ELSEVIER

Blood 142 (2023) 6858–6859

The 65th ASH Annual Meeting Abstracts

ONLINE PUBLICATION ONLY

704.CELLULAR IMMUNOTHERAPIES: EARLY PHASE AND INVESTIGATIONAL THERAPIES

Reinfusion of Varnimcabtagene Autoleucel (IMN-003A) in Patients with Relapsed Refractory B Cell Malignancies Is Feasible with Sustained Responses

Sharat Damodar, MBBS, MD DM[1], *Raja Thirumalairaj, MDDM*[2], *Akshatha Nayak, MD*[1], *Shilpa Prabhu, MD*[1], *Rameez Ahamed, MD*[2], *Deepak MB, MD*[1], *Sudarshan Chougule, MD*[1], *Lakshman Vaidhyanathan, MD*[2], *Karthik GA, MD*[1], *Sunil HV, MD*[1], *Shelley Simon, MD*[2], *Jayaraj Govindaraj, MD*[2], *Pallavi Arasu*[3], *Sri Ramulu Elluru*[3], *Mohammed Manzoor Akheel, MPH MBA*[3], *Anil Kamat, MDFRCP FRCPath MBA*[3]

[1] Mazumdar Shaw Medical Centre, Narayana Health City, Bengaluru, India
[2] Apollo Speciality Hospital, Chennai, India
[3] Immuneel Therapeutics Private Limited, Bengaluru, India

Background: Varnimcabtagene autoleucel, a CD19 directed CAR-T cell therapy with a 4-1BB co-stimulatory domain and a non-FMC63 based murine scFv (A3B1 binder), has demonstrated remarkable responses in relapsed/refractory B cell malignancies (RR BCM) in the IMAGINE study. Reinfusion of var-cel is an option to improve functional persistence for CD19+ relapsed disease. This abstract describes the clinical outcomes following reinfusion of var-cel in patients (pts) who relapsed after first infusion.

Methods: Patients (pts) aged 3 to 45 years (B-ALL) and ≥ 18 years (B-NHL) with RR BCM were eligible for IMAGINE study 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).

The primary 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 infused over 3 days (10%/30%/60% fractions). 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. Adverse events (AEs) were graded using CTCAE v5.0. CRS and ICANS were graded according to ASTCT criteria.

Criteria for reinfusion was: 1) achieved response with subsequent disease progression and presence of CD19 positive malignant cells; 2) available second dose for retreatment from initial apheresis and manufacturing run; and 3) after primary endpoint at D+90.

This abstract evaluates the outcomes at D+28 after var-cel reinfusion.

Results: At data cut-off, 25 pts were enrolled (median age 31 yrs, range 3 - 66) with RR BCM (n=13 B-ALL; n=12 B-NHL). 24 pts received var-cel (1 withdrawal) with majority of infusions on Days 0, +3, +7. ORR was 91.7% at D+28 and 80.9% at D+90. 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).

Nine pts had relapsed disease (37.5%) with median PFS of 178 days (range 28-319). Of these 9 pts, 7 had CD19+ relapse (77.8%) and 2 (with B-ALL) had CD19- relapse. Four of these pts received second infusion at full dose (same as primary infusion) fractionated over 3 days (10%, 30%, 60%). For these 4 pts, duration of B cell aplasia after primary infusion was 90 days to NR (range); var-cel was detectable in 1 pt (n=1/4) at relapse; and median PFS was 166 days (range 90-275). Tumour burden at relapse was: Ph+ B-ALL (n=1) with 22% blasts (p210 BCR ABL transcript 36.7%); B-NHL (n=3) with TMTV range 7.5 to 277 ml and SPD range 660.5 to 8686 mm ^{2} (Table 1). PDL1 exhaustion marker was expressed in one B-NHL pt only. Salvage regimen in B-NHL pts was involved field radiotherapy (n=2); 1 B-NHL pt was reinfused without salvage treatment. B-ALL pt received Dasatinib, Inotuzumab and CNS prophylaxis. Preparative conditioning regimen for these 4 patients were: Fludarabine-Cyclophosphamide (n=1), with Rituximab (n=2) and Rituximab with Nivolumab (n=1).

Post reinfusion, var-cel was not detected in 1 pt (B-ALL) however B cell aplasia was persistent. In B-NHL pts, Cmax range was 7222 to 31846 CAR+ copies / ug genomicDNA; Tmax was D+2 after reinfusion and duration of var-cel persistence was range 2 days to NR (Figure 1).

Post reinfusion, no CRS (0%) or ICANS (0%) was reported. Hematotoxicity was the most common AE (100%) with neutropenia (G3+ 100%); anemia (G3+ 66.7%); and thrombocytopenia (G3+ 33.3%;). Hypogammaglobulinemia (IgG <4g/L) was seen in

2 pts (50%, new onset 1 pt). Time to first response after reinfusion was 28 days. The D+28 ORR for evaluable pts (n=2) was 100%. Median PFS after reinfusion is NR. Post reinfusion 1 pt (Ph+ B-ALL) died of disease progression at 313 days (50 days after reinfusion). The evaluable B-NHL pts are in remission.

Conclusions: Reinfusion of varnimcabtagene autoleucel (IMN-003A) is feasible, safe and well tolerated. Preparative conditioning regimen for reinfusion needs personalization guided by CAR persistence, disease biology (CD20, PDL1 expression) and haematological reserve. After reinfusion, prolonged B cell aplasia was observed with 100% ORR at D+28 in evaluable pts. Var-cel was detected post reinfusion in B-NHL patients with sustained responses. Reinfusion may be considered in preference for some pts. The ideal preparative regimen and pt characteristics to guide reinfusion outcomes remains an area of research.

Disclosures Arasu: *Immuneel Therapeutics Private Limited:* Current Employment. **Elluru:** *Immuneel Therapeutics Private Limited:* Current Employment. **Akheel:** *Immuneel Therapeutics Private Limited:* Current Employment. **Kamat:** *Immuneel Therapeutics Private Limited:* Current Employment.

Table 1: Characteristics of reinfused patients in IMAGINE study

Patient Characteristics	B-ALL	B-NHL
	N = 1	N = 3
Age (years); median (range)	43	53 (31 - 59)
Disease burden at relapse		
Blasts (%)	22	-
TMTV (mL) range	-	7.5 - 277
SPD (mm^2) range	-	660.5 - 8686
Var-cel persistence after first infusion (days)	28	56 - NR
CRS (Reinfusion)	No	No
ICANS (Reinfusion)	No	No
ORR at D+28 (Reinfusion) evaluable pts (%)	100	100

Figure 1: Persistence and expansion of varnimcabtagene autoleucel and percentage B cell count after reinfusion

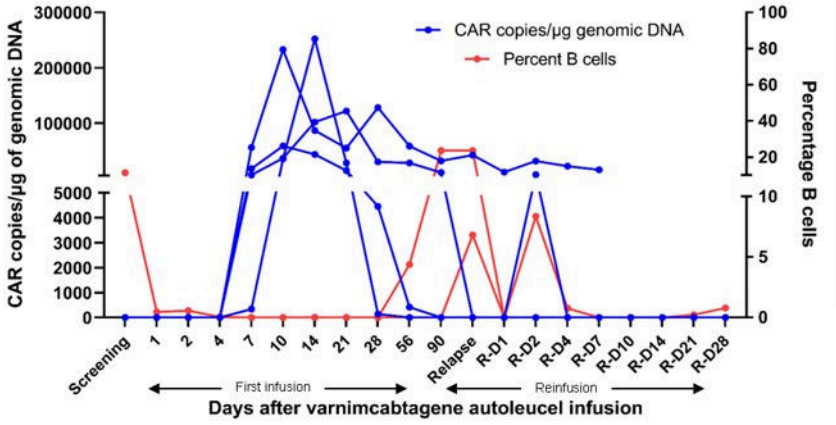

Figure 1

https://doi.org/10.1182/blood-2023-181106