P862 SERUM MASS SPECTROMETRY TO ANALYZE DISEASE RESPONSE IN PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA RECEIVING ARI0002H, AN ACADEMIC BCMA-DIRECTED CAR T-CELL THERAPY

**Topic:** 13. Myeloma and other monoclonal gammapathies - Biology & Translational Research

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**Background:**
ARI0002h is an academic BCMA-directed CAR T-cell that has been reported as effective in patients (pts) with relapsed/refractory multiple myeloma (RRMM). In these pts, next generation flow cytometry (NGF) in bone marrow (BM) allows the identification of deeper responses than serum protein immunofixation (IFE) after treatment.

**Aims:**
Here, we explore EXENT Quantitative Immunoprecipitation Mass Spectrometry (EXENT QIP-MS) as a highly-sensitive, serum-based, alternative monitoring technique and able to identify therapeutic monoclonal antibodies (t-mAb) interferences.

**Methods:**
Thirty-three RRMM pts with measurable disease in serum by IFE or free light chains were included. All of them received ≥2 prior regimens including a proteasome inhibitor, an immunomodulatory drug and daratumumab, and were refractory to the last one. These pts were treated with ARI0002h, 30 in the setting of the CARTBCMA-HCB-01 clinical trial (NCT04309981) and 3 as compassionate use. The M-protein (MP) was analyzed in serum by EXENT QIP-MS using IgG/A/M/κ/λ isotypic beads at three time points: before ARI0002h infusion, and 28 and 100 days post-infusion. Finally, 98 samples were analyzed by EXENT QIP-MS. Every patient had received daratumumab previously, but the last infusion date varied widely. The presence of disease in BM was also investigated by NGF (sensitivity ≥ 2x10^-6) at 28 and 100 days post-infusion. The median follow-up of the pts was 15 months (range 5 to 20).

**Results:**
Before ARI0002h infusion, MP could be identified in 33 (100%) pts by EXENT QIP-MS. After 28 and 100 days post-infusion, MP was also detected by this method in serum in 24 (72.7%) and 18 (56.3%) pts, respectively.

Investigating the ability of EXENT QIP-MS to identify the patient’s MP, interferences due to daratumumab and tocilizumab were successfully detected in serum with a IgG-kappa peak in the mass spectrum of 11693 and 11750.
Before AR10002h, daratumumab was identified in 10 pts (30.3%) and persisted even at day +100 in 5 of them (15.2%). Tocilizumab was detected at day +28 in 15 (71.4%) pts out of the 21 receiving it, persisting at day +100 in 3 of them (14.3%).

Then, we compared the results obtained by EXENT QIP-MS and IFE at the two time-points analyzed (n=63). Results were concordant in 81% of samples and discordant in 19% (p<0.0001). All discordances were due to EXENT QIP-MS(+)/IFE(-) results, except in one case. In this patient, the serum was mistakenly considered as IFE(+) (IgG-kappa) owing to the interference of daratumumab. Discordant results were equally noted at day +28 and +100 (Fig.1).

From 25 and 26 MRD-evaluable pts at day +28 and +100, 96% and 92% were MRD(-) in BM by NGF, respectively. NGF was discordant in all cases (EXENT QIP-MS(+)/NGF(-)), except in 1 patient at +28 days and 3 pts at +100 days, reflecting the MP persistence in the absence of BM disease. After 16 months, 75% of pts with EXENT QIP-MS(-)/NGF(-)/IFE(-) at day +28 were alive and without progression, and only 2 pts have relapsed from the disease, both after 12 months (14 and 16 months, respectively).

Image:

**Figure 1.** Concordance of EXENT QIP-MS in serum and IFE at the two time-points analyzed.

|          | +28rd AR10002h | +100rd AR10002h |
|----------|----------------|-----------------|
| EXENT QIP-MS (+) | 17             | 0               |
| EXENT QIP-MS (-) | 8              | 14              |
| IFE (+)   | 1              | 12              |
| IFE (-)   | 8              | 5               |

*False positive due to daratumumab interference.

Summary/Conclusion:

In this study including pts with RRMM and measurable disease, serum EXENT QIP-MS allowed the identification of the MP in all cases with high sensitivity. EXENT QIP-MS was also able to differentiate between the MP and t-mAb, which translated in a correct labeling of treatment response. As compared to both IFE in serum and NGF in BM, EXENT QIP-MS was able to identify residual disease in a higher proportion of cases.