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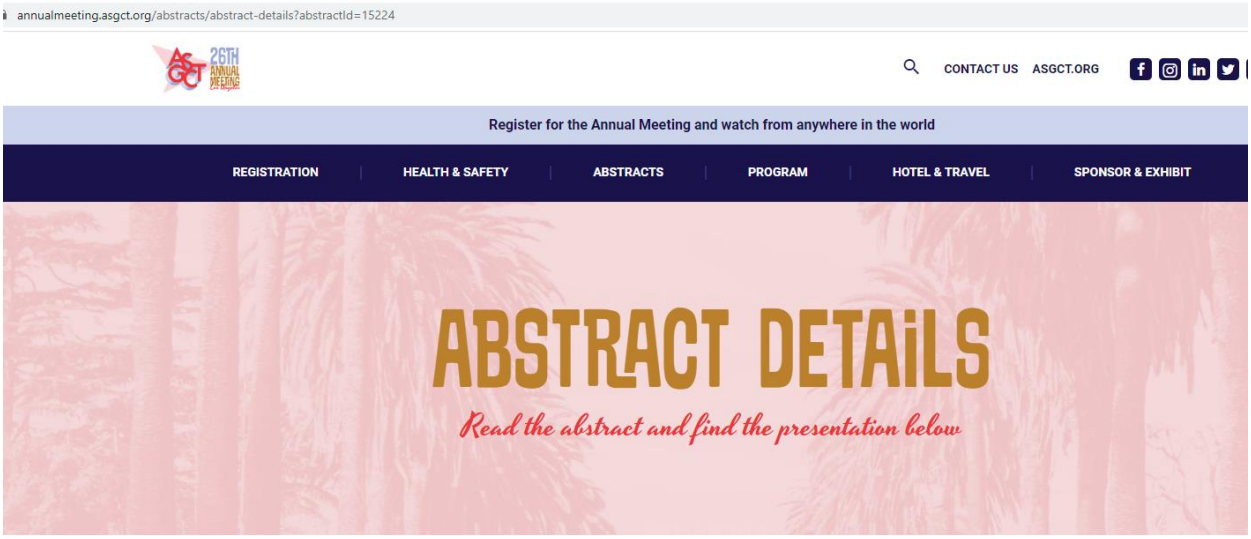

Full text and presentation details

I – Gene & Cell Therapy Trials in Progress -> Gene & Cell Therapy Trials in Progress

BCMA-Targeted CART (HBI0101), a Safe and Efficacious Novel Modality of Treatment for LC Amyloidosis Patients

Type: Oral Abstract Session

Presentation Details

Session Title: Late-Breaking Abstracts 1
Location: Room 515 AB
Start Time: 5/19/2023 9:15
End Time: 5/19/2023 9:30

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BACKGROUND. Multiple myeloma (MM) is an incurable plasma cell malignancy. Light chain amyloidosis (AL) is a rare plasma cell disorder characterized by an overproduction and accumulation of immunoglobulin light chains, resulting in amyloid fibril formation and organ deposition. While BCMA-CART approved therapies have proven safe and efficient in MM

patients, their application to other plasma cell dyscrasias, such as AL, has been restricted, due to the frailty of this patient population. HBI0101 therapy is a novel anti-BCMA CART-based therapy developed and launched at Hadassah Medical Center for MM treatment (NCT04720313). In this phase Ia/b study, HBI0101 has demonstrated manageable safety profile, with therapeutic efficacy in over 50 MM patients. **RATIONALE.** Although BCMA targeting in the treatment of AL has been questioned because of the lower expression of this antigen on AL plasma cell surface in comparison with its expression on MM plasma cells, we have previously reported that this level of expression is sufficient to enable plasma cell recognition and subsequent eradication by HBI0101 CART cells *ex vivo*. Based on this observation, we have included eight AL patients in our study cohort. **METHOD.** We present here the interim results of eight AL patients, which represent the largest cohort of AL patients treated with BCMA-CART-based therapy reported in the literature so far. All eight patients reported here had clinically active, relapsing and progressive disease following a median of 6 lines of treatment (range: 3-10), and all were resistant to their last line of therapy. Of these patients, six were penta-refractory, including five patients resistant to anti-BCMA antibody conjugates. Seven of the patients had cardiac involvement. Three with MAYO-stage IIIa cardiac involvement and one with stage IIIb. Six patients had elevated proBNP ranging from 731-28000 pg/ml. The patients were treated within the following HBI0101 cohorts: one received $150x10^6$ CAR+, two received $450x10^6$ CAR+ and five received $800x10^6$ CAR+ cells. Two patients were treated on a compassionate basis due to concomitant myelodysplastic syndrome (MDS) and to ECOG 4 performance status, respectively. **RESULTS.** Adverse events (AEs) were manageable, and included Grade 1-3 CRS observed in 5 of 8 patients. Hematologic AEs included: Grade 3-4 neutropenia in 5 of 8 patients, Grade 2-3 anemia in two patients, and in one case Grade 4 pre-existing thrombocytopenia (related to MDS). None of the patients developed ICANS. HBI0101 therapy induced remarkable responses in these eight heavily pretreated AL patients, achieving a fast and efficient complete response (CR) in five patients, a very good partial response (VGPR) in two patients, and a partial response (PR) in one patient. A significant reduction in the difference in Involved and Uninvolved Free Light Chain (dFLC) 0-50 mg/L dFLC levels was observed in all eight patients, and flow cytometry 10^{-5} minimal residual disease (MRD) negativity was achieved in five of the patients. With a relatively median follow-up period of 7.3 months (range: 1.5-15.5), the median duration of response (DOR) was 5 months (range: 1.5-15). In five of the patients, the deep responses observed correlated with clinical improvement and translated into organ responses. **CONCLUSION.** In this largest cohort of AL patients reported to date, HBI0101 demonstrated acceptable toxicity in this frail patient population. Moreover, all patients responded to therapy, implying that CART therapy may become a powerful clinical tool to improve patient and organ survival even in advanced AL patients.

N. Asherie: None.