic HSCT recipients (n=53, 84.1%). In 43 of 54 studies reporting on incidence of CMV infection, estimates were uniformly distributed between 24.8% and 61.2% within 1 y post-HSCT (Figure 1). Estimates were lower in autologous HSCT recipients (5.3%) and younger pts at the time of transplantation (9.3% in adults with a median age of 25 y and 18.6% in pts aged ≤20 y). In 8 studies from China and South Korea, estimates were higher (range: 69.4%- 88.2%) and most had a follow-up period >1 y (median: 27-54 months in 5 studies). Incidence of CMV disease following HSCT was <20%, with estimates uniformly distributed between 0% and 15.7% in allogeneic HSCT. In 11 studies, reported rates of CMV recurrence ranged between 19.8% and 37.9%. Commonly reported risk factors for CMV infection or disease in HSCT recipients were high-risk CMV serostatus (R+) (hazard ratio [HR]: 2.6 and 3.7, odds ratio [OR]: 2.2 and 5.4), older age of recipients (HR for each additional year: 1.03-1.04), presence of acute or chronic graft versus host disease (HR: 1.1-2.5), haploidentical HSCT (HR: 2.7-6.4), and use of immunosuppressive agents (OR: 5.0-9.3). CMV-related mortality was reported in up to 10% of pts following HSCT (n=30 studies; assessment period not reported).
Discussion and Conclusion: Relatively high rates of CMV infection, CMV disease and CMV recurrence were reported post-HSCT, with CMV-related mortality seen in up to 1 in 10 pts. High rates of CMV infection and disease post-HSCT may impact outcomes and increase disease burden in pts post-transplantation.

Disclosure of Interest: C. M. Machado Research Grant from: See presenting author's COI., S.-Y. Cho Research Grant from: See presenting author's COI., M. Slavin Research Grant from: This research was supported by Takeda Pharmaceuticals International AG – Singapore Branch. The company was involved in data analysis and abstract preparation following the direction of the authors. Editorial support for this encore abstract was provided by Bena Lim, PhD, of MediTech Media Ltd and funded by Takeda Pharmaceuticals International AG – Singapore Branch. CMM has received honoraria from Takeda and MSD (advisory board, speaker, educational events, meeting); S-YC has served as a consultant for Takeda Pharmaceutical, and has received research support and payment for lectures from Merck Sharp & Dohme, Pfizer and Gilead; MS has received grants from F2G, Gilead, Merck and personal fees from Gilead, Pfizer, Takeda and Roche for work outside of this research; IS is an employee of Takeda Pharmaceuticals India Pvt Ltd; AS and DD are employees of Takeda International AG – Singapore Branch and hold stock options; WD has no conflicts of interest to disclose. The original abstract titled “Epidemiology of cytomegalovirus infection and disease in hematopoietic stem cell transplant recipients in selected countries outside of North America and Europe: A systematic review” was presented at the 29th International Congress of The Transplantation Society (TTS 2022)., I. Singh Research Grant from: See presenting author's COI., A. Sandhu Research Grant from: See presenting author's COI., D. Demuth Research Grant from: See presenting author's COI., D. Wu Research Grant from: See presenting author's COI.

Keywords: cytomegalovirus, epidemiology, hematopoietic stem cell transplant, real-world evidence

Poster Presentation

INFECTIONS (151)

HCRU IN TRANSPLANT RECIPIENTS WITH CMV: EXPLORATORY ANALYSIS OF THE PHASE 3 SOLSTICE TRIAL

Ishan Hirji[1], Kim Cocks[*2], Alejandro Moreno-Koehler[3], Aimee Sundberg[1]
[1]Takeda Development Center Americas, Inc., Lexington, United States, [2]Adelphi Values, Bollington, Cheshire, United Kingdom, [3] Adelphi Values, Boston, United States

Aims & Objectives: Increased healthcare resource utilization (HCRU) has been associated with cytomegalovirus (CMV) infection following transplantation, especially in patients (pts) requiring >1 antiviral course. In the Phase 3 SOLSTICE study (NCT02931539), maribavir (MBV) was superior to investigator-assigned therapy (IAT; val/ganciclovir, foscarnet, cidofovir) for CMV clearance at Wk 8 and clearance plus symptom control Wk 8 maintained through Wk 16 in transplant recipients with refractory CMV infection with/without resistance (R/R). This exploratory analysis of SOLSTICE evaluated HCRU for the MBV and IAT arms.
Patients / Materials & Methods: Transplant recipients with CMV R/R to prior treatment (tx; failure to achieve >1log10 decrease in CMV DNA after ≥14 days, with/without genotyped resistance) were randomized 2:1 to MBV 400 mg BID or IAT for 8 wks with 12 wks of follow-up. After ≥3 wks of tx, pts in the IAT arm with pre-specified criteria could enter a MBV rescue arm (8 wks of MBV tx, 12 wks of follow-up). Data on hospital admissions were collected at each study visit and analyzed by tx during the tx and follow-up phases. Analyses included the number of pts with ≥1 hospitalization and length of hospital stay (LOS). Hospitalization rates and LOS (per person/year) were estimated using negative binomial models adjusting for exposure time. Adjusted incidence rates (IR), 95% CIs, IR ratios (IRR) and percent reduction in IRRs were calculated. Supplementary analyses described hospitalizations and LOS for the rescue arm and individual IAT groups.
Results: A total of 352 pts were randomized (MBV: 235; IAT: 117), of whom 22 (18.8%) entered the MBV rescue arm. While on tx, pts on MBV versus IAT had reductions of 34.8% in hospitalizations (p=0.021) and 53.8% in LOS (p=0.029; Table). Hospitalization rates were lower during the follow-up than the tx phase, with no differences between tx in the follow-up (off-tx) period (Table). The hospitalization rate in the IAT group prior to rescue with MBV (IR=6.98; 95% CI: 4.06, 12.03) was 2.54 times higher (IRR=2.54; 95% CI: 1.28, 5.04; p=0.008) than on or after rescue with MBV (IR=2.75; 95% CI: 1.81, 4.18); increased LOS pre-rescue was also noted (IRR=2.25; 95% CI: 0.72, 7.01) but not statistically significant. In the IAT arm, foscarnet pts tended to have higher hospitalizations (5.5 admissions/person/year) and longer LOS (51.7 days/person/year) during the tx phase compared with pts on val/ganciclovir or MBV (Figure).
Discussion and Conclusion: Results from this analysis quantify the HCRU experience of pts requiring tx for post-transplant CMV. Hospitalizations and LOS were lower for pts on MBV than IAT. Pts who received MBV rescue reported lower hospitalization rates on or after rescue than pre-rescue. Reducing hospitalizations is critical for alleviating disease burden to healthcare systems.

Disclosure of Interest: I. Hirji Research Grant from: See presenting author's COI, K. Cocks Research Grant from: This research was supported by Takeda Development Center Americas, Inc. The company was involved in data analysis and abstract preparation following the direction of the authors. Editorial support for this encore abstract was provided by Bena Lim, PhD, of MediTech Media Ltd and funded by Takeda Pharmaceuticals International AG – Singapore Branch. I.H. and A.S. are employees of Takeda. K.C. and A.M-K are employees of Adelphi Values, funded by Takeda Development Center Americas, Inc., for contracted research. K.C. is also a consultant for Endomag Ltd and Xiros Ltd. The original abstract titled "Healthcare Resource Utilization in Transplant Recipients With Cytomegalovirus Infection Refractory/Resistant to Treatment Receiving Maribavir Versus Investigator-Assigned Therapy: Exploratory Analysis of a Phase 3 Trial" was presented at the Transplantation & Cellular Therapy Meetings of ASTCT and CIBMTR (TCT 2022) and subsequently at the 29th International Congress of The Transplantation Society (TTS 2022). The full original abstract is published in Transplantation and Cellular Therapy 2022;28(3):S45–S46., A. Moreno-Koehler Research Grant from: See presenting author's COI,
A. Sundberg Research Grant from: See presenting author's COI

Keywords: cytomegalovirus, healthcare resource utilization, maribavir, transplantation/transplant recipients

Poster Presentation

INFECTIONS (152)

MARIBAVIR VS IAT FOR REFRACTORY CMV IN HCT RECIPIENTS: SUBGROUP SAFETY ANALYSIS OF A PHASE 3 STUDY

Catherine Cordonnier*[1], Patrice Chevallier[2], Anke Verlinden[3], Drew Winston[4], Joan Gu[5], Martha Fournier[5]
[1]Henri Mondor Hospital and University Paris-Est-Créteil, Créteil, [2]CHU Hôtel Dieu, Nantes, France, [3]Antwerp University Hospital, Edegem, Belgium, [4]UCLA Medical Center, Los Angeles, [5]Takeda Development Center Americas, Inc., Lexington, United States

Aims & Objectives: Conventional anti-cytomegalovirus (anti-CMV) therapies are associated with myelotoxicity, nephrotoxicity, and electrolyte abnormalities, limiting their use in hematopoietic cell transplant (HCT) recipients. In the Phase 3 SOLSTICE study (NCT02931539), maribavir was superior to investigator-assigned therapy (IAT; valganciclovir/ganciclovir, foscarnet, or cidofovir) in CMV viremia clearance at Week 8 (primary endpoint; 55.7% vs 23.9%) in HCT/solid organ transplant (SOT) recipients with refractory CMV (with/without resistance [R/R]) (Avery et al. CID 2021). A consistent benefit for maribavir vs IAT for the primary endpoint was seen for HCT recipients (55.9% vs 20.8%) in a subgroup analysis. Here, we report safety data from the HCT subgroup.
Patients / Materials & Methods: HCT/SOT recipients ≥12 years old with confirmed CMV (plasma viral load ≥910 IU/mL) R/R to prior treatment (tx) were included and randomized 2:1 to maribavir 400 mg BID or IAT for 8 weeks of tx , with 12 weeks of follow-up. Pre- specified safety analyses for HCT recipients included evaluation of graft outcomes (graft-vs-host disease [GvHD], graft loss; randomized set), any tx-emergent adverse events (TEAEs), and tx-related TEAEs (safety set).
Results: Of 352 randomized patients (pts), 141 (40.1%) were HCT recipients (93 maribavir, 48 IAT [20 val/ganciclovir, 18 foscarnet, 5 cidofovir, 4 >1 IAT, 1 not treated]). Baseline characteristics for HCT recipients included (maribavir vs IAT) documented resistance mutations (19.4% vs 27.1%) and acute GvHD (24.7% vs 16.7%). Overall, 140 pts received allogeneic transplants; 1 pt had an autologous transplant. During the study, 25 (26.9%) pts treated with maribavir and 10 (20.8%) with IAT had new GvHD; 1 pt in the maribavir arm had graft loss after 124 days on study. Median (range) time to new GvHD after first dose of study tx was 33.0 (4–98) days for maribavir and 47.0 (2–123) days for IAT. TEAE rates (% pts) were 98.9% for maribavir and 95.7% for IAT; the most common TEAEs are shown (Table). More pts experienced dysgeusia with maribavir than IAT (25 [27.2%] vs 3 [6.4%]). With maribavir, the frequency of hypokalemia was lower than with foscarnet (6 [6.5%] vs 6 [33.3%]) and the proportion of pts who had neutropenia was lower than with val/ganciclovir (16 [17.4%] vs 9 [45.0%]). Tx-related TEAEs were seen in 46 (50.0%) pts treated with maribavir and 25 (53.2%) with IAT. Tx-related dysgeusia was more prevalent with maribavir (23 [25.0%]) vs IAT (1 [2.1%]) and fewer tx-related neutropenia cases were reported with maribavir (4 [4.3%]) vs val/ganciclovir (6 [30.0%]).
Discussion and Conclusion: In both tx groups, few pts experienced adverse graft outcomes. Lower rates of neutropenia and hypokalemia were seen with maribavir vs val/ganciclovir and foscarnet, respectively. More pts had dysgeusia with maribavir than with IAT.

Disclosure of Interest: C. Cordonnier Research Grant from: This research was supported by Takeda Development Center Americas, Inc. The company was involved in data analysis and abstract preparation following the direction of the authors. Editorial support for this encore abstract was provided by Bena Lim, PhD, of MediTech Media Ltd and funded by Takeda Pharmaceuticals International AG – Singapore Branch. CC is a consultant for Takeda, has received honoraria from Merck Sharp & Dohme and Takeda and is on the speakers bureau of Merck Sharp & Dohme and Takeda. PC has received honoraria from Amgen, Medac, Pfizer, Servier and Takeda. AV has no disclosures to declare. DW has received grant/research support from Takeda. JG and MF are employees of Takeda and have stock options with Takeda. The original abstract titled “Maribavir Versus Investigator-Assigned Therapy for Refractory CMV Infection (With/Without Resistance) in Hematopoietic Cell Transplant Recipients: Subgroup Safety Analysis of a Phase 3 Study” was presented at the 48th Annual Meeting of the European Society for Blood and Marrow Transplantation (EBMT 2022). The full abstract will be published in the supplement of Bone Marrow Transplantation (details were not available at the time of submission of this abstract)., P. Chevallier Research Grant from: See presenting author’s COI, A. Verlinden Research Grant from: See presenting author’s COI, D. Winston Research Grant from: See presenting author’s COI, J. Gu Research Grant from: See presenting author’s COI , M. Fournier Research Grant from: See presenting author’s COI

Keywords: cytomegalovirus, hematopoietic cell transplant, maribavir, safety

Poster Presentation

INFECTIONS (153)

REAL-WORLD TREATMENT PATTERNS AND OUTCOMES FOR CMV IN HSCT RECIPIENTS: A SYSTEMATIC REVIEW

Sung-Yeon Cho[1], Depei Wu[2], Clarisse Martins Machado[3], Inderjeet Singh[4], Anudeep Sandhu[5], Dirk Demuth[5], Monica Slavin[*6]
[1]Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea, South, [2]First Affiliated Hospital of Soochow University, Suzhou, China, [3]Institute of Tropical Medicine, University of São Paulo (IMT-FMUSP), São Paulo, Brazil, [4] Takeda Pharmaceuticals India Pvt Ltd, Haryana, India, [5]Takeda Pharmaceuticals International AG – Singapore Branch, Singapore, Singapore, [6]Victorian Infectious Diseases Service, Royal Melbourne Hospital, Melbourne, Australia

Aims & Objectives: Real-world data on treatments (tx) used for cytomegalovirus (CMV) in hematopoietic stem cell transplant (HSCT) recipients differ across countries and are limited outside developed markets. To address this knowledge gap, a systematic review (PROSPERO; CRD42020205559) evaluated current tx patterns for CMV infection and disease following HSCT in selected countries outside North America and Europe and described related outcomes.
Patients / Materials & Methods: Information sources (search period: 01 Jan 2011–21 Jul 2021) included indexed literature (Ovid® MEDLINE and Embase, Cochrane Database of Systematic Reviews and World Health Organization database Global Index Medicus), conference abstracts, pragmatic searches of the grey literature and snowballing of references lists of retained studies. Observational studies of interest included HSCT recipients (any age) who developed CMV infection or disease in 15 selected countries in Asia-Pacific, Latin America, Russia, and the Middle East. Outcomes of interest were tx patterns for CMV infection and CMV disease, proportion of patients (pts) with resistant and refractory CMV including definitions, tx-related outcomes and adverse events (AEs).
Results: Out of 25 retained studies (33 to 475 pts), most included allogeneic HSCT recipients (n=21, 84.0%) and adult pts (n=20, 80.0%). In HSCT recipients, pre-emptive therapy with intravenous ganciclovir (IV GCV) and/or valganciclovir (VGCV) was the conventional first-line (1L) approach for CMV infection prevention, with a median tx duration of 14-24 days (5 studies). GCV IV was also a conventional tx for CMV disease (5 studies), with tx lasting 12-30 days (3 studies). Neutropenia was seen in 30.0% and 39.8% pts treated with GCV and, in 3 studies, neutropenia, myelosuppression, and nephrotoxicity led to GCV discontinuation in 13.6%, 10.0%, and 2.3% of pts, respectively. In 3 studies, ≤10.0% of pts had second-line (2L) tx with foscarnet, due to GCV-related myelosuppression. The proportion of pts with resistant CMV (definition not specified) ranged between 0% and 7.7% (5 studies; Figure 1). These pts received foscarnet or cidofovir as 2L tx for a mean duration of 14 days (no data on AEs). In 3 studies, estimates of refractory CMV were 2.9%, 13.0%, and 49.4% (latter estimate reported in 39 pts, of whom 56.0% had recurrent CMV).
Discussion and Conclusion: In selected countries outside North America and Europe, conventional therapeutic options for pre-emptive and tx of CMV infection and CMV disease following HSCT were IV GCV and VGCV. However, premature tx discontinuation occurred in up to 1 in 8 pts, highlighting an unmet need with current standard of care. Real-world outcomes in pts with refractory CMV (with or without resistance) were scarce and warrants further investigation in this pt population, including therapeutic management.

Disclosure of Interest: S.-Y. Cho Research Grant from: See presenting author's COI., D. Wu Research Grant from: See presenting author's COI., C. M. Machado Research Grant from: See presenting author's COI., I. Singh Research Grant from: See presenting author's COI., A. Sandhu Research Grant from: See presenting author's COI., D. Demuth Research Grant from: See presenting author's COI., M. Slavin Research Grant from: This research was supported by Takeda Pharmaceuticals International AG – Singapore Branch. The company was involved in data analysis and abstract preparation following the direction of the authors. Editorial support for this encore abstract was provided by Bena Lim, PhD, of MediTech Media Ltd and funded by Takeda Pharmaceuticals International AG – Singapore Branch. S-YC has served as a consultant for Takeda Pharmaceutical, and has received research support and payment for lectures from Merck Sharp & Dohme, Pfizer and Gilead; WD has no conflicts of interest to disclose; CMM has received honoraria from Takeda and MSD (advisory board, speaker, educational events, meetings); IS is an employee of Takeda Pharmaceuticals India Pvt Ltd; AS and DD are employees of Takeda Pharmaceuticals International AG – Singapore Branch and hold stock options; MS has received grants from F2G, Gilead, Merck and personal fees from Gilead, Pfizer, Takeda and Roche for work outside of this research. The original abstract titled "Real-world treatment patterns and outcomes for cytomegalovirus (CMV) infection and disease in hematopoietic stem cell transplant (HSCT) recipients in selected countries outside of North America and Europe: A systematic review" was presented at the 29th International Congress of The Transplantation Society (TTS 2022).

Keywords: cytomegalovirus, hematopoietic stem cell transplant, real-world evidence, treatment patterns

Poster Presentation

INFECTIONS (154)

TIME TO FIRST CMV VIREMIA CLEARANCE IN TRANSPLANT RECIPIENTS: SUBGROUP ANALYSES OF A PHASE 3 TRIAL

Sophie Alain[1], Diana Florescu [2], Deepali Kumar[3], Jingyang Wu[4], Martha Fournier[4], Anudeep Sandhu[* 5]
[1]University of Limoges, Limoges, France, [2]University of Nebraska Medical Center, Omaha, United States, [3]University Health Network, Toronto, Canada, [4]Takeda Development Center Americas, Inc., Lexington, United States, [5]Non-author presenter from Takeda Pharmaceuticals International AG – Singapore Branch, Singapore, Singapore

Aims & Objectives: In the Phase 3 SOLSTICE study of haematopoietic cell/solid organ transplant (HCT/SOT) recipients with refractory cytomegalovirus (CMV) infection with/without resistance (NCT02931539), maribavir was superior to investigator-assigned therapies (IAT; val/ganciclovir, foscarnet or cidofovir) for CMV viremia clearance at Week 8 and maintenance of viremia clearance plus symptom control from Week 8 to Week 16. Median time to first CMV viremia clearance within study Week 8 occurred earlier in the maribavir than IAT groups. This post-hoc analysis reports the time to first CMV viremia clearance in subgroups within study Week 8.
Patients / Materials & Methods: Transplant recipients with confirmed CMV infection were randomized 2:1 to maribavir (400 mg BID) or IAT for 8 weeks' treatment, with 12 weeks' follow-up. Time to first CMV viremia clearance (2 consecutive post-baseline confirmed plasma viral load [VL] <137 IU/mL, ≥5 days apart) within study Week 8 was an exploratory endpoint and calculated as the first date of two consecutive CMV DNA results meeting CMV viremia clearance minus the randomization date plus 1 day; patients without viremia clearance by Week 8 were censored on the last CMV assessment date before initiating rescue/alternative anti-CMV treatment. Post-hoc subgroup analyses were performed by baseline resistance status, VL (low, <9,100; intermediate/high, ≥9,100 IU/mL [plasma]) and transplant type. Data were summarized using Kaplan–Meier method.
Results: Overall, 352 patients were randomized (235 maribavir, 117 IAT). Median time (days) to first viremia clearance in patients with baseline resistance was 27.0 for maribavir and 44.0 for IAT; and without resistance 17.0 and 22.0, respectively (Table). In patients with low baseline VL, median time (days) to first viremia clearance was 15.0 for maribavir and 22.0 for IAT, and 43.0 and 44.0, respectively, in patients with intermediate/high VL. Median time (days) to first viremia clearance was 25.0 for maribavir and 30.0 for IAT in SOT recipients, and 15.0 and 22.0, respectively, in HCT recipients (Table).
Discussion and Conclusion: These post-hoc analyses by subgroups are consistent with the previously reported pre-specified analysis from SOLSTICE, where time to first confirmed CMV clearance was shorter for maribavir than IAT in the randomized set.

Disclosure of Interest: S. Alain Research Grant from: See presenting author's COI, D. Florescu Research Grant from: See presenting author's COI, D. Kumar Research Grant from: See presenting author's COI, J. Wu Research Grant from: See presenting author's COI, M. Fournier Research Grant from: See presenting author's COI, A. Sandhu Research Grant from: This research was supported by Takeda Development Center Americas, Inc. The company was involved in data analysis and abstract preparation following the direction of the authors. Editorial support for this encore abstract was provided by Bena Lim, PhD, of MediTech Media Ltd and funded by Takeda Pharmaceuticals International AG – Singapore Branch. SA received research support from Altona, BioMerieux, Biotest, GlaxoSmithKline, Merck, Qiagen and Takeda, conference support from BioMerieux and Biotest, and honoraria from Biotest, Merck and IQone, and is on the advisory board of QCMD. DF is on the advisory board of Takeda, received research support from Astellas, Merck, Nobelpharma, Novavax and Takeda, and is on the data safety monitoring board of Amplyx. DK has received grants/research support from GlaxoSmithKline, Merck, Qiagen, Roche and Takeda, and consultation fees from GlaxoSmithKline, Merck, Roche, Sanofi and Takeda, and participated in a speaking engagement by Astellas. JW and MF are employees of Takeda and have stock options with Takeda. The original abstract titled "Time to First Cytomegalovirus Viremia Clearance in Transplant Recipients with Refractory Cytomegalovirus Infection With or Without Resistance Receiving Maribavir Versus Investigator-Assigned Therapy: Subgroup Analyses of a Phase 3 Trial" was presented at the 32nd European Congress of Clinical Microbiology & Infectious Diseases (ECCMID 2022).

Keywords: cytomegalovirus, maribavir, transplantation/transplant recipients, viremia clearance

Poster Presentation

INFECTIONS (159)

A THIRD DOSE COVID-19 VACCINES IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION PATIENS

Marika Watanabe[*1], Kimikazu Yakushijin[1], Yohei Funakoshi[1], Goh Ohji[2], Hironori Sakai[3], Wataru Hojo[3], Miki Saeki[1], Yuri Hirakawa[1], Sakuya Matsumoto[1], Hiroya Ichikawa[1], Rina Sakai[1], Shigeki Nagao[1], Akihito Kitao[1], Yoshiharu Miyata[4], Taiji Koyama[1], Yasuyuki Saito[5], Shinichiro Kawamoto[1], Mitsuhiro Ito[1, 6], Tohru Murayama[7], Hiroshi Matsuoka[4], Hironobu Minami[1, 8]
[1]Division of Medical Oncology/Hematology, Department of Medicine, [2]Division of Infectious Disease Therapeutics, Department of Microbiology and Infectious Diseases, Kobe University Hospital and Graduate School of Medicine, Kobe, [3]R&D, Cellspect Co., Morioka, [4]BioResource Center, Kobe University Hospital, [5]Division of Molecular and Cellular Signaling, Kobe University Graduate School of Medicine, [6]Laboratory of Hematology, Division of Medical Biophysics, Kobe University Graduate School of Health Sciences, Kobe, [7]Hematology Division, Hyogo Cancer Center, Akashi, [8]Cancer Center, Kobe University Hospital, Kobe, Japan

Aims & Objectives: We have previously shown that a second dose of COVID-19 mRNA vaccines is safe and effective for hematopoietic stem cell transplantation (HSCT) patients. However, some of these patients could not achieve seroconversion. This study investigated the safety and efficacy of a third dose of COVID-19 mRNA vaccines for Japanese HSCT patients.
Patients / Materials & Methods: We prospectively evaluated the safety and efficacy of a third dose of COVID-19 mRNA vaccines in Japanese allogeneic HSCT patients who had been enrolled in a previous study about a second dose of COVID-19 vaccines from March 2021 to August 2021. They all had undergone allogeneic HSCT at Kobe University Hospital. Peripheral blood samples were collected 1 to 4 weeks after the third vaccination. Antibody titers against the S1 spike protein were measured using the QuaResearch COVID-19 Human IgM IgG ELISA kit. The exclusion criteria were COVID-19 infection. Vaccine-related adverse events were graded according to Common Terminology Criteria for Adverse Events version 5.0, except for fever, which was categorized as follows: grade 1, 37.5–37.9 ºC; grade 2, 38.0–38.9 ºC; grade 3, 39.0–39.9 ºC; and grade 4, >40.0 ºC in the axilla. The optimal optical density S1 IgG cut-off was 0.26, as previously reported.
Results: The previous study included 25 HSCT patients who received two doses of COVID-19 mRNA vaccines. Three patients were excluded because of the development of COVID-19 (two cases) and loss to follow-up (one case). The study evaluated 22 HSCT patients who received a third dose of COVID-19 mRNA vaccines (BNT162b2 [n = 15] and mRNA-1273 [n = 7]). The median age at the time of the first vaccination was 52 (range, 22–63) years. The median time from HSCT to the third vaccination and from the second to the third vaccination was 1842 (range, 378-4279) days and 219 (range, 194-258) days, respectively. There were five patients who were receiving immunosuppressants at the vaccination; calcineurin inhibitors (CI) alone (n = 1), steroids alone (n = 2), or CI combined with steroids (n = 2). The median optical density of S1 IgG titers before and after the third dose was 0.099 (range, 0.001-0.713) and 1.315 (range, 0.006-1.730), respectively. Twenty-one patients (95%) seroconverted after receiving the third dose. Four out of five patients treated with steroids or CI seroconverted after the third vaccination. One patient who received CI and steroids could not achieve seroconversion, whose serum IgG level was 173 mg/dL. None of our patients had serious adverse events (> grade 3), new-onset graft-versus-host disease (GVHD), or GVHD exacerbation after vaccination. The most frequent adverse event was mild pain at the injection site.
Discussion and Conclusion: A third dose of the BNT162b2 and mRNA-1273 COVID-19 vaccines is safe and effective for Japanese allogeneic HSCT patients.

Disclosure of Interest: M. Watanabe: None Declared, K. Yakushijin: None Declared, Y. Funakoshi: None Declared, G. Ohji: None Declared, H. Sakai But No Conflict with: Hironori Sakai is employed by Cellspect. , W. Hojo But No Conflict with: Wataru Hojo is employed by Cellspect. , M. Saeki: None Declared, Y. Hirakawa: None Declared, S. Matsumoto: None Declared, H. Ichikawa: None Declared, R. Sakai: None Declared, S. Nagao: None Declared, A. Kitao: None Declared, Y. Miyata: None Declared, T. Koyama: None Declared, Y. Saito: None Declared, S. Kawamoto: None Declared, M. Ito: None Declared, T. Murayama: None Declared, H. Matsuoka: None Declared, H. Minami: None Declared

Keywords: allogeneic stem cell transplantation, COVID-19, vaccine

Poster Presentation

INFECTIONS (169)

RELATION OF CRP VALUES AND ANC IN BLOOD CULTURE POSITIVE PATIENTS IN BMT & HAEMATOLYMPHOID CANCER

Pratik Poladia*[1], UMAKANT GAVHANE[1]
[1]COMPOSITE LAB, TATA MEMORIAL CENTRE ACTREC, MUMBAI, India

Aims & Objectives: Selecting patients' with true bacteremia to initiate appropriate antibiotic therapy is important in controlling the mortality, especially in the oncology ward. Hence, this study was performed to see the sensitivity and relevance of CRP and ANC in culture confirmed infections in BMT and haematolymphoid cancer patients.

Patients / Materials & Methods:
A total of 238 blood culture samples were received during a period of January 2022 and May 2022 of BMT and haematolymphoid cancer patients. Out of these 21 samples were confirmed positive for infection. 42.85% of these confirmed positive for infection cases were BMT patients and rest were hematolymphoid cancer patients. All of these patients were tested for CRP, ANC and Blood cultures testing was performed in the Bactec 9050 automated Blood culture system. ANC was performed in Advia 2120i by Siemens Healthcare , CRP in the Siemens Dimension RXL 200 analyzer by immunoturbidimetric method.

Results: CRP was high in 100% of the cases. ANC was high in 34.3% cases accompanied by leukocytosis. But in cases with leukopenia ANC was low in 92.33% of cases .Common organisms isolated included Klebsiella pneumoniae(14), E.coli (2), staphylococci (2), Streptococcus(1), Acinetobacter (1) and Salmonell typhi (1)

Discussion and Conclusion: Infections are an important cause of morbidity and mortality in immunocompromised cancer patients. The gold standard for diagnosis of bacterial infections is isolation of the organism by culture but it takes more time to get the report an alternative early marker for detecting the infections would be very useful.
A higher absolute neutrophil count (ANC) is a marker for bacterial infection, but this is beset by the fact that many cancer patients on treatment may be neutropenic, since the immune system is suppressed by extensive chemical therapies, fever can be considered as the only positive finding as a probable infection that should be further investigated.
C- Reactive protein (CRP) is an acute phase reactant and is a useful marker for inflammation and infection. Higher levels have been shown to be associated with invasive bacterial infections.
CONCLUSION
- CRP was high in all of the culture confirmed infections. However, ANC was high in only 34.33% of cases with leukocytosis. Culture confirmed infection cases with leukopenia showed rise in ANC in only 5.66% of cases, while CRP was significantly increased in all cases with or without leucopenia. Though CRP is a non-specific marker for inflammation, especially in leukopenic and immunosuppressed patients of haematolymphoid malignancy as well BMT, it could be a more reliable indicator for infections than ANC and should be more frequently requested.
- It is an inexpensive test available in almost all healthcare centres

Disclosure of Interest: P. Poladia But No Conflict with: NA, U. GAVHANE But No Conflict with: NA

Keywords: ANC ABSOLUTE NEUTROPHIL COUNT, BMT BONE MARROW TRANSPLANT, CRP C REACTIVE PROTEIN

Poster Presentation

INFECTIONS (242)

LOW DOSE CIDOFOVIR IN CMV INFECTION POST PEDIATRIC HSCT–SAFE & EFFECTIVE APPROACH IN CYTOPENIA

Amit Jain*[1], Rajesh Patil[1], Ratna Sharma[1], Pranoti Kini[1], Ashutosh Walawalkar[1], Poulami Das[1], Srishti Srivastava[1], Mamta Manglani[1]
[1]Department of Pediatric BMT, MCGM – Comprehensive Thalassemia Care, Pediatric Hematology – Oncology & BMT Centre, Borivali, Mumbai, India

Aims & Objectives: Cytomegalovirus (CMV) infections are associated with significant morbidity and mortality after pediatric hematopoietic stem cell transplantation (HSCT). Ganciclovir and Valganciclovir is commonly used as pre-emptive therapy. However, cytopenia being a relative contraindication. Cidofovir is (CDV) considered a third-line therapy in the management of CMV infection with dose-limiting nephrotoxicity. A modified dose regimen of 1 mg/kg 3 times per week, described by Hoffman et al (2001) in adenoviral infection, seems to be less nephrotoxic.
Patients / Materials & Methods: We reviewed our experience with low dose CDV in treatment of CMV infections in HSCT patients with cytopenias at our centre July 2017 through June 2022. Peripheral blood was screened on all patients for CMV by quantitative real-time PCR as per standard protocol. Upon detection of CMV by PCR or tissue histopathology, CDV was given intravenously at 1 mg/kg thrice weekly for 2-4 weeks, until 2 consecutive CMV-negative samples were documented from all previously involved sites. The incidence of renal injury, data on CMV viral load and CDV dosing required to clear virus was documented.
Results: Overall, 9 children received low dose CDV during this period. The median age of the cohort was 9.5 years (range 5-18) with a male-female ratio of 8:1. Seven out of 9 patients underwent haplo-identical HSCT for malignant indication while 2 were match sibling donor HSCT for benign indications. All patients had viremia with median viral load of log 3 (range: log 2.1 – log 4.8) and one had CMV colitis additionally. Low dose CDV treatment resulted in complete response in 6 (67%) patients in whom the virus became undetectable and resolution of clinical symptoms. Median number of doses required to clear virus in these 6 patients were 12 (range: 7-14). All patients tolerated CDV well and none of them was required to interrupt or stop the drug. No cases of dose-limiting nephrotoxicity were observed; however, one patient developed transient tubulopathy.
Discussion and Conclusion: Low dose CDV appeared safe and effective for the treatment of CMV infection in patients with cytopenia where ganciclovir or valganciclovir is avoided. A larger prospective study is needed to determine further the role of low-dose CDV in the treatment of CMV after HSCT.

Disclosure of Interest: None Declared

Keywords: CMV, cytopenia, low dose cidofovir

Poster Presentation

INFECTIONS (284)

INCIDENCE AND FACTORS AFFECTING CYTOMEGALOVIRUS REACTIVATION POST ALLOGENEIC STEM CELL TRANSPLANT

Bharath Ram S* [1], Akshatha Nayak[1], Nataraj K S[1], Shilpa Prabhu[1], Sharat Damodar[1]
[1]Adult hematology and BMT, Mazumdar Shaw Medical Center, Narayana Health City, Bangalore, India

Aims & Objectives: 1. To study the incidence of CMV infections in patients undergoing allogeneic hematopoietic stem cell transplantation
2. To study the factors affecting the reactivation and time to reactivation.
Patients / Materials & Methods: One fifty-eight consecutive patients undergoing allogeneic HSCT for malignant and non-malignant hematological diseases were analyzed retrospectively for cytomegalovirus reactivation till day +100 post-transplant from March 2017 to December 2021. Quantitative CMV PCR ≥500 copies/ml was considered positive for CMV infection. Information regarding donor and recipient CMV serology status, conditioning regimens, source of stem cells, HLA match, granulocytes infusions, immunosuppressants used, and acute graft versus host disease were collected and recorded.
Results: Baseline characteristics of the study population are as shown (Table.1). Seventy-seven patients (48.7%) developed CMV reactivation (Figure 1). The median day of reactivation of cytomegalovirus in this series was 35 days (Range 13-100 days) and the median number of CMV copies was 3546 copies/ml (Range 259 to 275,000 copies/ml). Thirty of 77 treated patients (38%) had undetectable CMV copies after 1 week of treatment. The majority of donors and recipients were positive for CMV IgG which constituted 147 (93%) patients. Multivariate analysis of factors affecting CMV reactivation revealed CMV infection was significantly higher in patients who underwent matched unrelated and haploidentical transplants (OR 2.25; 95% CI 1.34-3.76; P=0.002) compared to matched sibling transplants and also patients who were receiving steroids (Odds ratio [OR], 3.87; 95% confidence interval [CI] 1.48-10.33; P=0.007) had a significantly higher risk of reactivation. While other factors such as mycophenolate (OR 1.38; 95% CI 0.57-3.30; P=0.46) and grade 2-4 acute graft versus host disease (aGVHD) (OR 1.68; 95% CI 0.65 to 4.36; P=0.28) were associated with increased odds but were not significant statistically on multivariate studies (Table 2). Median time to reactivation was not significantly earlier in any of the groups (Not shown).
Discussion and Conclusion: This study shows that the incidence of CMV reactivation burden is significant (48.7%) in the post-transplantation period. Among factors affecting CMV reactivation, matched unrelated, haploidentical transplants and steroids were associated with a significantly increased risk of CMV reactivation. CMV reactivation leads to a significant additional treatment burden and hospital stay on patients and transplant centers. A prompt pre-emptive approach has led to a significant reduction in the CMV disease though there is a need for better prophylaxis to prevent CMV reactivation.

Disclosure of Interest: None Declared

Keywords: Allogeneic hematopoietic stem cell transplantation, Cytomegalovirus reactivation, factors affecting

Poster Presentation

INFECTIONS (294)

THE PATTERN OF EARLY INFECTION AND ITS OUTCOMES IN HEMATOPOIETIC STEM CELL TRANSPLANT

Nishil Gowda[1], Kalpana Rajesh[*1], Preethi Sathianathan[1], Karthikeyan Radhakrishnan[1], Smita kayal[1], Biswajit dubashi[1], Prasanth ganesan[1], Apurba Sastry[2]
[1]Medical Oncology, [2]Microbiology, Jawaharlal Institute of Postgraduate Medical Education & Research (JIPMER), Puducherry, India

Aims & Objectives: Hematopoietic stem cell transplant (HSCT) is complicated by infections in the pre-engraftment and early post-engraftment period (until Day+30), which may lead to significant morbidity and early mortality. There is a lack of contemporary regional data on early post-HSCT infection complications, and therefore we undertook this study to evaluate the infection pattern and its outcomes in HSCT recipients at our center.
Patients / Materials & Methods: Analysis was conducted on prospectively maintained data of all patients who underwent HSCT in our center from January 2019 to December 2021 (3 years). Baseline characteristics, patterns of infections, and outcomes (until d+30) were studied.
Results: Among the 86 patients who underwent HSCT, 62% (n=53) were males and the median age was 35 years (3-61 years). 64% (n=55) patients had undergone Autologous HSCT, and 36% (n=31) patients had undergone Allogenic HSCT. Baseline and pre-HSCT patient characteristics are described in Table 1. The overall median CD34 cell dose was 6.6×106 cells/kg. The median neutrophil engraftment was 11 days (8-17 days); 10 days (8-16 days) in the autologous HSCT and 11 days(9-17days) in the allogenic HSCT respectively. The median platelet engraftment was 12 days (7-26 days); 12 days (7-26 days) in the autologous HSCT and 12 days (7-19 days) in the allogenic HSCT respectively. Febrile episode (fever or hypotension) was documented in 94% (81 patients) of patients and the median day of onset was 5 days (range, -2 to 17 days). There was no difference in the proportion of patients having febrile episode in the autologous and allogenic HSCT (94% each). Infection related data is presented in Table 2. Clinically documented infection (CDI) was observed in 83% (n=67), of which 15 patients (19%) also had microbiologically documented infection(MDI). Mucositis and gut infections were the most common sites of CDI, constituting around 37% each. Further description of CDI is presented in Figure 1. Gram negative organisms constituted 87% (n=13) of MDI. The median duration of antibiotic usage was 10 days (5-24 days) and median number of antibiotics used was 3 (1-10); colistin was used in 31% of patients and empirical therapeutic antifungal agents were used in 40% of patients. All cause treatment related mortality (TRM) until D+30 was seen in two patients, both due to neutropenic sepsis; one in autologous HSCT on D+16 and one in allogenic HSCT on D+25.
Discussion and Conclusion: Although febrile neutropenia with documented infections was seen in the majority of post-HSCT patients, d+30 mortality in our present cohort was low (2.3%), comparable to data from advanced centers. Periodic audits of infection patterns, gram-negative being the most common MDI in our cohort, guide to developing center-specific antibiotic policy.

Disclosure of Interest: None Declared

Keywords: Antibiotic, Early infection, Febrile neutropenia, HSCT

Poster Presentation

INFECTIONS (307)

POST HSCT CD4 AND CD19 SUBSET ANALYSIS AS A GUIDE FOR VACCINATION INITIATION-A RETROSPECTIVE STUDY

Poojitha Byreddy*[1], Pavitra DS[1], M J. John[1], Markas Masih[1], Ketan Modak[1]
[1]Clinical Hematology, Bone Marrow Stem Cell Transplantation, CMC Ludhiana, Ludhiana, India

Aims & Objectives: To measure the CD4 and CD19 lymphocyte count recovery in post-transplant patients.
Primary Objective:
- To measure the median CD4 and CD19 counts of the patients undergoing stem cell transplant prior to vaccination.

Secondary Objective:
- To analyze the median time to of recovery of counts.

Patients / Materials & Methods: Lymphocyte subset analysis of patients who underwent stem cell transplantation and have completed 6 months of post autologous HSCT and 12 months post allogeneic HSCT were analysed. Peripheral blood samples were collected at the time of decision of vaccine initiation. CD4 and CD19 subset analysis was done by flow cytometry.

Results: A total of 220 transplants were conducted at our institute. Retrospective data collection over the last five years of patients was done. In 60 patients Lymphocyte recovery data was available for 60 patients. Among the 60 patients, 20 (33.3%) patients underwent autologous transplant, 27 (45%) patients underwent matched related allogeneic hematopoietic stem cell transplantation, and 9 (15%) underwent matched unrelated HSCT and 4 (6.6%) underwent Haploidentical HSCT. The lymphocyte counts were assessed at 6 months in autologous HSCT patients and at 12 months in allogeneic transplant patients.
Median CD4 count in MRD group was 714/ul (range of 306-1374), in MUD group was 1052/ul (range of 168-3969), in Haploidentical group was 730/ul (range of 365-1304) and in Auto HSCT group was 378/ul (range of 161-734). (p – 0.00)
Median CD19 count did not vary significantly across the transplant groups Median CD19 count in MRD group was 465/ul (range of 100-1098), in MUD group was 314/ul (range of 40-582), in Haploidentical group was 542/ul (range of 202-1124) and in Auto HSCT group was 302/ul (range of 86-1494). (p=0.106).
Median time for the count recovery was 13.8 months in MRD patients (range of 11.8 to 70 months), 13.5 months in MUD group (range of 12.1 to 37.3 months), and 7.9 months in Haplo patients (range of 6.1 to 21 months) and in Auto HSCT patients it was 6.18 months (range of 3.3 to 10.3 months).

Discussion and Conclusion: For a vaccine to mount a response thought to be clinically relevant, adaptive T- and B-cell immunity after transplant must be at least partially reconstituted. In our patients, median CD4 and CD19 count recovery was optimal across all the subsets. All the patients had count recovery and had vaccination as per the institutional protocol.
The findings of the study suggest that CD4 and CD19 count varied across the subsets and it was lower in the Auto HSCT group which could be secondary to early count recovery analysis in this subgroup. However, most of the patients had optimal count recovery and lymphocyte subset analysis may be safely avoided. This will also reduce the financial burden incurred on the patient.

Disclosure of Interest: None Declared

Keywords: Immune reconstituion, Transplant, Vaccination

Poster Presentation

INFECTIONS (313)

IMPROVED SURVIVAL IN HSCT RECIPIENT: NEUTROPENIC CARE A KEY TO ENHANCED SURVIVAL

Joshy P. Joy*[1], princy T. p[1]
[1]oncology, aster mims , calicut, India

Aims & Objectives: The purpose of this study is to make the awareness of importants of good neutropenic care in patients and care-takers. And hope this research will help to improve survival rate in hcst recipient.
Patients / Materials & Methods: We used a covert-observational study to assess the effectiveness of neutropenic care during neutropenic stage in hcst recipient in all age group Between 19/12/20, and 16/07/22, we observed patients with neutropenia at BMT unit in 30 patients. We estimated neutropenic care effectiveness by observing the neutropenic care result in pre bone marrow transplant procedures, mobilization period and post bone marrow transplant among patients with neutropenia
Results: As a result of covert-observational study we observed that among 30 patients
25 patients were survived the neutropenic stage well with out major complications and 3 of them survived the neutropenic stage with some complications like tachycardia fever and 2 patients were died because of their gut infections
Discussion and Conclusion: Patients for hcst are at high risk for complications of infections in neutropenic stage and are dangerously affected with poor neutropenic care. In this study shows that good neutropenic care is the key to survival of hcst recipients

Disclosure of Interest: None Declared

Keywords: enhanced survival, neutropenic care, survival of hcst recipient

Poster Presentation

INFECTIONS (344)

PROFILE OF VIRAL INFECTIONS IN POST HEMATOPOIETIC STEM CELL TRANSPLANT PATIENTS.

Pavitra DS[*1], Poojitha Byreddy[1], M Joseph John[1]
[1]Clinical Hematology, Christian Medical College Ludhiana, Ludhiana, India

Aims & Objectives: To study the profile of viral infections in post-hematopoietic stem cell transplant patients.
Patients / Materials & Methods: Data of post HSCT patients with viral infections was collected through a retrospective chart review from the year 2009 to 2022. Diagnosis, type of hematopoietic stem cell transplantation, day of diagnosis of viral infection post-HSCT, immunosuppression and concurrent diagnosis of GVHD during viral infection were analyzed.
Results: In the 220 transplants performed at our center from 2009 to 2022, viral infections were documented in 31(14%). These were noted in the 20 (15%) of the 130 total matched related donor transplants, and 11 (33%) among the 33 matched unrelated donor transplants, none of the autologous transplants had viral reactivation.
The underlying spectrum of diseases included 16 (19%) among the 85 Thalassemia major, 4(17%) of 23 severe aplastic anemia, 4 (25%) of 16 ALL, 3 (13%) of 23 AML, Wiskot Aldrich syndrome in 2 and 1 each in Fanconi anemia and MDS. CMV reactivation was noted in 25 (74.%) patients, BK virus infection in 7 (21%), 1 (3%) each in herpes zoster and Epstein Bar virus infection. 2 patients had both CMV and BK virus infection and 1 patient had CMV reactivation at two different points post-transplant. The median time to CMV reactivation was day + 51 post-transplant (Range 15 - 196), BK virus infection at day +10 (Range 6 – 63), EBV and herpes zoster at day +80 and day + 335 respectively.
Response to ganciclovir was noted among 92% (23) of patients and 2 (8%) required second-line agent cidofovir. All the patients with CMV reactivation were on immunosuppression.
12 of 25 (48%) patients had active or resolving GVHD at the time of CMV reactivation and 24 % (6) were on ruxolitinib along with steroids and immunosuppression. CMV colitis and CMV pneumonitis was documented in 2 patients along with CMV viremia. CMV related death was seen in 3 patients.
All patients with BK virus infection had hemorrhagic cystitis, 3 received ciprofloxacin and the rest had spontaneous resolution. In the patient with EBV infection, PTLD was suspected, and he responded to the tapering of CNIs and steroids.
Discussion and Conclusion: CMV reactivation was the most common viral infection documented in post-transplant patients. BK viral infection with hemorrhagic cystitis was the second most common infection noted with spontaneous resolution seen in most of the patients.
Response to ganciclovir was seen in a majority of the patients and in patients with clinical resistance in the absence of genotypic analysis showed response to cidofovir. Use of ruxolinitib showed an increased trend towards risk of CMV reactivation.

Disclosure of Interest: None Declared

Keywords: BK virus, CMV, post hematopoietic stem cell transplant, Viral infections

Poster Presentation

INFECTIONS (349)

POST HSCT CD4 AND CD19 SUBSET ANALYSIS AS A GUIDE FOR VACCINATION INITIATION-A RETROSPECTIVE STUDY

Poojitha Byreddy*[1], Pavitra DS[2], M J. John[1], Markas Masih[1], Ketan Modak[1]
[1]Clinical Hematology, Bone Marrow Stem Cell Transplantation, CMC Ludhiana, [2]Clinical Hematology, Christian Medical College, Ludhiana, India

Aims & Objectives: To measure the CD4 and CD19 lymphocyte count recovery in post-transplant patients. Primary Objective:
● To measure the median CD4 and CD19 counts of the patients undergoing stem cell transplant prior to vaccination.
Secondary Objective:
● To analyze the median time to of recovery of counts.
Patients / Materials & Methods: Lymphocyte subset analysis of patients who underwent stem cell transplantation and have completed 6 months of post autologous HSCT and 12 months post allogeneic HSCT were analysed. Peripheral blood samples were collected at the time of decision of vaccine initiation. CD4 and CD19 subset analysis was done by flow cytometry.
Results: A total of 220 transplants were conducted at our institute. Retrospective data collection over the last five years of patients was done. In 60 patients Lymphocyte recovery data was available for 60 patients. Among the 60 patients, 20 (33.3%) patients underwent autologous transplant, 27 (45%) patients underwent matched related allogeneic hematopoietic stem cell transplantation, and 9 (15%) underwent matched unrelated HSCT and 4 (6.6%) underwent Haploidentical HSCT. The lymphocyte counts were assessed at 6 months in autologous HSCT patients and at 12 months in allogeneic transplant patients.
Median CD4 count in MRD group was 714/ul (range of 306-1374), in MUD group was 1052/ul (range of 168-3969), in Haploidentical group was 730/ul (range of 365-1304) and in Auto HSCT group was 378/ul (range of 161-734). (p – 0.00).
Median CD19 count did not vary significantly across the transplant groups Median CD19 count in MRD group was 465/ul (range of 100-1098), in MUD group was 314/ul (range of 40-582), in Haploidentical group was 542/ul (range of 202-1124) and in Auto HSCT group was 302/ul (range of 86-1494). (p=0.106).
Median time for the count recovery was 13.8 months in MRD patients (range of 11.8 to 70 months), 13.5 months in MUD group (range of 12.1 to 37.3 months), and 7.9 months in Haplo patients (range of 6.1 to 21 months) and in Auto HSCT patients it was 6.18 months (range of 3.3 to 10.3 months).
Discussion and Conclusion: For a vaccine to mount a response thought to be clinically relevant, adaptive T- and B-cell immunity after transplant must be at least partially reconstituted. In our patients, median CD4 and CD19 count recovery was optimal across all the subsets. All the patients had count recovery and had vaccination as per the institutional protocol.
The findings of the study suggest that CD4 and CD19 count varied across the subsets and it was lower in the Auto HSCT group which could be secondary to early count recovery analysis in this subgroup. However, most of the patients had optimal count recovery and lymphocyte subset analysis may be safely avoided. This will also reduce the financial burden incurred on the patient.

Disclosure of Interest: None Declared

Keywords: Immune reconstitution, transplantation/transplant recipients, Vaccination

Poster Presentation

INFECTIONS (357)

CMV REACTIVATION IN PEDIATRIC ALLOGENIC HSCT: EARLY DETECTION AND TREATMENT OPTIMISATION

Srishti Srivastava*[1], Ratna Sharma[2], Rajesh Patil[1], Mamta Manglani[1], Pranoti Kini[1], Amit Jain[1], Leo Mathan[1], Ashutosh Walawalkar[1], Krisha Shah[1], Pranoti Chiwarkar[1]
[1]Pediatrics, [2]MCGM CTC PHO BMT Center, Mumbai, India

Aims & Objectives: To assess the incidence, risk factors and treatment outcomes of CMV reactivation in children who underwent allogenic hematopoietic stem cell transplant (HSCT).
Patients / Materials & Methods: Retrospective analysis was done of all consecutive patients who underwent allogenic HSCT at our centre from June 2018 to June 2022. CMV reactivation by qualitative PCR was done monthly in matched transplants and weekly in haploidentical HSCT post engraftment till day +100 as well as when indicated. Pre-emptive treatment with IV Ganciclovir (5mg/kg/dose BD) or oral Valganciclovir (20-40 kg: 450 mg BD and >40 kg: 900 mg BD) was initiated when CMV PCR copies were more than log 3. CMV copies were reassessed after 2 weeks and an additional week of IV Ganciclovir was given for persistent viremia. All the patients received maintenance with Valganciclovir for 2 weeks. Low dose intravenous Cidofovir (1mg/kg alternate day) was administered in patients with concurrent cytopenia as front-line therapy. Tapering of immunosuppression was done wherever feasible as a part of management.
Results: Out of the total of 127 patients, 77 underwent matched donor transplants while 50 underwent haploidentical transplants. 39 episodes of CMV viremia occurred in 37/127 (29.1%) patients (M:F - 2.7:1) with median age of 9 years (Range: 3 years to 14 years). The median follow-up was 18 months (1 to 48 months). CMV viremia was seen in 19.4% (15/77) of matched transplants and 44% (22/50) of haploidentical transplants. CMV viremia was detected on median day +38 (Day+12 to Day+478) post-transplant, with median of log10 3.4 copies (log10 2.9 to log10 5.1 copies). Out of 39 episodes, 4 were associated with CMV disease (2 colitis and 2 interstitial pneumonia). As per serology, 36 patients were CMV D+/R+ and one was CMV D-/R+. Active GVHD was present in 27/39 (69.2%) episodes at the time of CMV detection. Valganciclovir was used in 21/39 (53.8%) episodes while Ganciclovir was used as first-line therapy in 15/39 (38.4%) episodes. Low dose Cidofovir was used upfront in 7.6% (3/39) episodes. Three patients on Ganciclovir were switched to low dose Cidofovir due to persistent cytopenia. The median time to resolution of viremia was 17 days (14 days to 35 days). CMV resistance was not encountered in any of these episodes.
Discussion and Conclusion: Cytomegalovirus reactivation remains a challenge in allogenic HSCT especially with Haplo-HSCT and in patients with GVHD. Pre-emptive therapy and tapering of immunosuppression are effective in clearance of CMV viremia. A fixed dose of Valganciclovir, as per weight band, is tolerated well in children. Low dose Cidofovir is efficacious for clearance of viremia and is a good alternative in those with cytopenia.

Disclosure of Interest: None Declared

Keywords: Allogenic HSCT, Cidofovir, CMV Viremia, Ganciclovir, Valganciclovir

Poster Presentation

INFECTIONS (362)

PREDICTORS OF SEVERE SARS-COV2 AND MORTALITY IN HSCT RECIPIENTS: A SINGLE CENTRE RETROSPECTIVE STUDY

Ashray Kole[*1], Sharon Lionel[1], Sushil Selvarajan[1], Uday Kulkarni[1], Anu Korula[1], Fouzia NA[1], Kavitha Lakshmi[1], Alok Srivastava[1], Aby Abraham[1], Vikram Mathews[1], Biju George[1]
[1]Clinical Haematology, Christian Medical College , Vellore, India

Aims & Objectives: In the COVID19 era, patients undergoing hematopoietic stem cell transplant (HSCT) infected with the SARS-CoV-2 may be at a higher risk of complications and death.
We aimed to analyse risk factors, severity and outcomes of COVID-19 illness in HSCT recipients who presented to our institution.
Patients / Materials & Methods: All HSCT recipients who were detected to have COVID19 illness since the beginning of the pandemic (Jan 2020 to May 2022) were included in this retrospective analysis, which was conducted at a single tertiary care centre in south India.
Results: Between January 2020 and May 2022, 43 HSCT recipients (34 allogeneic and 9 autologous) were detected to have COVID19. Baseline characteristics are given in Table 1. 11 (25%) patients succumbed to the illness. Factors associated with mortality were severe COVID19 ($p<0.01$), shorter time interval from transplant to COVID (median of 139 days vs 63 days, IQR 1.0 – 8.0 months, $p=0.022$), longer duration of admission (median of 20 days to 41 days, $p=0.025$) and presence of concomitant infections ($p=0.038$). Significant factors associated with severe COVID19 infection were male sex ($p=0.021$), longer time interval from transplant to infection (157 days vs 63 days, $p=0.020$) and longer hospitalization (38 days vs 8 days, $p=0.023$).
Other factors such as haematological diagnosis, type of transplant, presence of acute or chronic GVHD, ongoing immunosuppression, comorbid illnesses did not significantly impact overall survival.
A limitation is that many HSCT recipients who had COVID 19 infection may have sought treatment at local hospitals in view of travel restrictions and the mild cases may not have presented to the hospital at all.
Discussion and Conclusion: Infection with SARS-CoV-19 in HSCT recipients resulted in a mortality of 25% with more deaths in the immediate post-transplant period, confirming the intense degree of immunosuppression and immature immune reconstitution that leads to this frailty.

Disclosure of Interest: None Declared

Keywords: COVID-19, HSCT, Infections post HSCT

Poster Presentation

INFECTIONS (365)

CYTOMEGALOVIRUS REACTIVATION POST ALLOGENEIC TRANSPLANT AT A TERTIARY CANCER CENTER IN EASTERN INDIA

Vinay Anand Guntiboina[*1], Arijit Nag[1], Rizwan Javed[1], Dibakar Podder[1], Jeevan Kumar[1], Saurabh Bhave[1], Gaurav Goel[2], Sanjay Bhattacharya[2], Reena Nair[1], Mammen Chandy[1]
[1]Clinical Hematology & HCT, [2]Clinical Microbiology, Tata Medical Center, Kolkata, India

Aims & Objectives: Cytomegalovirus (CMV) reactivation and disease is a significant cause for morbidity and mortality in patients undergoing allogeneic hematopoietic cell transplantation (allo HCT) especially in developing countries with a high CMV seropositivity rate. There are limited studies on the patterns of CMV reactivation in developing countries. This study aims to review the epidemiology of CMV reactivation post allogeneic stem cell transplantation at our center.
Patients / Materials & Methods: This was a single center, retrospective audit of patients had undergone allo HCT at Tata Medical Center, Kolkata between 2017 to 2021. Data collection was done through electronic medical records and patient files. Data analysis was done using R version 3.6 and GraphPad Prism v9.
Results: Out of 160 patients undergoing allo SCT at our center, the incidence of CMV reactivation in the post-transplant period was 62.5% (n=100). Patients who had CMV-reactivation (CMV+) had a median age of 20.5 years (range: 2-60 years) compared to 25.5 years (range: 2-59 years) in the non-CMV reactivation (CMV-) cohort. Both groups had similar disease distribution. All patients received prophylactic Acyclovir in the peri-transplant period. Haploidentical transplants were more in patients developing CMV reactivation (44% compared to 31.7% in the non-CMV cohort). Most (92%) of the patients developed viremia within day 100 post-transplant, detected at a median of 35 days. In the R+ > D- (Donor seronegative, Recipient seropositive) cohort (n=11), 5 patients (45.4%) developed CMV reactivation. Patients had a median duration of viremia for 9 days (range: 2 to 62 days) with a median titre value of 1642 copies. Half (50%) of the patients developed recurrent viral reactivation, with the maximum being 5 recurrences noted in two patients. Four patients (4%) developed features of CMV disease and this contributed to death in 1 patient. Patients with CMV reactivation had an overall survival of 62% at 1 year with an event free survival of 60%. The median OS in the cohort was not reached in both the CMV+ and CMV- cohorts. The overall survival (OS) was not significantly different in the two groups (OS at 2 years: 62.6% for CMV- and 70.9% for CMV+, p=0.14). Uncontrolled sepsis was the most common cause of death (20% and 16.6%, respectively) in both cohorts.
Discussion and Conclusion: In this study, we have described the characteristics of CMV reactivation in patients undergoing allo SCT at our center over the last 5 years. This risk of developing CMV reactivation will only increase with higher numbers of haploidentical transplants performed across the country, which highlights a need for better and safer prophylactic agents.

Disclosure of Interest: None Declared

Keywords: Allogeneic Hematopoietic Stem Cell Transplantation, Cytomegalovirus reactivation, Viral infections

Poster Presentation

INFECTIONS (374)

IS THERE A ROLE OF FLUOROQUINOLONE(FQ) PROPHYLAXIS IN ALLOGENEIC HCT IN HIGH FQ RESISTANCE REGIONS??

Ashwin V. Nair*[1], Shaweta Kaundal[1], Kripa Shanker Kasudhan[1], Madhu Chopra[1], Charanpreet Singh[1], Aditya Jandial[1], Arihant Jain[1], Gaurav Prakash[1], Alka Khadwal[1], Pankaj Malhotra[1], Deepesh Lad[1]
[1]Clinical Hematology and Medical Oncology, PGIMER, Chandigarh , India

Aims & Objectives: There is data from developed regions with less prevalence of fluoroquinolone (FQ) resistance that FQ prophylaxis decreases the risk of gram-negative bacilli (GNB) bacteremia in allogeneic hematopoietic cell transplant (allo-HCT) recipients, leading it to be recommended by several guidelines. However, recent data also suggest that antibiotic prophylaxis increases the risk of acute graft versus host disease (GVHD), leading to questioning the role of FQ prophylaxis. We aimed to study the impact of levofloxacin prophylaxis on GNB bacteremia and acute GVHD in allo-HCT recipients in a high FQ resistance region like ours.
Patients / Materials & Methods: In this single-center study, allo-HCT recipients until the year 2016 were given levofloxacin prophylaxis till the need for initiation of IV antibiotics. After the year 2016, the decision for levofloxacin prophylaxis was physician based. We retrospectively analyzed this data to compare the incidence of GNB bacteremia, duration of IV antibiotics, hospitalization, acute GVHD, and overall survival between these two cohorts.Overall Survival (OS) was defined as the time from HCT to death from any cause.
Results: A total of 135 patients (43 in the levofloxacin cohort and 92 in the no levofloxacin cohort) were analyzed in this study. The age and sex were comparable between the two cohorts. The no levofloxacin cohort had a higher proportion of malignant diagnoses (80% vs. 58%, p = 0.01) and haploidentical transplants (46% vs. 14%, p = 0.004) compared to the levofloxacin cohort. The conditioning intensity was also matched between the cohorts. Though the neutrophil engraftment was significantly delayed by one day in the no-levofloxacin cohort (13 vs. 14 days, p=0.03), the incidence of GNB bacteremia was also comparable between the two cohorts (37% vs. 34% p = 0.690). The median duration of IV antibiotics (16 vs. 12.5, p = 0.05) and hospital stay (20 vs. 22.5, p=0.2) were also similar between the two cohorts. The incidence of acute GVHD was also comparable between the two cohorts (53% vs. 53%, p = 0.3). The infection (19% vs. 14%, p=0.7) or GVHD (16% vs 12%, p=0.7) attributable deaths were comparable between the two cohorts. The median OS was not reached in both cohorts. The one-year OS was comparable in the two cohorts (66.8% vs. 65.5%, p = 0.6).
Discussion and Conclusion: The role of levofloxacin as bacterial prophylaxis in HCT is controversial, especially in a country like ours where there is a wide prevalence of fluoroquinolone and multi-drug resistance. With limitations of a retrospective period study, our study shows that fluoroquinolone prophylaxis did not make a difference in the incidence of GNB bacteremia, antibiotic duration, hospitalization, acute GVHD, and overall survival outcomes post-HCT.

Disclosure of Interest: None Declared

Keywords: Allogeneic HSCT, FLUOROQUINOLONES, Gvhd, INFECTIONS

Poster Presentation

INFECTIONS (388)

COVID-19 IN TRANSPLANT RECIPIENTS – A COMPARISON OF THREE WAVES FROM A TERTIARY CENTER IN INDIA

Sumeet Mirgh[*1,2], Anant Gokarn[1,2], Ashwini More[3], Sujit Kamtalwar[3], Sachin Punatar[1,2], Nishant Jindal[1,2], Akanksha Chichra[1,2], Minit Shah[1], Kaumil Patel[1], Malini Garg[1], Akhil Rajendra[1], Nikhil Patkar[2,4], Sweta Rajpal[2,4], Gaurav Chatterjee[2,4], Prashant Tembhare[2,4], Papagudi Subramanian[2,4], Navin Khattry[1,2]
[1]BMT unit, Department of Medical Oncology, ACTREC Tata Memorial Centre, [2]Homi Bhabha National Institute, [3]Dept of Medicine, [4]Dept of Hematopathology, ACTREC Tata Memorial Centre, Mumbai, India

Aims & Objectives: We conducted this retrospective analysis to compare the pattern of presentation, severity and treatment of COVID-19 in post-HSCT patients in the three waves of the pandemic.
Patients / Materials & Methods: This is a retrospective analysis of 59 COVID-19 infected HSCT recipients from 1st May, 2020 to 30th April, 2022. Severity of infection was graded as per ordinal scale. In the 1st wave (Wuhan variant; March, 2020 – November, 2020), antivirals used were Lopinavir/ritonavir+Ribavirin+Interferon-β-1b combination (prior to availability of remdesivir) and later on remdesivir. Remdesivir was used exclusively in 2nd wave (Delta variant; March, 2021 – October, 2021), while either remdesivir or oral molnupiravir was given in 3rd wave (Omicron variant; January 2022 – April 2022). Low molecular weight heparin (LMWH) was instituted according to physician's discretion. Repeat SARS-CoV-2 RT-PCR swabs were done between day7-14 of initial positivity, followed by weekly thereafter until negativity.
Results: Total 59 patients with median age 40 years (range – 3-64), 25 (42%) autologous, and 34 (58%) allogeneic HSCT patients developed COVID-19 disease. Baseline characteristics are shown in Table 1. Majority of patients in 1st wave had comorbidities (93% vs 40% vs 42%; p<0.01). Fever (53% vs 80% vs 47%; p=0.05) and cough (53% vs 88% vs 37%; p<0.01) were predominant presenting manifestations in the 2nd wave. Higher number of patients in 1st wave had breathlessness at presentation (26% vs 16% vs 0; p=0.05). Similarly, more patients in 1st wave presented with moderate-severe disease (33.3% vs 16% vs 5.3%; p=0.09), had higher incidence of hospitalization (66% vs 36% vs 31%; p=0.08) and had longer hospital stay (median - 13.5 days vs 8 days vs 6 days; p<0.01). More patients in 1st and 2nd wave received remdesivir (26% vs 24% vs 15.8%; p=NS). Lesser patients in 3rd wave required steroids or tocilizumab (33% vs 16% vs 5.3%; p=0.09) and LMWH (46% vs 24% vs 0; p=0.08). Amongst 34 allogeneic HSCT recipients, 79% (n=27) patients had prior history of GVHD, of which, all 5 patients with prior lung GVHD developed moderate-severe disease. Three patients developed new-onset or worsening GVHD within 3 months of COVID-19 disease. Seven patients in 3rd wave were vaccinated with both doses prior to the development of COVID-19. There was no mortality till hospital discharge in our cohort.
Discussion and Conclusion: The severity of COVID-19 disease has decreased over time. Less virulent variant, ease of availability of antivirals and widespread vaccination might have contributed to favorable outcomes over time. While HSCT patients are presumed to have higher mortality with COVID-19 disease, outcomes of our patients were not compromised.

Disclosure of Interest: None Declared

Keywords: COVID-19, Gvhd, India, SARS-CoV-2, transplantation/transplant recipients

Poster Presentation

INFECTIONS (394)

BK VIRUS REACTIVATION IN PATIENTS UNDERGOING ALLOGENEIC STEM CELL TRANSPLANT- AN AUDIT

Dibakar Podder*[1], Vinay Anand[1], Satarupa Mohapatra[2], Rizwan Javed[1], Arijit Nag[1], Jeevan Kumar[1], Saurabh Jayant Bhave[1], Reena Nair[1], Mammen Chandy[1]
[1]Clinical Hematology, Tata Medical Centre, Kolkata, [2]Clinical Hematology, AIIMS, Bhubaneshwar, India

Aims & Objectives: BK polyoma virus hemorrhagic cystitis is a common viral reactivation in patients undergoing allogeneic stem cell transplant (allo HCT). This study analyzed the demographics, donor characteristics, risk factors and mortality in patients who had BK polyoma virus reactivation post allogeneic HCT.
Patients / Materials & Methods: This is a single center retrospective analysis of the patients Patients who had urinary tract symptoms and who had BK polyoma virus detected in urine or blood were included. Data was collected from electronic medical records. Only transplants performed between January 2017 and June, 2022 were included in this analysis. Statistical analysis was done by SPSS 22.
Results: Total number of patients that underwent allo HCT during the study period was 194. Patient who had a BK polyoma positive in blood or urine was 21 (10.8%) cases. Median age was 26 years (range: 11-55 years). 18 cases were male patients (85.7%) and 3 cases were females (14.3%). 12 (57.1%), 5 (23.8%) and 4 (19%) of the reactivations were seen in haplo matched, matched unrelated donor and matched sibling donor respectively. Macroscopic hematuria, microscopic hematuria and no hematuris was seen in 12 (57.1%), 5 (23.8%) and 4 (19%) cases respectively. Median time to reactivation post allo HCT was 2.21 months (range: 0.53 to 5.8 months). 12 patients (57.1%) was having graft versus host disease (GVHD) at the time of reactivation. 12 cases (57.1%) was treated with Ciprofloxacin as first line, 1 patient (4.8%) each received Leflunomide and Cidofovir as first line treatment. 2nd line therapy was required in only 4 (19%) cases and in 2 cases each (9.5%), Leflunomide and Cidofovir was used. At last follow up 7 patients died (33.3%). None of the death were attributed directly due to BK polyoma cystitis.
Discussion and Conclusion: BK polyoma hemorrhagic cystitis is a common complications in patients undergoing allo HCT. GVHD and immunosuppression remains one of the major cause of reactivation. Although it is not directly associated with mortality, but it causes significant morbidity.

Disclosure of Interest: None Declared

Keywords: Allogeneic HSCT, BK virus, Hemorrhagic Cystitis

Poster Presentation

INFECTIONS (404)

CIDOFOVIR AS PRE-EMPTIVE THERAPY IN CYTOMEGALOVIRUS INFECTIONS POST ALLOGENIC STEM CELL TRANSPLANT

Neha R. Panda*[1], Vikas Dua[2], Rahul Bhargava[2], Meet Kumar[2], Minakshi Bansal[2], Arun Danewa[2], Santosh Rout[2]
[1]Department of Infectious Diseases, [2]Department of Hematology and BMT, Fortis Memorial Research Institute , Gurugram, India

Aims & Objectives: To analyse clinical efficacy of Cidofovir as first line pre-emptive therapy in Cytomegalovirus (CMV) infections post allogenic stem cell transplant (SCT) recipients.
Patients / Materials & Methods: This was a prospective study done in post allogenic SCT patients who were admitted in Department of Paediatric and Adult haematology and Bone Marrow transplant at Fortis Memorial Research Institute, Gurugram over a period of 6 months (July2021-Dec2021). Cidofovir along with probenecid and appropriate hydration was administered as pre-emptive therapy in patients with detectable CMV viremia (>1000 copies/ml) after informed consent. Patients with upfront CMV disease, deranged renal parameters and those who received even a single dose of ganciclovir or foscarnet were excluded. Cidofovir was administered at dosage of 5 mg/kg on weekly basis with laboratory monitoring till two consecutive undetectable viral loads as per standard guidelines. We also analysed adverse effects and incidence of breakthrough CMV infections.
Results: Of total 48 allogenic SCT done over the study period (23 paediatric, 25 adults), CMV viremia was observed in 68.3% (33/48) patients. Median time to detect CMV viremia (>1000 copies/ml) was 18±2 days post-transplant. Cidofovir after meeting inclusion criteria was administered in 71.8% (23) patients. Median viral load before initiation of therapy was 5500 copies/ml. Successful CMV viremia resolution was observed in 65.2% (16/23) patients. All the patients who responded to Cidofovir had baseline CMV viral load <40,000 copies/ml. Median time to clear CMV viremia was 2 weeks post Cidofovir administration. 13% (3/23) patients had grade 3/4 cytopenias and 17.3% (4/23) developed acute kidney injury during therapy. On Cidofovir therapy, 13% (3/23) developed CMV disease and 17.3% (4/23) had persistent rise in CMV viral load in blood and they were shifted to ganciclovir /foscarnet therapy. Recurrence rate of CMV viremia in cidofovir treated patients was 12.5% (2/16).
Discussion and Conclusion: Though ganciclovir still remains the first line pre-emptive therapy in CMV infections post allogenic SCT settings but it has limitations in terms of causing myelosuppression. Cidofovir can be a potential pre-emptive strategy to combat CMV infections, especially in patients with poor graft function and pre-existing cytopenias where it's difficult to administer ganciclovir limited by its myelotoxicity and also in resource limited settings like ours having poor availability of foscarnet

Disclosure of Interest: None Declared

Keywords: Allogenic stem cell transplant, myelosuppression, pre-emptive, viremia clearance

Poster Presentation

INFECTIONS (414)

PATTERNS OF INFECTION IN HEMATOPOIETIC STEM CELL TRANSPLANTATION RECIPIENTS

Manthan Kathrotiya*[1], velu nair[1], ankit jitani[1], hemant menghani[1], vijay shirure[1], shruti bhise[1], mayur mundhe[1], wajid hussain kazi[1]
[1]clinical hematology, apollo cbcc cancer centre, gandhinagar, India

Aims & Objectives: Analyse incidence, risk factors, and outcome of various infections in Hematopoietic Stem Cell Transplant (HSCT) recipients.
Patients / Materials & Methods: We collected and analyzed data of patients who underwent HSCT between April 2019 and May 2022. Conditioning regimen were decided as per diagnosis, performance status and comorbidities. In allogeneic HSCT GVHD prophylaxis was decided as per donor type. Documented positive bacterial, viral and fungal infection were considered for analysis.
Results: We included 67 patients: Male 60%, Female 40%, Median age 38 years (1.6 years to 69 years), Autologous HSCT (autoHSCT) 55%, Allogenic HSCT (alloHSCT) 45% [Haploidentical HSCT (62%), Matched Sibling Donor (MRD) (35%), and Matched Unrelated Donor (MUD) (3%)]. Overall incidence of bacterial infection was 57.1% and 24.3% among alloHSCT and autoHSCT respectively (P value 0.007). Nocardiosis Farcinica (lung involved) was seen in one patient after 100 days of transplant and was treated successfully. Incidence of viral and fungal infection was 71.4%, and 7.1% respectively in alloHSCT patients while none were seen in autoHSCT patients. MDRO incidence was 21% and 22% in alloHSCT and autoHSCT patients respectively while all isolates were susceptible to colistin. Central catheter removal was done in 3 alloHSCT patient for infection and fever. Within autoHSCT, multiple myeloma patients had higher incidence of bacterial infection compared to others diseases (39% vs 10.5%; P value 0.05). Viral infection were more common in cohort where PTCy was used (68% vs 32%; P value 0.05), while fungal infection were more common acute GVHD group (33% vs none; P value 0.03). No significant impact of age, sex, previous lines of treatment received, HCT comorbidity index, donor type, intensity of conditioning regimen, chronic GVHD and severity of mucositis on incidence and severity of infection noted. In autoHSCT cohort, patients who had median neutrophil engraftment in ≤10 days had less incidence of bacterial infection (P value 0.05). Among alloHSCT cohort cost of transplant was significantly higher in patient with diagnosed infection (2765450 vs 2522354, P value 0.007). NRM due to documented bacterial and fungal infection was 7% in alloHSCT group while there was no mortality in autoHSCT group. MDRO bacterial infection lead to 1 Peritransplant and 1 post-transplant death.
Discussion and Conclusion: Bacterial and viral infections were more common in alloHSCT group. Viral infections were more common in patients with PTCy use. Search for atypical organism where the cause of fever cannot be ascertained. MDRO infections and related deaths are concern in HSCT recipients. Acute GVHD is an independent predictor for fungal infections warranting use of aggressive anti-fungal prophylaxis.

Disclosure of Interest: None Declared

Keywords: BK virus, CMV Viremia, fungal infection, Infections post HSCT, nocardia infection

Poster Presentation

CONDITIONING REGIMENS (128)

INTERNATIONAL SURVEY FOR ANTIEMETICS IN HEMATOPOIETIC STEM CELL TRANSPLANTATION IN APBMT

Kimikazu Yakushijin[*1], Jacinta Perram[2], Aloysius Ho[3], Tasneem Farzana[4], Hiroatsu Iida[5], Jong W. Lee[6], Yoshihiro Inamoto[7], Biju George[8], Depei Wu[9], Ritsuro Suzuki[10], Maryam Behfar[11, 12], He Huang[13], Thiti Asawapanumas[14], Philip Rowlings[15], Bishesh S. Poudyal [16], Damai Santosa[17], Aye A. Gyi[18], Otgonbat Altangerel[19], Chinadol Wanitpongpun[20], Gan G. Gin[21], Satoshi Iyama[22], Shahid Iqbal[23], Mani Ramzi[24], Alka Khadwal[25], Jun Kato[26], Joycelyn Sim[27], Jessica Cheng[28], Chua Y. Xuan[29], Shinichiro Okamoto [26], Minako Iida[30], Shigeo Fuji[31]

[1]Medical Oncology and Hematology, Kobe University Hospital, Kobe, Japan, [2]Department of Haematology and BM Transplant, St Vincent's Hospital Sydney, NSW, Sydney, Australia, [3]Haematology, Singapore General Hospital, Singapore, Singapore, [4]BMT, National Institute of blood diseases and bone marrow transplantation, Karachi, Pakistan, [5]Hematology/ Cell Therapy, National Hospital Organization Nagoya Medical Center, Nagoya, Japan, [6]Hematology, Seoul St. Mary's Hospital, Seoul, Korea, South, [7] Hematopoietic Stem Cell Transplantation, National Cancer Center Hospital, Tokyo, Japan, [8]Haematology, Christian Medical College , Vellore, India, [9]Hematology, National Clinical Research Center for Hematologic Disease. The First Affiliated Hospital of Soochow University. Jiangsu Institute of Hematology, Suzhou, China, [10]Hematology and Oncology, Shimane University, Izumo, Japan, [11] Pediatric Cell and Gene Therapy Research Center, Gene, Cell and Tissue Research Institute, [12] Children's Medical Center, Pediatrics Center of Excellence, TUMS, Tehran, Iran, [13]Bone Marrow Transplantation Center, First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, China, [14]Medicine, King Chulalongkorn Memorial Hospital, Bangkok, Thailand, [15] Haematology, Calvary Mater Newcastle, Waratah, Australia, [16]Clinical hematology and bone marrow transplant, Civil service hospital , Kathmandu, Nepal, [17]Hematology-Medical Oncology, Internal Medicine, Dr. Kariadi Hospital, Semarang, Indonesia, [18]Clinical Haematology Department, North Okkalapa General and Teaching Hospital, Yangon, Myanmar (Burma), [19]Department of Hematology, School of Medicine, Mongolian National University of Medical Sciences, Uloonbaater, Mongolia, [20]Internal Medicine, Srinagarind, Khon Kaen University Hospital, Khon Kaen, Thailand, [21]Medicine, University Malaya Medical Centre, Kuala Lumpur, Malaysia, [22]Hematology, Sapporo Medical University, Sapporo, Japan, [23]Bone Marrow Transplant Data Management Section, Armed Forces Bone Marrow Transplant Centre (AFBMTC) Rawalpindi Pakistan, Rawalpindi, Pakistan, [24]hematology and medical oncology &stem cell transplantation, Shiraz university of medical sciences-Shiraz stem cell transplant center, Shiraz, Iran, [25]Clinical Hematology & Medical Oncology, Post Graduate Institute of Medical Education & Research, Chandigarh, India, [26]Division of Hematology, Department of Medicine, Keio University School of Medicine, Tokyo, Japan, [27]Medicine, Queen Mary Hospital, Hong Kong, Hong Kong, China, [28]Haematology and Bone Marrow Transplant, St Vincent's Hospital Sydney, Sydney, Australia, [29] Pharmacy, KK Women's and Children's Hospital, Singapore, Singapore, [30]Promotion for Blood and Marrow Transplantation, Aichi Medical University, School of Medicine, Nagakute, [31]Hematology, Osaka International Cancer Institute, Osaka, Japan

Aims & Objectives: Chemotherapy and irradiation therapy require appropriate antiemetic medications, for which guidelines and recommendations have recently been published. A triple combination of 5-HT3 receptor antagonist, dexamethasone, and NK1-receptor antagonist is recommended in hematopoietic stem cell transplantation (HSCT); the addition of olanzapine is optional. However, clinical practices in the field of HSCT possibly vary among countries/regions, resulting in instances where these guidelines are not followed. We have conducted an international questionnaire survey to get a better understanding of the current policy on antiemetic use in the participating countries and regions of the Asia-Pacific Blood and Marrow Transplantation Group (APBMT).

Patients / Materials & Methods: A web-based questionnaire survey was conducted via e-mail between December 7, 2021 and January 21, 2022. The draft of the questionnaire was prepared and discussed in the Nutrition Support Working Group of APBMT, and confirmed in the annual meeting held in Thailand in 2021. The questionnaire was approved by the executive board of APBMT.

Results: Twenty-nine sets of data from 14 countries were collected. The categories of approximate allo-HSCT numbers in a year were "0, autologous HSCT only" (n = 2), "1 to 50" (n = 13), "51 to 100" (n = 6), and more than 100 (n = 8). The decision regarding the antiemetics for each regimen was made by physicians (93%), the pharmacist (3%) and the multidisciplinary team (3%). Major conditioning regimens often used were Bu-CY (72%), Flu-Bu (62%), TBI-CY (55%), and Flu-Mel (55%) for allogeneic HSCT, and high dose Mel (83%), BEAM (69%), Bu-Mel (14%), and LEED (14%) for autologous HSCT. Four respondents showed that there were different policies for antiemetics in allogeneic and autologous HSCT. In allogeneic HSCT patients, more potent antiemetics were used and dexamethasone was preferably avoided. Main results of antiemetics for each treatment are shown in Table 1. While 5-HT3 receptor antagonist was often used for antiemetics even in minimal to low emetic risk, olanzapine was not routinely used even in high emetic risk in several hospitals.

It is categorized as high emetic risk in radiation therapy, and 5-HT3 and dexamethasone are recommended. However, 5 respondents did not use dexamethasone.

Discussion and Conclusion: Olanzapine is not used widely in HSCT yet. Further data on the efficacy and safety of olanzapine is required in HSCT setting. Especially in the case of dexamethasone, proposed guidelines for antiemetics are sometimes not followed in allogeneic HSCT, to avoid clinically relevant complications due to steroids.

Disclosure of Interest: None Declared

Keywords: antiemetics, emetic risk, hematopoietic stem cell transplantation

Poster Presentation

CONDITIONING REGIMENS (165)

SECOND ALLO-HSCT WITH REDUCED-INTENSITY CONDITIONING IN RELAPSED HEMATOLOGICAL MALIGNANCIES

Yongqiang Zhao* [1], Yanzhi Song[1], Zhihui Li[1], Fan Yang[1], Feifei Li[1], Dongfang Yang[1], Tong Wu[1]
[1]beijing boren hospital, beijing, China

Aims & Objectives: In present study, the safety and efficacy of the second allogeneic hematopoietic stem cell transplantation (allo-HSCT) with reduced-intensity conditioning (RIC) in the patients with hematological malignancies who relapsed after the first allo-HSCT were evaluated.
Patients / Materials & Methods: Between April 2018 and June 2021, total 45 patients with hematological malignancies (B-ALL 24, T-ALL/LBL 4, AML15, MDS 2) who relapsed after the first allo-HSCT and underwent the second allo-HSCT in our hospital were enrolled and analyzed retrospectively. Donor type was either unrelated (n=11) or haploidentical (n=33). For the second allo-HSCT, donors were changed in 44/45 cases. The best related donor was determined by hematological and immunological hereditary predisposition genes, and hematopoietic and immune function tests. RIC regimens were mainly total body irradiation (TBI)/fludarabine (FLU)-based (n=38) or busulfan (BU)/FLU-based (n=4).Two patients were with total marrow irradiation (TMI)/FLU-based regimen and one patient received BU/cladribine-based regimen. Cyclosporine, mycophenolate mofetil, short-term methotrexate and ATG were employed for graft-versus-host disease (GVHD) prophylaxis. Nineteen of 45 (42.2%) patients who has targeted medicines available received maintenance therapy up to 2 years post-transplant.
Results: The median age was 25 (7–55) years old. Before the second allo-HSCT, 34 (75.6%) patients were in complete remission (CR), and 11 (24.4%) cases were in non-remission (NR). All patients achieved durable engraftment. The incidences of grade II-IV and severe acute GVHD were 20.0%, 8.9% respectively. Chronic GVHD were 20.0% in limited and 22.2% in extensive patterns. The incidences of CMV and EBV reactivation were 28.9%, 6.7% respectively. Hemorrhage cystitis developed in 15.2% cases and all in grade I or II. With the median follow-up 13(1–38) months, one-year disease-free survival (DFS), overall survival (OS) and cumulative recurrence incidences (RI) of all patients were 71.4%, 79.8% and 28.6%. Eight patients died (relapse 7, infection 1). Non-relapse mortality (NRM) was only 2.2%. One-year RI in CR patients was significant lower than in NR patients (16.9% vs. 49.7%, p=0.021). There was a trend of higher DFS in CR patients than NR patients but without statistical difference (78.9% vs. 51.9%, p=0.064). Univariate analysis showed that CR before the second allo-HSCT was an important factor on prognosis.
Discussion and Conclusion: With our strategies of RIC regimens, donor change, and maintenance therapy post-transplant, the second allo-HSCT in relapsed hematological malignancies after the first allo-HSCT is safe and effective treatment with high OS and DFS, and low NRM and relapse rate. The most important factor on prognosis of the second allo-HSCT is disease status before transplant.

Disclosure of Interest: None Declared

Keywords: Hematological malignancy, Reduced-intensity conditioning, Second allogeneic hematopoietic stem cell transplantation

Poster Presentation

CONDITIONING REGIMENS (183)

HIGH DOSE ETOPOSIDE CHEMO-MOBILIZATION FOR AUTOLOGOUS STEM CELL TRANSPLANTATION - REVISITED

Jayachandran Perumal Kalaiyarasi*[1], Nadeem Ahmed[1], Parathan Karunakaran[1], Nikita Mehra[1], Krishnarathinam Kannan[1]
[1]Medical Oncology, Cancer Institute (WIA), Chennai, India

Aims & Objectives: Patients with relapsed lymphoma who have undergone multiple lines of chemotherapy will need consolidation with Autologous stem cell transplantation (ASCT). Chemo-mobilization was used routinely before granulocyte–colony stimulating factor (G-CSF) was available. Most centers have now switched to G-CSF-based stem cell mobilization ± Plerixafor. Despite the usage of plerixafor, about 6%-23% of patients may fail mobilization. Such patients either undergo allogeneic stem cell transplantation which carries increased mortality or they do not undergo any consolidation which carries an increased risk of relapse. So we started using high-dose etoposide with GCSF and plerixafor as mobilization (chemo-mobilization) in patients who failed conventional GCSF with plerixafor (G-CSF mobilization). Here we present a short series of seven patients who underwent chemo-mobilization after the failure of G-CSF mobilization.
Patients / Materials & Methods: The treatment details, mobilization details, collection details, and transplant details of those who underwent chemo-mobilization from Jan 2021 – June 2022 were collected from patient records and analyzed. The patients were given high dose etoposide 1.6g/m2 on D1 followed by G-CSF 300mcg daily till the morning of collection. Peripheral blood CD34 was done daily in the morning from the day when total WBC counts raise above 1000 cell/cc and once the peripheral blood CD 34 count reaches 5 cells/cc, Plerixafor was given on that day night and the collection was done the next day morning.
Results: There were 7 patients who underwent chemo-mobilization in the above period. Males were five. The median age was 35 years (Range: 19-49). Four patients were primary progressive Hodgkin Lymphoma, two were relapsed Non-Hodgkin Lymphoma, and one was HIV-positive plasmablastic lymphoma. The median number of lines of chemotherapy received by these patients before ASCT was 2 (1-4). Six out of 7 patients failed G-CSF mobilization. One patient was taken up for direct chemo-mobilization as we anticipated failure with G-CSF mobilization due to four lines of prior chemotherapy. Out of the 7 patients, six patients had a successful mobilization with chemo-mobilization. The success rate was 85.7%. The only patient who failed chemo-mobilization was the HIV-positive plasmablastic lymphoma who has got only one line of therapy. Only one patient had febrile neutropenia during the chemo-mobilization. The median stem cell dose (n=6) collected during chemo-mobilization was 6.35x106 cells/kg (2.89-10.4). All 6 patients had engraftment before D15 of ASCT.
Discussion and Conclusion: This series is presented to increase awareness of the usage of chemo-mobilization in patients who fail conventional G-CSF mobilization before offering the allogeneic stem cell transplantation which carries increased morbidity and mortality.

Disclosure of Interest: None Declared

Keywords: Chemomobilization, High dose etoposide, Mobilization failure

Poster Presentation

CONDITIONING REGIMENS (196)

EFFECT OF REDUCED-INTENSITY FLU COMBINED WITH DIFFERENT DOSES OF BU ON THE PROGNOSIS OF ALLO-HSCT

Mingyue Pan[*1,2,3], Yibo Wu[1,2,3], Luxin Yang[1,2,3], Panpan Zhu[1,2,3], Jimin Shi[1,2,3], Xiaoyu Lai[1,2,3], Lizhen Liu[1,2,3], Yanmin Zhao[1,2,3], Jian Yu[1,2,3], He Huang[1,2,3], Yi Luo[1,2,3]
[1]Bone Marrow Transplantation Center, the First Affiliated Hospital, Zhejiang University School of Medicine, [2]Liangzhu Laboratory, Zhejiang University Medical Center, [3]Institute of Hematology, Zhejiang University, Hangzhou, China

Aims & Objectives: To evaluate the effects of a reduced-intensity conditioning regimen of fludarabine (Flu) combined with different doses of busulfan (Bu) on transplantation safety, long-term survival, and complications in patients with malignant hematologic diseases.
Patients / Materials & Methods: Fifty patients who received their first allogeneic hematopoietic stem cell transplantation (allo-HSCT) on a reduced-intensity regimen at the Bone Marrow Transplantation Center of the First Affiliated Hospital of Zhejiang University School of Medicine from December 2016 to June 2021 were included.. The patients were divided into two groups, Flu6Bu2 and Flu6Bu3, depending on the dose of Bu used. Overall survival, disease-free survival, cumulative relapse rate, non-relapse mortality, and cumulative incidence of graft-versus-host disease (GVHD) were observed in both groups.
Results: The median age of patients in the entire cohort was 55 (32~67) years. In the subgroups, the median age of patients in the Flu6BU2 (30 patients) and Flu6BU3 (20 patients) groups was 57 (32~67) and 61(41~66) years, respectively (P=0.081), and the median follow-up time was 355 (83-1853) and 414 (156-1471) days, respectively (P=0.657). 2-year overall survival rates in the Flu6BU2 and Flu6BU3 groups were 54.2% vs 83.1% (P=0.199); 2-year disease-free survival was 50.5% vs 72.9% (P=0.075); 2- year relapse rate was 30.0% vs 15.0% (P=0.258); and 2-year non-relapse mortality was 11.8% vs 11.9% (P=0.315). The cumulative incidence of 100-day acute GVHD and 2-year chronic GVHD were similar in both groups. Multifactorial analysis showed lower overall survival in patients with pre-transplant disease status of CR3/NCR compared to CR1/2. [HR 8.25, 95% CI 0.99-68.53; P=0.05]. Independent risk factors affecting disease-free survival included pretreatment regimen of Flu6BU3 [HR 4.76, 95% CI 1.16- 20.0; P=0.030], disease type of myelodysplastic syndrome [HR 0.13, 95% CI 0.03-0.59; P=0.008], positive pre-transplant MRD [HR 9.41, 95% CI 1.72-51.54; P=0.010].
Discussion and Conclusion: RIC-HSCT is a safe and effective treatment for elderly patients and young patients in poor physical functional status who are intolerant to myeloablative transplantation, and a relatively high-intensity Flu6Bu3 pretreatment regimen significantly improves patient disease-free survival.

Disclosure of Interest: None Declared

Keywords: ALLOGENEIC HAEMATOPOIETIC STEM CELL TRANSPLANTATION, MALIGNANT BLOOD DISEASES, REDUCED-INTENSITY CONDITIONING REGIMEN

Poster Presentation

CONDITIONING REGIMENS (207)

BLINATUMOMAB AS A PART OF CONDITIONING REGIMEN FOR ALLO-H FOR MRD POSITIVE ADULT A：A CASE REPORT

Jian Yu[*1,2,3], Hui Fu[1,2,3], Yanmin Zhao[1,2,3], Huarui Fu[1,2,3], Li Yang[1,2,3], Meng Liu[1,2,3], He Huang[1,2,3], Jimin Shi[1,2,3]
[1]Bone Marrow Transplantation Center, the First Affiliated Hospital, Zhejiang University School of Medicine, [2]Liangzhu Laboratory, Zhejiang University Medical Center, 1369 West Wenyi Road, Hangzhou 311121, China, [3]Institute of Hematology, Zhejiang University , Hangzhou, China

Aims & Objectives: To explore the optimal conditioning regimen for MRD positive adult ALL receiving allo-HSCT.
Patients / Materials & Methods: From November 2021 to January 2022, three MRD positive ALL patients received allo-HSCT at our center. Two patients were ph+ ALL, and one patient was ph- ALL with E2A-PBX1 fusion gene positive. Two women and one man. The median age was 44 (range 21-55) years old. All three patients underwent HRD allo-HSCT. At the time of transplantation, all three patients were morphologic remission, but MRD by multiparameter flow cytometry were 0.014%, 0.013% and 4.06% respectively. All three patients received conditioning regimen consisting of blinatumomab.
For the first ph+ ALL female patient, the conditioning regimen consisted of blinatumomab 28ug IV on days -21 to -15, Ara-C 4g/m2/d IV on days -10 to -9, BU 3.2mg/kg/d IV on days -8 to -6, CTX 1.8g/m2/d IV on days -5 to -4, MECCNU 250mg/m2/d on day -3, ATG 6mg/kg total dose IV on days -5 to -2. For the second ph+ ALL male patient, the conditioning regimen consisted of blinatumomab 28ug IV on days -17 to -11, Flu 30mg/m2/d IV on days -10 to -5, BU 3.2mg/kg/d IV on days -6 to -5, ATG-F 20mg/kg total dose IV on days -4 to -1. For the third ALL female patient, the conditioning regimen consisted of blinatumomab 28ug IV on days -17 to -11, Ara-C 4g/m2/d IV on days -10 to -9, BU 3.2mg/kg/d IV on days -8 to -6, CTX .8g/m2/d IV on days -5 to -4, MECCNU 250mg/m2/d on day -3, ATG 6mg/kg total dose IV on days -5 to -2. All patientss received the same GVHD prophylaxis consisting of CsA, MTX, and MMF.
Results: The median follow-up for all patients was 181 (range 150-198) days, and they achieved sustained engraftment successfully. The median time of neutrophil and platelet engraftment were 14 days and 13 days. One patient suffered Grade I aGVHD at days +17, one ph+ ALL patient suffered Grade II aGVHD at day +32. One ph+ ALL patient experienced CNS infiltration two months after transplantation, then he received intrathecal Ara-C/MTX/DXM injection, and achieved complete remission again. Five months after transplantation, he suffered cGVHD with CNS, skin and liver. The other two patients maintained the persistent MRD negative after transplantation.
Discussion and Conclusion: Allo-HSCT is a curable therapy for adult ALL patients. Negative pre-transplantation MRD status is associated with significantly lower incidences of relapse in ALL patients. For treatment of MRD positive adult ALL, we applied blinatumomab-based conditioning regimen followed by allo-HSCT, and all three patients achieved fast MRD negative after blinatumomab administration, and engrafted successfully without severe adverse effect and GVHD. Our preliminary result showed blinatumomab-based conditioning regimen followed by allo-HSCT might be a well-tolerated and effective regimen for adult MRD positive ALL.

Disclosure of Interest: None Declared

Keywords: Allo-HSCT, blinatumomab, MRD positive

Poster Presentation

CONDITIONING REGIMENS (224)

AN EFFECTIVE DESENSITIZATION STRATEGY FOR CHILDREN WITH VERY HIGH DSA UNDERGOING HAPLOIDENTICAL HSCT

Vimal Kumar*[1], Rishab Bharadwaj[1], Deenadayalan Munirathnam[1]
[1]PAEDIATRIC HAEMATOLOGY, ONCOLOGY & BMT, DR RELA INSTITUTE & MEDICAL CENTRE, CHENNAI, India

Aims & Objectives: Introduction:
Advances in techniques of haploidentical hematopoietic stem cell transplantation (HSCT) including post-transplant Cyclophosphamide (PTCy) and TCRαβ-Cd19 depletion has enabled near universal availability of donors for children requiring HSCT when no HLA-matched donors are available. Children with prior history of multiple blood transfusions especially hemoglobinopathies, aplastic anemia etc, often have very high titres of donor specific anti-HLA antibodies (DSA), thereby posing significant risk for primary graft failure. Several desensitization strategies have been developed to decrease these antibodies pretransplant based on studies from solid organ transplantation. However, there is still no consensus for desensitization strategies in paediatric HSCT
Aim:
To assess the efficacy of desensitization strategy comprising plasmapheresis, IV immunoglobulin (IVIG) and Rituximab +/- pretransplant immune suppression (for thalassemia) in children who underwent haploidentical HSCT at our centre over the last 2 years (2021 -2022).
Patients / Materials & Methods: Five out of the 17 patients who underwent haploidentical HSCT with PTCy approach for various indications at our hospital were found to have significantly elevated titres of DSA. The MFI cut-off used was 3000 units. Indications of HSCT were Thalassemia (3), Fanconi anaemia (1) and hypoplastic MDS (1). Our desensitization strategy included Plasmapheresis – alternate days on day-16, day-14 and day-12, followed by IV Immunoglobulins 1gm/kg on day-11, and Ritiximab 375mg/m2 on day-10 prior to HSCT. Plasmapheresis were continued on alternate days post HSCT in case of persistent high titres. Children with Pesaro Class III Thalassemia underwent 2 cycles of pretransplant immune suppression (PTIS) in addition to desensitization protocol.
Results: All our cohort of patients had high tires of DSA to multiple antigens. The mean DSA titres were 18363 units (range 3170U-51899U). The desensitization protocol was well tolerated without much adverse effects. The mean DSA titres post desensitization was 1956 units. (range 450U to 5600U). One out of the 5 children developed primary graft failure (Class III Thalassemia). Median time to engraftment was 14 days. All children who engrafted have persistent full donor chimerism on median follow-up of 11 months.
Discussion and Conclusion: The desensitization protocol comprising plasmapheresis, IVIG, Ritiximab +/- PTIS forms an effective strategy to decrease the very high DSA titres in heavily transfused children undergoing haploidentical HSCT when no full HLA matched donors are available, thereby significantly reducing the chances for primary graft failure.

Disclosure of Interest: None Declared

Keywords: DESENSITIZATION, DONOR SPECIFIC ANTIBODIES, HAPLOIDENTICAL

Poster Presentation

CONDITIONING REGIMENS (226)

FACTORS INVOLVED IN DOSIMETRIC UNCERTAINTIES IN CONVENTIONAL TOTAL BODY IRRADIATION (TBI)

Venkata Krishna Reddy Pilaka[*1], Srinu Aketi[2], Boopathi Rajan P[2], Rakesh Reddy Boya[3], Chandrasekhar Bendi[4], Murali Krishna Voonna[5]
[1]Department of Radiation Oncology, [2]Department of Medical Physics, [3]Department of Medical Oncology, [4]Department of Clinical Haematology, [5]Department of Surgical Oncology, Mahatma Gandhi Cancer Hospital & Research Institute, Visakhapatnam, India

Aims & Objectives: Conventional Total Body Irradiation (TBI) is considered as gold standard TBI technique in myeloablative regimens. The dose inhomogeneity should be less than 10% in order reduce treatment failures or side effects. This study aims to identify variations between calculated and measured doses and its likely causative factors.
Patients / Materials & Methods: Dosimetric data of ten consecutive TBI patients from April 2021 to May 2022 was taken and analyzed. Midline doses and compensator thickness of skull, neck, shoulder, chest, umbilicus, thigh, knee and ankle were calculated according to corresponding separations. Semiconductor diodes were used to measure the corresponding delivered doses. The mean percentage deviations between the measured and calculated doses at sites mentioned above were analyzed during the first two fractions of TBI.
Results: A total of 38 measurements for each site from ten patients were collected and analyzed. The mean percentage of deviation between calculated and measured doses of skull, neck, shoulder, chest, umbilicus, thigh, knee and ankle were -3.14, -3.20, +6.41, +2.36, +1.28, +1.71, -3.15, -1.54 respectively. The percentages of deviations were negative as distance increases from the central axis. This observation was likely due to larger source to surface distance (SSD) and lesser lateral scatter at the peripheries. On adoption of inverse square law (in view of larger SSD) into the calculation process, the mean percentage deviations of skull, shoulder, knee and ankle were changed to positive, i.e +3.48, +0.92, +4.63 and +4.20 respectively. The compensator hanging bars may contribute to reduced measured dose up to 5%.
Discussion and Conclusion: The measured negative percentage deviations at the periphery do not necessarily mean under dosing and immediate compensator corrections are not needed. Taking into consideration the inverse square law, lateral scatter and attenuation due to hanging bars in the calculation would reduce the dose variation between measured and calculated doses during TBI.

Disclosure of Interest: None Declared

Keywords: Invivo Dosimetry, Myeloabalative regimens, Total Body Irradiation

Poster Presentation

CONDITIONING REGIMENS (247)

MANAGEMENT OF DONOR SPECIFIC ANTIBODIES IN HAPLO-IDENTICAL HEMATOPOIETIC STEM CELL TRANSPLANTATION

Rasmi Palassery*[1], Aditi Raghunathan[1], Deepa D[2], Santhosh K. Devadas[1]
[1]Medical Oncology, [2]Transfusion Medicine, Ramaiah Medical College, Bengaluru, India

Aims & Objectives: Haplo-identical hematopoietic stem cell transplants (haplo-HSCT) are becoming increasingly common in the treatment of various blood disorders and haematological malignancies, since there is always a shortage of full-matched related or unrelated donors and because of the improving outcomes with newer advances in the conditioning regimens and supportive care. Primary graft failure (PGF) secondary to the donor-specific anti-HLA antibodies (DSA) in the recipient is one of the dreaded complications of haplo-HSCT. There are sensitive assays to identify and quantify DSAs in the recipients and various strategies to minimise them prior to HSCT. Here, we describe our experience of desensitisation techniques in patients with DSAs undergoing haplo-HSCT using a combination of bortezomib, plasma exchange (PE), intravenous immunoglobulin (IVIG) infusion, Rituximab (RTX), and donor buffy coat (BC) or single donor platelet (SDP) transfusions.
Patients / Materials & Methods: Twenty one patients who underwent haplo-HSCT were tested for DSAs by solid phase immuno-assays in multiplexed multianalyte bead arrays using Luminex. Six patients had DSA titers >2000 MFI and underwent desensitisation. Five patients had aplastic anemia and one had a myelo-proliferative disorder. Patients with DSA MFI >10000 received at least 2 doses of Bortezomib, 3 doses of RTX, 3 or more sessions of PE, IVIG infusions and either donor SDP (for DSAs against HLA Class I MHC antigens only) or BC (for DSAs against HLA Class II MHC antigens only or both Class I and II MHC antigens). Patients with DSA MFI >5000, but <10000 received RTX, PE and IVIG. For patients with DSA MFI >2000, but <5000, PE with or without RTX was given. Repeat DSA testing was done post day 0 for five patients. Three patients (all had DSA MFI >5000 prior to desensitisation) had positive DSA with MFI >2000, one had DSA with MFI <1000 and the fifth patient's DSA test was negative. The patients with DSA MFI >2000 received IVIG in the post-transplant period.
Results: Five out of six patients engrafted and the median day of engraftment was +16. One patient had primary graft rejection and died of infectious complications. Two patients developed calcineurin inhibitor (CNI) associated thrombotic microangiopathy (TMA) later; one survived and one succumbed to the complications. Yet another patient developed post-HSCT hemophagocytic lymphohistiocytosis (HLH), likely secondary to Hepatitis B reactivation and died. The remaining three patients are alive at 3, 5 and 7 months post-HSCT respectively.
Discussion and Conclusion: High DSA titers can be seen in patients who are heavily transfused pre-HSCT with non-leukodepleted blood products. The use of desensitisation treatment can reduce the DSA titers and result in successful engraftment in these patients.

Disclosure of Interest: None Declared

Keywords: DESENSITIZATION, DONOR SPECIFIC ANTIBODIES, HAPLOIDENTICAL

Poster Presentation

CONDITIONING REGIMENS (272)

FLUDARABINE-CYCLOPHOSPHAMIDE-ATG-TBI CONDITIONING FOR APLASTIC ANEMIA WITH HLA 9/10 MATCHED DONOR

Shreyas Hanmantgad[*1], Rohtih Chitrapur[1]
[1]Dept. of Haematology & Bone Marrow Transplant, Bangalore Baptist Hospital, Bengaluru, India

Aims & Objectives: Fludarabine and cyclophosphamide with or without ATG have been used as conditioning regimens in allogeneic stem cell transplant for aplastic anemia with matched related donors. Addition of TBI to the conditioning lends an immunosuppressive effect. Various centers use different conditioning and GVHD prophylaxis strategies where mismatched donors are used.
AIM: To demonstrate the use of FLUDARABINE-CYCLOPHOSPHAMIDE-ATG-TBI conditioning in a stem cell transplant for aplastic anemia with HLA single antigen mismatched donor.
Patients / Materials & Methods: A 16 years old male presented with pancytopenia of 3 months. He was diagnosed to have severe aplastic anemia. Stress cytogenetics was negative. A minor PNH clone was detected. His 14 years old female sibling was found to be a HLA 9/10 match with a single A* antigen mismatch with mismatch vector directed towards rejection. Probable DSA against donor class I antigen was detected with an MFI of 1505. Red cell ABO was a minor mismatch with donor being O blood group and recipient being A. No other donor sources were available. Allogeneic stem cell transplant was done with conditioning of Fludarabine 30 mg/m2/day for 4 days (from day -5 to day -2); Cyclophosphamide 25 mg/kg/ day for 4 days (from day -5 to -2) and Rabbit Anti Thymocyte Globulin 2.5 mg/kg/day for 3 days (from day-4 to -2). A single fraction of 2Gy Total Body Irradiation was added on day-1. GVHD prophylaxis was Cyclosporine 5 mg/kg/day in 2 divided doses from day – 1 and Methotrexate 15 mg/m2 on day +1; 10 mg/m2 on day+3 and day+6 and day+11. Posaconazole was used for fungal prophylaxis.
Results: Peripheral blood stem cell mobilization was done with filgrastim. A dose of 8.5 x 106 CD34+ stem cells/kg body weight of recipient was infused with no complications. Neutrophil engraftment occurred on day+26 and platelet engraftment occurred on day+21.Bone marrow studies done on day+28 to rule out poor graft function showed a normocellular marrow. Chimerism assessment by STIRs showed 96% and 99.5% donor chimerism on day+28 and day+60 respectively. He had persistent high grade fever from day+10 to day+26. No focus of infection was found. Fever settled with withdrawal of antibiotics. He had minimal WHO grade 1 mucositis. There was no evidence of GVHD. There was significant interaction between ciclosporin and Posaconazole leading to fluctuating trough levels of ciclosporin. Doses were adjusted as per trough levels. Patient recovered without major setbacks.
Discussion and Conclusion: FLUDARABINE-CYCLOPHOSPHAMIDE-ATG-TBI conditioning can be used in single HLA antigen mismatched related donor transplant in aplastic anemia. Cyclosporin with methotrexate at 15 mg/m2 on Day+1 and 10 mg/m2 on day+3, +6 and day+11 can be effectively utilized and GVHD prophylaxis. Trough levels of cyclosporine must be closely monitored.

Disclosure of Interest: None Declared

Keywords: CSA, FLU-CY-TBI-ATG, mismatched related donor

Poster Presentation

CONDITIONING REGIMENS (287)

HAPLO-IDENTICAL TRANSPLANT – THE WALK THROUGH DEEP WOODS – DONOR SPECIFIC ANTIBODIES

Rohith Chitrapur*[1], SHREYAS HANMANTGAD[1]
[1]HEMATOLOGY AND BONE MARROW TRANSPLANT, BANGALORE BAPTIST HOSPITAL, BENGALURU, India

Aims & Objectives: Introduction:
Haplo- identical peripheral blood stem cell transplant(T- replete) is a feasible option for many of the Benign and Malignant blood disorders. Inspite of conditioning regimen becoming better and better for the outcomes of transplant as well as GVHD, the main hurdle being the presence of Donor specific antibodies(DSA) in the recipient.Prescence of DSA in the recipient is a risk for Primary graft Failure.DSA > 1000MFI is considered positive and requires a de-sensitisation or search for a alternative donor. In absence of a alternative donor, DSA needs to be de-sensitised before the graft infusion. There are no consensus protocols for de-sensitisation. Aim: Haplo-SCT in High Risk Acute Myeloid leukemia with FLU/TBI conditioning with a de-sensitisation protocol used at our center(Plasmapheresis/Rituximab/Bortezomib/IvIg)
Patients / Materials & Methods: A 17 years old male with no co morbid illnesses presented with history of neck swellings, fever of 1 month duration. In view of high white count and blasts on peripheral smear. Bone marrow was done,IPT-Acute Myeloid Leukemia (non-M3).Karyotyping normal.FLT3-ITD mutated with High Allele ratio. He was induced with 3+7 ,following which Bone marrow was MRD +ve.He received 1 cycle of HIDAC and was considered for Allogeneic transplant. Patient did not have a sibling or the mother, Hence father was screened who was a Haplo Match. DSA done showed both Class I and II antibodies(C*06;02-1637,B*57;01-1341,A*01;01-1229,DQB1*03;03-2112) .The following de-sensitisation protocol was followed along with the conditioning for the transplant. It was adapted from MDACC and Spanish protocols. Inj Rituximab 375mg/m2 on Day- 15,Inj Bortezomib 1.3mg/m2 on Day -14 and Day-10,Plasmapheresis on Day -12,Day-8 and Day -1 and IVIG 5G on Day -5. Conditioning started on Day-7 with Fludarabine (30mg/m2/day for 3 days) and from Day-4 to Day -1,TBI (1.5Gy BD).GVHD prophylaxis with High dose Cyclophosphamide and Tacrolimus .G-CSF from Day +5
Results: DSA done on Day -1 was negative. Peripheral blood stem cell mobilisation was done with Filgrastim. A dose of 7.5 x 106 CD34+ stem cells/kg body weight of recipient was infused with no complications. Neutrophil engraftment occurred on day+16 and platelet engraftment occurred on day+27. Bone marrow studies done on day+28 showed a normocellular marrow. Chimerism assessment by STIRs showed 99% donor Chimerism on day+28 . He had persistent low grade fever post engraftment, evaluated to have Cytomegalovirus viremia, was treated with Ganciclovir and IvIG. Post 1 year of transplant patient is doing well, with good graft function and no signs of GvHD
Discussion and Conclusion: De-sensitisation protocol(Plasmapheresis/Rituximab/Bortezomib/IvIg) along with FLU/TBI conditioning is a feasible option for Haplo SCT with Donor specific antibodies.

Disclosure of Interest: None Declared

Keywords: CONDITIONING, DONOR SPECIFIC ANTIBODIES, Haplo-identical/mismatched HSCT

Poster Presentation

CONDITIONING REGIMENS (309)

AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANT IN PCNSL USING BUSULPHAN THIOTEPA CONDITIONING

Vibhor Sharma*[1], RANGARAJU R. RAO[2]
[1]medical oncology, yatharth hospital, noida, [2]medical oncology, paras hospital, gurugram, India

Aims & Objectives: We present an elderly patient of primary central nervous system lymphoma (PCNSL) who underwent autologous hematopoietic stem cell transplant in first complete remission (CR 1).
Patients / Materials & Methods: A sixty three years old lady, with known comorbidities of diabetes mellitus, systemic hypertension and hypothyroidism, was diagnosed as primary central nervous system lymphoma in November 2020. She had ECOG Performance Status 1 to begin with and had mini mental status examination score [MMSE] of 30/30. She was treated with four cycles of Induction chemotherapy as per MATRIX protocol [Rituximab 375mg/m2 on days minus 5 and day 0, high dose methotrexate 3.5 gram/m2 on day 1, Cytarabine 2 gram/m2 q 12 hourly on day 2 and 3, and Thiotepa 30mg/m2 on day 4). Induction chemotherapy was well tolerated. She attained Partial response at the end of 2 cycles and complete response at the end of 4 cycles of induction chemotherapy. Options of whole brain radiotherapy and autologous stem cell transplant were discussed as consolidation strategies. She was planned for autologous hematopoietic stem cell transplant [HSCT] in view of her excellent tolerance to induction chemotherapy, good performance status, good diabetes control and normal organ functions. Rectal swab sent pre-transplant showed the growth of ESBL organism.
Results: After written informed consent, she was planned for autologous HSCT. Stem cell mobilization was done with inj filgrastim and plerixafor (single dose). Single session of Peripheral blood stem cell [PBSC] harvest was done. CD 34 cell dose collected was 6.79 million / kg body weight. PBSC product was cryopreserved using controlled rate freezing. She was given conditioning chemotherapy with busulphan and thiotepa [Busulphan 3.2mg/kg iv once daily on days minus 7 and minus 6, Thiotepa 5mg/kg iv once daily on days minus 5 and minus 4]. Stem cell infusion was done on day zero. Stem cell viability was 96%. PBSC infusion was well tolerated. She achieved WBC engraftment on day +10. Her course in the bone marrow transplant unit was complicated by raised blood sugars, oral mucositis grade 1, diarrhea grade 2 and febrile neutropenia [blood culture- no growth]. In the last follow up after 1 year for ASCT, she was in complete remission.
Discussion and Conclusion: Newer conditioning regimes have been explored in order to make autologous peripheral blood stem cell transplant more feasible in the elderly patients of PCNSL. A single centre study by Schorb et al [MARiTA study] has explored Busulphan-Thiotepa conditioning protocol for patients over the age of 65 years. They found it to be well tolerated with zero transplant related mortality, 2 year OS of 92% and 2 year PFS of 89%. A select group of elderly patients with PCNSL can be offered autologous HSCT as a consolidation strategy.

Disclosure of Interest: None Declared

Keywords: BUSULPHAN THIOTEPA, CONDITIONING, pcnsl

Poster Presentation

CONDITIONING REGIMENS (371)

COMPARATIVE STUDY OF FLU-BU ,FT10 & FT14 IN PATIENTS UNDERGOING HEMATOPOITEIC TRANSPLANT

Amrita Gope*[1], Rizwan Javed[1], Mammen Chandy[1], Mita Roy Chowdhury[1], Sourav Jayant Bhave[1], Jeevan Kumar[1], Dibakar Poddar[1], Reena Nair[1]
[1]CLINICAL HEAMTOLOGY AND CELLULAR THERAPY, TATA MEDICAL CENTER, KOLKATA, India

Aims & Objectives: To compare transplant outcomes in patients receiving FT10, FT14 and Flu-Bu regimens before MRDT
Patients / Materials & Methods: Retrospectively data of 15 patients with sibling MRDT from the year 2017 to 2022 . Data was collected from hospital records of a tertiary care center from East India.
Results: Our result of comparison of Flu-Bu verses different doses of Flu - Treo shows that Treosulfan based regimen causing less mucositis , less need of total parenteral nutrition & less incidence of nausea, vomiting & diarrhea.
Up to 100 days follow up one patient was relapse in FT10, another one patient in FT14 regimen but no patient has relapsed in Flu-Bu regimen.
Discussion and Conclusion: It was observed regimen related toxicities are significantly less in Flu –Treo as compared to Flu-Bu

Disclosure of Interest: None Declared

Keywords: Flu-Bu, FT10, FT14, MRDT- MATCHED RELATED DONOR TRANSPLANT, pt-patients

Poster Presentation

CONDITIONING REGIMENS (381)

FLUDARABINE AND 7.2 GY TBI AS A CONDITIONING REGIMEN IN HAPLOIDENTICAL STEM CELL TRANSPLANT

Malini Garg*[1], Akanksha Chichra[1], Kaumil Patel[1], Muralidharan C[1], Sachin Punatar[1], Anant Gokarn[1], Sumeet Mirgh[1], Nishant Jindal[1], Lingaraj Nayak[1], Avinash Bonda[1], Bhausaheb Bagal[1], Sadhana Kannan[2], Komal Kumbhalwar[1], Libin Mathew[1], Navin Khattry[1]
[1]BMT, [2]Biostatistics, ACTREC, TATA MEMORIAL CENTRE, MUMBAI, India

Aims & Objectives: Haploidentical HSCT (haplo-HSCT) is an attractive strategy for patients as it offers advantages of readily available donors. The initial John Hopkins protocol [Fludarabine (Flu) +2Gy TBI] showed a 2-year EFS & OS of 26% & 36%, respectively, with low non relapse mortality (NRM) (15%), but high relapse rates (51%). We used Flu + 7.2-8 Gy TBI as conditioning regimen, in order to possibly decrease the relapse rates, without increasing regimen related toxicity and deliver effective immunosuppression. We analysed the outcomes and toxicities of this regimen in our cohort of patients.
Patients / Materials & Methods: This is a retrospective single centre analysis of all consecutive patients with haematological malignancies who received Flu with 7.2 Gy-8 Gy TBI from 2016 to 2021 for haplo-HSCT. The regimen was Flu 150 mg/m2 (30mg/m2 on days −7 to −3) with 7.2-8.0 Gy TBI in 4 divided fractions on day -2 and -1. No lung shields were used. Standard anti-infective prophylaxis were used. Prophylaxis for GVHD consisted of post-transplant cyclophosphamide (PTCy) with calcineurin inhibitors (CNI) and mycophenolate mofetil (MMF). Comorbidities were scored according to the HCT-CI. Disease Risk Index (DRI) and EBMT score were recorded for all patients. Neutrophil (NE) and platelet engraftment (PE) were graded as per standard criteria. Early toxicity after haplo-HSCT was graded according to CTCAE version 5. Acute GVHD and chronic GVHD were graded as per standard criteria. All patients underwent chimerism studies at day 15, 30 and then monthly for 1 year.
Results: Nineteen patients with characteristics as given in Table 1 were included. The median age was 24 years (range 9-52 years). Peripheral blood stem cell (PBSC) was the stem cell source in all patients. Engraftment kinetics, toxicities and outcomes are given in Table 2. Acute regimen related toxicity (grade >3 mucositis and diarrhea) was seen in 20% patients. Neutrophil and platelet engraftment occurred in all except 1 patient who had graft rejection but eventually had an autologous recovery. Grade 2-4 acute GVHD was seen in 15 patients (79%). The cumulative incidence of grade 3-4 acute GVHD was 31% and chronic GVHD was 31%. The 1-year OS was 39.5% (Fig 1). Six patients died due to acute GVHD and 2 due to MDR sepsis. No factor analyzed had any impact on OS. Two year cumulative incidence of relapse was 16.92% with NRM as the competing event.
Discussion and Conclusion: The incidence of acute regimen related toxicities (mucositis, diarrhea and organ toxicity) were acceptable with this regimen and the relapse rates were low. Flu-7.2 Gy TBI can be considered as a conditioning regimen in haploidentical transplants. Measures need to be taken to decrease bacterial multidrug resistant sepsis and acute GVHD, which were the main cause of mortality in our cohort of patients.

Disclosure of Interest: None Declared

Keywords: conditioning, Haplo-HSCT, TBI

Poster Presentation

CONDITIONING REGIMENS (393)

CLINICAL OBSERVATION OF R/R AML TREATED WITH RIC-ALLO-HSCT CONTAINING TBI-BASED CONDITIONING REGIMEN

Fan Yang[1], Pengfei Shi[*1], Shenxian Qian[1]
[1]Affiliated Hangzhou First People's Hospital · Zhejiang University School of Medicine, HangZhou, China

Aims & Objectives: To investigate the safety and efficacy of allo-HSCT containing reduced-intensity TBI(4 or 6 Gy) for refractory/relapsed acute myeloid leukemia(R/R AML).
Patients / Materials & Methods: Clinical data of 11 R/R AML patients who received allo-HSCT containing reduced-intensity TBI between Feb 2020 to Mar 2022 was analysed in this retrospective.
Results: ①Of the 11 patients,4 were males and 7 females, with a median age of 49(31-58)years. The donors were identical sibling(1), haploidentical family member(8) and unrelated cord blood(2),respectively. 4 patients reached partial remission,5 patients remained no remission and 2 patients reached complete remission before allo-HSCT.② Conditioning regimen: TBI 4 or 6 Gy,d-10;Fludarabine 30mg/m^2·d,d-9 to d-5;Cytarabine Arabinoside 1.5g/m^2·d ,d-9 to d-5;Cyclophosphamide 1g/m^2·d,d-4 to d- 3;Rabbit anti-human thymocyte immunoglobulin(ATG)2.5mg/kg·d,d-4d to d-1(haplo-HSCT).③ Of the 11 patients, 10 patients attained complete haploidentical engraftment, one case died from infection at d+6. The median durations for neutrophils and platelet innplantations were 14(10-23)and 14.5(11-39)days respectively.④Acute GVHD grade Ⅰ was found in 1 case, Acute GVHD grade Ⅱ was found in 3 cases.No Acute GVHD grade Ⅲ-Ⅳ was Observed.Chronic GVHD occurred in 2 cases.1 case was dignosed as bronchiolitis obliterans(BO).⑤The 10 patients who attained complete haploidentical engraftment reached complete remission after allo-HSCT.Of the 11 patients,the median follow-up was 304(6-700)days.Leukemia relapse occurred in 1 patients at time of 320 days after allo-HSCT.The estimated 1-year OS and DFS were(75.8±15.6)% and(60.6±18.4)%,respectively .
Discussion and Conclusion: Allo-HSCT containing reduced-intensity TBI was a feasible choice with favorable outcome for refractory/relapsed AML patients with comorbidities and frailty.

Disclosure of Interest: None Declared

Keywords: acute myeloid leukemia, refractory, relapsed, total body irradiation;

Poster Presentation

BONE MARROW FAILURE SYNDROMES INCLUDING MDS. (240)

SECOND HAPLOIDENTICAL BONE MARROW TRANSPLANTATION FOR GRAFT FAILURE IN SEVERE APLASTIC ANEMIA

Zhang Chengtao*[1], Jingjing zhang[1], Mohammad Arian Hassani[1], Yan Yang[1], Xiaoli Zheng[2], Jinsong Yan[1]
[1]The Second Hospital of Dalian Medical University, Dalian, [2]Air Force Medical Center, Beijing, China

Aims & Objectives: To date, the efficacy of second haploidentical bone marrow transplantation with antithymocyte antibody-contained conditioning remained limited information for severe aplastic anemia (SAA) patients with graft failure (GF).In this study, the outcome of second haploidentical bone marrow transplantation with antithymocyte antibody-contained conditioning for graft failure in eight patients with severe aplastic anemia was investigated.
Patients / Materials & Methods: Eight patients developed GF after first allogeneic transplantation and were treated with a second haploidentical BMT in the department of hematology in second hospital of Dalian Medical University (China) and Air Force Medical Center of PLA (China) from May 2011 to December 2020. The follow-up period was up to December 31, 2021. Flu/Cy/ATG was used as conditioning regimen, containing fludarabine (Flu, 30 mg/m2) once a day for 4 consecutive days, cyclophosphamide (Cy, 30 mg/kg) once a day for 4 days, and rabbit ATG (SangStat, France) of 2.5 mg/kg once a day for 2 days. G-CSF-primed HSCs plus marrow grafts were infused into recipients.
Results: Eight SAA patients with GF were retrospectively reviewed, who had median age of 12.5 (range, 3–22) years. They received a median mononuclear cell number of 15.7 (range, 11.2–20.9) × 10^8/kg, or median CD34+ cell number of 6.2 (range, 2.5–17.5) × 10^6/kg. They were all successfully engrafted with a median time for neutrophil or platelets of 12.5 (range, 11–16) and 24 (range, 14–50) days, respectively. Three patients developed skin acute graft versus host disease grades I–II, and another 3 developed limited chronic graft versus host disease. They all successfully recovered by treating with methylprednisolone (0.5–1 mg/kg/day) and tacrolimus. Two patients died of respiratory failure caused by pneumonia at 8 months and 23 months post-transplantation, respectively. Six patients survived with a 2-year estimated overall survival of 75%, with a median follow-up time of 48 (range, 8–116) months.
Discussion and Conclusion: This retrospective investigation indicated second haploidentical bone marrow transplantation based on antithymocyte antibody-contained regimen was feasible for salvaging SAA with GF.

Disclosure of Interest: None Declared

Keywords: Antithymocyte antibody, Graft failure, Overall survival, Second haploidentical bone marrow transplantation, Severe aplastic anemia

Poster Presentation

BONE MARROW FAILURE SYNDROMES INCLUDING MDS. (319)

PURE REDCELL APLASIA FOLLOWING ABO MISMATCHED TRANSPLANTATION-ROLE OF IBRUTINIB

Ranjit Kumar CS*[1], Anil Aribandi[1]
[1]Hemato-oncology and BMT, American Oncology Institute, Hyderabad, India

Aims & Objectives: To assess the efficacy of Ibrutinib in post transplant associated PRCA following major ABO incompatible matched related donor allogenic stem cell transplantation.
Patients / Materials & Methods: we are presenting two cases developed PRCA with transfusion dependency following allogenic stem cell transplantation, data was captured from case records.
Results: Case 1:
A 17yrs old female, severe aplastic Anemia- 46XX, undergone Matched sibling donor allogenic stem cell transplantation from her brother with major ABO incompatibility. Post transplant she had Neutrophil engraftment Day+13 and platelet engraftment on Day+14.She had complete donor chimerism on Day+30.She was on transfusion dependency for red cells, requiring about 2transfusions per month.On Day+80 she was having persistent low hemoglobin and transfusion dependency, hence Anti A and Anti B titers were checked which was anti A 1:16 and anti B 1:8, had Reticulocytopenia 0.1%, Bone marrow aspiration and biopsy suggestive of PRCA, CMV was negative and Parvovirus B serology negative.
She was initiated on Darbopoietin 100mcg s/c weekly for 8wks but no major improvement, then added Bortizomib but not had any response, later initiated Ibrutinib at 140mg once a day and gradually escalated to 420mg/day over 2weeks duration. Post Ibrutinib she become transfusion dependent within 4wks duration, within 8wks of Ibrutinib her hemoglobin was >10gm/dl. Following 2months of therapy she developed periungual granulation tissue around great toe, asymptomatic improved on boric acid powder topically, currently she is transfusion independent since march 2022, with decreasing of Anti B titers latest titers were 1:4.
Case2:
A 57yrs old gentleman, Acute Myeloid Leukemia-NPM1+,TET2+,DNMT+. Received 7+3 induction, post induction Bone marrow in remission,he received 2nd cycle of High dose cytarabine, he had 10/10 HLA matched sibling with Major ABO incompatability,he undergone transplant. Engrafted Neutrophil on Day+13,platlet Day+15.Day+30 chimerism was 100% donor chimerism.post transplant he was requiring transfusion support until Day+130 he received about 14 PRBC transfusions and he was initiated on Darbopoietin however no response. Tapered Stopped immunosuppression, however he was transfusion dependent. Bone marrow suggestive of PRCA, Parvo viral was negative. He was initiated on Ibrutinib at 140mg daily once for a week on Day +130 and escalated to 280mg once a day after a week, from Day+ 160 his hemoglobin was stabilized and transfusion free.
Discussion and Conclusion: Major ABO incompatible allogenic stem cell transplants are at risk of PRCA, which is challenging to manage, Ibrutinib small molecule tyrosine kinase inhibitor which was approved for 2nd line GVHD therapy has a role in management of PRCA following Major ABO incompatible stem cell transplantation.

Disclosure of Interest: None Declared

Keywords: Acute Myeloid Leukaemia (AML), Ibrutinib, PRCA, Severe aplastic anemia

Poster Presentation

BONE MARROW FAILURE SYNDROMES INCLUDING MDS. (354)

HAPLOIDENTICAL VERSUS MATCHED SIBLING DONOR TRANSPLANTATION IN CHILDREN WITH SEVERE APLASTIC ANEMIA

Neha Rastogi*[1], Sunisha Arora[1], Upasana kartik[1], Anjali Yadav[1], Dhwanee Thakkar[1], Satya Prakash Yadav[1]
[1]Dept. of Pediatric Hemat-oncology & BMT, Medanta- The Medicity, Gurugram, India

Aims & Objectives: Hematopoietic stem cell transplantation (HSCT) is the treatment of choice in severe aplastic anemia (SAA). However, many patients lack matched sibling donor (MSD). Therefore, alternate donor HSCT especially Haploidentical HSCT is the upcoming modality. Here, we compare outcomes of patients undergoing MSD HSCT vs. Haploidentical HSCT with post-transplant cyclophosphamide (PTCy) for SAA at our centre.
Patients / Materials & Methods: 16 children with acquired SAA who underwent HSCT in our centre, (10 Haploidentical, 6 MSD) from Jan 2017 to June 2022 were included in the study. Conditioning regimen for MSD: Horse ATG 90 mg/kg/total (day-4 to -2), Fludarabine 40mg/m2/d for 4 days (day-7 to -4), Cyclophosphamide 60mg/kg/d for 2 days (day-3 and -2). Conditioning regimen for Haploidentical: Rabbit ATG 4.5 mg/kg/total (day-4 to -2), Fludarabine 40mg/m2/d for 4 days (day-6 to -3), Cyclophosphamide 14.5mg/kg/d for 2 days (day-6 and -5) and total body irradiation 2Gy on day-1. Graft source was PBSC in all. PTCy 50 mg/kg on day+3 & +4, MMF and Cyclosporine were used as GvHD prophylaxis in haploidentical while Methotrexate and Cyclosporine were used in MSD.
Results: Mean age- 10.3 yrs (Range: 4-11.5 yrs) for MSD and 10.15 yrs (Range: 2.1-15.6 yrs) for Haploidentical. Mean CD34 cell dose was 6.62 X 106/kg (3.8-11.8) for MSD and 7.73 X 106/kg (3.5-11.8) for haploidentical. All 6 patients engrafted in MSD group. Among haploidentical group, one child died on day+15 before engraftment with E. coli sepsis and two had primary rejection while remaining 7 engrafted. Mean neutrophil and platelet engraftment was 14.5 days (Range: 12-16) and 12.8 days (Range: 12-24) in MSD and 17.8 days (Range: 16-24) and 18.8 days (Range: 12-27) in haploidentical. Among 2 rejections in haploidentical, 1 patient underwent second HSCT from the same donor and rejected again and died while second patient underwent second HSCT from other family donor, engrafted and doing well. Among engrafted patients, 4/6 had full donor chimerism in MSD group and 7/7 had full donor chimerism in Haploidentical group at day+100. In MSD group, none had viral reactivations or acute GVHD and 2/6 had limited chronic GVHD. However, in Haploidentical group 6/10 had viral reactivations (CMV-6, BKV-3, Adenovirus-1) and Grade II acute GvHD was seen in 2 (Liver-1, Gut-1) and limited skin chronic GvHD was seen in one. Mean follow up duration was 295.5 days in MSD group and 592.7 days in haploidentical. Overall survival and event free survival for MSD group were 100% and 100% whereas for haploidentical group it was 80% and 70%.
Discussion and Conclusion: Haploidentical HSCT with PTCy represents a potential treatment option for children with SAA when MSD is unavailable. However, complications are more common in Haploidentical HSCT in comparison to MSD HSCT.

Disclosure of Interest: None Declared

Keywords: aplastic anemia, Haploidentical transplants, Matched sibling donor

Poster Presentation

BONE MARROW FAILURE SYNDROMES INCLUDING MDS. (378)

OUTCOMES OF ALLOGENEIC HSCT FOR APLASTIC ANEMIA – A SINGLE CENTRE EXPERIENCE FROM NORTHERN INDIA.

Gopinathan Mathiyazhagan*[1], Nihar Desai[1], Archit P[1], Ashish Mishra[1], Manoj Singh[1], Mathuri Smith[1], Priyanka Chauhan[1], Manish Singh[1], Sanjeev Yadav[1], Dinesh Chandra[1], Anshul Gupta[1], Naresh Tripathi[1], K Rehman[1], Ruchi Gupta[1], Rajesh Kashyap[1], Soniya Nityanand[1]
[1]HEMATOLOGY, SGPGI, LUCKNOW, India

Aims & Objectives: Allogeneic Hematopoietic stem cell transplant (HSCT) remains the promising option for patients less than 40 years with Severe Aplastic Anemia(SAA).
To analyse the clinical profile and outcomes of patients undergoing HSCT for SAA from a tertiary care centre in Northern India.
Patients / Materials & Methods: This is a retrospective analysis of 43 patients who had undergone HSCT for AA at our centre. The clinico-demographic profile, time from diagnosis to transplant, prior transfusions to HSCT, gender and blood group disparity were retrieved. Their conditioning regimens and GVHD prophylaxis, time to engraftment, rates of acute and chronic GVHD, all cause mortality were analysed. Descriptive statistics was used to express data and analysis using SPSS software (version 20).
Results: The median age of the entire cohort was 24 years (range 4-62), most were males (65.1%, n=28) and 41.8% (n=18) qualified the criteria for VSAA. The causes include acquired (n=40, 93%) in majority, followed by Fanconi Anemia (n=1) and Dyskeratosis Congenita (n=1). Graft source were predominantly MSD (n=41) followed by haplo-SCT (n=2) in young acquired AA due to absence of MSD and failure of IST. The median time to transplantation from diagnosis was 6 months (range 2-48) with a median of prior 20 (range 6-53) PRBC and 34 (range 12-72) RDP transfusions. ATG based conditioning regimens (Flu-Bu-ATG, Flu-Cy-ATG, FLUCAB- Prime) were predominantly used (n=38, 88.3%) and made a difference with respect to primary graft failure (p=0.00011) and mortality (p =0.04) in comparison with Flu-Cy alone. CSA/MTX was used in majority (n=41,95.3%) as GVHD prophylaxis with PTCY in 2 haplo-transplants. Neutrophil and platelet engraftment occurred with a median of 13 days (range 9-19) and 14 days (range 12-22) respectively. Though PBSC was our preferred graft source the overall incidence of acute (n=8, 18.6%) and chronic GVHD (n=6, 13.9%, 3 were limited) were minimal. Time to transplant from diagnosis (early vs late as defined by 6 months) and old age (>40 years) didn't impact outcome (p=0.36, 0.63) though the latter were represented few (n=5). CMV and BK virus reactivation was noted in 14 and 4 patients, including both haplo transplants. There were 3 primary graft failures with overall mortality rate of 30.2% (n=13). Sepsis (gram negative=7, fungal=1) accounted for majority followed by SR GVHD (n=2) and TMA (n=2) in rest. There was no clonal evaluation and mean survival time of the entire cohort was 103 months (+ 11.59).
Discussion and Conclusion: The outcomes of aHSCT for SAA has improved overall due to improvised supportive care despite a infections and alloimmunisation. There is an ongoing need to develop better haplo conditioning regimens for those young patients with SAA lacking MSD and failure of first line IST.

Disclosure of Interest: None Declared

Keywords: aplastic anemia, Graft failure, Gvhd, INFECTIONS, Transplant Outcome

Poster Presentation

HEMOGLOBINOPATHIES, PRIMARY IMMUNE DEFICIENCY DISEASES AND METABOLIC DISORDERS. (215)

CLINICAL SPECTRUM AND ROLE OF HSCT IN PRIMARY IMMUNE REGULATORY DISORDERS IN CHILDREN

Vimal Kumar*[1], Rishab Bharadwaj[1], Meena Sivasankaran[2], Deenadayalan Munirathnam[1]
[1]PAEDIATRIC HAEMATOLOGY, ONCOLOGY & BMT, DR RELA INSTITUTE & MEDICAL CENTRE, [2]PAEDIATRIC HAEMATOLOGY, ONCOLOGY & BMT, KANCHI KAMAKOTI CHILDS TRUST HOSPITAL, CHENNAI, India

Aims & Objectives: INTRODUCTION:
Primary Immune Regulatory Disorders (PIRD) comprise a spectrum of diseases caused due to monogenic defects in immune regulatory pathways resulting in multisystem autoimmunity, lymphoproliferation and hyperinflammation. Most of these children present with organ specific autoimmune features like cytopenia, inflammatory bowel disease etc. as well as with non-malignant lymphoproliferation. Advances in next generation sequencing have enabled diagnosis of many of these disorders, as well as development of disease specific treatment modalities. Haematopoietic stem cell transplantation is often the curative option for most of these disorders.
AIM:
To assess the clinical spectrum and treatment outcomes including HSCT in children diagnosed with any of the PIRD in our hospital over the last 2 years
Patients / Materials & Methods: Retrospective case review of the presentation, diagnosis, next generation sequencing, and treatment outcomes
Results: A total of seven 7 children with different varieties of PIRD were diagnosed and treated at our hospital over the last 2 years. It included 2 children with LRBA deficiency, 2 children with DOCK8 mutation, 1 child each with Familial HLH (PRF gene mutation), STAT1-GOF mutation, IL2RA deficiency respectively. Four out of the 7 children presented with features of eczema, autoimmune enteropathy and nonmalignant lymphoproliferation (DOCK8 mutation-2, LRBA deficiency-1, IL2RA deficiency-1). Autoimmune cytopenias were the presenting feature in 2 children (LRBA deficiency-1, IL2RA deficiency-1). One child with DOCK8 mutation presented with recurrent abscess involving liver, lung, brain and mandible, while 11 child with STAT1-GOF mutation presented with Chronic mucocutaneous candidiasis. Four out of these 7 children underwent HSCT (DOCK8 mutation-2, LRBA deficiency-1, HLH-1), one child with LRBA mutation has a sustained response on treatment with Abatacept and awaiting HSCT.
Discussion and Conclusion: PIRD predominantly present with features of autoimmunity, hyperinflammation, lymphoproliferation, and severe atopy with comparatively lesser features of immune deficiency. Next generation sequencing has enabled diagnosis and characterization of PIRDs, their underlying molecular defects and an opportunity to treat with novel therapeutic drugs to modulate the immune system. HSCT is still the permanent curative treatment for many of these PIRD.

Disclosure of Interest: None Declared

Keywords: DOCK-8, HSCT, LRBA

Poster Presentation

HEMOGLOBINOPATHIES, PRIMARY IMMUNE DEFICIENCY DISEASES AND METABOLIC DISORDERS. (241)

ALLOGENIC STEM CELL TRANSPLANT IN SICKLE CELL DISEASE

Pravas Mishra*[1], Prachi Jain[1]
[1]Hematology/ BMT, Max Hospital, Delhi, India

Aims & Objectives: To study the outcome of patients with sickle cell disease (SCD) undergoing alternative transplant protocols
Patients / Materials & Methods: We are prospectively enrolling patients with SCD into a transplant program with protocols tailored as per the patient/ donor characteristics. Patients with matched sibling donor upto the age of 15 receive Treosulfan based protocol whereas those above 15 years are offered the TBI/ Alemtuzumab protocol. Haploidentical transplant followed the standard protocol with added thiotepa and two fractions of 200 cGy TBI. After the first two patients, the TBI dose was changed to single fraction 300 cGy. All patients after the first case now undergo red cell exchange transfusion, simple exchange or apheresis based, to reduce the HbS to < 30%. Post transplant GVHD prophylaxis is tacrolimus/ cyclosporine in matched sibling donors and post transplant cyclophosphamide/ mycophenolate/ tacrolimus in haploidentical transplants. The TBI/ alemtuzumab group receive sirolimus indefinitely based on the chimerism data at followup.
Results: 9 patients have been enrolled so far, age range 1 year 9 months to 19 years; 7 males. Four patients had a fully matched sibling donor of which 3 received a TBI/ alemtuzumab protocol (age greater than 15 years). All received PBSC grafts. (Table 1). 6 patients had major ABO mismatch. Table 2 summarises the outcomes and complications. All patients and donors were CMV IgG positive at baseline. CMV reactivation was noted in 5 patients in the immediate post transplant phase. These included 2 haploidentical transplants and all 3 TBI/alemtuzumab patients.
8 patients are alive at follow ups ranging from 3-24 months. 1 patient (haploidentical) died of sepsis prior to engraftment. 1 patient (TBI / Campath) failed to engraft and had autologous recovery. Acute grade II gut / skin GVHD was seen in 2 patients. Four have developed mild chronic GvHD primarily involving skin. Infectious complications were noted in 5 patients. Carbapenem resistant klebsiella developed in the one patient who died. CLABSI was noted in one patient. 3 patients had diarrhea. None except the one patient with engraftment failure received any red cell support in the post transplant phase. All haploidentical transplants had cytokine release syndrome grade 1.
Discussion and Conclusion: PBSCT is safe in patients with sickle cell disease. Alternate transplant protocols including haploidentical transplants in selected cases and non chemotherapy based protocols have expanded the eligibility for transplant in patients with sickle cell disease .

Disclosure of Interest: None Declared

Keywords: outcome, sickle, transplant

Poster Presentation

HEMOGLOBINOPATHIES, PRIMARY IMMUNE DEFICIENCY DISEASES AND METABOLIC DISORDERS. (289)

STEM CELL MOBILIZATION AND APHERESIS IN DONORS WITH SICKLE CELL TRAIT.

Shailesh Lavana*[1]
[1]stem cell transplant, Kailash cancer hospital and research centre, Goraj (Vadodara), India

Aims & Objectives: To report of safety and feasibility of stem cell mobilization and apheresis in donors with sickle cell trait.
Patients / Materials & Methods: Retrospective analysis of stem cell mobilization and apheresis in two donors with sickle cell trait. The G-CSF 5 mcg/kg/dose twice a day was given for stem cell mobilization. Peripheral blood stem cell harvests were performed with "spectra Optia" using cell separators MNC programme. Participant's health records were reviewed for reported adverse events. In addition, patients also reviewed for use of analgesia during mobilization and apheresis.
Results: • Donor characteristics:
Both Donors were from India, first one from Maharashtra and the second one from Gujarat. First donor is 3 year old boy and second one is 22 year old girl.
• Stem cell mobilization
Both donors mobilized without unanticipated adverse events. None of them experienced sickle cell crisis. Only second donor experience myalgia, however it was graded as 1 as per severity score (Table 2). None of them required analgesia during mobilization. One dose of GCSF was held on 3rd day of mobilization in second donor due to high counts (Table 1). Spleen was not enlarged in both donors during mobilization.
• Stem cell apheresis
PBSC apheresis was done under general anesthesia without complication for first 3 year old male donor. Second female donor experienced hypocalcemia related symptoms during apheresis. None of them required apheresis on second day. Adequate stem cells were collected from both donors (1st donor: 7.73 x106 CD34 cells /kg, 2nd donor: 8.26 x106 CD34 cells/kg). None of them required special care following stem cell apheresis.

Discussion and Conclusion: Stem cell mobilization is appears to be safe and feasible in donor with sickle cell trait.
However, prospective and larger studies are needed to confirm same.

Disclosure of Interest: None Declared

Keywords: safety and feasibility, sickle cell trait, stem cell mobilization and apheresis

Poster Presentation

HEMOGLOBINOPATHIES, PRIMARY IMMUNE DEFICIENCY DISEASES AND METABOLIC DISORDERS. (297)

HEMATOPOIETIC STEM CELL TRANSPLANTATION IN PRIMARY HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS

Ritu L*[1], Pooja M[1], shobha B[1], Ravi J[1], Santosh K. A[1], Swathi P M[1], Shweta P[1], Monika B[1], Gayathri s[1], Manojit C[1], Lakshmi T[1], Kamini K[1], Sunil B[1]
[1]Pediatric Hematology,Oncology and Bone marrow Transplantation, Mazumdar Shaw Medical Center, Bengaluru, India

Aims & Objectives: Primary hemophagocytic lymphohistiocytosis (HLH) is a life-threatening hyperinflammatory syndrome with multiorgan involvement which exhibit an autosomal recessive inheritance and usually present during infancy.Hematopoietic stem cell transplantation (HSCT) is the only curative treatment option for patients diagnosed with primary HLH.
Patients / Materials & Methods: In this retrospective study, records of pediatric patients with Primary Hemophagocytic lymphohistiocytosisundergoing hematopoietic stem cell transplant (HSCT) at Mazumdar Shaw Medical Center, Bangaluruwere analyzed.
Results: Total 13 patients underwent hematopoietic stem cell transplant). Out of which, 8 (62%) were Primary HLH and 6(38%) were Gricelli Syndrome. Median age of presentation was 26 (8-23) months with M:F ratio of 5:8. Median age of HSCT was 42 (30-62) months. All patients received chemotherapy as per HLH 2004 protocol prior to transplant. Seven (54%) patients underwent Matched Sibling Donor transplant, 5 (38%) had Haploidentical HSCT with TCRalpha/beta depletion and 1(8%) received Haploidentical HSCT with Post Transplant cyclophosphamide. For GvHD propylaxis, Cyclosporin and Methotrexate (54%) combination was most frequently used. Peripheral blood stem cell (54%) was common stem cell source than bone marrow (46%). Thiotepa, fludarabine, treosulphan and anti-thymocyteglobulin (54%) was the most common conditioningregimen used. The mean MNC and CD34 count was 8.1 x 108 and 14.2 x 106/kg respectively. The mean time to neutrophil and platelet engraftment was 14 and 16 days respectively. Sepsis (31%), CMV reactivation (31%), Acute GvHD (23%) were the common complications observed post-transplant. 23% patients required PICU care. Total of 2(15%) patients died, mostly from acute respiratory distress syndrome.The Overall Survival (OS) was 84%.
Discussion and Conclusion: Primary HLH is associated with high morbidity and mortality rate. HSCT is the only curative option for primary HLH. Early recognitionis crucial for any reasonable attempt at curative therapy.Haploidentical HSCT is a feasible option for those with no fully matched donors.

Disclosure of Interest: None Declared

Keywords: Gricelli syndrome, Hematopoietic stem cell transplantation, Primary hemophagocytic lymphohistiocytosis

Poster Presentation

HEMOGLOBINOPATHIES, PRIMARY IMMUNE DEFICIENCY DISEASES AND METABOLIC DISORDERS. (300)

REDUCED INTENSITY CONDITIONING RESULTS IN MIXED CHIMERISM IN WISKOTT ALDRICH SYNDROME

Sohini Chakraborty*[1], Kavitha Ganesan[1], Suresh R Duraisamy[1], Satish K. Meena[1], Vigneswar Venkatesan[1], Venkateswaran V. Swaminathan[1], Ramya Uppuluri[1], Revathi Raj[1]
[1]Paediatric Haematolog y, oncology and Blood and Marrow Transplantation, Apollo Cancer Centre, chennai, India

Aims & Objectives: Wiskott Aldrich syndrome (WAS) is an X-linked genetic disorder characterized by thrombocytopenia, primary immune deficiency, autoimmunity and malignancy. Hematopoietic stem cell transplantation (HSCT) is the only available curative option. The aim of this study was to analyse the outcome of patients with WAS who underwent HSCT at our centre.
Patients / Materials & Methods: We performed a single centre retrospective study in children up to 18 years of age with WAS who underwent HSCT between January 2009 to December 2021 at our centre. Data was collected through retrospective review of patient charts and medical records. Institutional ethics committee approval was obtained prior to the study.
Results: A total of 25 patients were included in the study. Five underwent matched family donor (MFD) HSCT, 10 had matched unrelated donor (MUD) HSCT and 10 underwent haplo-identical HSCT. Stem cell source was bone marrow in 3 children, peripheral blood (PBSC) in 18 and umbilical cord in 4 patients. The conditioning regimen used in majority of patients was Fludarabine/ Busulfan in those undergoing MRD HSCT with the addition of anti-thymocyte globulin in those undergoing MUD HSCT and Fludarabine, melphalan with post-transplant cyclophosphamide as GVHD prophylaxis in those undergoing haplo-identical HSCT. The median age at transplantation was 1 year and the median duration of follow up was 80 months (1-153 months). Twenty-one (84%) patients engrafted. Two children in the study group received treosulfan based protocol both of whom had primary graft failure and died. Secondary graft failure occurred in 2 patients. Acute and chronic GVHD rates were high seen in 14 (66.6%) and 13 (61.9%) patients respectively. Mixed chimerism was documented in 5 (20%) requiring donor lymphocyte infusions. Autoimmune manifestations included thrombocytopenia and immune haemolytic anaemia in patients with mixed chimerism. There was a total of 13 deaths in the group (MUD cord =4, MUD PBSC =2, MFD =1 and Haploidentical =6). The cause of death was graft failure in 3, infections in 4, GVHD in 3 and refractory immune cytopenia in 3 patients. The overall survival in the cohort was 53%, with 80% in the MFD group, 66.6% in the MUD group and 40% in the haploidentical group.
Discussion and Conclusion: Allogeneic HSCT from matched family donor using myeloablative conditioning (MAC) confers excellent outcome. However, the outcomes in the haploidentical group still remains sub optimal. Mixed chimerism is associated with auto-immune manifestations and hence complete chimerism is desirable in patients with WAS unlike other inborn errors of immunity. Based on our experience, we have altered the haploidentical HSCT regimen to a MAC regimen using rabbit ATG, fludarabine, busulfan and melphalan.

Disclosure of Interest: None Declared

Keywords: mixed chimerism, Transplant Outcome, wiskott aldrich,

Poster Presentation

HEMOGLOBINOPATHIES, PRIMARY IMMUNE DEFICIENCY DISEASES AND METABOLIC DISORDERS. (341)

SPECKLE TRACKING ECHOCARDIOGRAPHY - LEFT VENTRICULAR GLOBAL LONGITUDINAL STRAIN IN EX-THALASSAEMICS

Amal Paul*[1], Uday Kulkarni[1], Fouzia N A[1], Bijesh Yadav[1], Anup Devasia[1], Anu Korula[1], Aby Abraham[1], Biju George[1], Paul George[1], Alok Srivastava[1]
[1]Christian Medical College, Vellore, India

Aims & Objectives: Long term survivors of haematopoietic stem cell transplantation (HSCT) for β-thalassemia major are designated "ex-thalassaemics". Whether ex-thalassaemics continue to harbour residual myocardial dysfunction and thereby stand the risk of heart failure-related morbidity and mortality is unknown. The aim of this study was to assess the prevalence and predictors of subclinical left ventricular (LV) dysfunction in an apparently normal ex-thalassaemic population.
Patients / Materials & Methods: We conducted a single centre cross-sectional study among 62 ex-thalassaemic patients, who had undergone HSCT for β-thalassaemia major at our centre. The primary outcome variable was LV systolic dysfunction, as assessed by 1) LV global longitudinal strain (GLS) derived by 2D speckle tracking echocardiography and 2) LV ejection fraction (EF) derived by 2D Simpsons Biplane method.
Results: Among the 62 patients included in the study, 9 [14.5%] were found to have LV systolic dysfunction, all of which were subclinical. Of these, 4 [6.5%] had abnormal GLS and LVEF, 4 [6.5%] had abnormal GLS with normal LVEF, and 1 [1.6%] had abnormal LVEF with low normal mean GLS. Older age at the time of HSCT was found to be a significant predictor of LV systolic dysfunction [OR = 1.15].
Discussion and Conclusion: There was a high prevalence of subclinical myocardial dysfunction in the ex-thalassaemic population reiterating the need for close follow up of these patients.2D Speckle tracking echocardiography-derived LV global longitudinal strain is an effective tool in detecting subclinical myocardial dysfunction in this cohort.

Disclosure of Interest: None Declared

Keywords: Allogeneic Hematopoietic Stem Cell Transplantation, Ex thalassaemics, LV GLS, Myocardial dysfunction

Poster Presentation

HEMOGLOBINOPATHIES, PRIMARY IMMUNE DEFICIENCY DISEASES AND METABOLIC DISORDERS. (356)

SAFETY AND EFFICACY OF DONOR TYPE RBC TRANSFUSION PRIOR TO MAJOR ABO INCOMPATIBLE BMT.

Shailesh Lavana*[1], Pallavi Mehta[2]
[1]Stem cell Transplant, KCHRC, Goraj, [2]Hematology, RGCI, Delhi, India

Aims & Objectives: To report a safety and efficacy of donor type RBC to decrease isohemagglutinin titters in MAJOR AND BI-DIRECTIONAL ABO incompatible BMT

Patients / Materials & Methods: This is a retrospective study was done at two centers, KCHRC, Goraj and RGCI, Delhi.

Patients:

Recipients of major and Bidirectional ABO incompatible transplant with corresponding Anti A and Anti B titers of ≥ 1:32 were given donor type of RBC prior to Bone marrow stem cell infusion.

Donor type RBC:

Donor type RBC(PCV) was not cross matched with recipients as it is ABO incompatible. Donor type RBC (PCV) was irradiated.

Infusion protocol

Donor type irradiated PCV was given for 4 days as an incremental volume after completion of ATG during conditioning. Donor type RBC infusion given under steroid and antihistamic cover along with hydration.

Analysis:

Reaction to donor type RBC and graft transfusion, number of donor type RBC transfusions, and trend of isoagglutinin titers, and engraftment data were observed.

Results: Total 74 bone marrow stem cell transplants were done at two centers from May 2019 to May 2022. Donor type RBC was given to 8 recipients. Major ABO incompatible transplants were 6 (8.1%) and bidirectional ABO incompatible transplants were 2(2.7%). Six was MRD transplant & one was MUD transplant for transfusion dependent thalassemia and one was haploidentical transplant for acquired aplastic anemia. Mean age & weight of patient was 7.6 (3-20) years and 22.2 (13.2-46.6) Kg respectively.

Efficacy of Donor type RBC

All the patients had reduction in titers to clinically insignificant level after donor type RBC.
Median Pre-procedure isoagglutinin titers were 1: 32 (1:32 - 1:64).
Median post-procedure titers were 1:4 (1:2 - 1:16).
Mean volume of donor type RBC (PCV) infused was 78.1(75-100) ml.
Mean volume of bone marrow stem cells infused was 401.6 (215- 500) ml.

Engraftment

All of them achieved engraftment. All of them except 2 patients had complete donor chimerism. Median time to neutrophil & platelet engraftment was 17.3 (15-21) days & 19.4 (13-42) days respectively.

Safety of Donor type RBC

None of them had severe hemolysis or anaphylaxis. Mild hemolysis/ hemoglobinuria was observed in 5 (62.5%) of patient at donor type RBC, however none of them had hemolysis/hemoglobinuria at bone marrow stem cell infusion. All patients were managed with adequate hydration with diuresis. Only one (12.5%) of them had febrile reaction at donor type RBC and one (12.5%) had febrile reaction at bone marrow stem cell infusion.

Discussion and Conclusion: Donor type RBC is efficacious & well tolerated procedure to decrease isoagglutinin titers & to avoid clinical significant hemolysis at bone marrow stem cell infusion in ABO incompatible BMT.

It is very simple method &allows infusion of unmanipulated bone marrow stem cells also.

Disclosure of Interest: None Declared

Keywords: Donor type RBC, major and Bi directional ABO incompatible, safety and efficacy

Poster Presentation

HEMOGLOBINOPATHIES, PRIMARY IMMUNE DEFICIENCY DISEASES AND METABOLIC DISORDERS. (408)

LONG-TERM OUTCOME OF HAEMATOPOIETIC STEM CELL TRANSPLANTATION IN OSTEOPETROSIS

Mithun A. Prakash*[1], Fouzia Nambiatheyil Aboobacker[1], Uday Kulkarni[1], Anu Korula[1], Anup Devasia[1], Sharon Lionel[1], Sushil Selvarajan[1], Aby Abraham[1], Biju George[1], Vikram Mathews[1], Alok Srivastava[1]
[1]Department of Clinical Haematology , CMC Vellore, Vellore , India

Aims & Objectives: To assess long term outcomes after Haematopoietic stem cell transplantation (HSCT) in osteopetrosis
Patients / Materials & Methods: A retrospective analysis was made of 7 children who had received an allogeneic HSCT for osteopetrosis between 2000 and 2021. Conditioning regimen used was Thiotepa, Treosulfan and Fludrabine in 6 patients and Busulfan and Cyclophosphamide in one patient. GVHD prophylaxis used was Cyclosporine and Methotrexate in matched related transplants and Cyclosporine or Tacrolimus with MMF and post-transplant cyclophosphamide in Haploidentical stem cell donors.
Results: 7 Children (all male), with a median age of 12 months (range: 5-12) underwent allogeneic HSCT for osteopetrosis. Six of them were born to consanguineous parents. Genetic work up was positive in three patients. (CLCN7, TNFRSF11A and TC1RG1 mutation respectively). Three children had deafness and hydrocephalus, one of whom required a VP shunt for the same and two had bilateral optic atrophy.
The donor was a matched sibling donor in 1 patient, matched related donor (grandmother =1, mother=2) in three patients, matched unrelated donor in one and haploidentical (parents) in two patients. Source of stem cells was bone marrow in five and PBSC in two patients. Median CD 34 Cell dose was 12.4 x 106 cells/kg (10.2 - 18.4). All patients had successful engraftment; median time to myeloid engraftment by day+18 (range: 13-27) and platelet engraftment by day + 33 (range15-52). Four patients developed acute GVHD (Grade 2 Skin in 3 and Grade 4 Gut & Liver in one) and one had severe veno-occlusive disease. Hypercalcemia as a complication was present in three, with median highest calcium of 15.6mg/dl(range 10.7 to 16.8, requiring treatment with corticosteroids, forced diuresis, calcitonin and bisphosphonates. Hypercalcemia settled by day +21 and day +25 in 2 children, while the third child (who had maximum calcium of 16.8mg%) required treatment till day +353 post SCT. One child developed a left gluteal tuberculous abscess by day +202 post-transplant and was treated with 12 months of anti-tuberculous therapy. At last review, with a median follow up of 30 months (range 1.13 – 69.6), 4/7 (57%) were alive and well with no evidence of chronic GVHD. In the 3 patients who died, causes of death were Infection, GVHD and cardiac failure in each.
Discussion and Conclusion: HSCT remains the only curative treatment option for osteopetrosis and should be offered as early as possible. Hypercalcemia is a common complication that should be actively managed.

Disclosure of Interest: None Declared

Keywords: Osteopetrosis, Pediatric, stem cell transplantation

Poster Presentation

HEMOGLOBINOPATHIES, PRIMARY IMMUNE DEFICIENCY DISEASES AND METABOLIC DISORDERS. (410)

LONG TERM OUTCOME OF ALLOGENEIC STEM CELL TRANSPLANTATION IN PATIENTS WITH CEREBRAL LEUKODYSTROPHIES

Fouzia Nambiatheyil Aboobacker*[1], Uday Kulkarni[1], Anu Korula[1], Anup Devasia[1], Sharon Lionel[1], Sushil Selvarajan[1], Aby Abraham[1], Alok Srivastava[1]
[1]Department of Clinical Haematology , CMC Vellore, Vellore , India

Aims & Objectives: The prognosis of cerebral leukodystrophies (CLD) with neurological involvement is generally dismal; however, allogeneic stem cell transplantation (allo SCT) is recognized as an effective therapy to stabilize or improve the clinical outcome of CLD.
To assess the long-term clinical outcome of consecutive patients with CLD who underwent allo SCT with myeloablative conditioning at our institution.
Patients / Materials & Methods: Retrospective analysis of patients who underwent allo SCT for X-linked adrenoleukodystrophy (X-ALD) and metachromatic leukodystrophy (MLD) at our center between 2007 to 2022 were included in the analysis. The conditioning regimen prior to transplantation was myeloablative and consisted of fludarabine and Busulfan. Low dose total body irradiation (TBI) (200 cGy in a single fraction) was added for haplo-SCT. Graft versus host disease (GVHD) prophylaxis was with cyclosporine and methotrexate for HLA identical and cyclophosphamide, tacrolimus and mycophenolate for haplo-SCT.
Results: Thirteen male patients underwent allo SCT for leukodystrophies from 2007 to 2022; twelve patients with X-ALD and a median age of 8 years (5-27), and one child aged 6 years for MLD. The pre-SCT Loes score ranged in X-ALD from 1-14; 9/12 had adrenal insufficiency at diagnosis and one patient (age 27yrs) presented with spastic paraparesis. The child with MLD was diagnosed pre-emptively at 5 years of age in view of the history of elder sibling death with progressive neurological symptoms. The stem cell source was bone marrow (n = 2), or peripheral blood (n=11) from HLA identical donor (related =3 carrier sister, unrelated=1) or haplo identical donor (father=5, carrier mother=2, sister=1, cousin=1). Primary engraftment was obtained in all 13 patients.Four had grade 1-2 acute GVHD and 3 had limited chronic GVHD. None had grade 3-4 acute or extensive chronic GVHD. Loes score stabilized or improved in 7/13 patients by 12 months post-SCT, one patient who is only 5 months post-SCT had stable disease, and 5 had progressive disease. Among those with progressive disease, 2 succumbed at 1 and 3 years post-SCT respectively, while 3 of them stabilised with no further progression after 3-4 years of transplant. At a median follow up of 22 months (range:5-173) post-SCT, the overall and event-free survival were 84.6% and 44.4% respectively.
Discussion and Conclusion: Allo SCT with myeloablative conditioning for patients with CLD can be safely performed without major transplant-related complications. Allo SCT is the only therapeutic approach that can arrest cerebral demyelination, and results in longterm good quality of life, provided the procedure is performed at an early stage of disease.

Disclosure of Interest: None Declared

Keywords: LEUKODYSTROPHIES, Pediatric, Stem Cell Transplant,

Poster Presentation

HEMOGLOBINOPATHIES, PRIMARY IMMUNE DEFICIENCY DISEASES AND METABOLIC DISORDERS. (419)

DKMS-BMST THALASSEMIA PROGRAM: IMPROVING SITUATION OF THALASSEMIA PATIENTS IN INDIAN SUBCONTINENT

Jothi K*[1], Nitin Agarwal[1]
[1]DKMS BMST, Bangalore, India

Aims & Objectives: DKMS BMST foundation India is able to fight against life-threatening blood diseases from many different angles by employing a wide range of programs and services. One among them is our Thalassemia Program with the following objectives:
1. To increase the collaboration with institutions engaged in the fight against thalassemia.
2. To support these Thalassemia Program Partners to increase the awareness about the option of HSCT as a permanent cure for Thalassemia amongst Thalassemia patient families.
3. To provide access to free high-resolution HLA typing for patients and their related donors (siblings, parents).
4. To provide access to free searches for matched unrelated donors, in the absence of any matched related donors, for the patients without a matched related donor.

Patients / Materials & Methods: DKMS BMST has 11 transplant centers and 7 NGOs as our program partners. These partners work on ground with their sub partners and patient organizations to create awareness about the disease and educate them about the potential curative option as a stem cell transplantation within the related family members or with an unrelated donor from worldwide database. We at DKMS-BMST, train and support all these partners to create awareness and collect samples from poor patients in Indian subcontinent. We also provide access to free searches for finding an unrelated donor, in the absence of any matched related donors within the family.

Results: Since the inception of this program in 2018, 5493 plus Indian patients and their families have been benefited. Totally we have typed more than 9221 samples from 2018 to 2022 through our DKMS-BMST Thalassemia program. We consider the successful transplant as an impact of our program. Through our program, we are able to help 102 matched sibling transplant, 37 haploidentical transplants and 15 matched unrelated (MUD) transplants.

Discussion and Conclusion: India is the Thalassemia capital of the world, with the incidence of around 12,000 every year. The major challenge to access stem cell transplant is the associated costs, as most of the payment is out of pocket. The Indian Government supports the ongoing patient needs for their monthly blood transfusions, iron chelation medicines, however, these funds do not cover the costs of the high-resolution HLA typing, which is the start of the medical assessment for a HSCT. DKMS-BMST Thalassemia Program aims to facilitate the access to the potentially curative option of a stem cell transplant treatment for poor Thalassemia children in Indian subcontinent.

As we see from the results, DKMS-BMST thalassemia program has Increased the number of stem cell transplantations for poor patients in India and other neighboring countries. We hope to increase these numbers in future thus providing the second chance at life for more Thalassemia patients.

Disclosure of Interest: None Declared

Keywords: DKMS BMST, HLA, Thalassemia

Poster Presentation

HEMOGLOBINOPATHIES, PRIMARY IMMUNE DEFICIENCY DISEASES AND METABOLIC DISORDERS. (420)

MLASA-1: A RARE CAUSE OF SIDEROBLASTIC ANEMIA WITH MYOPATHY

Benazer Sait*[1], Aakash Chandran Chidambaram[1], Dinesh Babu R M[1], Krishnamoorthy Vidhyasagar[1], Joshua Xavier Rajan[1], Benjamin Sagayaraj[1]
[1]Paediatrics, Saveetha Institute of Medical and Technical Sciences, Chennai, India

Aims & Objectives: Myopathy, lactic acidosis, and sideroblastic anemia-1 (MLASA-1) is an ultra-rare mitochondrial disorder that involves skeletal muscle and erythrocytic cell-line of the bone marrow. It is characterised by mutations in PUS1 gene, with varying severity of presentation. Herein, we describe a 3 year old girl who presented with severe failure to thrive, cardiomyopathy, transfusion dependent anemia, myopathy and lactic acidosis.
Patients / Materials & Methods: A 3-year-old girl, born to non-consanguineous parents, was brought with complaints of pallor, failure to thrive and floppiness of all limbs noted since early infancy. Her perinatal history was uneventful. There was a significant family history in the form of early sibling deaths. Her developmental milestones were delayed in all domains. She was admitted twice in the past for anemia, requiring blood transfusions. Her anthropometric parameters revealed severe undernutrition (weight-7.8kg (< -3Z score); height-86cm (< -3 Z score) and microcephaly (43cm). General examination revealed severe pallor, mild facial dysmorphism in the form of frontal bossing, flat nasal bridge and high arched palate. Neurological examination revealed generalised wasting, hypotonia, muscle power of 4/5, exaggerated reflexes and flexor plantar response.
Results: The initial investigations revealed microcytic hypochromic anemia with increased serum lactate levels. Her serum iron and serum ferritin levels had improved on oral iron therapy but there was no concomitant increase in hemoglobin, arousing the suspicion of sideroblastic anemia. Echocardiography was suggestive of cardiomyopathy. Clinical exome sequencing revealed a novel homozygous missense variation in PUS1 gene suggestive of MLASA-1.
Discussion and Conclusion: MLASA is an ultra-rare genetic disease that manifests with sideroblastic anemia and myopathy. Knowledge about this disease will help clinicians in early diagnosis of the condition, that would aid in providing appropriate genetic counselling to the parents.

Disclosure of Interest: None Declared

Keywords: MLASA, MYOPATHY, SIDEROBLASTIC ANEMIA

Poster Presentation

BASIC SCIENCE (140)

PROVISION OF HEMATOPOIETIC BONE MARROW STEM CELL DONATIONS BY THE TZU CHI BONE MARROW DONOR REGISTRY

Kuo-Liang Yang*[1]
[1]Tzu Chi Stem Cells Centre and Department of Biotechnology, Hualien Tzu Chi Hospital and Tzu Chi University, Hualien, Taiwan, China

Aims & Objectives: The provision of bone marrow stem cell donations by Tzu Chi Stem Cells Centre at the time of COVID-19 pandemic.
The impact of global COVID-19 pandemic has taken a disastrous human toll so far. It has crippled many facets of our daily living and disabled confidence on world economy, security, and health. The pandemic has forced countries to isolate themselves within their own boundaries and stop transportations by land, sea, and air in and out of their countries except for humanitarian and certain diplomatic or other justified trade reasons. The enforced quarantines and restrictions hamper the transport of bone marrow stem cell donations to cross country boundaries and jeopardize transport of the life-saving gifts for blood diseased patients waiting for transplant therapies.
Patients / Materials & Methods: With cryopreservation method frozen hematopoietic stem cells are transported to domestic and international transplant centres to rescue patients' lives.
Results: Buddhist Tzu Chi Bone Marrow Donor Registry of Buddhist Tzu Chi Stem Cells Centre (BTCSCC) overcomes the many difficulties to successfully deliver bone marrow stem cell donations from Taiwan to patients being treated domestically and internationally continuously. BTCSCC employs cryopreservation protocol to deliver frozen bone marrow stem cell donations to international and domestic patients for timely transplant schedules. Extraordinarily, BTCSCC delivered a bone marrow stem cell donation to a patient in Singapore employing a charter flight plane to complete a smooth transferring of the stem cell donation in-transit fashion without border entrance of the flight crew and the courier personnel.
Discussion and Conclusion: Our experience on the success of case management to facilitate the delivery of bone marrow stem cell donations for patients under the stress of the COVID-19 pandemic circumstance will be shared in detail.

Disclosure of Interest: None Declared

Keywords: Blood diseases, COVID-19 pandemic, Cryopreservarion of bone marrow stem cells, Hematopoietic stem cells, Tzu Chi Marrow Donor Registry

Poster Presentation

BASIC SCIENCE (364)

BLOOD TYPE AND ANTIBODY SCREEN POST HSCT IN ABO INCOMPATIBLE TRANSPLANTS- WHAT'S THE MANDATE

Kalpana D. Velaskar*[1], RUCHIRA MISRA[2]
[1]TRANSFUSION MEDICINE, [2]BONE MARROW TRANSPLANT, NH SRCC CHILDREN'S HOSPITAL, MUMBAI, India

Aims & Objectives: To access blood group change and antibody detection post ABO mismatched hemopoietic stem cell transplant in varied pediatric diseases so as to establish a mandate for regular testing.
Patients / Materials & Methods: A total of 38 patients were screened for blood group and antibody using solid phase and column gel techniques.
-7 AML cases age: 2-11Yrs; one female 6 males; 6 haploidentical and 1 MUD transplant; 3 major mismatches and 4 minor mismatches.
-9 ALL cases age: 4-16Yrs; one female 8 males; 6 haploidentical , 2 MUD and 1 related full match transplant; 2 major mismatches and 7 minor mismatches.
-11 Thal Major cases age: 2-13Yrs; 3 females 8males; 6 haploidentical, 2 MUD and 3 related full match transplants; 7 major mismatches and 4 minor mismatches.
-11 other congenital diseases age: 3-9Yrs; 3 females 8 males; 6 haploidentical, 2MUD and 3 related full match transplants; 7 major mismatches and 4 minor mismatches. *(details in table below.)
Results: -AML: 3 major mismatches, one showed group change 195 days and other 2 showed no change, of the 4 minor mismatches one group shows change in 40 days and other 3 show no change.
-ALL: 2 major mismatches, group change in 77 and 88 days, however RhD was weak and no antibody was detected in the serum of other case, of the 7 minor mismatches group change was detected in 2 however no corresponding antibodies were detected in serum within 95 to 125 days.
-Thal Major: 7 major mismatches, group change was noted in 3 cases in 67 to 484 days, 4 cases of minor mismatches with group change only in 1 case.
-Others: 7 major mismatches, group change was noted in 2 cases with corresponding antibody and other 5 cases showed no change, of the 4 minor mismatches 2 cases showed group change but no corresponding antibodies.
Discussion and Conclusion: Blood group change and antibody detection post hemopoietic stem cell transplant is variable. Most survivors with prolonged hospital stay and regular follow-up for post transplant complications are tested and the change is noted. However those who succumb and those survivors who do well are not tested or documented. This analysis reveals that this detection is essential and a mandate should be established by common consensus.

Disclosure of Interest: K. Velaskar But No Conflict with: NONE, R. MISRA But No Conflict with: NONE

Keywords: antibody screen, Blood group,, post ABO incomatible hsct

Poster Presentation

BASIC SCIENCE (380)

ENHANCING STORAGE OF CANINE PLATELET CONCENTRATES USING SSP+ PLATELET ADDITIVE SOLUTIONS

Baranidharan G.R*[1], Paunas Kamlesh Joshi[1], Kavitha S[1], Mangala Gowri A[2]
[1]Veterinary Medicine, [2]Centralised Instrumentation Laboratory, Madras Veterinary College, chennai, India

Aims & Objectives: Severe thrombocytopenia (less than 25,000 cells/cmm)in dogs results from impaired thrombopoiesis, increased platelet destruction,consumption and sequestration of platelets with clinical signs of bleeding diatheses. Owing to the less conventional storage days of the platelets (5 days). an in vitro research was attempted during 2019-20 to study the extended storage time for SSP+ Platelet Additive Solutions (PAS) added Canine Platelet Concentrates (CPC) beyond five days at 22°C.
Patients / Materials & Methods: The study was conducted at the Animal Blood Bank facility at Madras Veterinary College and Teaching Hospital, TANUVAS, Chennai during the period 2020-21. CPC was prepared from eligible donor dogs (n = 6) as per standard protocols after proper client consents. The total amount of CPC was divided into four aliquots of 15 ml to which SSP+ was added at concentrations of 65%, 75% and 85% of the total final volume. The PSL markers and platelet indices were measured for the above parameters on days 1, 5, 9 and 13 during storage and were screened for contamination.
Results: There was statistically significant ($p < 0.05$) difference between the swirling observed in the control and 65% SSP+ PAS added CPC group and that the swirling quality of 65% SSP+ PAS added CPC was well maintained till day 9 (Table 1). The mean pH of the control CPC on day 5 was 7.28 ± 0.0384 which similar to that 9th day of 65% SSP+ PAS added CPC. (Table 2) The mean glucose in the control CPC (441 ± 5.19 mg/dl) was significantly high ($p < 0.01$) when compared to that of the SSP+ PAS added PC groups. Similarly, mean lactate concentrations evidenced a statistically significant difference ($p < 0.01$) between the control group and the SSP+ PAS added CPC group.
Discussion and Conclusion: The study of PSL markers in SSP+ added CPC concludes that 65% SSP+ PAS added CPC with 35% of plasma spill over was the ideal concentration to help maintain near ideal conditions for CPC storage with minimal deterioration in the quality and platelet viability. Further, ascertained by the retention of moderate swirling properties at day 9, maintenance of a constant pH,flatter curve of increase in lactate and decreased bicarbonate consumption during storage, the use of 65% PAS in CPCs was advantageous. The increased duration of storage of CPCs will help increase the availability of the CPCs for treatment of severe thrombocytopenia and various bleeding emergencies in a emergency and critical care set up. Addition of 65% SSP+ PAS to CPC evidenced increased shelf life up to 9 days at 22°C under agitation without significant deterioration in product quality.

Disclosure of Interest: None Declared

Keywords: Canines, clinical bleeing diathesis, Platelet Additive Solutions, Platelet Concentrates, severe thrombocytopenia

Poster Presentation

BASIC SCIENCE (399)

USE OF PEGYLATED GCSF FOR STEM CELL MOBILIZATION IN HEALTHY DONOR FOR ALLOGENIC STEM CELL TRANSPLANT

Rohan K. Tewani*[1], Pavan Kumar Boyella[1], Krishna Mohan MVT[1], Vijay Ram Reddy[2]
[1]Medical Oncology and Hematology, [2]Transfusion Medicine, Basavatarakam Indo American Cancer Hospital & Research Institute, Hyderabad, India

Aims & Objectives: To evaluate safety and efficacy of Pegylated Granulocyte colony stimulating factor in mobilizing stem cells of donors for allogenic stem cell transplant
Patients / Materials & Methods: We retrospectively evaluated data of 30 patients and their donors whose stem cells were collected during 2021 and 2022. All the donors were healthy and received subcutaneous 6mg of Pegylated Granulocyte Colony Stimulating factor and harvesting was done on day 5. In cases where yield was less than desired value, collection was attempted on Day 6 also.
Results: 90% of the donors achieved desired stem cell yield on Day 5 while remaining 10% required apheresis process on next day also. Failure rate was 0% on day 6. 28(93%) out of 30 donors had skeletal pain after Peg GCSF and was managed with NSAIDs. No severe adverse event was seen. None of the donors required plerixafor for stem cell mobilisation.
Discussion and Conclusion: 6mg of Pegylated GCSF was well tolerated and achieved optimal collection of CD34+ stem cells from all the donors. Skeletal pain is the most common symptom and is well manageable.

Disclosure of Interest: None Declared

Keywords: Allogenic stem cell transplant, GCSF, stem cell mobilization and apheresis

Poster Presentation

CELL AND GENE THERAPY (109)

CYTOKINE PROFILES OF CYTOKINE RELEASE SYNDROME DURING CAR-T CELL THERAPY

Linqin Wang[*1,2,3], Yuqi Lv[1,2,3], Linghui Zhou[1,2,3], Ruimin Hong[1,2,3], Mingming Zhang[1,2,3], Houli Zhao[1,2,3], Alex H. Chang[4,5], Yongxian Hu[1,2,3], He Huang[1,2,3]
[1]Bone Marrow Transplantation Center, The First Affiliated Hospital, School of Medicine, Zhejiang University, [2]Institute of Hematology, Zhejiang University, [3]Liangzhu Laboratory, Zhejiang University Medical Center, Hangzhou, [4]Tongji University, [5]Shanghai YaKe Biotechnology Ltd., Shanghai, China

Aims & Objectives: Chimeric antigen receptor (CAR) engineered T cell therapy has revolutionized the efficacy and prognosis of relapsed or refractory B-cell hematological malignancies. Whereas, cytokine release syndrome (CRS), the most common toxicity after CAR-T cell infusion, remains to be an unsolved problem which poses potential threat for patients. Therefore, in clinical practice, it's necessary to find out indicative biomarkers for the early warning of severe or durable CRS.
Patients / Materials & Methods: In this study, 85 patients with relapsed or refractory hematological malignancies from four clinical trials were integrated, including 72 patients on BCMA CAR-T therapy (ChiCTR1800017404), 8 on CD19 CAR-T therapy (ChiCTR-ORN-16008948), 2 on CD22 CAR-T therapy (ChiCTR1800017402), and 3 on CD19/CD22 CAR-T therapy (ChiCTR1800015575). The CRS grade was assessed according to a revised grading system, and grade 3-4 CRS was recognized as severe. Besides, temporal profiles of CRS were assessed according to the clinical symptoms and signs. We defined "CRS occured within 2 (≤2) days" as "early-onset CRS" , and "CRS persisted longer than 1 (≥1) week" as "prolonged CRS". Blood were collected from patients around the timepoint of CRS peak. And forty-five serum cytokines were analyzed via Luminex platform. Levels of cytokines were log-transformed, and continuous variables were analyzed using the Mann-Whitney U test.
Results: A total of 85 patients receiving CAR-T cell therapy between January, 2017 and September, 2021, were reviewed. Among them, 15.29% (13/85) were diagnosed with acute lymphoblastic leukemia, and 84.71% (72/85) suffered from multiple myeloma. All of them developed CRS with varying degrees. CRS mostly occurred with a median of 2 days (range, 0-17 days) after CAR-T cell infusion, and the median duration was 7 days (range, 1-37 days). Moreover, 56.47% (48/85) developed early-onset CRS, 62.35% (53/85) developed prolonged CRS, and 55.29% (47/85) developed severe CRS. It is noteworthy that CRS profile of 23 patients (27.06%) was early-onset, prolonged and severe. Furthermore, we dissected the differential serum cytokines among patients with different CRS profiles, and found 35 differential serum cytokines during CRS peak (Figure 1). Of note, there were several overlaps of differential cytokines among three groups (Table 1). Cytokines, including CCL20, CXCL1, and IL-8, were common biomarkers that significantly elevated among those who developed early-onset, prolonged or severe CRS.
Discussion and Conclusion: Serum cytokines are useful and accessible biomarkers correlated with the severity and temporal characteristics of CRS. Our research provided a clue for constructing clinical models to predict the severity and temporal features of CRS, which would contribute to the optimized clinical management of toxicities after CAR-T cell therapy.

Disclosure of Interest: None Declared

Keywords: CAR-T cell therapy, cytokine profiles, cytokine release syndrome

Poster Presentation

CELL AND GENE THERAPY (130)

CHARACTERIZATION OF TUMOR LYSIS SYNDROME IN MULTIPLE MYELOMA FOLLOWING BCMA CAR T-CELL THERAPY

Qiqi Zhang[*1,2,3], Cheng Zu[1,2,3], Youqin Feng[1,2,3], Yuqi Lv[1,2,3], Mingming Zhang[1,2,3], Yongxian Hu[1,2,3], He Huang[1,2,3]
[1]Bone Marrow Transplantation Center, the First Affiliated Hospital, Zhejiang University School of Medicine, [2]Liangzhu Laboratory, Zhejiang University Medical Center, [3]Institute of Hematology, Zhejiang University, Hangzhou, China

Aims & Objectives: Chimeric antigen receptor (CAR) T-cell therapy has revolutionized the field of cancer treatment. B-cell maturation antigen (BCMA) targeted CAR T-cell therapy has shown remarkable efficacy and safety in chemotherapy refractory or relapsed (R/R) multiple myeloma (MM) patients. But toxicities following CAR-T therapy remain major challenges for its clinical application. Tumor lysis syndrome (TLS), a life-threatening complication, has been reported in patients administered with CD19 targeted CAR-T cells. However, a comprehensive characterization of BCMA CAR-T cell therapy associated TLS in relapsed/refractory multiple myeloma (R/R MM) is lacking.
Herein we report the incidence, characteristics and clinical outcomes of TLS in R/R MM following BCMA CAR-T cell therapy.
Patients / Materials & Methods: This is a retrospective, single-institution analysis of R/R MM patients treated with BCMA CAR T-cell therapy at our center from July 2018 to December 2021 (n=99). Patients' characteristics, laboratory parameters, and clinical data were obtained from medical record. TLS was identified based on a constellation of laboratory parameters and clinical manifestations per Howard criteria. CRS was graded per Lee criteria. Univariate analysis and multivariate logistic regression were performed to evaluate the risk factors of TLS following BCMA CAR T-cell therapy.
Results: Among the 99 patients, 17 (17.2%) cases of TLS were noted. Median onset of TLS was 8 days (range, 4-14), lagging behind the onset of cytokine release syndrome (CRS). Most common TLS-related symptoms were renal dysfunction and arrhythmia. The median overall survival (OS) was poorer in TLS patients (median: 194 days in TLS group vs 1194 days in non-TLS group, $p<0.01$, HR=3.8 [95% CI 1.3-11.1]) (Figure 1A). The development of TLS exhibited no significant effect on progression-free survival (median: 215 days in TLS group vs 434 days in non-TLS group, $p>0.05$) (Figure 1B). Univariate analysis revealed higher levels of baseline uric acid, serum creatinine and max CRS grade were associated with TLS (Table 1). Another intriguing finding is that max CRS grade and cytokine profile of TLS patients were distinguished from non-TLS patients. The peak levels of IL-6, IL-10, IFN-γ and ferritin were significantly higher in TLS patients ($P<0.05$) (Figure 2). Multivariate logistic regression demonstrated baseline creatinine (OR=1.015, $P<0.01$) and CRS grade (OR=9.371, $P<0.01$) as risk factors.
Discussion and Conclusion: Our results indicated R/R MM patients undergoing BCMA CAR T-cell therapy had relatively high incidence of TLS. TLS significantly affected the overall survival of patients. Elevated level of serum creatinine and severe CRS were independent risk factors. These results provided a new insight of toxicities related with CAR T-cell therapy.

Disclosure of Interest: None Declared

Keywords: Chimeric antigen T cell, Multiple myeloma, Tumor lysis syndrome

Poster Presentation

CELL AND GENE THERAPY (166)

PROMISING OUTCOME WITH 3RD-GENERATION CART-CELL TARGETING BCMA FOR REL/REF MULTIPLE MYELOMA

Kannadit Prayongratana[*1], Rong He[2], Tanapun Thamgrang[1], Dollapak Apipongrat[1], Pornpavee Siricharoenthai[1], Pornpavee Siricharoenthai[1], Warunporn Maneechote[1], Panachai Silpsamrit[1], Piyarat Pimsi[3], Apichai Leelasiri[1], Wichean Mongkonsritragoon[4]
[1]Department of Medicine, Phramongkutklao Hospital, Bangkok, Thailand, [2]Swiss R&D Laboratory, Baar, Switzerland, [3]Silapakorn University, Nakhon Pathom, [4]Horizon Cancer Center, Bumrungrad International Hospital, Bangkok, Thailand

Aims & Objectives: To express the efficacy and safety of 3rd generation Chimeric antigen receptor (CAR)T cell targeting B cell maturation antigen (BCMA) in patients with heavily pre-treated multiple myeloma (MM).
Patients / Materials & Methods: Study design: Retrospective pilot study.
Patients and methods: Patients with relapsed/refractory MM were enrolled to this cohort. Third generation CART cell targeting BCMA engineered by lentivirus vector were used as the salvage treatment for these patients with a target dose of 5 x 10^6 cells/kg. Fludarabine and cyclophosphamide were used as a lymphodepletion regimen. Cytokine level (IL6, IFN-gamma) was measured by ELISA. In addition, if patient develop symptoms indicated severe CRS, cytokine levels were also measured. Tocilizumab was given for Gr>2 CRS or significant cytokine increased. Monoclonal(M) protein was measured to monitor response and bone marrow study was done when M-protein was unmeasurable.
Results: From Jan-Sep 2020 (with limitation by COVID-19 pandemic, the enrollment was held) 5 pts were included with a median age of 58 years old (range;37-61). Median prior lines of treatment were 6 (range;4-7). Median percentage of plasma cell before CART-cell therapy was 30% (range;2-70). Four patients had high-risk cytogenetics. Median BCMA expression was 16.1% (range;2.7-30.6). All of them priorly underwent autologous stem cell transplantation with a median 21 months (12-77) prior to CART cell therapy. Four of them (80%) respond to CART, of these 3 achieved stringent complete response (60%). With median follow up duration of 24 months, median overall survival was 24 months, 2-year overall survival was 60%, and 2-yr progression-free survival was 60%. (Fig 1,2). Regarding safety profile, CRS occurred in all patients; none of them developed > Gr2 CRS or required tocilizumab treatment. Neutropenia occurred in all patients with >Gr 2 of 80%. Neutropenia with infection happened in 3 patients but none of them had >Gr2 febrile neutropenia.
Discussion and Conclusion: BCMA CART cell therapy was effective in treatment of patients with heavily pretreated relapsed/refractory MM.

Disclosure of Interest: None Declared

Keywords: B cell maturation Antigen, chimeric antigen receptor T cell, cytokine release syndrome, Multiple myeloma

Poster Presentation

CELL AND GENE THERAPY (177)

REAL-WORLD DATA OF TISAGENLECLEUCEL FOR TREATMENT OF AGGRESSIVE LYMPHOMA IN HONG KONG CHINESE

Thomas S. Y. Chan*[1], Yok Lam Kwong[1], Garret M. K. Leung[1], Eric W. Tse[1]
[1]Medicine, Queen Mary Hospital, Hong Kong, Hong Kong, China

Aims & Objectives: Tisagenlecleucel (Tisa-cel) is a CD19-chimeric receptor T cell (CAR-T cell) therapy that is approved for the treatment of relapsed/refractory large B-cell lymphoma. In the JULIET trial that led to its approval, the best overall response rate was 52% with approximately 35% of patients achieving long-term disease control. Real-world data continues to emerge, showing similar results to the trial in terms of efficacy and toxicity. Data from Asian countries, particularly Chinese, is scarce. In Hong Kong, Tisa-cel is provided to suitable patients under government subsidy since 2021. Here we analyze the results of our patients who received Tisa-cel at Queen Mary Hospital, the only public hospital currently providing adult CAR-T service in Hong Kong.
Patients / Materials & Methods: Retrospective analysis of all consecutive patients who received Tisa-cel since the introduction of the government subsidy program in May 2021 was performed. Baseline data were collected. Details on the CAR-T cell treatment were also recorded. Data cut-off was on May 30, 2022. Responses were evaluated using Lugano 2014 criteria. Statistical analysis performed included chi-square for independence and logistic-regression analysis for binary outcome. Survival analyses were performed using Kaplan-Meier method.
Results: There were 21 patients accepted into the CAR-T program. One patient passed away before apheresis because of rapid disease progression. Data on the 20 patients who underwent apheresis are summarized in table 1. Out of these 20 patients, two patients passed away before CAR-T infusion because of disease progression (n=1) and sepsis (n=1). Manufacturing of CAR-T cells were still on-going for two patients. There were no manufacturing failures or out-of-specification products. Sixteen patients received CAR-T infusion. Results for one-month PET-CT assessment (number of evaluable patients: 14): CR: n=5(35.7%), PR: n=4 (28.6%), NR/PD: n=5 (35.7%), three-month PET-CT assessment (number of evaluable patients: 13): CR: n=4 (30.7%), PR: n=2 (15.4%), NR/PD: n=7 (53.8%). Cytokine release syndrome (CRS) occurred in 12 patients (75%), and grade 3 or above CRS occurred in 6 patients (38%). Immune-effector cell-associated neurotoxicity syndrome (ICANS) occurred in one patient (6%, grade 1). The median duration of follow-up is 4.5 months. Progression-free survival and overall survival of 16 patients who received Tisa-cel infusion were presented in figure 1. The median PFS is 3 months and OS is not reached.
Discussion and Conclusion: To the best of our knowledge, this is the first report of real-world data on Tisa-cel in Chinese patients. Our results show similar efficacy when compared with the pivotal trial and registry data. A major limitation of this study is the short duration of follow-up and the small number of patients.

Disclosure of Interest: None Declared

Keywords: CAR-T, Chinese, Lymphoma, Real-world, Tisagenlecleucel

Poster Presentation

CELL AND GENE THERAPY (178)

A MODEL FOR LOW, MIDDLE INCOME COUNTRIES FOR IMPROVING ACCESS TO SCT: EXPERIENCE FROM 10 SCT CENTERS

Sachin Jadhav[*1], Sonu Tony[1], Raj Badavath[1], Aswathy Sajith[1], Ayon Sett[1]
[1]HealthCare Global, Bengaluru, India

Aims & Objectives: Availability of clinical programs for stem cell transplantation (SCT) in low- and middle-income countries (LMIC) is sub-optimal. We have created a model for improving access to Stem Cell Transplantation (SCT) in LMIC, with acceptable clinical outcomes.
Patients / Materials & Methods: A methodology for creating SCT programs in LMIC was created and is being implemented for over the last one decade. This analysis is about the processes, strategies and the core requirements which were required to build new SCT programs within existing hospitals, with restricted resources in LMICs. The outcomes of stem cell transplantation in these Centers are also reported.
Results: Between February 2013 and October 2021, 10 SCT programs were created, out of which 10 (91%) were in India and 1 (9 %) was in Dar es Salaam (Tanzania). A total of 145 patients underwent SCT which consisted of 85 (58.6%) autologous SCTs, an average of 7.73 per hospital, and 60 (41.4%) allogeneic SCT, with an average of 3.76 per hospital. At last follow-up 105 (72.41%) patients were alive.
Discussion and Conclusion: Multiple SCT programs can be created in LMIC with ample opportunities to improvise the technique to make it more accessible and also chieve acceptable clinical outcomes.

Disclosure of Interest: None Declared

Keywords: LMIC, low and middle-income countries, stem cell transplantation

Poster Presentation

CELL AND GENE THERAPY (193)

TRENDS IN SURVIVAL AND LATE MORTALITY AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

Linnan Wu[*1,2,3], Yibo Wu[1,2,3], Jimin Shi[1,2,3], Yanmin Zhao[1,2,3], Xiaoyu Lai[1,2,3], Weiyan Zheng[1,2,3], Yamin Tan[1,2,3], Yongxian Hu[1,2,3], Lizhen Liu[1,2,3], Jian Yu[1,2,3], Wenjun Wu[1,2,3], Yuanyuan Zhu[1,2,3], Luxin Yang[1,2,3], Panpan Zhu[1,2,3], He Huang[1,2,3], Yi Luo[1,2,3]
[1]Bone Marrow Transplantation Center, the First Affiliated Hospital, Zhejiang University School of Medicine, [2]Liangzhu Laboratory, Zhejiang University Medical Center, [3]Institute of Hematology, Zhejiang University, Hangzhou, China

Aims & Objectives: Most events after allogeneic hematopoietic stem cell transplantation (allo-HSCT) occur within the first 2 years, whereas the outcomes of long-term survivor populations who survived at least 2 years post HSCT without relapse are not clear. To explore whether trends in life expectancy have improved in contemporary HSCT survivor generation and assess main death-specific factors.
Patients / Materials & Methods: We analyzed the records of consecutive patients receiving allo-HSCT for hematologic malignancies from 2007 to 2019 in our center, who were alive in remission for the first two years. Characteristics and parameters of patients were provided by our institutional database.
Results: A cohort of 834 patients over a 14-year period met the criteria with a donor graft including haploidentical related donor (HRD) 61%, matched sibling donor (MSD) 22%, and unrelated donor (URD) 17%. The estimated overall survival (OS), disease-free survival (DFS) and chronic graft-versus-host disease-relapse-free survival (CRFS) at 10 years were 92%, 88% and 78%, respectively. The major risk factors for late mortality included prior grade III-IV acute GVHD ($P = 0.004$) and severe chronic GVHD ($P < 0.001$). The cumulative incidence of late relapse continued to increase and reached 8.6% at 10 years, which was influenced by high/very high disease risk index (DRI) ($P = 0.002$) and prior grade III-IV acute GVHD ($P = 0.038$). The incidence of non-relapse mortality was 3.6%, which was associated with the occurrence of severe chronic GVHD ($P < 0.001$). The three most common causes of late mortality were disease relapse (49%), chronic GVHD (28%) and infections (13%).
Discussion and Conclusion: The projected long-term survival of 2-year survivors following allo-HSCT is excellent, even though some patients remain at high risk of late relapse or death. Strategies should be taken to minimize the late death-specific hazards of transplant recipients and improve the quality and quantity of life.

Disclosure of Interest: None Declared

Keywords: Allogeneic Hematopoietic Stem Cell Transplantation, Hematologic malignancy, Late Mortality, Long-term Survival

Poster Presentation

CELL AND GENE THERAPY (200)

HBV REACTIVATION IN PATIENTS WITH CHRONIC OR RESOLVED HBV INFECTION AFTER BCMA-CAR-T CELL THERAPY

Cheng Zu[* 1, 2, 3], Fang Ni[1, 2, 3], Qiqi Zhang[1, 2, 3], Mingming Zhang[1, 2, 3], Guoqing Wei[1, 2, 3], He Huang[1, 2, 3], Yongxian Hu[1, 3, 4]
[1]Bone Marrow Transplantation Center, the First Affiliated Hospital, Zhejiang University School of Medicine, [2]Liangzhu Laboratory, Zhejiang University Medical Center, 1369 West Wenyi Road, Hangzhou 311121, China, [3]Institute of Hematology, Zhejiang University , [4]Liangzhu Laboratory, Zhejiang University Medical Center, Hangzhou, China

Aims & Objectives: CAR-T therapy has changed the treatment paradigm of relapsed/refractory (R/R) multiple myeloma (MM), resulting in CR rates of 33~86%. Hepatitis B virus (HBV) reactivation is a well-recognized complication in patients exposed to chemotherapy and/or immunotherapy, and may exert negative effects on clinical outcomes. Occasional cases of HBV reactivation have been reported in patients receiving CAR-T cells, mostly in the setting of CD19 CAR-T therapy. Herein, we performed a post-hoc analysis of R/R MM patients who received BCMA CAR-T in our center, aimed to explore the risk of HBV reactivation in patients with resolved or chronic HBV infection.
Patients / Materials & Methods: We reviewed the status of HBV infection in R/R MM patients treated with BCMA CAR-T cells at our center from Jul. 2018 to Dec. 2021 (n = 99). Pre-treatment serological HBsAg+ identifies patients with chronic HBV infection, pre-treatment serological HBsAg-HBcAb+ identify patients with resolved HBV infection, and the rest are considered HBV-uninfected. Following conditions are considered reactivation of HBV: 1) a ≥ 10-fold increase in HBV DNA in patients with detectable HBV DNA at baseline; 2) detection of HBV DNA in patients with undetectable HBV DNA at baseline; 3) reverse seroconversion from HBsAg- to HBsAg+.
Results: 7 (7.07%) patients had chronic HBV infection, and 43 (43.43%) patients had resolved HBV infection. All 7 patients with chronic HBV infection received entecavir or tenofovir throughout the course of treatment and follow-up. A total of 4 patients experienced HBV reactivation, 3 with resolved HBV infection at 103, 285, and 119 days after infusion, respectively, and 1 with chronic HBV infection at 31 days. (Figure 1) Of interest, a patient negative for HBV-related antigens, antibodies and HBV DNA developed HBV infection 11 months after infusion. Serum HBsAb were negative in all 4 patients, and one was under entecavir administration when HBV reactivated. Serum IgG experienced a drop around the date of HBV reactivation in patient 48, 60, and 94. (Figure 2A) Our analysis showed that liver function (peak ALT, AST, TB) after CAR-T therapy didn't differ among patients with different status of HBV infection. (Figure 2B) Patients with HBV reactivation achieved 2 CR and 2 SD, compared to an overall response rate (ORR) of 95.79% (CR rate: 55.79%) in the whole cohort. (Table 1) Also, chronic or resolved HBV infection had no impact on the levels of IL-6, IFN-γ, and CRP. (Figure 2C)
Discussion and Conclusion: Taken together, these results indicates that this population are at risk of HBV reactivation, but chronic or resolved HBV infection may not be considered a contraindication against BCMA CAR-T since the safety and efficacy were not affected. Close monitoring of HBV serology and DNA during follow-up is required, especially in those who are HBsAb-.

Disclosure of Interest: None Declared

Keywords: CAR-T cell therapy, HBV, Multiple myeloma

Poster Presentation

CELL AND GENE THERAPY (248)

ESTABLISHMENT & VALIDATION OF IN-HOUSE QUALITY CONTROL ASSAYS FOR GM/NGM IMMUNOTHERAPEUTIC PRODUCTS

Albeena Nisar*[1], Gaurav Narula[1], Khushali P. Pandit[1], Deepali Pandit[2]
[1]Medical Oncology, [2]BSBW, tata memorial hosital, Mumbai, India

Aims & Objectives: The Cell Therapy Product Development for various targets and malignancies is emerging successfully worldwide, and more specifically in LMICs like India, an increasing number of investigational new drug applications (INDs) for CAR-T cell products and other non-genetically modified cell therapy products (CTPs) are expected in the coming years. The manufacturing processes for each CTP is complex and the Quality Control testing is critical to ensure safety and effectiveness. Most academic & commercial centres face serious challenges of a single Quality control unit for handling the complete spectrum of QC testing for all products.
Our aim was to develop and optimize in-house centralized quality control of all Cell Therapy products (GM/NGMs) encompassing Process & Product development at a centralized cGMP facility in an academic centre.
Patients / Materials & Methods: The Cell Therapy Product Development for various targets and malignancies is emerging successfully worldwide, and more specifically in LMICs like India, an increasing number of investigational new drug applications (INDs) for CAR-T cell products and other non-genetically modified cell therapy products (CTPs) are expected in the coming years. The manufacturing processes for each CTP is complex and the Quality Control testing is critical to ensure safety and effectiveness. Most academic & commercial centres face serious challenges of a single Quality control unit for handling the complete spectrum of QC testing for all products.
Our aim was to develop and optimize in-house centralized quality control of all Cell Therapy products (GM/NGMs) encompassing Process & Product development at a centralized cGMP facility in an academic centre
Results: For sterility, Endotoxin testing, two different systems, used LAL Chromogenic Endotoxin Quantitation and Endosafe® nexgen-PTS™ Endotoxin Testing, allowed for detection of endotoxin in low and high of detection range tailoring to different CTPs. VSVG PCR , Mycoplasma PCR and adventitious Viral testing was optimized using customized primer and assays. The multiplex PCR testing facilitated to test different CTPs in base line, in process and end point time points thereby making it time efficient. The identity of all CTPs is tested for customized panel of multi-parametric cell surface markers formed by FACS which demonstrated a correlation between T Cell Phenotypes and Expansion efficacy. For efficacy, cytoxicity testing using a wide panel of cell lines like NAML, K652, B-ALL Specific Cell lines and cytokines estimations of multiple cytokines, IL-6, IL-2, INFy , TNF, IL-15 has been optimized. The use of multiple cell line panel and estimation using multiplex kits for cytokines helped to estimate cytokines in different products at low cost. In addition, some QC tests, were tailored as per CTP type. For CAR T , the impact of two variables, multiplicity of infection and centrifugation, on transduction efficiency and copy number was also examined as a part of efficacy testing. Using FACS and a ddPCR assay, it was demonstrated that transduction efficiency and copy number increased as multiplicity of infection (MOI) – the virus:cell ratio – increased, and the low copy numbers observed at the lower range of MOIs increased with high-speed centrifugation. These are new novel additions to the efficacy testing of CAR T Cell products in particular.
Discussion and Conclusion: The QC testing Unit at CTCTC and the novel CTP tailored workflow will be a one stop solution for the QC testing of all academic & commercial centres. Our data demonstrates the capacity to perform concurrent QC testing for multiple CTPs Product for all end points including Non-clinical research (R & D), Product Development and Clinical Trials.

Disclosure of Interest: None Declared

Keywords: Cellular cancer immunotherapy, Chimeric antigen receptor (CAR) T-cells;, Multiparametric flow cytometry-based assay, Mutiplex PCR testing, Quality control

Poster Presentation

CELL AND GENE THERAPY (249)

COMPARATIVE EFFICACIES OF POINT OF CARE ENDOTOXIN ASSAYS FOR QUALITY CONTROL OF CAR T CELL PRODUCTS.

Albeena Nisar*[1], Gaurav Narula[1], Khushali P. Pandit[1], Shailender Gugalavath[1]
[1]Medical Oncology, tata memorial hosital, Mumbai, India

Aims & Objectives: Aim: To study the comparative efficacies of Endotoxin assays for Quality Control of CTPs.
Endotoxin from a part of lipopolysaccharide complex of outer membrane of gram negative bacteria released during the lysis of microbes or cell divisions during the development of CTPs. An essential part of Quality Control and Quality Assurance involves in testing of the end products. Therefore the testing of endotoxin become the standard test for release of the end product with maximum acceptable level ofendotoxin in these products is usually 5.0 EU/kg/dose. However, there are various kits based methods developed to study the efficacy level of the products with respect to the time sensitive, labor intensive CTPs. Here we studied the comparative efficacies of the commercially available kits.
Patients / Materials & Methods: Herein we compared the level of endotoxin using two different commercially available kits i.e. Endosafe System of Charles River and Pierce™ Chromogenic Endotoxin Quant Kit of Invitrogen. CTPs samples were collected at end manufacturedCTPs and assessed immediately for the Endotoxin levels. Endosafe systems uses Endosafe nexgen-PTS which is rapid, point of use handheld spectrophotometer that uses USP/BET-compliant disposable cartridges for accurate, convenient, and real-time endotoxin testing, glucan concentration determination, and Gram identification. Whereas, the Thermo Scientific Pierce™ Chromogenic Endotoxin Quant Kit is an efficientquantitative endpoint assay. We Investigated levels of endotoxin as per the manufacturers protocol and the assay accuracy and precision of Pierce™ Chromogenic Endotoxin and Endosafenexgen-PTS was determined between both assays.
Results: Endotoxin levels of sample was 0.016 EU/ml for Pierce™ Chromogenic Endotoxin Quant Kit and 2.50 EU/ml for Endosafe nexgen-PTS. Pierce™. Chromogenic Endotoxin Quant Kits displayed relative standard deviation (RSD) of 0.51% with error of 0.69% whereas Endosafe nexgen-PTS was with 3.17% RSD and 1.93% error.
Discussion and Conclusion: The study finding suggests that endotoxin levels studied by Pierce™ Chromogenic Endotoxin Quant Kit showed greater accuracy and precision compared to Endosafe nexgen-PTS. Pierce™ Chromogenic Endotoxin Quant Kit providedreliable results with CTPs typically produced in cell therapy manufacturing facilities, and would be an appropriate test. However, Endosafe nexgen-PTS system are found to be faster and easily executed but don't thrive with results.

Disclosure of Interest: None Declared

Keywords: CART Cell Therpay, Cell Therapy, Endotixin testing

Poster Presentation

CELL AND GENE THERAPY (251)

OPTIMIZATION OF AUTOLOGOUS LEUKAPHERESIS PROCEDURES FOR CAR T-CELL MANUFACTURING

Minal Poojary[*1], Shashank Ojha[1], Sumathi Hiregoudar[1], Hasmukh Jain[2], Rahul Purwar[3], Deepali Pandit[4], Albeena Nisar[4], Atharva Karulkar[5], Afrin Rafiq[5], Ankesh Jaiswal[5], Sweety Asija[5], Prashant Tembhare[6], P. G. Subramaniam[6], Anant Gokarn[7], Sachin Punatar[7], Akansha Chichra[7], Sumeet Mirgh[7], Nishant Jindal[7], Nikhil Patkar[6], Sumeet Gujral[6], Nirmalya Moulik[2], Bhausaheb Bagal[2], Manju Sengar[2], Shilpushp Bhosale[2], Jayshree Thorat[2], Lingaraj Nayak[2], Neha Sharma[8], Subhash Yadav[9], Shripad Banavali[10], Navin Khattry[11], Gaurav Narula[4]
[1]Transfusion Medicine, ACTREC, Kharghar, [2]Medical Oncology, TMH, Parel, [3]Bioengineering, IIT, Mumbai, [4]CAR T CELL THERAPY LAB, ACTREC, Kharghar, [5]Biosciences and Bioengineering department, IIT, Mumbai, [6]Hematopathology & Molecular hematology, [7]Medical Oncology, ACTREC, Kharghar, [8]Hematolymphoid, [9]Pathology, [10]Director Academics, TMH, Parel, [11]Deputy Director, ACTREC, Kharghar, India

Aims & Objectives: T lymphocyte collection by leukapheresis plays a substantial role in CAR (Chimeric antigen receptor) T cell manufacturing. However, heterogeneity in the cellular composition and timing of apheresis in heavily pre-treated patients makes it challenging. This study describes the optimization pattern associated with leukapheresis procedures for CAR T cell therapy in our tertiary care hemato-oncology centre.
Patients / Materials & Methods: We have analyzed a total of 16 unstimulated autologous leukapheresis procedures in 15 patients including 5 B-ALL pediatric patients and 10 DLBCL adult patients from May 2021 to April 2022. Descriptive statistics and frequencies were used for the data description.
Results: Adequate lymphocytes were harvested from all patients with median peripheral absolute lymphocyte counts of 878.8 (215-2451) cells/ µl. Only one patient required second consecutive leukapheresis session. All the leukapheresis procedures were performed on Fresenius COM.TECTM cell separator and the final products contained a median of 1.495 x 10^9 (0.47- 3.79 x 10^9) absolute lymphocytes with median collection efficiency (CE) of 13.825 % (4.12 %- 58.58 %). A median of 308 (253- 388) minutes and 3.84 (3.4- 5.01) number of times of total whole blood volume was processed to obtain adequate collection of lymphocytes. Only 2 pediatric patients required blood priming of apheresis circuit. An overall, 12 (75%) adverse events (AE) were observed in total 16 procedures which included citrate reactions in 10 (83.33%) and technical related AEs in 2 (16.66%) of procedures. All patients successfully donated and tolerated the leukapheresis procedures without any serious AE. Manufacturing of CAR T cell product was successful in all the products with Transduction Efficiency (TE) of 30-50%.
Discussion and Conclusion: Our study shows that optimal technical and procedural modification can facilitate collection of sufficient yield of lymphocytes for CAR T cell production and overcome the potential risks thereby, providing donor safety.

Disclosure of Interest: None Declared

Keywords: CAR T Cell therapy, Leukapheresis, lymphocyte apheresis

Poster Presentation

CELL AND GENE THERAPY (258)

RISK FACTORS FOR ACUTE KIDNEY INJURY AFTER BCMA CAR-T CELL THERAPY

Yuqi Lv*[1], Qiqi Zhang[1], Chen Zu[1], Yongxian Hu[1], He Huang[1]
[1]Bone Marrow Transplantation Center, the First Affiliated Hospital, Zhejiang University School of Medicine, Zhejiang, China

Aims & Objectives: Multiple myeloma (MM) is a malignant plasma cell disease, and nearly half of patients with MM are accompanied by proteinuria, tubular urine and renal insufficiency. Impaired renal function in MM patients is associated with poor prognosis and shorter survival. B cell maturation antigen (BCMA) chimeric antigen receptor (CAR) T therapy has shown an excellent therapeutic effect on patients with relapsed and/or refractory (RR) MM. However, CAR-T cell infusion, as an exposure factor for the development of acute kidney injury (AKI), may cause secondary damage to MM patients with fragile renal function. Hence, we aim to explore whether RRMM patients can withstand CAR-T treatment, and find out risk factors of AKI during BCMA CAR-T therapy.
Patients / Materials & Methods: The clinical data of 99 patients, with RRMM, who received BCMA CAR-T cell therapy in the First Affiliated Hospital of Zhejiang University from July 2018 to December 2021 was retrospectively analyzed. Autologous peripheral blood mononuclear cells were collected from patient within 1 month before CAR-T therapy. All patients were pretreated with fludarabine (30.0 mg/m2, -4~-2 days, a total of 3 days) + cyclophosphamide (500.0 mg/m2, -3~-2 days, a total of 2 days) chemotherapy regimen 2-4 days before CAR-T cell infusion. Dynamic changes of renal function before and after chemotherapy preconditioning and after CAR-T cell infusion were observed. Logistic regression was used to analyze the independent risk factors associated with the occurrence of AKI.
Results: Among 99 patients the AKI occurred in 25 cases with an incidence of 25.3%, and the median time was 8.0 (5.5,11.0) d. The AKI grade 1, 2 and 3 accounted for 8.0%, 12.0%, and 36.0%, respectively. Logistic regression analysis showed that serum creatinine (Scr) after chemotherapy preconditioning (OR=1.020, P<0.001), the grade of cytokine release syndrome (CRS) (OR=6.501, P<0.01) were independent risk factors for AKI during treatment. The area under the ROC curve (AUC) of Scr after chemotherapy preconditioning in predicting AKI was 0.80 (95%CI:0.694-0.904, P<0.001); using 83.0μmol/L as cut-off value, the sensitivity, specificity and Youden index of Scr were 72.0%, 80.8% and 0.528, respectively. The incidence of AKI in patients with CRS≥grade 3 was 39.1%, while that was 13.2% in patients with CRS<grade 3.
Discussion and Conclusion: AKI mostly occurred within 15.0 d after CAR-T cell infusion, causing transient severe renal damage. Patients with abnormal renal function after chemotherapy preconditioning should be alert to the occurrence of AKI and receive kidney-protecting treatment in a timely manner. During the BCMA CAR-T cell therapy, attention should be paid to the management of the CRS, in order to help patients to pass through the kidney damage periods smoothly.

Disclosure of Interest: None Declared

Keywords: B cell maturation antigen (BCMA), chimeric antigen receptor (CAR) T, Multiple myeloma (MM)

Poster Presentation

CELL AND GENE THERAPY (361)

HEMATOPOIETIC STEM CELL TRANSPLANTATION IN BANGLADESH : ACTIVITY AND OUTCOME UPDATE

Mafruha Akter*[1], Abu Jafar Mohammed Saleh[2], Col Mosleh Uddin[3], Col Md Mostafil Karim[3], Quazi Smita Haq[2], Mohiuddin Ahmed Khan[1]
[1]Hematology & BMT, Dhaka Medical College Hospital, [2]Hematology and Stem Cell Transplant, Evercare Hospital Dhaka, [3]Bone Marrow Transplant Center, Combined Military Hospital, Dhaka, Bangladesh

Aims & Objectives: HSCT is a potentially life saving curative modality of treatment that was first started in DMCH in Bangladesh in 2014. Since then it is growing in both public and private hospitals.
Patients / Materials & Methods: This is a multicenter retrospective study describing the demographics, activities and outcome of HSCT in Bangladesh. Data were collected from three eminent HSCT centres of Bangladesh, eg DMCH, Evercare hospitals and Combined Military Hospital(CMH) Dhaka and were analyzed.
Results: As of June 2022, total 163 HSCT have been done in three centers of Bangladesh as DMCH(52), Evercare hospital (62)and CMH Dhaka(49).
Mean age of all patients is 39.4 years(range 15-69 Y) and sex distribution is M:F 3:1. Total autologous transplants were 125(77%) for myeloma(52), Hodgkins lymphoma(27) ,non-Hodgkins lymphoma(39) and others(7). Total allogeneic transplants were 38(23%) for AML(23), ALL(6), other malignancy(03), Severe aplastic anemia (04) and thalassemia (02). Majority of allotransplants were matched sibling donor transplant (30/78%) from mostly male donor. Eight (08) haplo transplant were also done.
Conditioning chemo protocols that usually used are high dose melphalan for MM, BEAM(Carmustine, Etoposide, Ara-C and Melphalan) for lymphoma and Bu-Cy(Busulphan-Cyclophosphamide) based for acute leukemia. Some leukemia patients received total body irradiation(TBI), thiotepa and Fludarabine based conditioning chemotherapy. All centres use irradiated blood components as transfusion products to avoid transfusion associated GVHD.
As all centre used almost similar conditioning for particular disease, mean engraftment time in all centres were almost similar. Average time for neutrophil and platelet engraftment was 10-12 and 12-16 days post transplant respectively. Major early complications following transplant were neutropenic fever (>80%) and bacteraemia (25-30%) commonly with coagulase negative Staphylococcus, Pseudomonas sp, E. Coli and Klebsiella sp. Severe sepsis, pneumonia, typhlitis, CMV reactivation and hemorrhagic cystitis were in few cases. Acute GVHD was observed in almost all allogeneic transplanted patients. Mucositis, vomiting and diarrhoea were mild to moderate in most patients. Almost all patients required at least 1-3 red cell and platelet transfusion during the time waiting for engraftment. Progression free survival for all patients was variable in different centres (62% to 83%) since 2014. Transplant related mortality was 2% for auto and 5% for allogeneic transplant. Three early deaths were due to sepsis with COVID-19 infection in autologous transplant in pandemic period.
Discussion and Conclusion: Considering total population in Bangladesh, the number of transplant is very low and it needs to be grown more rapidly to provide maximum benefit.

Disclosure of Interest: None Declared

Keywords: AML, HSCT, TRM

Poster Presentation

ALLIED (NURSING, TECHNICAL ASPECTS SUCH AS GRAFT PROCESSING, CRYOPRESERVATION, ETC) (115)

NUTRITIONAL ASSESSMENT IN EARLY ALLOGENIC HEMATOPOIETIC STEM CELL TRANSPLANT PATIENTS

Pan Yang*[1], Yaya Song[2], Lu Lin[1], Xiuchen Jing[1], Yongqin Ge[3], Fang Tang[3], Ying Chen[3], Qin Li[3], Feng Wei[3], Yanqin Mao[3], Xiang Xu[3], Xiaming Zhu[3], Yin Lu[3]
[1]School of Nursing, Suzhou medical college of Soochow University, suzhou, [2]Shandong Province Qianfoshan Hospital, jinan, [3] Department of hematology, The First Affiliated Hospital of Soochow University, suzhou, China

Aims & Objectives: Our study aims to comprehensively assess nutrition status and malnutritional prevalence in early allogenic hematopoietic stem cell transplant patients.
Patients / Materials & Methods: This single-center, cross-sectional study included 171 patients within the 90 days post- transplantation (from September 2019 to April 2020). Data collected included demographic, 3 day 24-hour diet record, a Patient- Generated Subjective Global Assessment (PG-SGA) tool, laboratory tests, anthropometric indices, and body composition.
Results: One hundred and seventy-one patients with a mean age of 37.82±11.262 and a male to female ratio of 102 to 69 were included. According to PG-SGA,115(67.25%) indicated the critical need for nutritional intervention and symptom management (PG-SGA score>9). Forty-three (43.27%) of patients had experienced insufficient intakes of energy according to a 24-hour diet record. Our study found that 120(70.17%) patients had a body fat percentage and high triacylglycerol (64.91%). Reduced free fat mass index and low hand-grip strength were found in 133(77.78%) and 104(60.81%), respectively. The prevalence of malnutrition was 24.56% and the prevalence of sarcopenia was 13.45%.
Discussion and Conclusion: Although the prevalence was not high, this research has demonstrated a high risk of malnutrition and a lower muscle mass in early allo-HSCT. Furthermore, our study confirmed body composition assessment would be an excellent way to identify malnutrition precisely.

Disclosure of Interest: P. Yang But No Conflict with: No conflict of interest to disclose, Y. Song But No Conflict with: No conflict of interest to disclose, L. Lin But No Conflict with: No conflict of interest to disclose, X. Jing But No Conflict with: No conflict of interest to disclose, Y. Ge But No Conflict with: No conflict of interest to disclose, F. Tang But No Conflict with: No conflict of interest to disclose, Y. Chen But No Conflict with: No conflict of interest to disclose, Q. Li But No Conflict with: No conflict of interest to disclose, F. Wei But No Conflict with: No conflict of interest to disclose, Y. Mao But No Conflict with: No conflict of interest to disclose, X. Xu But No Conflict with: No conflict of interest to disclose, X. Zhu: None Declared, Y. Lu But No Conflict with: No conflict of interest to disclose

Keywords: Allogeneic hematopoietic stem cell transplantation, Body composition, Nutritional assessment, Nutritional status

Poster Presentation

ALLIED (NURSING, TECHNICAL ASPECTS SUCH AS GRAFT PROCESSING, CRYOPRESERVATION, ETC) (129)

NURSING EXPERIENCES OF CARING A HAPLO-IDENTICAL HSCT RECEIVER WITH GRAFT AND RESPIRATORY FAILURE

Shun-Ying Wang*[1], Wan-Yu Chen[1]
[1]Nursing department , NTUCC, Taipei City, Taiwan, China

Aims & Objectives: Hematopoietic stem cell transplantation has been a standard treatment for patients diagnosed with AML over the decades. With a high engraft rate, few physicians talked about what happened after graft failure. And how complicated the situation would be.
Patients / Materials & Methods: This patient had been diagnosed with AML about one year before receiving Haplo-identical hematopoietic stem cell transplantation. Under the DSA positive condition, she had MAC protocol plus plasma exchange, IVIG, and donor leukocyte before the BMSC and PBSC transfusion. Also, physicians prescribed intense immunosuppression after HSCT. By the 15th day after HSCT, the bone marrow test showed her transplantation had failed. She had been through tough days with continuing pancytopenia, hematuria, and pneumonia. She complained of shortness of breath and felt exhausted, for she could not even speak a complete sentence.
Results: Helping this lady and her family make intubation decisions in a short time seemed to be impossible at that time. Our nursing team urged the physician to hold a family conference. Since she was a Registered Nurse, she used to go outpatient and make all medical decisions by herself. Her family didn't realize how dangerous once graft failure would happen. The primary purpose was to help her family understand the risky situation she was in. They had to reach a consensus on whether she should receive intubation or not.
Discussion and Conclusion: Eventually, the lady wants to fight for herself and her mom again. She decided to receive intubation and strive for a second chance. Nevertheless, the consequences may be different than they expected. The family had gone through it together. By sharing the nursing experience, I hope we can learn more about the risk of Haplo-identical HSCT in DSA positive recipients and the more we need to discuss before starting transplantation.

Disclosure of Interest: None Declared

Keywords: Graft failure, haplo-identical, Nursing

Poster Presentation

ALLIED (NURSING, TECHNICAL ASPECTS SUCH AS GRAFT PROCESSING, CRYOPRESERVATION, ETC) (175)

CORRELATION IN PHYSICAL WELL-BEING AND LONGTERM SURVIVAL OF HEMATOPOIETIC STEM CELL TRANSPLANTATION

Yin Lu[*1], Tao You[1], Qin Ma[1], Weiquan Wang[1], Pan Yang[2], Liming Liu[1], Jianhong Fu[1], Xiaming Zhu[1]
[1]The First Affiliated Hospital of Soochow University, [2]School of Nursing, Suzhou medical college of Soochow University, Suzhou, China

Aims & Objectives: To explore the relationship between the state of Physical Well Being (PBW) in early stage of hematopoietic stem cell transplantation and their long-term survival.
Patients / Materials & Methods: Our study comprised 149 HSCT patients; their data were collected before transplantation and at 1, 3, 6, 12, 15, 36, and 60 months post-transplantation. The Functional Assessment of Cancer Therapy-Bone Marrow Transplant (FACT-BMT) questionnaire was used to assess Health related quality of life. We also evaluated the patients' demographic characteristic and the state of their survival.
Results: In the 149 cases, 5-years OS, PFS, NRM, and GRFS were 65%, 48%, 17%, and 36%. The trends of 5 years Health related quality of life are wavelike rising. According to latent class mixed model, 149 HSCT patients were divided into two groups depending on the PWB score trough 60 months of follow up period. Results showed the first class (Class 1) had a lower PBW score during the first 4 years after HSCT, whereas a gradual increasing trend was observed. In contrast, the second class (Class 2) maintained a higher and PBW level with a small slope during the follow up. Kaplan-Meier survival analysis showed that Class 1 had improved OS (70.9% vs. 52.9%, P=0.021), PFS (60.5% vs. 41.2%, P=0.039), and GRFS (35.1% vs. 29.3%, P=0.035) compared with Class 2.
Discussion and Conclusion: Patients maintaining a higher PBW score early after HSCT had improved survival compared to those with a lower initial PBW score. PBW score could be a useful predictor for long term prognosis of HSCT.

Disclosure of Interest: Y. Lu But No Conflict with: No conflict of interest to disclose, T. You But No Conflict with: No conflict of interest to disclose, Q. Ma But No Conflict with: No conflict of interest to disclose, W. Wang But No Conflict with: No conflict of interest to disclose, P. Yang But No Conflict with: No conflict of interest to disclose, L. Liu But No Conflict with: No conflict of interest to disclose, J. Fu But No Conflict with: No conflict of interest to disclose, X. Zhu But No Conflict with: No conflict of interest to disclose

Keywords: Correlation Analysis, Early Physical Well-being, Long-term Survival

Poster Presentation

ALLIED (NURSING, TECHNICAL ASPECTS SUCH AS GRAFT PROCESSING, CRYOPRESERVATION, ETC) (190)

NOVAL METHODOLOGY FOR ASSESSING NURSING COMPETENCY IN BMT UNIT

Aswathy Asokan*[1], Sachin S. Jadhav[1], Raj Badavath[1], Jemy A. Mathew[1]
[1]BMT, HCG Hospital, Bangalore, India

Aims & Objectives: To strategize nursing towards excellence
Patients / Materials & Methods: • Using Saville and Holdsworth Model (S&H), by in co-operating the recommendations of FACT committee and Assessment module of Oncology School of Nursing (US), an Occupational Personality Questionnaire (OPQ) is created to assess Knowledge, Skills and Attitude relevant to the performance of 18 BMT-Hematology nurses. The entire competency is classified into 3 levels based on over all scores.
Level :1: Threshold competency < 55
Level:2: Differentiating Competency 55-85
Level:3: Meta Competency > 85
■ Each level is sub classified into A B C for easy mapping for nurses in exact position/score.In all the 3 levels, the competency parameters are prepared, and distributed these parameters under Knowledge, Skills and Attitude clusters. Competency matrix is created based on S&H model using Repertoire method and devised evaluation forms for individual nurses. With the help of assessment Panel evaluation form for each nurse was discussed based on all the attributes across all levels and it took around 30-45 minutes for individual nurse. Primary data was collected. Evaluations, comparison and summary were made for analysis. Overall Competency Index of the department should be 85 points. It was only 59 points. A wide gap of 26 points. In many instances Knowledge and application of knowledge is also wanting. Some Nurses overall score show a downward trend as they increase in experience – denoting a Peters' Principle creeping in the system. A training deficiency is also seen
■ Following the assessment, the nurses underwent HSCT-Fellowship Training program for a duration of 8 months. Post fellowship program, nurses underwent competency assessment.
Results: Nurses reacted favorably to the fellowship training program and reported a significantly higher level of knowledge and competency in the next year competency assessment
Discussion and Conclusion: This methodology will be useful in creating a structured training plan and PIPE program (Personal Interpersonal Effectiveness Program for nurses. This can also be used as a career progression (from Level 1A to 3C) and job allocation and succession planning. Also, to assess and allocate salaries based on a composite of competency and years of experience. Impact of this can reflect in the quality of service to patients as well as the motivation to learn

Disclosure of Interest: None Declared

Keywords: Competency, Nursing excellence, Saville and Holdsworth Model

Poster Presentation

ALLIED (NURSING, TECHNICAL ASPECTS SUCH AS GRAFT PROCESSING, CRYOPRESERVATION, ETC) (192)

NURSING CARE FOR A CHILD AML PATIENT WHO RECEIVED CD33 CAR-T BRIDGING TO SECOND HSCT

Xiaoxia Wang[*1], Shasha Ji[1], Qishu Qin[1], Yanzhi Song[1]
[1]Gobroad Boren Hospital, Beijing, China

Aims & Objectives: Patients normally receive hematopoietic stem cell transplantation (HSCT) when all types of infections are treated. This case reports details of an acute myeloid leukemia (AML) patient who received a second HLA haploidentical HSCT in emergency with pulmonary infection, pleural effusion, post-CAR-T CRS, high fever and severe illness.
Patients / Materials & Methods: A severe 3-year-old female patient, weighing 12kg, presented with high fever, abdominal distension, jaundice and malaise on May 26th, 2021. Admitting diagnosis: AML relapse 10 months after HSCT; infections with sepsis; cardiac insufficiency; liver damage; grade 2 CRS 23 days after CD33-CAR-T infusion; and chronic GVHD. Condition treatment before 2nd HSCT began on May 28th with the regimen of VP-16/BU/FLU/ATG/MECCNU; PBSC was infused (B+ to B+, HLA 5/10 matched, mother to daughter) on June 7th; and MTX/CSA/Mycophenolate Sodium Enteric-coated Tablets were administered for prophylaxis of acute graft versus host disease (aGVHD). Nursing practice: Total environmental protection; HSCT nursing routine; serious illness management; pediatric care; close monitoring of vital signs to prevent septic shock; CRS care; GVHD care; special drug management; observation and nursing care of viscera function problems.
Results: High fever lasted until day -2. Diarrhea occurred at most 8 times per day during conditioning treatment. Blood pressure increased to 112/86 mmHg. Blood oxygen decreased to 88%. Heart rate raised to 173 beatsper minute. Blood culture and stool culture test indicated multidrug-resistant Enterococcus faecium. Patient's appearance showed facial flushing, edema on eyelid and limb which later aggravated to systemic edema and flushing. BNP significantly increased. Levels of cytokines and serum ferritin increased, and was corrected soon after. G0 phase of cell cycle lasted 24 days. No new infection sites detected. Pulmonary infections were well-controlled without progression. Oral and perianal mucosa stayed intact. There was moderate fever during the cellimplantation. On June 23rd (Day +16), patient left HSCT ward with white blood cells 2.64×109/L and neutrophils 1.49×109/L. By the time of 12-month follow-up in June 2022, the patient returned to a normal quality of life.
Discussion and Conclusion: The child patient received second HLA haploidentical HSCT in emergency with pulmonary infection, pleural effusion and post-CAR-T CRS. The patient's situation was extremely in danger of aggravate infection and organ failure after conditioning treatment, posing great challenges to medical staffs. As the development of medical technology, the medical protocol for leukemia becomes more complicated and no longer solely base on HSCT. Nurses at the HSCT division shall keep up with modern medical protocols to create miracles together with the physician team.

Disclosure of Interest: None Declared

Keywords: AML, Nursing Care, Second HSCT

Poster Presentation

ALLIED (NURSING, TECHNICAL ASPECTS SUCH AS GRAFT PROCESSING, CRYOPRESERVATION, ETC) (205)

AN AUDIT OF A GOVERNMENT HEALTH SCHEME IN IMPROVING ACCESS TO HSCT IN NON-AFFORDING PATIENTS

Rakesh Reddy Boya*[1], Chandrasekhar Bendi[2], Veni Prasanna Gedala[3], Praveena Voonna[1], Rajini Priya Yedla[1], Venkatesh Rongali[4], Srikanth Balduri[4], Jyothi Priyanka Viswanadhapalli[5], Murali Krishna Voonna[6]
[1]Medical Oncology, [2]Hematology, [3]Pathology and laboratory services, [4]Intensive care, [5]medical support service, [6]Surgical Oncology, Mahatma Gandhi Cancer Hospital and Research Institute, Visakhapatnam, India

Aims & Objectives: HSCT remains unaffordable to majority of patients who need it, due to the cost involved particularly in the low-middle income countries (LMIC). We aimed to study the utility of a Government-sponsored health scheme called Dr. Y.S.R. Arogyasree in enabling HSCT in non-affording patients in the state of Andhra Pradesh, India.
Patients / Materials & Methods: The study is conducted in the BMT unit of a tertiary care cancer centre over a period of two and a half years from January 2020 to June 2022. Data was taken for the cost incurred for undertaking the transplant, subsequent follow-up and treatment required. The scheme has a package cost system for different types of transplants. Autologous HSCT for multiple myeloma and pediatric conditions has a package cost of 650,000 rupees; for Lymphoma it is 900,000 rupees. For allogeneic HSCT for the pediatric age group (<15 years) the package cost is 1 million rupees and for adults, it is 1.1 million rupees. The package involves costs incurred in management from the time of admission until 8 weeks.
Results: A total of 59 cases were undertaken in the scheme in the period mentioned. The case distribution and the average costs incurred for taking up treatment are depicted in table 1. Cost for autologous HSCT is sufficient within the package limit for multiple myeloma and pediatric autologous transplant. For lymphoma, the package is adequate in 90% of cases. For allogeneic transplant, the cost incurred is adequate for the first 5 weeks of treatment on average. For Haploidentical transplant, the cost is adequate for first 4 weeks on average. GVHD is the most common cause of post discharge repeat admission, which couldn't be accommodated within the package cost.
Discussion and Conclusion: The government-sponsored health scheme Arogyasree is successfully utilized to undertake HSCT in non-affording patients needing this treatment in majority of scenarios of autologous HSCT. For allogeneic HSCT, though it could help in the first one month of treatment, subsequent admissions like GVHD management still remain an issue. This situation is even more apparent for Haploidentical transplant. Overall, it's a health scheme which has bridged the treatment gap in non-affording patients and improved access to cost-intensive treatments like HSCT in majority of situations.

Disclosure of Interest: None Declared

Keywords: ACCESS, LMIC, NON-AFFORDABILITY

Poster Presentation

ALLIED (NURSING, TECHNICAL ASPECTS SUCH AS GRAFT PROCESSING, CRYOPRESERVATION, ETC) (206)

UTILITY OF DOING A MID-CD34 IN EARLY STOPPAGE OF APHERESIS IN PATIENTS/DONORS IN A PBSCT PROCEDURE

Rakesh Reddy Boya[1], Veni Prasanna Gedala[*2], Praveena Voonna[1], Rajini Priya Yedla[1], Ashok Kumar Pangi[2], Tataji Vanamala[2], Murali Krishna Voonna[3], Chandrasekhar Bendi[4]
[1]Medical Oncology, [2]Pathology and laboratory services, [3]Surgical Oncology, [4]Hematology, Mahatma Gandhi Cancer Hospital and Research Institute, Visakhapatnam, India

Aims & Objectives: We aimed to study if doing a mid-CD34 count would help in early termination of the apheresis procedure without compromising on the final CD34+ stem cell yield. For patients who had a suboptimal collection in mid-CD34, we sought to see if extending procedure beyond Standard Volume Leukapheresis (SVL) is successful in getting adequate stem cell yield in a single session of apheresis.
Patients / Materials & Methods: Data of patients who underwent apheresis procedures between January 2020 and June 2022 in our BMT unit was analysed retrospectively. Mobilization regimen was G-CSF based, with plerixafor used as pre-emptive strategy by using day 4 PB-CD34 cut-off of 20 cells/µl. The apheresis machine used was Fresenius Kabi Com.Tec (v.04.03.08). The unit's criterion for standard volume leukapheresis (SVL) is processing of 2-3 times of total blood volume (TBV) for donors in an allogeneic transplant setting and 3-4 times of TBV for a patient in the case of autologous PBSCT. Mid harvest CD34 count is assessed after 1-1.5×TBV was processed in allogeneic PBSCT and 2×TBV in autologous PBSCT. Adequate CD34+ stem cell collection was defined as a count of 3 million cells/kg body weight of patients for autologous PBSCT; for matched sibling donor Allo-PBSCT its 4-6 million cells/kg body weight and for Haplo-identical allo-PBSCT its 8-10 million cells/kg body weight of patient. The strategy to do a mid-CD34 is deemed to be successful if the yield obtained is able to denote an expected adequate collection at double the volume it was checked at AND if the resultant stoppage is earlier than doing the total planned SVL. For patients, who had less than expected mid-cd34, procedure is extended beyond SVL to see if adequate stem cell yield can be collected for a maximum of 6 × TBV.
Results: A total of 102 apheresis procedures were done in the period, 58 of them for auto-PBSCT and 44 for allo-PBSCT. Mid-CD34 count enabled early stoppage in 42 of auto-PBSCT procedures (72.4%) and in 41 of allo-PBSCT (93%) procedures. For the 16 patients of auto-PBSCT which couldn't stopped early, extending procedure beyond SVL resulted in adequate yield in 13 patients in the first session itself; 1 patient had successful harvest on the 2nd day and the remaining 2 were truly poor mobilizers. For allo-PBSCT setting, extending procedure beyond SVL could salvage all the remaining 3 scenarios. The median time of procedure for auto and allo-PBSCT in patients who had successful early stoppage and those who needed extended procedure was shown in table 1.
Discussion and Conclusion: Mid-CD34 count has successfully enabled early termination of apheresis procedure without compromising on the CD34+ stem cell yield in the final product, thereby minimising the side effects and discomfort to the patient/donor. This was a particularly useful strategy in allo-PBSCT scenario.

Disclosure of Interest: None Declared

Keywords: APHERESIS, CD34, MID-HARVEST, PBSCT

Poster Presentation

ALLIED (NURSING, TECHNICAL ASPECTS SUCH AS GRAFT PROCESSING, CRYOPRESERVATION, ETC) (208)

CAUSE ANALYSIS AND NURSING EXPERIENCE OF PICC-RELATED THROMBOSIS IN AN ELDERLY PATIENT WITH TD-NSAA

Chunyan Chang[*1], Yan Cui[1]
[1]GCP, Institute of Hematology and Blood Diseases Hospital, Tianjin , China

Aims & Objectives: By analyzing the causes and comprehensive nursing intervention of PICC-related thrombosis in an elderly patient with TD-NSAA, we can reduce the probability of venous thrombosis falling off and alleviate the existing symptoms of the patient, so as to reduce the impact of venous thrombosis on the body during the period of indwelling PICC, and improve the attention of medical staff to the risk of elderly patients during the period of indwelling PICC.
Patients / Materials & Methods: 1. The causes of PICC-related thrombosis were analyzed from 3 aspects: patients, nurses and catheters. Patients' age (> 60 years old), BMI (> 25), poor activity status (ECOG score of grade 4) and chronic renal insufficiency are the risk factors of PICC-related thrombosis.
2. The nurse early judged that the patient may have venous thrombosis, suspended the use of PICC, and timely contacted the ultrasound department for vascular B-ultrasound diagnosis. When it is confirmed that there is thrombus, communicate with the doctor in time and contact the vascular surgery department for consultation. According to the advice of the consulting doctor and in combination with the patient's condition, thrombolysis was not performed. At the same time, instruct the patient to lift and brake the affected limb, prohibit hot compress and massage, and prohibit any operation on the affected limb.
Results: Through the comprehensive nursing care of the patients by the nursing staff, no serious complications occurred during the period when the patients took the tube. The symptoms such as swelling and pain of the arm on the side of the tube insertion caused by venous thrombosis gradually relieved, and the tube can be pulled out smoothly after the treatment.
Discussion and Conclusion: 1. PICC-related thrombosis in elderly patients is one of the most common complications of PICC catheterization. For elderly patients, before PICC catheterization, a comprehensive evaluation should be conducted to determine whether they have the risk of PICC-related venous thrombosis; After catheterization, patients should be regularly followed up by vascular ultrasound to screen for thrombosis, and formulate prevention and control strategies for PICC-related thrombosis in elderly patients.
2. In daily nursing, nurses should pay attention to the high-risk population of PICC-related thrombosis, focus on observing whether the patient has swelling, pain and other symptoms in the arm on the side of catheter insertion; At the same time, closely observe the changes of patients' consciousness, heart rate, respiration and other vital signs, and early warn whether patients have thrombus shedding, so as to win valuable time for patients' lives.
3. For elderly patients whose symptoms are not serious and the catheter is still useful, the PICC can be temporarily retained and removed after the treatment.

Disclosure of Interest: None Declared

Keywords: aplastic anemia, Elderly patients, PICC-related thrombosis

Poster Presentation

ALLIED (NURSING, TECHNICAL ASPECTS SUCH AS GRAFT PROCESSING, CRYOPRESERVATION, ETC) (221)

APHERESIS SETTINGS TO OPTIMIZE COLLECTION YIELD IN POTENTIAL POOR MOBILIZERS UNDERGOING AUTO-HSCT

Veni Prasanna Gedala[*1], Rakesh Reddy Boya[2], Ashok Kumar Pangi[1], Tataji Vanamala[1], Murali Krishna Voonna[3]
[1]Pathology and lab services, [2]Medical Oncology, [3]Surgical Oncology, Mahatma Gandhi Cancer Hospital and Research Institute, VISAKHAPATNAM, India

Aims & Objectives: Pre-apheresis day4- peripheral blood-CD34 (D4PBCD34) of less than 20 cells/µl with G-CSF alone is a good indicator of potential poor mobilization scenario. Plerixafor is used as a rescue medication in this situation. We aim to study if change in apheresis settings would benefit in getting an adequate mobilization apart from Plerixafor use.
Patients / Materials & Methods: This is a retrospective study of apheresis data in the BMT unit of a tertiary cancer hospital over a period of 2 years. Apheresis machine used is Fresenius Com-Tec (v.04.03.08). Mobilization strategy is uniform for all patients with G-CSF given at 10mcg/kg in 2 divided doses on day 1 to 4. Pre-apheresis CD34 is done on day4; a value of <20 is considered as indicator of potential poor mobilization scenario. Plerixafor is given to these patients at 0.24mg/kg, 10 hours before the start of apheresis. Apheresis settings were changed for these patients from the usual, with a V buffy of 5-7 ml, spill over of 15-18 ml (depending on Total WBC count on the day of harvest – lesser spill over for higher T.WBC count and vice-versa), RPM of1850, cycle volume of 300-350 ml Changes from routine settings are indicated in table 1. Standard volume apheresis (2-4 times of calculated blood volume of the patient) was used as a standard approach to minimize discomfort for the patient. Successful mobilization was defined as a CD34+ stem cell yield of 2.5 million cells/kg body weight of recipient.
Results: A total of 46 patients who underwent autologous HSCT in the unit between July 2020 and June 2022 were included in the analyses. Of them 11 were Pediatric patients (<18 years), with neuroblastoma being the most common indication (n=5). Diagnosis wise, multiple myeloma was the most common indication (n=24) followed by Hodgkin and Non-Hodgkin lymphoma (8 each). D4PB-CD34 of <20 cell/µl was observed in 21 patients (45%) with 11 of them being lymphoma. With plerixafor and changed apheresis setting, 20 of these (95%) had a successful mobilization with just one session of apheresis. One case of primary refractory Hodgkin lymphoma couldn't be salvaged. The median time taken for the procedure was 319 minutes (range, 130-629). The median stem cell yield was 4.9 million CD34+ cells/ kg body weight (range, 2.5-8).
Discussion and Conclusion: Optimizing apheresis settings along with Plerixafor improves stem cell yield in a scenario of potential poor mobilization with G-CSF alone strategy in patients undergoing autologous HSCT. This can be achieved even with standard volume leukapheresis and in one single session, thereby minimizing the side-effects and financial burden on the patient.

Disclosure of Interest: None Declared

Keywords: APHERESIS, POOR MOBILIZATION, STEM CELL YIELD

Poster Presentation

ALLIED (NURSING, TECHNICAL ASPECTS SUCH AS GRAFT PROCESSING, CRYOPRESERVATION, ETC) (234)

PREDICTIVE FACTORS ASSOCIATED WITH SUCCESSFUL MOBILIZATION OF PERIPHERAL BLOOD STEM CELLS

Kannadit Prayongratana[1], Piyarat Pimsi[*2], Yotsaya Boonkorkue[2], Wannida Jindawattanawong[2], Supatcha Pombot[2]
[1]Pharmongkutklao Hospital, Bangkok, [2]Silpakorn University, Nakhorn Pathom, Thailand

Aims & Objectives: Currently, the study of predictive factors of the successful mobilization of peripheral blood hematopoietic stem cell (PBSC) in patients with hematological malignancies has no definitive conclusion.
This Retrospective study aims to investigate predictive factors associated with successful mobilization of peripheral blood hematopoietic Stem Cells.
Patients / Materials & Methods: Patients who underwent mobilization of PBSC were analyzed by collecting data from the patients' electronic medical records at the Bone Marrow Transplant Unit. Division of Medicine, Phramongkutklao Hospital from Jan 2015-Dec 2021. The association between possible predictive factors such as mobilization strategy, Baseline platelet count, white blood cell count, absolute neutrophil count and monocyte before mobilization were analyzed by logistic regression.
Results: 94 patients with hematological malignancies who underwent mobilization of Peripheral Blood Hematopoietic Stem Cells were included. This result demonstrated mobilization strategy (Odd ratio, 2.242; 95% CI 0.850-5.914; P= 0.103), white blood cell count (Odd ratio 1.857; 95% CI 0.409-8.437; P= 0.423), absolute neutrophil count (Odd ratio ,0.877; 95% CI 0.256-3.003; P= 0.834) and monocyte (Odd ratio 0.697; 95% CI 0.255-1.903; P= 0.481) did not predict the successful mobilization. Only Platelet counts higher than 163,500 cells/mm3 could serve as a predictive factor significantly associated with successful mobilization (Odd ratio, 3.500; 95% CI 1.336-9.169; P = 0.003).
Discussion and Conclusion: Platelet counts higher than 163,500 cells/mm3 was the predictive factor of the successful mobilization of peripheral blood hematopoietic stem cells.
No conflict of interest to disclose

Disclosure of Interest: None Declared

Keywords: Peripheral Blood Hematopoietic Stem Cells Collection, stem cell transplantation, Successful Mobilization

Poster Presentation

ALLIED (NURSING, TECHNICAL ASPECTS SUCH AS GRAFT PROCESSING, CRYOPRESERVATION, ETC) (254)

ADVERSE EVENTS AND PREDICTED FACTORS OF CRYOPRESERVED CORD BLOOD INFUSION

Yun Wu*[1], ying Y. Wang[1], Lu Huang[1], zhen C. Jia[1], Jin J. Jiang[1], di K. Song[1], lin B. Tang[1], yu X. Zhu[1], lan H. Liu[1], min Z. Sun[1]
[1]The First Affiliated Hospital of USTC, Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei , China

Aims & Objectives: Adverse events (AEs) associated with cryopreserved cord blood (CB) infusion after bedside thawing are common, severe AEs always life-threatening. The aim of this study was to determine the incidence, grade of AEs, and predicted factors during cryopreserved CB infusion.
Patients / Materials & Methods: In this observational study, 889 patients who received single CB transplantation (CBT) admitted from April 2013 and March 2020 were included, with the infusion time was controlled in 20 minutes. Random forest algorithms were trained for prediction of AEs and ranking predicted factors, with their accuracy quantified by area under the receiver operating curves (AUCs) for out-of bag samples.
Results: The incidence of AEs in cryopreserved CB infusion was 74.47% (662/889), hypertension was the most common AE, followed by hemoglobinuria and abdominal pain. Severe hypertension and headache, defined as grade 3 to 5, were occurred in 7.87% and 4.72% of infusions, respectively. The top 8 predicted factors were CB volume (≥30ml), patient weight (<44kg), age (<13 years old), infusion device (no filter), total nucleated cell (≥3.39×107/kg), CD34+ cell (≥1.93×105/kg), and thawing time (<2 min), with area under the curve (AUC) = 0.812.
Discussion and Conclusion: Our data based on random forest show that cryopreserved CB infusion risks vary by CB volume, age and weight of patients, may be severe, and should be closely monitored.

Disclosure of Interest: None Declared

Keywords: Adverse Events, Cord Blood Infusion, Cryopreserved, Predicted factors

Poster Presentation

ALLIED (NURSING, TECHNICAL ASPECTS SUCH AS GRAFT PROCESSING, CRYOPRESERVATION, ETC) (256)

BEST EVIDENCE SUMMARY OF EXERCISE FOR PATIENTS UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION

Yaqi Liu[*1], Chengyuan Li[1]
[1]The Third Xiangya Hospital of Central South University, Changsha, China

Aims & Objectives: To search,evaluate and summarize the best evidence of exercise intervention for patients undergoing hematopoietic stem cell transplantation in laminar flow chamber.
Patients / Materials & Methods: We searched relevant guideline networks and association websites,as well as the UpToDate,NGC,Cochrane Library, JBI, BMJ, Medline/Pubmed, Embase, Ovid, CNKI, Wanfang and other databases to collect relevant guidelines,expert consensuses,best practices and systematic reviews related to exercise intervention in patients during hematopoietic stem cell transplantation published from January 1,2012 to April 27,2022. Two researchers evaluated the quality of the included literature and extracted the evidence.
Results: 10 articles were included,including 5 guidelines,3 systematic reviews and 2 expert consensuses.29 pieces of evidence were summarized in 5 areas,namely exercise evaluation,exercise style,exercise intensity and time,safety management,promotion strategy.
Discussion and Conclusion: It is recommended that health care providers implement a supervised light-to-moderate intensity aerobic combined resistance training intervention for individuals undergoing HSCT.Exercise programs for patients undergoing HSCT should be adjusted day by day according to the patients'daily hematologic status,vital signs and their clinical symptoms.A variety of implementation promotion strategies should be used in full consideration of clinical reality.

Disclosure of Interest: None Declared

Keywords: Exercise, hematopoietic stem cell transplantation, laminar flow chamber

Poster Presentation

ALLIED (NURSING, TECHNICAL ASPECTS SUCH AS GRAFT PROCESSING, CRYOPRESERVATION, ETC) (275)

NINE YEARS ACTIVITY IN HSCT IN KERMANSH-BMT CENTER IN WEST OF IRAN

Mehrdad Payandeh*[1], Mehrak payandeh[1], Fatemeh Yari[1], Ms Najafi[1], Mrs Ezati[1], Farzane Chardoli[1]
[1]Kums , Kermanshah , Iran

Aims & Objectives: The Kermanshah Blood and Marrow Transplantation Center(KUMS-BMT) has been conducting annual surveys on the activity of hematopoietic stem cell transplants since 2012.
The KUMS-BMT Data Center collected the following data in 2022.
A total of 283 transplants were registered from KUMS-BMT center of the West of iran region.
The number of centers in iran are 20 Transplants.
Patients / Materials & Methods: The overall ratio between autologous and allogeneic transplants in our center was 63% and 37%, respectively, but the ratios varied significantly among regions. Autologous transplants have surpassed allogeneic trans- plant in our center and Iran.
The propor- tion of related and unrelated transplants also differed among countries/regions. The number of unrelated trans- plants was more than related ones in Japan (2,551 vs. 1,202) and Australia (329 vs. 291), whereas more than 80% of all transplants were related transplants in Malaysia (90.9%), India (89.5%), Iran (87.2%), Vietnam.
Regarding the indications for transplants, acute myeloid leukemia (AML) was the most common disease for allo- geneic transplant (62, 22% of allogeneic transplants), while plasma cell disorder (PCD) was the most com- mon disease for autologous transplant (117, 41% of all autologous transplants).
Results: Furthermore, the number of transplants for haploientical indications has steeply increased in this region compared with the rest of disease indica- tions (21, 7.5% of all transplants).
Discussion and Conclusion: Other transplanted cases during these 9 years consist of , Hodgkin (15.5% of total, 44),acute lymphoblastic leukemia (6.3% of total,18), NHL (4.9% of total,14), myelofibrosis (1%of total, 3) , CML (1%of total, 3), PCNS-NHL (1%of total, 3), MDS (2.1% of total , 6), Aplastic Anemia (2.1% of total , 6), Primary Amyloidosis (./ 7 % of total , 2) , Fanconi anemia (./ 3% of total ,1) , CLL (./ 3% of total ,1) , RCC (./ 3% of total ,1) , PNET (./ 3% of total ,1) , GCT (./ 3% of total ,1) .

Disclosure of Interest: None Declared

Keywords: AUTOLOGOUS FEMATOPOIETIC STEM CELL TRANSPLANTATION, Haploientical, HSCT

Poster Presentation

ALLIED (NURSING, TECHNICAL ASPECTS SUCH AS GRAFT PROCESSING, CRYOPRESERVATION, ETC) (283)

DIFFERENCES AND CHALLENGES OF PATIENTS RECEIVING HSCT VS CAR-T THERAPY: A NURSING PERSPECTIVE

Amish Kale*[1], Deepti Wairkar[1], Rosy Pinto[1]
[1]ACTREC, Tata Memorial Centre, Navi Mumbai, India

Aims & Objectives: To assess the differences and challenges among patients diagnosed with B-ALL who received HSCT vs CAR-T therapy from a nursing perspective.
Patients / Materials & Methods: A retrospective analysis of 5 post HSCT patients and 5 post CAR-T therapy patients diagnosed with ALL. Their baseline characteristic, baseline diagnosis, early complications and special nursing consideration following HSCT and CAR-T therapy was recorded for first 25 days post infusion. Early complications post HSCT were monitored. Post CAR-T patients were monitored for known complications like -cytokine release syndrome and neurological toxicity & B-cell aplasia.
Results: All patients had high risk B-ALL as baseline diagnosis. Pre transplant MRD was negative for all 5 patients whereas pre CART MRD was positive for all 5 patients. In HSCT group, 4 patients have undergone full match allogenic transplant and 1 patients MUD transplant. In CAR-T group all patients received their pre-collected and genetically engineered CAR-T cells.
Nursing care: HSCT: Neutropenic sepsis which was present in all patients, intensive monitoring of vitals sign, escalating antibiotics, strict intake & output charting and strict aseptic technique were followed. Mucositis assessment & grading done, diet modification, application of BG paint, SOS administration of analgesic and administered TPN. In diarrhoea, assessment of stool, maintaining electrolyte balance, maintaining strict intake-output and weight charting was done. For acute GUT GVHD, assessment of grading as per colour consistency frequency volume, diet modification, administration of steroids was done. For Engraftment syndrome, vigorous monitoring of patient for skin rashes, fever and weight gain was done, oxygen therapy, steroids and diuretics were administered as per need. For viral reactivation viral load was monitored and care is given accordingly.
CAR-T: Patients those who developed CRS, aggressive vital sign monitoring was done, strict intake -output and weight monitoring, monoclonal antibody(tocilizumab) administered, oxygen supplementation was provided, patient respond to CAR-T will develop B-cell aplasia leading to hypogammaglobulinemia treated with intravenous immunoglobulin, ICANS patients were monitored for mini mental status examination, confusion and behavioural changes, visual and auditory hallucination, language dysfunction, speech alteration, fine motor impairment, investigation sent for all patients including interleukins, tumor necrosis factor alpha (TNF- alpha), patient were protected from all types of fall.
Discussion and Conclusion: HSCT and CAR-T therapy requires close monitoring and skilled nursing care. Patients undergoing HSCT requires more intense care as compare to patients receiving CART therapy. But since CART therapy is novel therapy studies with more samples are required in this field.

Disclosure of Interest: None Declared

Keywords: CAR T Cell therapy, HSCT, NURSING PERSPECTIVE

Poster Presentation

ALLIED (NURSING, TECHNICAL ASPECTS SUCH AS GRAFT PROCESSING, CRYOPRESERVATION, ETC) (339)

STEM CELL DONATION: RELUCTANCE AND REFUSAL AMONGST HLA-MATCHED SIBLINGS

Sharon A. Lionel[*1], Sushil Selvarajan[2], Uday Kulkarni[2], Fouzia N.A[2], Anu Korula[2], Kavitha M.L[2], Aby Abraham[2], Alok Srivastava[2]
[1]Haematology, [2]Christian Medical College,Vellore, Vellore, India

Aims & Objectives: Introduction: Matched-related donors are meant to be among the most accessible options for allogeneic haematopietic stem cell transplantation (HSCT). There is limited information on reluctance and refusal amongst such donors as a barrier to HSCT. We describe our experience with such a phenomenon.
Patients / Materials & Methods: Patients and methods: A descriptive case series of patients with haematological conditions requiring allogeneic transplant whose matched sibling donors refused or showed reluctance to donate stem cells forms the basis for this report.
Results: We identified 5 recipients whose matched siblings were reluctant to or did not donate stem cells. Brief details are mentioned in table 1 below. One of these patients underwent HSCT in 2016 while all the other 4 were in 2020. During this period a total of 848 allogeneic HSCTs were performed at our centre, out of which 496 were matched related.
Discussion and Conclusion: Discussion: This data highlights an unfortunate situation that restricts access to matched sibling donors. Even among this small number, married female donors lacking autonomy and being subjected to the vagaries of their husbands or in-laws forms a major reason for restricting access. Increasing awareness of the safety of HSC donation as well as sensitization and appropriate general education could overcome some of these barriers. Still, the lack of autonomy of married female donors in some countries could be a more complex issue to resolve. As several of them happened during the COVID19 pandemic, it is unclear whether that also played a role in these refusals
Conclusion: This small series draws attention to this problem which restricts access to matched related donors for HSCT in some parts of the world. A prospective multicentre assessment is required to document the extent of the problem. Based on the reasons identified suitable remedial steps can be planned.

Disclosure of Interest: None Declared

Keywords: HSCT, Matched sibling donor, Refusal and Reluctance

Poster Presentation

ALLIED (NURSING, TECHNICAL ASPECTS SUCH AS GRAFT PROCESSING, CRYOPRESERVATION, ETC) (345)

"DUMP FREEZING" USING -80C MECHANICAL FREEZING FOR PEDIATRIC AUTOLOGOUS PBSCT

Satyam Arora[*1], Nita Radhakrishnan[2], Seema Dua[1], Manideepa Maji[2], Shruti Verma[1]
[1]Transfusion Medicine, [2]Pediatric Hemato Oncology, Post Graduate Institute of Child Health, Noida, India

Aims & Objectives: Controlled-Rate-Freezing (CRF) is one of the most widely used methods for the preservation of hematopoietic progenitor stem cells. CRF is a complicated, lengthy, expensive procedure and may not be a viable option in resource-constrained scenarios. Uncontrolled-rate-freeing (UCF) using -80C deep freezers provides a viable option for small centres and for shorter periods of preservations (< 6 month).
We present a retrospective analysis of the efficiency of UCF method to store the HPSC for paediatric autologous HSCT at a government paediatric tertiary care center.
Patients / Materials & Methods: Cryoprotectant solution consisting of 5% dimethyl sulfoxide (DMSO) & 5% albumin with 2% hydroxyethyl starch (HES) was used. An equal volume of PBSC product and cryoprotectant solution was mixed. The mix was stored at −80°C mechanical freezer till the transplant. Evaluation of cryopreservation was studied by analysing the variation in cellularity, viability and CD34+ stem cell dose recovery as well as clinical followup with engraftment.
Results: A total of 6 paediatric patients (4 male & 2 female) underwent auto HSCT from over a period of 10 months between October 2019 to September 2021 (BMT facility halted due to COVID-related issues in between). The mean age of patients was 9.5 yrs (5-18 yrs; median 7.5 yrs). Indications for autologous BMT included relapsed lymphomas in 3(ALCL in CR2-2, HL in CR2 -1), high-risk neuroblastoma in CR1 in 2 & relapsed APML in CR3 in 1 patient. GCSF was used in 2 patients whereas GCSF with one dose of Plerixafor was used in 4.
Total 7 harvest procedures were done on day 5 of mobilization using Optia cell separator (TERUMO BCT). Mean PBSC product volume was 230.8±55.7 ml. All the products were manipulated with plasma reduction, to have a more concentrated volume & to reduce the exposure of DMSO. The mean volume of the reduced product was 125.8±19.3 ml & 122.5±12.9 ml of cryoprotectant solutions was mixed.
The cryopreserved products were stored at −80°C for median 10d (9.3±1d) before infusion. Mean recovery post UCF at -80C mechanical freezing was 90.1%±11.2% for nucleated cells & 86.8%±4.54% viability. The mean dose of CD34+ cells recovered after the UCF was 4.6±1.5 million cells/kg body weight. The median days to neutrophil engraftment was 10 (8–12 d) and platelets engraftment was 14.5 (10–21 d). One child with ALCL relapsed at 10 months post-BMT. The EFS of this cohort is 83% at a median follow-up of 18 months post-transplant (11-33 months).
Discussion and Conclusion: Our results are similar to previously published work using same combination of cryoprotectant solutions. Our analysis shows that autologous PBSC can be successfully cryopreserved with mechanical UCF in paediatric patients as well. This is simpler, cost-effective and can be used in resourceconstrained settings.

Disclosure of Interest: None Declared

Keywords: Cryopreservarion of bone marrow stem cells, PBSCT, pediatrics

Poster Presentation

ALLIED (NURSING, TECHNICAL ASPECTS SUCH AS GRAFT PROCESSING, CRYOPRESERVATION, ETC) (402)

THE CHARACTERISTICS OF PATIENTS WITH HAEMATOPOIETIC STEM CELL TRANSPLANTATION AT INDONESIA

Sri Setyowati[*1], Aditya Tri Nugroho[1], Damai Santosa[2]
[1]Oncology Nursing, [2]Medical Hematology Oncology, Kariadi General Hospital , Semarang, Indonesia

Aims & Objectives: In Indonesia, bone marrow transplantation is a treatment which not known yet to some people. Kariadi Hospital is the one hospital that does bone marrow transplantation first. In 1987, the first bone marrow transplantation was successful for acute myeloid leukemia (AML) case with autologous bone marrow transplantation. Bone marrow transplantation or Hematopoietic stem cell transplantation (HSCT) is one of therapy used to treat patients with diagnosis leukemia, severe aplastic anemia, Hodgkin's disease, non-Hodgkin's lymphoma, myeloma multiple, many blood disorder and solid tumor (malignancy).
HSCT is a procedure that replaces bone marrow with good bone marrow. Prevalence of HSCT in the world in the year 2019 range amount to 1.5 million including HSCT autologous and allogeneic. This number has increased by almost 50 % since the year 2016. This study described the patient characteristics who did hematopoietic stem cell transplantation during 2017-2021 at Kariadi General Hospital Semarang, Indonesia.
Patients / Materials & Methods: This study is a quantitative research non-experiment with design retrospective analysis. Data or sample was taken with a total sampling are 20 patients. Data analysis by describing the criteria or group.
Results: The results study describe, that the sex of patients consist are 60% male and 40% female who doing hematopoietic stem cell transplantation. Most range age at 35-44 years amount 30% then followed 25% at range age 15-24 years and 55-64 years. For the diagnosis, the group is 40% in the case of Myeloma Multiple. Most of these HSCTs doing on autologous type are 80% of total cases. Then, it is indicated for 90% of malignancy cases. During the transplantation process, patients are 100% successful in engraftment, all of the patients happen neutropenia, thrombocytopenia, oral mucositis, gut disorder, and electrolyte imbalance. Almost 15% are hematuria and less than 10% are urticaria, VOD, sepsis, or brain hemorrhage.
Discussion and Conclusion: The conclusion is patients who did HSCT have various adverse events and complications depending on many factors or comorbids. These are age, sex, diagnosis, stage of disease, state of remission, regiment conditioning, comorbidity, etc. Health professionals should upgrade knowledge and skill for treatment and care for patients with HSCT.

Disclosure of Interest: None Declared

Keywords: Autologous Transplant, Haemopoietic stem cell transplantation, Patients Characteristics

Poster Presentation

ALLIED (NURSING, TECHNICAL ASPECTS SUCH AS GRAFT PROCESSING, CRYOPRESERVATION, ETC) (406)

EFFICIENT, COST-EFFECTIVE AND SAFE USE OF MAHURKAR CATHETER IN AUTOLOGOUS TRANSPLANT PATIENTS.

Rama Devi B R* [1], Anitha R[1], Santhosh K Devadas[2], Rasmi Palassery[2]
[1]Nursing, Ramaiah Memorial Hospital, [2]Medical Oncology, Ramaiah Medical College and Hospitals, Bangalore, India

Aims & Objectives: The insertion and maintenance of a central venous catheter (CVC) is a cornerstone in the care of patients undergoing hematopoietic stem cell transplant (HSCT). Autologous HSCT (auto-HSCT) often requires two separate CVCs: (1) for the peripheral blood stem cell (PBSC) harvest, a larger lumen stiff line and (2) for the actual HSCT, a multi-lumen, flexible, tunneled catheter. Our aim was to study the use, cost effectiveness and complications of a Mahurkar catheter for both PBSC harvest and the HSCT in auto-HSCTs done in our center.
Patients / Materials & Methods: Retrospective chart review of all auto-HSCT patients from November 2015 to July 2022 was done. Fifty-seven patients (Multiple Myeloma - 42, Hodgkin's Lymphoma - 8, Non-Hodgkin's Lymphoma - 7) underwent auto-HSCT during the study period. Double-lumen, 11.5 Fr, curved Mahurkar catheters were inserted into the right or left internal jugular veins of HSCT recipients by trained nephrologists. After G-CSF with or without Plerixafer mobilization, stem cell harvest was done using the Mahurkar catheter and cryopreserved/non-cryopreserved stem cells were infused via the same catheter after 24 hours of high dose chemotherapy. Mahurkar catheter care protocol included dressing with Chlorhexidine Gluconate Tegaderm changed every 5 days and flushing with Hep-lock solution daily of both the lumens. The catheters were removed at the time of discharge.
Results: Out of 57 patients, 55 were mobilized with G-CSF and 2 with chemotherapy and G-CSF. Two patients required a second Mahurkar catheter insertion, one due to catheter occlusion and the other one due to the delay between chemo-mobilization and stem cell infusion. Two catheters were removed due to continuous high fever, but negative blood culture. There were no major complications during the catheter placement. The median duration of the catheter in-situ was 21 days. The catheter related complications included: (1) line associated deep vein thrombosis (1/57), (2) catheter related bloodstream infection (CRBSI) (3/57), and accidental blood leak from catheter (2/57); the latter did not result in any morbidity. Comparison of the cost of (1) Mahurkar catheter for stem cell harvest followed by another CVC for transplant and (2) a single Mahurkar for both harvest and transplant, showed that the latter was associated with a significant reduction in the cost burden (table 1).
Discussion and Conclusion: The use of Mahurkar catheter as the single long term indwelling vascular access in patients undergoing autologous HSCT is a safe and financially viable option with minimal complications.

Disclosure of Interest: None Declared

Keywords: Autologous Transplant, cost effectiveness, Mahurkar Catheter, safety and efficac

Poster Presentation

ALLIED (NURSING, TECHNICAL ASPECTS SUCH AS GRAFT PROCESSING, CRYOPRESERVATION, ETC) (412)

MID APHERESIS WBC COUNT, MNC COUNT, IG COUNT AND CD34+ CELL COUNT IN OPTIMIZING DOSAGE OF PBSCH

Divya Setya[*1], Ankit Malhotra[2], Satyendra Katewa[3], Ravi Dara[1], Monica Singh[2], Rahul Sharma[3]
[1]Transfusion Medicine, [2]Hematopathology and Molecular Diagnostics, [3]Pediatric Hemato-Oncology and BMT, Manipal Hospital Jaipur, Jaipur, India

Aims & Objectives: The best parameter to predict hematopoietic progenitor cell yield in a graft is the viable CD34+ cell count. However, whenever in-house estimation of CD+ cell yield is not available, apheresis physicians rely on white blood cell (WBC) count or mononuclear cell (MNC) count or immature granulocyte (IG) count and other parameters which are easily available used to guide collection of peripheral blood stem cell (PBSC) harvest. To analyze mid apheresis PBSC harvest sample in order to investigate whether viable CD34+ cell counts correlate with parameters obtained by performing a complete blood count by a hematology coulter.
Patients / Materials & Methods: A retrospective study was performed in the department of Transfusion Medicine at a tertiary level healthcare setup. Fifty samples were included for analysis. Pre apheresis CD34 counts performed on the morning of the harvest were entered in the cell separator. Number of cycles were adjusted depending on the target dose per kilogram body weight. A mid apheresis sample was collected from the product collected at half the number of cycles. The sample was sent for a CBC followed by a viable CD34+ cell count. WBC count, MNC count, IG count were estimated by a coulter (Sysmex XN 300, Transasia, Japan) and viable CD34+ cell count was estimated by flowcytometry (BD Facs Canto, BD Biosciences, USA).
Results: There were 50 samples from allogeneic transplants in the study. A comparison of the test results showed that WBC count and MNC count have a significant but moderate correlation with viable CD34+ cell count ($r=0.72$, $p<0.05$ and $r=0.69$, $p<0.05$ respectively), whereas, IG count has a poor correlation with viable CD34+ cell count ($r=0.15$, $p<0.05$). Although none of the parameter estimated by CBC can replace CD34 cell count by flowcytometry, WBC and MNC count are better predictors of the hematopoietic progenitor cell content as compared to IG count in optimizing the PBSC collections.
Discussion and Conclusion: Collectively, the data demonstrated that WBC and MNC counts are better tools to guide PBSC collections as compared to IG counts. Whenever, CD34 estimation by flowcytometry is not available, a mid-apheresis complete blood count which has WBC and MNC count can be used to optimize the PBSC collections.

Disclosure of Interest: None Declared

Keywords: APHERESIS, CBC, CD34, immature granulocyte

Poster Presentation

ALLIED (NURSING, TECHNICAL ASPECTS SUCH AS GRAFT PROCESSING, CRYOPRESERVATION, ETC) (413)

PATTERN AND CHALLENGES IN HLA MATCH LIKELIHOOD : A STARTUP CENTRE EXPERIENCE FROM INDIA

Chepsy Philip*[1], Bobby george[1], Sruthy V[1], Nayana Reghu[1], Sheena Jacob[1]
[1]Believers Church Medical College Hospital, Thiruvalla, India

Aims & Objectives: Hematopoietic cell transplantation (HCT) remains a curative procedure to treat many diseases. Its success is multifactorial but depends greatly on the degree of HLA matching between donor and recipient. Although the number of successful HCT procedures carried out worldwide increases every year, many patients remain unable to receive this treatment because of the difficulty of finding an HLA-matching donor. We explored the patterns of HLA matching in identifying a fully matched donor at our center. We also analyzed the course of patients in whom a donor was identified.
Patients / Materials & Methods: All patients' files for HCT were retrospectively screened for HLA class I and class II typing of patients and their potential donors since the inception of our transplant program in October 2020 through May 2022.
Results: A total of 23 patients were screened for a potential HLA donor with the intent to transplant (Fig 1). There were 7 (30.4%) children (≤18 years) and 15 (65.2%) were males. A fully HLA matched donor was identified in 15 (65.2%) of the searches. In these a matched family donor was identified in 5 (21.7%). A matched unrelated donor was identified in 10 (43.4%). In those with a match identified; 4 (26.6%) patients underwent a transplant at our centre and 1 (6.6%) patient travelled to another centre for the transplant. 3 (30%) matched unrelated donors were unavailable for further donation after the initial screening. There was one (10%) delayed unrelated donor referral and further processing for one (10%) donor was denied due to the donor registry technical limitation. 5(21.7%) patients did not choose to proceed with the transplant in view of finances amongst whom 2 patients have died to disease. In those with no match identified 1 (12.5%) patient underwent a haploidentical transplant and a 9/10 donor has been identified for another patient.
Discussion and Conclusion: In this study, we investigated the chance of finding an HLA-matched donor for each patient requiring HCT at our centre. We found that overall, 65.2% of our patients had an identical matching donor. However only 21.7% patients could identify a matched sibling donor. Our data demonstrate that in a large country like India, it is still essential to consider alternative donor strategies. Also,only a minority of our patients proceed with further transplant. In our experience lack of finances and a suitable donor still remain significant challenges to stem cell transplantation.

Disclosure of Interest: None Declared

Keywords: donor type, hla, Transplantation