SUPPLEMENTAL TABLES

Table S1. Cy/Flu lymphodepletion regimens

Lymphodepletion regimen	Number of patients (%)
High-intensity lymphodepletion	31 (65)
Cy 60 mg/kg x 1 + Flu 25 mg/m^2 x 3	30 (63)
Cy 60 mg/kg x 1 + Flu 25 mg/m^2 x 5	1 (2)
Low-intensity lymphodepletion	17 (35)
Cy 30 mg/kg x 1 + Flu 25 mg/m^2 x 3	6 (13)
Cy 300 mg/m^2 x 3 + Flu 30 mg/m^2 x 3	10 (21)
Cy 500 mg/m^2 x 3 + Flu 30 mg/m^2 x 3	1 (2)
Total	**48 (100)**

Cy, cyclophosphamide; Flu, fludarabine

Table S2. List of factors considered in multivariable analyses

Variable	Variable
Pre-treatment	**Lymphodepletion**
Abnormal B cells in blood (cells/μL)	Low-intensity Cy/Flu†
Abnormal B cells in blood (%)	**Biomarkers**
Abnormal B cells in marrow (%)	IFN-γ#
Absolute lymphocyte count (cells/μL)*	IL-2 receptor α#
Absolute neutrophil count (cells/μL)*	IL-5#
Age	IL-6#
Ann Arbor stage	IL-7#
Anti-CD19 targeted therapy exposure†	IL-8#
Bulky disease (≥ 10 cm)†	IL-10#
$CD8^+$ T cell selection: bulk vs. CM-enriched	IL-15#
Corticosteroid requirement after leukapheresis†	IL-18#
ECOG performance-status score	IL-22#
Extranodal disease†	MCP-1#
International Prognostic Index score	MIP-1β#
Karnofsky performance-status score	Soluble Fas#
LDH pre-lymphodepletion elevated†	Soluble IL-6 receptor#
LDH, pre-lymphodepletion (U/L)	TGFβ-1#
Normal B cells in marrow (%)	TIM3#
Number of prior therapies	TNF-α#
Platelets (cells/μL)*	TNFRp55#
Prior hematopoietic cell transplantation†	TNFRp75#
Sex	**CAR-T cell kinetics**
Time from leukapheresis to last intensive chemotherapy	CAR-T cells by qPCR, peak (transgene copies/μg DNA)**
Total B cells in marrow (%)	$CD4^+$ CAR-T cells, peak (cells/μL)**
Treatment within 6 weeks before leukapheresis†	$CD8^+$ CAR-T cells, peak (cells/μL)**
Treatment within 9 weeks before leukapheresis†	**Toxicities**
Treatment after leukapheresis†	Cytokine release syndrome grade
Tumor cross-sectional area‡	Neurotoxicity grade
Manufacturing	
$CD4^+$ subsets, apheresis product (%)§	
$CD8^+$ subsets, apheresis product (%)§	
$CD4^+$ T cell fold expansion‖	
$CD4^+$ CAR-T cell fold expansion¶	
$CD8^+$ T cell fold expansion‖	
$CD8^+$ CAR-T cell fold expansion¶	
$CD8^+$ CAR-T cell subsets, infusion product§	

* Screening, pre-lymphodepletion, and day 0.

† Yes versus no.
‡ Sum of the product of the perpendicular diameters of up to 6 target measurable nodes and extranodal sites.
§ Naïve, central memory (CM), effector memory, and effector memory RA.
|| T cell fold expansion from day 0 to LCL (irradiated $CD19^+$ Epstein-Barr virus lymphoblastoid cell line) stimulation.
¶ CAR-T cell fold expansion from LCL stimulation to harvest.
# Pre-lymphodepletion; day 0; delta between pre-lymphodepletion and day 0; and peak.
** AUC0-28 (area under the curve from day 0 to 28) was highly correlated with peak and therefore not included in elastic net.

Table S3. Univariate analysis for factors impacting PFS in aggressive NHL

Variable	HR (95% CI)	*P* value*
Pre-treatment		
IPI score prior to lymphodepletion	1.91 (1.30-2.79)	.001
LDH pre-lymphodepletion > ULN (Y)†	3.70 (1.70-8.06)	.001
LDH, pre-lymphodepletion‡	1.24 (1.04-1.47)	.02
Abnormal B cells in blood (cells/μL)§	1.07 (1.02-1.11)	.003
Abnormal B cells in marrow (%)‖	1.03 (1.01-1.05)	.01
Corticosteroid dose within 6 weeks before apheresis¶	1.88 (1.20-2.93)	.01
Corticosteroid requirement after apheresis (Y)#	3.42 (1.43-8.22)	.01
Tumor cross-sectional area**	1.01 (1.00-1.02)	.01
Lymphodepletion		
Low-intensity Cy/Flu (Y)#	1.92 (0.99-3.72)	.05
Biomarkers		
MCP-1, fold change pre-lymphodepletion to day 0	0.34 (0.14-0.86)	.02
MCP-1, delta pre-lymphodepletion to day 0††	0.92 (0.85-0.99)	.03
MCP-1, day 0 (pre-CAR-T cell infusion)‡‡	0.25 (0.10-0.60)	.002
MCP-1, peak‡‡	0.31 (0.13-0.73)	.01
IL-7, pre-lymphodepletion[a]	0.73 (0.56-0.94)	.01
IL-7, fold change pre-lymphodepletion to day 0	1.26 (1.03-1.53)	.02
IL-7, peak[a]	0.84 (0.74-0.95)	.01
IL-7, AUC0-28	0.26 (0.08-0.82)	.02
IL-15, day 0 (pre-CAR-T cell infusion)‡‡	0.34 (0.12-1.00)	.05
IL-15, peak‡‡	0.36 (0.13-0.99)	.05
TGFβ-1, pre-lymphodepletion‡‡	0.26 (0.10-0.68)	.01
TGFβ-1, peak‡‡	0.26 (0.09-0.79)	.02
TGFβ-1, AUC0-28	0.21 (0.06-0.73)	.01
IFN-γ, pre-lymphodepletion[b]	0.43 (0.18-0.99)	.05
IFN-γ, delta pre-lymphodepletion to day 0[b]	2.08 (1.19-3.64)	.01
IL-18, pre-lymphodepletion‡‡	3.79 (1.33-10.83)	.01
IL-18, day 0 (pre-CAR-T cell infusion)‡‡	3.20 (1.15-8.94)	.03
IL-18, peak‡‡	2.27 (1.06-4.86)	.03
TNFRp75, pre-lymphodepletion‡‡	5.41 (1.51-19.33)	.01
TNFRp75, peak‡‡	5.08 (1.50-17.20)	.01
IL-10, AUC0-28	2.06 (1.09-3.88)	.03
CAR-T cell kinetics		
$CD8^+$ CAR-T cells, peak (log_{10} cells/μL)	0.70 (0.50-0.97)	.03
CAR-T cells by qPCR (log_{10} transgene copies/μg DNA)	0.69 (0.47-1.01)	.05

PFS, progression-free survival; HR, Hazard Ratio; 95% CI, 95% confidence interval; IPI, International Prognostic Index; ULN, upper limit of normal; AUC0-28, area under the curve from day 0 to 28
* Univariate Cox regression model.

† Above ULN, yes versus no.
‡ Per 100 U/L increment.
§ Per $10^3/\mu L$ increment.
|| Per percent increment.
¶ Cumulative corticosteroid dose within 6 weeks before leukapheresis (per $\log_{10}$ mg/m^2 prednisone equivalent dose increment).
# Yes versus no.
** Sum of the product of the perpendicular diameters of up to 6 target measurable nodes and extranodal site per cm^2 increment.
†† Per 50 pg/mL serum concentration increment.
‡‡ Per $\log_{10}$ pg/mL serum concentration increment.
[a] Per 5 pg/mL serum concentration increment.
[b] Per pg/mL serum concentration increment.

Table S4. Multivariable model for factors impacting PFS in aggressive NHL adjusting for new treatment after CAR-T cell infusion as a time-dependent covariate*

Variable	Hazard Ratio	95% CI	*P* value
LDH, pre-lymphodepletion†	1.37	1.14-1.63	.0007
MCP-1, day 0 (pre-CAR-T cell infusion)‡	0.29	0.09-0.90	.03
IL-7, peak§	0.89	0.77-1.04	.14
New treatment (Y)‖	1.12	0.45-2.78	.80

PFS, progression-free survival; HR, Hazard Ratio; 95% CI, 95% confidence interval

* Cox regression was performed to assess the association between PFS and variables of interest where $\log_{10}$ values were used to transform data as appropriate.

† Per 100 U/L increment.

‡ Per $\log_{10}$ pg/mL serum concentration increment.

§ Per 5 pg/mL serum concentration increment.

‖ Second CAR-T cell infusion, new antitumor therapy, or hematopoietic cell transplantation.

SUPPLEMENTAL FIGURES

Figure S1

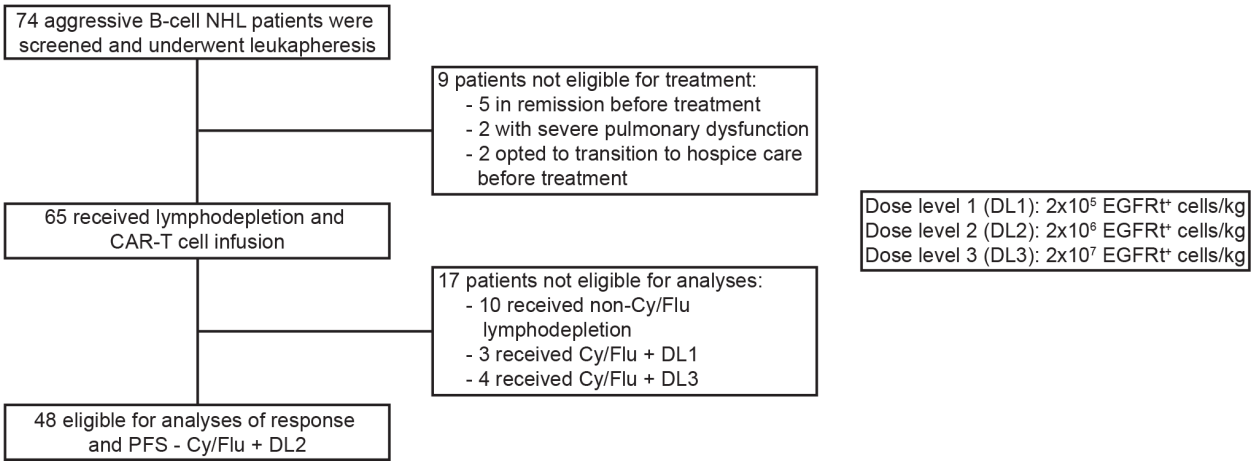

Figure S1. Flow chart of patient enrollment and eligibility for response and progression-free survival (PFS) analyses. NHL, non-Hodgkin lymphoma; CAR-T cell, CD19 chimeric antigen receptor-modified T cell; CR, complete remission; Cy, cyclophosphamide; Flu, fludarabine; DL, dose level.

Figure S2

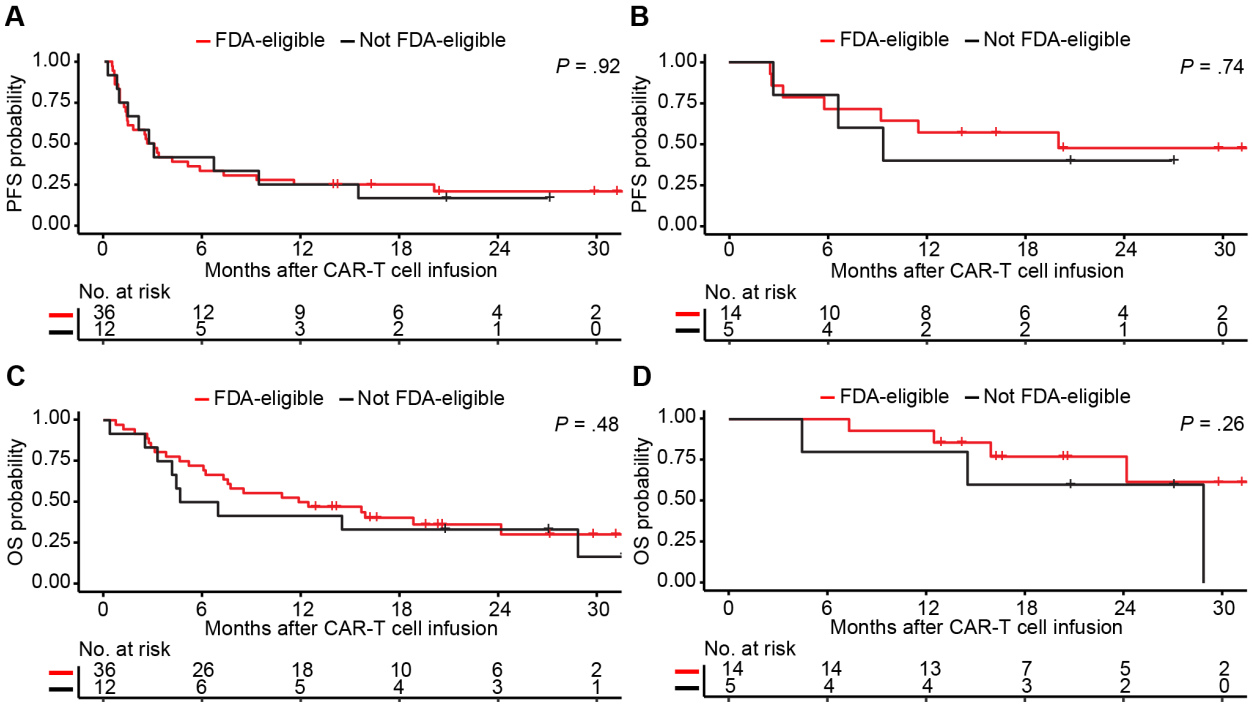

Figure S2. Progression-free (PFS) and overall survival (OS) in aggressive NHL according to FDA-approved histologic indications for CD19 CAR-T cell immunotherapy. (**A-B**) Kaplan-Meier estimates of PFS in FDA-eligible histologies (red) and histologies that are not FDA-eligible (black) in all patients (**A**) and patients who achieved CR (**B**). (**C-D**) Kaplan-Meier estimates of OS in FDA-eligible histologies (red) and histologies that are not FDA-eligible (black) in all patients (**C**) and patients who achieved CR (**D**). The numbers of patients at 6-month intervals are indicated. Log-rank tests were used to compare between-group differences in survival probabilities.

Figure S3

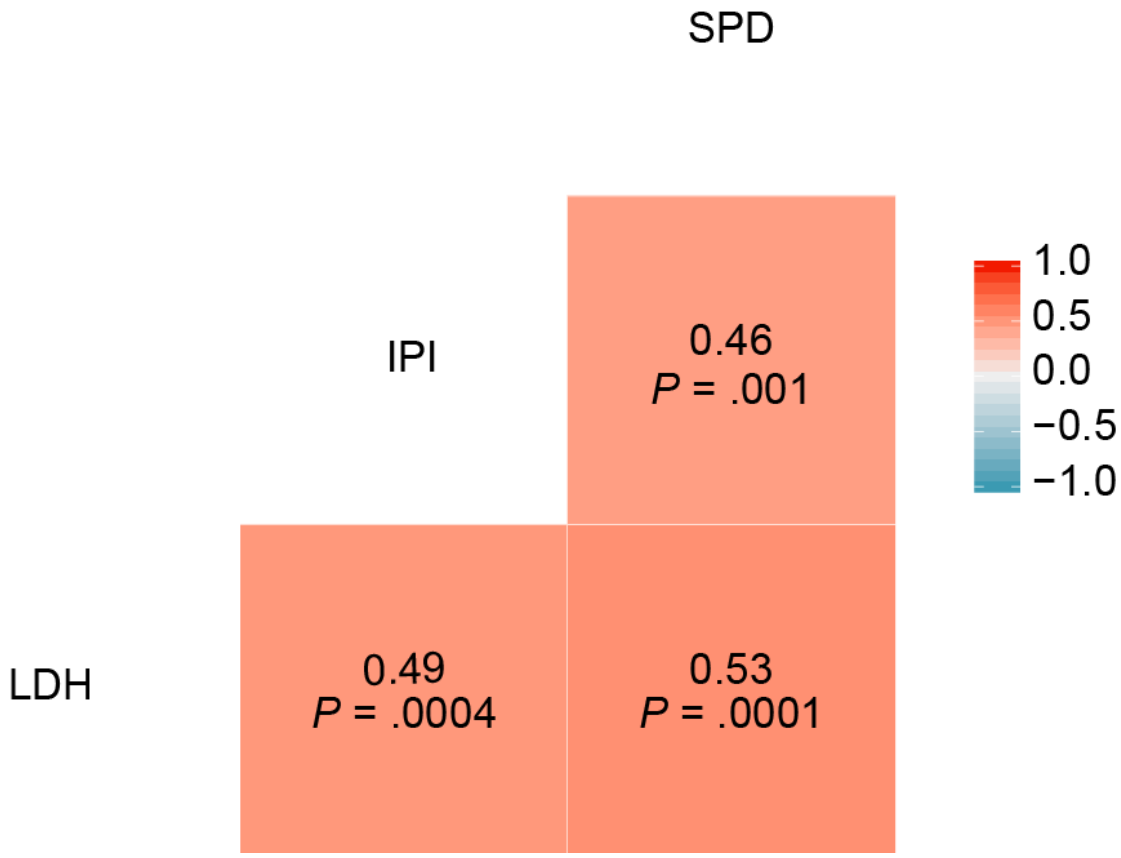

Figure S3. LDH, IPI, and SPD are highly correlated. Spearman correlation (*r* and *P* values) between serum lactate dehydrogenase (LDH), International Prognostic Index (IPI) score, and the sum of the product of the perpendicular diameters of up to 6 index lesions (SPD) before lymphodepletion.

Figure S4

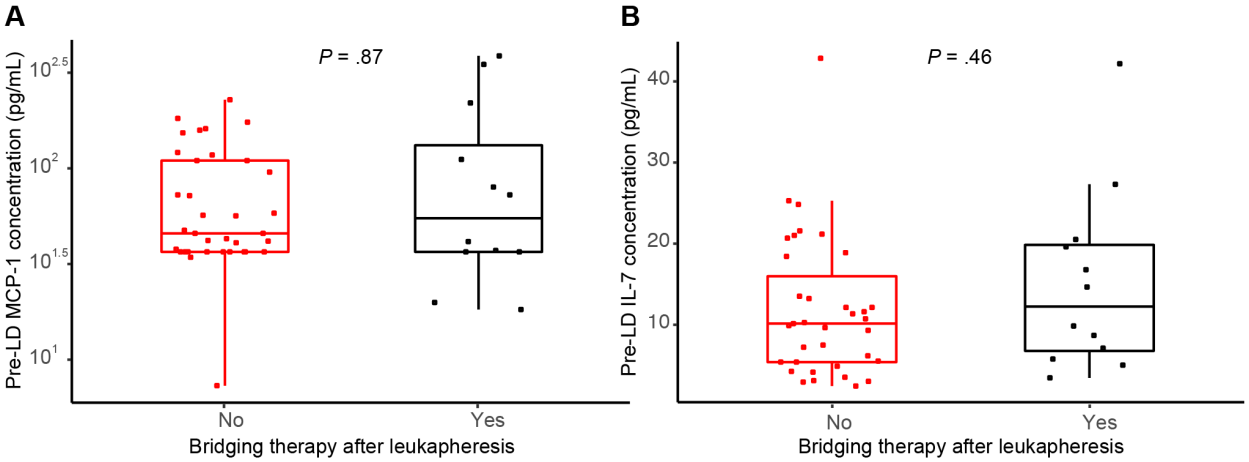

Figure S4. Serum MCP-1 and IL-7 concentrations before lymphodepletion in aggressive NHL patients. (**A-B**) Serum MCP-1 (**A**) and IL-7 (**B**) concentrations before lymphodepletion (pre-LD) in patients who did not receive bridging therapy (red) and in those who received bridging therapy (black) between leukapheresis and lymphodepletion. Each point represents data from a single patient. Box and whisker plots show the median (bar) and interquartile range (box).

Figure S5

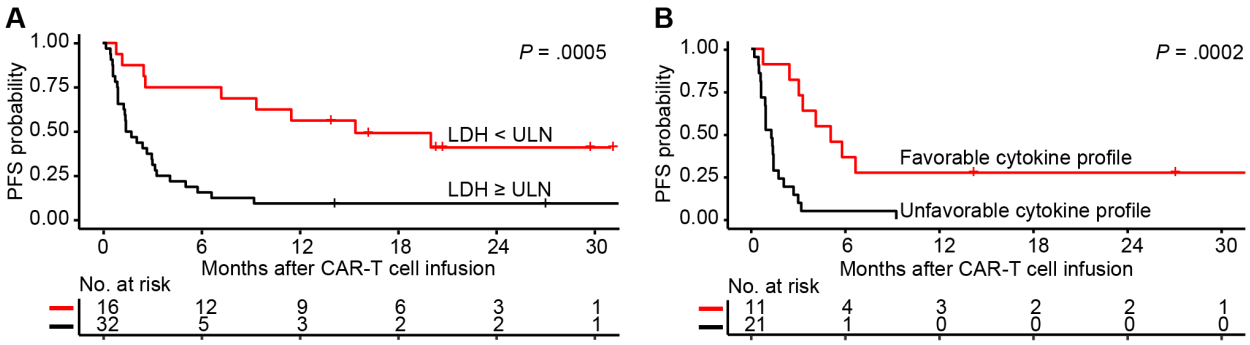

Figure S5. Progression-free survival (PFS) in aggressive NHL according to LDH concentration and in patients with LDH above normal. (**A**) Kaplan-Meier estimates of PFS in patients with pre-lymphodepletion LDH concentration below (red) or above or equal to the upper limit of normal (ULN; black). (**B**) Kaplan-Meier estimates of PFS in patients with pre-lymphodepletion LDH ≥ ULN according to development of favorable cytokine profile (serum day 0 MCP-1 and peak IL-7 concentrations above the median; red) compared to unfavorable cytokine profile (serum day 0 MCP-1 and/or peak IL-7 concentrations below or equal to the median; black). The numbers of patients at 6-month intervals are indicated. Log-rank tests were used to compare between-group differences in survival probabilities.