2026 ASCO® ANNUAL MEETING

Safety and Efficacy of Azer-cel, an Allogeneic CD19-Directed CAR T-Cell Therapy, in CAR T-Naive Patients with Relapsed/Refractory Non-Hodgkin Lymphoma and Chronic Lymphocytic Leukemia

Danielle Blunt, Matthew Ku, Houston Holmes, Nagendraprasad Sungala, Vinay Vanguru, Jean Yared, Scott Solomon, Hannah Rose, Aparna Raval, Grey Wilkinson, John Byon, Supriya Gupta

Supriya Gupta, MD, University of Minnesota

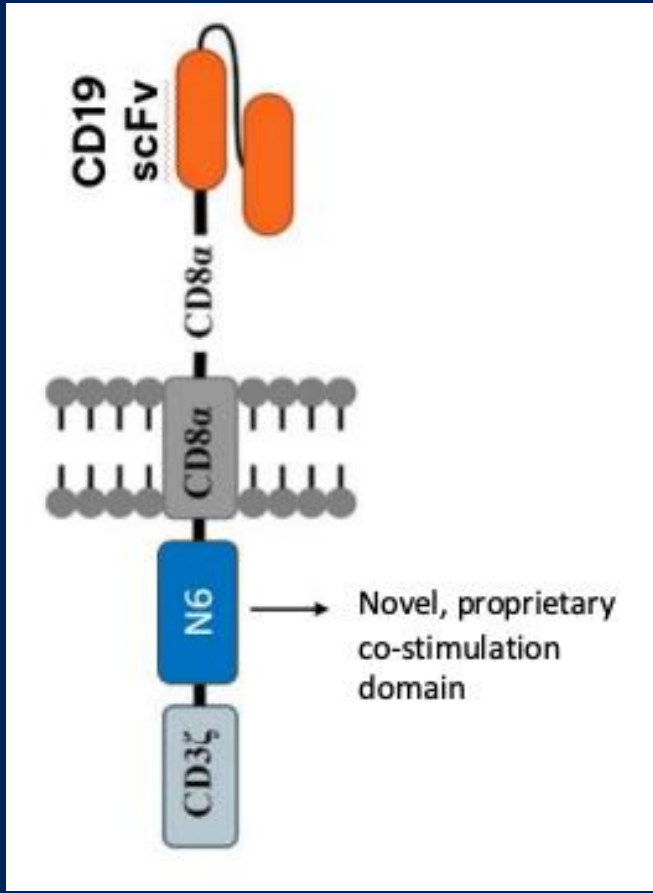
Key Takeaway

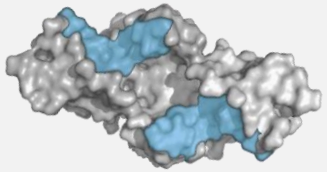
Azer-cel, an allogenic CAR T therapy, demonstrates promising clinical activity across a broad range of CD19+ B-cell malignancies, including MZL and CLL.

PRESENTED BY: Dr. Supriya Gupta, Assistant Professor of Medicine, University of Minnesota

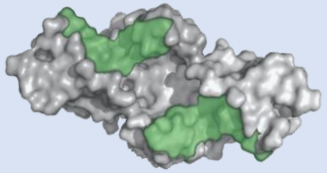
To Create Azer-cel, ARCUS Enables Precise Insertion of a CD19 CAR Into the *TRAC* Locus

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 (Complete)

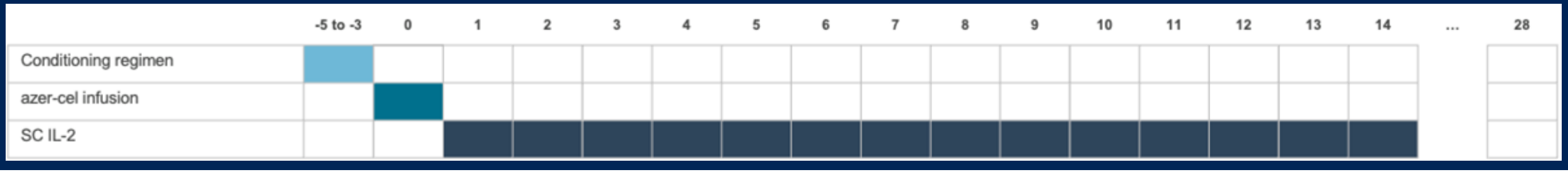
The Recommended Phase 2 Regimen was determined to be:

- 500M CAR T cells
- Aug/Cy – Flu 30mg/m^2 x 3 days, Cy 750mg/m^2 x 3 days
- Low-dose SC IL-2 (1 million IU, D1-14)

Dose Expansion (Currently enrolling)

- CAR T Relapsed
- **CAR T Naive**
- Concurrent BTKi

CAR T Naive cohort: Eligible patients with a CD19+ B-cell disease including DLBCL, HGBCL, FL (Grade1-3a), MZL, WM, PCNSL, and CLL/SLL. Patients must have had at least 1-2 prior lines of therapy.



Demographic & Disease Characteristics

Demographics	N=25
Median age (range), years	63.0 (56.0-69.0)
>65 years, n(%)	11 (44.0%)
Male, (%)	18 (72.0%)
Ethnicity, n (%)	
Hispanic or Latino	0
Not Hispanic or Latino	25 (100%)
Race, n (%)	
Black	2 (8.0%)
White	22 (88.0%)
Other	1 (4.0%)

Disease Characteristics	N=25
Histological subtypes, n (%)	
Diffuse Large B-cell Lymphoma Including Richter's Transformation	6 (24.0%)
Marginal Zone Lymphoma	6 (24.0%)
Chronic Lymphocytic Leukemia	4 (16.0%)
Primary Central Nervous System Lymphoma	4 (16.0%)
Follicular Lymphoma	3 (12.0%)
Primary Mediastinal B-cell Lymphoma	1 (4.0%)
Waldenstrom's Macroglobulinemia	1 (4.0%)

Prior Therapy	N=25
Median lines of prior therapy, n (range)	2 (1-7)
≥ 4 Lines	6 (24%)
Primary Refractory, n (%)	15 (60%)
Prior Bi-specific T-cell engager, n (%)	4 (16.0)
Prior BTK inhibitor, n (%)	14 (56.0%)
Prior BCL-2 inhibitor, n (%)	4 (16.0%)

Summary of Adverse Events, CRS, and ICANS

Treatment Emergent Adverse Events[1], n (%)	N=25 Any Grade	N=25 Grade ≥3
Any	24 (96.0%)	21 (84.0%)
Serious	13 (52.0%)	11 (44%)
Cardiac disorders[2]	4 (16.0%)	0
Infections	15 (60.0%)	7 (28.0%)
Heme Toxicity[3]		
Neutropenia	14 (56.0%)	12 (48.0%)
Thrombocytopenia	11 (44.0%)	7 (28.0%)
Anemia	8 (32.0%)	8 (32.0%)
Hypogammaglobulinemia	1 (4.0%)	0

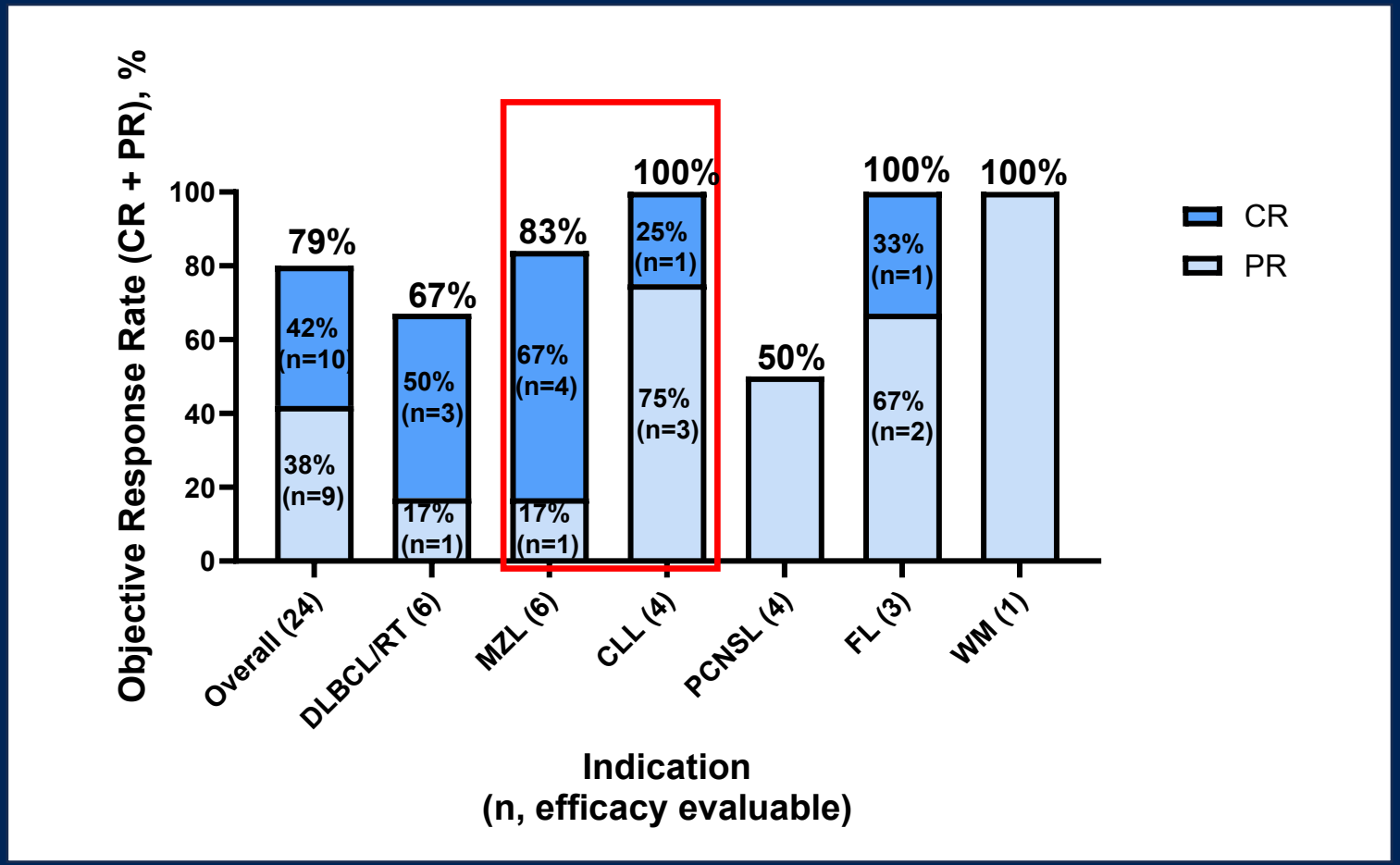
Summary includes the highest level CTCAE grade reported per participant.
[1]AEs that began on or after first administration of Azer-cel
[2]AEs included atrial fibrillation and tachycardia
[3]Heme Toxicity is based on the listed preferred term plus laboratory findings

AEs, n(%)	N=25 CRS	N=25 ICANS
Any grade, n(%)	21 (84.0%)	10 (40.0%)
Grade 1/2	21 (84.0%)	6 (24.0%)
Grade 3	0	3 (12.0%)
Grade 4	0	1 (4.0%)
Grade 5	0	0
Median time to onset (range), days	3 (1-10)	6 (2-19)
Median duration of event (range), days	2 (1-7)	2(1-7)

Summary includes the highest-level ASTCT grade reported for each participant.

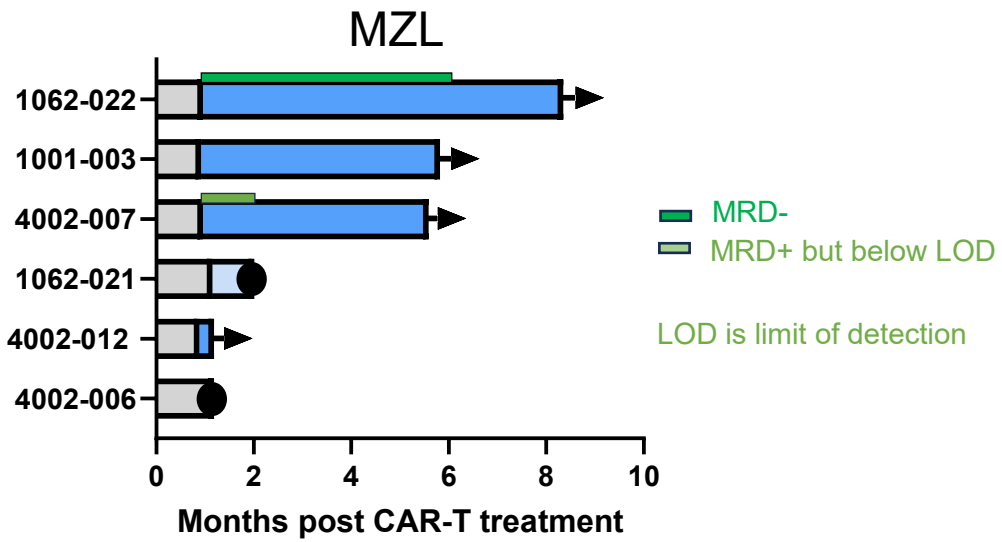
- No Grade ≥3 CRS events occurred
- ICANS was more frequent in patients with DLBCL (DLBCL: 67% any-grade, 33% Grade ≥3)
- CLL patients had no ICANS at any grade

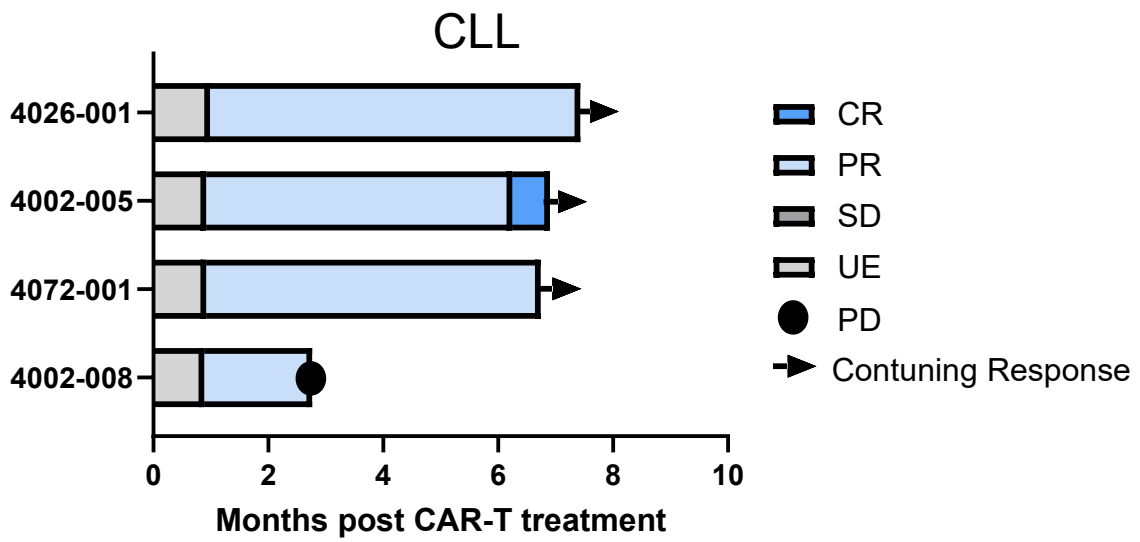
Responses Observed across All Indications



ORR is 93% among 14 patients with indolent disease

On-going Responses in MZL & CLL/SLL



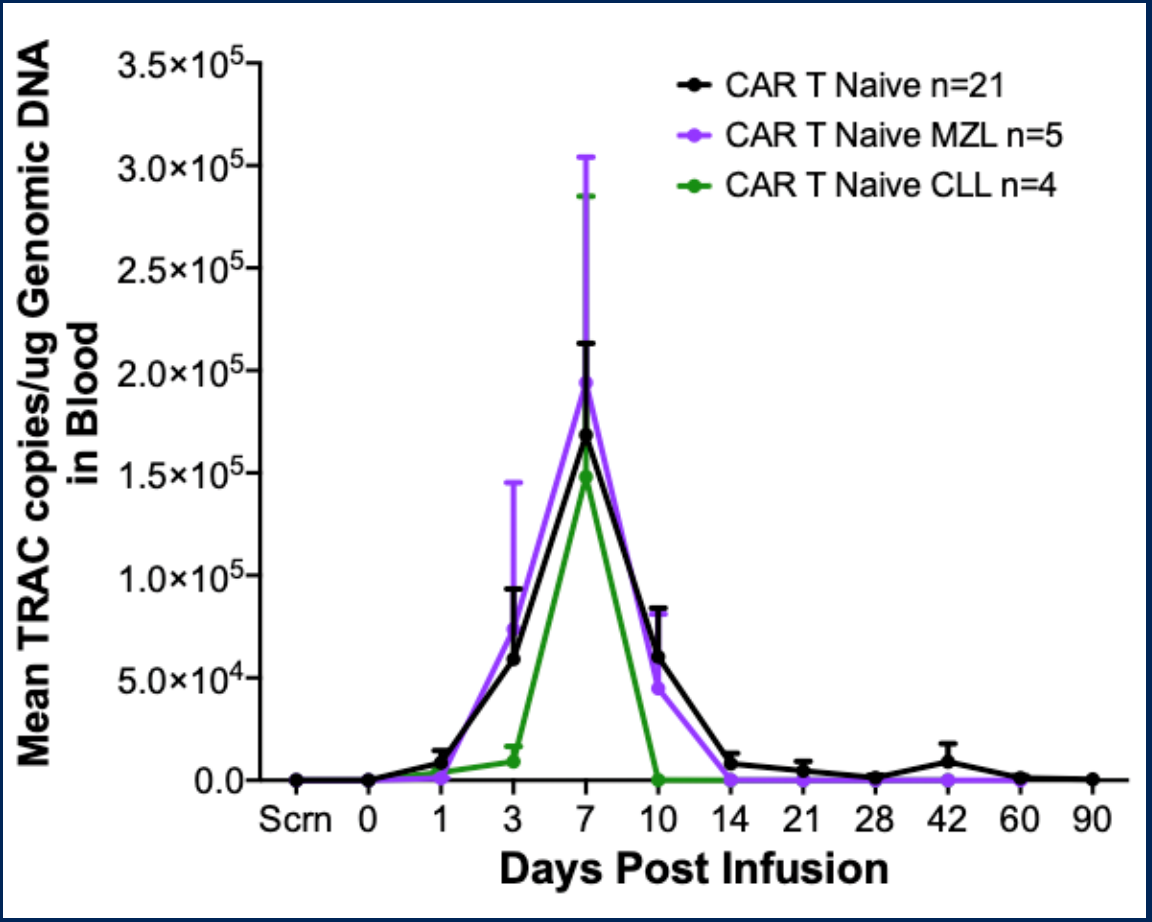


Median lines of prior therapy (range)	2 (2–6)
Median tumor burden, SPD cm² (range)	11.5 (3.5–34.6)
Refractory to most recent prior line	4/6 (67%)
Prior BTK inhibitor exposure	4/6 (67%) — 3/4 refractory
Prior anti-CD20 antibody	6/6 (100%)
High risk features	1062-022, 1062-021

Median lines of prior therapy (range)	3 (2–3)
Median tumor burden, SPD cm² (range)	42.5 (22.2–117.2)
Refractory to most recent prior line	3/4 (75%)
Prior BTK inhibitor exposure	4/4 (100%) — *3/4 refractory*
Prior BCL-2 inhibitor (venetoclax) exposure	3/4 (75%) — *2/3 refractory*
Double-refractory (BTKi + BCL-2i)	1/4 (25%) — 4002-008

Molecular disease burden reduction is observed in a subset of MZL subjects (ClonoSeq assay)

Robust CAR T Expansion is Observed in Subjects with MZL and CLL



Group	N	Peak CAR T (Cmax), copies/µg gDNA	AUC_{D0-28}, copies/µg gDNA	Time to peak (Tmax), in days
All CAR T-naive subjects	21	1.9×10^5 ($\pm0.5\times10^5$)	1.0×10^6 ($\pm0.3\times10^6$)	5.7 (±0.6)
Marginal Zone Lymphoma	5	1.9×10^5 ($\pm1.1\times10^5$)	1.1×10^6 ($\pm0.6\times10^6$)	5.8 (±1.2)
Chronic Lymphocytic Leukemia	4	1.5×10^5 ($\pm1.4\times10^5$)	5.5×10^5 ($\pm4.8\times10^5$)	4.5 (±1.5)

Data is shown as Mean (± SEM)

Conclusions / Key Takeaways

- Azer-cel, an off-the-shelf, allogenic CAR T cell therapy demonstrates promising clinical activity across a broad range of CD19+ B-cell malignancies, including MZL and CLL
- The safety profile was manageable with low-grade CRS. ICANS is consistent with auto CAR T therapy (brexu-cel and axi-cel) and seen primally in patients with DLBCL
- Robust CAR T-cell expansion is observed in the CAR T–naïve cohort
- MRD trends are consistent with the anti-tumor activity of azer-cel
- Enrollment in the US and Australia is ongoing in the CAR T–naïve cohort and a cohort exploring combination with a BTK inhibitor

Lay summary

What we tested: Azer-cel, an "off-the-shelf" cell therapy that targets the CD19 protein on cancerous B cells. It is made in advance from healthy donors so it is available within days, rather than the 4–6 weeks needed for traditional CAR T-cell therapies that are individually manufactured from each patient's own cells.

Who we treated: 25 adults with hard-to-treat lymphomas or leukemias (DLBCL, MZL, CLL, FL, PCNSL, WM, PMBCL) who had already received an average of 2 prior treatments and had not previously received CAR T therapy.

What we found: Most patients responded to azer-cel, including all 4 patients with chronic lymphocytic leukemia and most patients with marginal zone lymphoma. Side effects were mostly mild-to-moderate and manageable; serious neurologic and cardiac side effects were uncommon. The trial is still enrolling more patients.