IMPACT OF DOUBLE-HIT GENETICS ON REAL-WORLD OUTCOMES OF MULTIPLE MYELOMA PATIENTS UNDERGOING AUTOLOGOUS STEM CELL TRANPLANTATION (ASCT) – A UK ASCT CENTRE EXPERIENCE

Panopoulou, Katerina[1,2]

[1]Institute of Cancer Research, London, [2]Royal Marsden Hospital NHS Foundation Trust

Background: Despite the recent improvements in newly diagnosed (ND) Multiple Myeloma (MM) outcomes, remission times, in particular after ASCT, remain variable. Better outcome prediction post-ASCT could highlight populations in particular need for individualised post-ASCT management and potentially inform optimal allocation of resources. Genetic biomarkers including chromosomal aberrations t(4;14), t(14;16), and t(14;20) translocations, gain(1q) and del(17p), have been associated with adverse outcome, and co-occurrence of ≥2 such aberrations (a Double-Hit) is predictive of especially aggressive disease. We investigated the prognostic impact of genetics in a real-world setting.

Methods: Electronic records of all ASCT recipients for NDMM indication at the Royal Marsden Hospital between January 2014-October 2019, were retrospectively reviewed.
Only patients with a full complement of cytogenetic risk by Fluorescent *in situ* Hybridisation (FISH) reported for the above lesions were included. Co-occurrence of ≥2 lesions was classified as Double-Hit, and a single lesion as Single-Hit.

Results: We identified 139 patients eligible for evaluation. Clinical and genetic characteristics were representative of a transplant-eligible cohort with regards to age, sex, ISS and number of genetic lesions.
Double-Hit patients had significantly shorter median PFS (15.1 months, 95%CI: 95% CI: 2.73-NA) compared with Single-Hit (24.6 months, 95%CI: 20.12-27.6) and No-Hit (35.7 months,95% CI: 28.8-39.7), (p =0.00063). Median OS for Double-Hit was 49.2 months, whereas it was not reached for the remaining groups (p =0.034). In only 1.4% of the No-Hit cohort did the myeloma relapse within 6 months post-ASCT, whereas relapses in the same timeframe were observed in 7.3% and 30.8% of the Single-Hit and Double-Hit cohorts respectively.

Conclusions: We demonstrate that detailed genetic profiling, specifically the combined assessment of adverse genetics, can help stratify NDMM patients undergoing ASCT in a standard of care setting. This approach can support identifying patients with particular need for intensified monitoring and post-ASCT therapy in a standard clinical setting already at diagnosis.