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ISATUXIMAB IN COMBINATION WITH BORTEZOMIB, LENALIDOMIDE, AND DEXAMETHASONE (ISA-VRD) IN NEWLY DIAGNOSED MULTIPLE MYELOMA PATIENTS NOT CANDIDATES FOR TRANSPLANTATION: CLINICAL PRACTICE EXPERIENCE IN FIVE HOSPITALS IN ANDALUSIA, SPAIN

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INTRODUCTION

Newly diagnosed multiple myeloma (NDMM) in patients not candidates for transplantation poses a therapeutic challenge due to its clinical heterogeneity and associated frailty. Isa-VRd (Isatuximab, Bortezomib, Lenalidomide, and Dexamethasone) is the first quadruple anti-CD38 + VRd regimen approved by the EMA and funded in Spain for this population, offering the potential to improve response rates and progression-free survival.

Objective:

To evaluate the safety, clinical management, and efficacy of Isa-VRd in NDMM patients who are not candidates for transplantation treated in routine clinical practice.

Methods:

A retrospective analysis was conducted on 38 NDMM patients treated with Isa-VRd as first-line therapy from five centers from February 2025 to February 2026. Baseline characteristics and treatment tolerability were analyzed. Toxicities and treatment responses were reported according to standard IMWG criteria

RESULTS

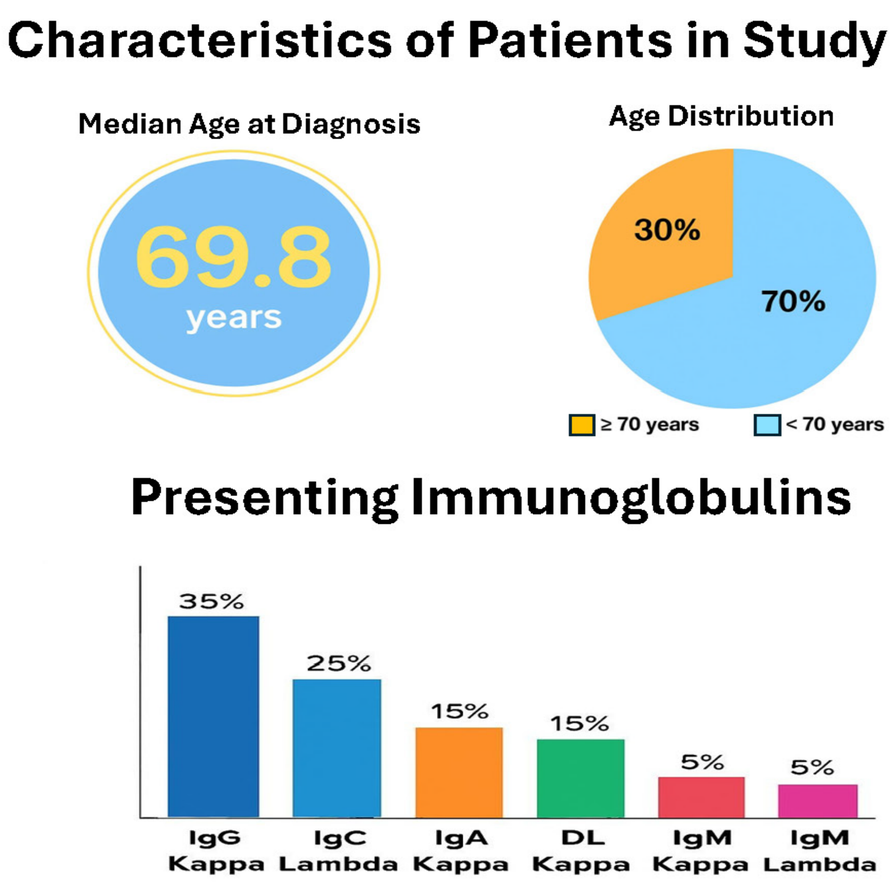
The median age at diagnosis was 69.8 years, with 70% of patients being ≥70 years old. The presenting immunoglobulins were: IgG Kappa (35%), IgG Lambda (25%), IgA Kappa (15%), CL Kappa (15%), IgM Kappa (5%), IgM Lambda (5%), and one case of oligosecretory macrofocal (5%) IgG Kappa. At baseline, 26.32% of patients had an estimated glomerular filtration rate (eGFR) <60 mL/min, and 60% of patients had an ISS-R ≥2. Cytogenetic analysis performed via FISH revealed that 39.47% of patients had Gain1q as the most frequent anomaly, while more than 50% of patients did not have chromosomal abnormalities identified by FISH.

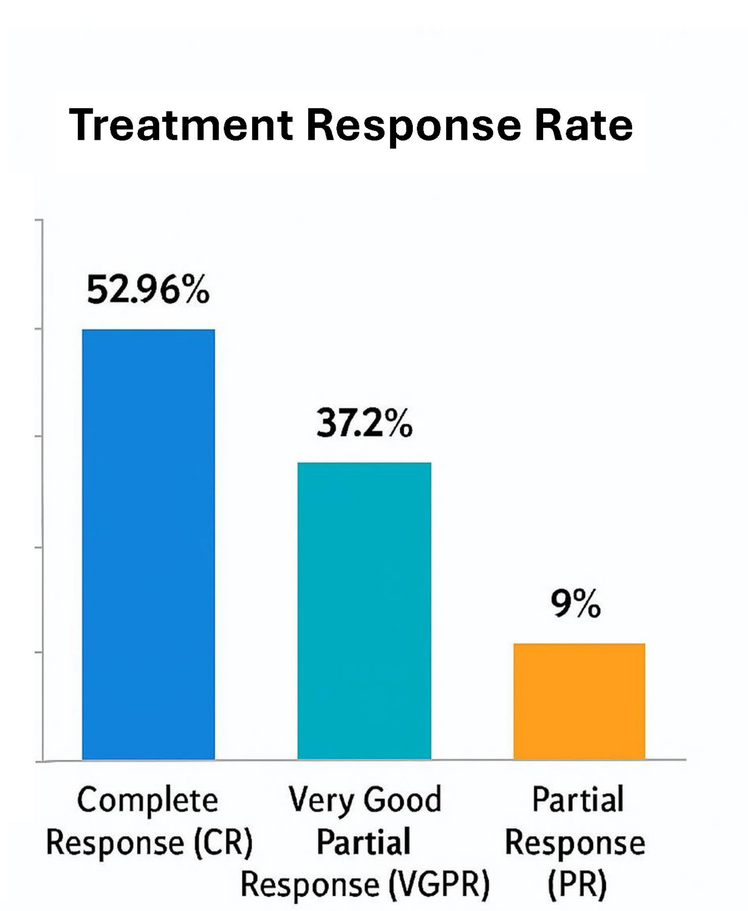
All patients included in the observational study were treated with Isa-VRd as first-line therapy, thus none had been previously exposed to or refractory to Daratumumab, Bortezomib, and/or Lenalidomide. Among the 38 patients treated with Isa-VRd, 55% started with a dose-reduced regimen, and only 3 patients experienced infusion reactions to Isatuximab.

Of the 38 patients included, 75% underwent G8 scale assessment, and 35% were assessed with the GAH scale. 60% of the studied patients were considered frail based on G8 scores <14 and/or GAH frailty scale at the start of treatment. In this subgroup of patients, a therapeutic regimen with adjusted doses was initiated in 72.3% of patients. Among the studied patients, 35% initiated the regimen with a reduction in Lenalidomide, 25% with a reduction in Bortezomib, and 20% with reductions in both Lenalidomide and Bortezomib.

During treatment, 45.45% of patients required dose reductions due to toxicity (neuropathy, DVT, or neutropenia); however, overall, they exhibited adequate tolerability, with no severe infections or fatalities.

100% of our patients demonstrated a response: 52.96% achieved complete response (CR), 37.2% very good partial response (VGPR), and 9% partial response (PR). The median time to achieve ≥VGPR was 3.5 months (range 2-6 months). Notably, EMR (-) was observed in 8 of the 15 patients in CR after the 5th cycle, all of whom were confirmed to have strict CR through imaging studies (PET/CT).





CONCLUSION

Isa-VRd is an effective and well-tolerated regimen in older patients with NDMM who are not candidates for transplantation. The high response rate and manageable safety profile support its incorporation into clinical practice as a first-line option, including in frail patients.

REFERENCES

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