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Durable Clinical Responses With Rondecabtagene Autoleucel (Dual-Targeting CD19/CD20 CAR-T Cell) are Associated With Higher Proportion of Cytotoxic T Cells With Memory Potential in Infusion Products

Poster # PF1097

Akil Merchant,[1] Tahir Latif,[2] Umar Farooq,[3] Locke Bryan,[4] Stefan O. Ciurea,[5] Nebu Koshy,[6] Ben Harris,[7] Viola Lam,[7] Shobha Potluri,[7] Sarah M. Larson[8]

[1]Samuel Oschin Cancer Center, Cedars-Sinai Medical Center, Los Angeles, CA, USA; [2]University of Cincinnati Medical Center, Cincinnati, OH, USA; [3]University of Iowa, Iowa City, IA, USA; [4]Augusta University, Augusta, GA, USA; [5]University of California, Irvine, Irvine, CA, USA; [6]Baylor Scott & White Health, Dallas, TX, USA; [7]Lyell Immunopharma, South San Francisco, CA, USA; [8]UCLA Medical Center, Los Angeles, CA, USA

Two pivotal trials are underway for ronde-cel:

PINACLE – A single-arm pivotal trial evaluating the efficacy and safety of ronde-cel in R/R LBCL (3L+)

PiNACLE-H2H – A head-to-head trial evaluating the efficacy and safety of ronde-cel versus investigator's choice of CD19 CAR T-cell therapy in R/R LBCL (2L+)

For more information contact;
spotluri@lyell.com@lyell.com

Introduction

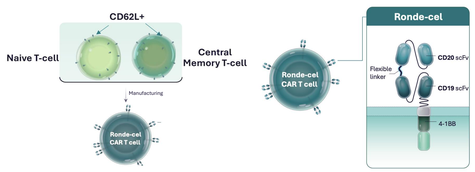
- More durable responses are needed in relapsed/refractory large B-cell lymphoma (LBCL). Rondecabtagene autoleucel (ronde-cel) has reported a median progression-free survival (mPFS) of 18 months in the 3L+ setting.

Table 1. Best overall response in 3L+ LBCL (ASH 2025 presentation)

Best Overall Response (3L+)	N = 29
Overall Responses, n (%)	**27 (93%)**
Complete Responses, n (%)	**22 (76%)**
Partial Response, n (%)	5 (17%)

- **Cytotoxic Effector product composition has been linked to CAR T response[5,6], but durable activity may require cytotoxic cells that retain memory potential**
- Ronde-cel is a dual-targeting CD19/CD20 CAR T-cell product candidate designed with full potency at either CD19 or CD20 and manufactured with CD62L-selection to enrich for naïve and central memory T-cells in the infusion product
- The purpose of this study was to explore the roles of CD62L+ enrichment and CD19/CD20 dual-targeting in ronde-cel infusion products on clinical response observed in patients with LBCL

Figure 1. Ronde-cel is a dual-targeting CD19/CD20 CAR T-cell candidate enriched for naïve and central memory T cells



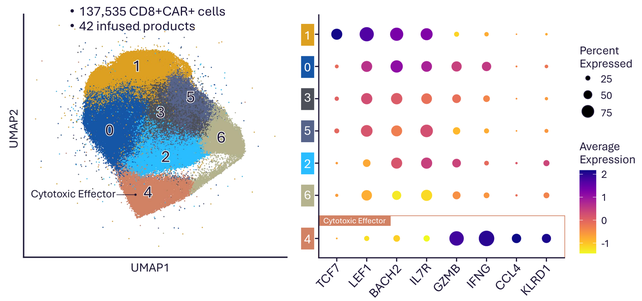
Methods

- Single-cell RNA-sequencing (scRNAseq) was performed to characterize ronde-cel products and to assess for the memory potential of cytotoxic effector cells compared to published gene datasets for axi-cel and tisa-cel
- Proportions of stemlike and cytotoxic effector cells were evaluated for correlation with response rates from the ongoing Phase 1/2 trial of ronde-cel in patients with LBCL
  - An in vitro study was subsequently performed to functionally evaluate the cytotoxic effector cells from either CD62L enrichment (T_{cmp}) or bulk enrichment derived products to assess the memory potential (survival and proliferation) in a homeostatic cytokine (IL7 + IL15) assay
- Peripheral blood samples were collected from patients, then co-cultured with a tumor cell line and CAR+ cells were assessed for proliferation, cytotoxicity, and cytokine secretion
- Co-culture of ronde-cel with Raji cells expressing CD19, CD20 or both were conducted to evaluate potency of the tandem dual-targeting CD19/CD20 CAR
- Immunohistochemical staining on baseline tumor biopsies for CD19/CD20 were performed and to understand impact on clinical response

Results

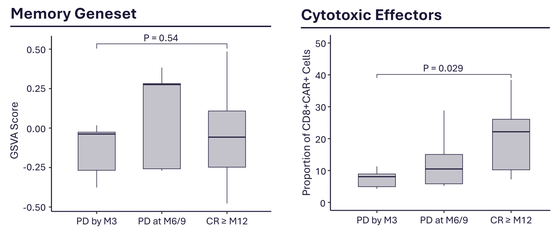
Identification of cytotoxic effector cluster in scRNAseq of ronde-cel infusion products

Figure 2. Characterization of ronde-cel products through scRNAseq



Patients with durable responses after ronde-cel have a higher proportion of Cytotoxic Effector cells in their drug products

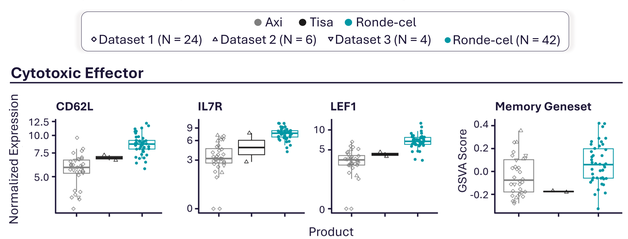
Figure 3. Comparison of memory geneset in products and T_{cmp} proportion in CD8+CAR+ cells across patients with durable responses (CR ≥ month 12) and early progressors (PD by month 3)



N = 20, patients with ongoing complete response before M12 excluded

Cytotoxic Effectors in ronde-cel have stronger memory potential (T_{cmp}) compared to approved CD19 CAR products (axi-cel and tisa-cel)

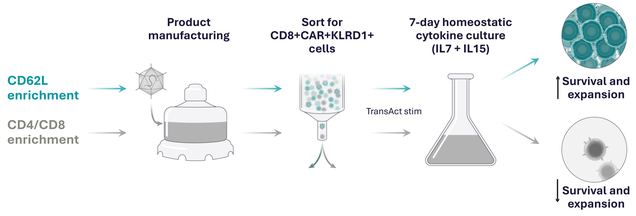
Figure 4. Normalized expression of memory genes and memory geneset score of ronde-cel products compared to axi-cel and tisa-cel in cytotoxic effector cells

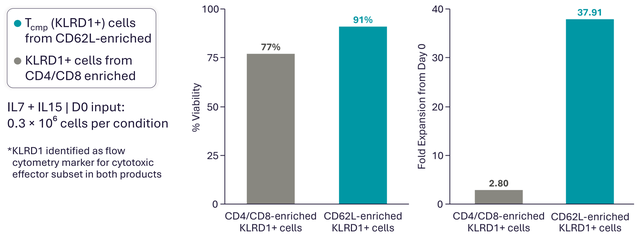


Publicly available infusion products were re-analyzed[7,8,9] to identify cytotoxic effector clusters using enrichment of cytotoxic effector genes (GZMB, IFNG, CCL4, CCL5, KLRD1). Pseudobulk analysis of 42 ronde-cel and publicly available products within cytotoxic effector clusters was performed (only products with > 20 cells in cytotoxic effector clusters were included).

T cells with cytotoxic memory potential (T_{cmp}) from ronde-cel have higher survival and expansion compared to cytotoxic effector cells from bulk-enriched products

Figure 5. Comparison of viability and proliferation of cytotoxic effector (CAR+CD8+KLRD1+) cells from small scale CD4/CD8 enriched and CD62L enriched products

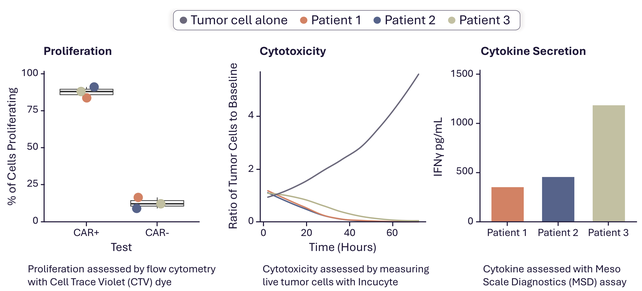




CAR+ T cells two months after patient infusion: effectively proliferate, kill, and secrete cytokines

Strong memory phenotype that persists and enhanced expansion of ronde-cel enable sustained functional capacity

Figure 6. Assessment of proliferation, cytotoxicity, and cytokine secretion of peripheral blood mononuclear cells from patients two-months post ronde-cel infusion



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

Cytotoxicity assessed by measuring live tumor cells with Incucyte

Cytokine assessed with Meso Scale Diagnostics (MSD) assay

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

Abbreviations:
Axi-cel, axicabtagene ciloleucel; CEM, T lymphoblast cell line that is CD19-CD20-; E:T, Effector to target; KO, knockout; LBCL, Large B-cell lymphoma; Liso-cel, lisocabtagene maraleucel; scRNAseq, single cell RNA sequencing; Tisa-cel, tisagenlecleucel

References:
[1]Neelapu et al *NEJM* 2017; [2]Abramson et al *Lancet* 2020; [3]Gattinoni et al *Nature Medicine* 2017; [4]Larson et al *Blood* 2025; [5]Rezvan et al *Nature Cancer* 2024; [6]Mauer et al *Blood* 2024; [7]Li et al *Cancer Cell* 2023; [8]Haradhvala et al *Nature Medicine* 2022; [9]Yu et al *JITC* 2025

Acknowledgments
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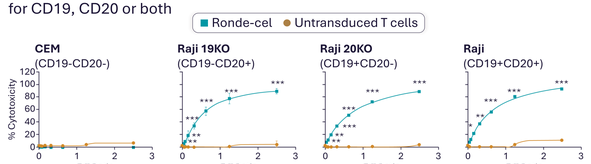
Ronde-cel exhibits robust antigen-specific cytotoxicity in co-culture with CD19 and CD20 single and dual-antigen expressing Raji tumor cells

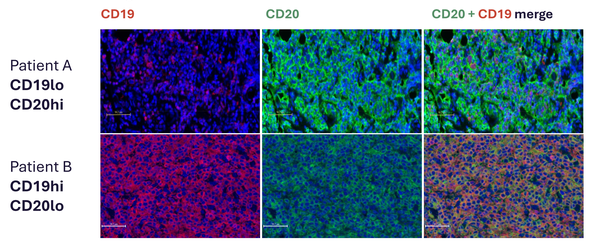
Figure 7. Assessment of cytotoxicity of ronde-cel to cell lines that are positive for CD19, CD20 or both



*P < 0.05, **P < 0.01, ***P < 0.001

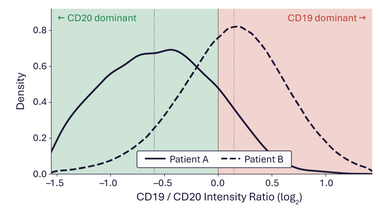
Ronde-cel exhibits durable responses in patients with variable levels of CD19 and CD20 antigen at baseline

Figure 8. Immunohistochemical staining on baseline tumor biopsies from two patients for CD19/CD20 and assessment of relative intensities of the CD19/CD20 antigens



Patient A and Patient B both achieved durable complete responses (> 12 month response)

Distribution of per-cell CD19/CD20 intensity ratio quantified using Halo HighPlex FL



Conclusion

CD62L+ enrichment of T cells achieves memory phenotype associated with durable responses in patients with large B-cell lymphoma

Summary of key findings:

- Ronde-cel drug products cytotoxic effector cells (T_{cmp}) have a **stronger memory potential** compared to axi-cel's cytotoxic effector cells
- Ronde-cel's T_{cmp} cells are associated with durable responses and have better capacity to survive and proliferate in vitro
- Ronde-cel CAR+ T cells collected from patients two months after infusion **sustain the capacity to proliferate, kill tumor cells, and secrete cytokines**
- Durable complete responses are observed in patients with large B-cell lymphoma with low CD19 or low CD20 antigen expression on tumor biopsies at baseline