S103 EFFICACY AND SAFETY OF ARI0002H, AN ACADEMIC BCMA-DIRECTED CAR-T CELL THERAPY WITH FRACTIONATED INITIAL THERAPY AND BOOSTER DOSE IN PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA

Topic: 14. Myeloma and other monoclonal gammopathies - Clinical

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Background: ARI0002h is a lentiviral autologous CAR T-cell product with a 4-1BB co-stimulatory domain and a humanized single chain variable fragment targeting BCMA. In pre-clinical studies, this academic CAR-T has demonstrated potent in vitro and in vivo activity.

Aims: We report the safety and efficacy results of the CARTBCMA-HCB-01 multicenter clinical trial for patients with relapsed/refractory multiple myeloma (RRMM) (NCT04309981) who received ARI0002h in 5 Spanish centers.

Methods: Patients (pts) aged 18-75 years old with RRMM were eligible for this study if they had measurable disease, received ≥2 prior regimens, including a proteasome inhibitor, an immunomodulatory drug and an anti-CD38 antibody, and were refractory to the last line of treatment. Bridging therapy was allowed after apheresis. Cyclophosphamide (300 mg/m²) and fludarabine (30 mg/m²) were used as lymphodepletion regimen. The targeted dose was 3x10⁶/kg CAR+ cells and was administered in a fractionated manner (10%/30%/60%), with at least 24 h between infusions. A second dose of 3x10⁶ CAR+ cells/kg was planned at least 4 months after the first dose in pts who achieved any grade of response any response and had not or serious complications after the first administration. Primary objectives were overall response rate (ORR; at least partial response -PR-) within 3 months of the first infusion and rate of cytokine release syndrome (CRS) and/or neurological toxicity in the first 30 days. Response was assessed as per IMWG criteria and bone marrow minimal residual disease (MRD) was analyzed by next-generation flow (NGF).

Results:

As of February ⁹th 2022, 35 pts (median age 61 years) with RRMM were included in the trial. Four pts could not receive ARI-0002h due to MM progression and one died of infection. Therefore, 30 pts received ARI0002h cells (modified intention-to-treat population), of which 47% received bridging therapy. Median CAR-T cell production time was 11 days (range 9-14) with a 100% manufacture success.

Median follow-up after ARI0002h administration for surviving pts was 16 months. The ORR of 30 evaluable pts was 100%, with a stringent complete remission (sCR) plus very good partial response (VGPR) rate of 90%. Median time to first response was one month. Of 26 MRD- evaluable pts at day +100, 92% were MRD-negative in bone marrow by NGF. 53% of patients were alive and without progression at 16 months. Median overall survival (OS) was not reached and the 16-month OS rate was 80% (Figure 1).

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AEs reported in >70% of pts were CRS (87%; grade [gr] 3/4 0%; gr 1 73%), neutropenia (97%; gr 3/4 100%), anemia (85%; gr 3/4 43%), and thrombocytopenia (79%; gr 3/4 70%). Median duration of CRS was 4 days (range 1-12). No CAR-T cell-related neurotoxicity cases were reported. Tocilizumab and corticosteroids were administered in 76% (mainly for persistent grade 1 CRS) and 12% of pts, respectively.

ARI0002h cells demonstrated peak expansion on day 14 (range 7 days-6 months). 24 out of 28 eligible pts (86%) received the second dose (range 1.2-3x10^6 CAR+ cells/kg). Median time after first infusion was 4 months and 38% received a second lymphodepletion regimen. No relevant toxicities after second infusions were reported. 7 pts (29%) improved their response after reinfusion.

Summary/Conclusion: ARI0002h is the first European academic CART for RRMM that has demonstrated deep and durable responses and a favorable safety profile, including the absence of neurotoxicity and the feasibility of a second booster dose.