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Real-World Outcomes of Isatuximab-Carfilzomib-Dexamethasone in Relapsed/Refractory Multiple Myeloma: A Single-Center Analysis Using the IMS/IMWG Consensus Genomic Staging

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Background

Isatuximab-carfilzomib-dexamethasone (IsaKd) demonstrated superiority over Kd in RRMM in the IKEMA phase III trial. Real-world data applying the IMS/IMWG Consensus Genomic Staging (CGS) binary classification remain scarce.

Purpose

To describe response and survival outcomes of RRMM patients treated with IsaKd at a single center

Methods

Retrospective single-center analysis (N=27). Cytogenetic risk was classified using the IMS/IMWG CGS binary system. Kaplan-Meier estimates for PFS (event: progression or death) and OS (event: death). Treatment duration (DOT) used as follow-up proxy. Data cutoff: February, 2026.

Results

27 patients were included. Median age was 62 years (51-79); R-ISS staging was I/II/III in 24%/32%/44% of patients, 63% received a prior autologous transplantation, 92.6% were Lenalidomide refractory. The median number of prior lines was 1 (range 0-5), with 14.8% triple-refractory. 37.0% of patients (n=10) were classified as high risk (HR) and 40.7% (n=11) as standard risk (SR); 14.8% had incomplete evaluation (TP53 status) and 7.4% non-classifiable.

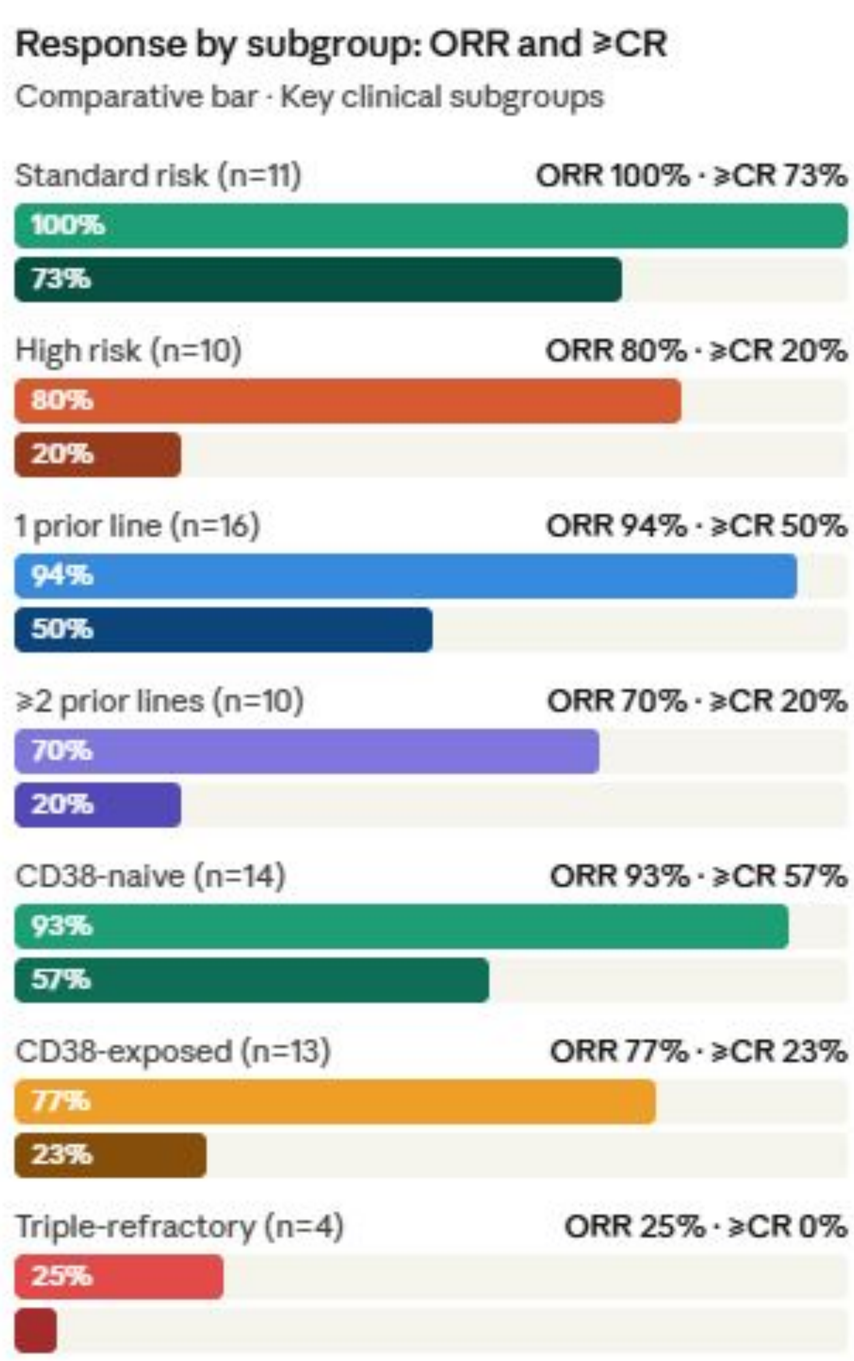
ORR was 85.2%,with ≥VGPR in 77.8%, ≥CR in 40.7%, and MRD-negative CR in 22.2% of patients. SR patients achieved deeper responses than HR patients (ORR 100% vs. 80%; ≥CR 73% vs. 20%), while the triple-refractory subgroup showed poor outcome, with an ORR of 25% and 3 of 4 deaths recorded.

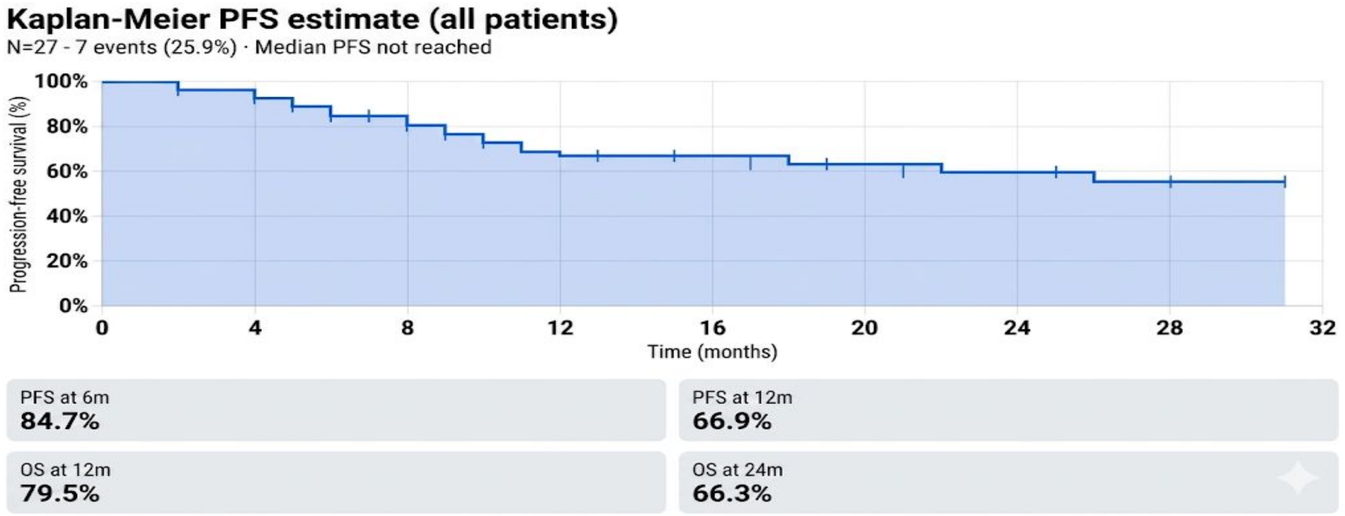
Median DOT was 10 months (range 2-31); 13/27 on active treatment at cutoff. With 7 events (25.9%) recorded, median PFS and OS were not reached; PFS at 6/12 months: 84.7%/66.9%. OS at 12/24 months: 79.5%/66.3%. PFS at 12 months: 75% (SR) vs. 57% (HR).

Table 1. Baseline patient characteristics (N=27)

Variable	n / Median	% / Range
Age (median, range)	62 years	51-79
Male sex	13/27	48.1%
Frailty	2/27	7.4%
Extramedullary disease	7/27	25.9%
Renal impairment	9/27	33.3%
R-ISS I / II / III	6/8/11 (NE: 2)	24% / 32% / 44%
High risk	10/27	37%
Standard risk	11/27	41%
Prior autologous transplant	17/27	63.0%
Median prior lines (range)	1	0-5
Prior anti-CD38 exposure	13/27	48.1%
PI refractory	8/27	29.6%
IMiD refractory	25/27	92.6%
Anti-CD38 refractory	7/27	25.9%
Triple refractory	4/27	14.8%

IMiD: immunomodulatory drug - NE: not evaluable - PI: proteasome inhibitor - R-ISS: Revised International Staging System





Conclusions

IsaKd achieves high ORR and durable responses in RRMM. The IMS/IMWG CGS 2024 system classified 37% as HR; while ORR was preserved (80%), depth of response (>=CR) was markedly lower vs. SR (20% vs. 73%). Triple-refractory patients showed poor outcome (ORR 25%). Earlier use was associated with superior responses.

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