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

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INTRODUCTION

Anti-B-cell maturation antigen (BCMA) chimeric antigen receptor T-cell (CART) therapy shows remarkable efficacy in patients with relapsed/refractory (R/R) multiple myeloma (MM), however, access to commercial CART products is a major barrier. 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 1a study evaluating HBI0101 (NCT04720313) demonstrated a manageable safety profile and an initial high efficacy (Asherie, Haematologica 2022). Here, we present the updated results of the additional phases 1b/2, with 50 patients receiving 800x10^6 CART cells in the NCT04720313.

METHODS

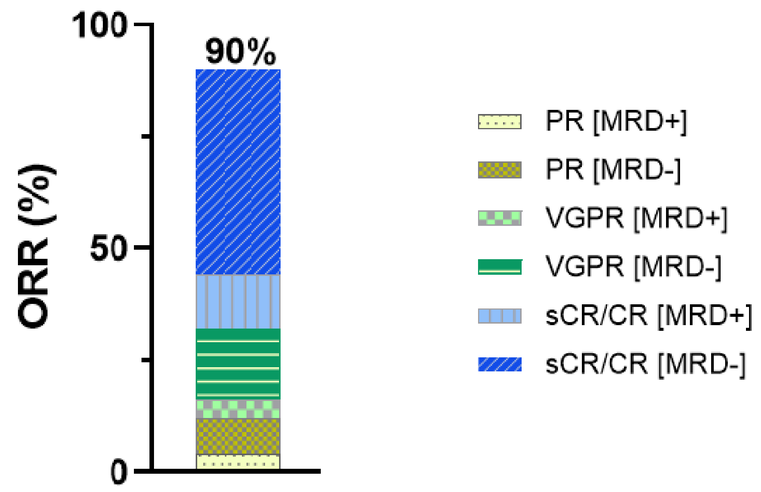
The phase 1a study with HBI0101 which first evaluated 20 R/R MM patients with ≥3 prior lines of therapy, including a PI, IMiD and anti-CD38 antibody, revealed a dose of 800x10^6 CART cells to be safe and effective. Phases 1b/2 of study further evaluated this dose.

Inclusion criteria were relatively permissive with minimum creatinine clearance of 20ml/min, platelet count of $30x10^9$/ml 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 for patients with creatinine clearance <30ml/min).

Planned manufacturing time was 10 days.

Table 1- Characteristics of the 50 patients included

Age	median 65 (40-84)
Prior lines of therapy	median 4 (3-13)
Triple refractory	47/50 (94%)
Penta-refractory	20/50 (40%)
Prior BCMA-targeted therapy	12/50 (24%)
Extra-medullary disease	16/50 (24%)
High-risk FISH (t(4:14)/t(14:16)/-17p)	12/50 (24%)
High-risk FISH incl. +1q	31/50 (62%)

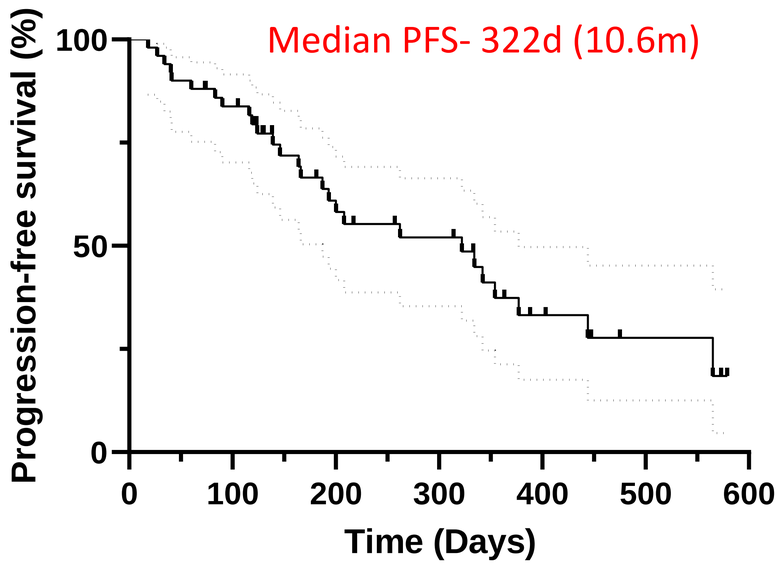


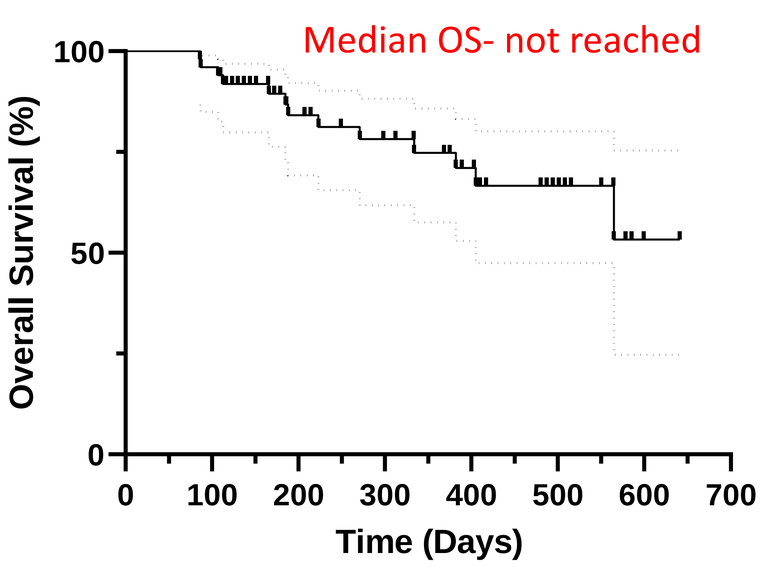
RESULTS

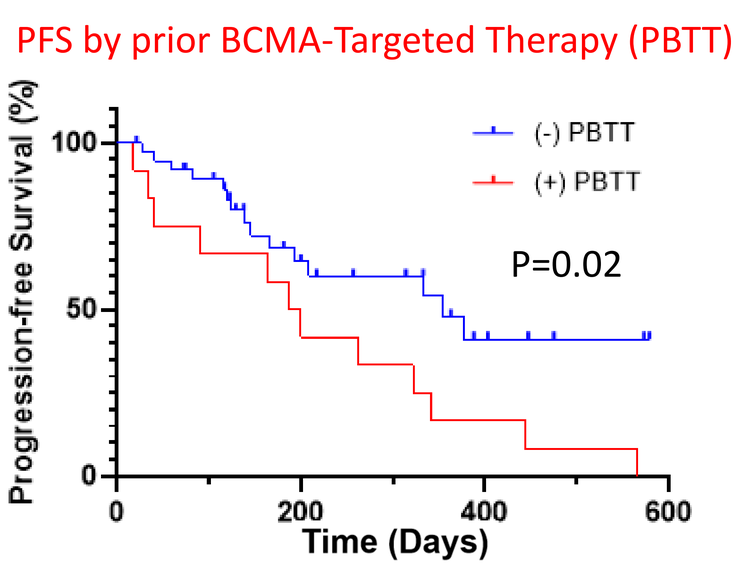
Of 51 patients who underwent lymphocyte apheresis, 50 (98%) were infused. HBI0101 production success rate was 100%, with manufacturing time of 10 days for all patients.

Patients' characteristics are detailed in **Table 1.**

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. Although the presence of extra-medullary disease and prior BCMA-targeted 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 BCMA-targeted therapy, respectively).







Safety: 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- 41 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.

CONCLUSIONS

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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