Vispa-cel, an allogeneic anti-CD19 CAR-T cell therapy with a PD-1 knockout, in patients with relapsed/refractory B cell non-Hodgkin lymphoma

Long-term follow-up results from the ANTLER phase 1 trial

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Disclosures

Bristol Myers Squibb, Arovella Therapeutics, Kite/Gilead, Novotech CRO, and Prescient Therapeutics

Most 2L LBCL patients do not receive treatment with curative intent

75%

of 2L LBCL patients do **not** receive autologous CAR-T cell therapies[1]

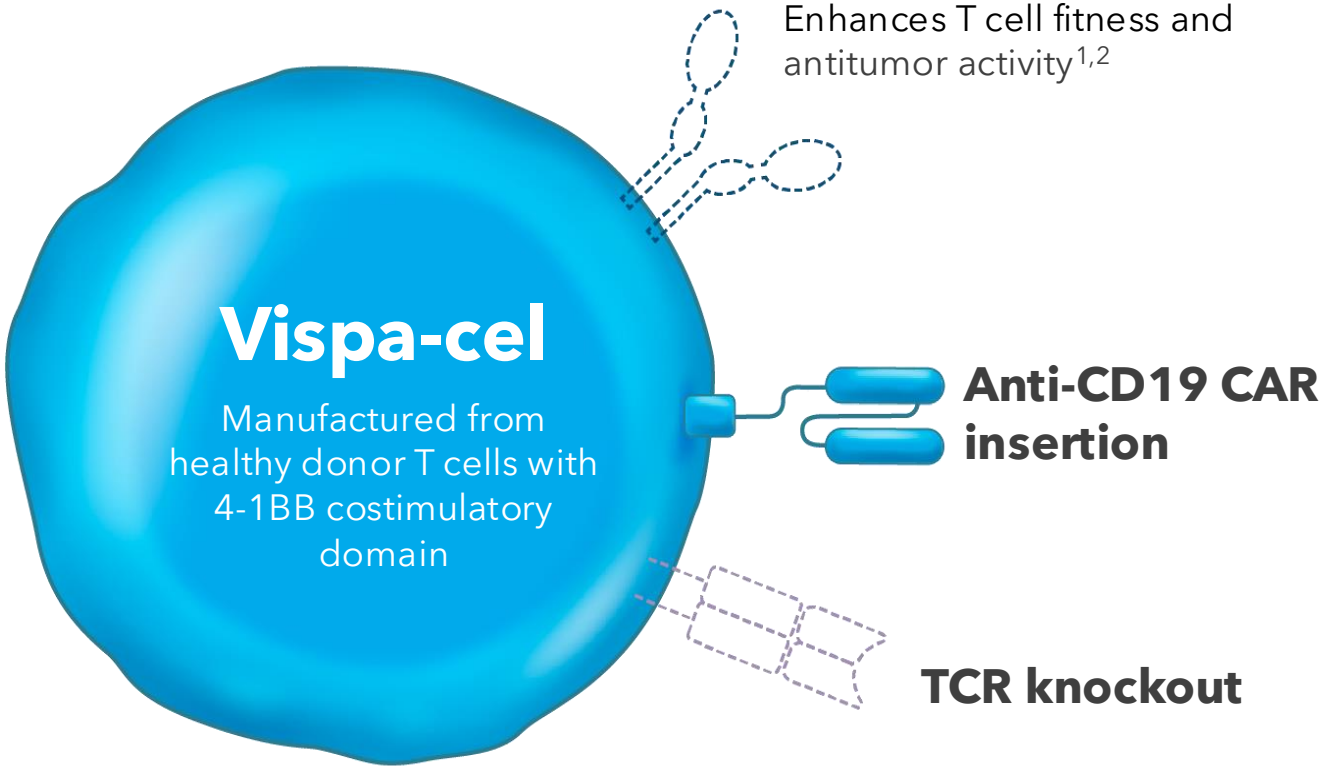
No time to wait due to rapid disease progression or CAR-T manufacturing failure

Geographic, financial, socioeconomic, or insurance issues impact CAR-T accessibility

Alternative therapies require **continuous treatment without curative potential**

[1]Perales, M-A, et al. Poster 549, 2025 TANDEM Meetings

Vispa-cel: a differentiated allogeneic CAR-T cell therapy for 2L LBCL



Optimized vispa-cel includes:

- **Young donor age (<30 years old)**
- **HLA matched to ≥2 alleles**

Single infusion of optimized vispa-cel demonstrates **efficacy, safety, and durability on par with auto CAR-Ts[2]**

Potential to address **unmet need in rapidly progressing, difficult-to-treat, 2L LBCL patients**

[1] Lau E et al. Cytotherapy. 2023;25(7):750–762
[2] Hamadani M et al. TANDEM 2026 presentation

85 patients dosed with vispa-cel in ANTLER trial

Eligibility

- **Dose escalation**: third- or later-line or primary refractory aggressive r/r B-NHL[1]
- **Dose expansion**: second-line LBCL[2] (primary refractory disease or relapse ≤12 months after first-line therapy)

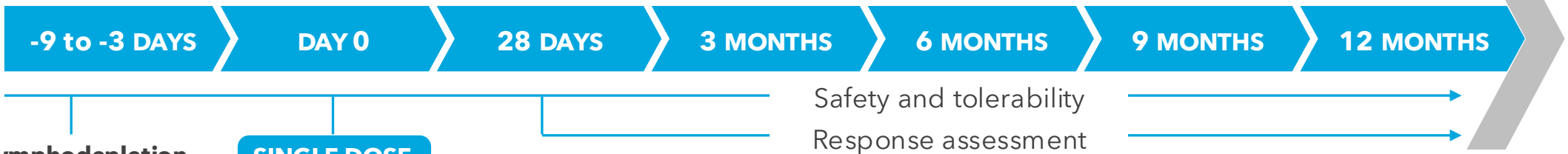
Exclusion

- Prior CD19-targeted therapy for CD19-naïve cohorts

Vispa-cel dose levels evaluated

- 40, 80, and 120x10^6 CAR-T cells
- 80x10^6 CAR-T cells determined as RP2D

ANTLER trial design for all cohorts



Lymphodepletion
Cyclophosphamide (60 mg/kg/d for 2 days) followed by fludarabine (25 mg/m^2/d for 5 days)[3]

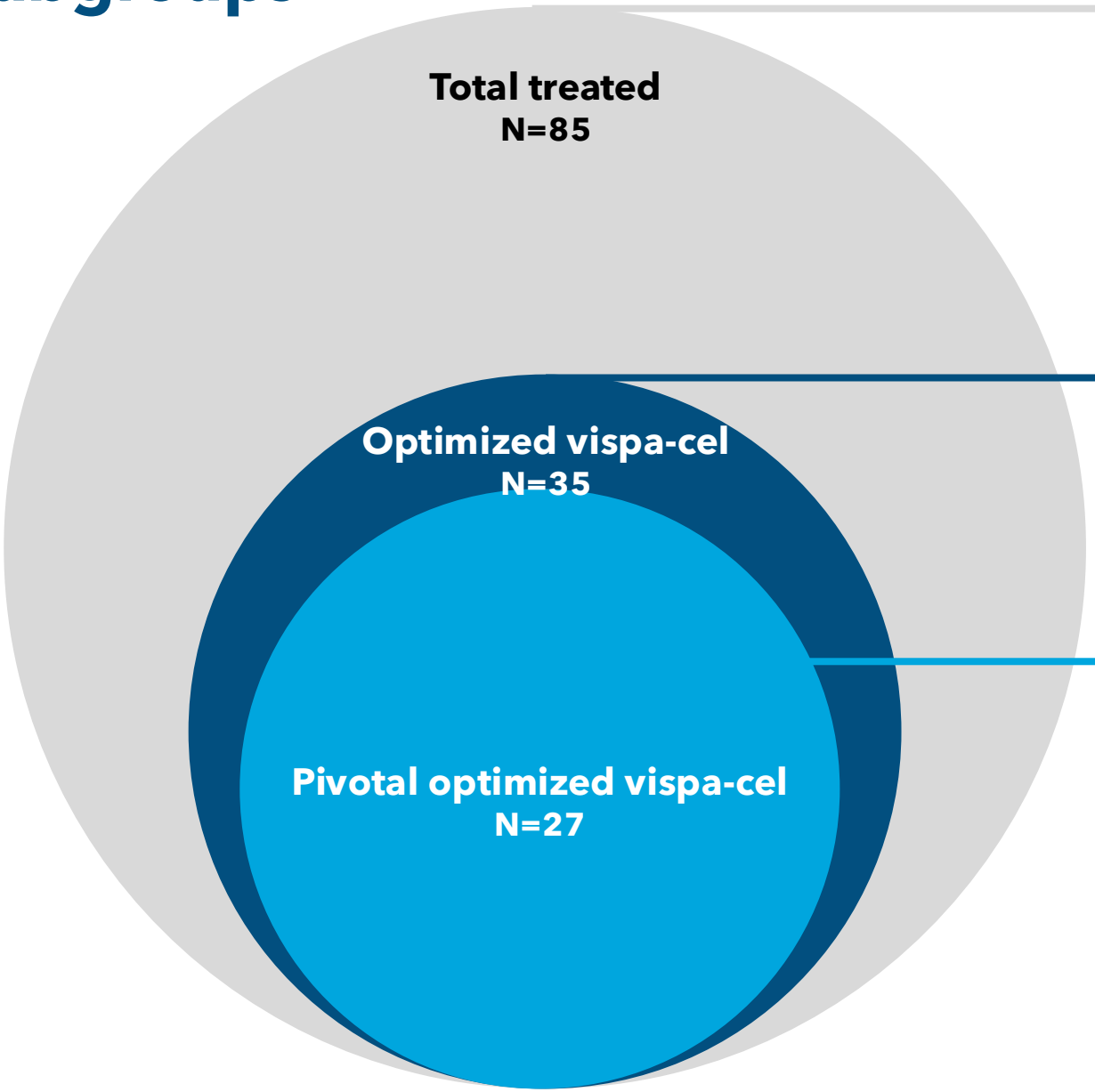
SINGLE DOSE of vispa-cel

Part of trial	Patient population	N	CD19-naïve
Dose escalation	r/r B-NHL	16	Yes
Dose expansion	2L LBCL	63	Yes
CD19 relapsed	LBCL	6	No

Rapidly progressing disease, patients unwilling to go through apheresis or bridging therapy, insurance rejection, or preference for an off-the-shelf therapy are key reasons why investigators enrolled patients in ANTLER trial[4]

NCT04637763
[1]B-NHL subtypes include: DLBCL (diffuse large B cell lymphoma), HGBL (high-grade B cell lymphoma), tFL (transformed DLBCL from follicular lymphoma), PMBCL (primary mediastinal large B cell lymphoma), FL (follicular lymphoma, with POD24 (high risk)), MCL (mantle cell lymphoma), MZL (marginal zone lymphoma)
[2]LBCL subtypes include: DLBCL NOS (not otherwise specified), HGBL, transformed DLBCL from FL or MZL, and PMBCL
[3]Clin Cancer Res. 2011 July 1; 17(13): 4550–4557. doi:10.1158/1078-0432.CCR-11-0116
[4]Based on survey answers from ANTLER investigators asking why patients were dosed with vispa-cel versus autologous CAR-T cell therapy; 86% of ANTLER sites offer one or more of the approved auto CAR-Ts in 2L LBCL

ANTLER subgroups



R/R B-NHL
40M, 80M, 120M CAR-T cells

2L and 3L+ LBCL
40M, 80M, 120M CAR-T cells
Young donor (<30 yo)
2+ HLA matching

2L LBCL
80M CAR-T cells
Young donor (<30 yo)
2+ HLA matching

This subgroup best represents the treatment regimen and patient population for the planned pivotal trial

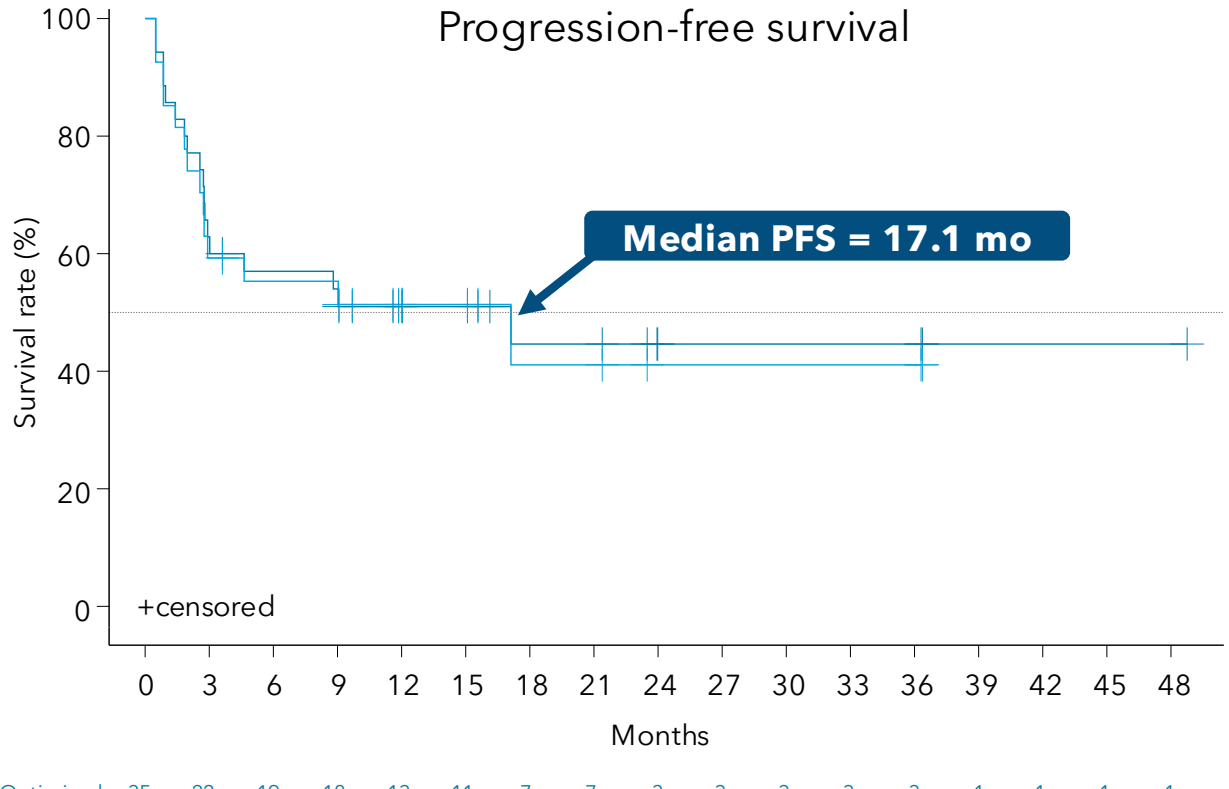
2L: second-line; 3L: third-line; B-NHL: b cell non-Hodgkin lymphoma; LBCL: large B cell lymphoma; HLA: human leukocyte antigen; M: million

Patient and disease characteristics in ANTLER (N=85)

Baseline characteristics	All treated patients N=85	Optimized vispa-cel[1] (All patients) N=35	Pivotal optimized vispa-cel[2] (2L LBCL, RP2D) N=27
Age, years, median (range)	66 (20-86)	63 (20-86)	66 (20-86)
Age ≥ 65 years, n (%)	45 (53)	17 (49)	14 (52)
Male, n (%)	65 (77)	25 (71)	20 (74)
ECOG, n (%)[3]			
1	45 (53)	16 (46)	13 (48)
NHL subtype, n (%)			
DLBCL, NOS	48 (57)	21 (60)	16 (59)
HGBL	14 (17)	5 (14)	5 (19)
tFL/tMZL	15 (18)	8 (23)	6 (22)
PMBCL	2 (2)	1 (3)	-
MCL/FL/MZL	6 (7)	-	-
Disease status, n (%)			
Refractory to 1L therapy[4]	67/79[5] (85)	30 (86)	25 (93)
No CR to 1L therapy	51/79[5] (65)	24 (69)	19 (70)
Prior lines of therapy, n (%)			
1	67 (79)	32 (91)	27 (100)
≥2	18 (21)	3 (9)	-
Age-adjusted IPI (%)			
2	32 (38)	10 (29)	7 (26)
≥3	20 (24)	7 (20)	7 (26)
Baseline LDH status (%)			
>ULN	48 (57)	19 (54)	16 (59)
Bulky disease[6]	18 (21)	5 (14)	4 (15)

[1]2L (N=32) and 3L+ (N=3) LBCL patients treated with 40M, 80M, or 120M vispa-cel CAR-T cells optimized for multiple factors, including 2+ HLA matched and young donor
[2]2L LBCL patients treated with 80M vispa-cel CAR-T cells optimized for multiple factors, including 2+ HLA matched and young donor
[3]ECOG of 0 or 1 eligible for ANTLER trial
[4]Includes patients with no CR to 1L therapy or CR with duration from end of therapy to PD of ≤6 months
[5]LBCL subgroup only
[6]Bulky disease defined by maximum baseline lesion diameter ≥7.5 cm
Data cutoff 06March2026

Optimized vispa-cel delivered durable, long-term efficacy in ANTLER

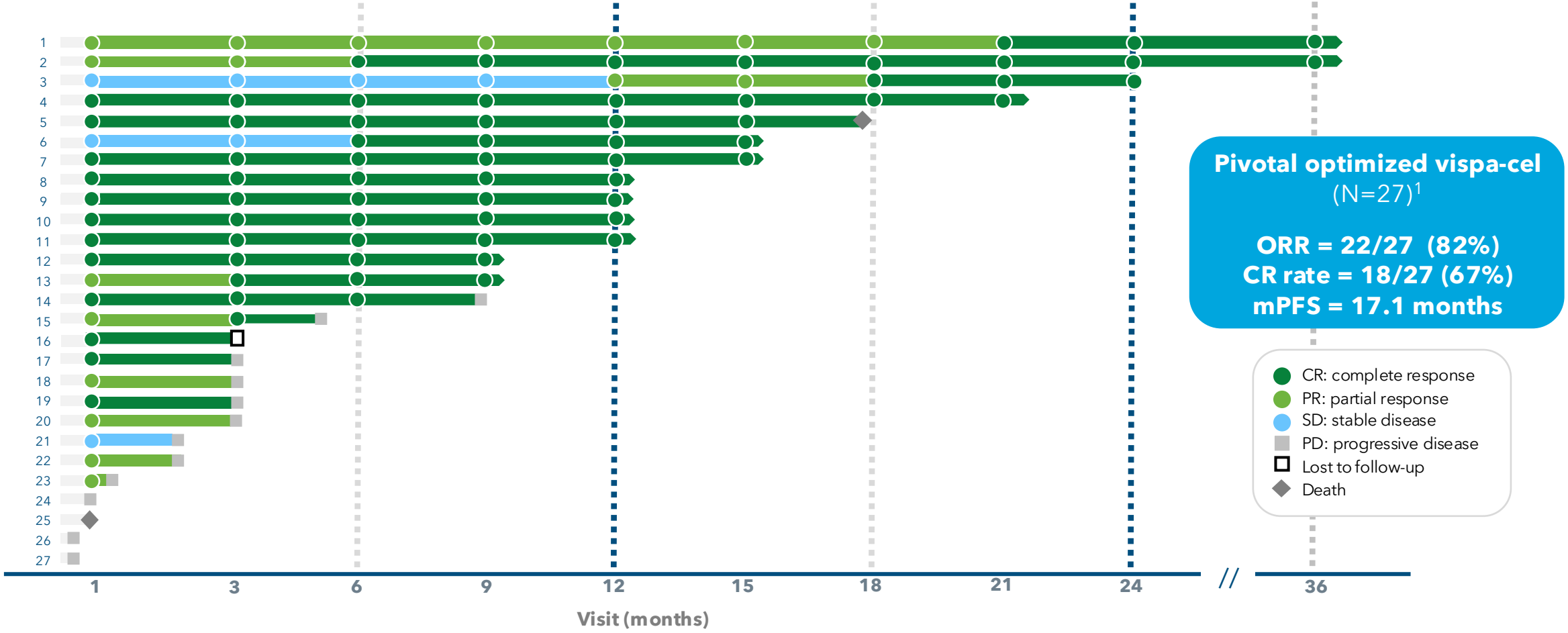


	Optimized vispa-cel[1] (All patients) N=35	Pivotal optimized vispa-cel[2] (2L LBCL, RP2D) N=27
ORR	**83%**	**82%**
CR rate	**66%**	**67%**
Median PFS[3] (95% CI)	**17.1 mo** (2.8, NE)	**17.1 mo** (2.6, NE)
12-mo PFS (95% CI)	**51%** (34, 66)	**51%** (31, 68)
Median DoR[4] (95% CI)	**NR** (3.7, NE)	**16.2 mo** (2.0, NE)

[1]2L (N=32) and 3L+ (N=3) LBCL 2+ HLA matched, dosed with vispa-cel from young donors (40M, 80M, or 120M doses)
[2]2L (N=27) LBCL patients treated with 80M vispa-cel CAR-T cells optimized for multiple factors, including 2+ HLA matched and young donor
[3]Median follow-up for PFS is 16.1 mo for optimized vispa-cel (all patients), and 15.1 mo for pivotal optimized vispa-cel
[4]Median follow-up for DoR is 14.2 mo for optimized vispa-cel (all patients), and 11.2 mo for pivotal optimized vispa-cel

CR: complete response; DoR: duration of response; HLA: human leukocyte antigen; NE: not estimable; NR: not reached; mo: month; ORR: overall response rate; PFS: progression-free survival
Data cutoff 06March2026

Single 80M dose of pivotal optimized vispa-cel in 2L LBCL patients drives long-term, potentially curative responses



[1]2L LBCL patients treated with 80M vispa-cel CAR-T cells optimized for multiple factors, including 2+ HLA matched and young donor
Long-term follow-up data reflect the last known response; marked timepoints indicate confirmation of no disease progression
Two grade 5 AEs occurred: IEC-HS (day 25 post-infusion; related to vispa-cel) and PML (day 520 post-infusion; possibly related to vispa-cel.
Certain patients converted from CR or PR to PD at various assessments time points as indicated in the chart above
CR: complete response; HLA: human leukocyte antigen; IEC-HS: immune effector cell-associated hemophagocytic lymphohistiocytosis-like syndrome; mo: months; mPFS: median progression-free survival; ORR: overall response rate; PML: progressive multifocal leukoencephalopathy; RP2D: recommended phase 2 dose
Data cutoff 06March2026

Vispa-cel has a generally well-tolerated safety profile

Enables outpatient administration and further expansion to community sites

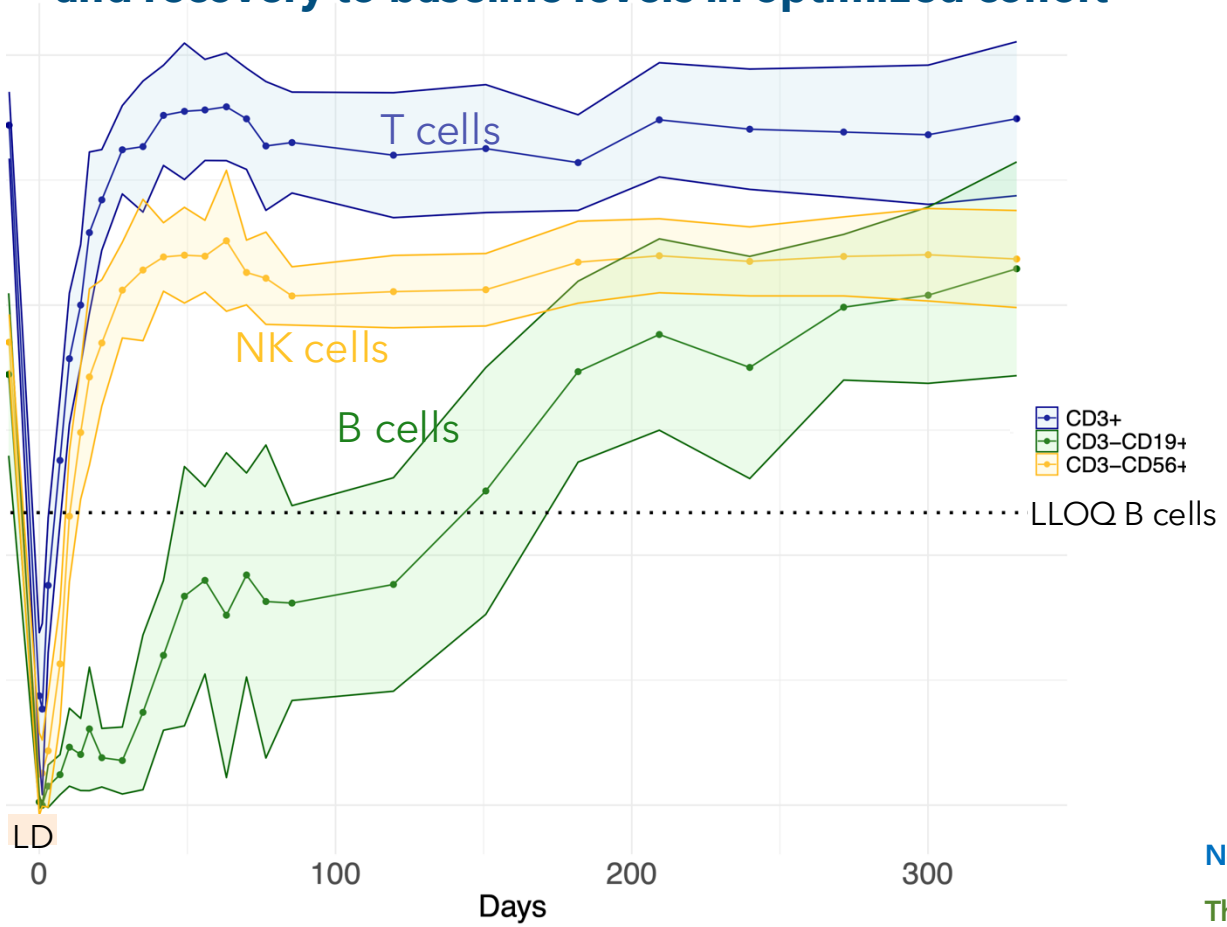
	Vispa-cel					
	All treated patients N=85		**Optimized vispa-cel** (All patients) N=35[1]		**Pivotal optimized vispa-cel** (2L LBCL, RP2D) N=27[2]	
	All grade	**≥Gr 3**	**All grade**	**≥Gr 3**	**All grade**	**≥Gr 3**
ICANS, n (%)	12 (14)	3 (4)	1 (3)	--	1 (4)	--
CRS, n (%)	46 (54)	1 (1)	19 (54)	1 (3)	17 (63)	1 (4)
Infections, n (%)	45 (53)	22 (26)	21 (60)	7 (20)	14 (52)	6 (22)
Prolonged cytopenias[3]	NA	22/82 (27)	NA	6/32 (19)	NA	5/24 (21)
IEC-HS, n (%)	2 (2)	2 (2)	1 (3)	1 (3)	1 (4)	1 (4)
GvHD, n (%)	--	--	--	--	--	--

- Six grade 5 AEs: 2 related, 1 possibly related, 3 unrelated (bladder perforation secondary to BK virus [related]; IEC-HS [related]; PML [possibly related]; acute respiratory failure [unrelated]; acute respiratory distress syndrome [unrelated]; HHV6 encephalitis [unrelated])

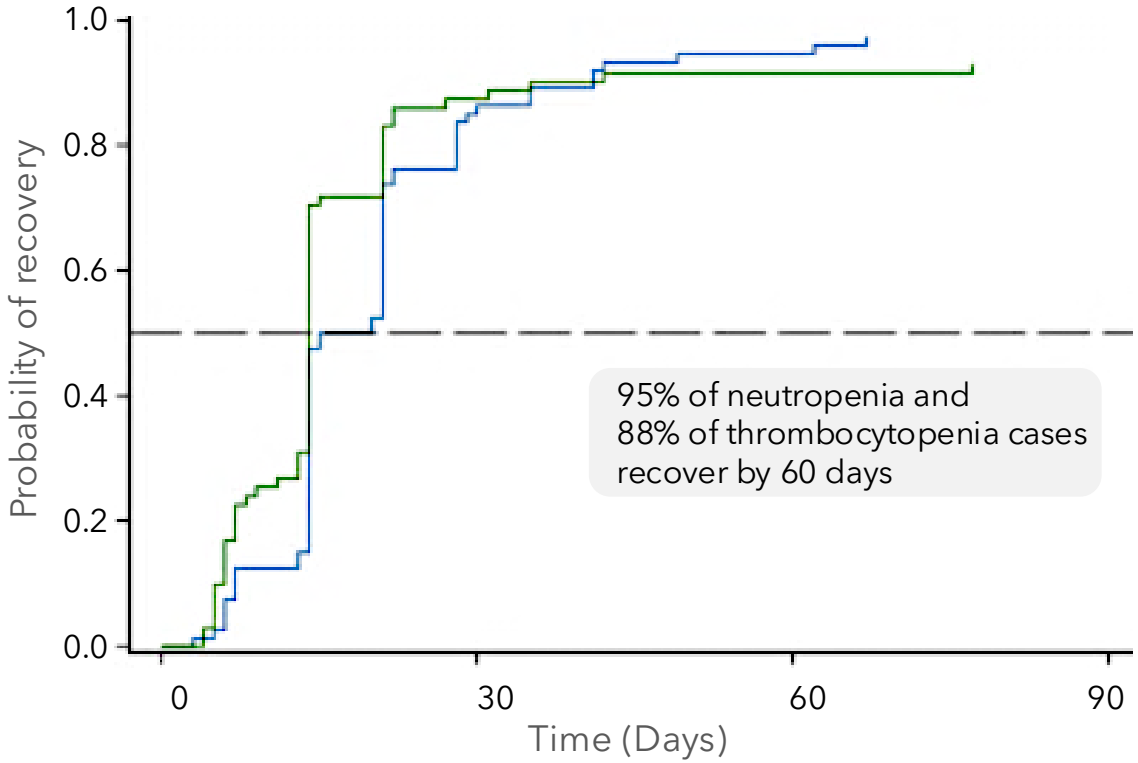
[1]2L (N=32) and 3L+ (N=3) LBCL patients treated with 40M, 80M, or 120M vispa-cel CAR-T cells optimized for multiple factors, including 2+ HLA matched and young donor
[2]2L LBCL patients treated with 80M vispa-cel CAR-T cells optimized for multiple factors, including 2+HLA matched and young donor
[3]For vispa-cel, prolonged cytopenias are defined as Grade 3 or 4 neutropenia, thrombocytopenia, or anemia ongoing at day 30 (+/ 5 days) post CAR-T infusion, based on laboratory data, distinct from investigator-reported clinical adverse events. Analysis includes patients with assessments at day 30 (+/-5 days).
CRS: cytokine release syndrome; GvHD: graft-versus-host disease; ICANS: immune effector cell-associated neurotoxicity syndrome; IEC-HS: immune effector cell-associated hemophagocytic lymphohistiocytosis-like syndrome; PML: progressive multifocal leukoencephalopathy; NA: not applicable
Data cutoff 06March2026

Rapid hematologic and immunologic recovery after vispa-cel contributes to generally well-tolerated safety profile

B cell, T cell, and NK cell depletion and recovery to baseline levels in optimized cohort



Absolute neutrophil and platelet count recovery to Grade ≤2



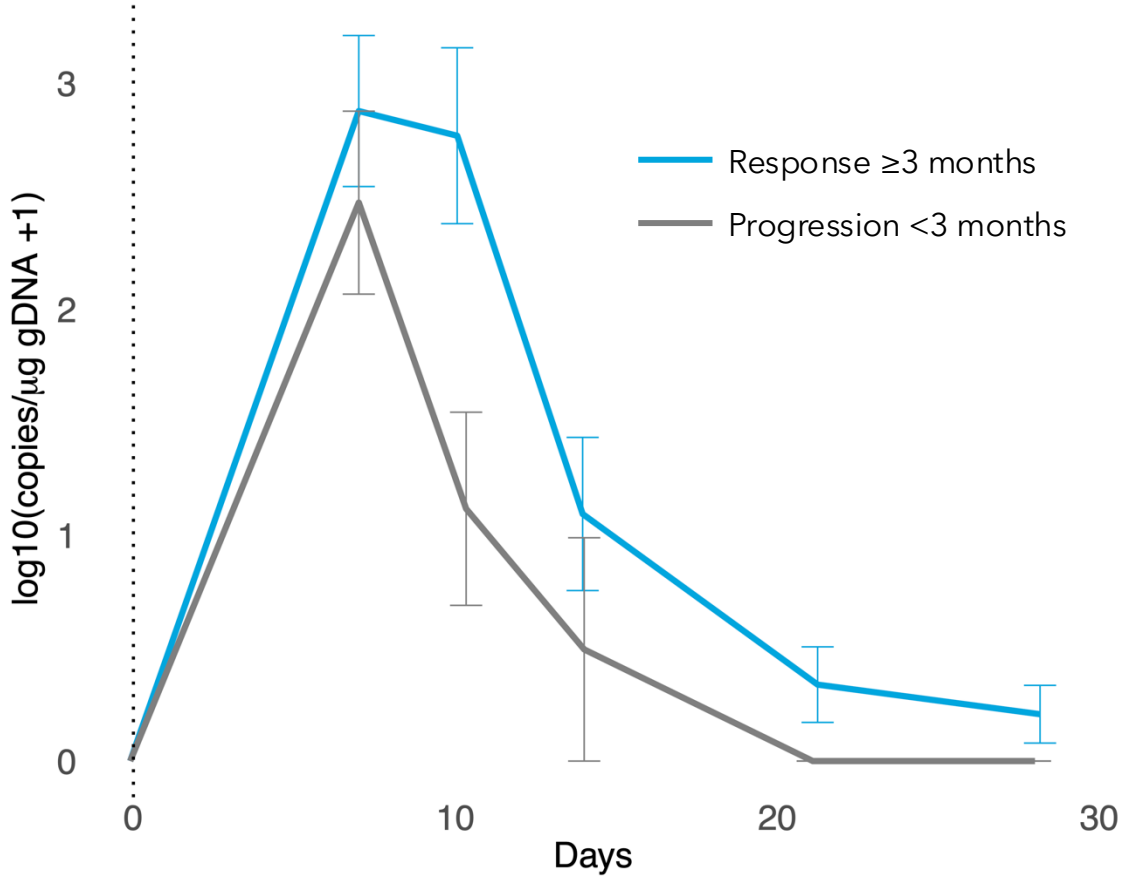
Neutropenia	80	10	3	1
Thrombocytopenia	71	8	4	1

Optimized cohort N=35; average of log transformed values shown with ribbons reflecting standard error;
Baseline B cells absolute levels calculated with data points ≥ LLOQ;LD: lymphodepletion; LLOQ: lower limit of quantification
Data cutoff 06March2026

CAR-T cell expansion and functional persistence correlate with duration of response and HLA match level

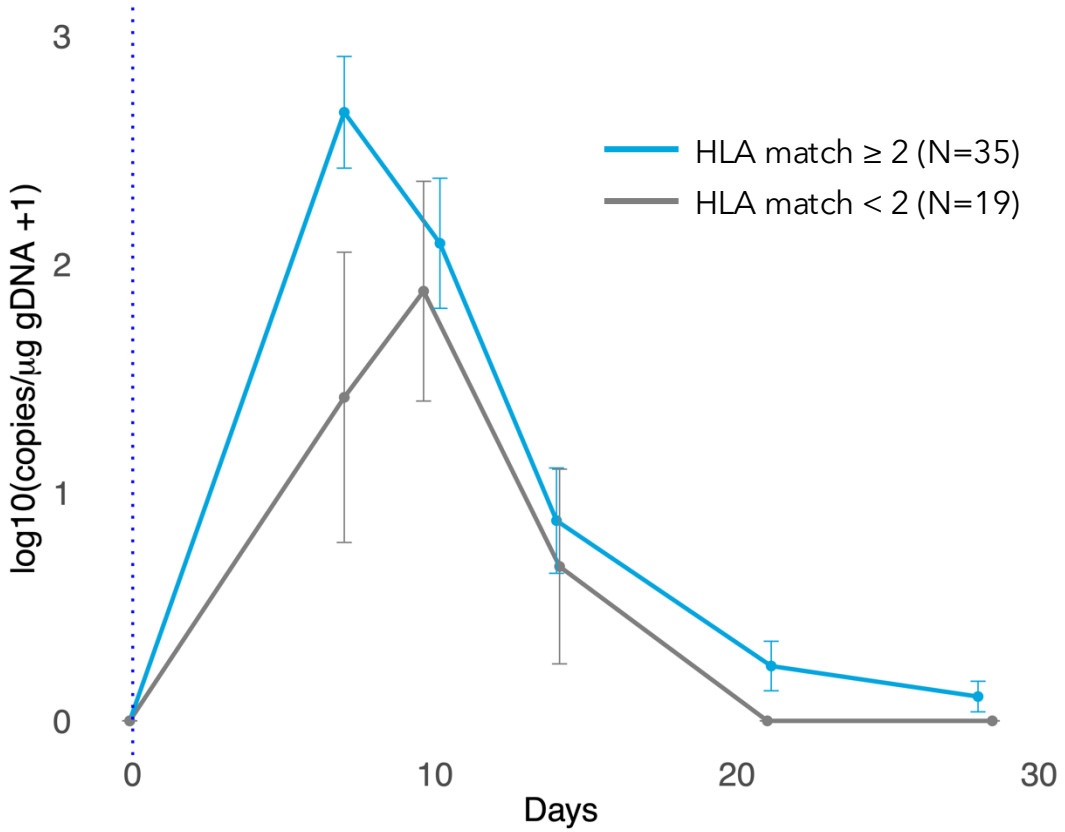
All patients who received optimized vispa-cel

N=35[1]



HLA match level (<2 vs ≥2) impact on PK for vispa-cel manufactured from young donor T cells

N=54



Average of log transformed values shown; error bars represent standard error

[1]Progression <3 mo N=14; response ongoing ≥3 months N=21

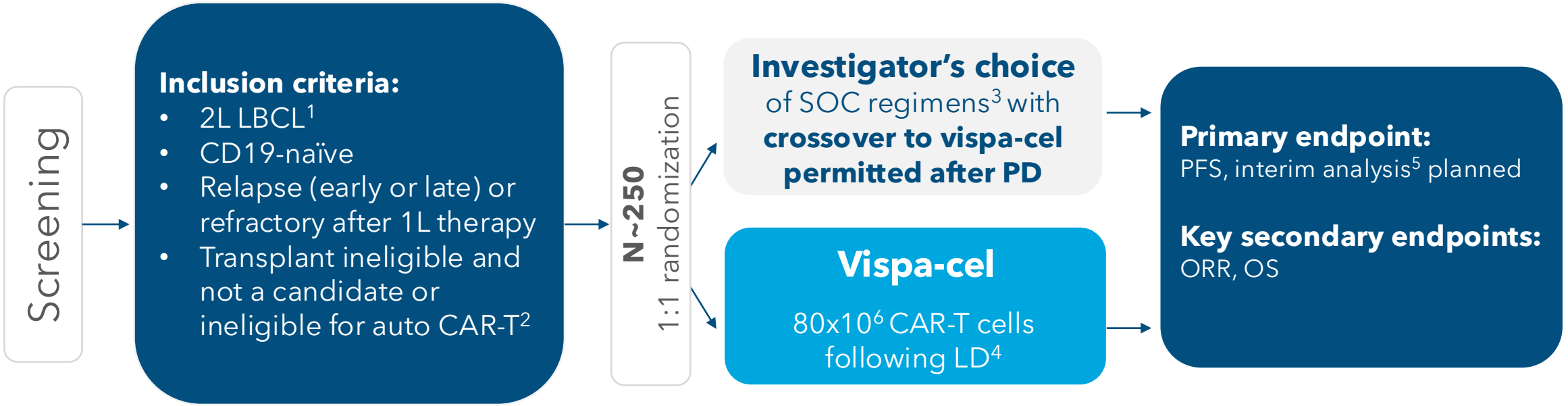
Response categories determined at Month 3/Week 12 visit; visits with <50% subject data available are excluded

Data cutoff 06March2026

Next steps for vispa-cel in 2L LBCL

- Vispa-cel is a potential paradigm shift towards an off-the-shelf, scalable, CAR-T approach in 2L LBCL patients that achieves durable remissions
- Vispa-cel can overcome the logistical barriers of auto CAR-T and the need for continuous infusions of bispecific antibodies
- **A phase 3 pivotal trial (ANTLER-3) is planned in 2L LBCL patients who are transplant ineligible and not a candidate or ineligible for auto CAR-T**

ANTLER-3: phase 3 randomized pivotal trial design



[1]LBCL subtypes include DLBCL NOS, HGBL (with MYC and BCL2 and/or BCL6), HGBL NOS, transformed DLBCL from FL or MZL, FL3B, PMBCL
[2]Enrollment to include patients who are ineligible for transplant and not a candidate or ineligible for auto CAR-T cell therapy based on access challenges or medical criteria, including the need for urgent therapy
[3]Patients in the comparator arm to be treated with an investigator's choice of SOC regimens: R+gemcitabine+oxaliplatin (R-GemOx); Pola-R-GemOx (Pola-RGO); or tafasitamab+lenalidomide
[4]Single infusion of vispa-cel following a lymphodepletion regimen of cyclophosphamide 60 mg/kg/d x 2d and fludarabine 25 mg/m^2/d x 5d
[5]Will only be performed after study is fully enrolled

ANTLER phase 1 trial conclusions

- **Vispa-cel is a differentiated allogeneic CAR-T cell therapy**
  - ✓ PD-1 knockout potentially contributes to enhanced antitumor activity
  - ✓ Donor age and partial HLA matching improve clinical outcomes
- Long-term durable remissions demonstrated after a single infusion of optimized vispa-cel in 2L LBCL patients, most with rapidly progressing disease
  - ✓ 82% ORR, 67% CR rate, and **17.1 mo median PFS**
- Generally well-tolerated safety profile enables outpatient administration and use in the community setting
- **Rapid hematologic and immunologic recovery**, unique to vispa-cel, contributes to the generally well-tolerated safety profile

Gratitude for our patients, caregivers, investigators, and site staff

ANTLER trial sites in US

Israel - ANTLER

Hadassah University Hospital
Rabin Medical Center
Tel Aviv Sourasky Medical Center
The Sheba Fund for Health Services and Research

Australia - ANTLER

Epworth HealthCare
Royal Perth
Westmead Hospital