First-in-human trial of LB2501, an *in vivo* CD19/CD20 dual-target CAR-T therapy, in relapsed/refractory B-cell NHL

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Disclosures

- No conflicts of interest to declare.

Background

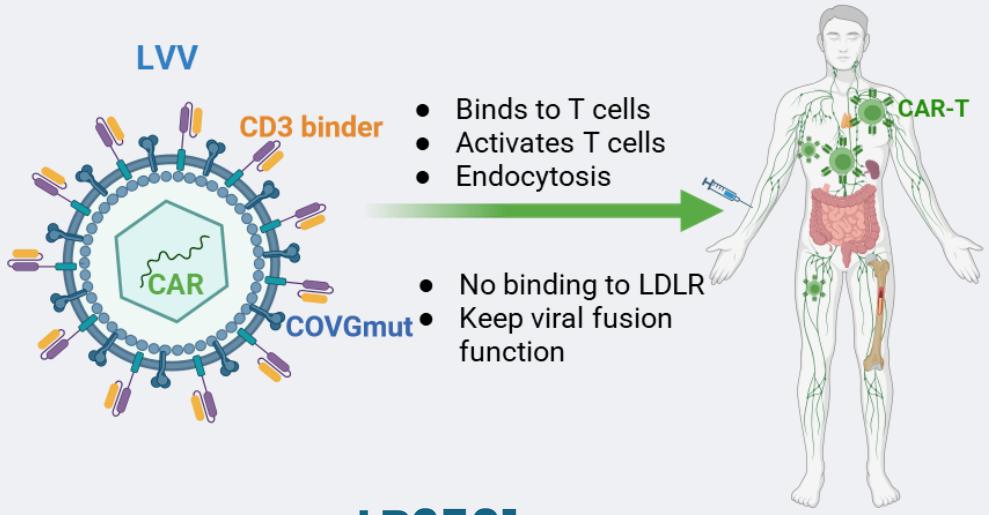
- For patients with chemotherapy-refractory B-cell lymphoma, conventional salvage therapies achieve overall response rate (ORR) of 26%, a complete response (CR) rate of 7%, and a median overall survival time of approximately 6 months – underscoring a persistent unmet medical need[1]
- CD19-directed autologous CAR T-cell therapy has substantially transformed the treatment landscape of R/R B-NHL[2–5]; however, *ex vivo* CAR-T manufacturing is complex and individualized, causing treatment delays, high costs, restricted access, and treatment-related morbidity[5–8]
- *In vivo* CAR-T cell generation addresses these constraints by delivering CAR-encoding genetic material directly to endogenous immune cells, producing CAR-T cells within the patient instead of via complex *ex vivo* processing[8–12]
- LB2501 is an engineered, third-generation, self-inactivating, replication-incompetent lentiviral vector (LVV) designed to generate CD19/CD20-directed CAR-T cells *in vivo*

We present preliminary data from an ongoing Phase 1 clinical trial (NCT07002112) evaluating the safety and preliminary efficacy of LB2501 in adults with R/R B-NHL

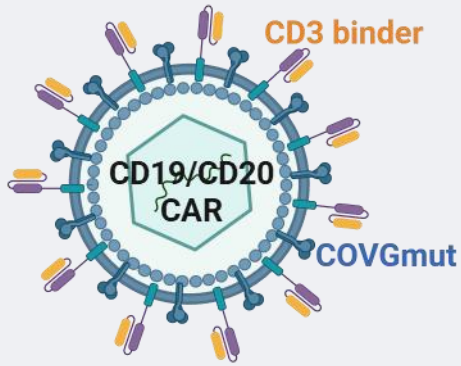
1. Crump M, et al. *Blood*. 2017;130(16):1800–1808. 2. Wang M, et al. *N Engl J Med.* 2020;382(14):1331–1342. 3. Neelapu SS, et al. *N Engl J Med.* 2017;377(26):2531–2544. 4. Schuster SJ, et al. *N Engl J Med*. 2019;380(1):45–56. 5. Westin JR, et al. *Am J Hematol*. 2021;96(10):1295–1312. 6. Sterner RC, et al. *Blood Cancer J*. 2021;11(4):69. 7. Kaparis S, et al. *Blood Rev*. 2025:101358. 8. Sorin M, et al. *Lancet Haematol*. 2026;13(2):e86–e97. 9. Bot A, et al. *Nat Rev Drug Discov*. 2026;25(2):116–137. 10. An N, et al. *Nat Med*. 2026;32(4):1257–1266. 11. Wang Q, et al. *N Engl J Med.* 2025;393(15):1542–1544. 12. Xu J, et al. *J Hematol Oncol*. 2025;18(1):105.

LB2501: Engineered LVV for *In Vivo* CD19/CD20 CAR-T

TaVec (T cell activation Vector) Platform

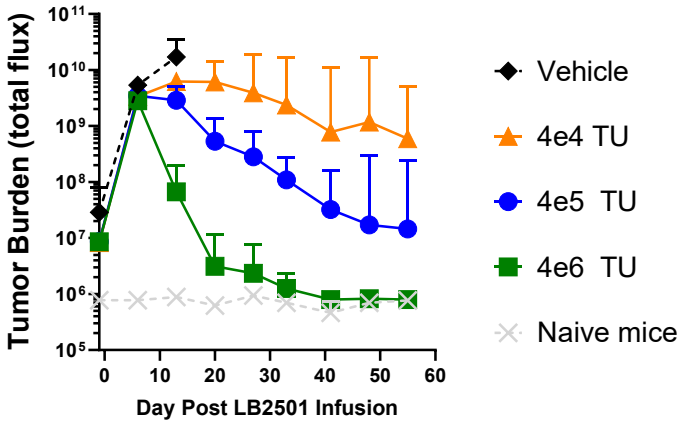


LB2501

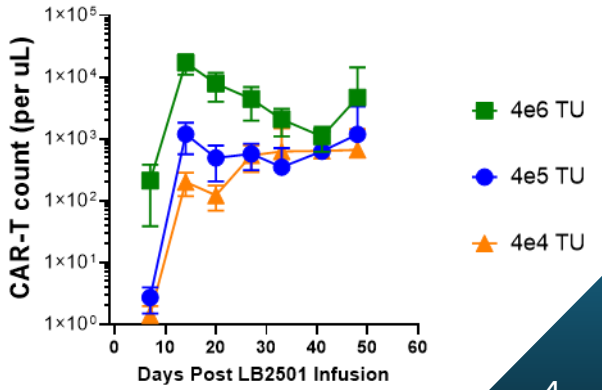


- **TaVec** is T cell-retargeting lentiviral vector (LVV) with CD3 binder and mutated COVG on surface
- **LB2501** is an engineered LVV for *in vivo* CD19/CD20 CAR-T based on TaVec platform
- Proprietary CD19/CD20 dual-target CAR design to broaden antigen coverage
- LB2501 generates CAR-T cells and controls tumor dose-dependently in human PBMC-reconstituted NSG mouse model

Tumor Burden

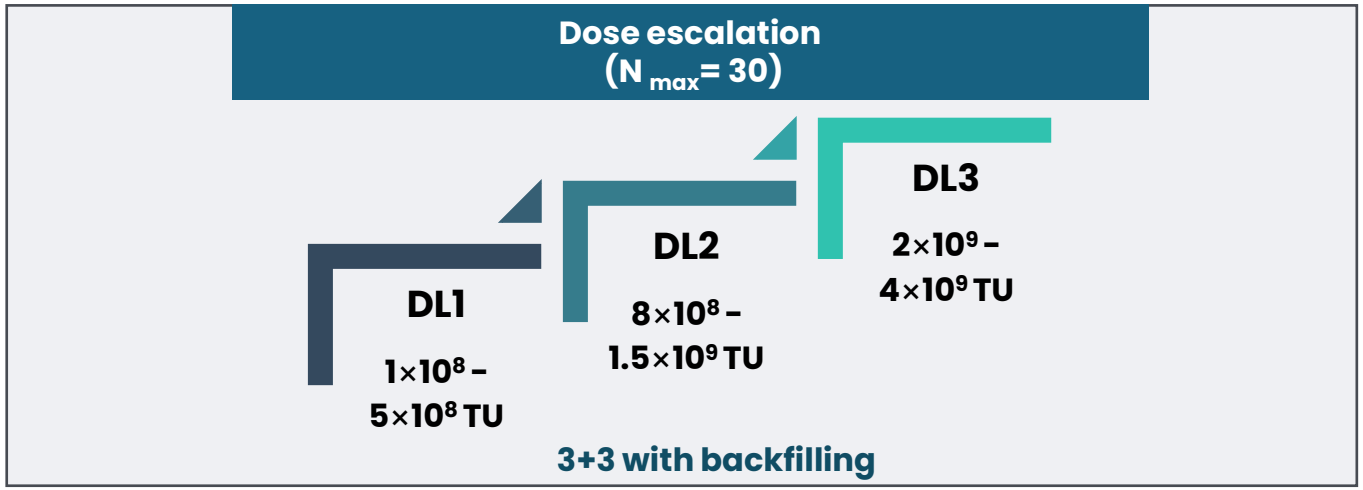


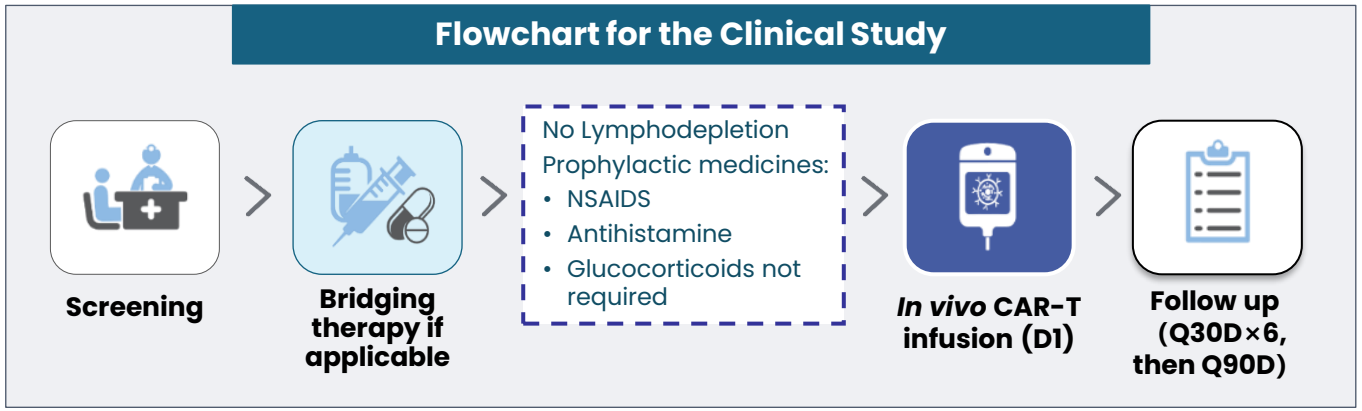
CAR-T Count



Study Design

An open-label, multi-center, dose-escalation phase 1 study to evaluate the safety and efficacy of *in vivo* CD19/CD20 dual-target CAR-T lentivirus therapy in adults with R/R B-NHL





Key eligibility criteria:

- Age ≥18 years
- ECOG PS 0-1
- Histologically confirmed LBCL (including transformed iNHL), iNHL, MCL, and confirmed CLL
- ≥2 prior lines or refractory to first-line* systemic therapy
- Previous CD19-autologous CAR-T and TCE therapy were allowed

Primary endpoints:

- Safety
- RP2D
- Pharmacokinetics of LVV and generated CAR-T

Secondary endpoints:

- Efficacy: ORR, TTR, DOR, PFS, and OS
- Immunogenicity: anti-LVV and anti-CAR-T

Median follow-up time was 4.0 months (range, 2.0~7.9 months) at data cutoff date of Apr 1, 2026

*Disease that did not respond to, or progressed within 12 months after completion of first-line therapy.
CLL, chronic lymphoblastic leukemia; DL, dose level; DLT, dose-limiting toxicity; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; iNHL, indolent non-Hodgkin lymphoma; LBCL, large B-cell lymphoma; MCL, mantle cell lymphoma; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetics; RP2D, recommended phase II dose; TCE, T-cell engager; TTR, time to response.

LB2501: Demographics and Baseline Characteristics

- As of April 1, 2026, a total of 12 patients dosed with LB2501, **6 patients in DL1 (4 at 2×10^8 TU and 2 at 5×10^8 TU) and 6 patients in DL2 (all at 1×10^9 TU)**
- No patients received bridging-therapy before infusion of LB2501. The median time from consent to infusion was 17.5 days

Baseline Characteristics	DL1 (N=6)	DL2 (N=6)	Total (N=12)
Age, median (range), years	50.0 (43, 63)	62.5 (36, 73)	58.5 (36, 73)
≥65 years, n (%)	0	2 (33.3)	2 (16.7)
Male, n (%)	4 (66.7)	1 (16.7)	5 (41.7)
ECOG PS 0/1, n (%)	5 (83.3)/1 (16.7)	1 (16.7)/5 (83.3)	6 (50.0)/6 (50.0)
Histology, n (%)			
DLBCL	3 (50.0)	3 (50.0)	6 (50.0)
FL	1 (16.7)	2 (33.3)	3 (25.0)
MCL	1 (16.7)	1 (16.7)	2 (16.7)
PMBL	1 (16.7)	0	1 (8.3)
Ann Arbor staging III-IV, n (%)	3 (50.0)	5 (83.3)	8 (66.7)
ALC, median (range), $\times10^9$/L	1.21 (0.93, 1.40)	0.77 (0.58, 1.44)	1.03 (0.58, 1.44)
CD3+, median (range), cells/µL	808 (453, 1713)	425 (311, 676)	557 (311, 1713)
No. of prior lines of treatment, median (range)	2.5 (2, 6)	3.5 (1, 7)	3.0 (1, 7)
Disease status to last line of prior therapy			
Relapsed, n (%)	3 (50.0)	2 (33.3)	5 (41.7)
Refractory, n (%)	3 (50.0)	4 (66.7)	7 (58.3)
SPD, median (range), mm^2	852.6 (144, 1041)	1444.1 (440, 2540)	921.4 (144, 2540)
Prior CD19 CAR-T cell therapy, n (%)	1 (16.7)	0	1 (8.3)
Prior T-cell engager* therapy, n (%)	1 (16.7)	1 (16.7)	2 (16.7)

*Both TCE therapies are CD20×CD3.
DL, dose level; DLBCL, diffuse large B-Cell lymphoma; ECOG, Eastern Cooperative Oncology Group; FL, follicular lymphoma; MCL, mantle cell lymphoma; PMBL, primary mediastinal large B-cell lymphoma; SPD, sum of the product of the diameters.

Safety Summary

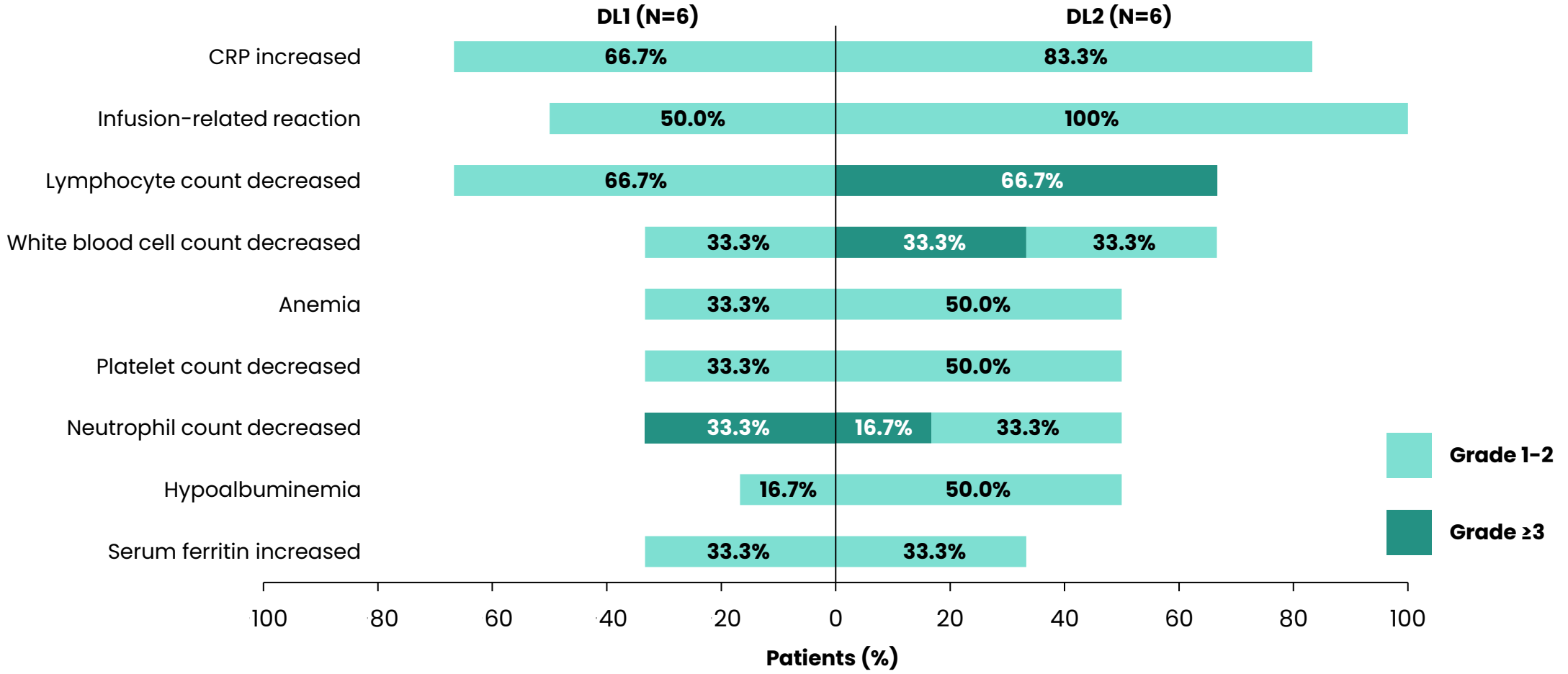
- LB2501 was well tolerated: **no DLT, no SAE, and no deaths**
- Most common AESIs were **IRR and CRS**, all **Grade 1-2**
- **No ICANS**

Treatment-emergent adverse events (TEAEs), n (%)	DL1 (N=6)		DL2 (N=6)		Total (N=12)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Patients with TEAE	6 (100.0)	5 (83.3)	6 (100.0)	6 (100.0)	12 (100.0)	11 (91.7)
Related to LB2501 LVV*	6 (100.0)	2 (33.3)	6 (100.0)	4 (66.7)	12 (100.0)	6 (50.0)
Related to generated CAR-T*	3 (50.0)	2 (33.3)	6 (100.0)	5 (83.3)	9 (75.0)	7 (58.3)
SAE	0	0	0	0	0	0
DLT	0	0	0	0	0	0
Adverse event of special interest (AESI)						
IRR	3 (50.0)	0	6 (100.0)	0	9 (75.0)	0
CRS	2 (33.3)	0	6 (100.0)	0	8 (66.7)	0
ICANS	0	0	0	0	0	0
Non-ICANS neurotoxicity	0	0	0	0	0	0
Second primary malignancy	0	0	0	0	0	0

*The relationship assessment was based on investigator decision.
CRS, cytokine-released syndrome; DLT dose-limiting toxicity; ICANS, immune effector cell-associated neurotoxicity syndrome; IRR, infusion-related reaction; SAE, severe adverse event.

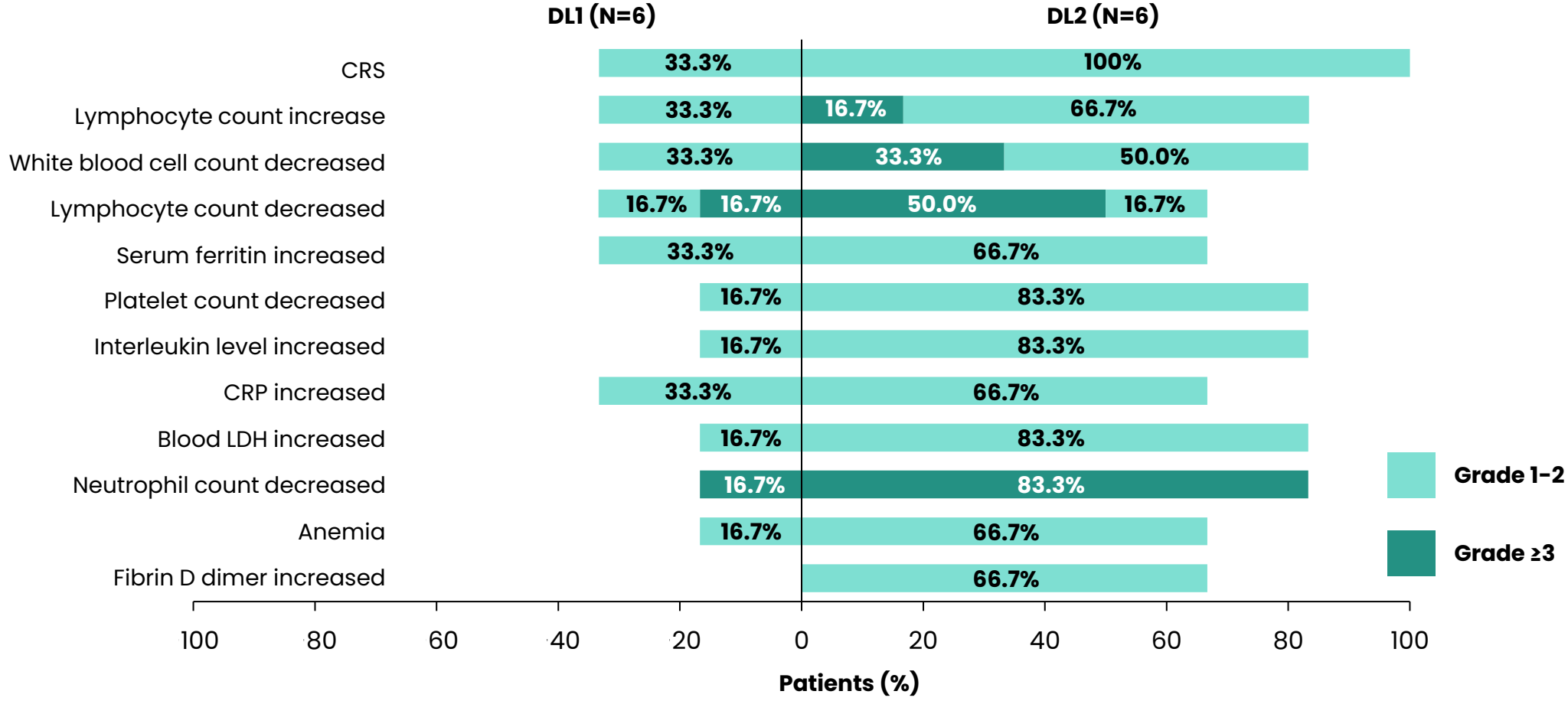
LB2501 LVV Infusion-Related TEAEs (≥30%)

- **IRR** occurred in 50% (DL1) and 100% (DL2), **all Grade 1–2 and manageable**, with a median onset of 1.4 h and recovery of 18.6 h
- No steroid prophylaxis. **No** IRR **required tocilizumab or glucocorticoids** for treatment
- Transient Grade ≥3 cytopenias resolved within a few days



LB2501 Generated CAR-T Related TEAEs (≥30%)

- **CRS** occurred in 33.3% (DL1) and 100% (DL2), **all grade 1–2 and manageable**, with a median onset at day 11 and duration of 4.5 days
- Tocilizumab given to 4 patients (DL1: 1, DL2: 3); **no glucocorticoids for CRS**
- Grade ≥3 cytopenias were observed, manageable, and recovered



Efficacy

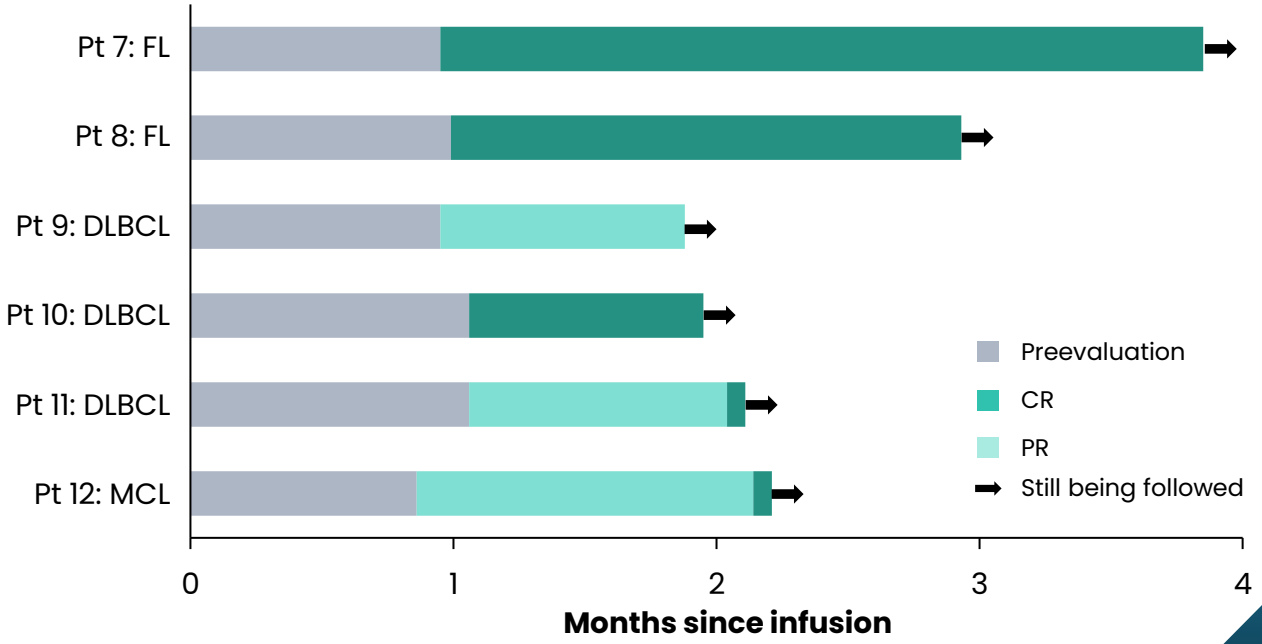
Response Rate	DL1 (N=6)	DL2 (N=6)	Total (N=12)
ORR, n (%) [95% CI]	0	6 (100) [54.1-100]	6 (50.0) [21.1-78.9]
CR, n (%) [95% CI]	0	5 (83.3) [35.9-99.6]	5 (41.7) [15.2-72.3]

- **At DL2, 100% ORR** and **83.3% CR** achieved across **DLBCL, MCL, and FL**
- **Deepening response** observed
- By data cutoff, all responses were ongoing

Percent Change from Baseline in SPD for Best Response (DL2)

The Lugano 2014 criteria were used to assess the response at each prespecified time point in patients with NHL

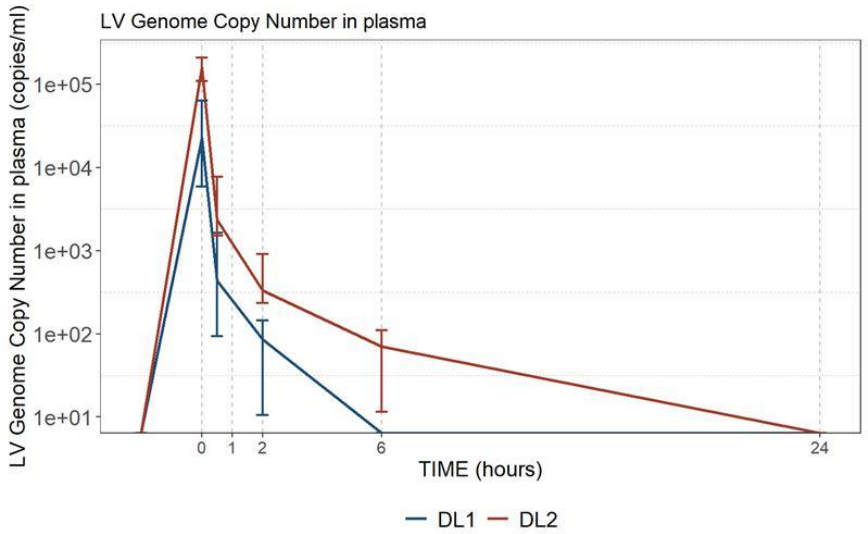
Duration of Responses in Patients (DL2)



The median follow-up for DL2 was 2.3 months (range, 2.0 to 4.5); Pt 8 had prior TCE with washout of 2.7 months

LB2501: Pharmacokinetics

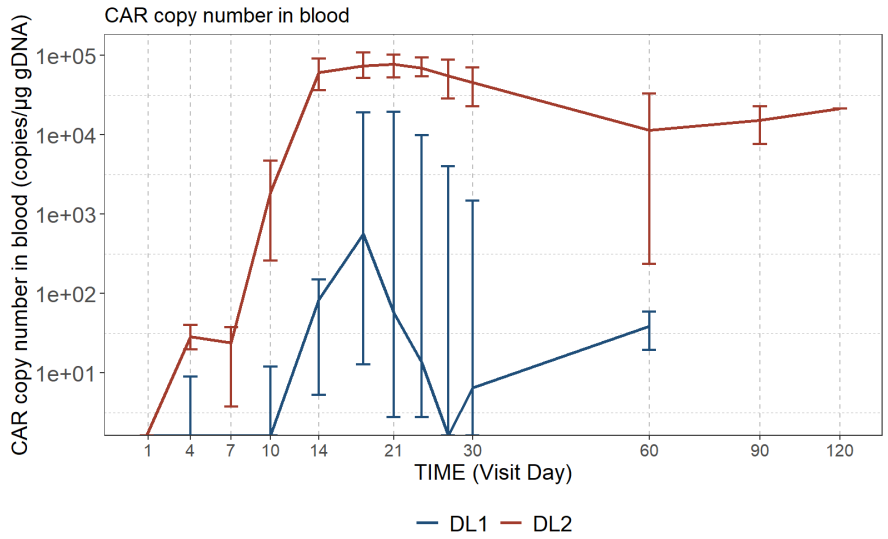
LVV PK



Data in plot presented as median and quartiles (Q1 and Q3)

		DL1 (N=6)	DL2 (N=6)	Total (N=12)
C_{max} (copies/mL)	Median (Min, Max)	22,540.5 (1,167, 83,666)	160,124.0 (36,755, 421,549)	79,905.0 (1,167, 421,549)
T_{max} (hours)	Median (Min, Max)	0.050 (0.02, 0.08)	0.050 (0.02, 0.07)	0.050 (0.02, 0.08)

***In vivo* CAR-T PK**



Data in plot presented as median and quartiles (Q1 and Q3)

		DL1 (N=6)	DL2 (N=6)	Total (N=12)
Patients with CAR-T expansion	N	5	6	11
C_{max} (copies/ug gDNA)	Median (Min, Max)	1,068.0 (51, 113,350)	109,117.5 (32,497, 137,457)	87,899.0 (51, 137,457)
T_{max} (day)	Median (Min, Max)	17.0 (14, 30)	15.0 (13, 18)	17.0 (13, 30)

- Viral copy number in peripheral blood peaked immediately after infusion and **decreased to undetectable concentrations within 24 hours**
- *In vivo* CAR-T expansion was detected by qPCR in 5/6 patients (83%) at DL1 and all patients (6/6, 100%) at DL2 in a **dose-dependent manner**. At the time of data cutoff, patients exhibited **persistent PK**, with CAR-T cells detectable in peripheral blood for up to 116 days

Integration Profile

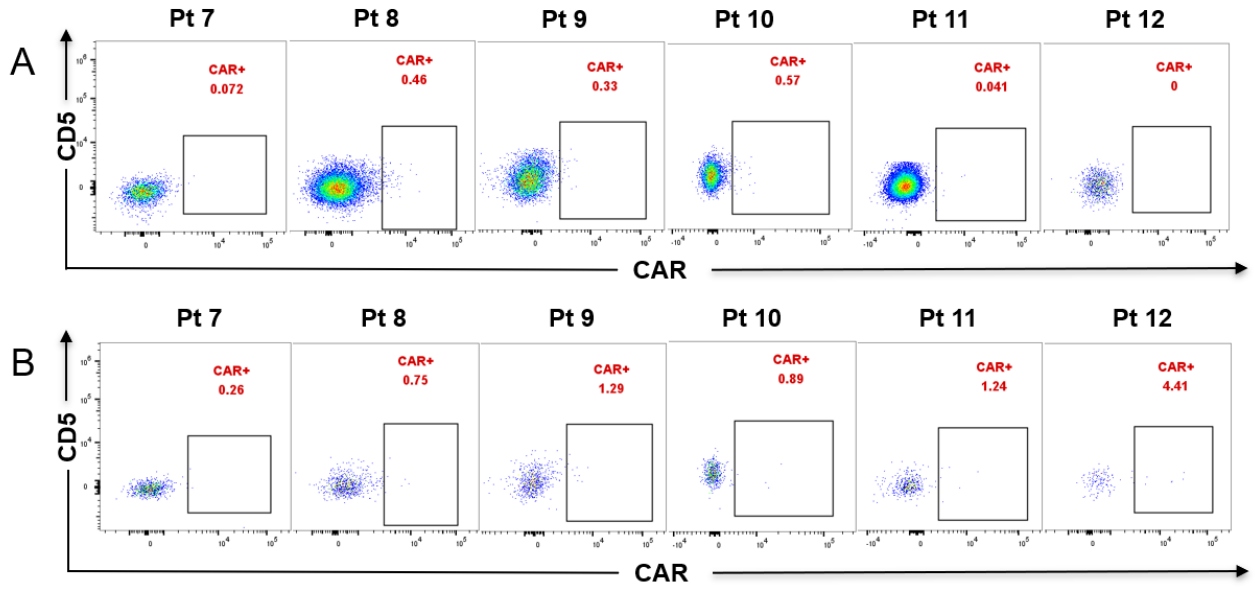
- Lentiviral integration analysis demonstrated a **safe transgene profile**

I. Integration profile was **highly polyclonal and diverse**, as confirmed by Simpson index and Evenness score

II. Integration patterns were concordant with established public HIV and LVV datasets[1,2] at both chromosomal and genomic functional region levels

III. Average vector copy number (VCN) of ≈1 per patient, indicating controlled transgene integration

IV. No evidence of **non-specific transduction** in non-T lymphocyte populations



No CAR transduction detected in non-T lymphocytes.
(A) NK cells and (B) CD19-CD56-CD3-CD5-lymphocytes

1. Citu C, et al. *Sci Data*. 2026;13(1):695. 2. Yan KK, et al. *Sci Adv*. 2023;9(40):eadg9959.

Conclusions

- In this FIH Phase 1 study in R/R B-NHL, LB2501 showed a **favorable safety profile and promising efficacy**:
  - LB2501 was well tolerated: no DLT, no SAE, no ICANS, and no deaths
  - IRR and CRS were all Grade 1–2; no glucocorticoid treatment
  - At DL2, 100% ORR and 83.3% CR achieved across DLBCL, MCL, and FL
- Dose-dependent expansion was observed, with consistent expansion at DL2
- **LB2501** establishes a **proof-of-concept** for **TaVec *in vivo* CAR-T platform** in clinic; it showed T-cell specific transduction and robust CAR-T expansion, polyclonal random integration, and rapid vector clearance

These findings support further development of LB2501 as potential first-in class
off-the-shelf, single-infusion, no lymphodepletion, outpatient use,
in vivo CD19/CD20 dual-target CAR-T therapy in R/R B-NHL

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