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894 Efficacy and Safety of Anti-BCMA Chimeric Antigen Receptor T-Cell (CART) for the Treatment of Relapsed and Refractory AL Amyloidosis

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BACKGROUND: While anti-BCMA chimeric antigen receptor T-cell therapy (CART) have proven safe and efficient in multiple myeloma (MM), its application to AL amyloidosis (AL), has been restricted due to the frailty of this population and rarity of disease. HBI0101 therapy is a novel academic anti-BCMA CART-based therapy. In a phase Ia-b/2 study (NCT04720313), HBI0101 has demonstrated manageable safety with therapeutic efficacy in over 90 MM patient. AL patients were included in our study from its beginning, and we reported on our experience at ASH conference 2023 (abstract 538). Herein, we aim to report on additional patients and update our results on the largest cohort of AL patients receiving CART.

METHODS: The patients were treated within the following cohorts: 1 received 150x10^6 CART cells, 2 received 450x10^6 CART cells and 13 received 800x10^6 CART cells. Two of the patients were treated on a compassionate basis due to concomitant myelodysplastic syndrome (MDS) / ECOG 4 performance status. Patients with creatinine clearance ≥30ml/min (n=13) received lymphodepletion with fludarabine 25mg/m^2 and cyclophosphamide 250mg/m^2 on days -

5 to -3 before infusion, and patients with creatinine clearance <30ml/min (n=3) received lymphodepletion with bendamustine 90mg/m^2 and on days -4 and -3 before infusion. Five patients with AL-related advanced heart failure were admitted electively to the intensive care unit before infusion for close monitoring.

RESULTS: Sixteen AL patients with relapsed/refractory disease were included, with a median of 4 prior lines of therapy (range: 3-10), all except one were refractory to their last line of therapy, 14/16 (88%) were triple refractory to PI, IMiD and anti-CD38 antibody and 6/16 (38%) were refractory to the anti-BCMA antibody drug conjugate belantamab mafodotin. Most (13/16, 81%) had cardiac involvement, including 5 with MAYO-stage 3a/3b at study entry.

Hematologic adverse events included: grade 3-4 neutropenia in 10/16, Grade 3-4 anemia in 5/16 with no grade 3-4 thrombocytopenia. There were 9 occurrences of AL-related organ deterioration, in a total of 7/16 patients: 3 events of grade 3 acute heart failure exacerbations, 4 events of acute kidney injury (all of grades 1-2) and 2 events of acute liver injury (both grade 3), all of which resolved to baseline function with supportive care.

Cytokine release syndrome (CRS) was observed in 14/16 (grade 1-2- 11 patients; grade 3- 3 patients; no grade 4 or 5 CRS), and was manageable with frequent use of tocilizumab (12/14). None of the patients developed immune effector cell-associated neurotoxicity syndrome (ICANS) or other neurotoxicity. There were no treatment-related deaths.

The overall hematological response rate was 15/16 (94%) and the complete response (CR) rate was 12/16 (75%). Minimal residual disease (MRD) negativity based on flow cytometry 10^-5 was achieved in 9/14 evaluable patients. The median time to response was 17 days. Six of twelve evaluable patients had organ responses (heart/kidney/liver/autonomic dysfunction) and 5/10 cardiac patients with baseline NYHA score above 1 had improvement in their score. Seven patients died during follow-up, of whom 3 while in hematologic response, and the median overall survival (OS) was 223 days (95% CI: 177-not reached). Updated results will be communicated at the presentation time.

CONCLUSION: In the largest cohort of AL patients treated with CART reported to date, we demonstrated acceptable toxicity in this frail population, with a remarkable hematologic efficacy, leading to organ responses in many patients. Among patients with baseline advanced cardiac disease, deaths in the first year were frequent, skewing the OS results and suggesting that this effective therapy should be considered earlier, before end-stage heart disease is established. Our data suggests that anti-BCMA CART modality may become a powerful clinical tool to improve organ function and survival in AL.

Disclosures: Lebel: *Pfizer:* Membership on an entity's Board of Directors or advisory committees; *BMS:* Membership on an entity's Board of Directors or advisory committees. **Elias:** *Novartis:* Honoraria. **Grisariu:** *Gilead, Medison, MSD, Novartis, Sanofi, Takeda:* Consultancy. **Avni:** *Medison:* Consultancy; *Johnson and Johnson:* Consultancy; *Takeda:* Consultancy; *MSD:* Consultancy; *Novartis:* Consultancy; *Sanofi :* Consultancy. **Cohen:** *Amgen:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Johnson and*

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