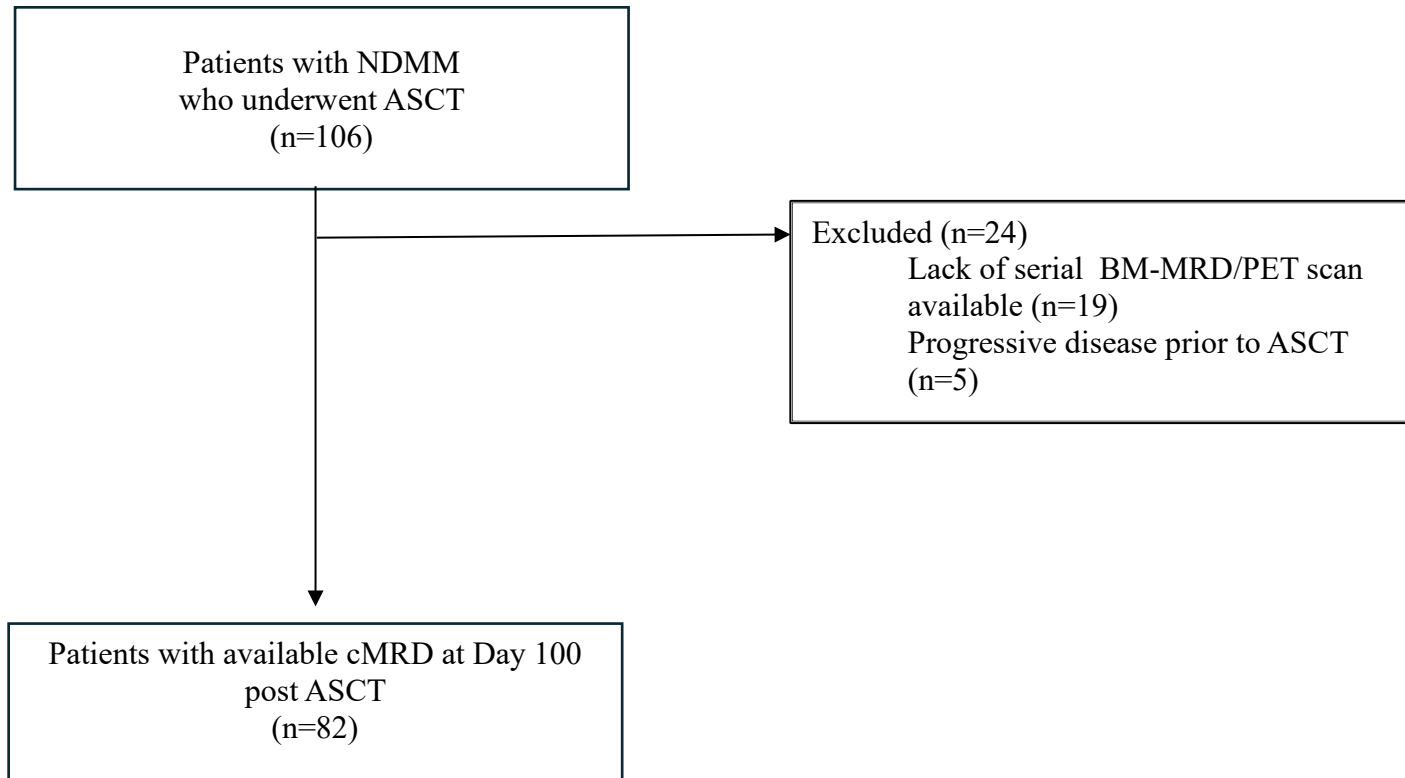


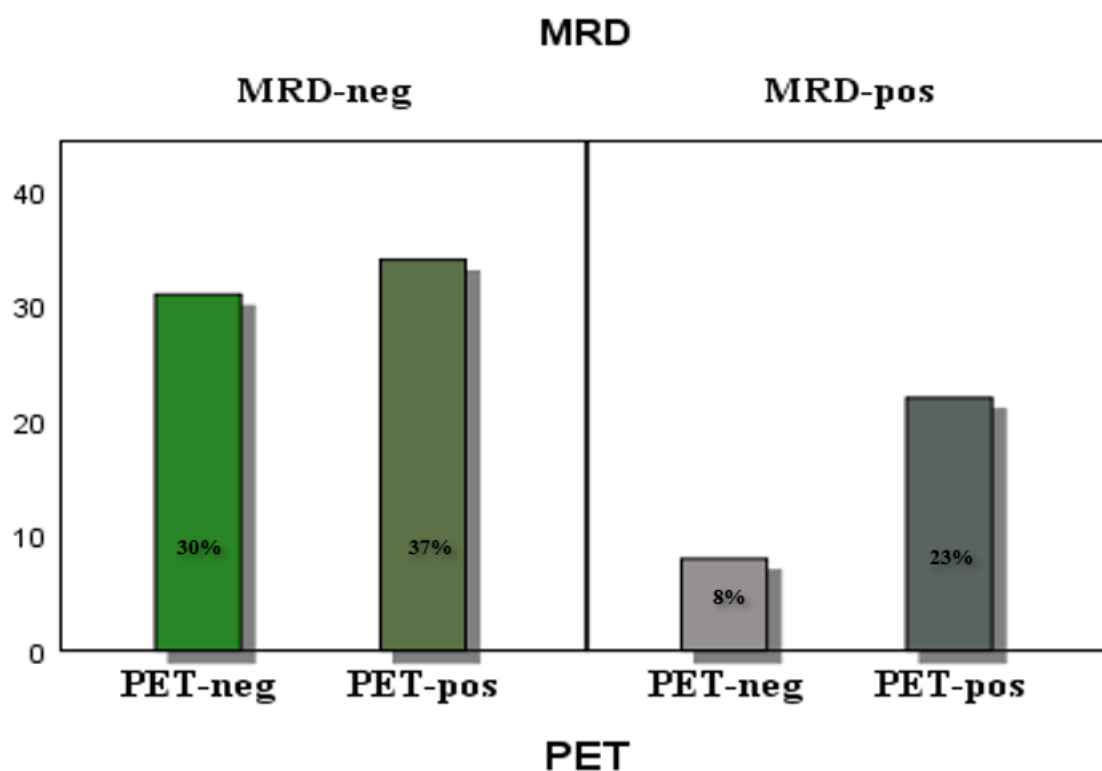
Supplementary Figure 1: Consort diagram of study



Supplementary Table 1: Comparison of baseline characteristics among the cMRD negative and positive group at both time point

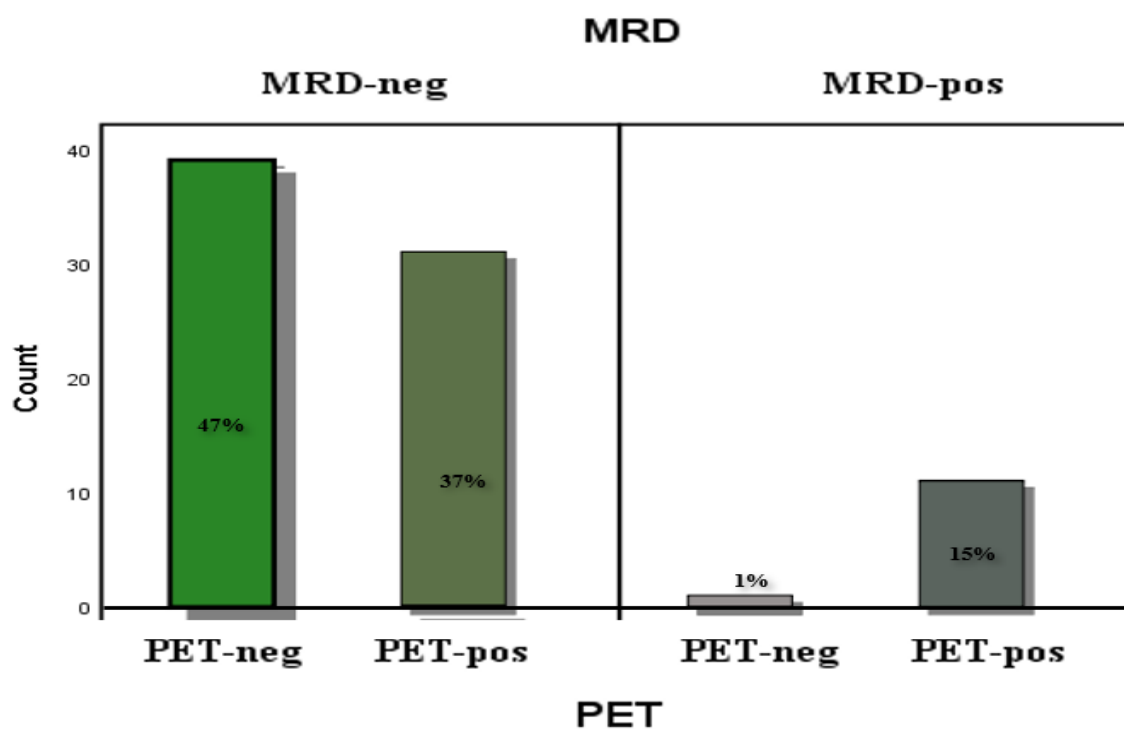
| Baseline characteristics | | cMRD ^{PRE-} N=25 | cMRD ^{PRE+} N=57 | P value | cMRD ^{POST-} N=39 | cMRD ^{POST+} N=43 | P Value |
|--|-------------|------------------------------|------------------------------|---------|-------------------------------|-------------------------------|---------|
| Median Age (IQR) | | 56(48-60) | 53(49.5-59) | 0.89 | 53(51-60) | 54(46-60) | 0.58 |
| Renal impairment at diagnosis (n,%) | | 12(48) | 19(33) | 0.226 | 19(49) | 12(28) | 0.069 |
| HRCA at diagnosis * (n,%) | | 5(20) | 13(22) | 1.00 | 8(20.5) | 10(23.3) | 0.79 |
| ISS(n,%) | 1 2 or 3 | 6(24) 19(76) | 10(47(| 0.9 | 12 27 | 7 36 | 0.139 |
| Initial treatment (n,%) | VRd | 8(32) | 28(49) | 0.22 | 15(38) | 22(52) | 0.61 |
| | VCd | 9(36) | 21(37) | | 17(43.5) | 13(30) | |
| | VTd | 4(16) | 5(9) | | 4(10) | 4(9) | |
| | Dara-VRd | 4(16) | 3(5) | | 3(7.5) | 4(9) | |
| Median duration of treatment in month prior to ASCT(IQR) | | 11(8.4-14) | 11(8-19.5) | 0.74 | 12(9-18) | 11(7-18) | 0.44 |
| Duration of anti-myeloma therapy pre-ASCT | | | | 0.4 | | | 0.054 |
| <6 months [n,%] | | 3(12) | 10(17.5) | | 3(7.7) | 10(23.2) | |
| ≥ 6 months [n,%] | | 22(88) | 47(82.5) | | 36(92.3) | 33(76.8) | |
| Prior line Treatment (n,%) | | | | 0.262 | | | 0.192 |
| 1 | | 20(80) | 43(75) | | 32(82) | 31(72) | |
| 2or more | | 5(20) | 14(25) | | 7(18) | 12(28) | |
| Response pre-ASCT (n,%) | | | | 0.151 | | | 0.264 |
| CR | | 18(72) | 31(54.5) | | 26(67) | 23(54) | |
| Not in CR | | 7(18) | 26(45.5) | | 13(33) | 20(47) | |
| Maintenance (n,%) | | | | 0.145 | | | 0.260 |
| Singlet | | | | | | | |
| IMiD | | 21(84) | 35(66) | | 30(76) | 26(60) | |
| PI | | 1(4) | 7(13) | | 5(14) | 3(7) | |
| Doublet(IMiD and PI) | | 2(8) | 11(21) | | 4(10) | 9(21) | |

Supplementary Figure 2 (A): Bar diagram representing the concordance between BM-MRD and PET-CT at the pre-ASCT time point S2a and S2b



Cohen's kappa for concordance was = 0.1

Supplementary Figure 2 (B):



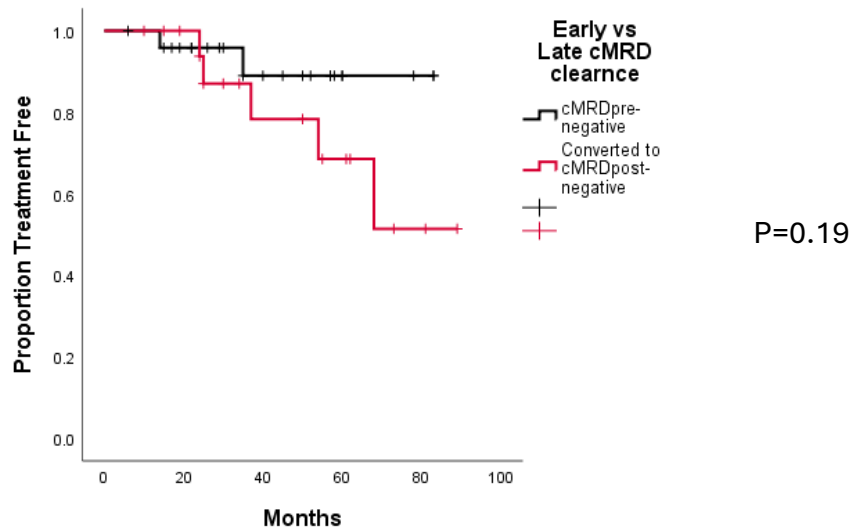
Cohen's kappa for concordance was = 0.23

Supplementary Table 2: Estimated Time to next treatment and Overall Survival in the study population amongst various MRD response categories

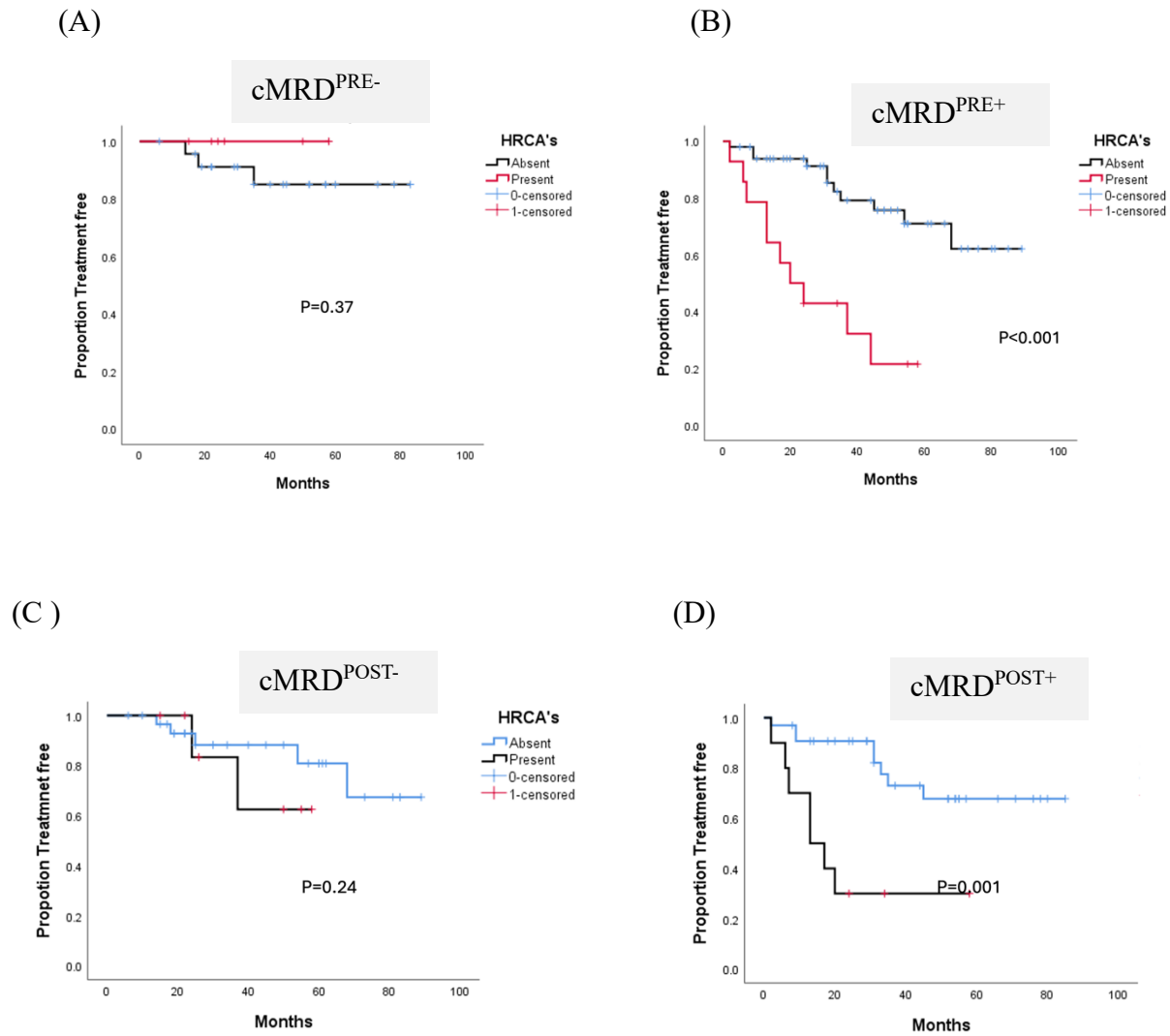
| | Proportion Treatment free at 3 year (%,SE) | P value | Proportion Surviving at 3 year (%,SE) | P value |
|--|---|----------------|--|----------------|
| Pre ASCT BM-MRD- BM-MRD+ | 84± 5 59 ± 10 | 0.002 | 86 ± 6 92± 3 | 0.24 |
| Pre ASCT PET-CT- PET-CT+ | 86 ± 7 69 ± 7 | 0.128 | 93 ± 3 88 ± 4 | 0.30 |
| Post ASCT BM-MRD- BM-MRD+ | 80±5 42±10 | 0.02 | 90±4 72±9 | 0.042 |
| Post ASCT PET-CT- PET-CT+ | 79±7 68±7 | 0.28 | 94±2 85±5 | 0.16 |
| Pre ASCT MRD-PET- Either Positive MRD+PET+ | 88±6 75± 8 53± 11 | 0.002 | 91±3 95± 2 80± 8 | 0.15 |
| Post ASCT MRD-PET- Either Positive MRD+PET+ | 82±7 70±9 48±16 | 0.089 | 92±5 90±5 70±14 | 0.02 |
| cMRD ^{PRE} - cMRD ^{PRE} + | 91±4 67±6 | 0.009 | 92±3 85±5 | 0.16 |
| cMRD ^{POST} - cMRD ^{POST} + | 82±7 65±7 | 0.116 | 92±5 85±5 | 0.169 |

Median follow-up 35 months (22-58)

*ASCT- Autologous Stem Cell Transplant, MRD- Minimal Residual Disease by BM FCM, cMRD- integrated MRD



Supplementary Figure 3: Kaplan Meir survival analysis for TTNT stratified according to early cMRD negativity defined by cMRD^{PRE-} vs late cMRD negative (Those having cMRD^{PRE+} but converted to cMRD^{POST-})



Supplementary Figure 4: (A) Kaplan Meir showing TTNT stratified according to presence or absence of HRCA's at diagnosis among (A)cMRD^{PRE-} cohort, (B) cMRD^{PRE+} cohort, (C) cMRD^{POST-} cohort, (d)cMRD^{POST}

Supplementary Table 3: summarises salient studies that have analysed the role of PET CT at various time points

| Study (Year) | Induction strategies | Timing of PET/CT | PET-Negativity Rate | Key Findings |
|--|--|---|----------------------------------|---|
| CASSIOPET (2021) (n=) | 4 cycles Dara VTD/VTD +ASCT +2 cycles DaraVTD/VTD | After consolidation, before maintenance | 64%* | PET-negativity associated with better progression-free survival (PFS); PET/CT negativity is a strong prognostic marker. |
| Zamagni et al. (2015) (n=282) | Conventional chemotherapy based , Bortezomib based and Thalidomide based | 3 month post ASCT | 70% | PET-negativity observed in 70% of patients; associated with improved PFS and OS. |
| Kaddoura et al. (2021) n=229 patients) | Conventional chemotherapy based , Bortezomib based and Thalidomide based | Day 100 post-ASCT | 35% | PET-negativity at day 100 post-ASCT associated with longer time to progression (TTP) and OS. |
| Imajem study (July 2017) N=155 patients (63 received ASCT) | 3 cycles VRd +ASCT+2 cycles VRd | At pre-maintenance | 75% | PET-negativity at maintenance associated with better PFS |
| Current study(N=82) | Median 11 cycle of VRd /VCd +ASCT | Pre Transplant and Day 100 post ASCT | Pretransplant 38% Day 100-49% | PET negativity before ASCT associated with longer Time to next treatment |