



The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

704.CELLULAR IMMUNOTHERAPIES: EARLY PHASE AND INVESTIGATIONAL THERAPIES

Safety and Efficacy of a Locally Produced Novel Anti-BCMA Chimeric Antigen Receptor T-Cell (CART) (HBI0101) for the Treatment of Relapsed and Refractory Multiple Myeloma

Eyal Lebel^{1,2}, Nathalie Asherie², Shlomit Kfir-Erenfeld^{3,2}, Batia Avni, MD^{3,4}, Sigal Grisariu, MD^{4,2}, Shlomo Elias^{3,2}, Miri Assayag^{3,2}, Tatyana Dubnikov^{3,2}, Nomi Zalcman^{5,3}, Marjorie Pick³, Eran Zimran, MD^{3,2}, Yael C. Cohen^{6,7}, Irit Avivi Mazza, MD⁸, Cyrille Cohen⁹, Moshe E Gatt, MD^{10,3}, Polina Stepensky^{2,3}

¹ Faculty of Medicine, the Hebrew University, Jerusalem, Jerusalem, Israel

² Department of Bone Marrow Transplantation and Cancer Immunotherapy, Hadassah Medical Center, Jerusalem, Israel

³ Faculty of Medicine, Hebrew University of Jerusalem, Jerusalem, Israel

⁴ Bone Marrow Transplantation & Cancer Immunotherapy Department, Hadassah-Hebrew University Medical Center and Faculty of Medicine, the Hebrew University of Jerusalem, Jerusalem, Israel

⁵ Bone marrow transplant and cellular therapy department, Hadassah Medical Center, Jerusalem, Israel

⁶ Department of Hematology, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel

⁷ Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

⁸ Hematology Division, Sourasky Medical Center and the Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

⁹ Laboratory of Tumor Immunology and Immunotherapy, The Mina and Everard Goodman Faculty of Life Sciences, Bar-Ilan University, Ramat Gan, Israel

¹⁰ Department of Hematology, Hadassah Medical Center, Jerusalem, Israel

BACKGROUND: Anti-B-cell maturation antigen (BCMA) chimeric antigen receptor T-cell (CART) therapy shows remarkable efficacy in patients with relapsed and/or refractory (R/R) multiple myeloma (MM), with recent phase 3 studies showing clear advantage of idecabtagene vicleucel (ide-cel) and ciltacabtagene autoleucel (cilta-cel) over standard-of-care. However, access to these commercial CART products is a major barrier, and it is estimated that only around a quarter of eligible R/R MM patients will receive CART nowadays.

HBI0101 is a novel second generation optimized anti-BCMA CART with 4-1BB co-stimulatory domain, that was developed in an academic setting, at Hadassah Medical Center and Bar-Ilan University. The phase Ia study evaluating HBI0101 (NCT04720313) demonstrated a manageable safety profile and an initial high efficacy (Asherie, Haematologica 2022). Here, we present the updated results of 50 patients receiving 800×10^6 CART cells in the NCT04720313 phases 1a-b / 2.

METHODS: The phase 1a study with HBI0101 which first evaluated 20 R/R MM patients with ≥ 3 prior lines of therapy, including a PI, IMiD and anti-CD38 antibody, revealed a dose of 800×10^6 CART cells to be safe and effective. The phase Ib and phase 2 of the study evaluated this dose infusion in 43 additional patients. Inclusion criteria were relatively permissive with minimum creatinine clearance of 20ml/min, platelet count of 30×10^9 /ml, left ventricular ejection fraction of 40%, and ECOG performance status of ≤ 2 . Lymphodepletion included fludarabine 25mg/m^2 and cyclophosphamide 250mg/m^2 on days -5 to -3 before infusion (bendamustine 90mg/m^2 and on days -4 and -3 for patients with creatinine clearance $< 30 \text{ml/min}$). Planned manufacturing time was 10 days.

RESULTS: Of 51 patients who underwent lymphocyte apheresis, 50 (98%) were treated with 800×10^6 CART cells; 7 patients in the phase Ia cohort and 43 in the phases 1b / 2 cohorts. HBI0101 production success rate was 100%, with manufacturing time of 10 days for all patients. The median age was 65y (range 40-84). The median number of prior lines was 4 (range 3-13) and most patients (47/50, 94%) were triple refractory to PI, IMiD and anti-CD38 antibody. Twenty patients (40%) were penta-refractory and 10 (20%) were refractory to the anti-BCMA antibody drug conjugate belantamab mafodotin. Forty-six patients (92%) were refractory to the last line of therapy. Twelve patients (24%) had high risk cytogenetics (t(4:14), t(14:16) or deletion 17p); 31 (62%) when 1q gain included. Sixteen patients (32%) had extramedullary involvement at study entry.

Grade 3-4 hematological toxicities were common (anemia- 62%, thrombocytopenia- 54%, neutropenia- 98%, lymphopenia- 100%). Cytokine release syndrome (CRS) occurred in 48/50 (96%)- grade 1/2- 17 patients (82%); grade 3- 7 patients (14%). Tocilizumab was used in 40/48 patients with CRS (median of 1 dose, range 1-4) and corticosteroids in 8/48. Two cases of immune effector cell associated neurotoxicity syndrome (ICANS) were observed (grade 1 and 2). Two patients developed

CART-associated hemophagocytic lymphohistiocytosis syndrome (HLH). No irreversible organ toxicities or treatment related deaths occurred.

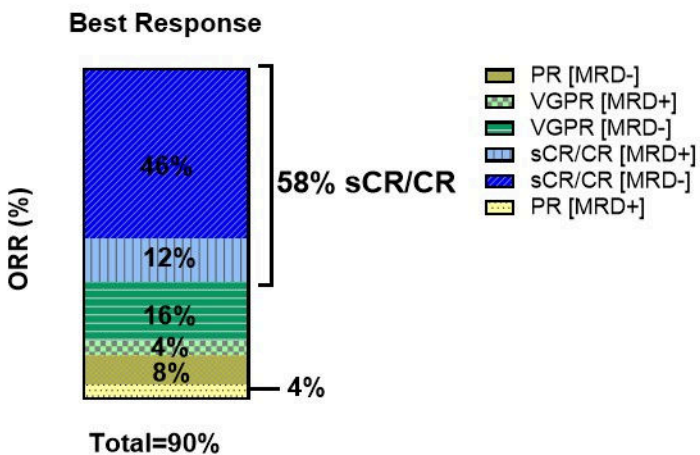
The overall response rate (ORR) was 45/50 (90%), including 29 patients (58%) with complete response (CR)/stringent CR, 10 (20%) with very good partial response and 6 (12%) with partial response. Thirty-five patients (70%) achieved minimal residual disease (MRD) negativity at day +30. At a median follow-up of 11.9 months (range: 0.6-19), the median progression-free survival was 10.6 months, and the median overall survival was not reached (Figure 1).

Although the presence of extra-medullary disease and prior anti-BCMA therapy correlated with worse outcome, high response rates were still observed (ORR of 98%/75% for patients without/with extra-medullary disease, respectively, and 95%/75% for patients without/with prior anti-BCMA therapy, respectively). Updated results will be communicated at the presentation time.

CONCLUSION: Our findings demonstrate the manageable safety and high efficacy profiles of HBI0101 also in high-risk patients. Fast production time enabled the timely treatment of 98% of apheresed patients. These favorable data are encouraging and support decentralization of CART production at an academic setting, ensuring a sufficient CART supply in the light of the increasing demand.

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ORR- overall response rate; sCR- stringent complete response; CR- complete response; VGPR- very good partial response; PR- partial response; MRD- minimal residual disease; PFS- progression-free survival; mPFS- median progression-free survival; mFU- median follow-up; OS- overall survival; mOS- median overall survival

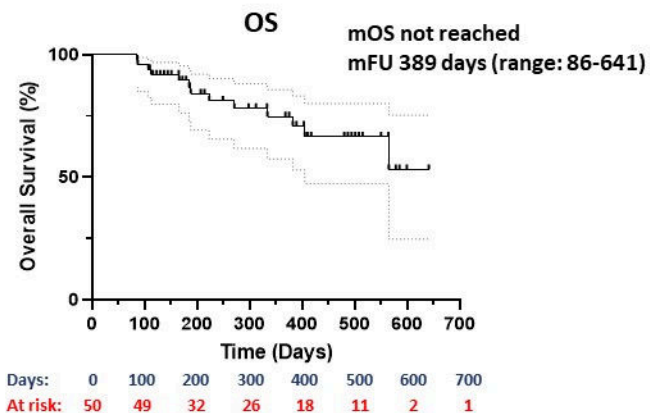
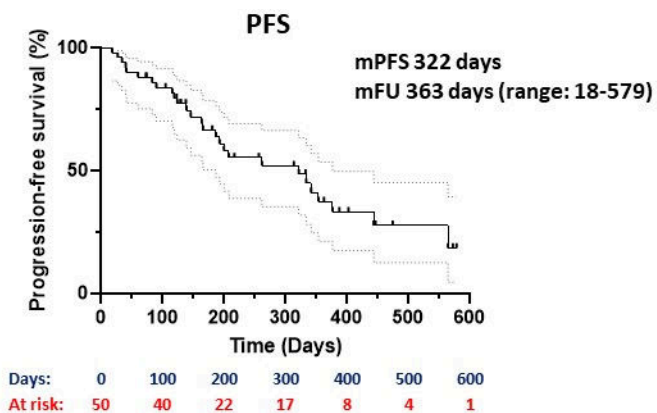


Figure 1