REAL-WORLD DATA ON VARNIMCABTAGENE AUTOLEUCEL (MURINE CD19 CAR-T) FROM INDIA: A STEP TOWARDS ENHANCED PATIENT ACCESS WITH EXCELLENT SAFETY AND EFFICACY

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INTRODUCTION

Varnimcabtagene autoleucel (varnim-cel), an autologous second-generation CAR T-cell product with a 4-1BB co-stimulatory domain and murine A3B1 binder, was approved in India in February 2024 for relapsed / refractory (r/r) B-cell Non-Hodgkin's Lymphoma (B-NHL) above 18 years based on safety and efficacy data (ASH 2022, 2023).

In this observational study, we present real-world data on the access, safety, and efficacy of the commercial use of this product across multiple clinical centres in India.

AIM

Evaluate safety and efficacy of varnimcabtagene autoleucel (varnim-cel) in patients with relapsed / refractory B-cell Non-Hodgkin's Lymphoma.

METHODS

Patients (pts) with r/r B-NHL aged 18+ years infused with varnim-cel as standard of care in a fractionated infusion protocol (10%/30%/60%) at target dose 5x10^6/kg CAR+ cells after Flu-Cy lymphodepletion regimen from 02 August 2024 till 31 October 2025 were included in this study. No adjuvant or maintenance treatment was administered post varnim-cel infusion.

Twenty centres across India were trained on clinical management and toxicity algorithms prior to initiation of treatment. Apheresis and infusion scheduling based on patient priority along with manufacturing was done centrally from a single facility.

Manufacturing parameters such as manufacturing success rate (MSR), OOS, vein to vein (leukapheresis to infusion) and brain-to-vein time (patient registration to infusion) were evaluated. Response was assessed as per IWG (B-NHL) criteria. Adverse events (AEs) including CRS, ICANS and IEC-HS were analysed as per published criteria.

RESULTS

As of data cut-off, 52 pts with B-NHL underwent leukapheresis, median age 57 years (range 21 to 79); Gender: Male 69%, Female 31%; Ethnicity: Asians 98% (Indians 88%, Arab 4%, Bangladeshi 2%, Mauritian 2%, Nepali 2%); African 2%, across 20 centres in India. Disease characteristics included: Subtypes - Large B-cell Lymphomas: 79% [Diffuse Large B-cell Lymphoma, NOS: 65%; High-grade B-cell Lymphoma, NOS: 6%; with MYC and BCL2 rearrangements: 2%; Primary Mediastinal Large B-cell Lymphoma: 2%; Primary Large B-cell Lymphoma of Immune-privileged Sites: 2%; T-cell / Histiocyte Rich Large B Cell Lymphoma: 2%]; Transformations of indolent B-cell lymphomas: 4%; Follicular Lymphoma: 10%; Mantle Cell Lymphoma: 8%; Extranodal involvement 85%; Bulky disease 35%; CNS involvement 10%. Median previous lines of treatment were 3 (range 1 to 6). Three patients had undergone previous autologous transplant.

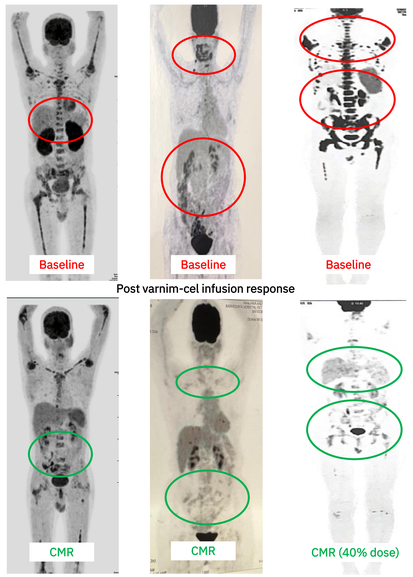
Centralized manufacturing ensured all patients received apheresis and manufacturing slots within a median of 6 days (range 1 to 81). Second apheresis was done in two patients (inadequate cell count – 1; sterility failure – 1). Temperature control for varnim-cel was maintained ≤ -150 C using ultracold chain logistics.

Of the 52 patients, 43 patients have been infused (patient death before infusion - 3; product not manufactured - 1; and 5 patients were awaiting infusion).

All patients received fractionated infusions, majority were on Days 0, +3, +7 and 26 patients (60%) underwent bridging therapy. One patient received only 2 fractions (40% dose) and in CR.

RWE Summary

Treatment Centres	20
Leukapheresis	52
Lines of Treatment (median)	1 to 6 (3)
Manufacturing Time (median), days	14 to 41 (24)
Manufacturing Success Rate (MSR)	98%
Distance travelled to access varnim-cel (median), Km	2 to 8889 (351)
Brain-to-Vein Time (median), days	25 to 113 (45)
Vein-to-Vein Time (median), days	20 to 72 (34)
ORR	73.5%
PFS (median)	NR
OS (median)	NR
CRS (G3+), %	40 (7)
ICANS (G3+), %	9 (5)
TRM, n (%)	3/43 (7)



Median CAR-T cell manufacturing time was 24 days (range 14 to 41) with 98% MSR (1 not manufactured).

Median distance travelled to access varnim-cel was 351 Km (range 2 to 8889). Median brain-to-vein time was 45 days (range 25 to 113). Median vein-to-vein time was 34 days (range 20 to 72). The B2V and V2V were not influenced by distance of the treatment centres to the manufacturing site.

Of the 34 evaluable patients, best overall response rate (ORR) post infusion was 73.5% (25/34) with 76% of responders achieving CR.

Median progression-free survival and overall survival were not reached.

In the pivotal Phase II study (IMAGINE), ORR was 91.7% at D+28 and 83.3% at D+90 and in both B-ALL and B-NHL cohorts.

AESIs reported were CRS (overall 40%; G3+ 7%); ICANS (overall 9%; G3+ 5%); Immune Cell Associated Haemato-Toxicity (ICAHT) – pancytopenia (overall 9%); neutropenia (overall 23%; G3+ 12%); anemia (overall 37%; G3+ 9%); and thrombocytopenia (overall 26%; G3+ 2%); Hypogammaglobulinemia (overall 16%); all received IVIg. CRS median onset was D+3 (range 0 to 8) and duration 3 days (range 1 to 14). Tocilizumab, steroids and anakinra usage was in 35%, 9% and 7% respectively. At data cutoff, 6 deaths were reported [Treatment-related mortality (TRM) – 3 (7%) due to Infection-1, IEC-HS-1, ICANS-1; Non-relapse mortality – 1; Disease progression – 2]. Safety profile compares favourably with the pivotal Phase II study (IMAGINE): CRS (overall 67%; G3+ 4%); ICANS (overall 4%; G3+ 0%) and ICAHT - neutropenia (overall 100%; G3+ 92%); anemia (overall 96%; G3+ 29%); and thrombocytopenia (overall 92%; G3+ 21%).

CONCLUSIONS

The real-world experience provides strong evidence of efficacy and safety of varnim-cel in B-NHL comparable with pivotal study. It also proves the robustness of trans-national ultracold chain logistics, safe and effective clinical delivery and management systems for commercial rollout across multiple centres in India to provide equitable access in South Asia.

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