2. NEWLY DIAGNOSED MULTIPLE MYELOMA

CORRELATION OF THE CIRCULATING TUMOR CELLS AND R2-ISS SCORE IN NEWLY DIAGNOSED MYELOMA PATIENTS: RWE EXPERIENCE

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Background. Several prognostic stratifications, as second revision of the ISS (R2-ISS) score have been established in order to define high-risk patients (pts) with multiple myeloma (MM). Circulating tumor cells (CTC) in MM emerged as a important and minimally invasive prognostic biomarker of tumor dissemination and disease aggressiveness, especially in the settings of the routine clinical practice. The aim of study was to evaluate in the real-world settings prognostic impact of CTC burden in correlation with R2-ISS stratification on the treatment response, and survival outcome in newly diagnosed MM (NDMM) pts.

Patients and Methods. During period March 2023-March 2025 at the Clinic of Hematology, University Clinical Center of Serbia, CTC presence was analyzed in 79 NDMM pts (male 33pts, 41.8%; female 46pts, 58.2%), with median age 67 yrs (range: 32–82yrs). According to the paraprotein type, IgG MM was found in 51 pts (64.6%), IgA in 14 pts (17.7%), and BJ in 13 pts. (16.5%). Clinical stage I (CS, Durie & Salmon, CS I) was confirmed in 8 pts (10.1%), II in 12 pts (15.2%,) and III in 59 pts (74.7%). Renal impairment was present in 16 pts (20.3%). Extramedullary disease (EMD) was present in 6pts (7.6%), while double-hit MM was identified in 14pts (17.7%). Regarding R2-ISS scoring system: R2-ISS 1 was confirmed in 14 pts (17.7%), R2-ISS 2 in 24 pts (30.4%), 34 pts (43%) had R2-ISS 3, and 7 pts (8.9%) had R2-ISS 4. Median CTC concentration was 0.6/μL (range 0.0–389.3), and median CTC percentage was 0.008% (range 0.0–4.424%). The CTC-high risk MM (CTC >0.02%) was identified in 49 pts (62.02%), and ultra-high risk MM (CTC ≥2%) in 4 pts (5.06%). Bortezomib plus immunomodulatory drugs (Bz+IMiD) based therapy was applied in 68 pts (53.7%) and Daratumumab-based in 11 pts (8.69%).

Results. CTC-high risk MM status correlated with the degree of bone marrow plasma cell infiltration (ρ = 0.34, p= 0.002). Double-hit MM was strongly associated with CTC burden, being present in 16.3% of CTC-high risk MM pts, and in all of CTC ultra-high MM pts (p = 0.002). Statistically significant correlation was observed between CTC high--risk MM and R2-ISS stage (ρ =0.31, p=0.005). Overall treatment response (≥ partial remission, PR) was achieved in 70pts (88.6%). During 24months of follow-up, progression of disease (PD) occurred in 13 pts (16.5%) with lethal events in 7 pts (8.9%).

Conclusion. CTC burden significantly correlates with established prognostic stratifications as R2-ISS score, possibly providing solid ground base for MM high-risk model incorporating both of these features.