VARNIMCABTAGENE AUTOLEUCEL IN RELAPSED / REFRACTORY B-CELL MALIGNANCIES: MANUFACTURING EXPERIENCE FROM INDIA

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INTRODUCTION

Varnimcabtagene autoleucel (varnim-cel), a CD19 antigen-directed chimeric antigen receptor (CAR) T cell therapy with murine A3B1 binder, is currently approved in Spain (Hospital Exemption) for r/r B-ALL (> 25 years) and in India for r/r B-NHL (>18 years) [ASH 2022, 2023].

This report looks at the manufacturing experience in India, both in clinical trial and commercial patients. The importance of scheduling (apheresis and infusion) and ultracold chain logistics in both clinical trial and commercial settings is of paramount importance in CAR-T cell therapy.

The manufacturing and logistic outcomes of varnim-cel over more than 3 years in India is reported here.

METHODS

This analysis includes patients with r/r BCM from manufacturing database who underwent leukapheresis for varnim-cel treatment between March 17, 2022, and October 31, 2025, and had final manufacturing outcomes available. Manufacturing success rate (MSR) was defined as the percentage of patients for whom the product was released that met quality release specifications. Manufacturing turnaround time (MT) was defined as the number of days from leukapheresis to product release. Varnim-cel was manufactured on CliniMACS Prodigy closed cGMP system. Ultracold chain logistics (temperature ≤-150°C) was maintained as per product specifications. A robust chain of identity, custody and condition was maintained using semi-automated measures. Scheduling for apheresis and infusion was also semiautomated with manual interventions. This was the first clinical experience using ultracold chain logistics for a personalized treatment in India.

Manufacturing process was centralized at a single cGMP compliant, regulator-approved, facility in India.

Target dose was $1x10^6$/kg CAR+ cells (B-ALL) and $5x10^6$/kg CAR+ cells (B-NHL) (overall range $0.1x10^6$ to $5x10^6$ per kg) administered in a 3-day fractionated schedule (10%/30%/60%).

RESULTS

At data cutoff, 77 patients underwent leukapheresis (total 81 procedures; 4 patients needed second apheresis (inadequate cell count – 2; sterility failure – 2), with an overall MSR of 99% (IMAGINE CT 100%; Com 98%).

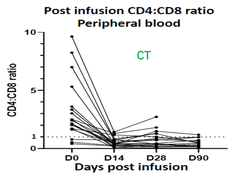
Median MT was 19 days (range 10 to 41); CT median MT 14 days (range 10 to 27); Com median MT 24 days (range 14 to 41). Median age for overall pts was 53 yrs (range 3 to 79) with median in CT 31 yrs (range 3 to 66) and median in Com 57 years (range 21 to 79). Median previous lines for overall pts was 3 (range 1 to 6) with median in CT 2 (range 1 to 5) and median in Com 3 (range 1 to 6). Median distance travelled by patients to access varnim-cel was 375 Km (range 2 to 8889).

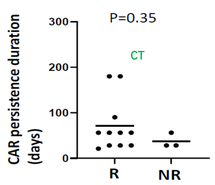
Distance covered by logistics for delivery of apheresis / final product ranged between 0 Km (onsite centre) to 2449 Km.

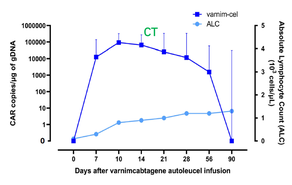
Cell dose within the approved range was achieved in 100% pts (B-ALL 100%, B-NHL 100%).

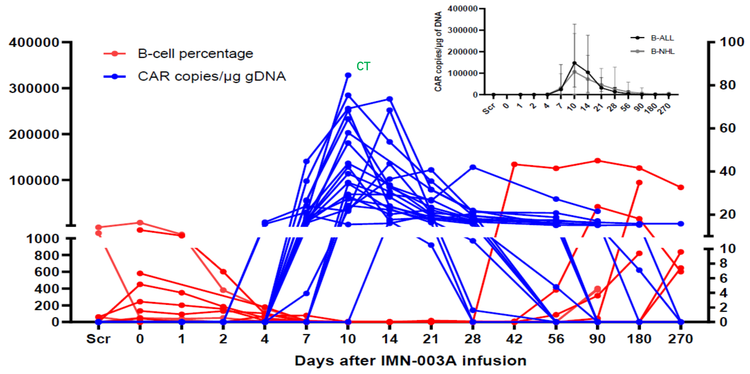
Manufacturing was not successful in one patient with TCRBCL in commercial due to poor expansion.

Median transduction % of var-cel was overall 42.4% (range 7.7 to 91.9) with median in CT 28.5% (range 8.5 to 58.4) and median in Com 50.5% (range 7.7 to 91.9).









Manufacturing Experience from India

Patients	77
Leukapheresis	81
MSR, %	99
Median MT, days (range)	19 days (10 to 41)
Median age, years (range)	53 (3 to 79)
Median previous lines (range)	3 (1 to 6)
Median distance travelled to access treatment, Km (range)	375 (2 to 8889)
Logistics distance, Km, range	0 to 2449
Approved dose achieved, %	100
Median transduction, % (range)	42.4 (7.7 to 91.9)
Median VCN, copies/genome (range)	3 (0.8 to 4.7)
Negative RCL, %	100
Median Product Doubling Time, days (range) in clinical trial	1.04 (0.74 to 4.2)
Median B2V, days (range)	45 (18 to 117)
Median V2V, days (range)	31 (10 to 95)

Median transgene copies / genome was overall 3 (range 0.8 to 4.7) with median in CT 2.6 (range 0.8 to 4.2) and median in Com 3.4 (range 0.9 to 4.7). RCL was negative in all batches. In the IMAGINE CT, mean CD4/CD8 ratio at apheresis and final product (CAR+ T cells) was 0.47 and 2.58 respectively. There was reversal of CD4/CD8 ratio from apheresis to final product which was statistically significant ($p<0.01$). Median product doubling time in CT was 1.04 days (range 0.74 to 4.2).

Median Brain-to-Vein (B2V) time for overall pts was 45 days (range 18 to 117) with median in CT 45 days (range 18 to 117) and median in Com 45 days (range 25 to 113). Median Vein-to-Vein (V2V) time for overall pts was 31 days (range 10 to 95) with median in CT 26 days (range 16 to 95) and median in Com 34 days (range 20 to 72).

CONCLUSIONS

Scheduling, delivery logistics, maintenance of ultracold chain logistics and close collaboration with clinical sites are important for effective delivery of CAR-T cell therapy products and optimizing outcomes. Varnim-cel has shown robust performance in clinical trials and sustained success in commercial manufacturing. This report reveals consistent success with manufacturing varnim-cel for patients in areas of high unmet need enabling efficient clinical implementation. This model establishes a strong foundation and provides confidence in the potential for global deployment of varnim-cel.

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