CD62L Enrichment Achieves Robust Expansion and Memory Phenotype Post-Infusion in Patients with LBCL Treated with Rondecabtagene Autoleucel, an Autologous, Dual-Targeting CD19/CD20 CAR T-Cell Candidate

Akil Merchant[1], Ben Harris[2], Lora Zhao[2], Sahithi Cheemalamarri[2], Shobha Potluri[2], Tahir Latif[3], Umar Farooq[4], Sarah M. Larson[5]

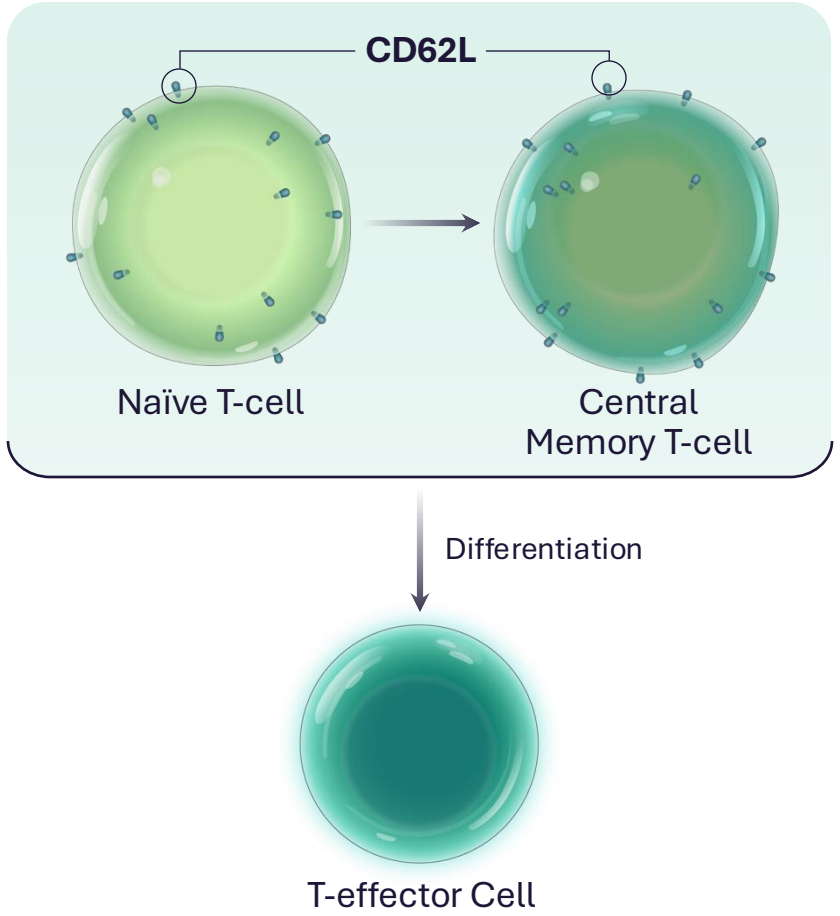
[1]**Samuel Oschin Cancer Center, Cedars-Sinai Medical Center, Los Angeles, CA, USA.**
[2]Lyell Immunopharma, South San Francisco, CA, USA.
[3]University of Cincinnati Medical Center, Cincinnati, OH, USA.
[4]University of Iowa, Iowa City, IA, USA.
[5]UCLA Medical Center, Los Angeles, CA, USA.

American Society of Hematology (ASH) | December 7, 2025 | Orlando, Florida | Publication Number 501

Higher Complete Response Rates and Longer Duration of Responses Needed in LBCL

Enrichment for stem-like CAR T-cells has promise in improving outcomes for patients

- Only ~50% of patients with 3L+ LBCL treated with approved CD19 CAR T-cell therapies (axi-cel, liso-cel) achieve a complete response
  - Higher CAR T-cell expansion is associated with better CAR T-cell response
  - Naïve T cells are associated with better CAR T-cell response
- CD62L is a surface protein that acts as a homing beacon, guiding white blood cells to sites of inflammation
- CD62L+-enriched cells include more naïve and central memory T-cells

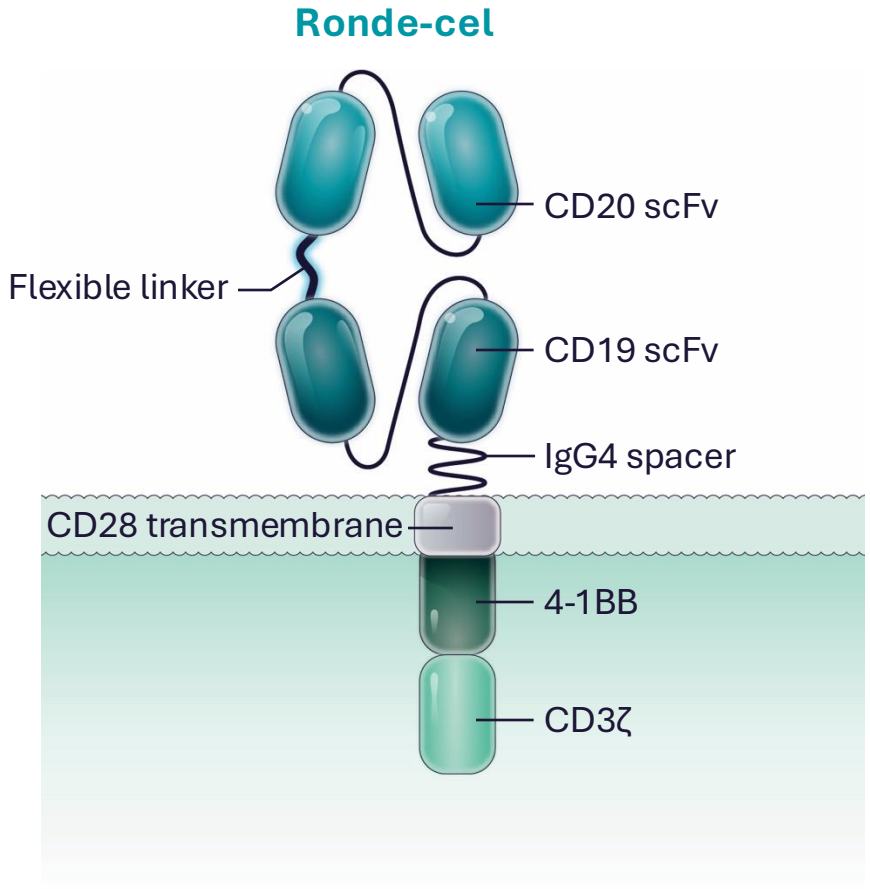


LBCL, large B-cell lymphoma; CAR, chimeric antigen receptor; 3L+, third- or later-line setting; axi-cel, axicabtagene autoleucel; liso-cel, lisocabtagene maraleucel.
Abramson et al. *Lancet* 2020, Arcangeli et. al. *JCI* 2022, Bishop et al. *NEJM* 2021, Harris et al. *Int J Mol Sci*. 2020, Neelapu et al. *N Engl J Med* 2017.

Dual-Targeting CD19/CD20 CAR T-Cells Enriched for Stem-Like Phenotype (CD62L+)

Rondecabtagene autoleucel (ronde-cel) designed to achieve high complete response rates and long duration of responses

- **Ronde-cel is a true CD19/CD20 "OR" logic-gated CAR**
  - Designed to target either CD19 and CD20 with full potency, overcome heterogeneous antigen density, and mitigate antigen loss following treatment.
- **CD62L+ enrichment selects for naïve and central memory T-cells**
  - CD62L+ cells are associated with improved persistence, reduced exhaustion, and lower adverse cytokine production.



Aldoss et al., *Clin Cancer Res* 2023, Arcangeli et. al. *JCI* 2022, Chen GM et. al. *Cancer Discovery* 2021, Sommermeyer et. al. *Leukemia* 2016.

High Overall Response Rate in Patients with 3L+ and 2L LBCL

Presented at the 18th International Conference on Malignant Lymphoma (ICML), Lugano, Switzerland, June 2025

Best Overall Response (3L+)	N = 25
Overall Responses, n (%)	**22 (88%)**
Complete Responses, n (%)	**18 (72%)**
Partial Response, n (%)	4 (16%)

Best Overall Response (2L)	N = 11
Overall Responses, n (%)	**10 (91%)**
Complete Responses, n (%)	**7 (64%)**
Partial Response, n (%)	3 (27%)

- Phase 1/2 multi-cohort, multi-center study with aggressive LBCL (CAR naïve), with the 3L+ cohort expanded into a single-arm, pivotal study called PiNACLE.

- Updated clinical data will be presented at ASH:
  - **Session:** 628
  - **Date:** 12/7/2025
  - **Time:** 4:45 PM – 5:00 PM ET
  - **Room:** OCCC - Tangerine Ballroom F3-4

Translational data from 2L and 3L+ LBCL patients treated with ronde-cel are included in this presentation

LBCL, large B-cell lymphoma.

CD62L+ Enrichment of T Cells Achieves Robust Expansion, Memory Phenotype, and Sustained Function After Infusion in Patients with Large B-Cell Lymphoma

Summary of Key Translational Findings

1. Ronde-cel drug products have a high proportion of CD62L+ cells with a **stronger memory-cell phenotype** compared to approved CD19 CAR T-cell products (axi-cel, tisa-cel) prior to infusion.

2. Ronde-cel has up to 3-fold **higher expansion** after infusion in patients compared to approved CD19 CAR T-cell products. A higher product memory-cell phenotype is positively correlated with expansion.

3. Ronde-cel has a **higher memory phenotype** at one month after infusion compared to axi-cel.

4. Ronde-cel CAR+ T cells collected from patients two months after infusion **sustain the capacity to proliferate, kill tumor cells, and secrete cytokines**.

Axi-cel, axicabtagene autoleucel; tisa-cel, tisagenlecleucel.

CD62L+ Enrichment of T Cells Achieves Robust Expansion, Memory Phenotype, and Sustained Function After Infusion in Patients with Large B-Cell Lymphoma

Summary of Key Translational Findings

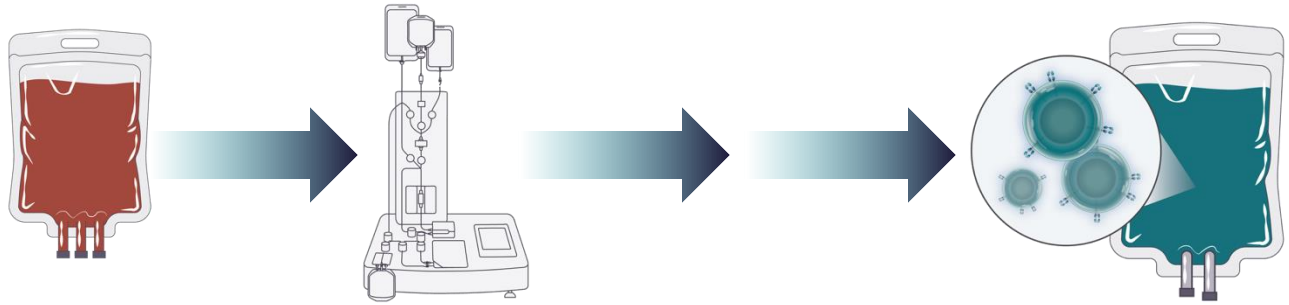
1. Ronde-cel drug products have a high proportion of CD62L+ cells with a **stronger memory-cell phenotype** compared to approved CD19 CAR T-cell products (axi-cel, tisa-cel) prior to infusion.
2. Ronde-cel has up to 3-fold **higher expansion** after infusion in patients compared to approved CD19 CAR T-cell products. A higher product memory-cell phenotype is positively correlated with expansion.
3. Ronde-cel has a **higher memory phenotype** at one month after infusion compared to axi-cel.
4. Ronde-cel CAR+ T cells collected from patients two months after infusion **sustain the capacity to proliferate, kill tumor cells, and secrete cytokines**.

Axi-cel, axicabtagene autoleucel; tisa-cel, tisagenlecleucel.

Ronde-Cel Has a High Percentage of CD62L+ Cells in the Final Drug Product

CD62L+ enrichment is a simple process that does not increase overall manufacturing time

Ronde-cel Manufacturing



Fresh Apheresis | CliniMACS | Standard CAR Process | **Ronde-cel**

Product Characteristics

- Ronde-cel drug products profiled with flow cytometry (N = 84)

	Median (Range)
% CD3+ of Viable Cells	**99 (90 - 99)**
% CD62L+ of CD3+ Cells	**96 (84 - 99)**

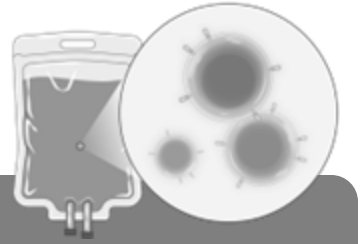
CD62L+ selection uses CliniMACS as part of an overall process with a vein-to-site median time of 16 days.

CAR, chimeric antigen receptor; CD62L or L-selectin positive T cells.
Aldoss et al., *Clin Cancer Res* 2023, Arcangeli et. al. *JCI* 2022, Chen GM et. al. *Cancer Discovery* 2021, Sommermeyer et. al. *Leukemia* 2016.

CD62L+-Enriched Ronde-Cel Has a Stronger Memory-Cell Phenotype Compared to Approved CD19 CAR T-Cell Products Prior to Infusion

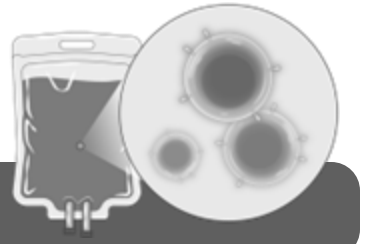
Transcriptional profiling performed using single-cell RNA-seq

Assess memory and effector phenotype of CAR+CD8+ cells at both individual genes and geneset (GSVA) level



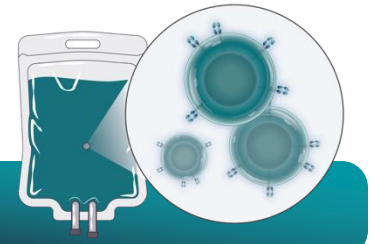
Axi-cel

- Single-cell RNA-seq data from Study 1 (N = 39), Study 2 (N = 12), Study 3 (N = 20), Study 4 (N = 39)



Tisa-cel

- Single-cell RNA-seq data from Study 2 (N = 13) and Study 4 (N = 18)



Ronde-cel

- Single-cell RNA-seq from Phase 1/2 study (N = 34)

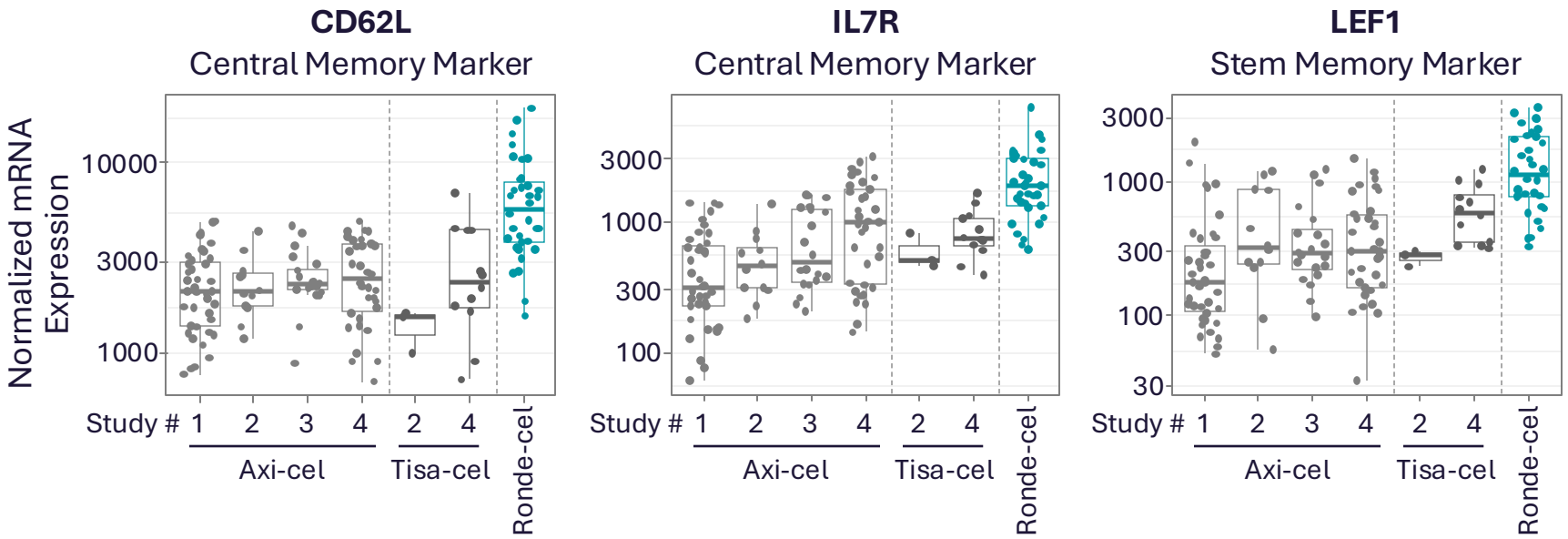
Note: No comparable data for liso-cel were available in the literature.

Single-cell RNA-seq is a technique that measures mRNA expression of all genes in individual CART-cells. Axi-cel, axicabtagene autoleucel; GSVA: GeneSet Variation Analysis; liso-cel, lisocabtagene maraleucel; tisa-cel, tisagenlecleucel.
Study 1: Deng et al. *Nat Med* 2020, Study 2: Haradhvala et al. *Nat Med* 2022, Study 3: Li et al. *Cancer Cell* 2023, Study 4: Yu et al. *JITC* 2025.

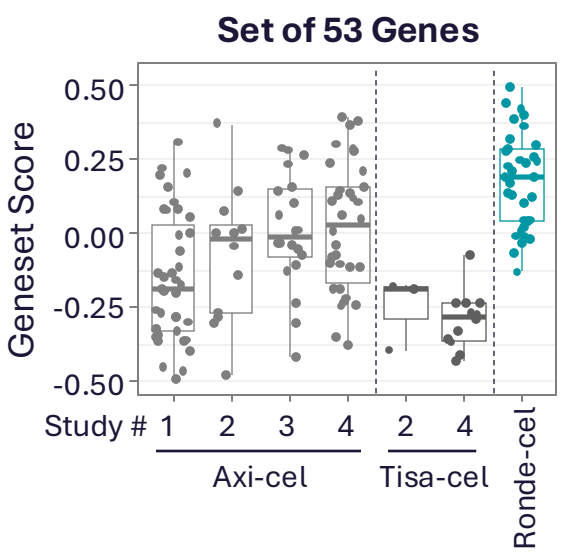
Ronde-Cel has a Stronger Memory Phenotype Compared to Approved CD19 CAR T-Cell Products

Higher relative expression of individual memory-related genes (CD62L, IL7R, LEF1) and memory geneset (group of 53 genes)

Individual Memory-Related Genes



Memory Geneset

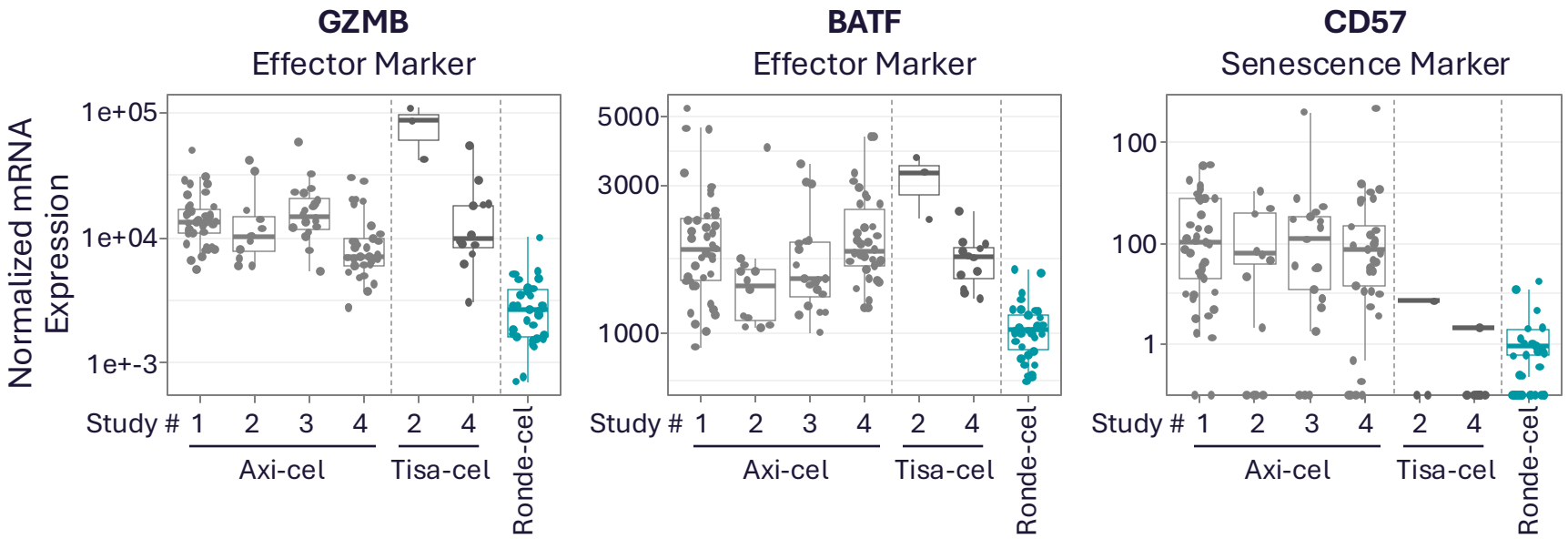


Axi-cel, axicabtagene autoleucel; tisa-cel, tisagenlecleucel.
Study 1: Deng et al. *Nat Med* 2020, Study 2: Haradhvala et al. *Nat Med* 2022, Study 3: Li et al. *Cancer Cell* 2023, Study 4: Yu et al. *JITC* 2025, Memory Geneset: Jansen et al. *Nature* 2019.

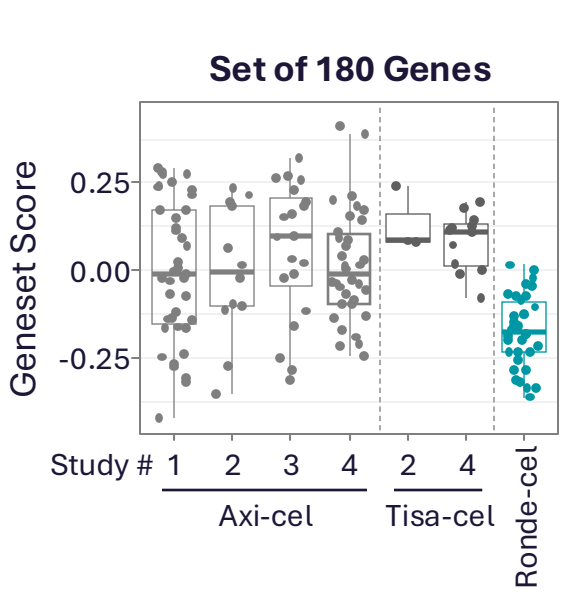
Ronde-Cel has Less of the Short-Lived Effector Phenotype Compared to Approved CD19 CAR T-Cell Products

Lower relative expression of individual effector-related genes (GZMB, BATF, CD57) and effector geneset (group of 180 genes)

Individual Effector-Related Genes



Effector Geneset



Axi-cel, axicabtagene autoleucel; tisa-cel, tisagenlecleucel.
Study 1: Deng et al. *Nat Med* 2020, Study 2: Haradhvala et al. *Nat Med* 2022, Study 3: Li et al. *Cancer Cell* 2023, Study 4: Yu et al. *JITC* 2025, Effector Geneset: Wherry et al. *Immunity* 2007.

CD62L+ Enrichment of T Cells Achieves Robust Expansion, Memory Phenotype, and Sustained Function After Infusion in Patients with Large B-Cell Lymphoma

Summary of Key Translational Findings

1. Ronde-cel drug products have a high proportion of CD62L+ cells with a **stronger memory-cell phenotype** compared to approved CD19 CAR T-cell products (axi-cel, tisa-cel) prior to infusion.

2. Ronde-cel has up to 3-fold **higher expansion** after infusion in patients compared to approved CD19 CAR T-cell products. A higher product memory-cell phenotype is positively correlated with expansion.

3. Ronde-cel has a **higher memory phenotype** at one month after infusion compared to axi-cel.

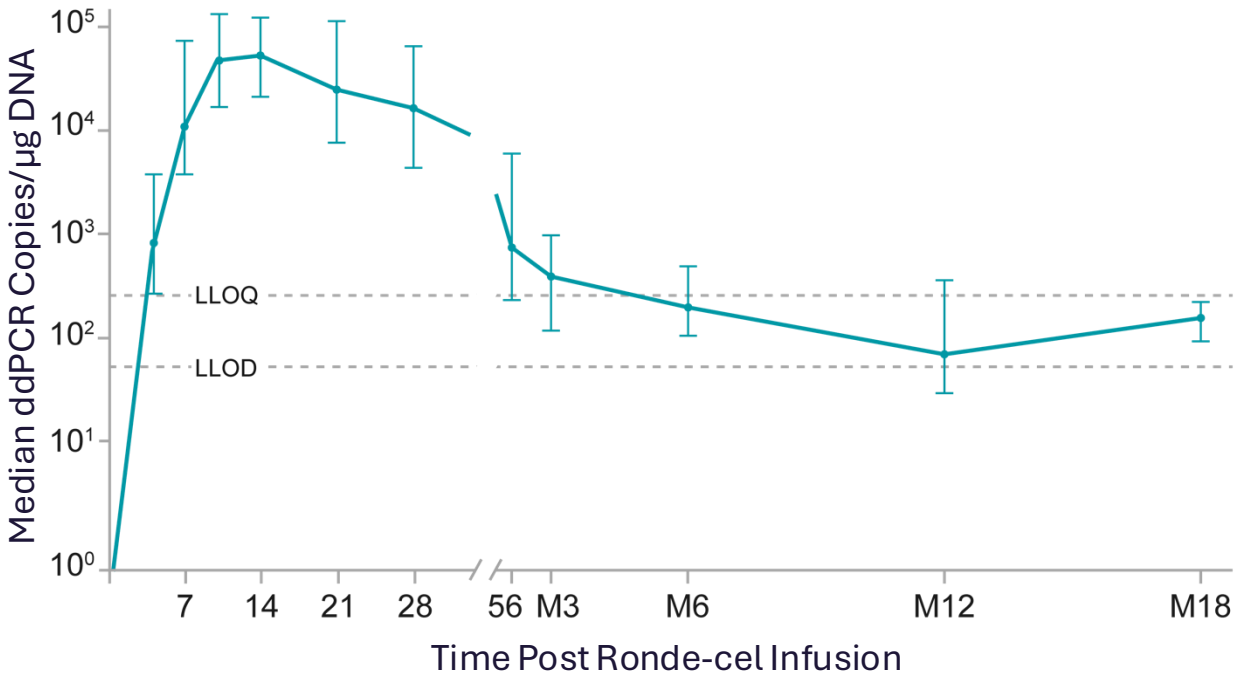
4. Ronde-cel CAR+ T cells collected from patients two months after infusion **sustain the capacity to proliferate, kill tumor cells, and secrete cytokines**.

Axi-cel, axicabtagene autoleucel; tisa-cel, tisagenlecleucel.

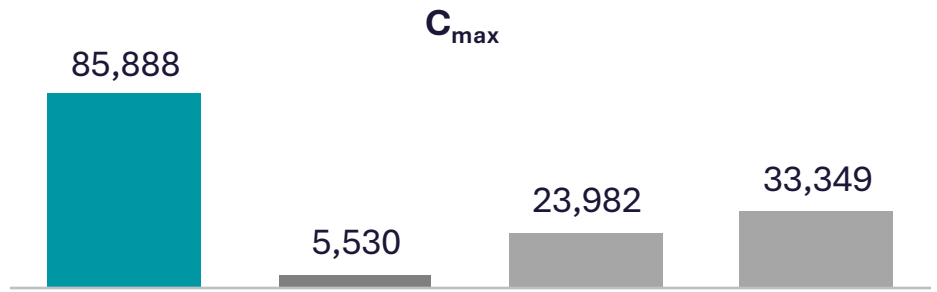
Up to 3-Fold Higher Cell Expansion with Ronde-Cel Compared to CD19 CAR T-Cell Products After Infusion

Better clinical response in CAR T-cell therapies has been shown to be associated with higher expansion

Ronde-cel Expansion



Ronde-cel vs CD19 CAR T-Cell Products



	Ronde-cel	Tisa-cel	Liso-cel	Liso-cel
	3L+, 2L N = 67	**3L+** N = 86	**3L+** N = 245	**2L** N = 83
$AUC_{[0-28]}$	819,198	64,600	213,730	270,345
T_{max}	14	9	12	12

Note: Axi-cel not included since cell expansion is assessed with a different method.

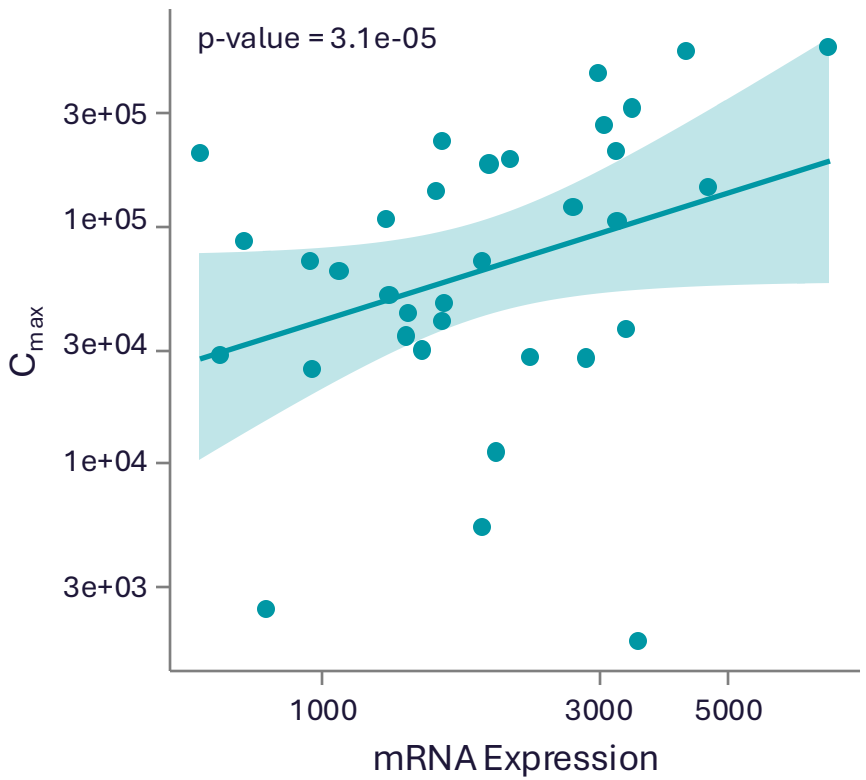
All metrics in table are median except tisa-cel is mean; C_{max} = peak concentration of CAR transgene in PBMCs post infusion (copies per ug DNA); AUC = days x copies/ug; T_{max} = days; Error bars = Interquartile range (IQR); M, month.
Abramson et al. *The Lancet* 2020, Abramson et al. *Blood* 2022, Schuster et al. *NEJM* 2018.

Ronde-Cel's Strong Product Memory Phenotype is Correlated with Higher Expansion

Patients with higher expression of memory-related genes have higher CAR T-cell peak expansion

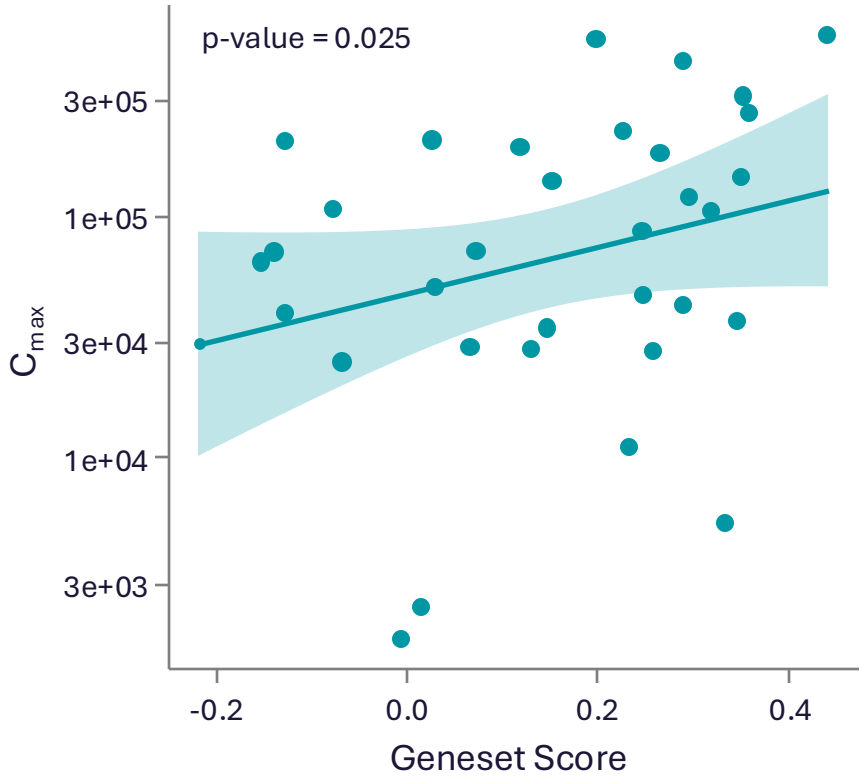
IL7R

Central Memory Marker Gene



Set of 74 Genes

Memory Geneset



A similar positive association is observed when evaluating overall CAR T-cell exposure ($AUC_{[0-28]}$)

AUC, area under the curve representing the total CAR-T product exposure integrated over time (days x copies/ug); Cmax, peak concentration of CAR transgene in PBMCs post infusion (copies per µg DNA); GSVA, gene set variation analysis; mRNA: messenger ribonucleic acid. Memory Geneset: Caushi et al. *Nature* 2021. p-value obtained from linear model fit using *lm* function in R.

CD62L+ Enrichment of T Cells Achieves Robust Expansion, Memory Phenotype, and Sustained Function After Infusion in Patients with Large B-Cell Lymphoma

Summary of Key Translational Findings

1. Ronde-cel drug products have a high proportion of CD62L+ cells with a **stronger memory-cell phenotype** compared to approved CD19 CAR T-cell products (axi-cel, tisa-cel) prior to infusion.

2. Ronde-cel has up to 3-fold **higher expansion** after infusion in patients compared to approved CD19 CAR T-cell products. A higher product memory-cell phenotype is positively correlated with expansion.

3. Ronde-cel has a **higher memory phenotype** at one month after infusion compared to axi-cel.

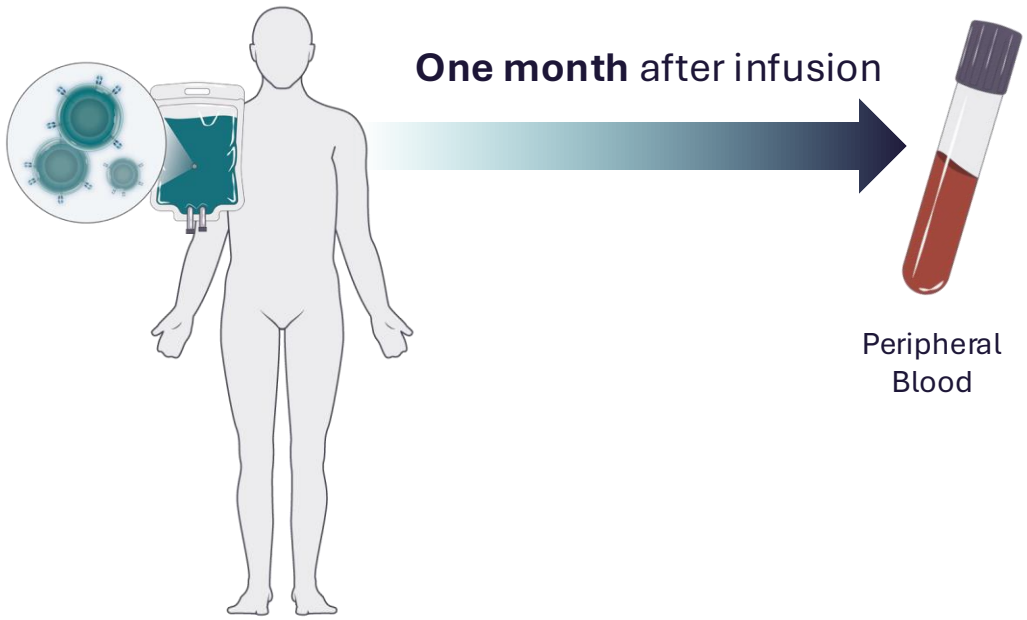
4. Ronde-cel CAR+ T cells collected from patients two months after infusion **sustain the capacity to proliferate, kill tumor cells, and secrete cytokines**.

Axi-cel, axicabtagene autoleucel; tisa-cel, tisagenlecleucel.

Ronde-Cel has a Higher Memory Phenotype One Month After Infusion Compared to Axi-Cel

Enhanced proportion of memory phenotype ($GZMB^{lo}KRLG1^{lo}$) may improve CAR-T cell persistence and durability

CAR T-Cell Infusion



Study Description

- Peripheral blood mononuclear cells were collected one month after treatment with ronde-cell
- CAR+ cells were sorted for single-cell RNA-seq
- **Memory phenotype** was assessed in CD8+ cells (N = 9) and compared with published axi-cel data

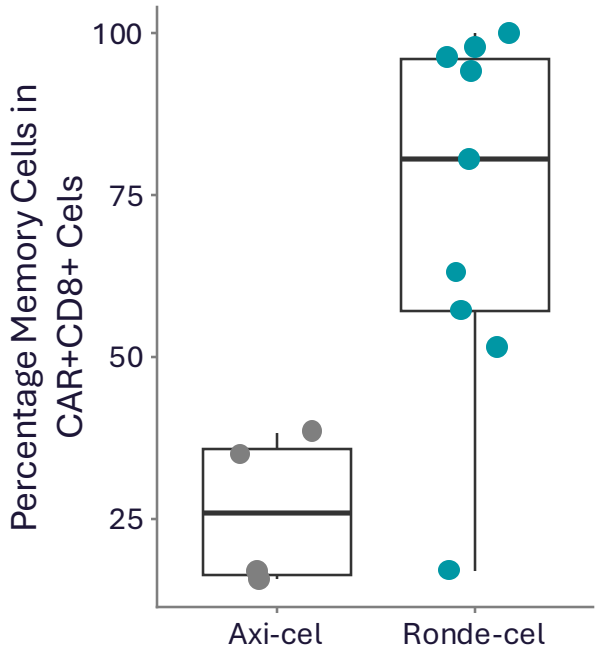
Post-infusion single-cell analyses are uncommon in CAR T-cell trials, yet provide insight into product behavior

Axi-cel, axicabtagene autoleucel.

Ronde-Cel has a Higher Proportion of Memory Cells and Higher Gene Expression of Cytokines One Month After Infusion Compared to Axi-Cel

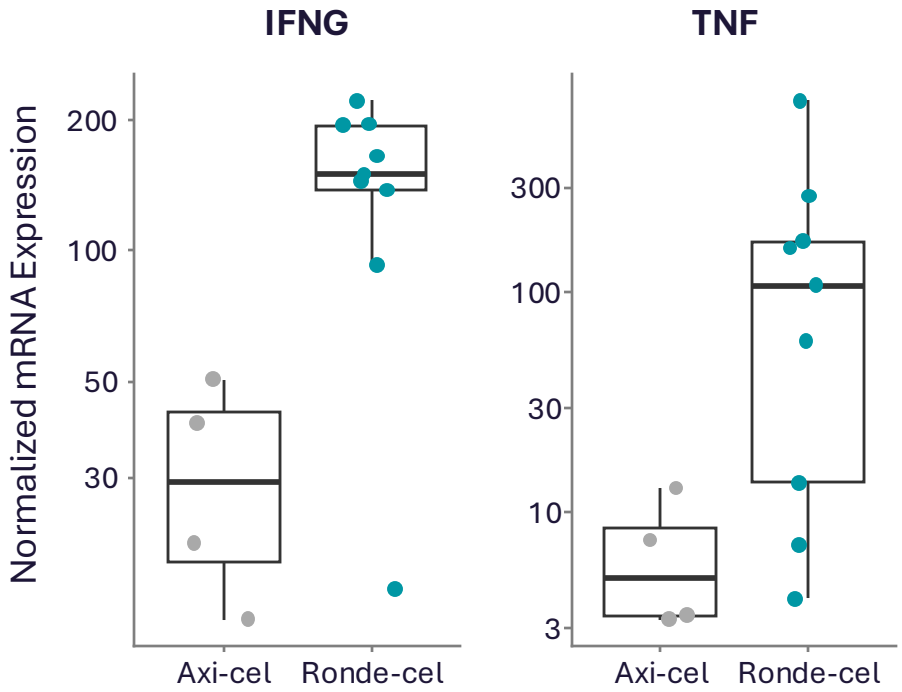
Higher proportion of GZMB^{lo}KLRG1^{lo} cells (T_{SCM}, T_{CM}, T_{EM}) and higher IFNG and TNF expression

Memory Cell Proportion (T_{SCM}, T_{CM}, T_{EM})



Note: No tisa-cel or liso-cel data available.

Cytokine Gene Expression



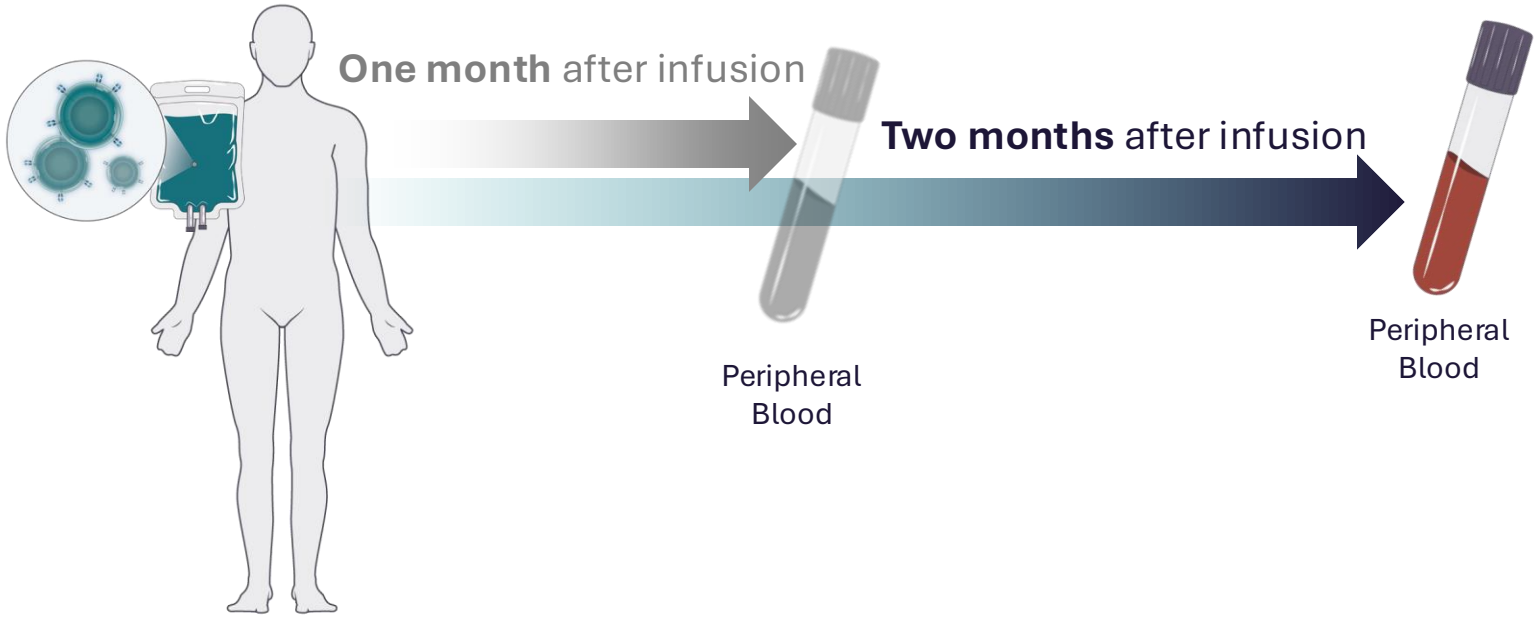
Note: No tisa-cel or liso-cel data available.

Axi-cel, axicabtagene autoleucel; GZMB, granzyme B; IFNG, interferon gamma; KLRG1, killer cell lectin-like receptor G1; liso-cel, lisocabtagene maraleucel; mRNA, messenger ribonucleic acid; T_{SCM}, stem cell memory; T_{CM}, central memory; T_{EM}, effector memory; TNF, tumor necrosis factor.
Restricted to patients with >500 CD8+CAR+ cells; Axi-cel dataset: Cao et al. *bioRxiv* 2025.

Sustained Anti-Tumor Activity of Ronde-Cel's CD62L+ Enriched Cells Were Assessed After Infusion

Experimental method enabled by high numbers of CAR T-cells in circulation two months after infusion

CAR T-Cell Infusion



Study Description

- Co-culture peripheral blood cells with tumor cell line
- Assess **functional activity** of CAR+ cells for proliferation, cytotoxicity, and cytokine secretion (N = 3)

Post-infusion functional analyses not reported in CD19 CAR T-cell trials, yet provide key insight into function

CD62L+ Enrichment of T Cells Achieves Robust Expansion, Memory Phenotype, and Sustained Function After Infusion in Patients with Large B-Cell Lymphoma

Summary of Key Translational Findings

1. Ronde-cel drug products have a high proportion of CD62L+ cells with a **stronger memory-cell phenotype** compared to approved CD19 CAR T-cell products (axi-cel, tisa-cel) prior to infusion.

2. Ronde-cel has up to 3-fold **higher expansion** after infusion in patients compared to approved CD19 CAR T-cell products. A higher product memory-cell phenotype is positively correlated with expansion.

3. Ronde-cel has a **higher memory phenotype** at one month after infusion compared to axi-cel.

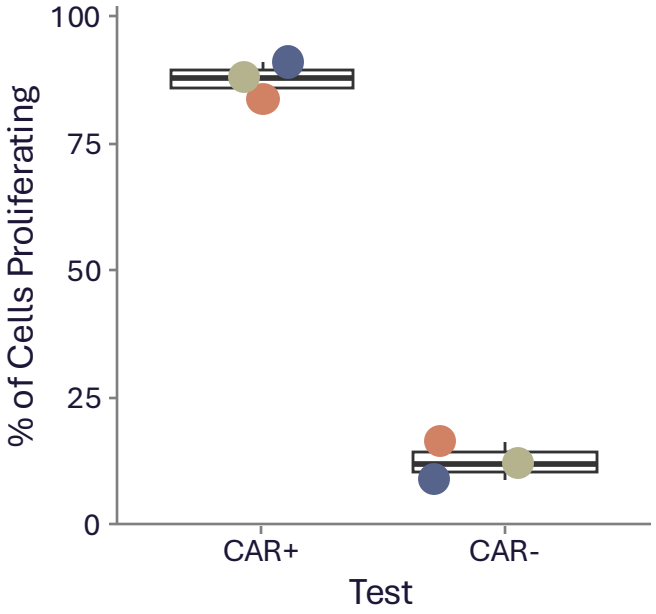
4. Ronde-cel CAR+ T cells collected from patients two months after infusion **sustain the capacity to proliferate, kill tumor cells, and secrete cytokines**.

Axi-cel, axicabtagene autoleucel; tisa-cel, tisagenlecleucel.

Ronde-Cel Two Months After Infusion Proliferates, Kills, and Secretes Cytokines

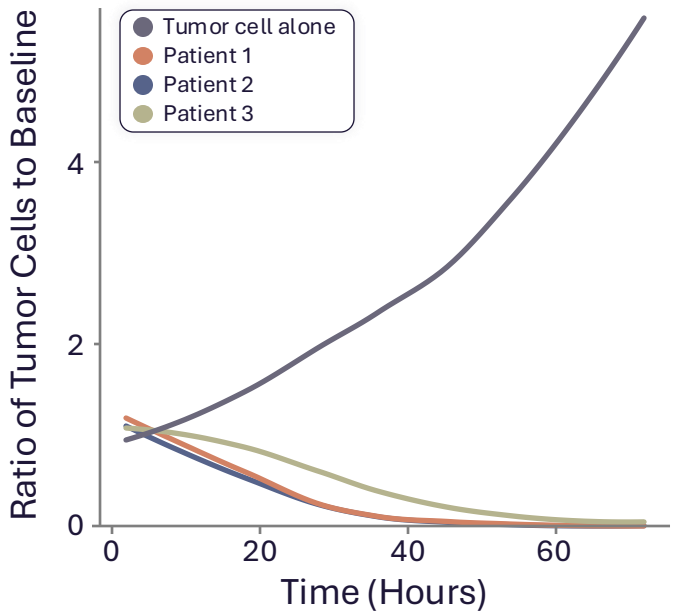
High memory phenotype and enhanced expansion of ronde-cel enable sustained functional capacity

Proliferation



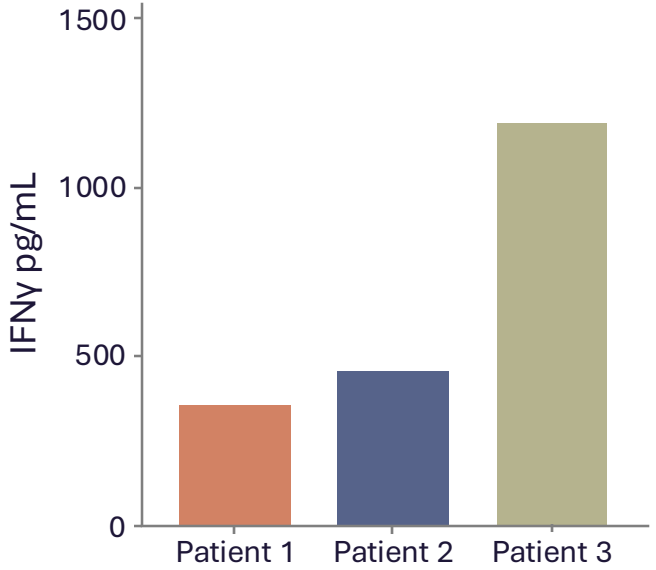
Proliferation assessed by flow cytometry with Cell Trace Violet (CTV) dye at Day 5

Cytotoxicity



Cytotoxicity assessed by measuring live tumor cells with Incucyte

Cytokine Secretion



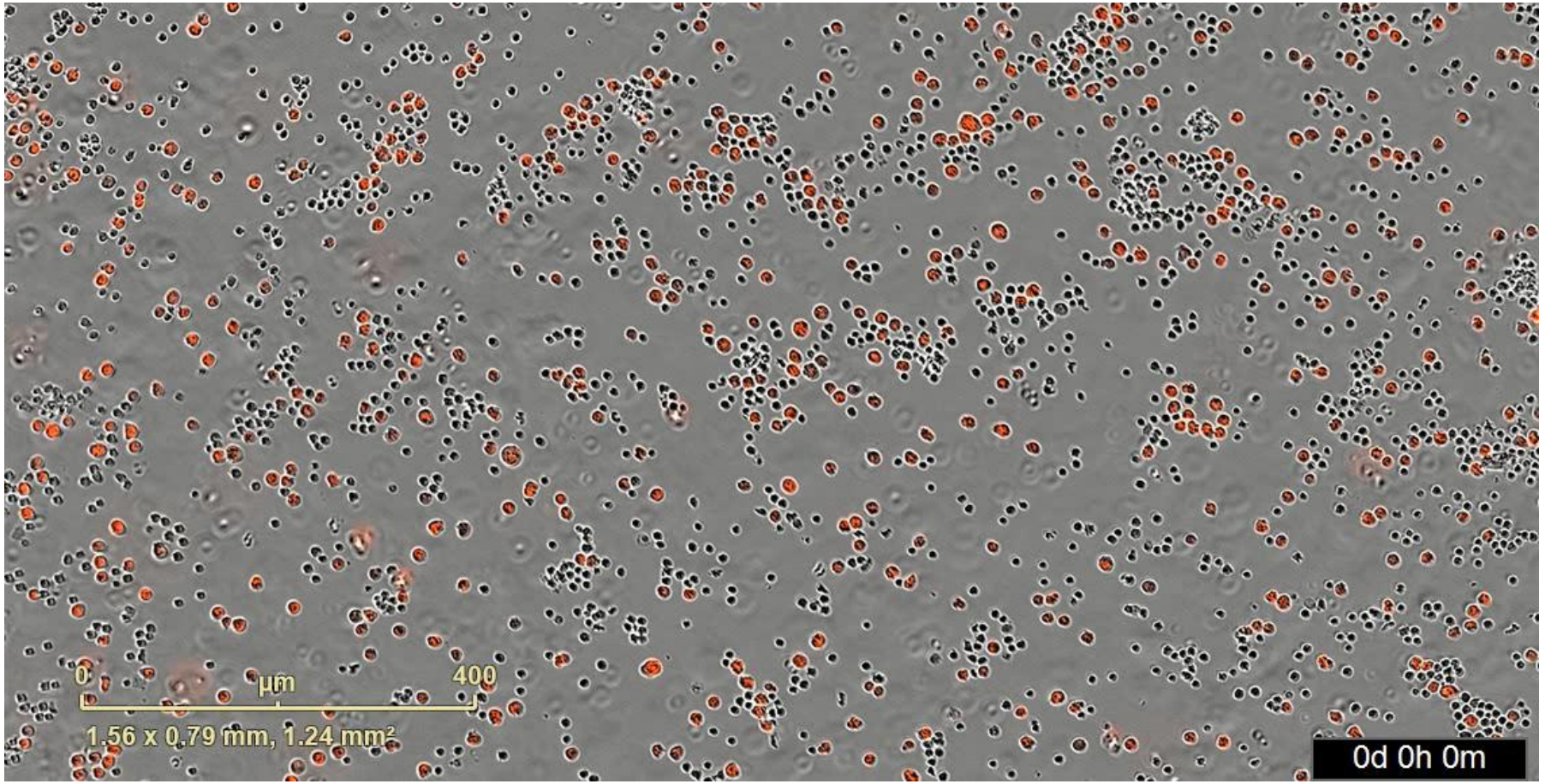
Cytokine assessed with Meso Scale Diagnostics (MSD) assay

Similar functional data also obtained on seven patient samples collected at one month after infusion

Tumor cell line used is Nalm6. The PBMC alone and the tumor cell alone controls are below the limit of detection in the cytokine secretion assay.
CAR, chimeric antigen receptor; PBMC, peripheral blood mononuclear cells.

Ronde-Cel from Two Months After Infusion Kills Tumor B-Cells in In Vitro Co-Culture

Pink cells = tumor cells; grey cells = patient peripheral blood mononuclear cells



Ronde-cel demonstrates sustained tumor killing two months after infusion (72-hour timelapse video)

Tumor cell line used is Nalm6.

CD62L+ Enrichment of T Cells Achieves Robust Expansion, Memory Phenotype, and Sustained Function After Infusion in Patients with Large B-Cell Lymphoma

Summary of Key Translational Findings

1. Ronde-cel drug products have a high proportion of CD62L+ cells with a **stronger memory-cell phenotype** compared to approved CD19 CAR T-cell products (axi-cel, tisa-cel) prior to infusion.

2. Ronde-cel has up to 3-fold **higher expansion** after infusion in patients compared to approved CD19 CAR T-cell products. A higher product memory-cell phenotype is positively correlated with expansion.

3. Ronde-cel has a **higher memory phenotype** at one month after infusion compared to axi-cel.

4. Ronde-cel CAR+ T cells collected from patients two months after infusion **sustain the capacity to proliferate, kill tumor cells, and secrete cytokines**.

Correlative analysis of translational data to clinical response from PiNACLE (single-arm, pivotal trial in 3L+ patients) is ongoing