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Monoclonal Gammopathies & Multiple Myeloma

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

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Introduction: In Multiple Myeloma (MM) the cytogenetic abnormalities del(17p), t(4;14), and t(14;16) have been previously recognized as the most significant one with a negative prognostic impact and incorporated into the R-ISS staging system. More recently chromosome 1 abnormalities have shown a possible prognostic adverse impact with discordant results. In this study we have investigated the prognostic role of chromosome 1 abnormalities in newly diagnosed MM patients (NDMM).

Methods: We performed a retrospective study enrolling 95 patients with NDMM between 2017 and 2022. Patients were stratified into eligibles and ineligibles to autologous stem cell transplant (ASCT) according to the age and the comorbidities. The disease-free survival (PFS), overall survival (OS), and the time from first-line therapy to the need for second-line therapy (TTNT) were analyzed by Kaplan–Meier and log-rank test. The association of the cytogenetic factors and outcomes were assessed by Cox proportional-hazards models. Analyses were performed in R (v4.3) using survival and survminer packages.

Results: At baseline 58% of patients were defined as high risk (HR) an 42% as standard risk (SR); t(4;14) was present in 8.4%, t(14;16) in 2.1%, del(13p) in 47%, del(17p) in 19% (cut-off>20%) del(1p) in 21%, gain(1q) in 28% and amp(1q) in 17%. With a median follow-up of 66 months, the median PFS was 30 months, the TTNT was 50 months, with an OS of 50 months. SR patients showed a better prognosis rather than the HR ones (PFS p=0.014, OS p= 0.03). The presence of del(17p) showed a significant impact (PFS p0.001, OS p<0.0001) in contrast to t(4;14) (PFS p= 0.21, OS p=0.45), t(14;16) (PFS p=0.81, OS p=0.19) and t(14;20) (PFS p=0.79 OS p= 0.4). Del(13q) when isolated did not show a significant impact on survival (PFS p= 0.392, OS p= 0.385, TTNT p=0.057) but acquired a significant role in association with del(17p), giving lower survival (PFS: p<0.001, OS:p<0.001 TTNT: p=0.001). By the univariate analyses we found that gain/amp(1q21) did not show a significant negative impact as isolated abnormalities in NDMM (PFS p=0.690, OS p=0.305, TTNT p=0.910). On the other hand, patients carrying del(1p) isolated had a shorter PFS (HR= 2.0, p=0.007) and OS (HR=2.1, p=0.015). Moreover, the co-occurrence of gain/amp(1q21) and del(1p) showed an impact on PFS and OS. Finally, the co-occurences of del(17p) and del(1p) showed a significant adverse negative impact both in univariate (PFS HR=6.3 p<0.001, OS HR=4.7 p<0.001, TTNT HR=5.5 p=0.001) and multivariate analysis, adjusted for other HR cytogenetic abnormalities, ASCT, ISS and response to therapy (PFS HR=3.4 p<0.001, OS HR=3.1 p=0.019, TTNT HR=4.3 p=0.015).

Conclusions: Our study suggests that del (1p), rather than the 1q abnormalities is an independent adverse prognostic factor in NDMM patients either alone or in combination with the presence of the del(17p).