High efficacy and excellent safety profile of Actalycabtagene autoleucel, a humanized CD19 CAR-T product in r/r B-cell malignancies: A phase II pivotal trial

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INTRODUCTION AND AIM

- Commercially approved CD19 CAR-T cell therapies are effective in r/r B cell malignancies but are associated with significant albeit manageable toxicities.
- These toxicities contribute to significant morbidity.
- We have developed a novel, humanized CD19 CAR-T cell therapy, Actalycabtagene autoleucel (Actaly-cel) and previously reported the safety in Phase I study (Jain H et.al., 4641 ASH 2022)
- Here, we present the pooled results from Phase I and Phase II study evaluating Actaly-cel.
- Recently received market authorization by regulatory authorities of India (Brand name: NexCAR19).

MATERIALS AND METHODS

- Manufacturing Site: Immunoadoptive Cell Therapy Pvt. Ltd (ImmunoACT)
- Clinical Trial Sites: Tata Memorial Hospital, DMHRC, AOI, RGCI, SMBT hospital.

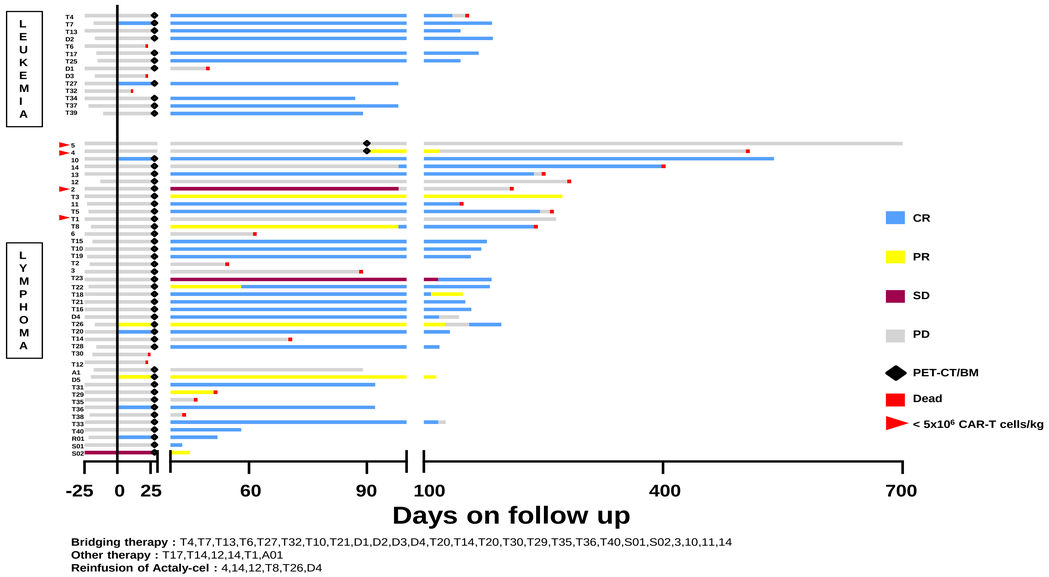
	Phase I	Phase II
Study Setting	Single -Centre	Multi centric
Population	High Grade Lymphoma	r/r B Cell Malignancies
Primary Objective	Safety and tolerability	Objective response rate
Dose	1 x 10^9 to 2 x 10^9	≥ 5 x 10^6 /kg
CTRI Registration	CTRI/2021/04/032727	CTRI/2022/12/048211

- Patients above the age of 15 with ECOG status 0-1, adequate organ function and no CNS involvement were screened for the study.
- Patients with relapsed/ refractory B-cell malignancies were included in the study.
- A lymphodepleting chemotherapy regimen of Fludarabine at 30mg/m2/day and cyclophosphamide at 500 mg/m2/day was administered.
- After 2 days rest period the patients were infused on day 0 with Actaly-cel.
- The response assessment was scheduled at day 28.

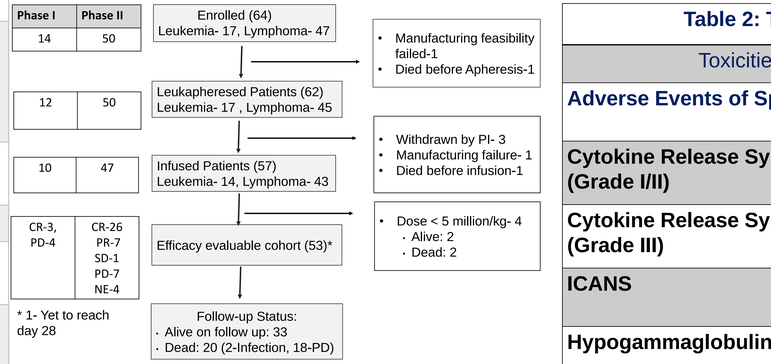
RESULTS

Table 1: Baseline Characteristics

Baseline Characteristics	Patients (N = 64)
Age Median (Range)	44 (16-71)
Gender n (%)	
Male	50 (78%)
Female	14 (22%)
ECOG	
0	2 (3%)
1	60 (94%)
2	2 (3%)
Diagnosis	
R/R DLBCL	43 (67%)
B-ALL	17 (27%)
Indolent lymphoma	4 (6%)
Disease Status at enrolment (Lymphoma)	
PD	43 (92%)
PR	2 (4%)
SD	2 (4%)
Disease Status at enrolment (Leukaemia)	
Relapsed	2 (12%)
Refractory	15 (88%)
Bulky Disease (>/= 7cm) n(%)	10 (21%)
Blast%, median (range)	61% (5-98)
Line of therapies Median (range)	2 (1-6)
Extranodal sites n (%)	
1	12 (25%)
>/=2	12 (25%)



Bridging therapy : T4,T7,T13,T6,T27,T32,T10,T21,D1,D2,D3,D4,T20,T14,T20,T30,T29,T35,T36,T40,S01,S02,3,10,11,14
Other therapy : T17,T14,12,14,T1,A01
Reinfusion of Actaly-cel : 4,14,12,T8,T26,D4



* 1- Yet to reach day 28

Responses

	Efficacy Evaluable Cohort (n=53)	Lymphoma (n= 38)	Leukemia (n=15)*
ORR	**36 (67%)**	**26 (68%)**	**10 (72%)**
CR	**29 (52%)**	**19 (37%)**	**10 (72%)**
PR	**7 (15%)**	**7 (18%)**	**0 (0%)**
SD	**1 (2%)**	**1 (3%)**	**0 (0%)**
PD	**11 (23%)**	**9 (24%)**	**2 (14%)**
NE	**4 (8%)**	**2 (5%)**	**2 (14%)**

Actaly-cel showed robust in vivo expansion and persistence

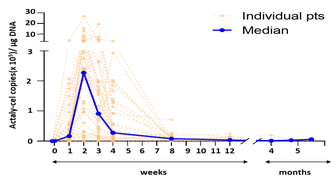


Table 2: Toxicities & responses

Toxicities	N = 57
Adverse Events of Special Interest	
Cytokine Release Syndrome (Grade I/II)	40 (70%)
Cytokine Release Syndrome (Grade III)	3 (5%)
ICANS	0 (0%)
Hypogammaglobulinemia	21 (37%)

CONCLUSIONS

- Actaly-cel (NexCAR19) is highly effective with a very favorable safety profile in relapsed/refractory B-cell malignancies.
- The absence of ICANS, shorter duration of cytopenias and a lower incidence of grade 3/4 CRS makes it one of the safest CD19 CAR-T cell therapy products.
- Actaly-cel (NexCAR19) can improve the ease of delivery of CAR T-cell therapy in a wide-range of settings.

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