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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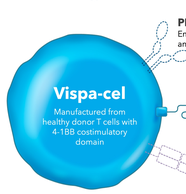
BACKGROUND

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**

Vispacabtagene regedleucel (vispa-cel): an allogeneic anti-CD19 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**[3]

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

METHODS

85 patients dosed with vispa-cel in ANTLER trial

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

Exclusion
- Prior CD19-targeted therapy for CD19-naïve cohorts

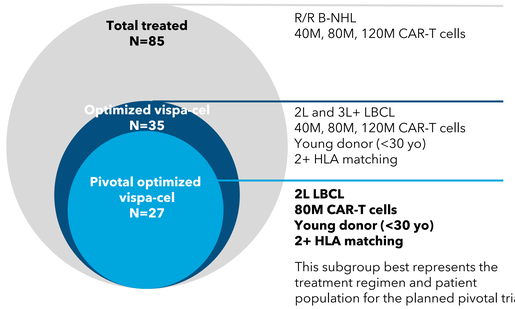
Vispa-cel dose levels evaluated
- 40, 80, and 120x10^6 CAR-T cells
- 80x10^6 CAR-T cells determined as RP2D

ANTLER trial design for all cohorts

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[c]

NCT04637763
[a]B-NHL subtypes include: DLBCL, HGBL, tFL, PMBCL, FL [follicular lymphoma, with POD24 (high risk)], MCL, and MZL
[b]LBCL subtypes include: DLBCL NOS, HGBL, transformed DLBCL from FL or MZL, and PMBCL
[c]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

PATIENT POPULATION



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

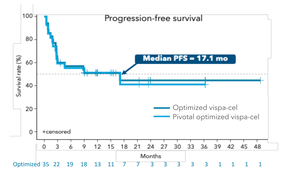
BASELINE CHARACTERISTICS

Baseline characteristics	All treated patients N=85	Optimized vispa-cel[a] (All patients) N=35	Pivotal optimized vispa-cel[b] (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 (%)[c]			
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[d]	67/79[e] (85)	30 (86)	25 (93)
No CR to 1L therapy	51/79[f] (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[f]	18 (21)	5 (14)	4 (15)

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

EFFICACY

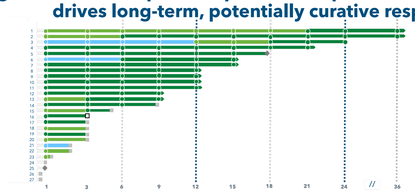
Optimized vispa-cel delivered durable, long-term efficacy



	Optimized vispa-cel[a] (All patients) N=35	Pivotal optimized vispa-cel[b] (2L LBCL, RP2D) N=27
ORR	**83%**	**82%**
CR rate	**66%**	**67%**
Median PFS[c] (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[d] (95% CI)	**NR** (3.7, NE)	**16.2 mo** (2.0, NE)

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

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



[a]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
Data cutoff 06March2026

SAFETY AND TOLERABILITY

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[a]		Pivotal optimized vispa-cel (2L LBCL, RP2D) N=27[b]	
	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[c]	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 (%)	--	--	--	--	--	--

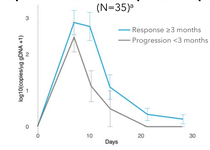
Six grade 5 AEs: 2 related, 1 possibly related, 3 unrelated (bladder perforation secondary to BK virus [related]; IEC-HS [related]; PML [possibly related]; acute respiratory failure [unrelated]; acute respiratory distress syndrome [unrelated]; HHV6 encephalitis [unrelated]

[a]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
[b]2L LBCL patients treated with 80M vispa-cel CAR-T cells optimized for multiple factors, including 2+HLA matched and young donor
[c]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).
Data cutoff 06March2026

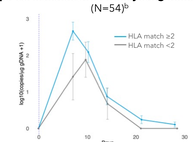
TRANSLATIONAL ANALYSES

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)[a]



HLA match level (<2 vs ≥2) impact on PK for vispa-cel manufactured from young donor T cells (N=54)[b]

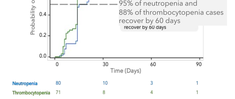


Average of log transformed values shown; error bars represent standard error; [a]Progression <3 mo N=14; response ongoing ≥3 months N=21; [b]HLA match <2 N=9, HLA match ≥2 N=45
Response categories determined at Month 3/Week 12 visit; visits with <50% subject data available are excluded; repeat assay results for the same subject sample were excluded (n=1 and n=3, respectively). Data cutoff 06March2026

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

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

Absolute neutrophil and platelet count recovery to Grade ≤2



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

NEXT STEPS

[a]LBCL subtypes include DLBCL NOS, HGBL (with MYC and BCL2 and/or BCL6), HGBL NOS, transformed DLBCL from FL or MZL, FL3B, PMBCL
[b]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
[c]Patients in the comparator arm to be treated with an investigator's choice of SOC regimens: R-GemOx (rituximab+gemcitabine+ oxaliplatin); Pola-RGO (polatuzumab vedotin+rituximab+gemcitabine+oxaliplatin); or tafasitamab+lenalidomide.
[d]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
[e]Will only be performed after study is fully enrolled

CONCLUSIONS

- **Vispa-cel is a 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

References:
1. **Perales, M-A, et al.** Poster 549, 2025 Tandem Meetings
2. **Lau E, et al.** *Cytotherapy*. 2023;25(7):750–762
3. **Hamadani M, et al.** TANDEM 2026 presentation
4. **Rosenberg S, et al.** *Clin Cancer Res.* 2011;17(13):4550–4557 doi:10.1158/1078-0432.CCR-11-0116

Abbreviations:
2L: second line; 3L: third line; ≥3L: third line or later; B-NHL: B cell non-Hodgkin lymphoma; CR: complete response; CRS: cytokine release syndrome; DLBCL: diffuse large B cell lymphoma; DLT: dose-limiting toxicity; DoCR: duration of complete response; DoR: duration of response; ECOG: Eastern Cooperative Oncology Group; FL: follicular lymphoma; GvHD: graft versus host disease; HGBL: high-grade B cell lymphoma; HLA: human leukocyte antigen; ICANS: immune effector cell-associated neurotoxicity syndrome; IEC-HS: immune effector cell-associated hemophagocytic lymphohistiocytosis-like syndrome; IPI: International Prognostic Index; LBCL: large B cell lymphoma; LD: lymphodepletion; LDH: lactate dehydrogenase; LLOQ: lower limit of quantification; LoT: line of therapy; M: million; MCL: mantle cell lymphoma; mo: months; mPFS: median progression-free survival; MZL: marginal zone lymphoma; NA: not applicable; NHL: non-Hodgkin lymphoma; NOS: not otherwise specified; NR: not reached; ORR: overall response rate; PMBCL: primary mediastinal large B cell lymphoma; PML: progressive multifocal leukoencephalopathy; POD24: progression of disease within 24 months; RP2D: recommended phase 2 dose; SOC: standard of care; tFL: transformed DLBCL from follicular lymphoma; tMZL: transformed marginal zone lymphoma; ULN: upper limit of normal; yo: years old

Disclosures for corresponding author:
- **BMS** (Speaker Bureau and Steering Committee)
- **Sanofi** (Speaker Bureau)
- **Pfizer** (Consultation/Advisory Board)
- **Caribou Bio** (Steering Committee)

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