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Management and Outcomes of Anti-CD38 Refractory Multiple Myeloma: Recycling of Therapies and Impact of PFS On Subsequent Treatments

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INTRODUCTION

- The management of refractory myeloma is challenging despite the increasing number of treatment options.
- In addition, the use of newer therapies such as anti-CD38 monoclonal antibodies (MoAbs) in earlier lines of treatment creates new challenges in the event of relapse, especially as more patients relapse during therapy with anti-CD38 MoAbs in combination with other agents.
- The management of such patients may be based either on the use of drugs with new mechanisms (if available) or on the recycling of drugs or drug classes used in prior lines, including anti-CD38 MoAbs.

AIM

Herein, we describe the outcomes of patients who failed on anti-CD38-containing therapy in the real-world practice.

METHOD

- The analysis included **183 patients** with RRMM who **progressed during therapy with a regimen that contained either daratumumab or isatuximab** (index therapy) and who received further therapy.
- Patients were treated in a single center (Department of Clinical Therapeutics) and started antiCD38 therapy from 1/1/2015 to 31/12/2021

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RESULTS

Characteristics of anti-CD38 treatment

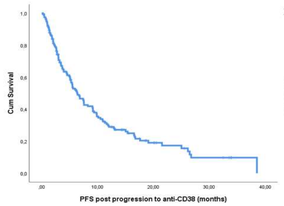
- The patients received index antiCD38 therapy after a median of 2 prior lines (range 1-10).
- The median age at the time of treatment initiation was 68 years (range 35-89).
- 38% had prior ASCT.
- 61% were PI-, 71% lenalidomide- and 29% pomalidomide- refractory.
- AntiCD38 was given as monotherapy (+/-dexa) in 50%, with IMiD in 25% and with PI in 25%.
- On ITT, ORR was 55% (CR: 5%, VGPR: 25%, PR: 25%).
- Median PFS on antiCD38 therapy for the whole cohort was 6.4 months; 5.5 months for antiCD38 +/-dexa vs 7.4 months for anti-CD38 triplets (p=0.055).

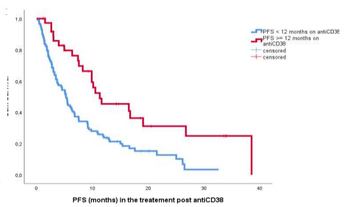
Characteristics of post anti-CD38 treatment

- Post antiCD38 progression (median 3 prior lines) all patients were PI and lenalidomide exposed.
- 82% were PI resistant, 75% lenalidomide resistant and 46% pomalidomide resistant.
- Treatments post antiCD38 failure included 40% PI regimens (23% carfilzomib-based), 30% pomalidomide containing, 23% antiCD38 triplet combinations, 15% belantamab mafodotin, 5% selinexor (+/-PI).
- 50% received a triplet and 50% a doublet.
- On ITT, ORR in the post antiCD38 line was 43%.

Progression-free survival (PFS) post anti-CD38 treatment

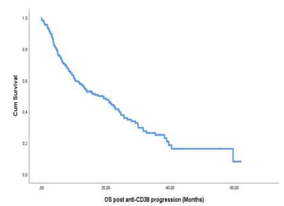
- On ITT, median PFS was 6.4 months.
- Median PFS was 5.5 months for patients who had progressed on antiCD38+/-dexa and 7.4 months for those progressing on antiCD38-combinations (p=0.195).
- Given the high rates of PI and lenalidomide resistance, only pomalidomide resistance was associated with poor PFS post anti-CD38 (median 7.5 vs 5.2 months, p=0.007).
- Median PFS was 4 months for patients who received anti-CD38 regiments and 9.1 months for belantamab mafodotin.
- A PFS >12 months during index antiCD38 therapy was the most important prognostic factor for PFS post antiCD38 failure (median PFS post antiCD38 of 11.3 months vs 5.2 months, p=0.001).
- This prognostic effect was independent of the number of prior lines, type of treatment or pomalidomide resistance.
- Notably, the use of antiCD38 combinations was associated with a PFS of 11.6 months in patients with a PFS ≥12 months during initial antiCD38 therapy.

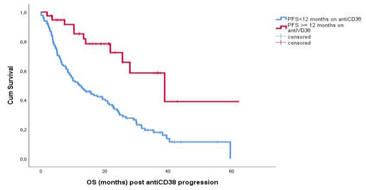




Overall survival (OS) post anti-CD38 treatment

- The median OS post antiCD38 progression was 17.6 months.
- The median OS was 12.8 vs 22.5 months for patients who had progressed on antiCD38+/-dexa vs antiCD38 combinations, respectively (p=0.327).
- The median OS post index therapy was 16.6 months for those who received antiCD38 containing regimens, 22.9 months for PI-based regimens (for carfilzomib 22.7 months), 20.9 months for pomalidomide-based therapies, 21 months for triplets (vs 19.3 for doublets), 24.5 months for belantamab and 30 months for the small group of selinexor-treated patients.
- OS post antiCD38 was 39 months for those with PFS ≥12 months on index therapy (vs 12 months, p<0.001) and this was the only important prognostic factor.
- This prognostic effect was independent of the number of prior lines, type of treatment or pomalidomide resistance.





CONCLUSIONS

- ✓ Outcomes after progression on antiCD38 therapy are poor, despite recent advances.
- ✓ Drugs with **new mechanisms of action** may improve PFS, but their use needs to be optimized, probably in the context of **triplet** combinations.
- ✓ **Recycling prior therapies** may be beneficial especially for patients who had **prolonged remissions** during the index antiCD38 treatment and could be useful as a bridge to further therapeutic options.
- ✓ In this subgroup of patients, maintaining an antiCD38 backbone could be a valid option.
- ✓ Participation in **clinical trials** should be highly encouraged.