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Monoclonal Gammopathies & Multiple Myeloma

BCMA GENOTYPES IN RELATION TO PROGNOSIS AND INDUCTION AND MAINTENANCE THERAPY IN MULTIPLE MYELOMA PATIENTS

M.L. Del Giudice[1], M. Magrini[2], M. Vitiello[2], S. Mori[2], R. Silvestri[2], F. Rea[2], M. Cipollini[2], R. Foddis[3], S. Galimberti[1], F. Gemignani[2], S. Landi[2], G. Buda[1]

[1]Hematology Unit, Department of Clinical and Experimental Medicine, University of Pisa; [2]Genetic Unit, Department of Biology, University of Pisa; [3]Department of Translational Research and of New Surgical and Medical Technologies, University of Pisa.

Introduction: Multiple myeloma (MM) is an incurable plasma cell malignancy, and predicting prognosis and personalising treatment remain key challenges. This study examines genetic variability in MM patients to enhance risk stratification, with a focus on BCMA, a plasma cell surface protein that is important for MM biology and targeted therapies. We genotyped polymorphisms in the BCMA gene and correlated them with MM risk, disease progression, treatment response and overall survival.

Methods: A total of 305 MM patients diagnosed according to IMWG criteria followed between 2020 and 2024 at the Hematology Unit, University Hospital in Pisa, Italy, were enrolled. A total of 193 patients underwent autologous stem cell transplantation (ASCT); 174 of these patients underwent VTD ± daratumumab as induction therapy. The present study examined the effects of VTD and Dara-VTD in a sample of 129 and 45 patients, respectively; 55 patients underwent maintenance therapy. Exposure to the main drug classes was documented, with particular attention paid to anti-CD38 antibodies: 146; proteasome inhibitors: 249; lenalidomide: 214. A tagging-SNP approach was applied using data from the Ensembl Project and LDlink, selecting SNPs with MAF ≥ 5% in the European population (in BCMA: rs3850997, rs11075036, rs11570151). A dominant model was applied, grouping rare homozygotes with heterozygotes. Analyses were performed using RStudio (v4.4.0) and MedCalc. Studies were approved by the Regional Ethics Committee (IDs: 18182 and 21498).

Results: This study identifies SNP rs3850997 in BCMA as a potential prognostic marker in MM patients undergoing autologous stem cell transplantation, particularly in the context of maintenance therapy decisions. T-allele carriers (G/T and T/T) in the no-maintenance cohort (n = 119) exhibited a longer progression-free survival (HR = 0.65, 95% CI: 0.35–0.88, p = 0.013). This effect was not observed when maintenance-treated patients were included.

Conclusions: These findings suggest that patients with the G/G genotype significantly benefit from maintenance therapy, whereas T-allele carriers may not benefit further and could potentially avoid unnecessary treatment. These results provide a basis for future studies involving anti-BCMA therapies and support the use of genetic stratification to guide therapy de-escalation for selected patients, thus reinforcing the concept of precision medicine in myeloma management. Further validation in larger, independent cohorts is required to confirm these findings and explore genotype–therapy interactions with targeted agents.