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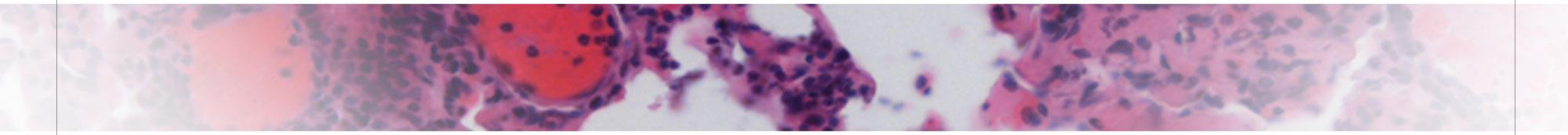

Safety and Efficacy of Azer-cel, an Allogeneic CD19 CAR T, Plus Low-Dose Interleukin-2 (IL-2) in Patients With Relapse/Refractory (r/r) Large B-Cell Lymphoma (LBCL) Who Relapsed After Autologous CAR T

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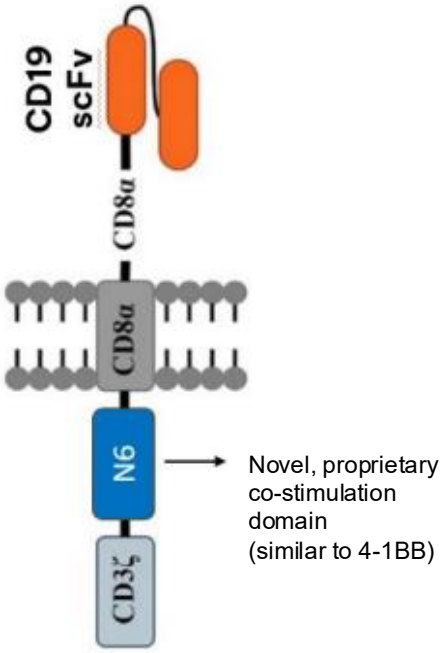
Background

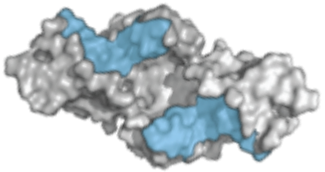
- Azercabtagene-zapraleucel (azer-cel, PBCAR0191) is an allogeneic anti-CD19 CAR T manufactured from healthy, adult donors
- During dose escalation, an optimized LD regimen has been identified (Aug/Cy – Flu 30mg/m^2 x 3 days, Cy 750mg/m^2 x 3 days) as well as the RP2D (500 million cells)
- In the current expansion cohort, low-dose SC IL-2 (1 million IU, D1-14) was added to the regimen as a form of exogenous armoring in order to improve clinical benefit

Abbreviations: TRAC, T-cell receptor alpha constant locus; LD, lymphodepletions; Aug/Cy, augmented cyclophosphomide; Flu, fludarabine; Cy, cyclophosphomide, RP2D, recomended phase 2 dose, SC, subcutaneous, IL-2, Interleukin-2. D1-14, study day 1-14.

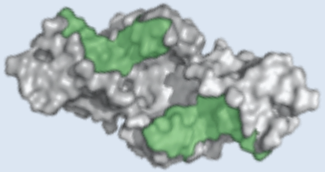
ARCUS Enables Precise Insertion of a CD19 CAR Into the *TRAC* Locus



Azer-cel



I-CreI: Nature's editing system, **evolved** for highly precise, versatile gene editing



ARCUS: I-CreI **engineered** to target desired genetic sites

KEY ADVANTAGES	
Safety	Non-integrating AAV vector, minimal off-target editing; natural "off switch"
Ease of delivery	Small size permits both mRNA, LNP and AAV delivery
Control of edits	Efficient knock-in or knockout

Azer-cel Phase 1/1b Study Design

Dose escalation completed; now in Phase 1b expansion

Dose Escalation (Parallel Groups)

n=84 patients

Subjects Treated to Date
B-ALL (N=23)
NHL (N=61)

Dose Escalation (Completed)

DOSE LEVEL	CONDITIONING REGIMEN
$500x10^6$ N=3-6	❑ **Aug Cy + IL-2**
$3x10^5$ N=3-6	✓ Standard LD ✓ Augmented Cy ✓ Modified LD ✓ Enhanced LD ✓ Augmented Flu ✓ Standard LD

Cohort Expansion Currently Enrolling

Patient Population
LBCL Relapsed after CD19 CAR T

Tumor Types of Interest
iDLBCL NOS
HGBCL
Transformed Indolent Lymphoma

Conditioning Regimen
Augmented Cy
(Flu 30mg/m2 & Cy 750mg/m2 x 3d) + low-dose SC IL-2 (1 million IU D1-14)

Key Inclusion Criteria (LBCL after CD19 CAR T)

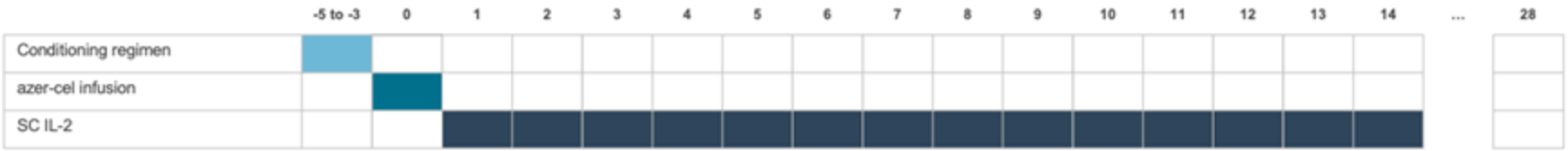
- CD19+ r/r DLBCL, NOS or other large B-cell lymphomas
- ≥2 prior therapies including autologous CD19 CAR T, with relapse after initial response

Endpoints

Primary: ORR by Lugano

Secondary: CR rate, DOR, PFS, OS, TNT, AEs

Treatment Schedule (One cycle)



Demographic & Disease Characteristics

Demographics & Characteristics	N=18
Median age (range), years	62.9 (28-86)
>65 years, n(%)	10 (55.5)
Male, (%)	13 (72.2)
Ethnicity, n (%)	
Hispanic or Latino	1 (5.6)
Not Hispanic or Latino	17 (94.4)
Race, n (%)	
Asian	1 (5.6)
White	17 (94.4)
Median Time since First Diagnosis, months	18.6 (11, 240)
Stage III/IV disease at study entry, n (%)	14 (77.8)
Histological subtypes, n (%)	
DLBCL	11 (61.1)
DLBCL, transformed from Follicular Lymphoma	3 (16.7)
Other[±]	4 (22.2)
Mean SPD (SD), cm^2	30.43 (3.1 – 123.5)

[±]*Other (1 Richter's Transformation, 1 HGBCL, 1 DLBC transformed from MZL, 1 EBV-positive DLBCL)*

Prior Treatment History

Prior Therapy	N=18
Median lines of prior therapy, n (range)	4 (2-7)
≥ 4 Lines	11 (61.1)
Prior anti-CD19 CAR T-cell therapy, n (%)	18 (100)
Primary Refractory, n (%)	10 (55.5)
Prior autologous stem cell transplant, n (%)	3 (16.7)
Prior Bi-specific T-cell engager, n (%)	8 (44.4)
Refractory to Bi-spcefic T-cell engager, n (%)	6 (33.3)
Duration of Response to Prior CAR T-cell therapy	
≤ 6 months	11 (61.1)
> 6 months	6 (33.3)

Summary of Adverse Events

No Evidence of GvHD

Adverse Events, n (%)	N=18	
	Any Grade	Grade ≥3
Any	18 (100)	14 (77.8)
Serious	6 (33.3)	4 (22.2)
Cardiac disorders	4 (22.2)	0
Infections*	9 (50.0)	6 (33)
Heme Toxicity**		
Neutropenia	18 (100)	18 (100)
Thrombocytopenia	18 (100)	9 (50)
Anemia	18 (100)	7 (38.8)
Hypogammaglobulinemia	2 (11.1)	0

AEs were graded according to the NCI CTCAE version 5.0
**One participant experienced Grade 5 bronchopulmonary aspergillosis and Grade 5 fungemia). Grade 3 CMV Infection, CMV viremia and HHV-6 were each reported in 1 (5.6%) participants.*
***AE based on laboratory values*

CRS and ICANS

AEs, n(%)	N=18	
	CRS	ICANS
Any grade, n(%)	13 (72.2)	3 (16.7)
Grade 1/2*	13 (72.2)	1 (5.6)
Grade 3	0	2 (11.1)
Grade 4	0	0
Grade 5	0	0
Median time to onset (range), days	3 (2-15)	5 (2-7)
Median duration of event (range), days	2 (1-9)	1 (1-10)

No Grade ≥3 CRS events occurred

ICANS Grade 3 events (N=2):

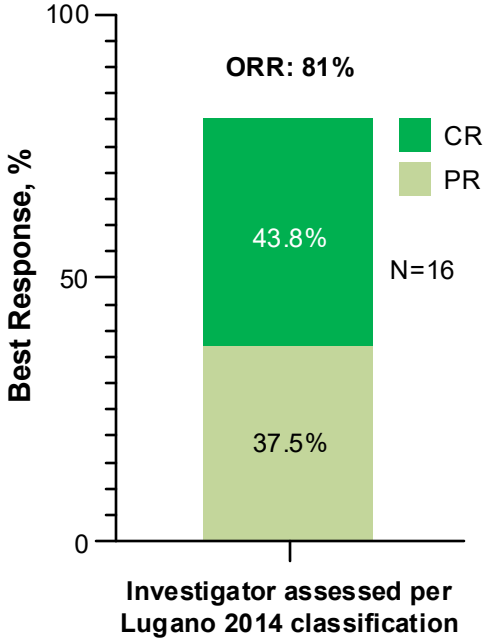
- 1 event resolved in 1 day
- 1 event resolved in 10 days

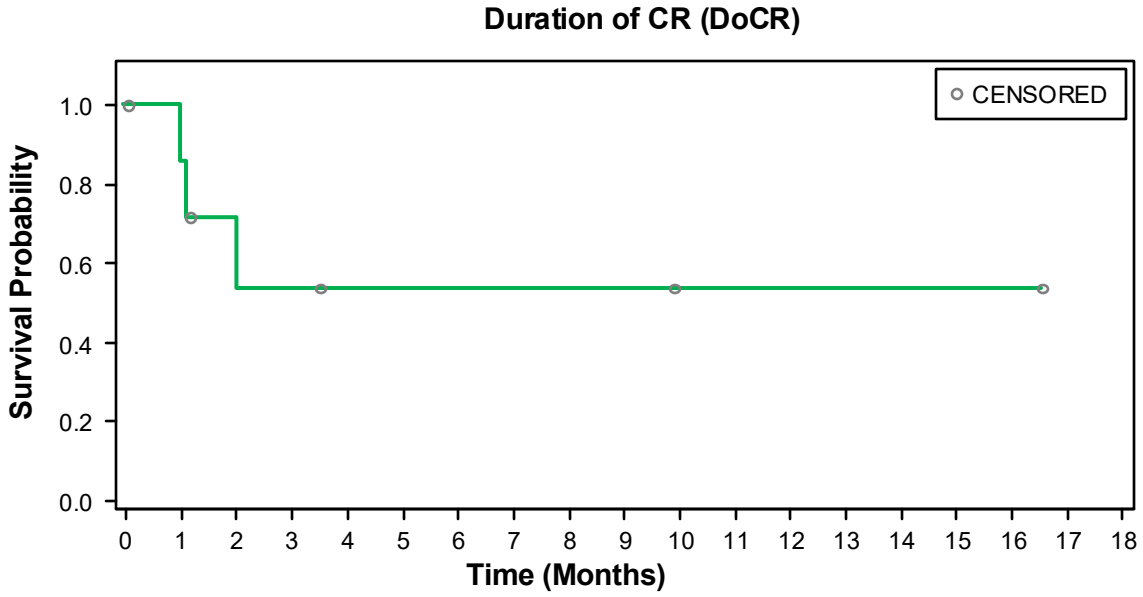
**2 serious CRS events: 1 Grade 1 and 1 Grade 2; 1 Serious ICANS event Grade 3*

Prolonged Cytopenias

Event	N=18
Participants with Prolonged Grade ≥3 Cytopenia present beyond D28, N (%)	9 (50)
Prolonged Anemia Grade ≥3, N (%)	2 (11.1)
Median time to recovery to Grade ≤ 2, median # of days (range)	33 (33, 33)
Prolonged Neutropenia Grade ≥3, N (%)	5 (27.8)
Median time to recovery Grade ≤ 2, median # of days (range)	25.5 (14, 38)
Prolonged Thrombocytopenia Grade ≥3, N (%)	6 (33)
Median time to recovery Grade ≤ 2, median # of days (range)	37 (13, 127)

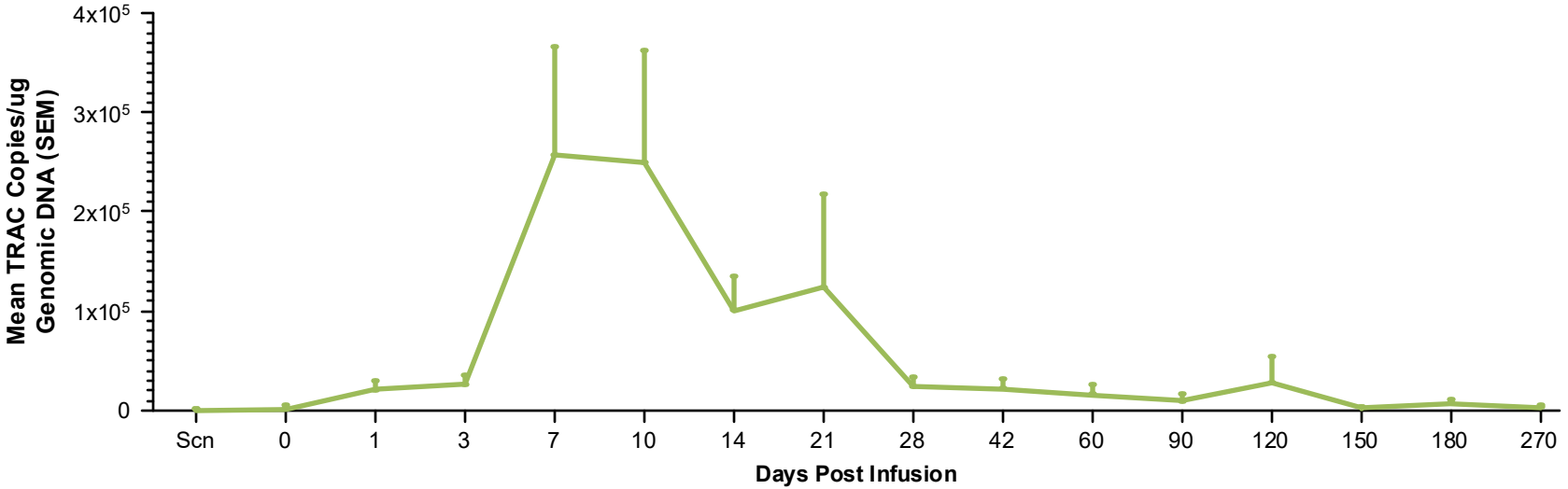
High Response Rates and Durable Responses Observed





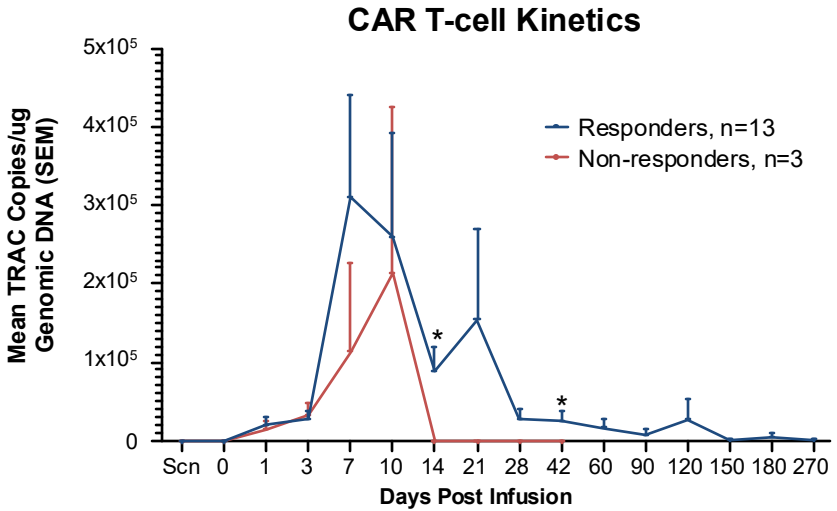
Median Duration of CR is Not reached (NR), range in months (1 – NR)

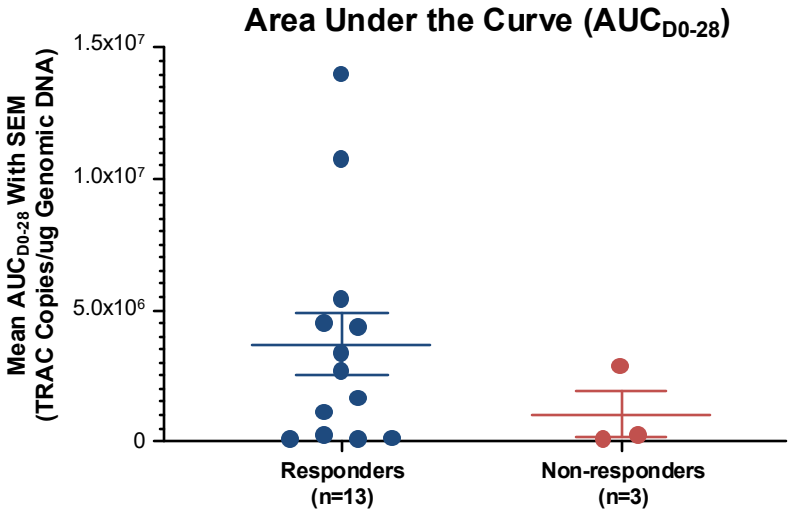
Robust CAR T-cell Expansion is Observed



Mean (± SEM)	N=16
Peak CAR T-cell, copies/ug of gDNA	$4.2x10^5$ ($\pm 1.3x10^5$)
AUC_{D0-28} CAR T-cell, copies/ug of gDNA	$3.2x10^6$ ($\pm 1.0x10^6$)
Time to peak, days	14.4 (±7.15)

Prolonged CAR T-cell Persistence Is Observed in Responders





Statistically significant difference, p value < 0.05

Mean (± SEM)	Responders (N=13)	Non-Responders (N=3)
Peak CAR T-cell, copies/ug of gDNA	$4.8x10^5$ ($\pm 1.5x10^5$)	$1.6x10^5$ ($\pm 1.3x10^5$)
AUC_{D0-28} CAR T-cell, copies/ug of gDNA	$3.7x10^6$ ($\pm 1.2x10^6$)	$1.0x10^6$ ($\pm 9.1x10^5$)
Time to peak, days	16.6 (±8.7)	4.7 (±2.7)

Statistics done using log transformed Anova test without BLQ imputation

Sustained MRD Negativity in Complete Responders

	Day 21/28	Day 60	Day 90	Day 120	Day 150/180	Day 270	Day 360
Patient 1	PR	CR	CR	CR	CR	CR	CR
Patient 2	CR	CR	CR	CR	CR	CR	
Patient 3	PR	PR	CR	CR			
Patient 4	CR	CR	CR				
Patient 5	PR	CR	CR				

MRD negative | MRD positive | Positive below LOD | Not done/data unavailable

LOD: Limit of detection

- MRD was assessed using the ClonoSEQ assay (Adaptive Biotechnologies)
- Dominant tumor cell clone for each subject is calibrated at screening using tumor tissue

Conclusions

- Azer-cel, followed by low-dose IL-2, demonstrates encouraging clinical activity in patients with LBCL relapsed after prior autologous CD19 CAR T therapy
- The safety profile was manageable with low-grade CRS and infrequent ICANS
- The median duration of CR has not yet been reached, underscoring the potential for long-lasting disease control even in this heavily pretreated, CAR T–relapsed population
- Robust CAR T-cell expansion and persistence observed in responders
- Sustained MRD negativity suggests deep remissions can be achieved
- Enrollment is ongoing in an additional cohort of CAR T–naïve patients (various indications) in the US and Australia

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