2. NEWLY DIAGNOSED MULTIPLE MYELOMA

THE LONG TERM PROGNOSTIC IMPACT OF CHROMOSOME 1 ABNORMALITIES IN NEWLY DIAGNOSED MULTIPLE MYELOMA PATIENTS

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The possible prognostic role of chromosome 1 abnormalities has been recently underlined by the revised International Staging System (R-ISS) and confirmed by the international myeloma working group (IMWG) which formulated a consensus genomic staging of high-risk multiple myeloma (MM). Nevertheless, the prognostic role of chromosome 1 abnormalities remains controversial. In this study we have investigated the prognostic role of chromosome 1 abnormalities in a cohort of newly diagnosed MM (NDMM) performing a retrospective monocentric analysis of 95 patients between 2017 and 2022. The median follow up was 66 months for the overall survival (OS) and progression free survival (PFS) and 55 months for the time to next treatment (TTNT) The prevalence of cytogenetic abnormalities was as follows: t(4;14) in 8.4%, t(14;16) in 2.1%, t(14;20) in 1.1%, del(13q) in 47.4%, del(17p) in 18.9% (cut off >20%), del(1p) in 21.1%, gain(1q) in 45.3%, and amp(1q) in 16.8%. By a univariate analyses gain/amp(1q) did not demonstrate a significant negative impact when present as an isolated abnormality. Conversely, isolated del(1p) was associated with significantly shorter OS (p=0.015), PFS (p=0.007), and TTNT (p=0.038). A sub analysis evaluating the combined effect of del(1p) and del(17p) confirmed a pronounced negative impact on PFS and OS (both p<0.0001), as well as on TTNT (p=0.015). Most paired cytogenetic combinations did not show a consistent additive prognostic effect. In several models, the adverse risk was primarily driven by a single lesion, most frequently del(1p) or del(17p), rather than by their co-occurrence. Interestingly, an additive effect was observed only for the combined presence of del(17p) and del(1p): patients harboring both alterations showed markedly inferior outcomes compared to those with single lesions or no alterations, with significantly increased hazards for OS (HR 6.97, 95%CI 2.94–16.54), PFS (HR 6.92, 95%CI 2.89–16.55), and TTNT (HR 5.21, 95%CI 1.69–16.05). On the other hand, combinations involving gain(1q) or amp(1q) did not demonstrate a consistent synergistic effect. To further assess the independent prognostic contribution of del(1p) we performed multivariate Cox proportional hazards models for OS, PFS, and TTNT. In the OS model, ISS III was associated with an increased risk of death (HR 4.15, 95%CI 1.64-10.46), while patients harboring both del(17p) and del(1p) exhibited markedly inferior survival (HR 6.67, 95%CI 2.39–18.61). Undergoing Autologous stem cell transplantation (ASCT) was independently associated with improved OS (HR 0.40, 95%-CI 0.17–0.94). For PFS, ISS III and the combined presence of del(17p) and del(1p) remained significantly associated with shorter time to progression (HR 5.92, 95%CI 2.24–15.62), whereas achieving ≥VGPR conferred a substantial protective effect (HR 0.26, 95%CI 0.15–0.48). Similar findings were observed for TTNT, where del(17p) plus del(1p) retained a strong negative impact (HR 5.21, 95%CI 1.53–17.7), and ≥VGPR was associated with prolonged treatment free intervals. Our study suggests that del(1p), rather than the gain/amp(1q) abnormalities is an independent adverse prognostic factor in NDMM patients either alone or in combination with the presence of the del(17p), in shaping the prognosis of NDMM.