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INTEGRATED ASSESSMENT OF MEASURABLE RESIDUAL
DISEASE (MRD) BY BONE MARROW FLOW CYTOMETRY AND
(18) F-FDG PET/CT SCAN IN MULTIPLE MYELOMA POST
TRANSPLANT : A PROSPECTIVE STUDY

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INTRODUCTION

- Measurable residual disease (MRD) in the bone marrow (BM) by flow cytometry is an important tool for assessing depth of treatment response and is strong predictor of progression free survival for multiple myeloma (MM) patients⁽¹⁾.
- 18F-FDG PET/CT is a non-invasive imaging technique that assesses overall disease burden by detecting metabolically active from inactive lesions, which makes it an appropriate method for evaluating treatment response in multiple myeloma patients⁽²⁾.
- We hypothesized that dual assessment of MRD using BM flow cytometry and PET/CT may be more robust rather than either of two methods.
- We prospectively evaluated MRD for MM patients on day +100 post autologous stem cell transplantation using BM flow cytometry and 18F-FDG PET/CT scan.

METHOD

- In this prospective study 37 consecutive MM patients who underwent ASCT between Nov, 2022 to Dec, 2024 were studied. All patients had received initial induction therapy 4 to 6 cycles followed by high dose melphalan and ASCT. Transplant response was assessed on day +100 as per IMWG criteria⁽³⁾.
- MRD by flow cytometry was performed by bulk lyse-stain-wash technique. A total of 5 million and more viable events were acquired per tube (detection limit $\geq 1 \times 10^{-5}$). Two tube 10 colour panel was used for surface and cytoplasmic markers. Gating was done using CD38 versus CD138 versus CD45. Adequacy was assessed by relative abundance of mast cell, hematolgones and myeloid precursors. Presence of MRD was assessed on the basis of aberrant immunophenotype and clonal restriction.
- 18F-FDG PET/CT data analysis was conducted using the IMPeTUs criteria⁽⁴⁾, which considered bone marrow metabolic status according to the 5-point Deauville score (DS), as well as the number and metabolic activity of focal lesions and paramedullary disease (PMD); PET negativity was defined as FDG uptake equal to or lower than the liver background.
- Data were analyzed using SPSS version 25.

RESULTS

- Patients median age was 57 years (range 43 to 71 years); 51.4% were males and 45.9% had ISS stage III. 21.6% patients had high risk cytogenetics.
- Pre-transplant 27% were in complete response(CR). 19 (51.4%) patients had very good partial response(VGPR), partial response(PR) in 6 (16.2%) and 2(5.4%) had a progressive disease(PD).
- Post ASCT- 34(91.9%) patients were in CR and 25(67.6%) were MRD negative on BM flow cytometry. Response to induction (CR+VGPR) ($p < 0.01$), pretransplant chemo-sensitive disease (CR+VGPR), $p < 0.02$ and response to transplant were predictive of MRD negativity.
- On Day +100 (± 7 days) post ASCT, 26(70.3%) patients were flow MRD negative and PET negative, 4(10.8%) each, were flow MRD negative and PET positive, flow MRD positive and PET negative and 3(8.1%) patients were both flow MRD and PET positive.
- Flow MRD negative patients had superior median progression free survival (mean PFS 27.7 months \pm 0.887 (SE), $p < 0.05$) compared to flow positive, regardless of PET/CT scan status.
- At a median follow up of 15.5 months, four patients had relapsed, 3 of them were flow MRD positive on day +100.

Data Analysis

Gender	MRD- PET-	MRD+ PET-	MRD- PET+	MRD+PET+	p Value
MALE	13	3	2	1	
FEMALE	13	1	2	2	0.691
ISS	MRD- PET-	MRD+ PET-	MRD- PET+	MRD+PET+	p Value
ISS I	7	0	1	0	
ISS II	9	2	1	0	
ISS III	10	2	2	3	0.471
R-ISS	MRD- PET-	MRD+ PET-	MRD- PET+	MRD+PET+	p Value
R-ISS I	4	0	0	0	
R-ISS II	4	2	1	0	
R-ISS III	13	2	2	3	0.554
Subtype	MRD- PET-	MRD+ PET-	MRD- PET+	MRD+PET+	p Value
Ig G K	5	2	2	0	
Ig G L	6	0	0	1	
Ig A K	1	0	2	1	
Ig A L	1	0	0	1	
K	11	1	0	0	
L	2	1	0	0	0.066
FISH	MRD- PET-	MRD+ PET-	MRD- PET+	MRD+PET+	p Value
Standard risk	11	4	1	1	
High risk	6	0	1	1	
Not known	5	0	2	1	0.433
Pretransplant status	MRD- PET-	MRD+ PET-	MRD- PET+	MRD+PET+	p Value
CR	8	0	1	1	
VGPR	15	3	1	0	
PR	3	1	2	0	
STABLE	0	0	0	0	
PD	0	0	0	2	<0.001
Day +100 response	MRD- PET-	MRD+ PET-	MRD- PET+	MRD+PET+	p Value
sCR	6	1	0	1	
CR	20	3	3	0	
VGPR	0	0	1	0	
PR	0	0	0	1	
<PR	0	0	0	1	<0.001

CONCLUSION

We conclude that MRD negativity by bone marrow flow and PET/CT scan on day +100 post- transplant identifies a subset of patients with superior outcome.

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