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1030 Efficacy of HBI0101, an Anti-BCMA Chimeric Antigen Receptor T-Cell (CART) for Relapsed/Refractory Multiple Myeloma

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BACKGROUND: Although anti-B-cell maturation antigen (BCMA) chimeric antigen receptor T-cell (CART) therapy proved unprecedented efficacy in patients with relapsed/refractory (R/R) multiple myeloma (MM), its availability remains limited. HBI0101 is a novel second generation optimized anti-BCMA CART, that was developed in an academic setting. The phase I study evaluating HBI0101 (NCT04720313) demonstrated manageable safety and high efficacy. Here we present the updated results of the phases 1b/2 study evaluating the efficacy and safety of 84 patients with R/R MM receiving the recommended phase II target dose (RP2D).

METHODS: The patients enrolled had R/R MM with at least 3 prior lines of therapy, including a proteosome inhibitor, immune modulator (IMiD) and anti CD38 antibody. Inclusion criteria were relatively permissive as compared with other CART clinical trials, including thresholds of $30x10^9$/ml platelets, creatinine clearance of 20ml/min and performance status of 2 by ECOG scale. The RP2D was 800x10^6 CART cells.

RESULTS: Eighty-four patients with a median of 4 prior lines (range 3-13) were included in the analysis. Most patients (73/84, 87%) were triple refractory, 32/84 (38%) were penta-refractory

and 14/84 (17%) had received prior anti-BCMA therapy, mostly belantamab mafodotin. Extra-medullary disease was evident in 22/84 (26%). Thirty three of 81 (41%) had high-risk cytogenetics (t(4:14)/t(14:16)/del17), and 61/81 (75%) including 1Q-gain. Nearly half of this cohort (48%) would not have met the inclusion criteria for the registrational trials of both approved anti-BCMA CART. The manufacturing success rate was 84/84 (100%), and all patients included were infused with the RP2D.

The overall response rate was 77/84 (92%) and the complete response (CR)/stringent CR rate was 46/84 (55%). The minimal residual disease negativity rate (10^-5 by flow-cytometry) was 62/84 (74%). At data cutoff, with a median follow-up of 12.0 months (95% CI: 8.8-14.6), the median progression-free survival was 11.6 months (95% CI: 8.6-14.6) and the median overall survival was not reached (NR) (95% CI: 19.6-NR).

Safety was manageable with grade 3-4 hematological toxicities common (anemia- 62%, thrombocytopenia- 42%, neutropenia- 99%). Cytokine release syndrome (CRS) occurred in 80/84 (95%), including 16 patients with grade 3 CRS (19%), but no cases of grade 4/5. Neurological toxicity (ICANS or other) was rare and mild (3 cases, all of grade 1-2). No irreversible organ toxicities or treatment related deaths occurred.

Updated results will be communicated at the presentation time.

CONCLUSION: HBI0101 BCMA CART results demonstrate high efficacy and manageable safety in a frailer and higher risk population as compared with the registrational studies with commercial products. This data not only supports further utilization of HBI0101 CART therapy, but also of CART production at an academic setting in general, ensuring a sufficient CART supply in the light of the increasing demand.

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