REAL WORLD EXPERIENCE OF PATIENTS WITH MULTIPLE MYELOMA RELAPSED/REFRACTORY TO DARATUMUMAB AFTER 1–2 LINES OF TREATMENT

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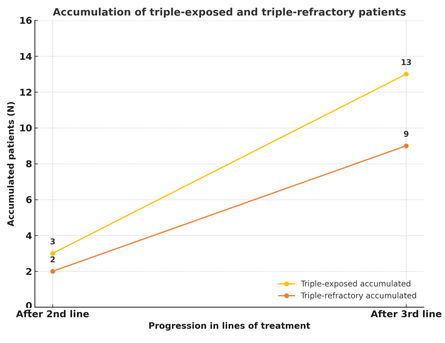
Introduction and Aim

Multiple myeloma (MM) remains an incurable malignancy, with inevitable relapses. Patients who become triple-refractory—that is, exposed and unresponsive to proteasome inhibitors (PIs), immunomodulatory drugs (IMiDs), and anti-CD38 monoclonal antibodies—face particularly poor outcomes. Despite their growing prevalence, these patients are underrepresented in pivotal clinical trials. Our study provides real-world data from a medium-sized Spanish hospital, aiming to identify the most effective salvage therapies for this high-risk group, and offering insight into routine clinical practice beyond controlled trial environments.

Methods

This was a retrospective, observational, single-center study conducted at the University Hospital of Jerez de la Frontera. The study included all patients diagnosed with MM who were refractory to anti-CD38 therapy in either first or second line of treatment. All patients initiated anti-CD38-based therapy between 2019 and 2024.Statistical analyses were performed using R software (version 4.3.3; R Core Team, 2021).

Baseline characteristics	N=18
Age (median/range)	73.5 (43-82)
Sex (male/female)	39.9%/61.1%
Induction regimen:	
- PIs	11.1%
- IMIDs	16.7%
- PIs + IMIDs	33.3%
- PIs + anti-CD38	16.7%
- IMIDs + anti-CD38	16.7%
- PIs + IMIDs + anti-CD38	5.5%
Autologous transplant (yes/no)	33.3%/66.7%
Anti-CD38 (1st line vs 2nd line)	39.9%/61.1%
Anti-CD38 regimen:	
- D-Vd	33.3%
- D-Rd	22.2%
- D-VMP	16.7%
- Isa-Kd	11.1%
- D-KRd	5.6%
- D-Kd	5.6%
- D-Pd	5.6%
Response to anti-CD38 treatment:	
- CR	50%
- VGPR	16.7%
- PR	27.8%
- SD	5.5%
Duration of anti-CD38 therapy (median/range)	11.27 (2.8-21.7)
PFS on anti-CD38 therapy (≥12 months / <12 months)	44.4%/55.6%
Plasmacytomas at relapse (yes/no)	22.2%/77.8%



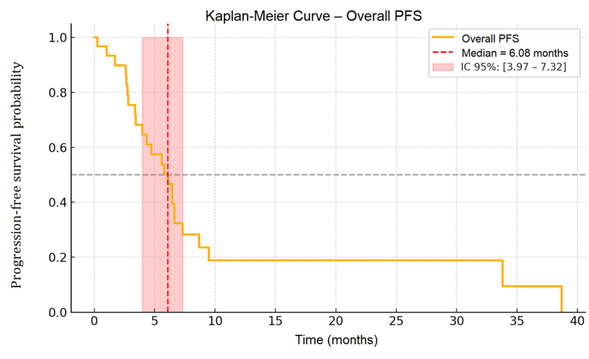
Results

Eighteen patients were included, with a median age of 73.5 years. Baseline characteristics are presented in Table 1. Anti-CD38 therapy was used in the first line in 38.9% and in the second line in 61.1% of cases. All patients were refractory to anti-CD38. In total, 72.2% were triple-exposed, and 50% were triple-refractory (Figure 2).

With a median follow-up of 12.35 months (95% CI: 4.53–13.53), median PFS following anti-CD38 refractoriness was 6.08 months (95% CI: 3.97–7.32), and the median OS was 11.4 months (95% CI: 1.6–33.3). In patients treated in second line, PFS was 6.44 months (95% CI: 3.45–7.32), and in third line 6.08 months (95% CI: 3.32–8.67).

The most frequently used salvage treatments, along with their corresponding response rates and PFS, are shown in Table 3. Among salvage therapies, bispecific antibodies –particularly teclistamab- showed the most promising results: all treated patients achieved complete response (CR) and the 6-month PFS was 100%.

SALVAGE TREATMENT REGIMEN AFTER ANTI-CD38 THERAPY	N patients	Median PFS	ORR	CR, n(%)
Teclistamab	5	Not reached	3(100%)	3(100%)
Kd	5	11.50 months [IC 95%, 2.73 - 36.29]	2 (40%)	1 (20%)
Poma-Cy-Dex	4	4.83 months [IC 95%, 2.86 - 6.43]	3 (75%)	1 (25%)
Alternating VBMCP–VBAD regimens	2	5.73 months [IC 95%, 2.60 - 8.87]	1 (50%)	0
KRd	2	6.80 months [IC 95%, 1.31 - 12.29]	1 (50%)	0
Belantamab	2	3.19 months [IC 95%, 2.78 - 3.59]	0	0



Summary

This real-world study highlights the clinical challenges of managing triple-refractory MM patients in a non-trial setting. Our findings support the role of bispecific antibodies as a promising treatment option and emphasize the importance of real-world evidence to guide clinical decisions in comparable healthcare settings.