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## Young Multiple Myeloma Patients (30-50 Years): The Depth of Response to First-Line Treatment Predicts Survival in a Single-Center Cohort Based on Real-World Data

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### ABSTRACT

#### Background

Multiple myeloma (MM) predominantly affects older adults, and real-world data focusing particularly on younger patients are limited. Single-center cohorts can provide detailed information about treatment patterns and outcomes in this subgroup.

#### Purpose

To describe the clinical characteristics and outcomes of young multiple myeloma patients and to identify prognostic factors for overall survival (OS) and disease-free survival (PFS).

#### Methods

We retrospectively analyzed 79 multiple myeloma patients aged 30-50 years who were treated at a single center. Baseline demographic, clinical, laboratory, and treatment-related variables were collected. Overall survival (OS) and disease-free survival (PFS) were estimated using the Kaplan-Meier method and compared using the log-rank test. Variables that were significant in univariate analyses were included in the multivariate Cox regression model.

#### Results

The average follow-up duration reached 46.6 months. Two- and five-year overall survival measured 84.4% and 62.3% respectively, yielding 96.9 months mean overall survival. Two- and five-year disease-free survival reached 86.0% and 64.6% respectively, yielding 75.7 months mean disease-free survival. IgG represented the predominant subtype (46.8%), while 78.5% exhibited bone involvement. Autologous stem cell transplantation (ASCT) occurred in 72.7% of subjects. Survival improved significantly following ASCT ( $p=0.026$ ) and very good partial response (VGPR) ( $p=0.011$ ). Multivariate analysis identified VGPR as the sole independent predictor regarding reduced mortality (HR 0.43; 95% CI 0.19–0.98;  $p=0.045$ ). Conventional clinical/laboratory parameters lacked significant mortality associations. PET-CT utilization correlated with lower PFS ( $p=0.048$ ).

#### Conclusions

In this single-center, real-world data-based cohort of young multiple myeloma patients, long-term survival was primarily driven by treatment-related factors. In this population, achieving a deep response, rather than key biomarkers, appears to be the determinant of outcome.

### RESULTS

#### 1) Patient characteristics

A total of 79 patients aged 30–50 years were included. The median age was 46 years (range, 30–50), and 67.1% were male. IgG was the most common subtype (46.8%), followed by kappa/lambda light-chain disease (26.6%) and IgA myeloma (19.0%). Bone involvement was present in 78.5% of patients. Autologous stem cell transplantation (ASCT) was performed in 72.7%, radiotherapy in 46.8%, and 38.0% achieved VGPR after first-line treatment. PET-CT was performed in 44.3% of the cohort. During follow-up, 45.6% of patients experienced progression and 45.6% died. The median follow-up duration was 46.6 months.

#### 2) Survival outcomes

For the whole cohort, 2-year and 5-year overall survival (OS) rates were 84.4% and 62.3%, respectively, with a median OS of 96.9 months. 2-year and 5-year progression-free survival (PFS) rates were 86.0% and 64.6%, respectively, with a median PFS of 75.7 months. Among the variables examined, ASCT was associated with superior OS ( $p=0.026$ ). Patients who underwent ASCT had a 5-year OS of 71.6%, compared with 41.3% in those who did not. Similarly, achieving VGPR after first-line therapy was associated with significantly improved OS ( $p=0.011$ ); the 5-year OS was 76.0% in patients with VGPR versus 54.5% in those without VGPR.

#### 3) PFS and prognostic analyses

Most baseline clinical and laboratory parameters were not significantly associated with survival outcomes. In ROC analysis for mortality discrimination, platelet count and LDH showed statistical significance, whereas NHR (Neutrophil-to-Hemoglobin Ratio) did not. Platelet count yielded an AUC of 0.675 ( $p=0.008$ ) and LDH an AUC of 0.631 ( $p=0.046$ ), while NHR had limited discriminatory ability (AUC 0.549,  $p=0.454$ ). In multivariable Cox regression, VGPR remained the only independent predictor of reduced mortality (HR 0.43, 95% CI 0.19–0.98;  $p=0.045$ ), whereas ASCT did not retain independent significance. Due to limited availability of cytogenetic and molecular testing in our center during a substantial part of the study period, genetic risk stratification could not be evaluated consistently across the cohort.

### CONCLUSION

Young patients account for only about 10% of all multiple myeloma cases and remain underrepresented in the literature, where many dedicated cohorts are still relatively small. In our real-world cohort of patients aged 30–50 years, survival was primarily associated with treatment-related factors, particularly ASCT and the achievement of a deep first-line response. Notably, in multivariable analysis, VGPR remained the only independent predictor of reduced mortality, emphasizing that depth of response is the dominant prognostic signal in this population. Beyond treatment response and transplant status, we could not identify a consistently significant conventional clinical or laboratory marker with robust prognostic value. Because cytogenetic and molecular testing was not uniformly available in our center during a substantial part of the study period, genetic risk stratification could not be systematically incorporated, which limits biologic interpretation of outcomes. Still, our findings support a practical message that is highly relevant for daily care in young myeloma: achieving a deep response to first-line therapy appears more informative for survival than routine baseline biomarkers when comprehensive genetic data are unavailable. Overall, our findings suggest that, beyond transplant status and treatment response, there is still no clearly reliable practical non-genetic marker for predicting disease course in young multiple myeloma, underlining the need for broader access to genetic risk assessment and for larger contemporary young-patient cohorts.

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