Rondecabtagene Autoleucel, an Autologous, Dual-Targeting CD19/CD20 CAR T-Cell Candidate Manufactured from CD62L+ Enriched T Cells, Achieves Durable Responses in Patients with Large B-Cell Lymphoma

Sarah M. Larson[1], Umar Farooq[2], Tahir Latif[3], Felix Mensah[4], Bradley D. Hunter[5], Stefan O. Ciurea[6], Nebu Koshy[7], Locke Bryan[8], Boyu Hu[9], William Clark[10], Hassaan Yasin[11], Yeonhee Kim[12], Greg Kaufman[12], Akil Merchant[13]

[1]**UCLA Medical Center, Los Angeles, CA, USA**; [2]University of Iowa, Iowa City, IA, USA; [3]University of Cincinnati Medical Center, Cincinnati, OH, USA; [4]Franciscan Health, Indiana Blood and Marrow Transplantation, Indianapolis, IN, USA; [5]Intermountain Health, Salt Lake City, UT, USA; [6]University of California, Irvine, CA, USA; [7]Baylor Scott & White Health, Dallas, TX, USA; [8]Augusta University, Augusta, GA, USA; [9]Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, USA; [10]Virginia Commonwealth University, Richmond, VA, USA; [11]University of Louisville, Louisville, KY, USA; [12]Lyell Immunopharma, South San Francisco, CA, USA; [13]Samuel Oschin Cancer Center, Cedars-Sinai Medical Center, Los Angeles, CA, USA

American Society of Hematology (ASH) | December 7, 2025 | Orlando, Florida | Presentation ID 668

CD19 CAR T-Cell Products Transformed the Treatment of LBCL, But Have Limitations

Despite these advances, next-generation CAR T-cell products with improved safety and efficacy are needed

- **Limited durability:**
  - ~40% of patients in 3L+ LBCL remain in complete response at 6 months
  - Median progression-free survival (mPFS) < 7 months in 3L+ LBCL
- **Exclusion of key populations:**
  - Axi-cel: Limited enrollment of age >75, no bridging therapy (ZUMA-1, 3L+) or steroids only (ZUMA-7, 2L)
  - Liso-cel: No patients > 75 (TRANSFORM, 2L)

- **Additional limitations:**
  - Complete response rate for liso-cel in older patients with primary refractory disease in the 2L setting (PILOT) was 42%
  - Limited data on duration of response have been published for patients in 2L with primary refractory disease (mPFS ~7 months in ZUMA-7)
  - Grade 3 and higher CRS and ICANS limit the use of the approved CD19 CAR T-cell products in the outpatient setting

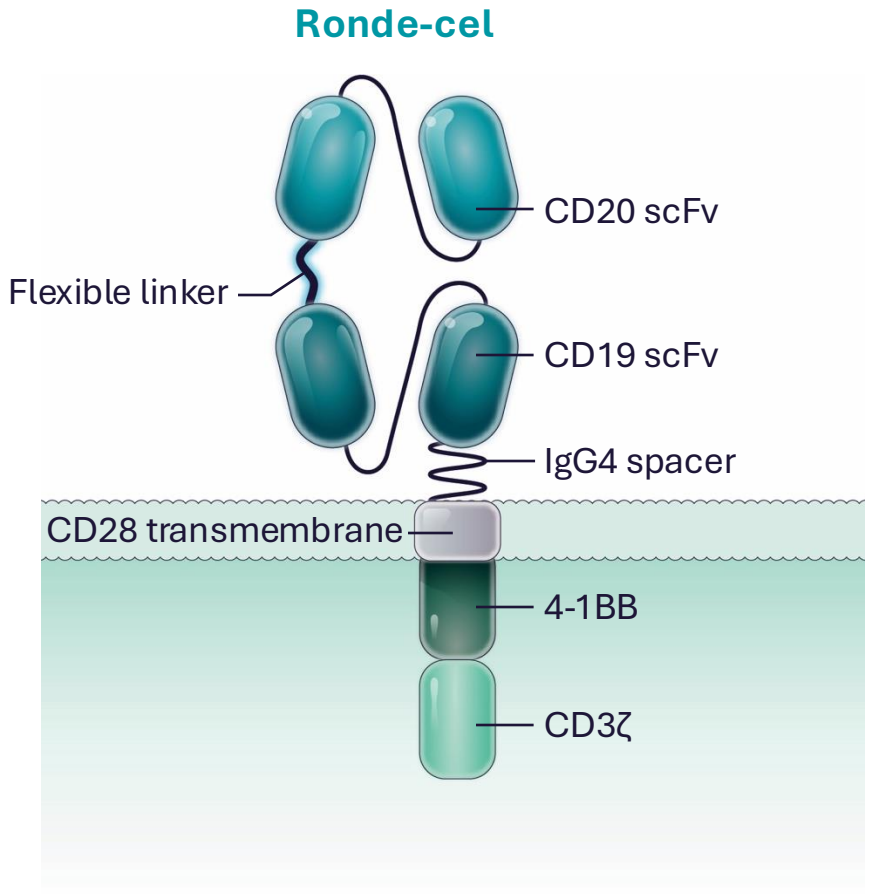
A product with higher complete response rates, longer duration of response, and fewer toxicities is needed

Abramson JS et al. *Lancet* 2020, Kamdar M et al. *Lancet* 2022, Locke FL et al. *Lancet Oncol* 2019, Neelapu SS et al. *N Engl J Med* 2017, Sehgal A et al. *Blood Adv* 2022, Westin JR et al. *N Engl J Med* 2023. Westin JR, et al. *TCT* 2025.
Axi-cel, axicabtagene autoleucel; CRS, cytokine release syndrome; ICANS, immune cell-associated neurotoxicity syndrome; LBCL, large B-cell lymphoma; liso-cel, lisocaptagene maraleucel; mPFS, median progression-free survival.

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

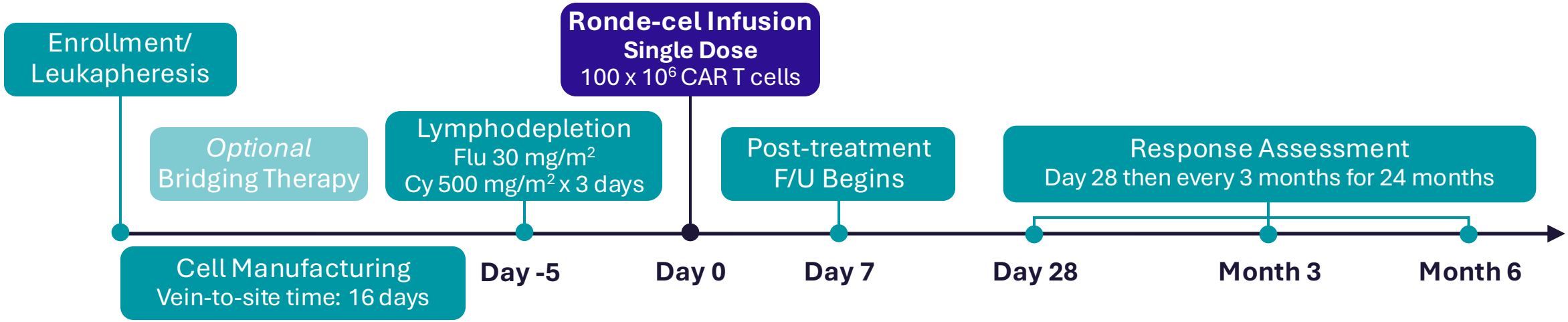
- **Ronde-cel is a true CD19/CD20 "OR" logic-gated CAR**
  - Designed to target either CD19 and CD20 with full potency, overcome heterogeneous antigen density, and mitigate antigen loss following treatment
- **Naïve T cells are associated with improved outcomes after CAR T-cell therapy**
- **CD62L+ enrichment 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, Filosto et. al. *Blood Cancer Discov* 2024, Sommermeyer et. al. *Leukemia* 2016.

Ronde-Cel Trial Schematic

Phase 1/2 multi-cohort, multi-center trial in aggressive large B-cell lymphoma (3L+ and 2L cohorts)



Patient Population

- Patients with relapsed/refractory DLBCL, PMBCL, HGBCL, Grade 3BFL, and tFL who have had ≥1 line of treatment
- CD19/CD20 expression testing not required for enrollment
- No prior treatment with CD19 CAR T-cell therapy
- No upper age limit

Trial Objectives

- Safety and tolerability
- Overall response rate, complete response rate
- Duration of response
- Selection of Phase 2 dose
- Cell expansion pharmacokinetics

The 3L+ cohort has expanded into a pivotal trial (PiNACLE) to enroll ~120 patients

PiNACLE (NCT05826535). Trial included two dose levels (DL1 = 100 x 10^6 CART cells; DL2 = 300 x 10^6 CART cells). 100 x 10^6 CART cells is the recommended Phase 2 dose.
Cy, cyclophosphamide; DL, dose level; Flu, fludarabine.

High-Risk, Heavily Pre-Treated, Multi-Center US Patient Population

Baseline characteristics in 3L+ and 2L patients consistent with high risk compared to historical studies

Demographics and Disease Characteristics	3L+ Overall N = 45	2L Overall N = 24
Median (range) age, years	64 (21, 87)	65 (26, 85)
≥ 75 years, n (%)	9 (20%)	5 (21%)
ECOG 1, n (%)	29 (64%)	14 (58%)
IPI score 3 or 4, n (%)	12 (27%)	8 (33%)
LBCL histology n (%)		
DLBCL	23 (51%)	15 (63%)
tFL	8 (18%)	2 (8%)
HGBCL	8 (18%)	6 (25%)
Primary refractory, n (%)	22 (49%)	22 (92%)
Elevated (above normal) LDH, n (%)	20 (44%)	10 (42%)
Bulky disease (≥ 7 cm), n (%)	10 (22%)	5 (21%)
Double-/triple-hit status, n (%)	7 (16%)	7 (29%)
Received bridging therapy, n (%)	23 (51%)	14 (58%)

Data cutoff: September 5, 2025. 67 of 69 patients received the recommended Phase 2 dose of 100 x 10^6 CART cells. 2 patients (in 3L+) received 300 x 10^6 CART cells.
LBCL includes DLBCL, PMBCL, Grade 3B FL, and tFL. HGBCL defined by disease histology at study entry.
Primary refractory defined as failure to achieve complete response to first-line therapy or complete response with relapse within 3 months.
Bridging therapy consisted of approved lymphoma therapies most commonly including corticosteroids or corticosteroids plus radiation.

Higher-Risk Demographic and Disease Characteristics in 3L+ HGBCL versus LBCL

Patients with HGBCL have bulkier disease, higher LDH, more extranodal disease, are older, and have more limited ECOG status

Demographics and Disease Characteristics	3L+ LBCL N = 37	3L+ HGBCL N = 8	3L+ Overall N = 45
Median (range) age, years	64 (21, 86)	68 (43, 87)	64 (21, 87)
≥ 75 years, n (%)	6 (16%)	3 (38%)	9 (20%)
ECOG 1, n (%)	22 (60%)	7 (88%)	29 (64%)
IPI score 3 or 4, n (%)	9 (24%)	3 (38%)	12 (27%)
LBCL histology n (%)			
DLBCL	23 (62%)	N/A	23 (51%)
tFL	8 (22%)	N/A	8 (18%)
Primary refractory, n (%)	16 (43%)	6 (75%)	22 (49%)
Elevated (above normal) LDH, n (%)	13 (35%)	7 (88%)	20 (44%)
Bulky disease (≥ 7 cm), n (%)	6 (16%)	4 (50%)	10 (22%)
Double-/triple-hit status, n (%)	3 (8%)	4 (50%)	7 (16%)
Received bridging therapy, n (%)	15 (41%)	8 (100%)	23 (51%)

Data cutoff: September 5, 2025.
LBCL includes DLBCL, PMBCL, Grade 3B FL, and tFL. HGBCL defined by disease histology at trial entry.
Primary refractory defined as failure to achieve complete response to first-line therapy or complete response with relapse within 3 months.
Bridging therapy consisted of approved lymphoma therapies most commonly including corticosteroids or corticosteroids plus radiation.

Overall Response Rate of 93% and Complete Response Rate of 76% (3L+ LBCL)

High rate of durable complete responses in LBCL

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

- **Median progression free survival (mPFS) was 18 months**
  - Median duration of follow-up 12 months
- 72% (13/18) of patients with complete response remained in complete response at ≥ 6 months

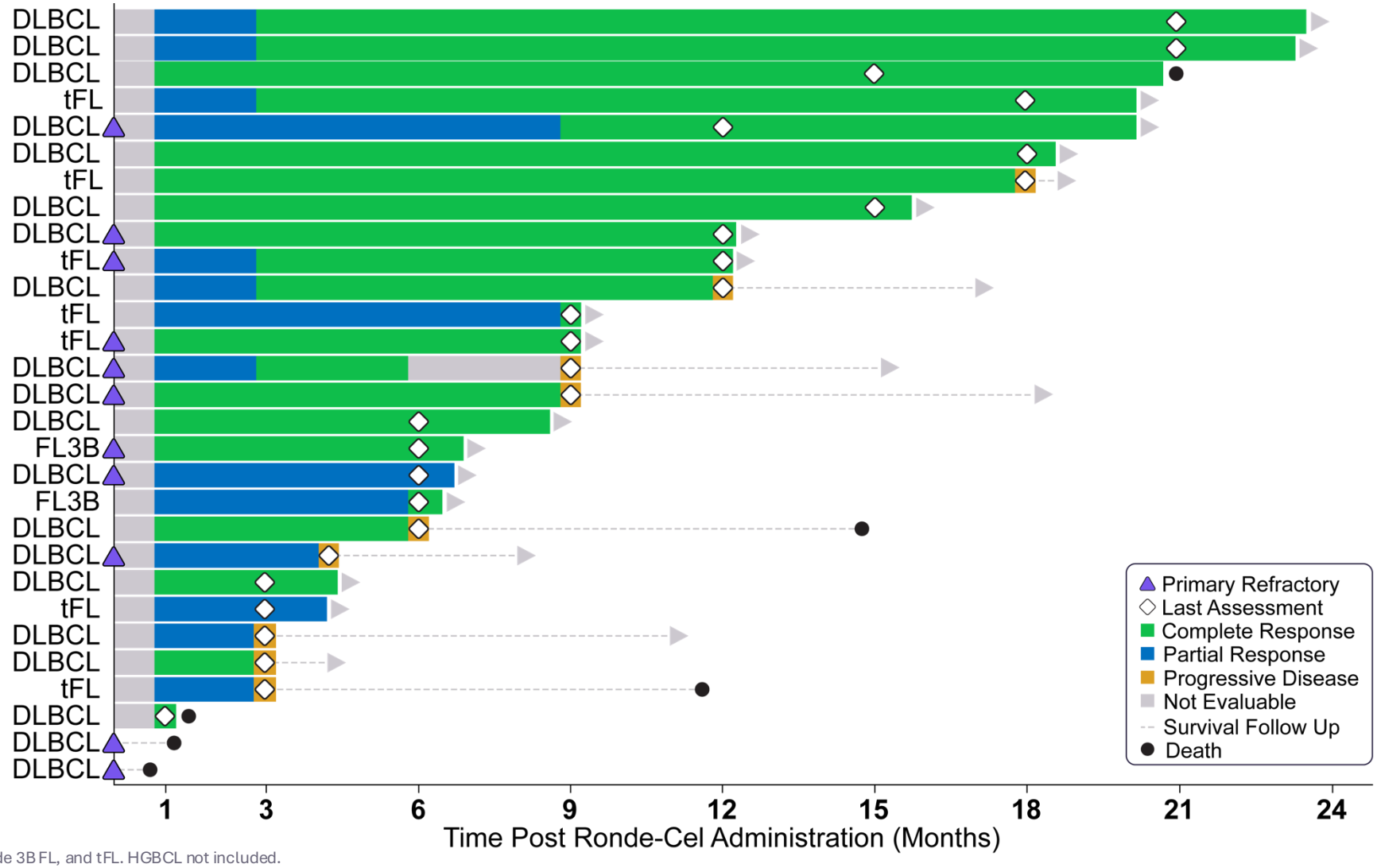
Best Overall Response (3L+ HGBCL)	**N = 8**
Overall Responses, n (%)	**7 (88%)**
Complete Responses, n (%)	**4 (50%)**
Partial Response, n (%)	3 (38%)

- 33% (1/3) of patients with complete response remained in complete response at ≥ 6 months
- PiNACLE will include only LBCL in order to enroll those patients most likely to receive durable benefit from ronde-cel in this single-arm trial

Data cutoff: September 5, 2025; all responses as determined by the Investigator.
LBCL includes DLBCL, PMBCL, Grade 3B FL, and tFL. HGBCL defined by disease histology at trial entry.
Patients were evaluable for efficacy if they had a Day 84 or later response assessment, disease progression, or death from any cause.
8 patients were dosed without Day 84 follow up, disease progression, or death.

Durable Responses in Patients with 3L+ LBCL

Median progression-free survival of 18 months; 72% of patients with CR remained in CR at ≥ 6 months



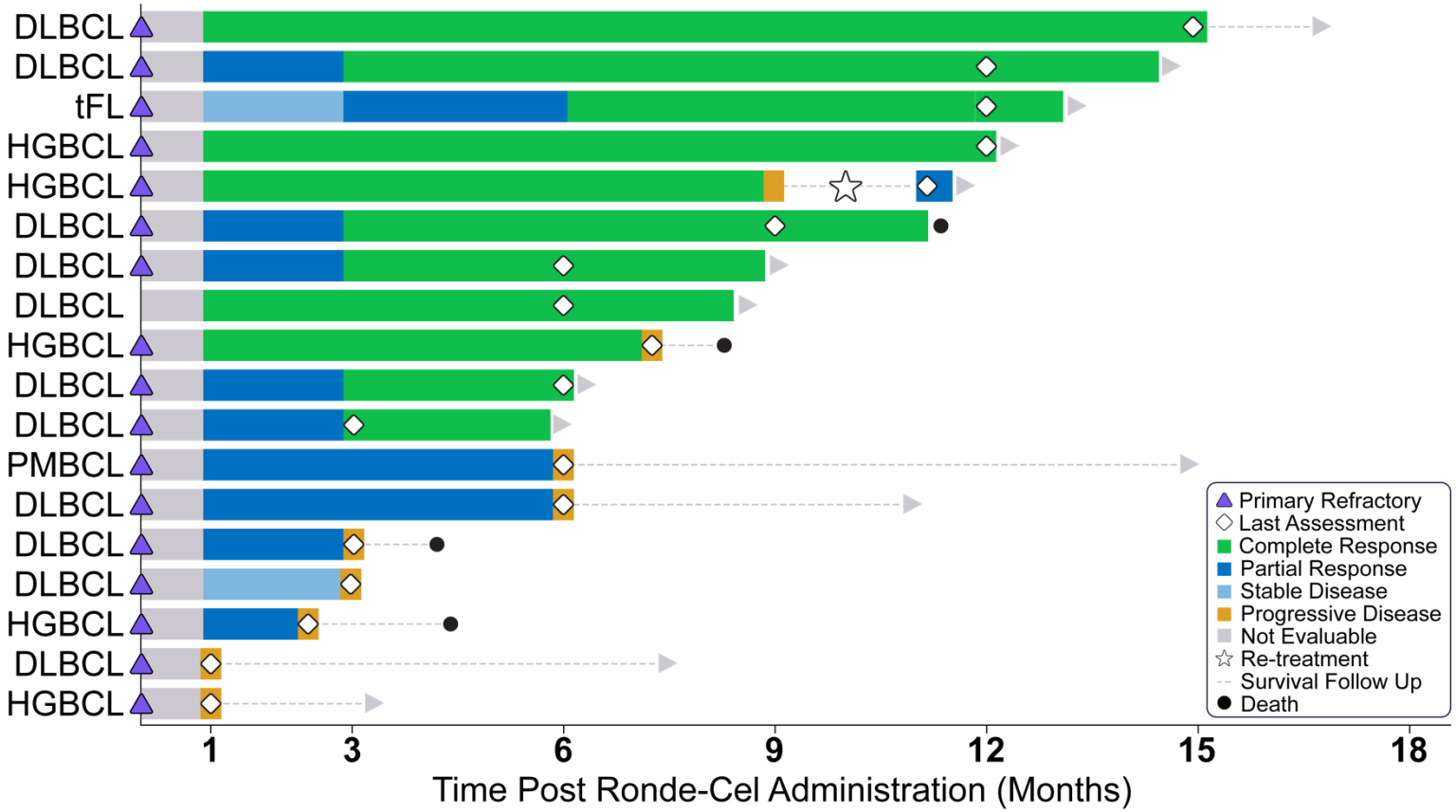
Data cutoff: November 11, 2025.
LBCL includes DLBCL, PMBCL, Grade 3B FL, and tFL. HGBCL not included.
CR, complete response.

High Overall Response Rate in Patients with 2L Aggressive B-Cell Lymphoma

High-risk characteristics including HGBCL with 94% of patients with primary refractory disease

Best Overall Response (2L Overall)	**N = 18**
Overall Responses, n (%)	**15 (83%)**
Complete Responses, n (%)	**11 (61%)**
Partial Response, n (%)	4 (22%)

- 70% (7/10) of patients with complete response remained in complete response at ≥ 6 months
- Median duration of complete response not reached
- Median duration of follow up 9 months



Data cutoff: September 5, 2025 (response rates); November 11, 2025 (swimmer plot). All responses as determined by the Investigator.
Patients were evaluable for efficacy if they had a Day 84 or later response assessment, disease progression, or death from any cause.
6 patients were dosed without Day 84 follow up, disease progression, or death.

Dexamethasone Prophylaxis Reduced Grade ≥ 3 ICANS to < 5% of Patients

Adverse events of interest (3L+ and 2L cohorts)

Adverse Event, n (%)	Prophylaxis N = 25	All N = 69
CRS	13 (52%)	42 (61%)
Grade 1	10 (40%)	22 (32%)
Grade 2	3 (12%)	20 (29%)
Grade ≥ 3	0 (0%)	0 (0%)
Median time to onset, days (range)	6 (3 - 18)	5 (1 - 18)
Median time to resolution, days (range)	2 (1 - 21)	3 (1 - 21)
ICANS	3 (12%)	16 (23%)
Grade 1	2 (8%)	6 (9%)
Grade 2	0 (0%)	2 (3%)
Grade ≥ 3	1 (4%)	8 (12%)
Median time to onset, days (range)	7 (4 - 14)	7 (2 - 14)
Median time to resolution, days (range)	4 (1 - 9)	4 (1 - 10)

Adverse Event, n (%)	Prophylaxis N = 25	All N = 69
IEC-HS		
Grade 1 or 2	1 (4%)	2 (3%)
Grade ≥ 3	0 (0%)	0 (0%)
Infections		
Grade 1 or 2	7 (28%)	19 (28%)
Grade ≥ 3	1 (4%)	8 (12%)
Prolonged cytopenias		
Grade ≥ 3	3 (12%)	15 (22%)

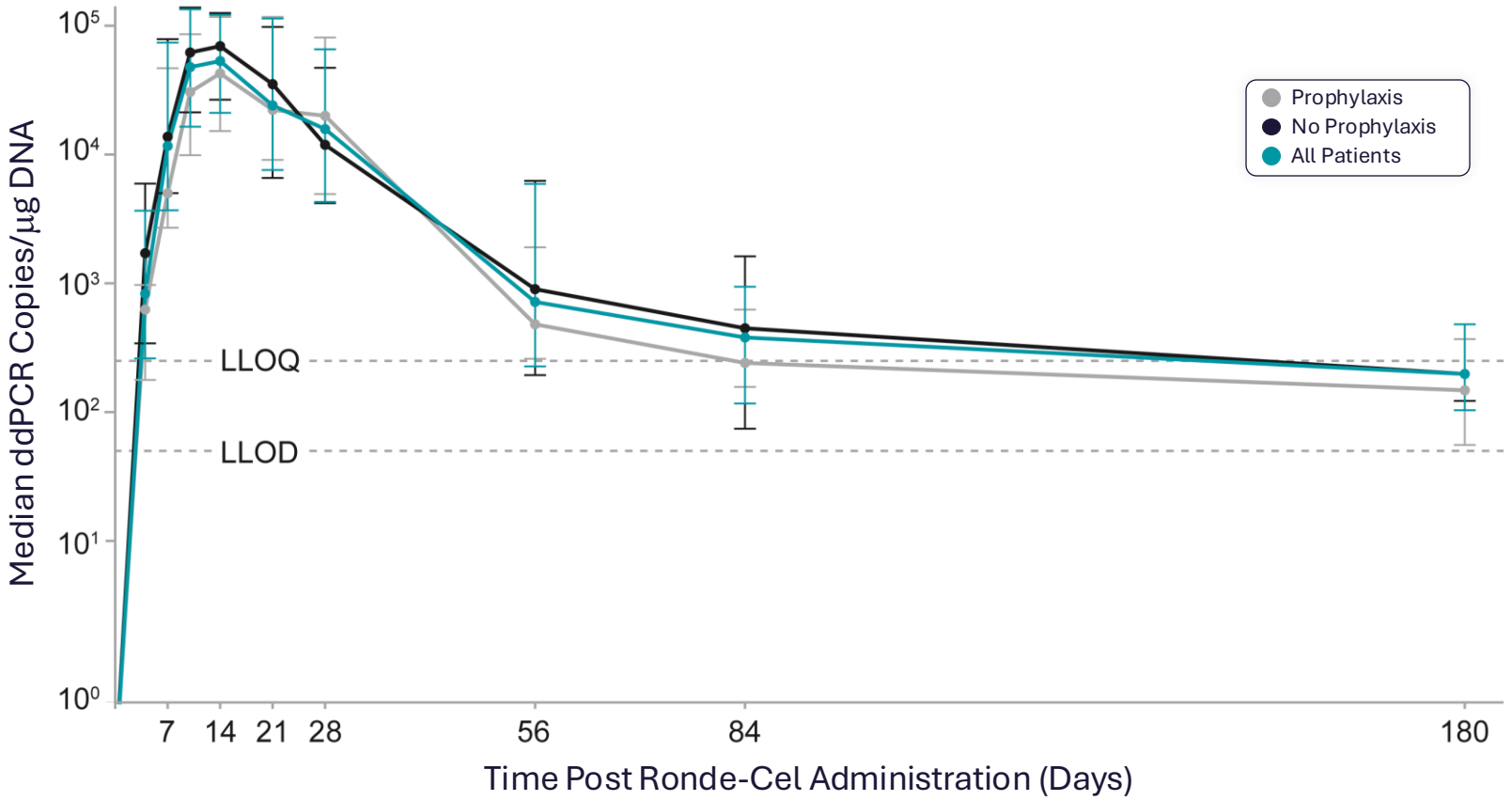
- Patients received 10 mg (IV/PO) of dexamethasone on Days 0, 1, and 2 after ronde-cel infusion
- Tocilizumab use in 37% of patients
- One case of Grade ≥3 ICANS was observed with dexamethasone prophylaxis in a patient with HGBCL, high tumor burden, and high LDH
- No deaths related to ronde-cel

Data cutoff: September 5, 2025.
Infections include all treatment emergent adverse events reported in the Infections and Infestations system organ class regardless of relationship to trial treatment.
Prolonged cytopenias defined as Grade 3 or 4 values of hemoglobin, platelets, or neutrophils beyond Day 28 post ronde-cel administration.
CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity; IV, intravenous; LBCL, large B-cell lymphoma; PO, orally.

Ronde-Cel Expansion is Robust in Patients with or without Dexamethasone Prophylaxis

Higher CAR T-cell expansion is associated with better CAR T-cell response

CAR T-Cell Expansion with or without Prophylactic Dexamethasone



- No significant differences were observed in peak CAR T-cell expansion (C_{max}) or overall exposure (AUC) between patients who received dexamethasone (N = 25) and those who did not (N = 42).

Data cutoff: September 5, 2025.
Assay used for measuring B cells/µl (Epiontis ID®) can detect as low as 2 cells/µl with high accuracy. IQR, interquartile range.
Neelapu et al. *N Engl J Med* 2017.

Conclusions

Phase 1/2 multi-cohort, multi-center trial evaluating ronde-cel in aggressive B-cell lymphoma (3L+, 2L)

- **High rate of durable complete responses** in high-risk patients in 3L+ LBCL:
  - Overall response rate of 93% and a complete response rate of 76%
  - Median progression-free survival of 18 months
- **High rate of durable complete responses in primary refractory patients** in the 2L setting:
  - Overall response rate of 83% and a complete response rate of 61%
  - 70% of patients with complete response remained in complete response at ≥ 6 months
- **Manageable safety profile appropriate for outpatient administration:**
  - No Grade ≥ 3 CRS
  - Single case of Grade ≥ 3 ICANS with dexamethasone prophylaxis (≤ 5%)
- **Robust CAR T-cell expansion** with final drug product enriched for stem-like cells (CD62L+):
  - Additional translational data on CD62L enrichment presented in separate oral presentation demonstrating sustained cytotoxicity of CAR T cells obtained from patients 2 months after infusion

Data cutoff: September 5, 2025, except for swimmer plots (November 11, 2025).

Ronde-Cel is a Promising CAR T-Cell Candidate for Large B-Cell Lymphoma

Two pivotal trials are underway for ronde-cel (PiNACLE – H2H, PiNACLE)

- **PiNACLE – H2H** has been initiated based upon these promising results:
  - Phase 3 head-to-head CAR T-cell therapy randomized controlled trial of ronde-cel vs Investigator's choice of axicabtagene autoleucel (axi-cel) or lisocabtagene maraleucel (liso-cel)
  - N = 200 patients per arm
  - No upper age-limit; early or late-relapsing/refractory patients; includes HGBCL
  - Primary endpoint: event-free survival
  - Key secondary endpoints: progression-free survival and overall survival

- **PiNACLE** enrollment continuing
  - Seamless expansion of the 3L+ cohort from the Phase 1/2 trial
  - N = 120 patients
  - No upper age-limit; early relapse or refractory patients; will not include HGBCL
  - Primary endpoint: overall response rate (and duration of response)