EJMA

DOI:10.14744/ejma.268062
EJMA 2026;(2):62–68

Research Article

Comparative Prognostic Value of the Durie–Salmon, ISS, and mSMART Staging Systems in Multiple Myeloma

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Abstract

Objectives: Multiple myeloma (MM) is a plasma cell malignancy characterized by marked interpatient variability in clinical course and prognosis. Accurate staging systems are essential for risk stratification and survival prediction. We aimed to compare the prognostic performance of the Durie–Salmon (DS), International Staging System (ISS), and Mayo Stratification of Myeloma and Risk-Adapted Therapy (mSMART) systems in predicting overall survival.

Methods: This retrospective study included 110 patients diagnosed with MM at a tertiary hematology center. Patients were staged according to the DS, ISS, and mSMART systems. Overall survival (OS) was evaluated using the Kaplan–Meier method, and prognostic factors were evaluated using univariate and multivariate Cox regression analyses.

Results: Advanced disease stages were significantly associated with poorer overall survival across all staging systems (Durie–Salmon, p<0.001; ISS, p=0.007; mSMART, p=0.001). Among the evaluated models, only DS stage IIIB remained an independent predictor of mortality in multivariate analysis (HR=11.55, 95% CI=3.29–40.56, p < 0.001). ISS stage and mSMART risk categories did not retain independent prognostic significance after adjustment.

Conclusion: The DS staging system showed the strongest association with overall survival among the evaluated models. Although biologically based risk stratification has advanced considerably, traditional clinical staging systems still provide valuable and practical guidance in routine clinical practice.

Keywords: Durie–Salmon; ISS, Multiple myeloma, mSMART, prognosis

Cite This Article: *Hendem E, Ayer M. Comparative Prognostic Value of the Durie–Salmon, ISS, and mSMART Staging Systems in Multiple Myeloma. EJMA 2026(2): 62-68.*

Multiple myeloma (MM) is a hematological cancer driven by the clonal expansion of plasma cells that produce monoclonal immunoglobulins. It constitutes a notable proportion of hematological malignancies and shows wide variability in clinical presentation and prognosis.[1] The International Myeloma Working Group (IMWG) has defined diagnostic criteria for MM, including clonal plasma cell infiltration in the bone marrow, the presence of monoclonal proteins, and evidence of end-organ damage.[2] Because of this variability, assessing prognosis at the time of diagnosis is particularly important. In everyday clinical practice, staging systems are commonly used to guide treatment choices, estimate risk, and inform patients about their disease. Among these, the International Staging System (ISS) is widely adopted, mainly due to its simplicity and reliance on routinely available laboratory parameters.[3] Nevertheless, other clinical and biological factors affecting survival have also been reported.[4] Moreover, variations in

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Submitted Date: April 29, 2026 **Accepted Date:** August 4, 2026

treatment response and patient-specific factors contribute to discrepancies in survival outcomes among multiple myeloma patients.

As knowledge of disease biology has evolved, more refined prognostic models have been developed. For example, the Revised International Staging System (R-ISS) includes biological markers in addition to traditional clinical variables to more accurately determine risk stratification.[5] Furthermore, the serum free light-chain ratio has been identified as a useful prognostic indicator in multiple myeloma patients; in parallel, risk-adapted approaches such as the Mayo Stratification of Myeloma and Risk-Adapted Therapy (mSMART) classification have been developed to integrate cytogenetic risk factors into clinical decision-making.[6] These developments aim to improve risk stratification and provide a more comprehensive understanding of the biological heterogeneity of the disease, including the effects of cytogenetic abnormalities and molecular subtypes.[7,8] Furthermore, response criteria and minimal residual disease (MRD) assessment have gained increasing importance in evaluating treatment response and long-term outcomes in multiple myeloma.[9]

Despite these advances, outcomes in multiple myeloma remain influenced by both biological factors and the initial disease burden. In many real-world settings, access to comprehensive cytogenetic and molecular analyses remains limited, which maintains the practical importance of conventional clinical staging systems. The Durie–Salmon (DS) system, one of the first clinically based staging systems, continues to be used in various centers due to its ability to reflect tumor burden and organ involvement. Owing to this feature, it maintains its importance as a valuable and practical tool in routine clinical practice, especially in settings where access to advanced molecular diagnostic methods is limited.

However, the comparative performance of these staging systems in real-world clinical settings remains to be fully clarified. Moreover, evidence from real-world patient cohorts remains relatively limited. In particular, direct comparisons between commonly used staging systems in routine clinical practice are still scarce.

In this context, we aimed to evaluate and compare the prognostic value of the DS, ISS, and mSMART staging systems in predicting overall survival in patients with multiple myeloma.

Methods

Study Population

This retrospective study included a total of 110 patients aged between 18 and 90 years who were diagnosed with multiple myeloma (MM) and followed at a tertiary hematology center. All patients had sufficient clinical and follow-up data available for evaluation. Patients with incomplete medical records or inadequate follow-up were excluded from the study. The diagnosis of MM was established according to standard international criteria.

Data Collection

Demographic characteristics, baseline laboratory parameters, and radiologic findings related to bone involvement were obtained from institutional medical records. Available cytogenetic data were reviewed when present. Patients were staged according to the Durie–Salmon (DS), International Staging System (ISS), and Mayo Stratification of Myeloma and Risk-Adapted Therapy (mSMART) systems at the time of diagnosis. Information regarding treatment responses and survival outcomes was also extracted from patient records. Treatment responses were assessed based on routine clinical evaluations documented in the patient files.

Ethical Approval

The study protocol was reviewed by the local Health Science University Haseki Education and Research Hospital Clinical Reserach Ethics Committee. According to the committee's decision (Approval No.: 298, Date: 02.12.2015), formal ethics committee approval was deemed unnecessary due to the retrospective nature of the study.

Statistical Analysis

Overall survival (OS) was defined as the time from diagnosis to death or the date of the last follow-up. Patients who were alive at the last follow-up were censored. Survival analyses were performed using the Kaplan–Meier method, and differences between groups were assessed with the log-rank test. Prognostic factors associated with overall survival were evaluated using univariate and multivariate Cox proportional hazards regression models. Variables that showed statistical significance in univariate analysis were included in the multivariate model. Statistical analyses were performed using SPSS software (version 22; IBM Corp., Armonk, NY, USA). A p-value of less than 0.05 was considered statistically significant.

Results

The basic demographic and clinical characteristics of the study population are presented in Table 1. The patient group exhibited a heterogeneous structure in terms of age distribution, clinical characteristics, and disease stages at diagnosis. Staging of patients according to the Durie–Salmon, International Staging System (ISS), and Mayo Strat-

Table 1. Baseline demographic and clinical characteristics of the study population

Characteristic	Value
Age (years)	67.3±11.1 (range: 37–86)
Sex, n (%)	
Male	63 (57.3)
Female	47 (42.7)
Myeloma type, n (%)	
IgG (κ/λ combined)	62 (56.3)
IgA (κ/λ combined)	23 (20.9)
Light chain only	18 (16.4)
IgD	4 (3.6)
Solitary plasmacytoma	3 (2.7)
Hypercalcemia, n (%)	13 (11.8)
Renal impairment, n (%)	25 (22.7)
Anemia, n (%)	56 (50.9)
Lytic bone lesions, n (%)	58 (53.2)

Data are presented as mean ± standard deviation or number (%). κ/λ indicates combined kappa and lambda light chain subtypes.

Table 2. Overall survival outcomes according to staging systems

Staging system	Category	Median OS (months)	95% CI	p
Durie–Salmon	IA	52	29.8–74.2	<0.001
	IIA	47	9.1–84.9	
	IIB	17	6.6–27.4	
	IIIA	19	11.3–26.7	
	IIIB	6	2.3–9.7	
ISS	I	52	35.4–68.6	0.007
	II	33	1.9–64.1	
	III	12	5.3–18.7	
mSMART	Standard risk	47	31.0–62.9	0.001
	High risk	7	0.0–15.6	

Overall survival (OS) was estimated using the Kaplan–Meier method. p values were calculated using the log-rank test. Median OS is presented in months, OS: Overall survival; ISS: International Staging System; mSMART: Mayo Stratification of Myeloma and Risk-Adapted Therapy.

ification of Myeloma and Risk-Adapted Therapy (mSMART) systems revealed the presence of different prognostic groups within the study population.

In overall survival analyses, significant differences were found between disease stages according to all three staging systems. Survival analyses based on the Durie–Salmon, ISS, and mSMART classifications showed significant differences between stages (Table 2; Figures 1–3). Kaplan–Meier curves demonstrated decreasing survival probabilities with advancing disease stage across all three models (Durie–Salmon, p<0.001; ISS, p=0.007; mSMART, p=0.001). Median overall survival was shorter in advanced-stage groups compared to early-stage patients.

Multivariate Cox proportional hazards regression analysis showed that only Durie–Salmon stage IIIB was independently linked to a higher risk of death (HR=11.55, 95% CI=3.29–40.56, p<0.001) (Table 3). After controlling for other variables in the model, ISS stage and mSMART risk category lost their independent prognostic significance. These results indicate that Durie–Salmon stage IIIB, which signifies advanced tumor burden and end-organ involvement, is the prognostic marker most closely correlated with overall survival in this cohort.

In addition to survival differences between staging categories, the distribution of patients across stages revealed a predominance of advanced disease at diagnosis. A substantial proportion of patients were classified as advanced stage according to the Durie–Salmon and ISS systems, while a smaller subset was categorized as high risk by mSMART. Advanced-stage patients more frequently showed clinical features indicative of higher disease bur-

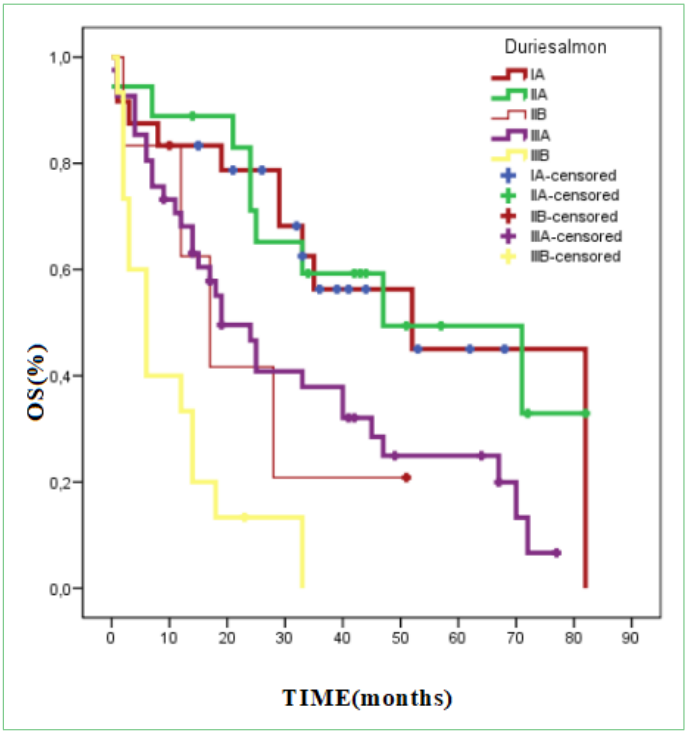

Figure 1. Durie–Salmon survival curves.
Kaplan–Meier overall survival curves according to Durie–Salmon staging system. Overall survival differed significantly among Durie–Salmon stages, with progressively shorter survival observed in advanced stages (log-rank test, p<0.001).

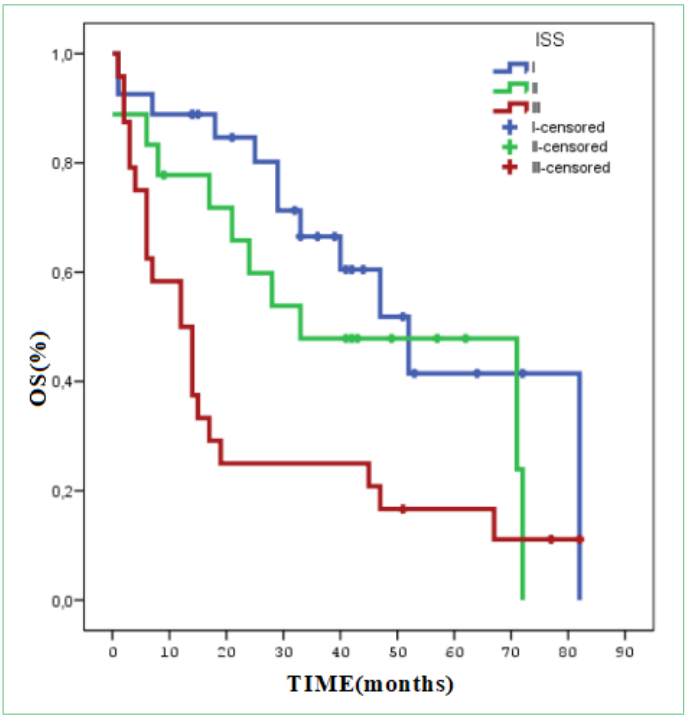

Figure 2. ISS survival curves.
Kaplan–Meier overall survival curves stratified by International Staging System (ISS). Patients with higher ISS stage demonstrated significantly inferior overall survival compared with lower stages (log-rank test, p=0.007).

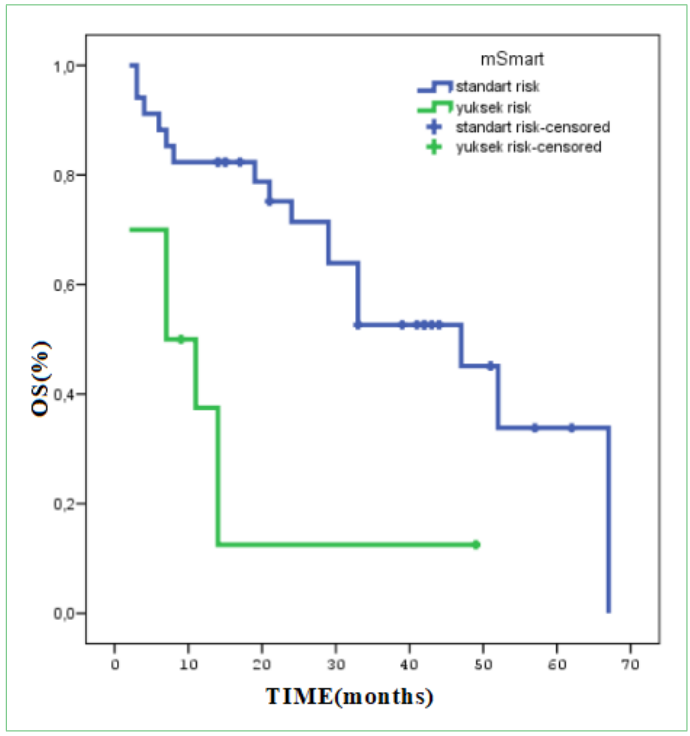

Figure 3. mSMART survival curves.
Kaplan–Meier overall survival curves according to mSMART risk stratification. High-risk patients exhibited significantly reduced overall survival compared with standard-risk patients (log-rank test, p=0.001).

den, including renal impairment, anemia, and extensive skeletal involvement (Table 1). These findings further support the observed differences in survival outcomes across staging groups.

When the staging systems were compared, greater agreement was observed in early-stage disease, whereas variability increased among advanced-stage categories. Notably, some patients categorized as advanced stage by the Durie–Salmon system were classified as intermediate or high risk according to ISS and mSMART. Despite these differences, each system was able to distinguish patients with poorer outcomes. Overlapping classifications indicate that disease severity may be captured differently across staging approaches used in routine clinical practice.

Table 3. Multivariate Cox regression analysis of prognostic factors associated with overall survival

Variable	Hazard Ratio (HR)	95% CI	p
Durie–Salmon stage			
IIIA	0.57	0.11–3.11	*0.520*
IIIB	11.55	3.29–40.56	*<0.001*
ISS stage			
II	0.98	0.24–3.94	*0.975*
III	3.14	0.55–17.83	*0.196*
mSMART risk category			
High risk	1.62	0.22–11.85	*0.635*

Multivariate Cox proportional hazards regression analysis included Durie–Salmon stage, ISS stage, and mSMART risk category. Durie–Salmon stage IA, ISS stage I, and standard-risk mSMART category were used as reference groups. Hazard ratios (HRs) and 95% confidence intervals (CIs) are shown. ISS: International Staging System; mSMART: Mayo Stratification of Myeloma and Risk-Adapted Therapy.

Discussion

In this retrospective cohort, the Durie–Salmon (DS) staging system was most strongly associated with overall survival compared with ISS and mSMART. This finding suggests that, even in the era of modern MM management, clinical burden and organ involvement—as reflected by the DS system—remain highly relevant for predicting patient outcomes at diagnosis.

DS stage IIIB appears to identify a subgroup of patients with more advanced disease, where renal impairment and extensive organ involvement play an important role in determining outcomes. In our cohort, Durie–Salmon stage IIIB was the strongest predictor of mortality (HR=11.55, 95% CI=3.29–40.56, p<0.001). Renal dysfunction is a frequent

complication of multiple myeloma and is linked to worse outcomes.[10] In this setting, staging systems that capture tumor burden and end-organ damage may provide clinically relevant prognostic information.[11]

The ISS is still commonly used in clinical practice, largely because it is simple and easy to apply across different settings. In our cohort, however, it did not appear to fully capture the complexity of disease burden and organ involvement. This may partly explain why its prognostic effect was no longer evident after adjustment for DS stage in the multivariate model. Similar patterns have been described in previous studies, particularly in real-world cohorts, where the performance of ISS has been less consistent.[3,4]

Multiple myeloma shows marked biological diversity, with molecular and cytogenetic features influencing both the disease course and response to treatment.[12] In particular, high-risk cytogenetic abnormalities are known to be associated with poorer clinical outcomes.[13] It is well established that multiple myeloma is often preceded by precursor conditions such as monoclonal gammopathy of undetermined significance (MGUS) and smoldering multiple myeloma, which follow a stepwise progression pattern.[14,15] The incorporation of cytogenetic abnormalities into prognostic models, as seen in the Revised International Staging System (R-ISS), represents an important step toward more refined risk stratification. However, the applicability of such models may be limited by the availability of comprehensive cytogenetic testing in routine clinical practice.

Advanced molecular diagnostics are not always available in many centers, especially those with limited resources. In these situations, clinically based staging systems like DS may still be very useful because they are easy to use and understand. Our findings affirm the enduring significance of these conventional models, particularly in instances where biological data are insufficient or inaccessible.

Recent advancements in treatment, encompassing autologous stem cell transplantation and the introduction of innovative therapeutic agents like proteasome inhibitors and immunomodulatory drugs, have significantly enhanced survival outcomes in patients with multiple myeloma.[16–18] Despite these therapeutic advances, baseline disease characteristics remain critical determinants of prognosis, underscoring the importance of accurate staging at diagnosis.

Frailty, age, and comorbidities also play an important role in determining outcomes, particularly in elderly patients.[19] These patient-related factors may influence both treatment selection and survival independently of disease stage. Therefore, integrating clinical staging with patient-specific factors may provide a more comprehensive approach to prognostic assessment.

Another significant finding in our study is the inconsistency noted among various staging systems, especially in advanced-stage disease. There is a general consensus in early-stage classifications; however, discrepancies become more evident in high-risk groups. This indicates that various staging methodologies may represent distinct facets of the disease's biology and clinical impact.

From a clinical perspective, these findings offer important practical implications. In routine clinical practice, where rapid decision-making is necessary and access to advanced diagnostic methods may be limited, simple and easily applicable staging systems like DS continue to provide valuable guidance.[20] Clinicians may benefit from using traditional staging systems in conjunction with modern prognostic tools to obtain a balanced and clinically relevant risk assessment. Newer approaches, such as the second revision of the International Staging System (R2-ISS), have been developed to make prognostic classification in multiple myeloma more precise.[21,22] In addition, some genomic profiles, defined as "double-hit" multiple myeloma, have been shown to be associated with a poor prognosis and a more aggressive disease course.[23] Minimal residual disease (MRD) status also stands out as a strong predictor of long-term outcomes in multiple myeloma.[24] Furthermore, patient-specific factors such as frailty and geriatric assessment have been reported to have a significant impact on survival outcomes, particularly in elderly patients.[25] When all these findings are considered together, it appears that while the importance of biology-based prognostic models is increasing, classical clinical staging systems—particularly the Durie–Salmon system—retain their status as a reliable source of prognostic information in routine clinical practice. The use of these systems is especially important in real-life situations where comprehensive molecular data are not always available.

Study Limitations

Several factors should be considered when interpreting these findings. The study was conducted retrospectively, which introduces an inherent risk of selection bias. The patient population was relatively limited and drawn from a single center, which may influence how broadly the results can be generalized. In addition, complete cytogenetic and molecular data were not consistently available across all cases, restricting a more detailed assessment of biologically based risk models. Variations in treatment practices among patients may also have affected survival outcomes and were not fully captured in this analysis.

Conclusion

Our results show that the Durie–Salmon (DS) staging sys-

tem remains closely related to overall survival in patients with multiple myeloma. Compared with ISS and mSMART, DS seemed to better identify patients with more advanced disease and less favorable outcomes.

While biologically driven risk models are becoming more common in clinical practice, traditional staging systems still have a clear role in everyday decision-making, particularly in settings with limited access to advanced molecular testing where clinicians rely on routinely available clinical data.

Expanding the evidence base with larger and more diverse patient cohorts may help clarify how clinical staging can be more effectively combined with emerging biology-based approaches in multiple myeloma.

Disclosures

Ethics Committee Approval: The study protocol was reviewed by the local Health Science University Haseki Education and Research Hospital Clinical Reserach Ethics Committee. According to the committee's decision (Approval No.: 298, Date: 02.12.2015), formal ethics committee approval was deemed unnecessary due to the retrospective nature of the study.

Informed Consent: Informed consent was waived due to the retrospective nature of the study.

Conflict of Interest: The authors declare that they have no conflict of interest.

Funding: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Use of AI for Writing Assistance: No artificial intelligence-assisted technologies were used in the preparation of this manuscript.

Authorship Contributions: Concept: EH, MA; Design: EH, MA; Supervision: MA; Materials: EH, MA; Data collection and/or processing: EH; Analysis and/or interpretation: EH, MA; Literature review: EH; Writing: EH; Critical review: MA.

Peer Review: Externally peer-reviewed.

References

1. Durie BGM, Harousseau JL, Miguel JS, Bladé J, Barlogie B, Anderson K, et al. International uniform response criteria for multiple myeloma. Leukemia 2006;20(9):1467–73. [CrossRef]
2. Rajkumar SV, Dimopoulos MA, Palumbo A, Blade J, Merlini G, Mateos MV, et al. International Myeloma Working Group updated criteria for the diagnosis of multiple myeloma. Lancet Oncol 2014;15(12):e538–48. [CrossRef]
3. Greipp PR, San Miguel J, Durie BGM, Crowley JJ, Barlogie B, Bladé J, et al. International staging system for multiple myeloma. J Clin Oncol 2005;23(15):3412–20. [CrossRef]
4. Fonseca R, San Miguel J. Prognostic factors and staging in multiple myeloma. Hematol Oncol Clin North Am 2007;21(6):1115–40. [CrossRef]
5. Palumbo A, Avet-Loiseau H, Oliva S, Lokhorst HM, Goldschmidt H, Rosinol L, et al. Revised international staging system for multiple myeloma: A report from International Myeloma Working Group. J Clin Oncol 2015;33(26):2863–9. [CrossRef]
6. Snozek CLH, Katzmann JA, Kyle RA, Dispenzieri A, Larson DR, Therneau TM, et al. Prognostic value of the serum free light chain ratio in newly diagnosed myeloma: proposed incorporation into the international staging system. Leukemia 2008;22(10):1933–7. [CrossRef]
7. Avet-Loiseau H, Attal M, Moreau P, Charbonnel C, Garban F, Hulin C, et al. Genetic abnormalities and survival in multiple myeloma: the experience of the Intergroupe Francophone du Myélome. Blood 2007;109(8):3489–95. [CrossRef]
8. Rajkumar SV. Multiple myeloma: 2020 update on diagnosis, risk-stratification and management. Am J Hematol 2020;95(5):548–67. [CrossRef]
9. Kumar S, Paiva B, Anderson KC, Durie B, Landgren O, Moreau P, et al. International Myeloma Working Group consensus criteria for response and minimal residual disease assessment in multiple myeloma. Lancet Oncol 2016;17(8):e328–46. [CrossRef]
10. Dimopoulos MA, Terpos E, Chanan-Khan A, Leung N, Ludwig H, Jagannath S, et al. Renal impairment in patients with multiple myeloma: a consensus statement on behalf of the International Myeloma Working Group. J Clin Oncol 2010;28(33):4976–84. [CrossRef]
11. Durie BGM, Salmon SE. A clinical staging system for multiple myeloma: correlation of measured myeloma cell mass with presenting clinical features, response to treatment, and survival. Cancer 1975;36(3):842–54. [CrossRef]
12. Fonseca R, Bergsagel PL, Drach J, Shaughnessy J, Gutierrez N, Stewart AK, et al. International Myeloma Working Group molecular classification of multiple myeloma: spotlight review. Leukemia 2009;23(12):2210–21. [CrossRef]
13. Sonneveld P, Avet-Loiseau H, Lonial S, Usmani S, Siegel D, Anderson KC, et al. Treatment of multiple myeloma with high-risk cytogenetics: a consensus of the International Myeloma Working Group. Blood 2016;127(24):2955–62. [CrossRef]
14. Landgren O, Kyle RA, Pfeiffer RM, Katzmann JA, Caporaso NE, Hayes RB, et al. Monoclonal gammopathy of undetermined significance (MGUS) consistently precedes multiple myeloma: a prospective study. Blood 2009;113(22):5412–7. [CrossRef]
15. Mateos MV, San Miguel JF. Smoldering multiple myeloma: when to observe and when to treat? Am Soc Clin Oncol Educ Book. 2015:e484–92. [CrossRef]
16. Attal M, Harousseau JL, Stoppa AM, Sotto JJ, Fuzibet JG, Rossi JF, et al. A prospective, randomized trial of autologous bone marrow transplantation and chemotherapy in multiple myeloma. N Engl J Med 1996;335(2):91–7. [CrossRef]
17. Child JA, Morgan GJ, Davies FE, Owen RG, Bell SE, Haw-

kins K, et al. High-dose chemotherapy with hematopoietic stem-cell rescue for multiple myeloma. N Engl J Med 2003;348(19):1875–83. [CrossRef]

18. Richardson PG, Sonneveld P, Schuster MW, Irwin D, Stadtmauer EA, Facon T, et al. Bortezomib or high-dose dexamethasone for relapsed multiple myeloma. N Engl J Med 2005;352(24):2487–98. [CrossRef]
19. Palumbo A, Bringhen S, Ludwig H, Dimopoulos MA, Bladé J, Mateos MV, et al. Personalized therapy in multiple myeloma according to patient age and vulnerability: a report of the European Myeloma Network (EMN). Blood 2011;118(17):4519–29. [CrossRef]
20. Moreau P, San Miguel J, Sonneveld P, et al. Multiple myeloma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2017;28(Suppl 4):iv52–61. [CrossRef]
21. D'Agostino M, Cairns DA, Lahuerta JJ, Wester R, Bertsch U, Waage A, et al. Second Revision of the International Staging System (R2-ISS) for overall survival in multiple myeloma: A European Myeloma Network (EMN) Report Within the HARMONY Project. J Clin Oncol 2022;40(29):3406–18. [CrossRef]
22. Kastritis E, Katodritou E, Badelita S, Bila J, Seval GC, Cvetkovic Z, et al. Validation of the second revision of the International Staging System (R2-ISS) for overall survival in multiple myeloma in a real-world cohort: an analysis by the Balkan Myeloma Study Group (BMSG). Leuk Lymphoma 2024;65(13):2064–7. [CrossRef]
23. Walker BA, Mavrommatis K, Wardell CP, Ashby TC, Bauer M, Davies FE, et al. A high-risk, Double-Hit, group of newly diagnosed myeloma identified by genomic analysis. Leukemia 2019;33(1):159–70. [CrossRef]
24. Munshi NC, Avet-Loiseau H, Rawstron AC, Owen RG, Child JA, Thakurta A, et al. Association of minimal residual disease with superior survival outcomes in patients with multiple myeloma: a meta-analysis. JAMA Oncol 2017;3(1):28–35. [CrossRef]
25. Palumbo A, Bringhen S, Mateos MV, Larocca A, Facon T, Kumar SK, et al. Geriatric assessment predicts survival and toxicities in elderly myeloma patients: an International Myeloma Working Group report. Blood 2015;125(13):2068–74. [CrossRef]