**P902 RELAPSED/REFRACTORY MULTIPLE MYELOMA PATIENTS. A MULTICENTER RETROSPECTIVE ANALYSIS OF ELIGIBILITY CRITERIA FOR CAR-T CELL THERAPY**

**Topic:** 14. Myeloma and other monoclonal gammapathies - Clinical

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**Background:** The overall survival (OS) of multiple myeloma (MM) patients (pts) has improved over the years due to the introduction of novel drugs, such as proteosome inhibitors (PI), immunomodulatory drugs (IMiDs) and anti-CD38 monoclonal antibodies (moAb). Nevertheless, the majority of pts continues to relapse and MM remains an incurable disease. No standard of care has been established for relapsed/refractory (RR) MM pts who have been exposed to the main anti-myeloma drugs. The outcome of pts failing standard of care regimens, which is now defined as triple-refractory, is poor, with a median progression-free survival (PFS) of 3-4 months and OS of 8-9 months. Novel therapeutic strategies are warranted to overcome the natural occurrence of relapse or therapy resistance in RRMM pts. Chimeric antigen receptor (CAR)-modified T cells are a promising new therapy approach for triple refractory RRMM. Specific CAR-T targets are being studied, but BCMA-directed CAR-T cells have so far provided the most convincing evidence of activity, with one product (idecabtagene vicleucel) recently approved by FDA and EMA.

**Aims:** The primary endpoint of this observational and retrospective study was to define the clinical characteristics and outcome of a cohort of RRMM pts potentially eligible to CAR-T cell treatment according to the KarMMa trial criteria. Secondary endpoints were aimed at defining specific factors influencing CAR-T cell therapy eligibility and at identifying a real-life estimate of RRMM pts truly eligible for CAR-T cells.

**Methods:** This is a cohort analysis on RRMM pts managed between January 2018 and July 2021 at 10 Italian hematology centers. At the time of data collection, 108 RRMM pts had underwent at least 3 prior therapy regimens; they had received a previous PI, IMiDs and a moAb, and were considered refractory to the last regimen.

**Results:**

Median age was 68 years (38-86); 63 (59%) pts were >65 years; 57 (53%) were male. Of 108 pts, 87 (80%) were ECOG 0-1 and 33 (35%) were ISS III. The majority of pts, 72 (67%), had undergone an autologous stem cell transplantation; 93 pts received >3 prior lines of therapy. Sixty-seven (62%) were triple-refractory and 41 (38%) were penta-refractory. Based on the KarMMa trial criteria, 49/108 pts (45%) would be defined as eligible and 59 (55%) not eligible for CAR-T cell therapy. Organ dysfunction such as impaired renal function, anemia, thrombocytopenia, neutropenia and a FEV <45% was the most common criteria for ineligibility (86%). Twenty-one pts (19%) were not eligible because of an ECOG >2. Of the 59 pts considered ineligible for CAR-T cell therapy, 46 (62%) presented ≥2 ineligibility criteria.
After a median follow-up of 27 months (mo) (8-40.5), the median OS for the entire cohort was 21.1 mo (Fig. 1A). The median OS was 33 mo in eligible pts vs 8.3 mo in non-eligible pts (p=0.002) (Fig. 1B). The median PFS of the entire cohort was 8.7 mo (Fig. 1C) and the median PFS was 19.4 mo in eligible pts vs 6 mo (p=0.001) in non-eligible pts (Fig. 1D).

**Summary/Conclusion:**

Despite the limits of a retrospective study and a limited cohort, our real-life analysis shows that heavily treated pts with RRMM are less likely to be eligible for CAR-T cell therapy. Considering the emergent role of quadruplet combined approaches for first-line therapy and given the therapeutic relevance of CAR-T cells for the management of RRMM pts previously exposed to PI, IMiDs and moAb, our data could help to better define pts who could benefit from CAR-T cells under the current indications, while waiting for an extension of this approach to earlier disease stages.