PHASE-2 STUDY OF VARNIMCABTAGENE AUTOLEUCEL (IMN-003A) FIRST-IN-INDIA INDUSTRY CD19-DIRECTED CAR-T WITH FRACTIONATED INFUSIONS FOR PATIENTS WITH RELAPSED REFRACTORY B CELL MALIGNANCIES: IMAGINE STUDY

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Abstract: P1409

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Session Title: Gene therapy, cellular immunotherapy and vaccination - Clinical

Background:

Varnimcabtagene autoleucel (IMN-003A) is an autologous second-generation CAR-T cell product with a 4-1BB domain and A3B1 binder, non-FMC63 based murine single chain variable fragment targeting CD19, manufactured in India. Pre-clinical studies and phase 1 clinical trial in Spain has demonstrated potent in vitro, in vivo and clinical activity. Safety and efficacy results of IMAGINE phase 2 clinical trial for patients in India with relapsed/refractory B cell malignancies (CTRI/2022/03/041162) are presented here.

Aims:

Evaluate safety and efficacy of IMN-003A in patients with relapsed refractory B cell malignancies (B-ALL and B-NHL).

Methods:

Patients (pts) 3 to 45 years (B-ALL) and ≥ 18 years (B-NHL) with relapsed refractory B cell malignancies (RR BCM) were eligible if they had measurable disease, assessed by lymphoid blasts (B-ALL) or metabolic tumour bulk (B-NHL), received ≥1 prior regimen, refractory to last line of treatment with ECOG 0 to 1. Bridging therapy was allowed after apheresis. Flu-Cy lymphodepletion was used on days -5 to -3. Target dose was $1x10^6$/kg CAR+ cells (B-ALL) and $5x10^6$/kg CAR+ cells (B-NHL) (overall range $0.1x10^6$ to $5x10^6$), with fractionated infusions (10%/30%/60%). 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 by NCCN (B-ALL) and IWG (B-NHL) criteria; 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.

Results:

At data cut-off, 22 pts (median age 31 yrs, range 3 - 66) with RR BCM (n=11 B-ALL; n=11 B-NHL) were enrolled. 18 pts received IMN-003A cells; 6 (33.3%) needed bridging therapy. Patient characteristics are described in Figure 1A. Median CAR-T cell manufacturing time was 14 days (range 10-27) with 100% manufacturing success.

Median follow-up after IMN-003A administration was 97 days (range 3 - 284). Overall response rate (ORR) was 88.2% at D+28 (B-ALL 85.7%; B-NHL 88.8%) and 72.7% at D+90 (B-ALL 71.4%; B-NHL 75%). Two pts relapsed by D+90. Of MRD-evaluable pts, response was 100% at day+28 (n=7) and 83.3% at D+90 (n=6). Median time to first response was 28 days.

Median progression-free survival (PFS, range 90-NR, Figure 1B) and overall survival (OS) were not reached (range 99-NR).

AESIs reported were CRS (Grade [G] 1 70.5%; G3+ 5.9%; overall 76.4%); ICANS (G1 5.9%; G3+ 0%; overall 5.9%); neutropenia (G3+ 94.1%; overall 100%); anemia (G3+ 35.3%; overall 100%); and thrombocytopenia (G3+ 23.5%; overall 94.1%). CRS median onset was D+6 and duration 3 days. No G3+ ICANS was reported. Tocilizumab usage was in 41.2% (n=7/17) (majority for persistent G1 CRS). Treatment related mortality was 5.9% (n=1/17); 2 pts died of disease progression.

IMN-003A cells demonstrated peak expansion on D+10 (range 7 – 21 days). 94% at D+28 and 36% at D+90 (range D+21 - NR) had measurable CAR+ T cells in peripheral blood. Updated results will be presented in the meeting.

Summary/Conclusion:

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

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 mEASIX	CRS	ICANS	Toci	Outcome	
																		D+28	D+90
1	31	F	0	-	B-ALL	RF	0.10%	None	No	No	No	2	BFM, 6MP	No	0.15	No	No	No	CR	CR
2	5	F	-	100	B-ALL	RF	0.01%	*iAMP21+*	No	No	No	2	BFM, HD MTX	No	0.04	G1	No	No	CR	CR
3	7	M	-	100	B-ALL	RL	0.63%	None	No	No	No	2	BFM, Pred	No	0.03	G1	No	No	CR	CR
4	43	F	0	-	B-ALL	RF	0.24%	*SETD2, BCR ABL*	No	Yes	No	3	BFM+TKI, H-CVAD, Ino	Yes (Dasatanib, Pred)	0.59	G1	No	Yes	CR	RD
5	11	M		100	B-ALL	RF	0.44%	*KRAS*	No	No	No	2	BFM, R3	No	0.03	G1	No	Yes	CR	CR
6	64	M	0	-	B-NHL	RL	24.9 ml	-	NA	NA	Yes	5	R-CHOP, R, R-GDP, Auto, R	No	0.43	G1	No	No	CR	CR
7	59	F	0	-	B-NHL	RF	416.9 ml	-	NA	NA	No	2	R-CHOP, R-DHAP	Yes (R-GDP)	0.05	G1	No	Yes	PR	PR
8	10	M	-	100	B-ALL	RF	10.1%	-	NA	Yes	No	3	BFM+RT, mCVAD, Ino	No	0.12	G1	No	Yes	CR	CR
9	34	M	0	-	B-NHL	RF	1177 ml	-	NA	No	No	3	R-CHOP, R-GDP	Yes (DHAP)	181.53	G1	No	Yes	PD	PD
10	40	M	0	-	B-NHL	RF	67.9 ml	-	NA	No	No	2	R-CHOP, R+Len	No	5.35	No	No	No	CR	CR
11	7	F	-	100	B-ALL	RL	0.02%	-	No	Yes	No	5	ICICLE, Maint, UK-ALL R1, mHyp CVAD, Ino	No	0.04	G5	G1	Yes	Deceased	
12	66	M	0	-	B-NHL	RL	-	-	NA	No	No	3	CHOP + RT , BR, R-GDP	No	63.81	G1	No	No	PR	-
13	53	M	0	-	B-NHL	RL	-	-	NA	No	No	4	BR, R-GDP, ICE, CHOP	No	24.29	G1	No	No	PR	-
14	53	F	0	-	B-NHL	RL	-	-	NA	No	No	4	BR, R, R, R-CHOP	Yes (R-CHOP)	0.89	G1	No	No	CR	-
15	14	M	-	100	B-ALL	RL	0.80%	None	No	No	No	5	ALL-REZ-BFM 85, Maint, TMC ALL R1, 6MP+ MTX	No	0.86	No	No	No	CR	-
16	3	M	-	100	B-ALL	RF	0.37%	None	No	No	No	1	BFM ALL 2002	Yes (6MP + MTX) (Ino + steroids)	-	-	-	-	-	-
17	31	F	0	-	B-NHL	RL	132.51 ml	-	NA	No	No	2	RCHOP, GCD	Yes (R-ICE)	1.39	G1	No	Yes	PR	-
18	53	M	0	-	B-NHL	RL	30.7 ml	-	NA	No	No	4	RCVP, BR, R, Obinutuzumab + CHOP	No	0.63	No	No	No	CR	-
18	9	F	-	100	B-ALL	RF	0.03%	TP53 del, NF1, POT1,	No	No	No	2	UK ALL 2011, FLA B	Yes (Dexa + MTX)	0.45	No	No	No	-	-

B

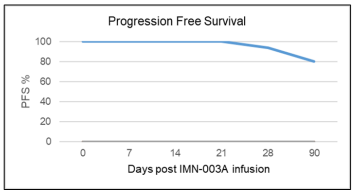

Figure 1:
(A) Patient characteristics, safety and efficacy outcomes,
(B) Progression Free Survival

Keywords: B cell acute lymphoblastic leukemia, Non-Hodgkin's lymphoma, Clinical trial, CAR-T