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Alternate Donor Transplantation

William YK Hwang[1,2,3], Piyanuch Kongtim[4], Navneet S Majhail[5], Ming Yao[6]

[1]National Cancer Centre Singapore, [2]Singapore General Hospital, [3]Duke-NUS Medical School Singapre, [4]Hematopoietic Stem Cell Transplantation and Cellular Therapy Program, Division of Hematology-Oncology, Department of Medicine, University of California Irvine, CA, USA, [5]Sarah Cannon Transplant and Cellular Therapy Network, Nashville, TN, USA, [6]Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan

Abstract

There is a significant need for alternative donors other than full-matched related or unrelated donors for allogeneic hematopoietic stem cell transplantation, especially in the Asia Pacific, where donor registries are smaller, and ethnicities are far more diverse. Both umbilical cord blood (UCB) and haploidentical transplantation can be carried out despite significant human leukocyte antigen (HLA) mismatches between patients and donors and help to meet this need. There are advantages and disadvantages to UCB and haploidentical transplantation, though enhancements in technology continue to improve outcomes in both. Donor selection for these cell sources is dependent on the presence of donor specific anti-HLA antibodies in the recipient's serum, degree and characteristics of donor-recipient HLA mismatches, ABO compatibility. Specific to haploidentical transplantation, additional factors like donor age, sex, donor-recipient CMV serology as well as NK cell alloreactivity are also important.

Key words umbilical cord blood, haploidentical, stem cell transplantation, bone marrow

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Correspondence: William YK Hwang, Department of Haematology, Singapore general Hospital, Outram Road, Singapore 169608, E-mail: williamhwang@duke-nus.edu.sg

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Introduction

Allogeneic hematopoietic stem cell transplantation (allo-SCT) remains a mainstay for the treatment of many hematological disorders but many patients in Asia are unable to find full matched unrelated donors due to small registry sizes and considerable human leukocyte antigen (HLA) diversity across Asia.

There is a significant need for alternative donors other than full-matched related or unrelated donors for allogeneic hematopoietic stem cell transplantation, especially in the Asia Pacific, where donor registries are smaller and ethnicities are far more diverse[1]. Both UCB and haploidentical transplantation can be carried out despite significant HLA mismatches between patients and donors and help to meet this need.

Allogeneic Stem Cell Transplantation Using Alternative Donor in Acute Leukemia - Current Status

Allogeneic stem cell transplantation using alternative donor

Allo-SCT is an established curative treatment for acute leukemia. It has been proven to improve survival in patients with intermediate or high-risk acute myeloid leukemia (AML) in first complete remission, or acute leukemia of any risk beyond first remission. However, only about 30% of patients have an available HLA-matched sibling donor[2]. Therefore searching for alternative donor had been developed in past three decades.

Up to present, there are three options for choosing alternative donor: matched unrelated donor (MUD) (or even mismatched unrelated donor) or UCB or mis-

matched related donor [including haploidentical (Haplo) related donor][2-4].

Unrelated donor stem cell transplantation

Firstly, the alternative strategy pursued for the remaining 70% of patients was an HLA MUD. Unfortunately, even with the use of large unrelated donor banks, such as the National Marrow Donor Program (NMDP), around 40% of patients are unable to find an HLA-matched donor among all ethnic groups. HLA-mismatched unrelated donors are available for some patients, but outcomes historically have been inferior to HLA-matched donor stem cell transplant (SCT)[2, 4].

UCB stem cell transplantation

UCB SCT offers several benefits such as immediate graft availability compared with other strategies using HLA mismatched donors; less strict HLA matching requirements; reduced incidence of chronic graft versus-host disease (GVHD), and favorable graft-versus-leukemia (GVL) effects. A reduced HLA matching requirement is especially helpful for finding donors for patients from ethnic minorities, providing an UCB unit of adequate dose for up to 81-91% of adult patients and 95-99% of patients below 20 years old. Experienced UCB SCT centers are currently reporting comparable disease-free and overall survival (OS) rates to MUD SCT, especially in patients with minimal residual disease prior to SCT. The main obstacles for UCB SCT remain the expense, high graft failure rate, delayed engraftment, slow immune reconstitution, high rates of opportunistic infections, and relatively high rate of non relapse mortality. There are additional difficulties with UCB SCT in the treatment of acute leukemia, including the inability to acquire new cells from the donor for use as donor lymphocyte infusions in cases of disease relapse or to perform a second transplant from the same donor in cases of graft failure or poor graft function. Novel strategies of ex vivo expansion of UCB and manufacturing UCB-derived virus-specific T cells to treat post-UCB SCT virus infections may hold promise to improve outcomes of UCB SCT[3].

Haploidentical stem cell transplantation

Haplo SCT has also been investigated in the past few decades and seemed more and more popular. The two most utilized approaches, either using G-CSF-primed grafts, Intensive postgrafting immunosuppression, Antithymocyte globulin (ATG), and Combined peripheral blood stem cell and bone marrow allografts (GIAC); or Post-Transplantation Cyclophosphamide (PTCy). The GIAC Haplo SCT approach has been shown to produce rates of OS comparable to that of HLA-matched related donors for patients with AML in first complete remission, or for patients with standard risk acute lymphoblastic leukemia (ALL)[4]. PTCy GVHD prophylaxis, developed by the Baltimore group, modulates host versus-graft and graft-versus-host reactions by directly impacting alloreactive T cells, while preserving regulatory T cells. PTCy-based Haplo SCT has been reported to be associated with high engraftment rates and low rates of infections, NRM, severe acute GVHD, and chronic GVHD[4]. The degree of HLA disparity also appears not to be associated with inferior outcomes after nonmyeloablative (NMA) Haplo SCT with PTCy. A growing number of studies have shown comparable outcomes of Haplo SCT versus HLA matched SCT using unrelated or even related donors in patients with acute leukemia. For improving outcome of Haplo SCT, several advances in development of optimal strategy of donor specific antibodies (DSAs) desensitization and in T-cell depleted (TCD) techniques including the use of immunomagnetic beads for CD34 selection, CD3/CD19 depletion, and ab CD3/CD19 depletion has been investigated. However, despite the technological innovation and resultant improvement in clinical outcomes, the extra cost and qualified laboratory requirements impacts its widespread application[4-6].

Potential benefits from HLA-mismatched stem cell transplantation

Interestingly, use of HLA-mismatched SCT provides several advantages for patients with AML in need of transplant. First, it provides rapid access to donors, allowing patients with high-risk leukemias to be transplanted quickly. Second, there is the potential that there may be more potent GVL with HLA-disparity in high-risk cases. For patients with AML in complete remission, UCB SCT had a similar relapse rate, but inferior OS when compared with MUD SCT. However, for acute leukemia patients with minimal residual disease (MRD) before SCT, retrospective analyses have shown that UCB SCT exhibited a lower relapse rate and similar OS in comparison with MUD SCT[4-6].

Perspectives

UCB SCT has the advantages of serving as an immediate 'off-the-shelf' graft source with excellent malignancy control and long-term outcome data. However, UCB SCT continues to require intensive management of opportunistic infections and also advanced cell processing laboratory demands for new strategies that manipulate the donor cells to shorten the time to engraftment or to provide viral-specific T-cell support. For Haplo SCT, especially PTCy-based approaches, its low NRM and opportunistic infection burden, inexpensive cost, and quick learning curve make it easily exportable

Table 1. Advantages and disadvantages of Haplo SCT and UCB SCT

UCB SCT		Haplo SCT	
Advantages	Disadvantages	Advantages	Disadvantages
*Readily & universally available	*Expensive	*Readily & universally available	*Relapse (BM/NMA)
*Low GVHD rates	*Inability to obtain more cells from the same donor for treatment of graft failure or relapse	*Lower cost	*Harvest in OR (if BM)
*Low relapse rates	*Delayed engraftment	*Additional donor cells readily available when needed for graft failure or relapse	
	*Delayed immune reconstitution & increased rates of infection	*Low GVHD rates	
	*Advanced laboratory requirements for attempted UCB manipulations and production of viral specific T cells	*Easy learning curve	

Modified from Liu JH, et al. Curr Opin Hematol 2018; 25: 103-111[4]

and have brought it into widespread use[5, 6]. The benefits and disadvantages of each platform are also influenced by current SARS-CoV-2 pandemic and should be balanced by institutional experience and preference, their ability to perform advanced stem cell processing and adoptive cell therapy and the availability of clinical trials[7] (**Table 1**).

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

PTCy platform for GVHD prevention has become standard of care for T-cell replete haploidentical SCT. 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[8]. Traditionally, it is recognized that there are advantages and disadvantages to using BM versus PBSC in human leukocyte antigen (HLA)-identical sibling and matched and mis-matched unrelated donor transplantation. The cellular composition of the two graft sources varies, which leads to differences in engraftment kinetics, immune reconstitution, and risks of acute and chronic GVHD. Hence, one graft source may be preferred over the other in certain clinical scenarios based on patient, disease, and donor related variables. In addition, there are logistical issues that need consideration such as harvest expertise and operating room resources for BM and apheresis facilities for PBSC. Given that it is still relatively new, there is considerable interest in understanding the use of PBSC and BM in recipients of T-cell replete haploidentical transplantation using PTCy for GVHD prevention.

Irrespective of the graft source, there are significant differences in T- and NK-cell reconstitution after T-cell replete haploidentical SCT using PTCy compared to sibling and unrelated donor SCT receiving conventional GVHD prophylaxis regimens, which explains the general lower incidence of GVHD and the higher incidence of infections such as cytomegalovirus (CMV) and BK virus[9]. Haploidentical SCT is characterized by delayed recovery of naïve T-cells and NK cells along with relative sparing of CD4+ regulatory T-cells, which leads to an immune milieu that promotes tolerance and lower rates of GVHD. Furthermore, B-cells remain phenotypically naïve through as long as 1-year post-transplantation, and with the delayed recovery of *de novo* T-cells, predisposes the recipients to viral infections. The kinetics of immune recovery after haploidentical SCT are generally complex and are also dependent on other variables such as conditioning regimen intensity, recipient-donor CMV status, and degree of HLA mismatch.

Table 2 summarizes large contemporary studies that have investigated the role of graft source in recipients of T-cell replete haploidentical SCT using PTCy as GVHD prevention strategy[10-16]. Notwithstanding the limitations typical of registry based retrospective analyses, there are common themes that can be identified with respect to the influence of graft source on outcomes. Similar to other donor sources, there are advantages and disadvantages to the use of PBSC and BM as a graft source in haploidentical SCT[17]. PBSC recipients have been observed to experience shorter time to neutrophil engraftment and lower rates of graft failure compared to BM recipients. However, patients receiving PBSC grafts have higher risks of acute and chronic GVHD. Arcuri et al, in a meta-analysis that compared the role of graft source and conditioning regimen intensity in haploidentical SCT recipients reported no difference in OS, progression free survival, GVHD-free relapse free survival, and non-relapse mortality with the use of PBSC or BM grafts. However, PBSC recipients had lower risk of relapse but higher rates of grade II-IV acute GVHD, grade III-IV acute GVHD, chronic GVHD, and extensive chronic GVHD[8]. Their results did not change in analyses that were stratified by conditioning regimen intensity.

Table 2. Highlights of contemporary large studies comparing bone marrow versus peripheral blood stem cells as graft source for T-cell replete haploidentical stem cell transplantation using post-transplant cyclophosphamide for graft-versus-host disease prevention

Reference*	Population	N	Results
Bashey et al (2017)[11]	Hematologic malignancies; adult patients	BM 481, PBSC 190	Higher risk of acute GVHD with PBSC; comparable risks of OS and NRM; higher relapse risk in BM recipients with leukemia
Ruggeri et al (2018)[15]	AML or ALL in CR1 or CR2; adult patients	BM 260, PBSC 191	Lower engraftment rates with BM and higher incidence of acute GVHD with PBSC; comparable chronic GVHD, relapse, NRM, LFS, and OS probability with BM and PBSC
Solomon et al (2019)[16]	AML, ALL, MDS; adult patients	BM 645, PBSC 680	Higher risks of acute GVHD and chronic GVHD in PBSC recipients
Bazarbachi et al (2020)[12]	Lymphoma; adult patients	BM 219, PBSC 255	Lower engraftment rates and lower risk of acute GVHD with BM; no difference in risks for OS, PFS, relapse, or chronic GVHD
Im et al (2020)[13]	AML, ALL, MDS, CML; adult patients	BM 271, PBSC 375	Higher risks of chronic GVHD and NRM in RIC PBSC vs. RIC BM recipients, no graft source effect on chronic GVHD or NRM in MAC recipients; no difference in risks of acute GVHD, relapse, GRFS, OS in RIC or MAC recipients
Nagler et al (2020)[14]	ALL in CR1 or CR2; adult patients	BM 157, PBSC 157	Higher engraftment rates with PBSC; lower LFS, OS, and GRFS with PBSC; no difference in relapse incidence
Baron et al (2022)[10]	Relapsed/refractory AML; adult patients	BM 249, PBSC 419	Higher incidence of acute GVHD in PBSC recipients; LFS comparable in patients <55 years; lower NRM and higher LFS in BM recipients among patients ≥ 55 years

AML: acute myeloid leukemia, ALL: acute lymphoblastic leukemia; CR: complete remission; BM: bone marrow; PBSC: peripheral blood stem cells; GVHD: graft-versus-host disease; NRM: non-relapse mortality; LFS: leukemia free survival; OS: overall survival; PFS: progression free survival; GRFS: GVHD-free relapse-free survival
*All studies described are retrospective cohort studies

With this background, how should clinicians determine which graft source is appropriate for a given patient who is being considered for T-cell replete haploidentical SCT with PTCy based GVHD prophylaxis? Foremost in this decision-making process are the data that OS in most studies has been shown to be comparable between BM and PBSC recipients. Hence, both graft sources are acceptable for proceeding with transplantation. Donor characteristics that are associated with SCT outcomes need to be considered in addition to the graft source (e.g., donor age and sex, presence of donor-specific antibodies, ABO compatibility, and CMV status)[18]. In our clinical practice, BM is the preferred graft source for haploidentical SCT given its association with lower risks of acute and chronic GVHD. This approach is definitely desirable in non-malignant diseases such as severe aplastic anemia where there is no need for an alloreactive graft-versus-tumor effect. However, we lean towards using PBSC in patients where there is higher risk of delayed engraftment or primary graft failure (e.g., older recipients and in diseases such as myelodysplastic syndromes, myeloproliferative neoplasms, and myelofibrosis) and in patients with high-risk leukemia given the suggestion that PBSC may possibly be associated with lower risks of relapse. An important caveat in graft source selection is logistics, since many centers do not have the experience, expertise, and set up to perform bone marrow harvests while PBSC collection using apheresis is more universally available.

In conclusion, BM and PBSC are acceptable graft sources for T-cell replete haploidentical SCT using PTCy based GVHD prophylaxis. The decision to use a specific graft source needs to be tailored towards patient characteristics and transplant center experience. Randomized clinical trials are needed to further clarify appropriate populations for the use of BM vs. PBSC in this setting.

Donor Selection for Haploidentical Hematopoietic Stem Cell Transplantation

Over the past two decades, significant advancement has been made in alleviating HLA alloreactivity between the donor and recipient, which has permitted an increase in use of haploidentical donors for transplantation, now the fastest growing source of hematopoietic stem cells, with 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. The great majority of patients have more than one potential haploidentical donor available for donation and it is clear that not all of these donors can provide equivalent transplant outcomes, making donor considerations become increasingly complex. In an effort to optimize donor selection strategies, multiple studies have been published on 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 al-

loreactivity[19]. It is also important to mention that these donor characteristics may have different impact on outcomes when different haploidentical transplant platforms are used, i.e., T-cell depleted (TCD) versus T-cell replete (TCR) haploidentical transplantation.

1. Donor specific anti-HLA antibodies (DSAs)

Approximately 10-20% of recipients of haploidentical transplant have pre-formed anti-HLA antibodies against their donor's HLA, with higher incidences in female and heavily transfused recipients. The presence of DSAs has been shown to be associated with primary graft failure, delayed engraftment, primary poor graft function as well as lower post-transplant survival[20-23]. The ability of DSAs in causing primary graft failure depends on both antibody levels and activation of the complement system[22]. It has been now recommended to routinely test for DSAs and their ability to activate complement pathway such as C1q assay before choosing haploidentical donors.

Using hematopoietic stem cells from a donor without the corresponding HLA antigens is an ideal option for a recipient with anti-HLA antibodies. However, if there are no such donors available, recipients with DSAs should undergo desensitization treatment prior to transplantation to prevent graft failure[24].

2. Donor age

Using stem cells from a younger donor has been associated faster immune recovery, less severe GVHD, low transplant-related mortality (TRM) and better survival in both TCD and unmanipulated haploidentical transplant with PTCy[3]. Not only better survival but younger donor can provide other potential benefits such as the ability to better tolerate the collection procedure, providing higher CD34+ cell yield and lower likelihood of clonal hematopoiesis and future risk of developing malignancies.

3. Donor Sex

It has been shown that minor HLA antigens in Y chromosome may increase GVHD as well as graft versus tumor effect in a setting of a female donor to a male recipient transplantation. We have previously shown in an HLA-matched SCT that female donors for male recipients associated with higher incidence of acute GVHD, higher TRM and lower relapse resulted in similar survival compared with other donor-recipient sex combinations[25]. This is particularly important when the main target of GVL from the graft is minor HLAs. However, in the setting of a major HLA mismatch like haploidentical transplantation, using stem cells from a female donor to a male recipient seems to have more negative impact on outcomes. In the PTCy platform, Kasamon and colleagues found that transplantation using a female donor to a male recipient resulted in lower survival[26]. It is therefore recommended that a male donor should be a preferred donor choice when selecting a donor for male recipients at least in the TCR haploidentical transplantation using PTCy.

4. Donor-recipient Relationship

In an unmanipulated haploidentical SCT, high risk of graft failure has been reported using a parent donor in comparison with an offspring. This impact is independent to donor age[27]. While in TCR haploidentical transplantation using the Beijing protocol, a higher NRM, acute GVHD and lower survival with mother than father donors has been reported[28]. On the contrary, in TCD haplo, it has been shown that a mother donor was associated with less relapse, lower NRM and better EFS compared with a father donor[29].

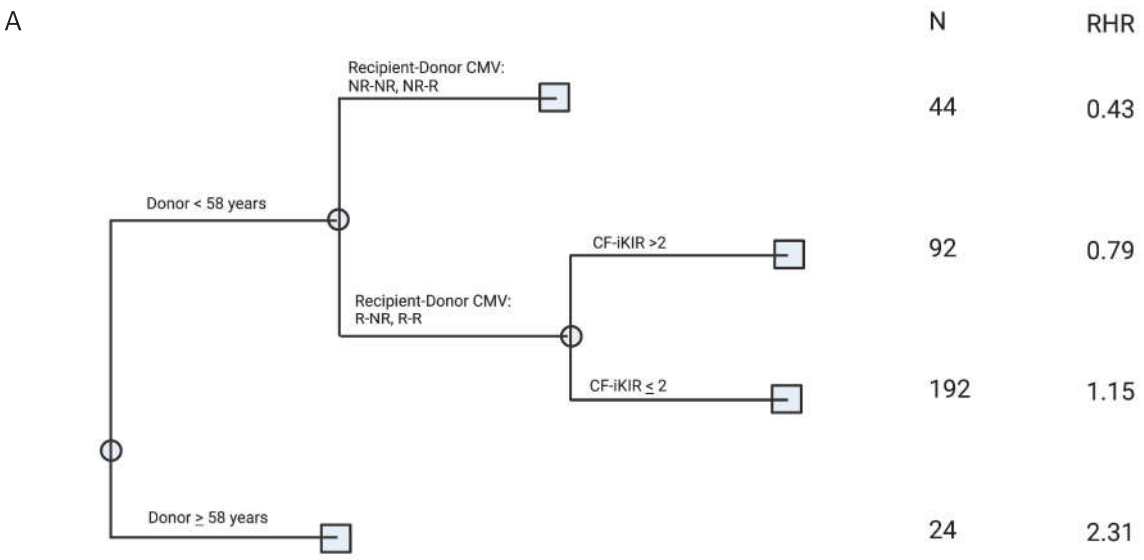
A second degree relatives have also been used as a haploidentical donor which showed similar results to first-degree relative donors[30]. However, using the Beijing protocol, Wang and colleagues found that second-degree haploidentical donors associated with higher TRM and lower survival in comparison with 1st degree relatives[28].

5. Donor-recipient ABO compatibility

ABO mismatch between a donor and a recipient can cause immunologic complications in allo-SCT. Major ABO mismatch can induce anti-donor isoagglutinin causing delayed RBC engratment, pure red cell aplasia as well as hemolytic anemia, while minor ABO mismatch can cause acute hemolysis from donor plasma or donor passenger lymphocyte syndrome. However, the impact of ABO mismatch on major transplant outcomes like NRM or survival remains controversy with conflicting data have been reported to date. Data from the EBMT showed that major ABO mismatch was associated with inferior engraftment rate whereas bi-directional mismatching increased risk of acute GVHD. Interestingly, this study also demonstrated that major ABO mismatch was associated with poor survival in patients receiving BM but not PB graft[31].

6. NK Cell Alloreactivity

NK cell alloreactivity has been shown to have different impact on outcomes of haploidentical SCT when different platforms and different KIR hypotheses are used. For instance, in the TCD and unmanipulated haploidentical SCT with PTCy, NK cell alloreactivity seems to have positive impact on outcomes, such as reduce risk of relapse and increase survival. On the other hand, in the Beijing protocol, higher incidence of GVHD, NRM and worse survival were reported when



	Donor age	Recipient-Donor CMV status	CF-iKIR score	N	3-yr OS	HR (adjusted)	95%CI	P value
Group 1: Best	<58	NR-NR or NR-R	Any	44	73.9	Ref		
Group 2: Better	<58	R-NR or R-R	>2	92	54.1	1.84	1.12-3.69	0.044
Group 3: Poor	<58	R-NR or R-R	≤2	192	44.5	2.70	1.41-5.19	0.003
Group 4: Worst	≥58	Any	Any	24	18.5	5.44	2.54-11.64	<0.001

Figure 1A. The algorithm to optimize donor selection by incorporating donor characteristics and NK cell alloreactivity

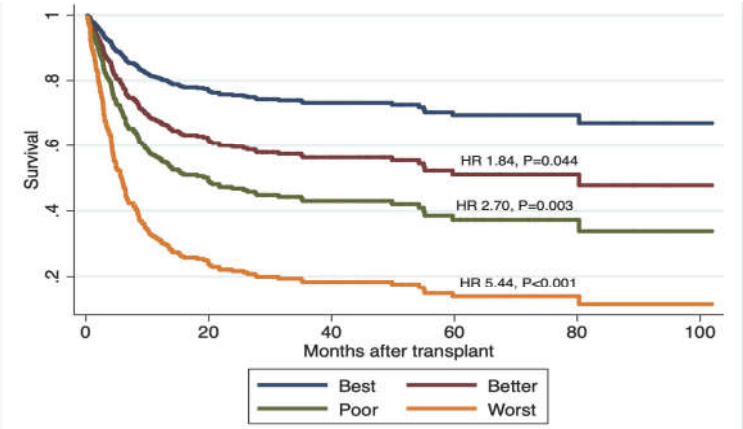


Figure 1B. Adjusted overall survival by donor risk group

having KIR ligand mismatch between the donor and recipient. We recently studied the impact of NK alloreactivity using several models on outcomes of haploidentical SCT and found that a donor with NK cell alloreactivity predicted by count functional inhibitory KIR score is associated with improved PFS and OS of patients. Based on this result, we developed an algorithm to optimize donor selection by incorporating donor characteristics and NK cell alloreactivity (**Figure 1A**) (Kongtim P et al, *Submitted manuscript*).

7. Donor-recipient CMV Serostatus

Conflicting data have been reported on the impact of donor-recipient CMV serostatus on clinical outcomes of haploidentical SCT. Our group has demonstrated that recipient- but not donor CMV serostatus influenced OS and PFS (**Figure 1B**) (Kongtim P et al, *Submitted manuscript*).

8. Degree and characteristics of HLA mismatch

In an HLA-matched SCT, higher degree of HLA mismatch is associated with poor outcomes. However, studies have demonstrated that in unmanipulated haploidentical SCT using either PTCy and the Beijing protocol, degree of HLA mismatching did not influence NRM, relapse, PFS or OS.

The impact of HLA mismatches at molecular level has also been studied and recently reported by our group which showed that HLA-A mismatch eplets in HVG direction is associated with a reduced risk of relapse and improved survival. Based on the result from this study, ME analysis of individual HLA loci might assist donor selection and risk stratification in haploidentical SCT[32].

In conclusion, data on the impact of different donor characteristics on outcomes of haploidentical SCT have emerged over the recent years. Carefully select donor who can provide the best outcomes for the recipient is one of the most important elements for successful haploidentical SCT.

Is It The End of the Road for Cord Transplant?

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 (e.g. with TCR α/β and CD19 depletion) or novel peri-transplant conditioning and prophylaxis protocols including the widely used PTCy regimen[33].

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[34]. Specifically, 2-year OS after UCB was 46% compared with 57% after haploidentical transplantation (p = .04). Studies using a uniform myeloablative regimen (comprising thiotepa, busulfan, and fludarabine with anti-thymocyte globulin) revealed similar results, with no significant differences in relapse, disease-free, or OS[35]. These results show that haploidentical transplant is at least equivalent to UCB transplantation in outcomes.

However, UCB has certain advantages including immediate availability. UCB in cord blood banks are fully tested and can be thawed from liquid nitrogen for transplantation upon request. Furthermore, despite the lack of donor lymphocyte infusion, UCB transplantation is associated with lower post-transplant relapse rates. A study of 582 patients comparing UCB and fully matched or mismatched adult donor transplantation revealed that mismatched UCB grafts had reduced relapse rates (hazard ratio 2.92, p=0.007 with HLA matched adult donors vs UCB) and superior leukemia-free survival versus fully-matched adult donor stem cells, suggesting superior leukemia control with UCB grafts despite more manageable GVHD[36]. This phenomenon could be related to the robust immunological potential albeit allogeneic pliability of UCB immune cells.

Ongoing studies show continued progress in UCB transplantation with improving outcomes with modifications in conditioning regimens as well as hematopoietic stem cell expansion. A prospective phase 3 multicenter study of ex-vivo expanded hematopoietic stem cell versus conventional UCB transplantation, patients who received expanded grafts experienced accelerated neutrophil engraftment (12 days vs 22 days; $p < 0.001$), faster platelet recovery, lower incidence of first grade 2 to 3 bacterial or invasive fungal infection, and spent more time out of hospital during the first 100 days after transplant (median, 61 vs 48 days; P = .005) than controls[37].

Haploidentical transplantation has largely 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[38] could result in a resurgence in usage if costs could be controlled.

Conclusions

Current results with both UCB and haploidentical transplantation are excellent. In the absence of a readily available full matched related or unrelated donor, no patient should have the lack of an immediately available stem cell donor for transplantation.

Author Contributions

WYKH wrote the abstract, introduction, and conclusions as well as the section on "Is it the end of the road for cord blood transplant". PK, NSM, and MY wrote the sections on "Donor Selection for Haploidentical Hematopoietic Stem Cell Transplantation", "Bone Marrow Or PBSC: Does It Really Matter In T-replete Haploidentical Transplantation", and "Allogeneic stem cell transplantation using alternative donor in acute leukemia - current status", respectively.

Conflicts of Interest

The authors declare that they have no relevant conflicts of interest. The disclosure forms provided by the authors are available online. WHYK is a member of the Editorial Board of Blood Cell Therapy and of the Board of Directors of the Singapore Cord Blood Bank. He is not involved in the editorial evaluation or the decision to accept this article for publication.

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