2104 Primary Analysis of Varnimcabtagene Autoleucel (IMN-003A) in Phase 2 Study (IMAGINE), a First-in-India Industry CD19-Directed CAR-T Cell Therapy for Patients with Relapsed Refractory B Cell Malignancies

Program: Oral and Poster Abstracts
Session: 704. Cellular Immunotherapies: Early Phase and Investigational Therapies: Poster I
Hematology Disease Topics & Pathways:
Research, clinical trials, Lymphoid Leukemias, ALL, Biological therapies, Lymphomas, non-Hodgkin lymphoma, Clinical Research, B Cell lymphoma, Chimeric Antigen Receptor (CAR)-T Cell Therapies, Diseases, indolent lymphoma, aggressive lymphoma, Therapies, Lymphoid Malignancies, Minimal Residual Disease

Saturday, December 9, 2023, 5:30 PM-7:30 PM

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Background: Varnimcabtagene autoleucel (IMN-003A) is an autologous second-generation CAR-T cell product with a 4-1BB co-stimulatory domain and a non-FMC63 based murine single chain variable fragment targeting CD19 (A3B1 binder), manufactured in India. Preclinical and Phase 1 study was conducted at HCB / IDIBAPS Spain. Here, we present the primary analysis of IMAGINE, a Phase 2, multicenter, single-arm study of var-cel for patients in India with relapsed/refractory B cell malignancies (RR BCM) (CTRI/2022/03/041162).

Methods: Patients (pts) aged 3 to 45 years (B-ALL) and ≥ 18 years (B-NHL) with RR BCM were eligible if they had measurable disease, as assessed by lymphoid blasts (B-ALL) or metabolic tumour bulk (B-NHL), received ≥1 prior regimen, refractory to the last line of treatment with good performance status (ECOG 0 to 1). Bridging therapy was allowed after apheresis. Cyclophosphamide (300 mg/m^2) and fludarabine (30 mg/m^2) on days -5 to -3 were used as preparative lymphodepletion regimen. The target dose was 1x10^6/kg CAR+ cells (B-ALL) and 5x10^6/kg CAR+ cells (B-NHL) (overall range 0.1x10^6 to 5x10^6) and was administered in a fractionated manner (10%/30%/60%) over 3 days with at least 24h between infusions. Primary objectives were overall response rate (ORR: CR + CRi in B-ALL and CR + PR in B-NHL) at day +90 after first infusion, and safety. Response was assessed as per NCCN (B-ALL) and IWG (B-NHL) criteria; bone marrow minimal residual disease (MRD) for B-ALL was analyzed by flow cytometry at 10^{-4} sensitivity and PET-CT for B-NHL. Adverse events (AEs) were graded using CTCAE v5.0. CRS and ICANS were graded according to the American Society for Transplantation and Cellular Therapy (ASTCT) criteria.

Results: At data cut-off, of 25 pts enrolled (median age 31 yrs, range 3 - 66) with RR BCM [n=13 B-ALL, median blasts 0.34% (range 0.01 - 27.2); n=12 B-NHL, median TMTV 67.9 ml (range 27.1 - 1177), median SPD 3846 mm^2 (range 1001 to 35849], 24 pts received var-cel (1 withdrawal) with majority of infusions on Days 0, +3, +7 and 12 pts (50%) needed bridging therapy. Median CAR-T cell manufacturing time was 14 days (range 10 - 27) with 100% manufacturing success.

Median follow-up after IMN-003A administration was 205 days (range 12 – 434). Overall response rate (ORR) was 91.7% (22/24) at D+28 (B-ALL 91.7%, MRD neg 83.3% (n=10/12); B-NHL 91.7%, CR 66.7%) and 80.9% (17/21) at D+90 [B-ALL 80%, MRD neg 80% (n=8/10); B-NHL 81.8% (9/11), CR 63.6%]. One B-NHL pt in PR at D+28 achieved CR at D+90. Three pts relapsed by D+90. Of MRD evaluable pts, response was 100% at day+28 (n=11/11) and 88.9% at D+90 (n=8/9). Median time to first response was 28 days.

Median progression free survival (PFS, range 12-NR), duration of response (DOR, range 0-NR) and overall survival (OS) were not reached (range 12-NR).

AESIs reported were CRS (Grade [G] 1 62.5%; G3+ 4.2%; overall 66.7%); ICANS (G1 4.2%; G3+ 0%; overall 4.2%); neutropenia (G3+ 91.7%; overall 100%); anemia (G3+ 29.2%; overall 95.8%); and thrombocytopenia (G3+ 20.8%; overall 91.7%). CRS median onset was D+5 and duration 3 days. No G3+ ICANS was reported. Tocilizumab, steroids and anakinra usage was in 37.5% (n=9/24, majority for persistent G1 CRS), 8.3% and 4.2% respectively. Treatment related mortality was 4.2% (n=1/24); 3 pts died of disease progression.

IMN-003A cells demonstrated peak expansion on D+10 (range 7 – 28 days). 79.2% at D+28 and 29.2% at D+90 had measurable CAR+ T cells in peripheral blood; median D+28 (range D+10 - NR). Updated results will be presented in the meeting.

Conclusions: Varnimcabtagene autoleucel (IMN-003A), a First-In-India Industry CD19-directed CAR-T Cell Therapy for RR BCM, has demonstrated manageable safety profile and durable efficacy outcomes with deep responses including absence of severe neurotoxicity. This offers a significant benefit over standard treatment options for patients with RR BCM.

A

Endpoints	ITT Set: 24 (n = 12 B-ALL; 12 B-NHL)
Efficacy	
Overall Response Rate (ORR) @ Day 90 Primary endpoint	**80.9%** (n= 17 / 21) B-ALL 80% (n = 8 / 10); B-NHL 81.8% (n = 9 / 11) B-ALL Adult 50% (n = 1 / 2); B-ALL Paed 87.5% (n = 7 / 8) MRD neg (B-ALL): 77.8% (n = 7 / 9) B-NHL CR 63.6% (n = 7/11); PR 18.1% (n = 2 / 11)
Overall Response Rate (ORR) @ Day 28	**91.7%** (n = 22 / 24) B-ALL 91.7% (n = 11 / 12); B-NHL 91.7% (n = 11 / 12) B-ALL Adult 100% (n = 3 / 3); B-ALL Paed 88.9% (n = 8 / 9) MRD neg (B-ALL): 91.7% (n = 11 / 12)* B-NHL CR 66.7% (n = 8/12); PR 25% (n = 3 / 12)
Progression Free Survival	**NR**
Duration of Response	**NR**
Overall Survival	**NR**
Safety	
Cytokine Release Syndrome (CRS)	**G4 4.2% (n = 1/24); G1 62.5% (n = 15/24)**
Immune Effector Cell Associated Neurotoxicity Syndrome (ICANS)	**G1 4.2% (n = 1/24); G3+ 0%**
TRM	**4.2% (n = 1/24); CRS**
Tocilizumab Use	
CRS (n = 16 / 23)	**37.5% (9 / 24)**

B

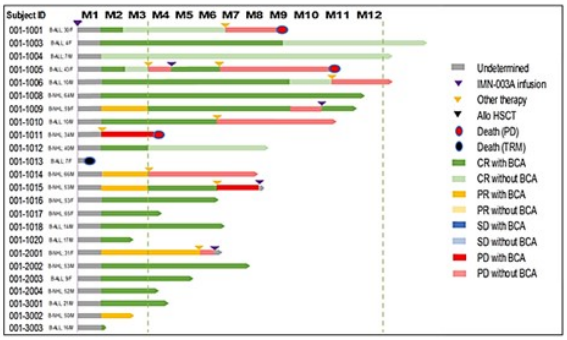

Figure 1: (A) Summary of safety and efficacy outcomes; **(B)** Swimmer plot