Supplemental Table S1. Patient and treatment characteristics by CRS grade

CRS Grade (n, %)	0 (n=52, 30%)	1 (n=40, 23%)	2 (n=55, 32%)	3-5 (n=26, 15%)
Age (years) – median (IQR) [range]	56 (44, 64) [24 – 71]	54 (46, 62) [23 – 73]	55 (42, 66) [20 – 74]	53 (41, 60) [20 – 76]
Sex – n (%)				
Female	19 (37)	9 (22)	16 (29)	14 (54)
Male	33 (63)	31 (78)	39 (71)	12 (46)
Race – n (%)				
White	47 (90)	31 (78)	49 (89)	24 (92)
Non-white	5 (9.6)	8 (20)	6 (11)	2 (7.7)
Unknown	0 (0)	1 (2.5)	0 (0)	0 (0)
Disease Type (n, %)				
ALL	14 (27)	12 (30)	23 (42)	13 (50)
CLL	8 (15)	15 (38)	18 (33)	7 (27)
NHL	30 (58)	13 (32)	14 (25)	6 (23)
Number of prior therapies – median (IQR) [range]	4 (2, 5) [1 – 11]	4 (3, 6) [1 – 10]	4 (3, 5) [1 – 11]	4 (3, 5) [1 – 9]
Prior HSCT – n (%)				
Allogeneic	7 (13)	11 (28)	13 (24)	4 (15)
Autologous	11 (21)	4 (10)	6 (11)	2 (7.7)
Both	1 (1.9)	2 (5.0)	0 (0)	0 (0)
None	33 (63)	23 (57)	36 (65)	20 (77)
Pre-lymphodepletion marrow abnormal B-cells (%) – median (IQR) [range]	0 (0, 2) [0 – 98]	10 (0, 59) [0 – 92]	24 (0, 58) [0 – 96]	75 (18, 86) [0 – 98]
Pre-lymphodepletion ANC (x 10^3/μl) – median (IQR) [range]	2.46 (1.61, 3.51) [0.17-12.4]	2.92 (1.20, 5.00) [0 – 23.17]	2.50 (1.40, 4.72) [0 – 13.65]	1.95 (0.68, 2.54) [0 – 8.06]
Pre-lymphodepletion ALC (x 10^3/μl) – median (IQR) [range]	0.6 (0.4, 1.4) [0.3 – 32.6]	1.0 (0.7, 2.4) [0.1 – 11.4]	1.0 (0.6, 1.6) [0.2 – 58.9]	0.9 (0.3, 2.1) [0 – 42.8]
Pre-lymphodepletion Hgb (g/dL) – median (IQR) [range]	11.1 (9.8, 12.6) [7.5 – 15.0]	10.7 (9.6, 11.6) [7.4 – 16.0]	11.0 (10.0, 12.4) [8.9 – 15.1]	10.2 (9.3, 11.8) [7.2 – 13.9]
Pre-lymphodepletion Plt (x 10^3/μl) – median (IQR) [range]	128 (80, 197) [9 – 448]	119 (66, 200) [7 – 339]	139 (84, 212) [10 – 434]	66 (36, 141) [11 – 212]
Lymphodepletion – n (%)				
High-intensity CyFlu	22 (42)	20 (50)	25 (45)	13 (50)
Low-intensity CyFlu	21 (40)	13 (32)	24 (44)	8 (31)
Non-CyFlu	9 (17)	7 (18)	6 (11)	5 (19)
CAR-T cell dose – n (%)				
DL1	12 (23)	10 (25)	16 (29)	9 (35)
DL2	37 (71)	29 (72)	36 (65)	12 (46)
DL3	3 (5.8)	1 (2.5)	3 (5.5)	5 (19)
Neurotoxicity grade – n (%)				
0-1	52 (100)	31 (78)	33 (60)	5 (19)
2-3	0 (0)	9 (22)	22 (40)	14 (54)
4-5	0 (0)	0 (0)	0 (0)	7 (27)

High-intensity CyFlu, cyclophosphamide (Cy) 60 mg/kg or >1500 mg/m^2 with fludarabine (Flu) 75-125 mg/m^2; low-intensity CyFlu, Cy 30 mg/kg or ≤1500 mg/m^2 with Flu 75-90 mg/m^2; Non-CyFlu, any conditioning regimen other than as noted above including single agent Cy or Flu. CAR-T cell dose level (DL) - DL1 = 2 x 10^5 cells/kg, DL2 = 2 x 10^6 cells/kg, DL3 = 2 x 10^7 cells/kg. CRS grade as defined by Lee criteria[1]. Neurotoxicity grade as defined by CTCAE 4.0.3. HSCT, hematopoietic stem cell transplant; IQR, interquartile range; LD, lymphodepletion.

Supplemental Table S2. Lymphodepletion regimens prior to CAR T-cell infusion

Lymphodepletion Regimen	Number of Patients
Cyclophosphamide 2 g/m^2 Day 1; Etoposide 200 mg/m^2 Days 2-4	2
Cyclophosphamide 3 g/m^2 Day 1; Etoposide 200 mg/m^2 Days 2-4	2
Cyclophosphamide 4 g/m^2 Day 1; Etoposide 200 mg/m^2 Days 2-4	3
Cyclophosphamide 2 g/m^2 Day 1	14
Cyclophosphamide 3 g/m^2 Day 1	2
Cyclophosphamide 4 g/m^2 Day 1	1
Fludarabine 25 mg/m^2 Day 1-3	2
Cyclophosphamide 30 mg/kg Day 1; Fludarabine 25 mg/m^2 Day 2-4	5
Cyclophosphamide 60 mg/kg Day 1; Fludarabine 25 mg/m^2 Day 2-4	66
Cyclophosphamide 60 mg/kg Day 1; Fludarabine 25 mg/m^2 Day 2-6	12
Cyclophosphamide 1 g/m^2 Day 1; Fludarabine 25 mg/m^2 Day 2-4	1
Cyclophosphamide 3 g/m^2 Day 1; Fludarabine 25 mg/m^2 Day 2-4	1
Cyclophosphamide 300 mg/m^2 and Fludarabine 30 mg/m^2 Day 1-3	59
Cyclophosphamide 300 mg/m^2 and Fludarabine 20 mg/m^2 Day 1-3	1
Cyclophosphamide 500 mg/m^2 and Fludarabine 30 mg/m^2 Day 1-3	2
Total	**173**

Supplemental Table S3. Univariate analysis of patient, disease, and treatment variables (A, C) and serum cytokine levels (B, D) affecting ANC (A, B) and platelet recovery (C, D).

A. Day-28 ANC recovery

Variable	Coefficient	Standard Error	Test Statistics	p-value	95% CI
Pre-LD platelet	0.612	0.101	6.09	0	0.414 - 0.811
Bone marrow disease burden	-0.074	0.025	-2.967	3.46E-03	-0.123 - -0.025
NHL	0.272	0.099	2.751	6.63E-03	0.077 - 0.467
CAR-T dose level	0.212	0.077	2.737	6.90E-03	0.059 - 0.364
CRS grade	-0.093	0.037	-2.519	1.27E-02	-0.167 - -0.02
Ferritin MI	-0.139	0.062	-2.242	2.63E-02	-0.261 - -0.017
Age	0.006	0.003	2.117	3.58E-02	0 - 0.012
CLL	0.198	0.106	1.873	6.28E-02	-0.011 - 0.406
Pre-LD ANC	0.024	0.014	1.757	8.08E-02	-0.003 - 0.051
PT MI	-0.072	0.042	-1.689	9.32E-02	-0.155 - 0.012
Prior allogeneic HSCT	-0.149	0.102	-1.465	1.45E-01	-0.35 - 0.052
Prior autologous HSCT	0.164	0.118	1.386	1.68E-01	-0.07 - 0.398
ICANS grade	-0.036	0.033	-1.067	2.88E-01	-0.102 - 0.03
Female sex	0.07	0.092	0.765	4.45E-01	-0.111 - 0.252
Number of prior treatments	-0.014	0.02	-0.71	4.79E-01	-0.053 - 0.025
Pre-LD ALC	-0.016	0.077	-0.201	8.41E-01	-0.168 - 0.137
PTT MI	0	0.009	-0.041	9.67E-01	-0.018 - 0.017

B. Serum cytokine levels and day-28 ANC recovery

Variable	Coefficient	Standard Error	Test Statistics	p-value	95% CI
Pre-LD platelet	0.612	0.101	6.09	0	0.414 - 0.811
TGF-beta-1	0.527	0.11	4.804	3.50E-06	0.31 - 0.744
IL-6	-0.222	0.046	-4.783	3.90E-06	-0.314 - -0.131
IL-8	-0.22	0.065	-3.371	9.36E-04	-0.349 - -0.091
MCP-1	-0.254	0.083	-3.052	2.66E-03	-0.418 - -0.089
IL-2R-alpha	-0.189	0.067	-2.832	5.21E-03	-0.321 - -0.057
sTNFR1 (p55)	-0.386	0.152	-2.544	1.19E-02	-0.686 - -0.086
IL-10	-0.149	0.059	-2.53	1.24E-02	-0.264 - -0.033
IL-18	-0.159	0.074	-2.146	3.33E-02	-0.306 - -0.013
IFN-gamma	-0.111	0.052	-2.146	3.34E-02	-0.214 - -0.009
IL-6R	-0.362	0.176	-2.053	4.16E-02	-0.71 - -0.014
TIM-3	-0.178	0.087	-2.036	4.34E-02	-0.351 - -0.005
IL-15	-0.249	0.134	-1.862	6.44E-02	-0.513 - 0.015
Pre-LD ANC	0.024	0.014	1.757	8.08E-02	-0.003 - 0.051
sTNFR1 (p75)	-0.203	0.124	-1.642	1.02E-01	-0.448 - 0.041
MIP-1	-0.14	0.09	-1.556	1.22E-01	-0.319 - 0.038
IL-2	-0.156	0.103	-1.515	1.32E-01	-0.359 - 0.047

C. Day-28 platelet recovery

Variable	Coefficient	Standard Error	Test Statistics	p-value	95% CI
Pre-LD platelet	0.526	0.071	7.44	0	0.386 - 0.666
CRS grade	-0.092	0.027	-3.415	8.07E-04	-0.145 - -0.039
Number of prior treatments	-0.037	0.014	-2.632	9.32E-03	-0.066 - -0.009
Bone marrow disease burden	-0.04	0.018	-2.189	3.00E-02	-0.077 - -0.004
NHL	0.14	0.073	1.907	5.83E-02	-0.005 - 0.285
Ferritin MI	-0.085	0.046	-1.865	6.41E-02	-0.176 - 0.005
ICANS grade	-0.04	0.024	-1.636	1.04E-01	-0.088 - 0.008
Prior allogeneic HSCT	-0.121	0.075	-1.627	1.06E-01	-0.269 - 0.026
PT MI	-0.039	0.031	-1.246	2.15E-01	-0.101 - 0.023
Pre-LD ANC	0.012	0.01	1.171	2.43E-01	-0.008 - 0.032
Age	0.002	0.002	1.018	3.10E-01	-0.002 - 0.007
Pre-LD ALC	0.057	0.057	1.013	3.13E-01	-0.054 - 0.169
CAR-T dose level	0.045	0.058	0.776	4.39E-01	-0.069 - 0.159
Female sex	-0.04	0.068	-0.592	5.54E-01	-0.173 - 0.093
Prior autologous HSCT	0.044	0.087	0.498	6.19E-01	-0.129 - 0.216
PTT MI	0	0.007	-0.055	9.56E-01	-0.013 - 0.012
CLL	-0.003	0.078	-0.037	9.70E-01	-0.158 - 0.152

D. Serum cytokine levels and day-28 platelet recovery

Variable	Coefficient	Standard Error	Test Statistics	p-value	95% CI
TGF-beta-1	0.642	0.07	9.198	0	0.504 - 0.78
Pre-LD platelet	0.526	0.071	7.44	0	0.386 - 0.666
IL-18	-0.22	0.052	-4.191	4.55E-05	-0.324 - -0.116
sTNFR1 (p55)	-0.448	0.108	-4.146	5.44E-05	-0.661 - -0.235
IL-6	-0.141	0.035	-4.046	8.03E-05	-0.209 - -0.072
IL-7	0.408	0.114	3.585	4.46E-04	0.183 - 0.633
IL-10	-0.127	0.043	-2.97	3.43E-03	-0.212 - -0.043
sTNFR1 (p75)	-0.256	0.089	-2.859	4.81E-03	-0.432 - -0.079
IFN-gamma	-0.102	0.038	-2.709	7.48E-03	-0.177 - -0.028
IL-2R-alpha	-0.121	0.049	-2.457	1.51E-02	-0.219 - -0.024
IL-15	-0.204	0.098	-2.079	3.92E-02	-0.397 - -0.01
TIM-3	-0.118	0.064	-1.833	6.86E-02	-0.245 - 0.009
IL-6R	-0.221	0.13	-1.697	9.16E-02	-0.478 - 0.036
IL-8	-0.079	0.049	-1.607	1.10E-01	-0.176 - 0.018
Fas	-0.164	0.109	-1.502	1.35E-01	-0.379 - 0.052
MCP-1	-0.087	0.062	-1.387	1.67E-01	-0.21 - 0.037
Pre-LD ANC	0.012	0.01	1.171	2.43E-01	-0.008 - 0.032

Supplemental Table S4. Tocilizumab

A. Tocilizumab use

Tocilizumab administrations	Number of patients (%)
0	139 (80)
1	23 (13.3)
2	7 (4)
3	2 (1.2)
4	3 (1.7)

B: Sensitivity analysis - IL6 serum concentrations and tocilizumab administrations

ANC Recovery

Variable	Univariate		Multivariate (IL6+Toci_n)		Multivariate (IL6+Toci_n+IL6*Toci_n)	
	beta	p-value	beta	p-value	beta	p-value
IL6	-0.22	$3.9e^{-6}$	-0.26	$7.9e^{-6}$	-0.28	$1.6e^{-5}$
Toci_n	-0.11	0.12	0.08	0.29	-0.086	0.68
IL6*Toci_n					0.067	0.38

Plt Recovery

Variable	Univariate		Multivariate (IL6+Toci_n)		Multivariate (IL6+Toci_n+IL6*Toci_n)	
	beta	p-value	beta	p-value	beta	p-value
IL6	-0.14	$8.0e^{-5}$	-0.12	0.004	-0.10	0.03
Toci_n	-0.14	0.006	-0.05	0.41	0.066	0.67
IL6*Toci_n					-0.045	0.43

Toci_n (number of tocilizumab administrations); IL6 (peak serum IL6 level)

Supplemental Table S5. Proportion of variables missing values

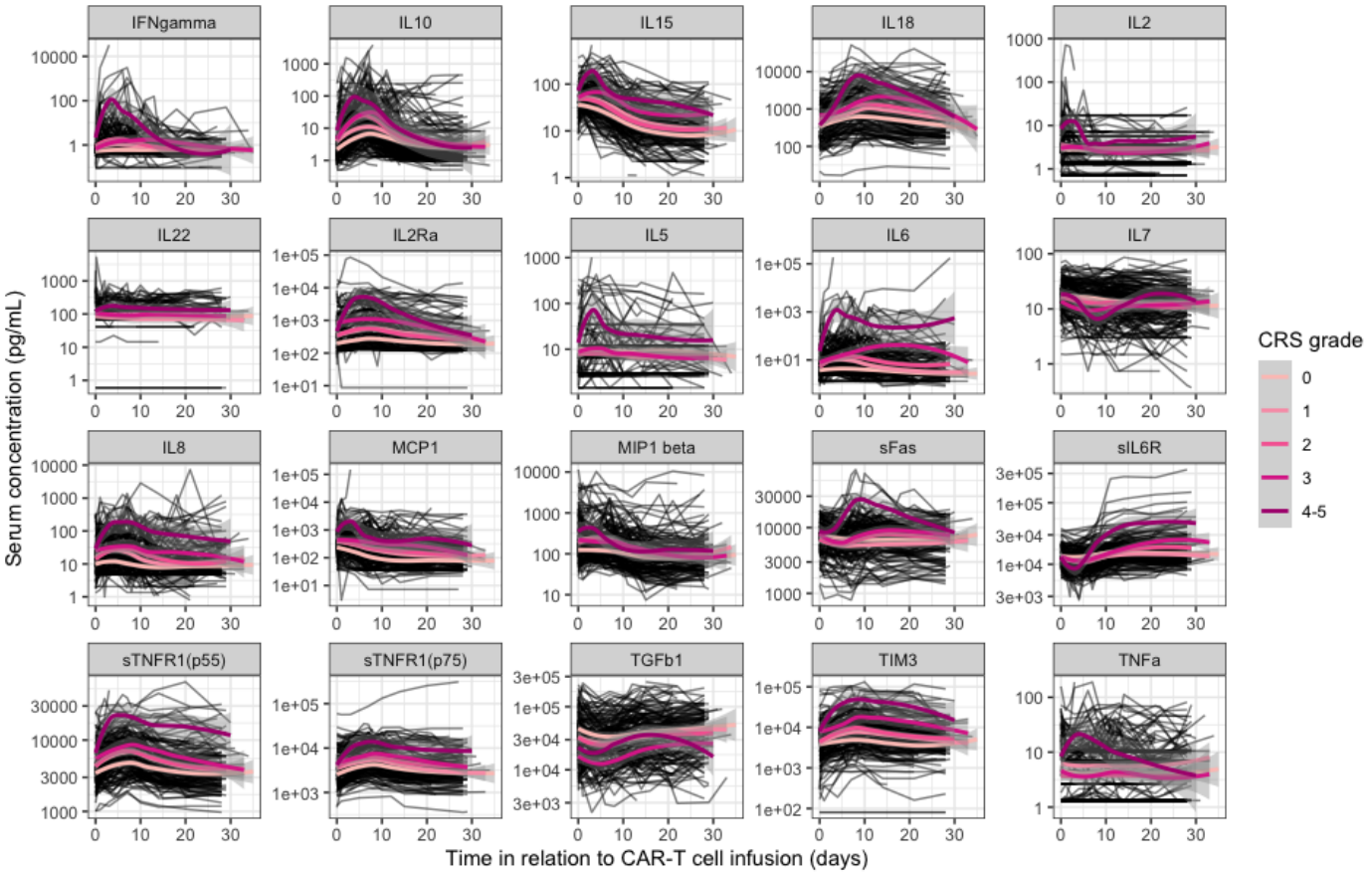
Variable	Number `	Proportion
D-dimer	72	0.44
CRP	66	0.4
Fibrinogen	57	0.35
Pre-LD PTT	39	0.24
Pre-LD PT	38	0.23
Pre-LD ferritin	34	0.21
IL-5	16	0.1
sTNFR1 (p75)	16	0.1
IL-22	15	0.09
Fas	15	0.09
MCP-1	10	0.06
TGF-beta-1	9	0.05
IL-15	9	0.05
IL-18	9	0.05
sTNFR1 (p55)	7	0.04
MIP-1	4	0.02
TIM-3	2	0.01
IL-2	1	0.01
IL-2R-alpha	1	0.01
IL-7	1	0.01
IL-8	1	0.01
IL-6R	1	0.01
TNF-alpha	1	0.01
Pre-LD ALC	1	0.01
Bone marrow disease burden	1	0.01
IFN-gamma	0	0
IL-10	0	0
IL-6	0	0
Female sex	0	0
Age	0	0
CLL	0	0
NHL	0	0
Prior allogeneic HSCT	0	0
Prior autologous HSCT	0	0
ICANS grade	0	0
CRS grade	0	0
Number of prior treatments	0	0
Pre-LD ANC	0	0
Pre-LD platelet	0	0
CAR-T dose level	0	0

Supplemental Table S6: Patient and treatment characteristics by ANC or platelet recovery

Hematopoietic Recovery	ANC Recovery n=157 (90.1%)	ANC Non-Recovery n=16 (9.2%)	Platelet Recovery n=148 (86%)	Platelet Non-recovery n=25 (14.5%)
Age (years) – median (IQR) [range]	55 (43, 64) [20 – 76]	50 (37, 58) [20 – 70]	55 (44, 64) [20 – 76]	52 (35, 59) [20 – 76]
Sex – n (%)				
Female	54 (34)	4 (25)	51 (34)	7 (28)
Male	103 (66)	12 (75)	97 (66)	18 (72)
Race – n (%)				
White	137 (87)	14 (88)	127 (86)	24 (96)
Non-white	19 (12)	2 (12)	20 (14)	1 (4.0)
Unknown	1 (0.6)	0 (16)	1 (0.7)	0 (0)
Disease Type (n, %)				
ALL	53 (34)	9 (56)	51 (34)	11 (44)
CLL	42 (27)	6 (38)	40 (27)	8 (32)
NHL	62 (39)	1 (6.2)	57 (39)	6 (24)
Number of prior therapies – median (IQR) [range]	4 (3, 5) [1 – 11]	5 (3, 7) [2 – 10]	4 (3. 5) [1 – 11]	5 (4, 6) [2 – 10]
Prior HSCT – n (%)				
Allogeneic	31 (20)	4 (25)	28 (19)	7 (28)
Autologous	23 (15)	0 (0)	20 (14)	3 (12)
Both	3 (1.9)	0 (0)	3 (2.0)	0 (0)
None	100 (64)	12 (75)	97 (66)	15 (60)
Pre-lymphodepletion marrow abnormal B-cells (%) – median (IQR) [range]	3 (0, 55) [0 – 98]	52 (30, 80) [0 – 96]	4 (0, 50) [0 – 98]	40 (0, 87) [0 – 96]
Pre-lymphodepletion ANC (x 10^3/µl) – median (IQR) [range]	2.50 (1.39, 4.36) [0 – 23.17]	1.06 (0.20, 2.53) [0 – 6.91]	2.62 (1.41, 4.47) [0 – 23.17]	1.67 (0.59, 2.41) [0 – 8.06]
Pre-lymphodepletion ALC (x 10^3/µl) – median (IQR) [range]	0.9 (0.5, 1.7) [0 – 58.9]	0.9 (0.7, 1.1) [0.1 – 42.8]	0.9 (0.5, 1.8) [0 – 58.9]	0.8 (0.4, 1.1) [0 – 42.8]
Pre-lymphodepletion Hgb (g/dL) – median (IQR) [range]	10.8 (9.8, 12.1) [7.2 – 16]	10.5 (9.5, 12.3) [7.3 – 14.1]	11.00 (9.9, 12.3) [7.3 – 16.0]	10.3 (9.6, 10.7) [7.2 – 14.0]
Pre-lymphodepletion Plt (x 10^3/µl) – median (IQR) [range]	129 (76, 200) [9 – 448]	36 (22, 94) [7 – 261]	139 (83, 202) [9 – 448]	36 (22, 108) [7 – 412]
Lymphodepletion – n (%)				
High-intensity CyFlu	75 (48)	5 (31)	71 (48)	9 (36)
Low-intensity CyFlu	58 (37)	8 (50)	55 (37)	11 (44)
Non-CyFlu	24 (15)	3 (19)	22 (15)	5 (20)
CAR-T cell dose – n (%)				
DL1	41 (26)	6 (38)	38 (26)	9 (36)
DL2	105 (67)	9 (56)	102 (69)	12 (48)
DL3	11 (7.0)	1 (6.2)	8 (5.4)	4 (16)
CRS grade – n (%)				
0	51 (32)	1 (6.2)	48 (32)	4 (16)
1	36 (23)	4 (25)	36 (24)	4 (16)
2	50 (32)	5 (31)	48 (32)	7 (28)
3-5	20 (13)	6 (38)	16 (11)	10 (40)
Neurotoxicity grade – n (%)				
0-1	112 (71)	9 (56)	105 (71)	16 (64)
2-3	42 (27)	3 (19)	41 (28)	4 (16)
4-5	3 (1.9)	4 (25)	2 (1.4)	5 (20)

High-intensity CyFlu, cyclophosphamide (Cy) 60 mg/kg or >1500 mg/m^2 with fludarabine (Flu) 75-125 mg/m^2; low-intensity CyFlu, Cy 30 mg/kg or ≤1500 mg/m^2 with Flu 75-90 mg/m^2; Non-CyFlu, any conditioning regimen other than as noted above including single agent Cy or Flu. CAR-T cell dose level (DL) - DL1 = 2 x 10^5 cells/kg, DL2 = 2 x 10^6 cells/kg, DL3 = 2 x 10^7 cells/kg. CRS grade as defined by Lee criteria[1]. Neurotoxicity grade as defined by CTCAE 4.0.3. HSCT, hematopoietic stem cell transplant; IQR, interquartile range; LD, lymphodepletion.

Supplemental Figure S1. Kinetics of cytokines following CAR T-cell infusion

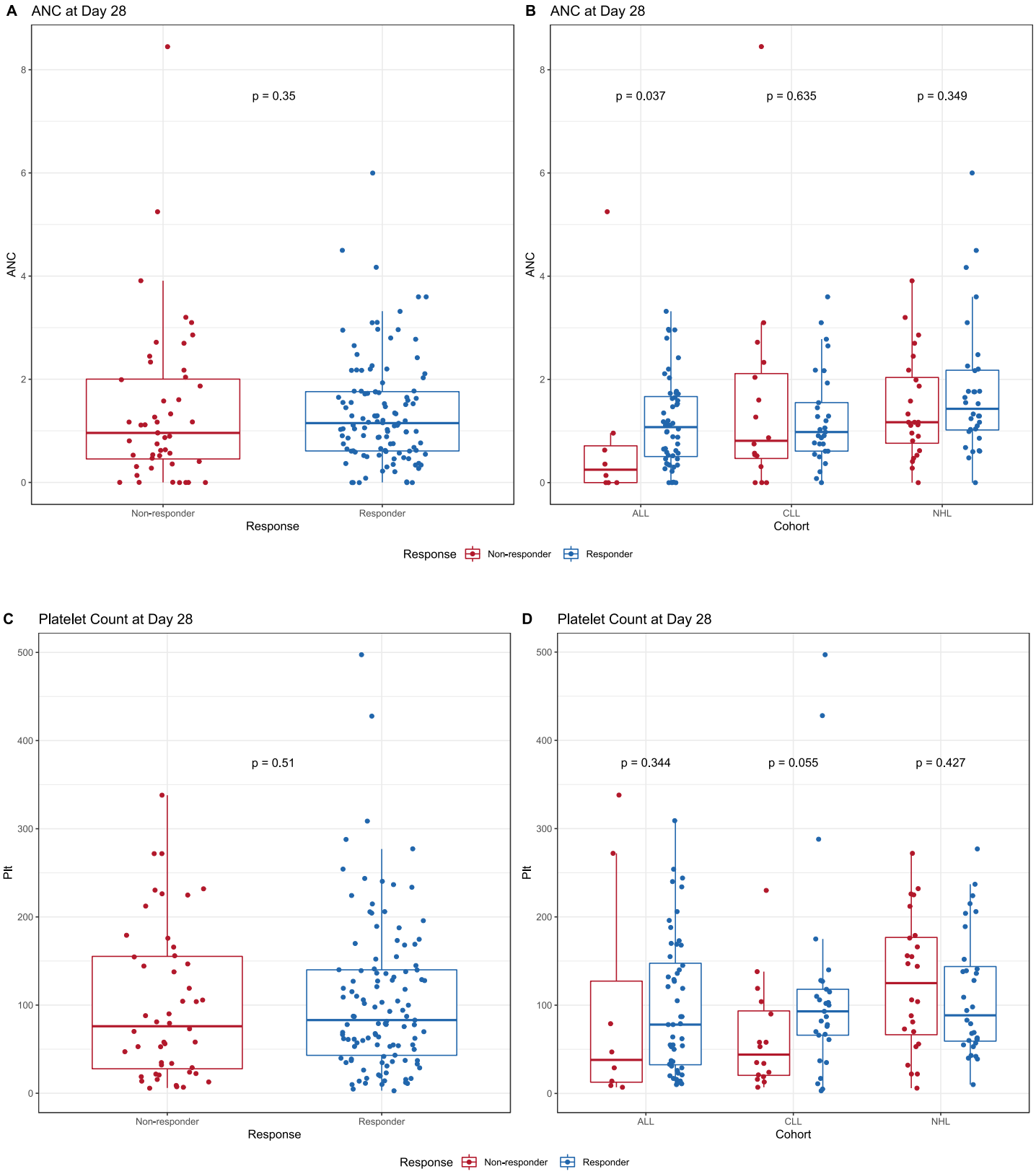


Serum concentration (pg/mL) of various cytokines at the indicated times following CAR T-cell infusion for all patients in study cohort (black lines). Non-parametric smoothing using locally estimated scatterplot smoothing (LOESS) stratified by CRS-grade.

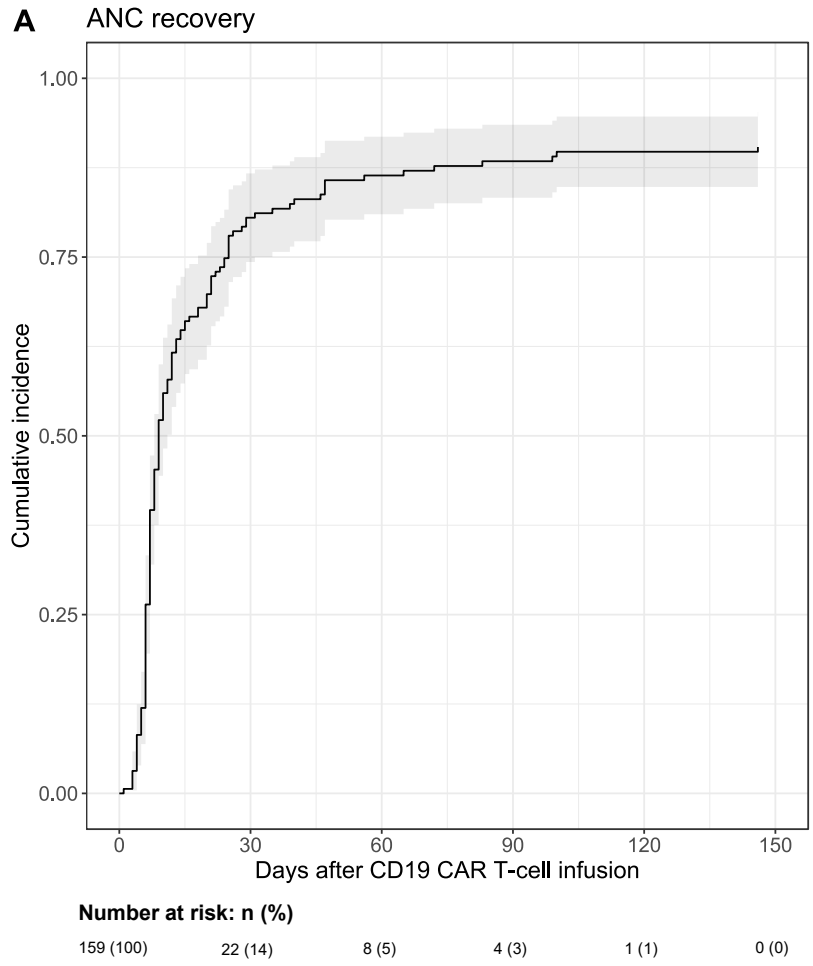
Supplemental References

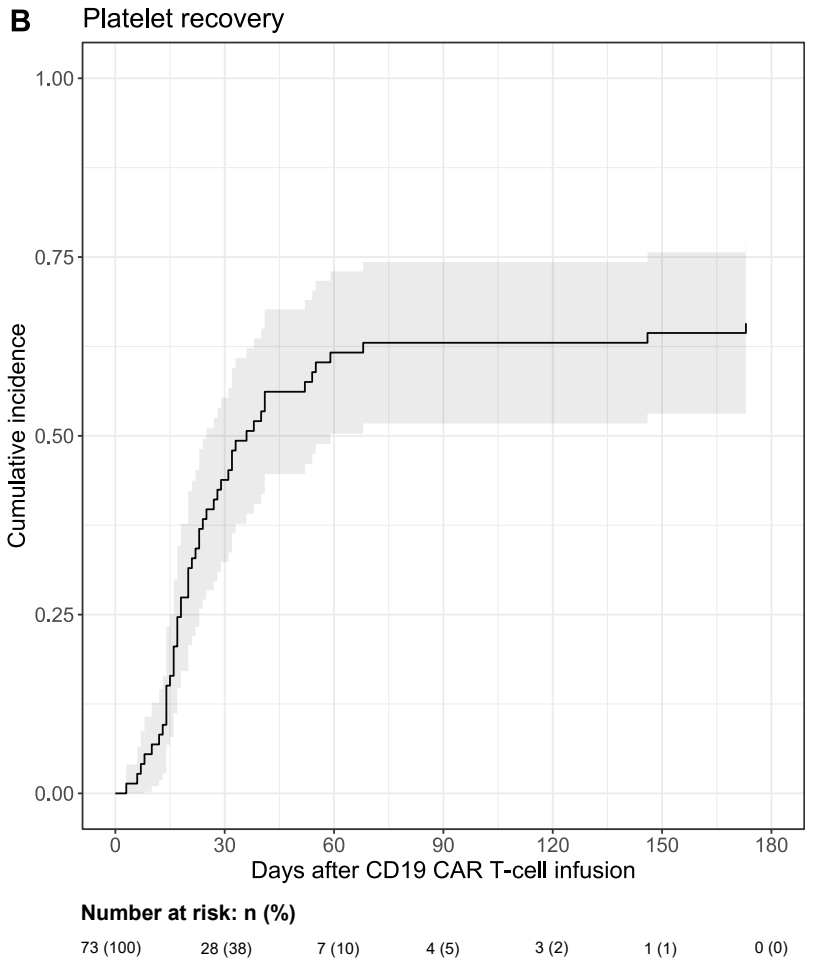
1. Lee DW, Gardner R, Porter DL, et al. Current concepts in the diagnosis and management of cytokine release syndrome. *Blood*. 2014;124(2):188-195.

Supplementary Figure S2. Day 28 ANC and Platelet Count by Response Status

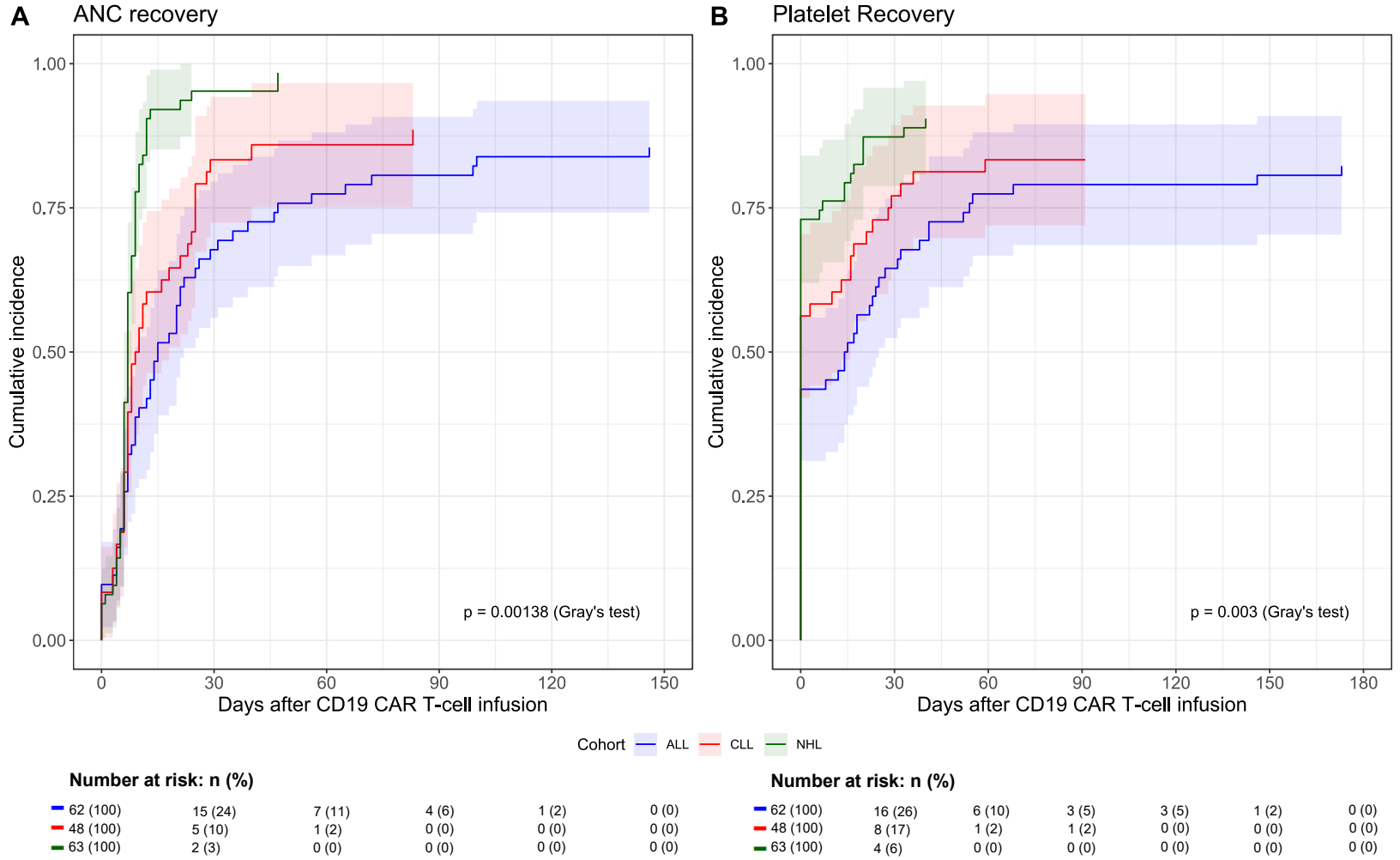


Supplemental Figure S3. Cumulative Incidence of Hematopoietic Recovery





Supplemental Figure S4. Cumulative Incidence of Hematopoietic Recovery by Disease Cohort



Number at risk: n (%)

62 (100)	15 (24)	7 (11)	4 (6)	1 (2)	0 (0)
48 (100)	5 (10)	1 (2)	0 (0)	0 (0)	0 (0)
63 (100)	2 (3)	0 (0)	0 (0)	0 (0)	0 (0)

Number at risk: n (%)

62 (100)	16 (26)	6 (10)	3 (5)	3 (5)	1 (2)	0 (0)
48 (100)	8 (17)	1 (2)	1 (2)	0 (0)	0 (0)	0 (0)
63 (100)	4 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)