Supplementary

Tables

Supplemental Table S1: Panel of antibodies used in peripheral blood flow cytometry.

Antibody/recombiant protein	Fluorochrome	Catalogue number	Vendor
BCMA/TNFRSF17 Fc	Alexa Fluor® 488	AFG193	R&D systems
CD2	BV421	562667	BD Horizon
CD3	Pe-Cy7	340948	BD Biosciences
CD5	PerCP-Cy5-5	341099	BD Biosciences
CD7	APC	17-0079-42	Invitrogen
CD8	APC-H7	6607102	Beckman-Coulter/immunotech
CD57	PE	560844	BD Pharmingen

Supplemental Table S2 Absolute Lymphocyte Count (ALC) variables after BCMA CAR-T treatment.

Variable	Overall N = 156[1]	Ide-cel N = 65[1]	Cilta-cel N = 91[1]	p-value[2]
Maximum ALC (cel/uL)	1.26 (0.65 - 2.7)	0.8 (0.5 - 1.1)	2 (0.9 - 4.4)	<0.001
Absolute Lymphocytosis (ALC_{max} >3.74 x10^3/uL)				
Had absolute lymphocytosis	29 (19)	0 (0.0)	29 (32)	<0.001
No absolute lymphocytosis	127 (81)	65 (100)	62 (68)	
ALC_{max} >1.0 x10^3/uL				
ALC_{max} ≤ 1.0 x 10^3 cel/uL	70 (45)	46 (71)	24 (26)	<0.001
ALC_{max} > 1.0 x 10^3 cel/uL	86 (55)	19 (29)	66 (74)	
ALC_{max} within above lower limit range (>1.17 cel/uL)				
No Normal ALC during day 0-15	76 (49)	49 (75)	27 (30)	<0.001
Normal ALC during day 0-15	80 (51)	16 (25)	64 (70)	
Absolute ALC Change	1.28 (0.6 - 2.9)	0.77 (0.4 - 1.1)	2.1 (0.9 - 4.4)	<0.001

Absolute Lymphocyte Count (ALC), ALC_{max} ($_{max}$imum ALC during day 0-15), interquartile range (IQR)

[1]Median (IQR); n (%)

[2]Wilcoxon rank sum test; Pearson's Chi-squared test

Univariable Regression - Max Absolute Lymphocyte Count

	Cilta-cel				Ide-cel			
Characteristic	**N**	**exp(Beta)**	**95% CI[1]**	**p-value**	**N**	**exp(Beta)**	**95% CI[1]**	**p-value**
Age at CAR-T Infusion	91	1.01	0.94 to 1.09	0.70	65	1.01	1.00 to 1.02	0.14
CRS after CAR-T	91			**0.013**	65			0.10
No		—	—			—	—	
Yes		12.6	1.69 to 93.0			1.38	0.94 to 2.03	
CRS Higest Grade	80			**0.007**	56			**0.040**
Grade I		—	—			—	—	
Grade II		13.5	2.02 to 89.6			1.09	0.77 to 1.56	
Grade III		28.1	1.57 to 504			2.31	1.21 to 4.42	
Grade IV		0.10	0.00 to 50.6					
ICANS after CAR-T	91			**0.009**	65			**0.038**
No		—	—			—	—	
Yes		13.0	1.90 to 88.8			1.57	1.03 to 2.40	
High-Risk Cytogenetics*	91			0.50	65			0.39
No High-Risk CG		—	—			—	—	
High-Risk CG		1.63	0.40 to 6.67			1.13	0.85 to 1.51	
Use of Tocilizumab after CAR-T	29			**0.027**	13			0.85
No		—	—			—	—	
Yes		16.9	1.39 to 206			1.06	0.58 to 1.93	
Number of Previous Lines	91	0.82	0.66 to 1.02	0.079	65	0.99	0.95 to 1.04	0.80
Non-Paraskeletal Extramedullary Disease	91			0.63	65			0.073
No Non-Paraskeletal EMD		—	—			—	—	
Non-Paraskeletal EMD		0.70	0.16 to 3.09			0.73	0.52 to 1.03	
Received Bispecific Agent prior to CAR-T	91	0.71	0.10 to 4.89	0.73	65	0.89	0.47 to 1.70	0.72
ISS_Stage	76			0.22	49			0.39
I		—	—			—	—	
II		0.24	0.04 to 1.47			1.12	0.77 to 1.63	
III		1.15	0.17 to 7.73			0.81	0.52 to 1.26	
Setting of CAR-T Administration	85			0.70	64			0.83
Commercial		—	—			—	—	
Other clinical trial (Non-OOS)		0.69	0.14 to 3.41			0.91	0.66 to 1.26	
Out-of-spec protocol/study		0.43	0.06 to 3.22			0.83	0.26 to 2.60	
Out-of-specification CAR-T	85			0.48	64			0.84
Non Out-of-spec		—	—			—	—	
Out-of-spec protocol/study		0.51	0.08 to 3.32			0.89	0.29 to 2.71	
Dose of CAR-T (based on FDA approved dose)	59			0.74	51			0.081
Lower than SOC Dose		—	—			—	—	
Standard of Care Dose		2.15	0.02 to 190			1.66	0.94 to 2.95	

High-Risk Cytogenetics: del 17p, t(4;14), t(14;16), gain 1q. Cytokine Release Syndrome (CRS), Immune effector cell-associated neurotoxicity syndrome (ICANS)

[1] CI = Confidence Interval

Supplemental Table S3: Univariable regression for max absolute lymphocyte count by BCMA CAR-T product.

Characteristic	N	HR[1]	95% CI[1]	p-value	q-value[2]
ALCmax	155	0.83	0.72 to 0.95	**0.002**	**0.011**
Age at CAR-T infusion	155	0.97	0.95 to 1.00	**0.037**	**0.053**
ISS Staging	124			0.55	0.57
I		—	—		
II		1.23	0.68 to 2.21		
III		0.83	0.43 to 1.63		
ALCmax levels	155			**<0.001**	**<0.001**
high		—	—		
Int		2.93	1.72 to 4.99		
low		6.00	3.27 to 11.0		
Bone marrow plasmacytosis	123	1.01	1.00 to 1.02	**0.044**	**0.060**
M-protein	149	1.25	1.01 to 1.55	**0.049**	**0.062**
FLC ratio	153	1.00	1.00 to 1.00	**0.036**	**0.053**
Ferritin pre-lymphodepletion	155	1.00	1.00 to 1.00	**0.006**	**0.018**
D-dimer pre-lymphodepletion	98	1.55	1.09 to 2.19	**0.021**	**0.041**
C reactive protein pre-lymphodepletion	150	1.35	1.10 to 1.66	**0.010**	**0.028**
ALC~max~ > 1x10^3/uL	155			**<0.001**	**<0.001**
ALC <= 1 x 10^3 cel/uL		—	—		
ALC > 1 x 10^3 cel/uL		0.27	0.17 to 0.44		
Previous transplant	155	1.60	0.80 to 3.22	0.16	0.19
Out of specification product	148			0.70	0.70
No		—	—		
Yes		1.21	0.48 to 3.06		
ALC~max~ <= 0.5x10^3/uL	155			**<0.001**	**<0.001**
ALC > 0.5 x 10^3 cel/uL		—	—		
ALC <= 0.5 x 10^3 cel/uL		3.84	2.25 to 6.53		
Last line Alkylating Chemotherapy	153	1.68	1.05 to 2.70	**0.035**	**0.053**
bendamustine	153	3.23	1.47 to 7.11	**0.012**	**0.029**
cyclophosphamide	153	1.83	1.12 to 2.98	**0.020**	**0.041**
High-Risk Cytogenetics	155			**0.024**	**0.042**
No High-Risk CG		—	—		
High-Risk CG		1.75	1.06 to 2.91		
CAR-T product	155			**0.003**	**0.012**
Abecma		—	—		
Carvykti		0.51	0.32 to 0.80		
Cytokine Release Syndrome (CRS) during admission	155			0.50	0.55
No		—	—		
Yes		0.80	0.42 to 1.52		
ICANS during admission	155			0.34	0.39
No		—	—		
Yes		1.40	0.72 to 2.73		
Non-Paraskeletal EMD	155			**<0.001**	**0.002**
No Non-Paraskeletal EMD		—	—		
Non-Paraskeletal EMD		2.49	1.55 to 3.99		
Number of previous lines	155	1.08	1.02 to 1.15	**0.012**	**0.029**

[1] HR = Hazard Ratio, CI = Confidence Interval

[2] False discovery rate correction for multiple testing

Supplemental Table S4A: Univariable Analysis for Progression Free Survival in patients with >1 month of Follow-up.

Supplemental Table S5B: Univariable Analysis for Progression Free Survival in patients with >1 month of Follow-up and according to the CAR-T product received.

Univariable Cox PFS

	PFS - Carvikty					PFS - Abecma				
Characteristic	**N**	**HR[1]**	**95% CI[1]**	**p-value**	**q-value[2]**	**N**	**HR[1]**	**95% CI[1]**	**p-value**	**q-value[2]**
ALCmax	91	0.94	0.82 to 1.08	0.37	0.43	65	0.43	0.21 to 0.86	**0.010**	**0.042**
ALCmax tiles	91			**0.010**	**0.026**	65			**0.006**	**0.035**
1		—	—				—	—		
2		0.31	0.13 to 0.71				0.46	0.22 to 0.94		
3		0.37	0.16 to 0.84				0.28	0.13 to 0.62		
ALC~max~ > 1x10^3/uL	91			**<0.001**	**<0.001**	65			**0.018**	**0.057**
ALC <= 1 x 10^3 cel/uL		—	—				—	—		
ALC > 1 x 10^3 cel/uL		0.24	0.11 to 0.48				0.45	0.22 to 0.91		
ALC~max~ <= 0.5x10^3/uL	91			**0.016**	**0.032**	65			**0.001**	**0.024**
ALC > 0.5 x 10^3 cel/uL		—	—				—	—		
ALC <= 0.5 x 10^3 cel/uL		4.09	1.52 to 11.0				3.07	1.59 to 5.96		
High-Risk Cytogenetics	91			0.19	0.25	65			0.077	0.18
No High-Risk CG		—	—				—	—		
High-Risk CG		1.62	0.77 to 3.40				1.81	0.91 to 3.59		
CRS during admission	91			0.84	0.90	65			0.79	0.96
No		—	—				—	—		
Yes		0.90	0.31 to 2.56				0.89	0.38 to 2.09		
ICANS during admission	91			0.14	0.20	65			0.86	0.96
No		—	—				—	—		
Yes		2.06	0.85 to 5.01				1.09	0.43 to 2.77		
Non-Paraskeletal EMD	91			**<0.001**	**<0.001**	65			0.21	0.34
No Non-Paraskeletal EMD		—	—				—	—		
Non-Paraskeletal EMD		3.91	1.97 to 7.77				1.61	0.79 to 3.27		
Age at CAR-T infusion	91	1.00	0.96 to 1.04	0.98	0.98	65	0.96	0.93 to 0.99	**0.007**	**0.035**
Number of previous lines	91	1.09	1.00 to 1.19	0.058	**0.093**	65	1.08	1.00 to 1.18	0.067	0.18
Bone marrow plasmacytosis	62	1.02	1.01 to 1.03	**0.007**	**0.021**	61	1.00	0.99 to 1.01	0.96	0.96
M-protein	85	1.24	0.90 to 1.70	0.20	0.25	65	1.25	0.92 to 1.69	0.17	0.33
FLC ratio	89	1.00	1.00 to 1.00	**<0.001**	**0.001**	65	1.00	1.00 to 1.00	0.62	0.83
Ferritin at baseline (Log)	91	2.08	1.54 to 2.82	**<0.001**	**<0.001**	65	1.10	0.88 to 1.38	0.41	0.60
C reactive protein (CRP)	90	1.48	1.05 to 2.09	**0.047**	**0.083**	61	1.21	0.93 to 1.57	0.18	0.33
Last line Alkylating Chemotherapy	89	2.63	1.27 to 5.43	**0.011**	**0.026**	65	0.96	0.52 to 1.80	0.91	0.96

[1] HR = Hazard Ratio, CI = Confidence Interval

[2] False discovery rate correction for multiple testing

Multivariable Cox DoR - All Patients

Characteristic	N	HR[1]	95% CI[1]	p-value
ALCmax >1 10^3/uL	137			
ALC <= 1 x 10^3 cel/uL 1		—	—	
ALC > 1 x 10^3 cel/uL		0.43	0.22 to 0.84	**0.013**
Non-Paraskeletal Extramedullary Disease	137			
No Non-Paraskeletal EMD		—	—	
Non-Paraskeletal EMD		2.03	1.10 to 3.74	**0.024**
CAR-T product	137			
Cilta-cel		—	—	
Ide-cel		2.02	1.03 to 3.99	**0.042**
Number of Previous Lines	137	1.04	0.97 to 1.13	0.28
High-risk cytogenetics*	137			
No High-Risk CG		—	—	
High-Risk CG		1.82	0.98 to 3.39	0.058

*High-Risk Cytogenetics: del 17p, t(4;14), t(14;16), or gain 1q

[1] HR = Hazard Ratio, CI = Confidence Interval

Supplemental Table S6: Multivariable Cox Proportional Hazard Model for Duration of Response (DoR) in BCMA CAR-T cohort.

Multivariable Regression of Achieving VGPR/CR by max ALC

Characteristic	OR[1]	95% CI[1]	p-value
ALCmax	1.37	1.07 to 1.94	0.037
Non-Paraskeletal Extramedullary Disease			
No Non-Paraskeletal EMD	—	—	
Non-Paraskeletal EMD	0.34	0.14 to 0.80	0.013

[1] OR = Odds Ratio, CI = Confidence Interval

Supplemental Table S7: Multivariable binomial regression for achieving VGPR/CR by ALC_{max} and presence of non-paraskeletal extramedullary disease.

Characteristic	Cilta-cel				Ide-cel			
	N	OR[1]	95% CI[1]	p-value	N	OR[1]	95% CI[1]	p-value
ALC max Group	62				56			
ALC <= 1 x 10^3 cel/uL		—	—			—	—	
ALC > 1 x 10^3 cel/uL		0.26	0.08 to 0.84	0.028		0.26	0.07 to 0.95	0.042

[1] OR = Odds Ratio, CI = Confidence Interval

Supplemental Table S8: Univariable logistic regression for no relapse at last follow up in patients with >6 months of follow up by CAR-T product.

Characteristic	OR[1]	95% CI[1]	p-value
ALCmax Group			
ALC <= 1 x 10^3 cel/uL	—	—	
ALC > 1 x 10^3 cel/uL	0.19	0.08 to 0.43	<0.001
Non-Paraskeletal EMD Status			
No Non-Paraskeletal EMD	—	—	
Non-Paraskeletal EMD	2.94	1.06 to 9.08	0.046

[1] OR = Odds Ratio, CI = Confidence Interval

Supplemental Table S8: Multivariable logistic regression for no relapse at last follow up in patients with >6 months of follow up by CAR-T product.

Characteristic	ALC <= 1 x 10^3 cel/uL 1, N = 70[1]	ALC > 1 x 10^3 cel/uL, N = 86[1]	p-value[2]
Age at CAR-T Infusion	61 (53 – 69)	63 (57 – 69)	0.25
Bone Marrow Plasma cells (%) pre-CAR-T	10 (2 – 40)	12 (2 – 45)	0.86
M-protein pre-CAR-T	0.92 (0.00 – 1.78)	0.30 (0.00 – 1.31)	0.20
Involved/Uninvolved Free Light at CAR-T	63 (5 – 308)	47 (5 – 266)	0.87
Lymphodepleting Conditioning			0.75
Bendamustine	5 (7.1)	5 (5.8)	
Flu/Cy	65 (93)	81 (94)	
Extramedullary Disease Previous to CAR-T			0.063
No Non-Paraskeletal EMD	48 (69)	70 (81)	
Non-Paraskeletal EMD	22 (31)	16 (19)	
ISS Stage at Diagnosis			0.32
I	19 (37)	36 (49)	
II	20 (39)	20 (27)	
III	12 (24)	18 (24)	
Previous Bispecific Use	8 (11)	8 (9.3)	0.66
High-risk Cytogenetics			0.79
No High-Risk CG	25 (36)	29 (34)	
High-Risk CG	45 (64)	57 (66)	
Cytotoxic Chemotherapy as most recent line before leukoapheresis	32 (46)	23 (27)	**0.018**
Last Line Contained Cyclophosphamide	25 (36)	18 (21)	**0.049**
Last Line Contained Bendamustine	7 (10)	1 (1.2)	**0.024**
Previous Autologous Stem Cell Transplant	61 (87)	72 (84)	0.55
ALC pre-lymphodepletion	0.70 (0.50 – 1.00)	1.00 (0.50 – 1.30)	**0.047**
ALC at day 0	0.04 (0.00 – 0.10)	0.04 (0.00 – 0.10)	0.86
Ferritin pre-lymphodepletion	170 (76 – 355)	143 (55 – 372)	0.53
C-Reactive Protein pre-lymphodepletion	0.40 (0.20 – 0.87)	0.39 (0.18 – 0.78)	0.33
D-Dimer Pre-lymphodepletion	0.71 (0.30 – 1.45)	0.55 (0.37 – 1.01)	0.37
Peak Ferritin day 0-30	536 (250 – 1,843)	1,040 (319 – 3,019)	0.12

High-Risk Cytogenetics: del 17p, t(4;14), t(14;16), gain 1q. Absolute Lymphocyte Count (ALC)

[1] Median (IQR); n (%)

[2] Wilcoxon rank sum test; Fisher's exact test; Pearson's Chi-squared test

Supplemental Table S9: Baseline characteristics across the three ALC_{max} subgroups (<= 1 and <= 1.0, and >1.0 $x10^3$/uL).

Characteristic	Infection Event, N = 33[1]	No Infection Event, N = 123[1]	p-value[2]
ALCmax day 0-15	1.40 (0.79 – 3.40)	1.25 (0.60 – 2.53)	0.20
ANCmax day 0-15	4.0 (2.4 – 5.5)	4.7 (2.7 – 7.1)	0.29
ALCmax >1 10^3/uL			0.75
ALC <= 1 x 10^3 cel/uL 1	14 (42)	56 (46)	
ALC > 1 x 10^3 cel/uL	19 (58)	67 (54)	
Number of Previous Lines of Treatment	5.0 (4.0 – 7.0)	5.0 (4.0 – 8.0)	0.70
Age at infusion CAR-T	66 (50 – 71)	62 (55 – 69)	0.68
Year of CAR-T Infusion			0.66
2017-2018	3 (9.1)	18 (15)	
2019-2021	12 (36)	48 (39)	
2022-2023	18 (55)	57 (46)	

Absolute Lymphocyte Count (ALC), Absolute Neutrophil Coun (ANC)

[1] Median (IQR); n (%)

[2] Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test

Supplemental Table S10: ALC and other baseline characteristics of patients who developed infection during the initial 30 day period compared to those without infection.

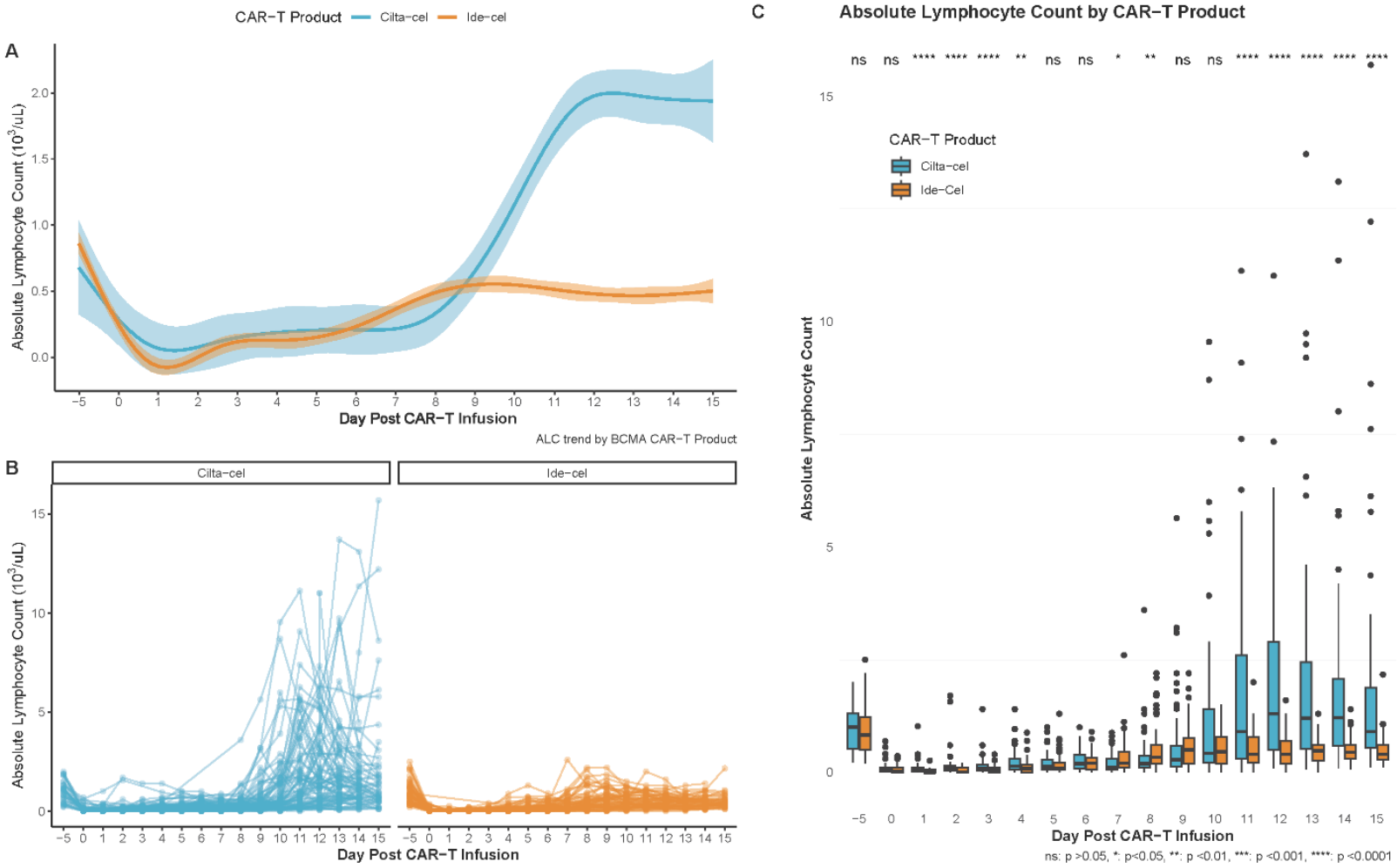
Characteristic	N = 33[1]
fungal	
No	33 (100)
bacterial	
No	26 (79)
Yes	7 (21)
viral	
No	21 (64)
Yes	12 (36)
Day after CAR-T of Infection	4 (1 – 17)
Receiving IVIG	
No	19 (58)
Yes	14 (42)
ANC at Infection Event	1.70 (0.90 – 2.50)
ALC at Infection Event	0.16 (0.03 – 0.40)

Absolute Neutrophil Count (ANC), Absolute Lymphocyte Count (ALC)

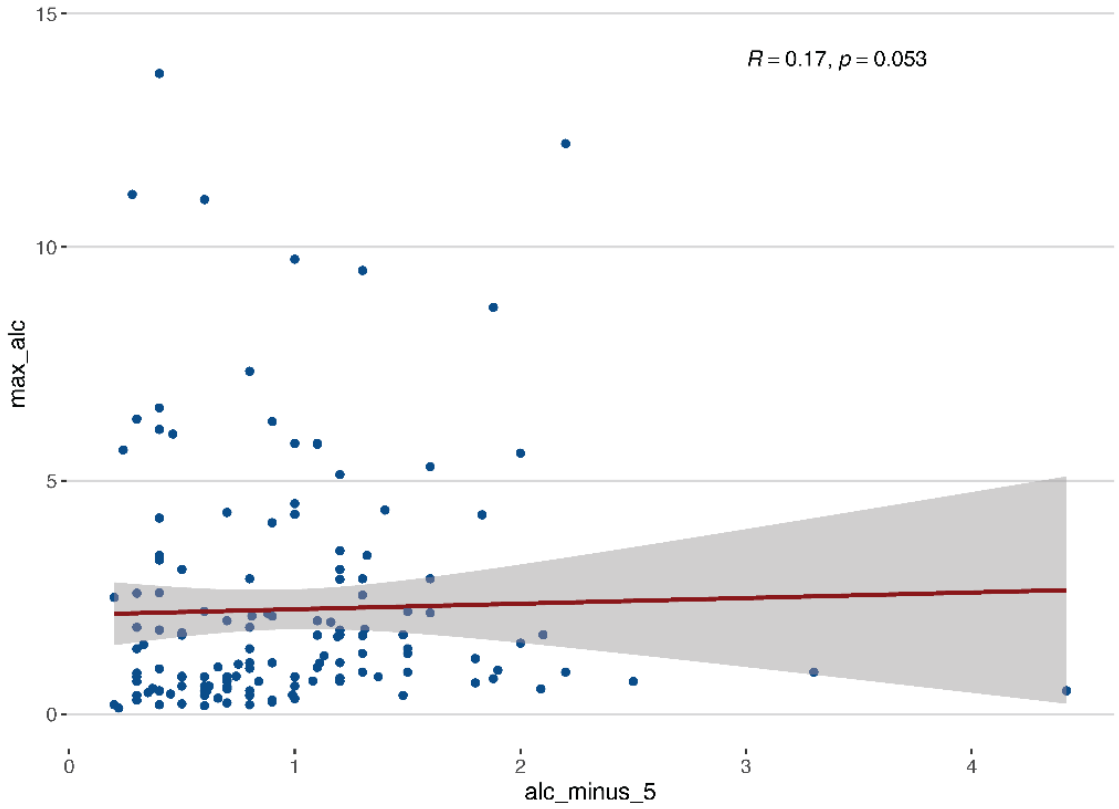
[1] n (%); Median (IQR)

Supplemental Table S11: Characteristics of non-neutropenic infectious event during the first 30 days in patients receiving BCMA CAR-T.

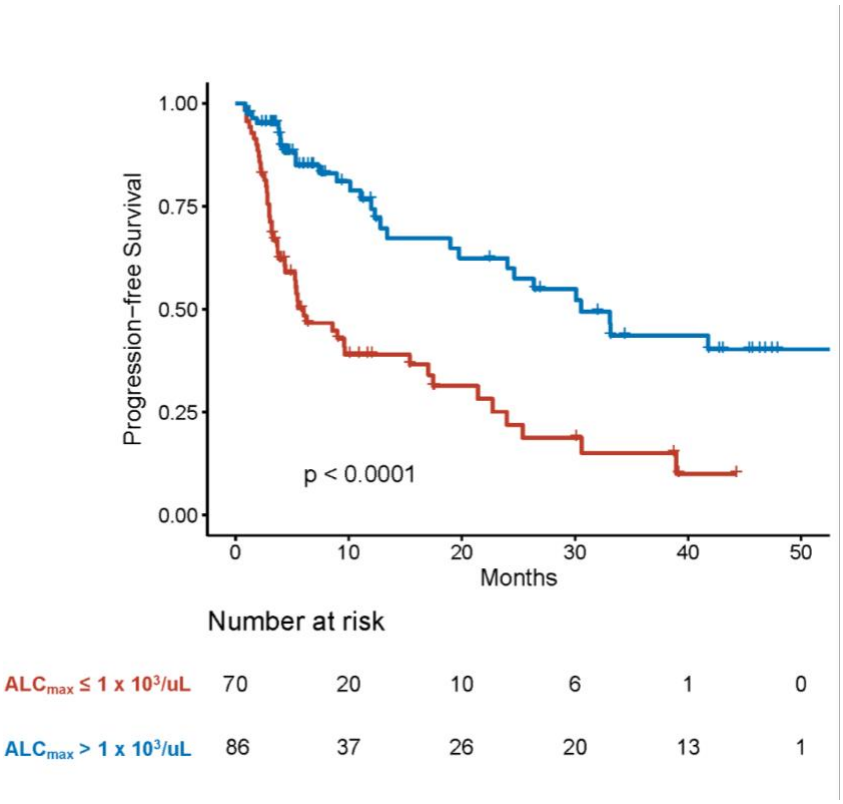
Supplemental Figures



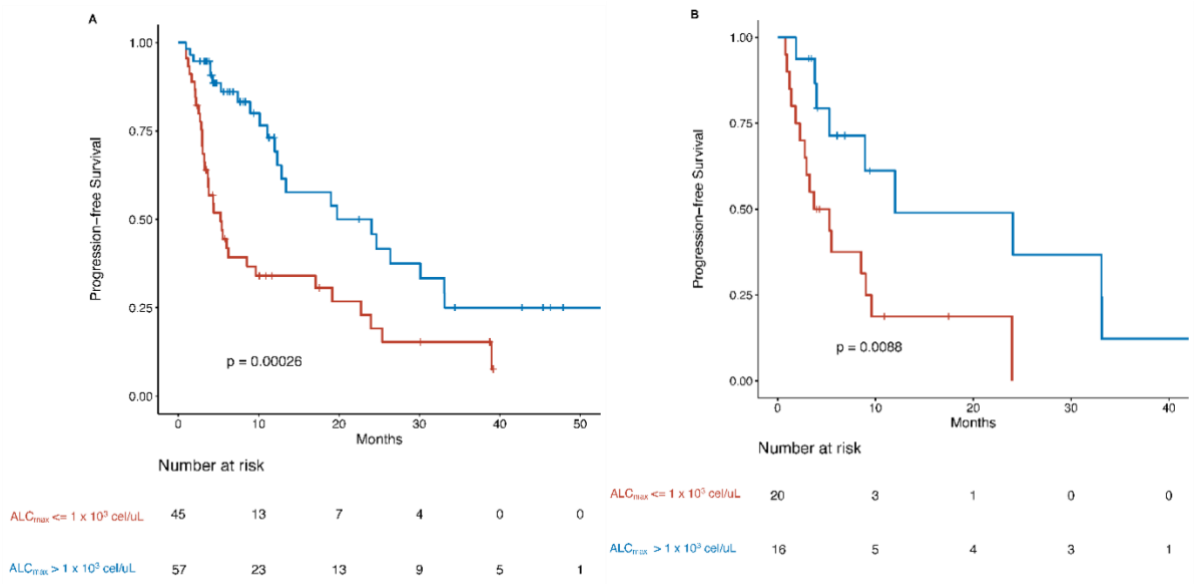
Supplemental Figure S1: Median absolute lymphocyte count during day -5 through +15 by BCMA CAR-T product, shaded areas represent 95% CI (**A**). Individual absolute lymphocyte count for each BCMA CAR-T product from day -5 through +15(**B**). Pairwise comparison between BCMA CAR-T products comparing median ALC (**C**).



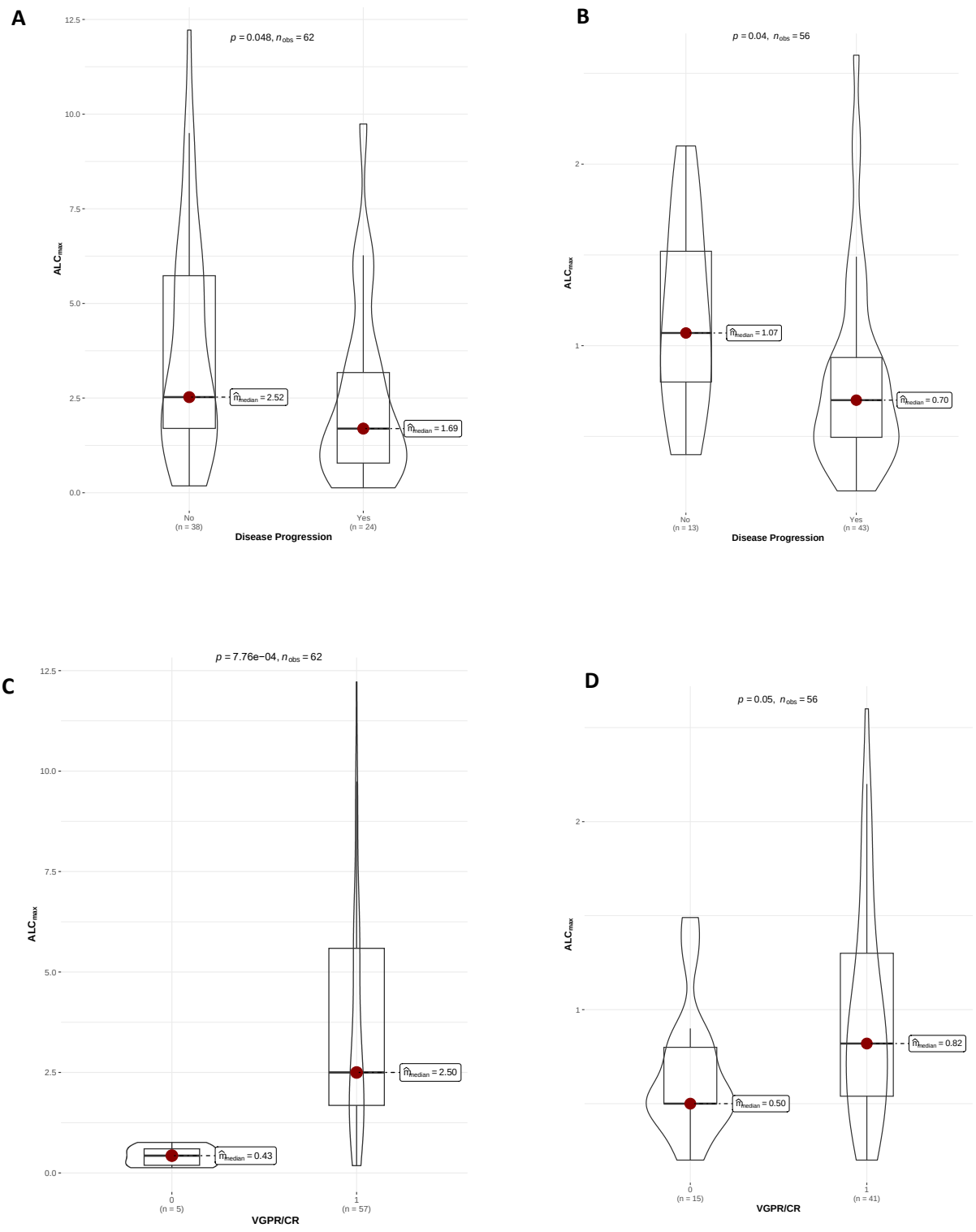
Supplemental Figure S2: Correlation of pre-conditioning (ALC_minus_5) and ALC_{max} for all patients treated with BCMA CAR-T.



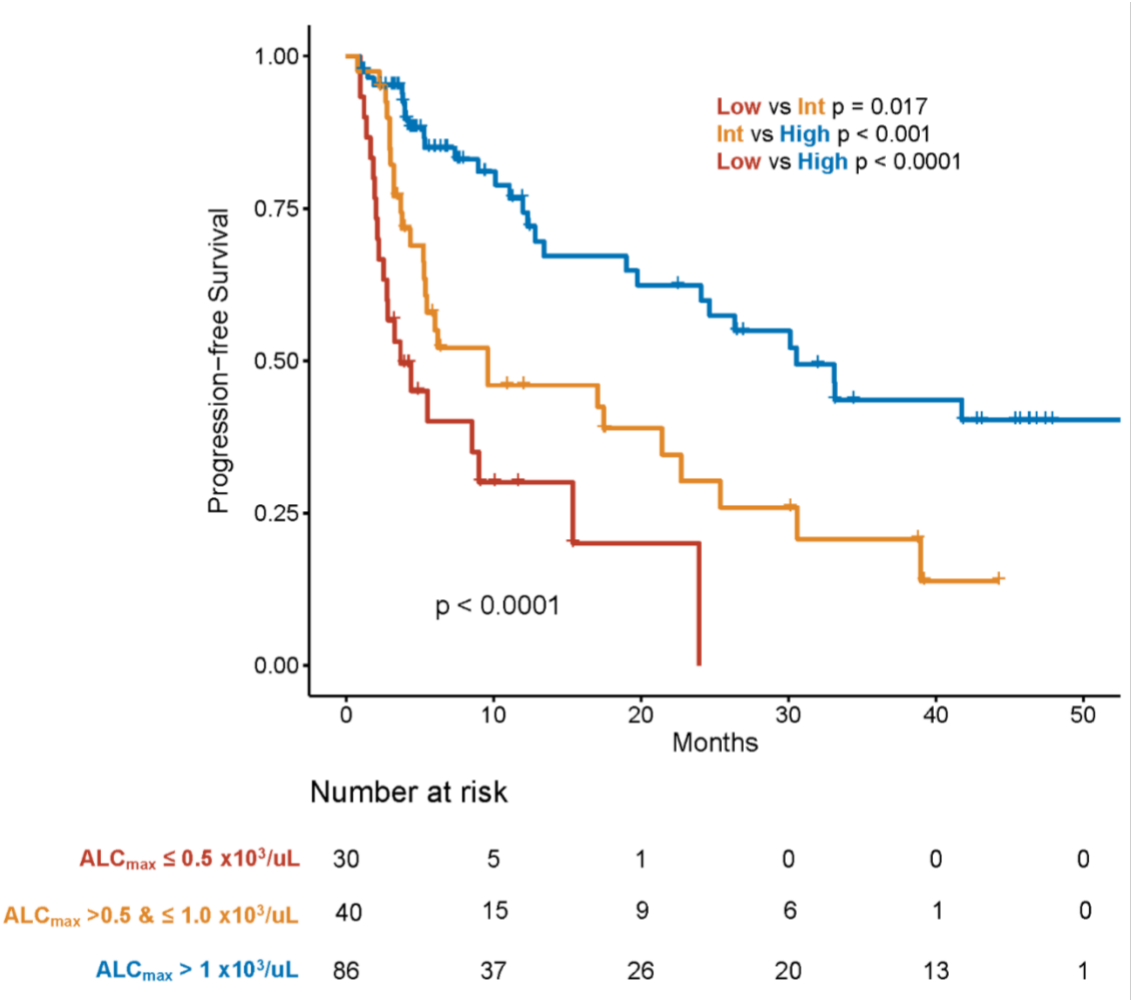
Supplemental Figure S3: Duration of Response by max absolute lymphocyte count subgroup in the BCMA CAR-T Cohort.



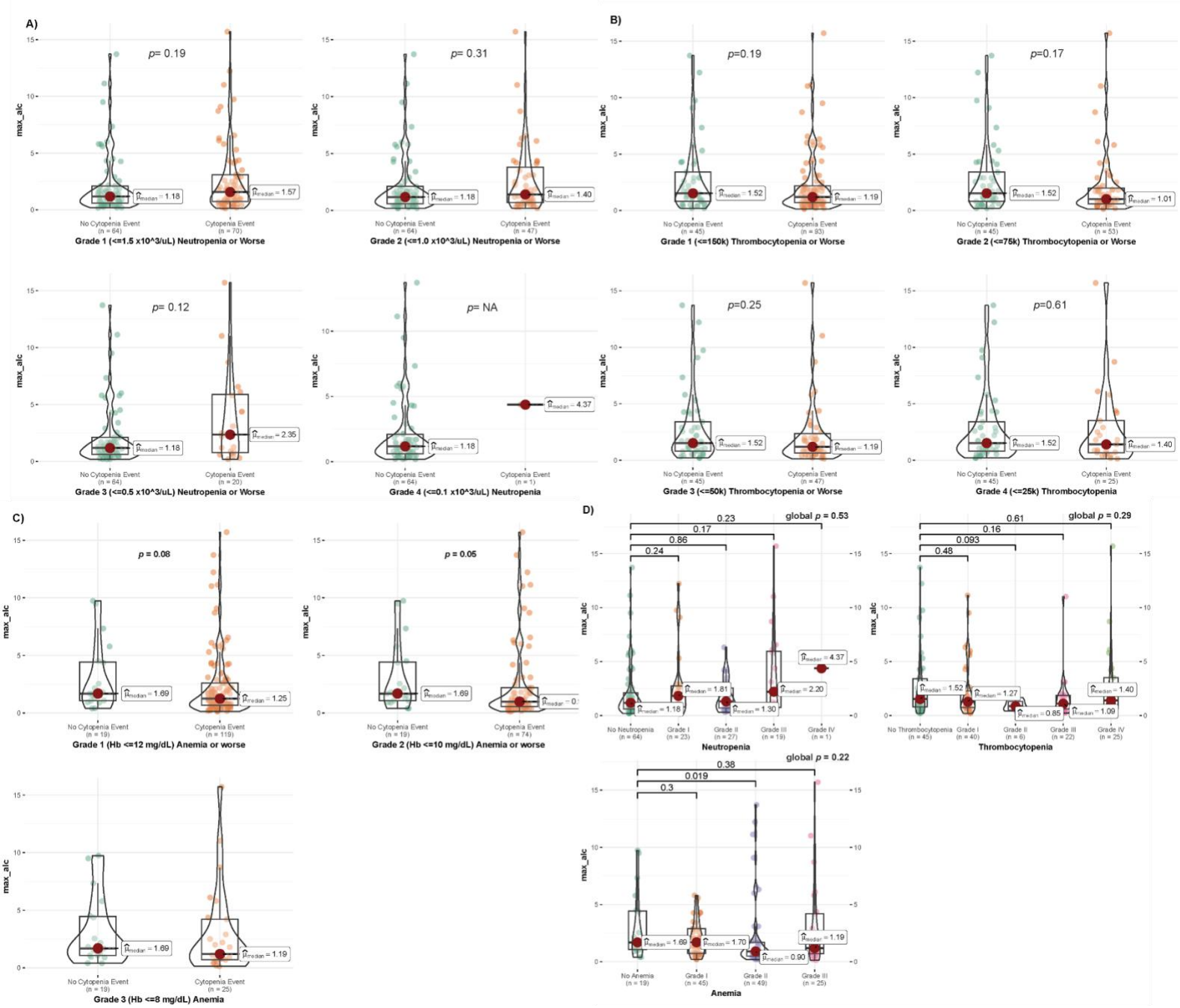
Supplemental Figure S4: Progression free survival in patients with High-Risk Cytogenetics (**A**) and non-paraskeletal extramedullary disease (**B**) by ALC$_{max}$ treated with BCMA CAR-T. High-risk cytogenetics defined as presence of any of Gain 1q, t(4;14), t(14;16) or deletion 17p.



Supplemental Figure S5: (A & B) ALC_{max} and Progression status for patients with more than 6 months follow up in cilta-cel and Ide-cel, respectively. **(C & D)** ALC_{max} between patients achieving VGPR or CR as best response for patients with more than 6 months follow up in cilta-cel and Ide-cel, respectively.

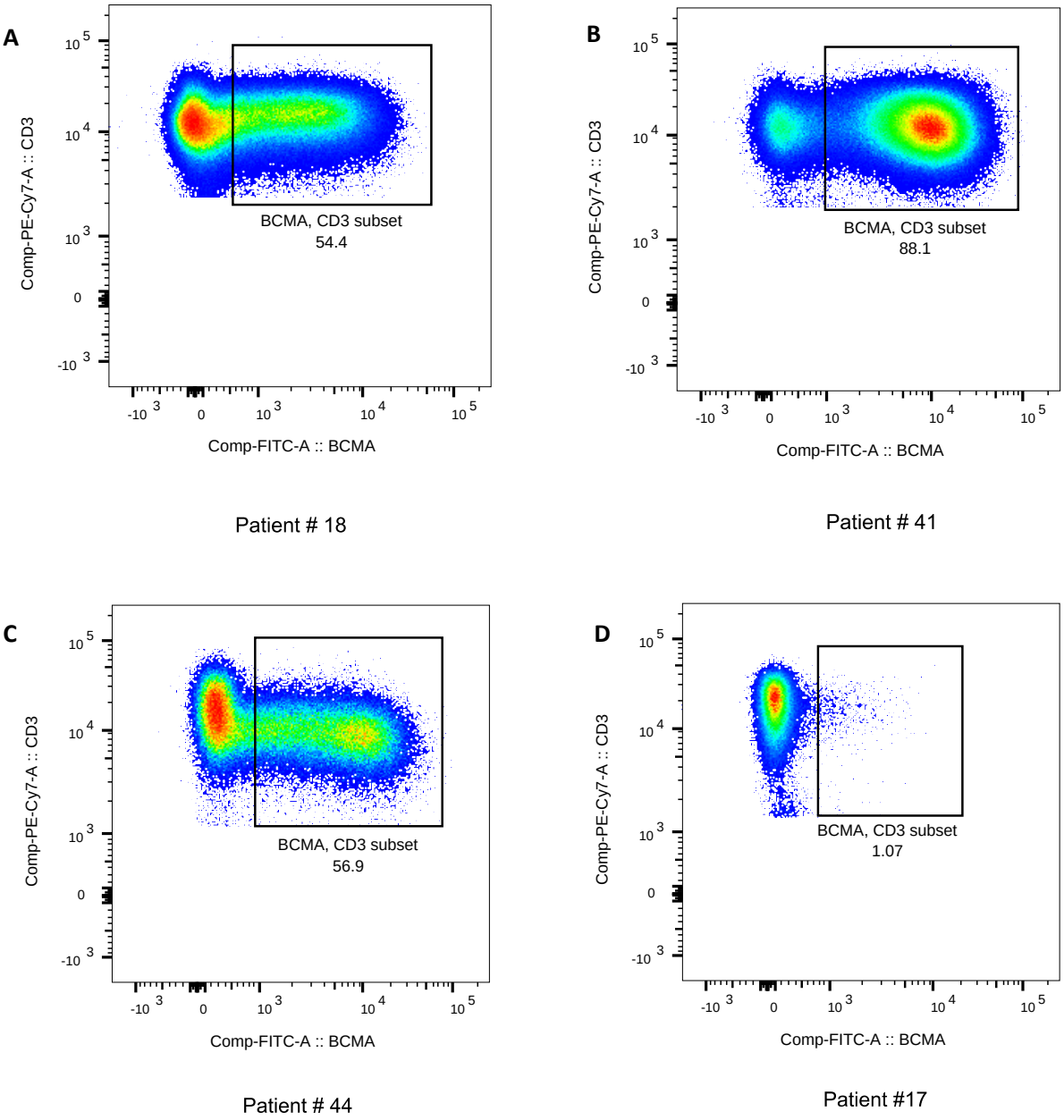


Supplemental Figure S5: Progression Free Survival by ALC_{max} group and pairwise-comparison between groups.



Supplemental Figure S7: median ALC_{max} comparison between non-cytopenia and those with grade 1-4 or greater delayed cytopenia for neutropenia (**A**), thrombocytopenia (**B**), and anemia (**C**). Figure **D** displays pairwise comparison of the non-cytopenia group with each individual cytopenia grade. Cytopenia was considered only if two consecutive values were below the prespecified value.

Supplemental Figure S8: Flow Cytometry analysis of four patients at day 14 showing the percentage of BCMA positive T cells from the CD3 lymphocytes gate. **(A-C)** Three patients who had high ALCmax and in remission as of last date of follow up. (D) A patient who has not responded to BCMA CAR-T therapy and relapsed within 2 months of CAR-T cells infusion.



Supplemental Figure S9: Graph plot of four patients the percentage of BCMA positive T cells from the CD3 lymphocytes gate at days 7, 14, and 21