median of 3-year PFS 61.1% (95%CI 43.7, 76.1) vs. 17.7% (95% CI 6.8, 23,9) (p = 0.045), median 3-year OS 72.2% (95%CI 58.2, 86,1) vs. 38.1% CI (27.6, 48,2) (p = 0.049) respectively was associated the achievement of any renal response.

To compare with patients who were the candidates for autoHSCT, but didn't undergo autoHSCT: median 3-year PFS 17,9% (CI 9.7, 31,2), 3-year OS – 33,7% (CI 16.7, 57.3) ($p = 0,036$) – median 3-year PFS in patients who underwent autoHSCT was 48,6% (CI 35.8, 67,2), median 3-year OS – 67,2% (CI 46.8, 78.9). There wasn't mortality associated with transplantation.

Conclusions: Achieving at least a minimal renal response during induction therapy and performing autoHSCT improve the PFS and OS in patients with newly diagnosed MM with dialysis-dependent RI.

Keywords: Multiple Myeloma, Stem Cell Transplant

No conflicts of interests pertinent to the abstract.

CAR-T (CELLULAR THERAPIES)

632 | PHASE-2 FIRST-IN-INDIA INDUSTRY STUDY OF VARNIMCABTAGENE AUTOLEUCEL (IMN-003A) IN RELAPSED REFRACTORY B CELL MALIGNANCIES: IMAGINE STUDY B-NHL SUBANALYSIS

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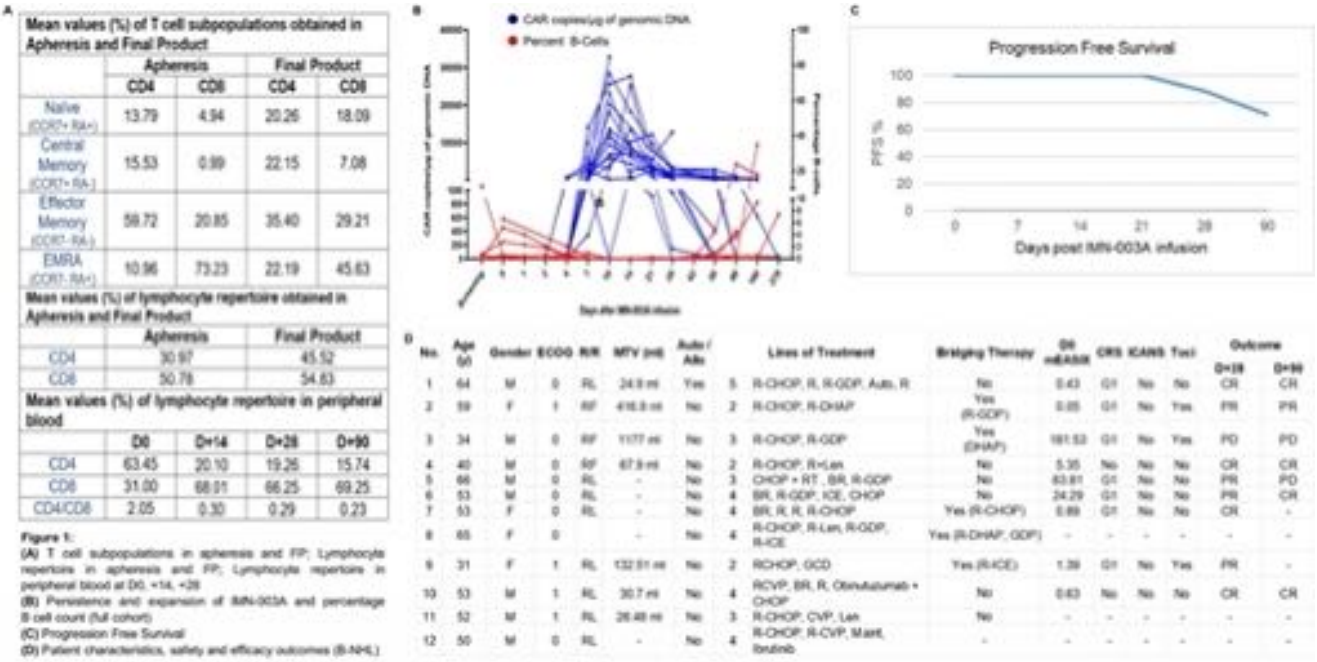
Introduction: Varnimcabtagene autoleucel (IMN-003A) is an autologous CD19 directed CAR-T with 4-1BB co-stim domain and A3B1 binder, a non-FMC63 murine scFv, manufactured in India for phase 2 study in patients (pts) with relapsed / refractory (r/r) B cell malignancies (CTRI/2022/03/041162). Target dose (B-ALL: 1×10^6 CAR+ cells/kg; B-NHL: 5×10^6 CAR+ cells/kg) was infused as 3 fractions (10%, 30%, 60%) after Flu-Cy lymphodepletion. B-NHL subanalysis is presented here.

Methods: Pts ≥ 18 yrs with r/r B-NHL, measurable disease, ≥1 prior regimen and ECOG 0-1 were eligible. IMN-003A persistence was evaluated by ddPCR. Manufacturing was in CliniMACS Prodigy. CAR-T % transduction and T cell subsets were analyzed by flow. Primary objectives were overall response rate (ORR: CR + PR; IWG criteria) at day +90, and occurrence of adverse events.

Results: Of 23 pts in study, 11 pts with B-NHL (median 53 yrs, range 31–66) underwent apheresis with 100% manufacturing success (median time 15d; range 11–27). Two needed second apheresis. Mean % transduction was 28.27% (range 8.50–51.07) with median transgene copies / genome of 2.36 (range 0.76–4.16). Mean CD4/CD8 ratio was 0.31 (apheresis); 0.62 (final product FP); 2.05 (Day 0) and 0.23 (Day 90) with reversal post infusion. Mean proportion of naïve cells (CCR7+ RA+) was >35% in FP (Fig 1A). Median Product Doubling time was 1.03d (range 0.88–2.12) and Apheresis to Infusion time was 30d (range 21–95).

Max IMN-003A expansion (Tmax) was at median 10d (range 7–21) with median Cmax 122,029 CAR copies / µg gDNA (range 24,624–284,498). IMN-003A persistence was 100% at D+28 and 40% at D +90 (range 28–NR) with concurrent B cell aplasia (Fig 1B) range 90–



A

Mean values (%) of T cell subpopulations obtained in Apheresis and Final Product

	Apheresis		Final Product	
	CD4	CD8	CD4	CD8
Naive (CCR7+ RA+)	13.79	4.94	20.26	18.09
Central Memory (CCR7+ RA-)	15.53	0.89	22.15	7.08
Effector Memory (CCR7- RA-)	59.72	20.85	35.40	29.21
EMRA (CCR7- RA+)	10.96	73.23	22.19	45.63

Mean values (%) of lymphocyte repertoire obtained in Apheresis and Final Product

	Apheresis	Final Product
CD4	30.97	45.52
CD8	50.78	54.83

Mean values (%) of lymphocyte repertoire in peripheral blood

	D0	D+14	D+28	D+90
CD4	63.45	20.10	19.25	15.74
CD8	31.00	68.01	66.25	69.25
CD4/CD8	2.05	0.30	0.29	0.23

Figure 1:
(A) T cell subpopulations in apheresis and FP; Lymphocyte repertoire in apheresis and FP; Lymphocyte repertoire in peripheral blood at D0, +14, +28
(B) Persistence and expansion of IMN-003A and percentage B cell count (full cohort)
(C) Progression Free Survival
(D) Patient characteristics, safety and efficacy outcomes (B-NHL)

B

C

D

No.	Age (y)	Gender	ECOG	R/R	MTV (ml)	Auto / Allo	Lines of Treatment	Bridging Therapy	D0 mRAISE	CRS	ICANS	Toci	Outcome D+28	Outcome D+90
1	64	M	0	RL	24.9 ml	Yes	5	R-CHOP, R, R-GDP, Auto, R	No	0.43	G1	No	No	CR	CR
2	59	F	1	RF	416.8 ml	No	2	R-CHOP, R-DHAP	Yes (R-GDP)	0.65	G1	No	Yes	PR	PR
3	34	M	0	RF	1177 ml	No	3	R-CHOP, R-GDP	Yes (DHAP)	181.53	G1	No	Yes	PD	PD
4	40	M	0	RF	67.9 ml	No	2	R-CHOP, R+Len	No	5.35	No	No	No	CR	CR
5	66	M	0	RL	-	No	3	CHOP + RT , BR, R-GDP	No	63.81	G1	No	No	PR	PD
6	53	M	0	RL	-	No	4	BR, R-GDP, ICE, CHOP	No	24.29	G1	No	No	PR	CR
7	53	F	0	RL	-	No	4	BR, R, R, R-CHOP	Yes (R-CHOP)	0.89	G1	No	No	CR	-
8	65	F	0	-	-	No	4	R-CHOP, R-Len, R-GDP, R-ICE	Yes (R-DHAP, GDP)	-	-	-	-	-	-
9	31	F	1	RL	132.51 ml	No	2	RCHOP, GCD	Yes (R-ICE)	1.39	G1	No	Yes	PR	-
10	53	M	1	RL	30.7 ml	No	4	RCVP, BR, R, Obinutuzumab + CHOP	No	0.43	No	No	No	CR	CR
11	52	M	1	RL	26.48 ml	No	3	R-CHOP, CVP, Len	No	-	-	-	-	-	-
12	50	M	0	RL	-	No	4	R-CHOP, R-CVP, Mant, Ibrutinib	-	-	-	-	-	-	-

NR. CD4+ T cell count recovery (>200/μL) was seen at median of 24.5 days (range 7- 42) post infusion.

Of 9 pts infused, 4 (44.4%) needed bridging therapy (patient characteristics in Figure 1D). Median follow-up was 99 days (range 58–226).

Overall response rate (ORR) was 88.8% at D+28 and 71.4% at D+90. Median time to first response was 28 days.

Median progression-free survival (PFS) and overall survival (OS) were not reached (Figure 1C).

AESIs reported were CRS (Grade [G] 1 77.8%; G3+ 0%; overall 77.8%); ICANS (G1 0%; G3+ 0%; overall 0%); hypogammaglobulinemia (8/9, 5 recd IVIg) neutropenia (G3+ 100%); anemia (G3+ 55.6%); and thrombocytopenia (G3+ 22.2%). CRS median onset was D+3 and duration 3 days. No G3+ ICANS was reported. Tocilizumab usage was in 33.3% pts (majority for persistent G1 CRS). There was no treatment related mortality with one death due to disease progression.

Conclusions: This First-In-India Industry study (IMAGINE) for varnimcabtagene autoleucel (IMN-003A) in B-NHL has demonstrated 100% manufacturing success with excellent safety and efficacy outcomes and durable responses including absence of neurotoxicity. This offers a significant benefit for patients in India.

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Keywords: Aggressive B-cell non-Hodgkin lymphoma, Cellular therapies, Indolent non-Hodgkin lymphoma

Conflicts of interests pertinent to the abstract

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633 | PRELIMINARY DATA FROM A FIRST-IN HUMAN PHASE II STUDY OF SEQUENTIAL USE OF SELINEXOR AND CD19 CART THERAPY IN PATIENTS WITH RELAPSED OR REFRACTORY B-CELL NON-HODGKIN LYMPHOMA

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Background: Preclinical trial has demonstrated that sequential use of Selinexor and Anti-CD19 directed chimeric antigen receptor modified T-Cell therapy (CART19) cells might improve the anti-tumor efficacy of CART 19 cells against lymphoma cells. However, the efficacy and safety of CART19 combined with Selinexor in lymphoma patients is unknown. We report preliminary data from a phase 2 trial of sequential use of Selinexor and CART19 in patients with relapsed or refractory B-cell non-Hodgkin lymphoma (R/R B-NHL).