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Early Results from a Phase-2 Study of Varnimcabtagene Autoleucel (IMN-003A), a First-in-India Industry CD19-Directed CAR-T Cell Therapy with Fractionated Infusions for Patients with Relapsed and/or Refractory B Cell Malignancies (IMAGINE Study)

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Abstract

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. As previously published, pre-clinical studies and phase 1 clinical trial in Spain, varnimcabtagene autoleucel (IMN-003A / ARI-0001) has demonstrated potent *in vitro*, *in vivo* and clinical activity. Here, we report the first safety and efficacy results of the IMAGINE phase 2 clinical trial for patients in India with relapsed/refractory B cell malignancies (CTRI/2022/03/041162).

Methods: Patients (pts) aged 3 to 45 years (B-ALL) and ≥ 18 years (B-NHL) with relapsed and/or refractory B cell malignancies (RR BCM) were eligible for this 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)

(30 mg/m^2) on days -5 to -3 were used as 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%), with at least 24h between infusions on days 0, +1, +2. 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 occurrence of adverse events including cytokine release syndrome (CRS) and/or Immune Effector Cell Associated Neurotoxicity Syndrome (ICANS). 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: As of data cut-off, eight pts (median age 21 yrs, range 5 - 64) with RR BCM (n=6 B-ALL; n=2 B-NHL) have been included in the trial. 6 pts received IMN-003A cells (intention-to-treat population), of which 2 (33.3%) received bridging therapy. The main characteristics of these pts and previous treatments are described in Figure 1A. Median CAR-T cell manufacturing time was 11 days (range 10-18) with 100% manufacturing success.

Median follow-up after IMN-003A administration was 50 days (range 5 - 117). Of the 5 evaluable patients, ORR at day +28 (n=4) and day +90 (n=1) was 100%. Median time to first response was 28 days. All pts were in CR at data cut-off.

Of 5 MRD-evaluable pts at day +28 (n=4) and +90 (n=1), 100% were MRD-negative. Median progression-free survival (PFS, Figure 1B) and overall survival (OS) were not reached.

AESIs reported in 8 pts were CRS (Grade [G] 1 50%; G3+ 0%; overall 50%), neutropenia (G3+ 50%; overall 62.5%), anemia (G3+ 0%; overall 62.5%), and thrombocytopenia (G3+ 0%; overall 62.5%). Median onset and duration of CRS was on Day +10 and 2 days respectively. No CAR-T cell-related neurotoxicity (ICANS) was reported. Tocilizumab was administered in 33.3% (n=2/6) (for persistent grade 1 CRS). No mortality has been reported in this study till date.

IMN-003A cells demonstrated peak expansion on day 10 (range 10 - 14 days). 80% (5/6 evaluable pts) had measurable CAR+ T cells in peripheral blood on day +28. Updated results will be presented in the meeting.

Conclusion: Varnimcabtagene autoleucel (IMN-003A) is a First-In-India Industry CD19-directed CAR-T Cell Therapy for RR BCM that has demonstrated excellent outcome in a clinical trial, with deep and durable responses and a favorable safety profile, including absence of neurotoxicity. Varnimcabtagene autoleucel offers a significant benefit over standard treatment options for

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Abstract

Disclosures

Figure 1 Author notes

A

No.	Age (y)	Gender	ECOG	Lansky	Cohort	R/R	Blasts (%) / MTV (ml)	Genomic aberration	EMD	Prior Inotuzumab	Auto / Allo		Lines of Treatment	Bridging Therapy	D0 mEASI	CRS	ICANS	Toci	Outcome
1	31	F	0	-	B-ALL	RF	0.10%	None	No	No	No	2	(BFM, 6MP)	No	0.15	No	No	No	D90 CR
2	5	F	-	100	B-ALL	RF	0.01%	iAMP21+	No	No	No	2	(BFM, HD MTX)	No	0.04	G1	No	No	D28 CR
3	7	M	-	100	B-ALL	RL	0.63%	None	No	No	No	2	(BFM, Pred)	No	0.03	G1	No	No	D28 CR
4	43	F	0	-	B-ALL	RF	0.24% (bcr abl 47.65%)	SETD2, BCR:ABL	No	Yes	No	3	(BFM+TKI, H-CVAD, Inc)	Yes (Dasatanib, Pred)	0.59	G1	No	Yes	D28 CR
5	11	M		100	B-ALL	RF	0.44%	KRAS	No	No	No	2	(BFM, R3)	No	0.03	G1	No	Yes	D28 CR
6	64	M	0	-	B-NHL	RL	25.9 ml	-	NA	NA	Yes	5	(R-CHOP, R, R-GDP, Auto, R)	No	0.43	-	-	-	-
7	59	F	0	-	B-NHL	RF	140 ml	-	NA	NA	No	2	(R-CHOP, R-DHAP)	Yes (R-GDP)	-	-	-	-	-
8	10	M	-	100	B-ALL	RL	10.1%	-	NA	Yes	No	3	(BFM+RT, mCVAD, Inc)	No	-	-	-	-	-

B

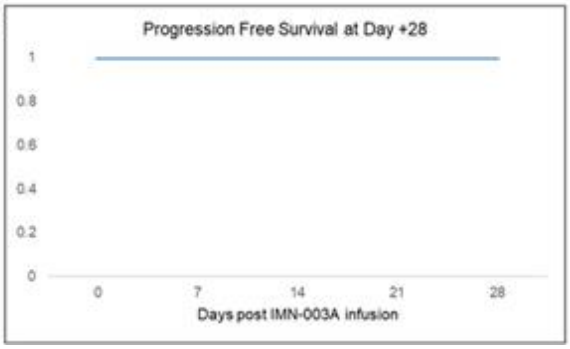

Figure 1:
(A) Patient characteristics, safety and efficacy outcomes,
(B) Progression Free Survival at day +28

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Disclosures

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