COULD DAY +30 T-CELL EXHAUSTION BIOMARKERS GUIDE MAINTENANCE CHOICE POST AUTOLOGOUS STEM CELL TRANSPLANTATION IN RELAPSED MULTIPLE MYELOMA

MM - 064

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INTRODUCTION

T-cell depletion and immunological dysfunction are key factors in multiple myeloma (MM) relapse. Immune competence is partially restored by autologous stem cell transplantation (ASCT), but the best post-ASCT maintenance in the context of relapse is still unknown.

AIM

We aimed to assess whether the immune checkpoint receptors PD-1, TIM-3, and LAG-3 expression early after ASCT indicate hallmark in maintenance choice of IMiDs in compare to anti-CD38.

METHOD

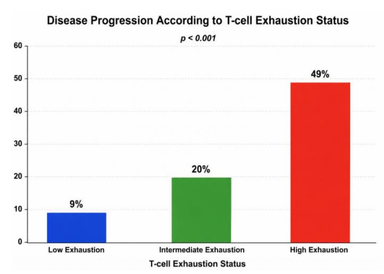
PD-1, TIM-3, and LAG-3 expression on CD8+ and CD4+ T cells was measured by flow cytometry in this prospective observational cohort of patients with relapsed MM following salvage therapy with Drara-RD followed by ASCT.

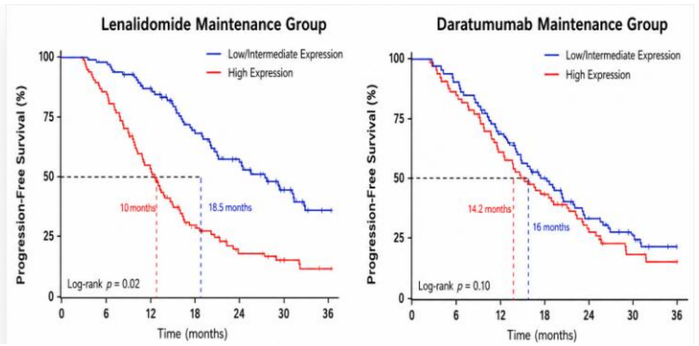
Peripheral blood immune profiling was conducted on Day +30 post-ASCT. Patients were classified as low (no marker elevated), intermediate (one marker elevated), or high (≥2 markers co-expressed). Elevated expression was defined as above predefined thresholds from healthy donor controls. Maintenance therapy (IMiD-based or Dara-based) was adopted. Progress-free survival (PFS) from a Day +100 served as the main endpoint.

RESULTS

High markers elevated (25 patients) were associated with more plasma cell infiltration (p = 0.03), higher β2-microglobulin (p = 0.04), lower hemoglobin at transplant (p = 0.02) and trend to be high cytogenetics risk (p = 0.06).

No correlation observed between markers expression and response immediately after ASCT (p = 0.1) or with negative MRD on Day +100 (p = 0.8). However, at 12 months post-ASCT, 9% of patients in the low exhaustion progressed, compared to 20% in the intermediate group and 49% in the high exhaustion group (p < 0.001). With median follow up of 22 months, PFS was significantly better in low versus intermediate versus high expression group (median PFS; 19.4 months vs 12 months versus 8.1 moths, respectively with p = 0.05). In lenalidomide maintenance group; median PFS was better in low/intermediate versus high expression (median PFS 18.5 versus 10 months, p = 0.02) while, in Daratumumab maintenance group; no significant difference in median PFS in low/intermediate versus high expression (median PFS 16 versus 14.2 months, p = 0.1).





CONCLUSIONS

In low/intermediate expression patients; Lenalidomide maintenance was effective and Daratumumab did not add advantage however, in high expression patients; Lenalidomide maintenance performed poorly while, Daratumumab maintenance showed improved PFS. This study supports early (Day +30) post-ASCT PD-1, TIM-3, and LAG-3 expression could guide selection of maintenance treatment.

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