Supplemental Data

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Full Listing of Study Sites

- H. Lee Moffitt Cancer Center, Tampa, FL, USA
- The University of Texas MD Anderson Cancer Center, Houston, TX, USA
- Vanderbilt University Medical Center, Nashville, TN, USA
- Sarah Cannon Research Institute, Nashville, TN, USA
- Washington University School of Medicine, St. Louis, MO, USA
- University of Rochester School of Medicine, Rochester, NY, USA
- University of California at San Diego, San Diego, CA, USA
- Mayo Clinic, Rochester, MN, USA
- University of California at Los Angeles, Los Angeles, CA, USA
- Emory University School of Medicine, Atlanta, GA, USA
- University of Chicago Medicine, Chicago, IL, USA
- Baylor University Medical Center, Dallas, TX, USA
- University of California San Francisco, San Francisco, CA, USA
- University of California Davis, Davis, CA, USA
- Icahn School of Medicine at Mount Sinai, New York, NY, USA
- University of Maryland Greenebaum Comprehensive Cancer Center, Baltimore, MD, USA
- Fred Hutchinson Cancer Research Center, Seattle, WA, USA
- Swedish Cancer Institute, Seattle, WA, USA
- Memorial Sloan Kettering Cancer Center, New York, NY, USA

Supplemental Methods

Additional eligibility criteria:

- Patients with Philadelphia chromosome (Ph)+ disease were eligible if they had disease intolerant to tyrosine kinase inhibitor (TKI) therapy, or if they had relapsed/refractory disease despite treatment with ≥2 different TKIs
- Absolute neutrophil count ≥500/μL unless in the opinion of the investigator cytopenia is due to underlying leukemia and is potentially reversible with leukemia therapy
- Platelet count ≥50,000/μL unless in the opinion of the investigator cytopenia is due to underlying leukemia and is potentially reversible with leukemia therapy
- Absolute lymphocyte count ≥100/μL
- Adequate renal, hepatic, pulmonary and cardiac function were defined as:
    - Creatinine clearance (as estimated by Cockcroft Gault) ≥60 cc/min
    - Serum alanine aminotransferase/aspartate aminotransferase ≤2.5 × upper limit of normal
    - Total bilirubin ≤1.5 mg/dL, except in patients with Gilbert's syndrome
    - Left ventricular ejection fraction ≥50%, no evidence of pericardial effusion as determined by an echocardiogram, no New York Heart Association class III or class IV functional classification, and no clinically significant arrhythmias
    - No clinically significant pleural effusion
    - Baseline oxygen saturation >92% on room air
    - Females of childbearing potential must have had a negative serum or urine pregnancy test
- Females of childbearing potential must have had a negative serum or urine pregnancy test
- Patients with central nervous system (CNS)-2 disease (cerebrospinal fluid [CSF] blast cells with <5 white blood cells (WBCs)/mm^3) without neurological changes were eligible
- In patients previously treated with blinatumomab, CD19 tumor expression on blasts obtained from bone marrow or peripheral blood must be documented after

completion of the most recent prior line of therapy. If CD19 expression is quantified, then blasts must be ≥ 90% CD19 positive. At the time of study initiation, limited data was available for CD19 expression in patients who had prior blinatumomab therapy. The expression rate was thus based on historical rates of CD19 expression in the literature for patients with CD19-expressing B-cell malignancies who relapsed following CD19-directed therapy.

Additional exclusion criteria:

- Diagnosis of Burkitt's leukemia/lymphoma according to World Health Organization classification or chronic myelogenous leukemia lymphoid blast crisis
- History of malignancy other than non-melanoma skin cancer or carcinoma in situ (eg, cervix, bladder, breast) unless disease-free for ≥3 years
- History of severe hypersensitivity reaction to aminoglycosides or any of the agents used in this study
- CNS abnormalities
    - Presence of CNS-3 disease defined as detectable cerebrospinal blast cells in a sample of CSF with ≥5 WBCs per mm^3 with or without neurological changes, and
    - Presence of CNS-2 disease defined as detectable cerebrospinal blast cells in a sample of CSF with <5 WBCs per mm^3 with neurological changes. Note: Patients with CNS-1 (no detectable leukemia in the CSF) and those with CNS-2 without clinically evident neurological changes are eligible to participate in the study
    - History or presence of any CNS disorder such as a seizure disorder, cerebrovascular ischemia/hemorrhage, dementia, cerebellar disease, any autoimmune disease with CNS involvement, posterior reversible encephalopathy syndrome, or cerebral edema
- History of severe hypersensitivity reaction to aminoglycosides or any of the agents used in this study
- History of concomitant genetic syndrome associated with bone marrow failure

- History of clinically significant cardiac disease within 12 months of enrollment
- History of symptomatic deep vein thrombosis or pulmonary embolism within 6 months of enrollment
- Primary immunodeficiency
- Known infection with HIV, hepatitis B, or hepatitis C virus. A history of hepatitis B or hepatitis C is permitted if the viral load is undetectable per quantitative polymerase chain reaction and/or nucleic acid testing
- Simple urinary tract infection and uncomplicated bacterial pharyngitis are permitted if responding to active treatment and after consultation with the Kite Medical Monitor
- Acute graft-vs-host disease (GVHD) grade II-IV by Glucksberg criteria or severity B-D by International Bone Marrow Transplant Registry index; acute or chronic GVHD requiring systemic treatment within 4 weeks prior to enrollment
- Prior medication:
    - Salvage systemic therapy (including chemotherapy, TKIs for Ph+ disease, and blinatumomab) ≤1 week or 5 half-lives (whichever is shorter) prior to enrollment
    - Prior CD19-directed therapy other than blinatumomab
    - History of Common Terminology Criteria for Adverse Events grade 4 neurologic event or grade 4 cytokine release syndrome with prior CD19-directed therapy
    - Treatment with alemtuzumab ≤6 months prior to enrollment, clofarabine or cladribine ≤3 months prior to enrollment, or PEG-asparaginase ≤3 weeks prior to enrollment
    - Donor lymphocyte infusion ≤4 weeks prior to enrollment
    - Treatment with any drug for GVHD and any immunosuppressive antibody ≤4 weeks prior to enrollment
    - At least 3 half-lives must have elapsed from any prior systemic inhibitory/stimulatory immune checkpoint molecular therapy prior to enrollment

    - Corticosteroid therapy at a pharmacologic dose (>5 mg/day of prednisone or equivalent doses of other corticosteroids) and other immunosuppressive drugs must be avoided for 1 week prior to enrollment
- Presence of any indwelling line or drain. Ommaya reservoirs and dedicated central venous access catheters are permitted
- Live vaccine ≤4 weeks prior to enrollment
- Women of childbearing potential who are pregnant or breastfeeding because of the potentially dangerous effects of the preparative chemotherapy on the fetus or infant
- Patients of both genders of childbearing potential who are not willing to practice birth control from the time of consent through 6 months after the completion of KTE-X19
- Patients who, in the investigator's judgment, are unlikely to complete all protocol-required study visits or procedures or comply with the study requirements for participation
- History of autoimmune disease resulting in end organ injury or requiring systemic immunosuppression or systemic disease modifying agents within the last 2 years

Dose formulations of 0.5 × 10^6 CAR T cells/kg

Two formulations were explored for patients receiving the lower dose 0.5 × 10^6 CAR T cells/kg, one with a total volume of 40 mL and the other with a volume of 68 mL. The 40-mL formulation was intended to maintain cell density and cell viability during the freezing/thawing process.

Study Design

In Phase 1, the Safety Review Team reviewed safety data after 3 patients in the dose-limiting toxicity (DLT)-evaluable set had the opportunity to be followed for 28 days after KTE-X19 infusion. Once the conditioning regimen and KTE-X19 dose evaluated in Phase 1 was determined to be safe based on the incidence of DLTs additional patients were enrolled at 2 lower dose levels to further evaluate safety and efficacy prior to commencing Phase 2.

DLT-evaluable set: All Phase 1 patients treated with the target KTE-X19 dose and followed for at least 28 days, or received a dose of KTE-X19 lower than the target dose but experienced a DLT during the 28 day post infusion period, up to the time at which a dose level has been evaluated for DLT and deemed safe. Additional Phase 1 patients enrolled and treated subsequently for the purpose of assessment of the overall safety in the same dose level or a lower dose level were not considered as part of the DLT evaluable set, and DLTs were not assessed for such patients.

Manufacturing

One patient was enrolled to receive 1×10^6 CAR T cells/kg and revised AE management, but only had sufficient product manufactured to receive 0.5×10^6 cells/kg. This patient was included in the analysis at the 1×10^6 dose level since the patient was treated under revised AE management guidelines.

Biomarker Analyses

Biomarker analyses were performed on blood and serum samples to evaluate predictive pharmacokinetics and pharmacodynamic markers for KTE-X19. As previously described, droplet digital polymerase chain reaction was used to measure the presence, expansion, and persistence of transduced CD19 CAR+ T cells in blood.[1] Serum was assessed for cytokines, chemokines, immune effector molecules, and markers of macrophage-activating syndrome using previously reported methods.[1]

Supplemental Table 1. Dose-limiting toxicities

DLTs were defined as the following KTE-X19-related events with onset within the first 28 days following KTE-X19 infusion:
• Grade 4 hematologic toxicity lasting more than 30 days (except lymphopenia) if not attributable to underlying disease
• All KTE-X19–related grade 3 non-hematologic toxicities lasting for >7 days and all KTE-X19–related grade 4 non-hematologic toxicities regardless of duration are considered DLTs, with the exception of the following: o Aphasia/dysphasia or confusion/cognitive disturbance which resolves to at least grade 1 or baseline within 2 weeks and to at least baseline within 4 weeks o Fever grade 3 or 4 o Immediate hypersensitivity reactions occurring within 2 hours of KTE-X19 infusion (related to KTE-X19 infusion) that are reversible to a grade 2 or less within 24 hours of KTE-X19 infusion with standard therapy o Renal toxicity which requires dialysis for ≤7 days o Intubation for airway protection if ≤7 days o TLS including associated manifestations attributable to TLS (eg, electrolyte abnormalities, renal function, hyperuricemia) o Grade 3 transaminase, alkaline phosphatase, bilirubin or other liver function test elevation, provided there is resolution to ≤ grade 2 within 14 days o Grade 4 transient serum hepatic enzyme abnormalities provided there is resolution to ≤ grade 3 within <72 hours o Hypogammaglobulinemia grade 3 or 4 o Grade 3 nausea and/or anorexia
• Adverse events attributed to CRS will be mapped to the overall CRS grading assessment for the determination of DLT o All occurrences of grade 3 CRS of duration >7 days and all occurrences of grade 4 CRS are considered DLTs, other than occurrences of CRS due to the exceptions listed above

CRS, cytokine release syndrome; DLT, dose-limiting toxicity; TLS, tumor lysis syndrome.

Supplemental Table 2. Original and revised neurotoxicity management guidelines

NE Grade	Original Management Guidelines	Revised Management Guidelines
Grade 1	• Supportive care • Neurological examination and additional work-up as clinically indicated	• Supportive care • Closely monitor neurologic status • Consider prophylactic antiepileptic
Grade 2	*Supportive Care and Evaluation* • Neurological examination, brain MRI, and evaluation of CSF; consider EEG as clinically indicated • Consider prophylactic antiepileptic	*Supportive Care and Evaluation* • Continuous cardiac telemetry and pulse oximetry as indicated • Serial neurological examinations to include fundoscopy and Glasgow Coma Score, brain MRI, evaluation of CSF, EEG; consider neurology consult • Administer antiepileptics for patients with seizures
	Tocilizumab • Consider tocilizumab 8 mg/kg IV over 1 hour (not to exceed 800 mg) for patients with comorbid conditions (eg, grade ≥2 CRS)	*Tocilizumab* • **For patients with concurrent CRS**, administer tocilizumab 8 mg/kg IV over 1 hour (not to exceed 800 mg); repeat every 4-6 hours as needed if not responsive to IV fluids or increasing supplemental oxygen, for a maximum of 3 doses in 24 hours • Discontinue tocilizumab if patient improves
	Corticosteroids • N/A	*Corticosteroids* • For patients without concurrent CRS, administer dexamethasone 10 mg IV every 6 hours • For patients with concurrent CRS, if no improvement within 24 hours after starting tocilizumab, administer dexamethasone 10 mg* IV every 6 hours • Taper corticosteroids if patient improves

Grade 3	*Supportive Care and Evaluation* • Per grade 2 • Monitor with continuous cardiac telemetry and pulse oximetry	*Supportive Care and Evaluation* • Manage in monitored care or ICU
	Tocilizumab • Consider tocilizumab 8 mg/kg IV over 1 hour (not to exceed 800 mg); repeat every 4-6 hours if symptoms have not stabilized or improved	*Tocilizumab* • Per grade 2 • Discontinue tocilizumab if patient improves
	Corticosteroids • Consider corticosteroids (eg, dexamethasone 10 mg IV every 6 hours or methylprednisolone 1 mg/kg BID) for worsening symptoms despite tocilizumab	*Corticosteroids* • Administer dexamethasone 10 mg* IV every 6 hours • Taper corticosteroids if patient improves
Grade 4	*Supportive Care and Evaluation* • Per grade 2 • Monitor with continuous cardiac telemetry and pulse oximetry	*Supportive Care and Evaluation* • Per grade 3 • Mechanical ventilation may be required • Administer immunosuppressants if patient does not improve
	Tocilizumab • Administer tocilizumab per grade 3 if not previously administered	*Tocilizumab* • Per grade 2
	Corticosteroids • Administer corticosteroids (eg, methylprednisolone 1g/d × 3 days, followed by 250 mg BID × 2 days, then 125 mg BID × 2 days, then 60 mg BID × 2 days)	*Corticosteroids* • Administer high-dose corticosteroids (eg, methylprednisone 1g/d × 3 days) • Taper corticosteroids if patient improves

* Or equivalent methylprednisolone dose (1 mg/kg).

BID, twice daily; CRS, cytokine release syndrome; CSF, cerebrospinal fluid; EEG, electroencephalogram; ICU, intensive care unit; IV, intravenous; MRI, magnetic resonance imaging.

Supplemental Table 3. Predefined bridging chemotherapy regimens

Bridging Chemotherapy Regimens	
Attenuated VAD	Vincristine non-liposomal (1-2 mg IV weekly) or liposomal (2.25 mg/m^2 IV weekly), and dexamethasone 20-40 mg IV or PO daily x 3-4 days per week. Optional doxorubicin 50 mg/m^2 IV x 1 (first week only)
Mercaptopurine (6-MP)	50-75 mg/m^2/day by mouth (administer at bedtime on an empty stomach to improve absorption)
Hydroxyurea	Doses titrated between 15-50 mg/kg/day (rounded to the nearest 500 mg capsule and given as a single daily oral dose on a continuous basis)
DOMP	Dexamethasone 6 mg/m^2/day PO (or IV) divided BID days 1-5, vincristine 1.5 mg/m^2 (maximum dose 2 mg) IV on day 1, methotrexate 20 mg/m^2 PO weekly, 6-MP 50-75 mg/m^2/day PO daily
Attenuated FLAG/FLAG-IDA	Fludarabine 30 mg/m^2 IV days 1-2, cytarabine 2 g/m^2 IV days 1-2, G-CSF 5 µg/kg SC or IV starts on day 3 and can continue until day before the start of conditioning chemotherapy. With or without idarubicin 6 mg/m^2 IV days 1-2
Mini-hyper CVAD (courses A and/or B)	Course A: Cyclophosphamide 150 mg/m^2 every 12 h x 3 days, dexamethasone 20 mg/d IV or PO daily days 1-4 and 11-14, vincristine 2 mg IV x 1 Course B: methotrexate 250 mg/m^2 IV over 24 hours on day 1, cytarabine 0.5 g/m^2 IV every 12 hours x 4 doses on days 2 and 3

Use of a TKI in combination with any of the above regimens is allowed for patients with Ph+ ALL and Ph-like ALL.

BID, twice daily; CVAD, cyclophosphamide, vincristine, doxorubicin, and dexamethasone; DOMP, dexamethasone, 6-mercaptopurine, methotrexate, and vincristine; FLAG, fludarabine, high-dose cytarabine, and G-CSF; G-CSF, granulocyte-colony stimulating factor; IDA, idarubicin; IV, intravenous; MP, 6-mercaptopurine; PO, oral; SC, subcutaneous; TKI, tyrosine kinase inhibitor; VAD, vincristine, doxorubicin, and dexamethasone.

Supplemental Table 4. Overall disease response classification

Response	BM		Peripheral Blood*		CNS EMD		Non-CNS EMD†
CR	≤5%‡	*and*	ANC ≥1000 and Plt ≥100,000	*and*	CNS-1	*and*	CR§
CRi			ANC ≥1000 and Plt <100,000 OR ANC <1000 and Plt ≥100,000				
CRh			ANC ≥500 and Plt ≥50,000 but not CR				
Blast-free hypoplastic or aplastic BM			Any values not meeting criteria for CR, CRi, or CRh				
PR	All criteria for CR, CRi, CRh, or blast-free hypoplastic or aplastic bone marrow are met					*and*	PR
Relapse	>5%‡	*or*	Circulating leukemia present¶	*or*	CNS-2 or CNS-3	*or*	PD
No response	All required assessments are performed with failure to attain the criteria needed for any response category						
Unknown	Assessment is not done, incomplete, or indeterminate Note: Overall disease response can be assessed as 'relapsed disease' if any single element of disease response assessment shows relapse, other unknown elements of disease response assessment do not need to be evaluated						

* The units for Plt and ANC are per uL. ANC and Plt values should be evaluated every time a BM evaluation is performed. If not done, ANC and Plt values used for response assessment can be from any time 7 days prior to the BM result to any time after the BM result.

† See supplementary Table 5 for disease assessment in patients with known baseline EMD. In patients evaluated for non-CNS EMD, imaging and BM results used for assessment of overall disease response must be within 30 days of each other.

‡ Blasts by morphology in BM.

§ If baseline EMD is present, then images must show CR. If no baseline EMD, then images are not required, but if performed, must show CR per Supplemental Table 5.

¶ No circulating leukemia is <1% circulating blasts by morphology. Circulating leukemia is ≥1% circulating blasts by morphology. If ≥1% blast by morphology and there is no other evidence of leukemia, then flow or molecular studies should be conducted to confirm that blasts are leukemia.

ANC, absolute neutrophil count; BM, bone marrow; CNS, central nervous system; CR, complete remission; CRh, complete remission response with partial hematologic recovery; CRi, complete remission response with incomplete hematologic recovery; EMD, extramedullary disease; PD, progressive disease; Plt, platelets; PR, partial response.

Supplemental Table 5. Extramedullary disease response classification

Response*	PET Baseline, On-study		Baseline Lesion(s) by CT or MRI		New Lesion(s)
CR	Neg, N/A	*and*	All of: • Disappearance of measurable and non-measurable nodal lesions: o Nodal masses >1.5 cm in GTD at baseline must have regressed to ≤1.5 cm in GTD o Nodes that were 1.1 to 1.5 cm in their long axis and more than 1.0 cm in their short axis before treatment must have decreased to 1.0 cm in their short axis after treatment • If testes, spleen and/or liver involvement, they must be normal size by imaging or physical examination	*and*	No
	Pos, Neg	*and*	Any	*and*	No
PR	Any	*and*	All of: • ≥50% decrease in SPD of up to 6 of the largest dominant masses. Dominant masses should be clearly measurable in at least 2 perpendicular dimensions, and should be from different regions of the body if possible • No increase in size of liver or spleen by imaging or physical exam • If multiple splenic and hepatic nodules are present, they must regress by ≥50% in SPD. There must be a >50% decrease in GTD for a single nodule	*and*	No
SD	Does not meet the criteria for CR, PR, or PD				

PD	Any	*and*	At least one of the following: • ≥50% increase from nadir in the sum of the products of at least two lymph nodes, or if a single node is involved at least a 50% increase in the product of the diameters of this one node • At least a 50% increase in the longest diameter of any single previously identified node more than 1 cm in its short axis • ≥50% increase in size of splenic, hepatic or any other non-nodal lesion	*or*	Yes

* Modified revised International Working Group criteria.[2]

CR, complete remission; CT, computed tomography; GTD, greatest transverse diameter; MRI, magnetic resonance imaging; N/A, not applicable; Neg, Negative; PD, progressive disease; Pos, Positive; PR, partial response; SD, stable disease; SPD, sum of the product of the diameters.

Supplemental Table 6. Bone marrow blasts by dose level

Median (range)	2×10^6 (n = 6)	1×10^6 Original AE Management (n = 14)	1×10^6 Revised AE Management (n = 9)	0.5×10^6 (n = 16)
BM blasts at screening, %	79 (48 – 100)	68 (5 – 97)	50 (10 – 96)	52 (5 – 91)
		Wilcoxon *P*=0.22		
BM blasts at preconditioning after bridging, %	70 (20 – 96)	81 (0 – 97)*	41 (2 – 96)*	64 (4 – 93)
		Wilcoxon *P*=0.10		

* Bridging therapy was administered to 14 of 14 patients (100%) in the 1×10^6 original AE management group, and 8 of 9 patients (89%) in the 1×10^6 revised AE management group.

AE, adverse event; BM, bone marrow.

Supplemental Table 7. Response to KTE-X19 among all enrolled patients (intent to treat)

Response Category, n (%)	2×10^6 (n = 6)	1×10^6 (n = 28)	0.5×10^6 (n = 20)	Total (N = 54)
Complete remission	4 (67)	19 (68)	8 (40)	31 (57)
Complete remission	3 (50)	15 (54)	6 (30)	24 (44)
Complete remission with incomplete hematologic recovery	1 (17)	4 (14)	2 (10)	7 (16)
Blast-free hypoplastic/aplastic bone marrow	0	1 (4)	1 (5)	2 (4)
Partial remission	0	1 (4)*	0	1 (2)
No response	1 (17)	2 (7)	6 (30)	9 (17)
Unknown or not evaluable	1 (17)	5 (18)	5 (25)	11 (20)†

* Patient had extramedullary disease at response assessment.

† One patient treated at the 2×10^6 CAR T cells/kg dose died on day 6 due to multiorgan failure secondary to CRS; 1 patient treated at the 0.5×10^6 CAR T cells/kg dose died on day 7 due to cerebrovascular accident (stroke) in the context of CRS and neurologic events; the other 9 patients discontinued prior to KTE-X19 infusion due to reasons described in **Supplemental Figure 2**.

Supplemental Table 8. CAR gene copies in blood over time

CAR Gene Copies per µg DNA in Blood	2×10^6	1×10^6 Original AE Management	1×10^6 Revised AE Management	0.5×10^6
Baseline	(n = 6)	(n = 14)	(n = 9)	(n = 16)
Median	0	0	0	0
Range	0 – 0	0 – 0	0 – 0	0 – 0
Day 7	(n = 4)	(n = 12)	(n = 9)	(n = 15)
Median	62,411	154,386	91,287	3702
Range	11,097 – 162,972	12,231 – 443,880	0 – 353,160	0 – 375,030
Week 2	(n = 5)	(n = 14)	(n = 8)	(n = 13)
Median	44,064	48,114	60,507	3669
Range	2228 – 106,110	7614 – 283,500	10,935 – 224,370	0 – 100,845
Week 4	(n = 5)	(n = 11)	(n = 9)	(n = 13)
Median	1304	3119	16,200	1588
Range	405 – 4860	1029 – 95,580	235 – 56,052	0 – 27,540
Week 8	(n = 0)	(n = 5)	(n = 7)	(n = 7)
Median	-	0	527	219
Range	-	0 – 907	0 – 972	0 – 9882
Month 3	(n = 4)	(n = 11)	(n = 6)	(n = 9)
Median	0	203	99	0
Range	0 – 0	0 – 1458	0 – 478	0 – 5508
Month 6	(n = 3)	(n = 8)	(n = 0)	(n = 7)
Median	0	0	-	0
Range	0 – 0	0 – 105	-	0 – 518
Month 9	(n = 1)	(n = 6)	(n = 0)	(n = 4)
Median	0	0	-	0
Range	0 – 0	0 – 138	-	0 – 0
Month 12	(n = 1)	(n = 4)	(n = 0)	(n = 3)
Median	65	0	-	0
Range	65 – 65	0 – 0	-	0 – 57

AE, adverse event; CAR, chimeric antigen receptor.

Supplemental Table 9. CAR gene copies in blood by grade ≥3 neurologic events and cytokine release syndrome

CAR Gene Copies per µg DNA in Blood	2×10^6 (n = 6)		1×10^6 (n = 23)		0.5×10^6 (n = 16)	
	Grade ≥3	Grade ≤2	Grade ≥3	Grade ≤2	Grade ≥3	Grade ≤2
Neurologic Events						
	(n = 3)	(n = 3)	(n = 10)	(n = 13)	(n = 4)	(n = 12)
Peak						
n	3	2	10	13	4	11
Median	106110.0	44185.5	201649.5	98820.0	127413.0	15147.0
Range	47790.0 – 162972.0	44064.0 – 44307.0	41553.0 – 443880.0	19602.0 – 353160.0	2122.0 – 375030.0	145.8 – 130653.0
AUC						
n	3	2	10	13	4	11
Median	1412169.5	601473.3	1759828.0	1549044.0	1198254.8	209590.5
Range	360753.8 – 1656550.0	552030.5 – 650916.0	474922.0 – 4082967.0	299033.0 – 5532786.0	7427.0 – 2808638.0	811.0 – 1054564.0
CRS						
	(n = 3)	(n = 3)	(n = 7)	(n = 16)	(n = 4)	(n = 12)
Peak						
n	2	3	7	16	4	11
Median	45927.0	106110.0	165483.0	107041.5	94081.5	15147.0
Range	44064.0 – 47790.0	44307.0 – 162972.0	51759.0 – 283500.0	19602.0 – 443880.0	2122.0 – 375030.0	145.8 – 130653.0
AUC						
n	2	3	7	16	4	11
Median	505834.9	1412169.5	1607844.0	1610990.5	705985.0	209590.5
Range	360753.8 – 650916.0	552030.5 – 1656550.0	654034.5 – 4082967.0	299033.0 – 5532786.0	7427.0 – 2808638.0	811.0 – 1277566.5

AUC, area under the curve; CAR, chimeric antigen receptor; CRS, cytokine release syndrome.

Supplemental Table 10. CAR gene copies in blood by bone marrow blasts at screening for enrollment and preconditioning after bridging

	2×10^6 (n = 6)		1×10^6 (n = 23)		0.5×10^6 (n = 16)	
	BM Blasts at Screening					
CAR Gene Copies per µg DNA in Blood	**BM Blasts 5%-50% (n = 1)**	**BM Blasts 50%-100% (n = 5)**	**BM Blasts 5%-50% (n = 8)**	**BM Blasts 50%-100% (n = 15)**	**BM Blasts 5%-50% (n = 7)**	**BM Blasts 50%-100% (n = 8)**
Peak						
n	1	4	8	15	7	7
Median	162972.0	46048.5	121054.5	111942.0	75006.0	2876.0
Range	162972.0 – 162972.0	44064.0 – 106110.0	51759.0 – 380700.0	19602.0 – 443880.0	145.8 – 153981.0	1077.0 – 375030.0
AUC						
n	1	4	8	15	7	7
Median	1412169.5	601473.3	1393176.8	1672937.0	750484.0	36945.3
Range	1412169.5 – 1412169.5	360753.8 – 1656550.0	654034.5 – 5532786.0	299033.0 – 4876767.0	1530.9 – 1277566.5	811.0 – 2808638.0
	BM Blasts at Preconditioning After Bridging					
CAR Gene Copies per µg DNA in Blood	**BM Blasts 0%-50% (n = 2)**	**BM Blasts 50%-100% (n = 4)**	**BM Blasts 0%-50% (n = 5)**	**BM Blasts 50%-100% (n = 12)**	**BM Blasts 0%-50% (n = 5)**	**BM Blasts 50%-100% (n = 9)**
Peak						
n	2	3	5	12	5	8
Median	105381.0	44307.0	290790.0	127615.5	85941.0	8161.0
Range	47790.0 – 162972.0	44064.0 – 106110.0	19602.0 – 380700.0	65124.0 – 283500.0	15147.0 – 153981.0	1077.0 – 100845.0
AUC						
n	2	3	5	12	5	8
Median	886461.6	650916.0	2128745.5	1640390.5	927612.0	123267.9
Range	360753.8 – 1412169.5	552030.5 – 1656550.0	299033.0 – 4876767.0	492723.0 – 4082967.0	188471.5 – 1118943.0	811.0 – 1277566.5

AUC, area under the curve; BM, bone marrow; CAR, chimeric antigen receptor.

Supplemental Table 11. Inflammatory markers in blood serum samples at baseline and at post-infusion peak

	2 × 10^6 cells/kg (n = 6)		1 × 10^6 cells/kg Original AE Management (n = 14)		1 × 10^6 cells/kg Revised AE Management (n = 9)		0.5 × 10^6 cells/kg (n = 16)	
	Baseline	**Peak**	**Baseline**	**Peak**	**Baseline**	**Peak**	**Baseline**	**Peak**
CCL17 (TARC), pg/mL								
Median	881.2	786.2	241.6	389.5	76.0	114.1	215.2	864.9
Range	93.3 – 4480.0†	220.1 – 1902.5	55.4 – 4480.0†	40.2 – 4480.0†	3.3* – 4480.0†	45.8 – 4480.0†	3.3* – 4480.0†	3.3* – 4480.0†
CRP, mg/L								
Median	79.1	193.0	17.1	93.0	10.0	94.8	59.5	138.4
Range	2.7 – 496.0†	7.3 – 272.1	0.5 – 183.5	3.5 – 496.0†	0.8 – 101.6	10.5 – 216.5	1.3 – 270.6	4.0 – 496.0†
CXCL10, pg/mL								
Median	230.8	2000.0†	289.1	2000.0†	298.9	1635.3	377.9	2000.0†
Range	113.3 – 515.5	663.3 – 2000.0†	88.6 – 2000.0†	525.3 – 2000.0†	134.6 – 1569.1	276.8 – 2000.0†	30.8 – 1682.4	309.5 – 2000.0†
Eotaxin-1, pg/mL								
Median	96.2	100.6	135.0	183.1	143.2	185.1	121.1	265.5
Range	12.3* – 480.9	12.3* – 222.3	12.3* – 277.6	59.9 – 346.2	74.6 – 342.0	69.0 – 636.2	59.4 – 401.8	77.0 – 594.7
Eotaxin-3, pg/mL								
Median	10.2*	10.2*	10.2*	10.2*	10.2*	10.2*	10.2*	10.2*
Range	10.2* – 10.2*	10.2* – 10.2*	10.2* – 10.2*	10.2* – 10.2*	10.2* – 96.3	10.2* – 307.4	10.2* – 10.2*	10.2* – 326.3
Ferritin, ng/mL								
Median	6963.1	20611.3	3126.7	14271.5	2769.1	7545.3	3816.9	9706.2
Range	2487.5 – 25000.0	9565.8 – 25000.0	0.8 – 17725.5	2758.8 – 25000.0	625.3 – 5299.5	1516.7 – 31620.0†	747.3 – 14020.1	875.2 – 31620.0†

GM-CSF, pg/mL								
Median	1.9*	11.9	1.9*	3.5	1.9*	1.9*	1.9*	5.7
Range	1.9* – 1.9*	1.9* – 78.9	1.9* – 1.9*	1.9* – 239.7	1.9* – 1.9*	1.9* – 64.6	1.9* – 5.9	1.9* – 189.1
Granzyme A, pg/mL								
Median	1194.1	685.9	20.0*	20.0*	20.0*	20.0*	20.0*	20.0*
Range	20.0* – 4634.0	20.0* – 5018.1	20.0* – 5804.6	20.0* – 3925.8	20.0* – 1818.5	20.0* – 2019.0	20.0* – 8664.7	20.0* – 14,625.9
Granzyme B, pg/mL								
Median	1.0*	43.4	1.0*	51.5	1.0*	29.6	1.0*	16.1
Range	1.0* – 117.5	1.0* – 473.8	1.0* – 394.3	1.0* – 2988.6	1.0* – 23.9	1.0* – 2499.7	1.0* – 14.4	1.0* – 10,000.0†
ICAM-1, ng/mL								
Median	691.0	1296.5	584.9	1236.0	572.6	882.7	711.4	1098.8
Range	395.1 – 1366.7	781.6 – 1777.4	313.5 – 1359.9	605.1 – 2332.3	137.1 – 857.4	270.7 – 3879.5	141.0 – 1538.5	543.5 – 4926.0
IFNγ, pg/mL								
Median	7.5*	703.6	7.5*	1415.3	7.5*	286.9	21.2	493.9
Range	7.5* – 7.5*	99.1 – 1876.0†	7.5* – 910.5	19.8 – 1876.0†	7.5* – 31.2	39.3 – 1876.0†	7.5* – 496.9	21.0 – 1876.0†
IL-1RA, pg/mL								
Median	357.6	1904.8	439.6	3360.9	308.3	1052.6	361.6	1154.6
Range	31.2 – 861.1	1034.7 – 4000.0	31.2 – 1672.7	431.2 – 4000.0	107.8 – 387.9	329.3 – 4224.3	31.2 – 975.7	371.3 – 4000.0
IL-1α, pg/mL								
Median	2.9*	2.9*	2.9*	2.9*	2.9*	2.9*	2.9*	2.9*
Range	2.9* – 2.9*	2.9* – 2.9*	2.9* – 2.9*	2.9* – 2.9*	2.9* – 2.9*	2.9* – 2.9*	2.9* – 2.9*	2.9* – 2.9*
IL-1β, pg/mL								
Median	2.1*	2.1*	2.1*	2.1*	2.1*	2.1*	2.1*	2.1*
Range	2.1* – 2.1*	2.1* – 2.1*	2.1* – 2.1*	2.1* – 2.1*	2.1* – 2.1*	2.1* – 2.1*	2.1* – 2.1*	2.1* – 2.1*
IL-10, pg/mL								
Median	1.8	57.3	0.7*	47.0	0.7*	15.9	0.7*	27.2
Range	0.7* – 7.7	0.7* – 113.8	0.7* – 85.2	3.0 – 466.0†	0.7* – 6.2	5.6 – 466.0†	0.7* – 16.8	0.7* – 466.0†
IL-12 P40, pg/mL								

Median	18.0	112.1	49.5	57.3	36.7	41.5	44.6	150.1
Range	5.7* – 83.7	16.6 – 177.1	14.2 – 466.3	5.7* – 418.4	5.7* – 372.8	5.7* – 283.5	5.7* – 674.6	5.7* – 4500.0†
IL-12 P70, pg/mL								
Median	1.2*	1.2*	1.2*	1.2*	1.2*	1.2*	1.2*	1.2*
Range	1.2* – 1.2*	1.2* – 1.2*	1.2* – 1.2*	1.2* – 16.7	1.2* – 5.2	1.2* – 4.7	1.2* – 1.2*	1.2* – 12.7
IL-13, pg/mL								
Median	4.2*	4.2*	4.2*	4.2*	4.2*	4.2*	4.2*	4.2*
Range	4.2* – 4.2*	4.2* – 4.2*	4.2* – 4.2*	4.2* – 13.1	4.2* – 4.2*	4.2* – 4.2*	4.2* – 4.2*	4.2* – 20.0
IL-15, pg/mL								
Median	8.3	66.3	7.3	39.6	4.5	39.6	6.8	52.8
Range	3.9 – 20.6	10.7 – 143.6	4.1 – 15.6	11.6 – 74.5	1.4* – 23.1	9.1 – 78.9	3.8 – 28.0	16.5 – 103.5
IL-16, pg/mL								
Median	103.1	173.9	255.8	462.8	122.6	248.7	272.7	650.5
Range	68.5 – 362.6	58.4 – 842.5	73.6 – 2216.9	85.4 – 3740.0†	71.2 – 935.7	92.5 – 803.7	88.3 – 3740.0†	132.4 – 3215.8
IL-17, pg/mL								
Median	9.3*	9.3*	9.3*	9.3*	9.3*	9.3*	9.3*	9.3*
Range	9.3* – 39.5	9.3* – 156.5	9.3* – 9.3*	9.3* – 35.7	9.3* – 9.3*	9.3* – 35.3	9.3* – 9.3*	9.3* – 41.6
IL-2, pg/mL								
Median	0.9*	18.8	0.9*	10.3	0.9*	4.2	0.9*	4.3
Range	0.9* – 0.9*	0.9* – 110.6	0.9* – 3.0	0.9* – 159.1	0.9* – 0.9*	0.9* – 49.5	0.9* – 3.8	0.9* – 359.1
IL-2Rα, pg/mL								
Median	5795.9	14016.8	4973.6	12766.2	4468.3	17904.8	4495.2	15104.8
Range	1210.9 – 35644.4	8277.2 – 22719.1	78.0 – 36533.8	3759.5 – 48150.8	1420.9 – 10663.5	8502.9 – 71270.8	78.0 – 92941.7	4893.7 – 100000.0†
IL-4, pg/mL								
Median	0.5*	0.5*	0.5*	0.5*	0.5*	0.5*	0.5*	0.5*
Range	0.5* – 0.5*	0.5* – 0.5*	0.5* – 0.5*	0.5* – 4.0	0.5* – 0.5*	0.5* – 5.6	0.5* – 0.5*	0.5* – 5.6
IL-5, pg/mL								

Median	6.3*	6.3*	6.3*	23.5	6.3*	6.3*	6.3*	24.1
Range	6.3* – 6.3*	6.3* – 32.7	6.3* – 14.2	6.3* – 111.8	6.3* – 6.3*	6.3* – 124.6	6.3* – 60.9	6.3* – 182.2
IL-6, pg/mL								
Median	7.1	91.9	1.6*	629.5	1.6*	60.0	5.5	213.9
Range	1.6* – 297.4	7.4 – 210.1	1.6* – 45.6	8.6 – 976.0†	1.6* – 19.8	16.8 – 976.0†	1.6* – 74.0	1.6* – 976.0†
IL-7, pg/mL								
Median	5.3	21.3	5.3	28.7	6.9	18.4	5.2	25.6
Range	2.9 – 14.7	15.1 – 58.1	1.4* – 36.6	10.9 – 46.9	1.4* – 15.5	9.0 – 38.6	1.4* – 25.1	1.4* – 47.6
IL-8, pg/mL								
Median	44.0	153.0	33.4	272.9	16.3	75.2	48.7	245.1
Range	6.5 – 130.5	29.0 – 750.0†	7.0 – 657.3	58.5 – 750.0†	13.3 – 258.0	37.1 – 750.0†	3.9 – 418.4	25.2 – 750.0†
MCP-1, pg/mL								
Median	878.5	1500.0†	872.2	1500.0†	777.1	1281.9	809.1	1500.0†
Range	786.5 – 1401.4	452.8 – 1500.0†	242.5 – 1500.0†	1090.8 – 1500.0†	405.4 – 1500.0†	495.8 – 1500.0†	191.4 – 1500.0†	627.4 – 1500.0†
MCP-4, pg/mL								
Median	77.3	189.0	83.5	245.8	70.1	112.3	102.0	214.4
Range	35.3 – 111.1	97.1 – 248.0	46.4 – 146.8	54.8 – 840.4	35.7 – 246.7	44.6 – 263.3	5.1* – 258.1	55.9 – 396.8
MDC, pg/mL								
Median	88.3*	600.8	395.0	396.1	392.8	407.2	238.1	445.7
Range	88.3* – 88.3*	88.3* – 1928.8	88.3* – 2285.8	88.3* – 1337.5	88.3* – 1256.1	88.3* – 927.6	88.3* – 740.5	88.3* – 1163.4
MIP-1α, pg/mL								
Median	13.8*	47.5	13.8*	75.0	13.8*	13.8*	13.8*	58.8
Range	13.8* – 13.8*	13.8* – 109.7	13.8* – 68.0	13.8* – 412.9	13.8* – 58.6	13.8* – 143.8	13.8* – 13.8*	13.8* – 182.6
MIP-1β, pg/mL								
Median	102.3	228.0	103.0	462.9	102.2	241.6	98.4	246.3
Range	56.1 – 132.7	163.6 – 891.4	32.4 – 346.8	58.2 – 2877.6	54.7 – 189.3	56.7 – 1644.5	34.8 – 240.7	122.2 – 992.7
PDL1, pg/mL								

Median Range	N/A	N/A	N/A	N/A	107.4 69.7 – 196.0	236.6 120.5 – 1137.0	86.9 86.9 – 86.9	153.8 153.8 – 153.8
Perforin, pg/mL								
Median	6263.5	7530.6	7811.5	22320.9	10674.7	20264.2	8418.8	16414.4
Range	2628.9 – 10482.2	3789.3 – 16842.9	2661.1 – 50032.0	6281.1 – 38643.4	7568.1 – 13712.9	5587.2 – 44195.4	2597.9 – 45816.7	5316.7 – 100000.0†
SAA, ng/mL								
Median	133028.2	359364.6	12121.4	116259.9	5984.5	176974.2	34725.5	250054.7
Range	44406.8 – 1380000.0†	20584.4 – 762894.4	2286.7 – 458693.3	13770.4 – 1380000.0†	2690.7 – 643970.0	15196.8 – 519874.5	2196.1 – 522644.6	12226.0 – 696334.1
SFASL, pg/mL								
Median	10.0*	10.0*	10.0*	10.0*	10.0*	10.0*	10.0*	10.0*
Range	10.0* – 1687.2	10.0* – 1978.1	10.0* – 178.9	10.0* – 164.1	10.0* – 936.1	10.0* – 554.5	10.0* – 859.8	10.0* – 856.6
TNF-α, pg/mL								
Median	3.6	8.0	4.8	12.6	3.0	5.6	4.1	8.3
Range	0.7* – 9.3	2.8 – 16.2	1.5 – 18.2	2.5 – 29.7	2.2 – 8.8	3.5 – 33.4	0.7* – 18.1	3.4 – 34.4
TNF-β, pg/mL								
Median	1.2*	1.2*	1.2*	1.2*	1.2*	1.2*	1.2*	1.2*
Range	1.2* – 1.2*	1.2* – 1.2*	1.2* – 1.2*	1.2* – 8.6	1.2* – 1.2*	1.2* – 1.2*	1.2* – 5.6	1.2* – 13.0
VCAM-1, ng/mL								
Median	1116.4	1186.6	1445.2	1782.7	599.4	1189.0	1277.4	2206.1
Range	744.5 – 7813.7	956.2 – 4743.1	543.4 – 3528.0	1089.5 – 2433.7	0.04* – 1808.7	627.2 – 3994.6	496.6 – 4447.2	817.1 – 8469.2

* Value represents lower limit of quantification in assay used.

† Value represents upper limit of quantification in assay used.

AE, adverse event; CAR, chimeric antigen receptor; CCL, C-C motif ligand; CRP, C-reactive protein; CXCL, C-X-C motif chemokine ligand; FGFBF, fibroblast growth factor basic form; FLT-1, fms related receptor tyrosine kinase 1; GM-CSF, granulocyte-macrophage colony-stimulating factor; ICAM-1, intercellular adhesion molecule 1; IFN, interferon; IL, interleukin; MCP, monocyte chemoattractant protein-1; MDC, macrophage-derived chemokine; MIP, macrophage inflammatory protein; PDL1, programmed death ligand 1; PLGF, placental growth factor; Rα, receptor alpha; RA, receptor antagonist; SAA, serum amyloid A; SFASL, soluble Fas ligand; TARC, thymus and activation-regulated cytokine; TNF, tumor

necrosis factor; VCAM, vascular cell adhesion protein; VEGF, vascular endothelial growth factor; VEGFC, vascular endothelial growth factor C; VEGFD, vascular endothelial growth factor D.

Supplemental Table 12. Association of serum biomarkers with cytokine release syndrome and neurologic events

		Cytokine Release Syndrome			Neurologic Events		
Function	**Peak Value - Median (range)**	**Grade ≥3 (n = 14)**	**Grade 0 – 2 (n = 31)**	***P* Value**	**Grade ≥3 (n = 17)**	**Grade 0 – 2 (n = 28)**	***P* Value**
Homeostatic/ proliferative	IL-15, pg/mL	31.9 (10.7 – 143.6)	55.1 (9.1 – 103.5)	**0.0372**	40.0 (21.2 – 84.0)	49.5 (9.1 – 143.6)	0.79
	IL-2, pg/mL	9.7 (0.9* – 110.6)	6.6 (0.9* – 359.1)	0.6846	10.9 (0.9* – 359.1)	5.3 (0.9* – 110.6)	0.1126
Pro-inflammatory	IL-6, pg/mL	213.9 (7.4 – 976.0†)	210.1 (1.6* – 976.0†)	0.7388	284.4 (7.4 – 976.0†)	188.5 (1.6* – 976.0†)	0.8596
	CRP, mg/L	96.0 (3.99 – 459.6)	133.7 (3.5 – 496.0†)	0.2646	145.7 (3.5 – 496.0†)	109.1 (7.3 – 496.0†)	0.708
	SAA, mg/L	173329.1 (14860.1 – 636991.2)	176974.2 (12226.0 – 1380000.0†)	0.3622	165464.6 (12226.0 – 1380000.0†)	211371.4 (13770.4 – 696334.1)	0.8621
	IL-5, pg/mL	6.3* (6.3* – 182.2)	23.2 (6.3* – 124.6)	0.6764	6.3* (6.3* – 86.5)	19.7 (6.3* – 182.2)	0.5092
	Ferritin, ng/mL	19490.9 (2758.8 – 29866.3)	10014.5 (875.2 – 31620.0†)	0.1643	9565.8 (2758.8 – 29866.3)	11486.6 (875.2 – 31620.0†)	0.8233
	IL-1RA, pg/mL	2227.8 (587.6 – 4224.3)	1313.9 (329.3 – 4000.0)	0.0925	2054.5 (431.2 – 4000.0)	1235.3 (329.3 – 4224.3)	0.2653
	IL-2Rα, pg/mL	17214.7 (5098.2 – 87978.1)	13246.7 (3759.5 – 100000.0†)	0.339	12776.3 (3759.5 – 87978.1)	17268.4 (4893.7 – 100000.0†)	0.1745
	GM-CSF, pg/mL	7.3	1.9*	0.6038	5.7	1.9*	0.5088

Immune-modulating		(1.9* – 112.5)	(1.9* – 239.7)		(1.9* – 239.7)	(1.9* – 197.8)	
	IFNγ, pg/mL	1365.8 (39.3 – 1876.0†)	551.6 (19.8 – 1876.0†)	0.3636	726 (19.8 – 1876.0†)	511.2 (21.0 – 1876.0†)	0.601
	IL-10, pg/mL	63.3 (0.7* – 466.0†)	21.4 (0.7* – 466.0†)	0.5558	26.3 (3.01 – 466.0†)	27.85 (0.7* – 466.0†)	0.5192
Chemokines	IL-8, pg/mL	277.9 (29.0 – 750.0†)	199.0 (25.2 – 750.0†)	0.4985	265.2 (52.6 – 750.0†)	212.4 (25.2 – 750.0†)	0.3532
	CXCL10, pg/mL	2000.0† (663.3 – 2000.0†)	2000.0† (276.8 – 2000.0†)	0.2668	2000.0† (525.3 – 2000.0†)	2000.0† (276.8 – 2000.0†)	0.3151
	MCP-1, pg/mL	1500.0† (452.8 – 1500.0†)	1500.0† (495.8 – 1500.0†)	0.3134	1500.0† (627.4 – 1500.0†)	1500.0† (452.8 – 1500.0†)	0.5301
Effector	Granzyme B, pg/mL	74.3 (1.0* – 10000.0 †)	22.1 (1.0* – 2499.7)	0.1124	57.5 (1.0* – 10000.0 †)	24.6 (1.0* – 2988.6)	0.4174

* Value represents lower limit of quantification in assay used.

† Value represents upper limit of quantification in assay used.

CRP, C-reactive protein; CXCL, C-X-C motif chemokine ligand; GM-CSF, granulocyte-macrophage colony-stimulating factor; IFNγ, interferon gamma; IL, interleukin; IP, interferon γ-induced protein; MCP, monocyte attractant protein; Rα, receptor alpha; RA, receptor antagonist; SAA, serum amyloid A.

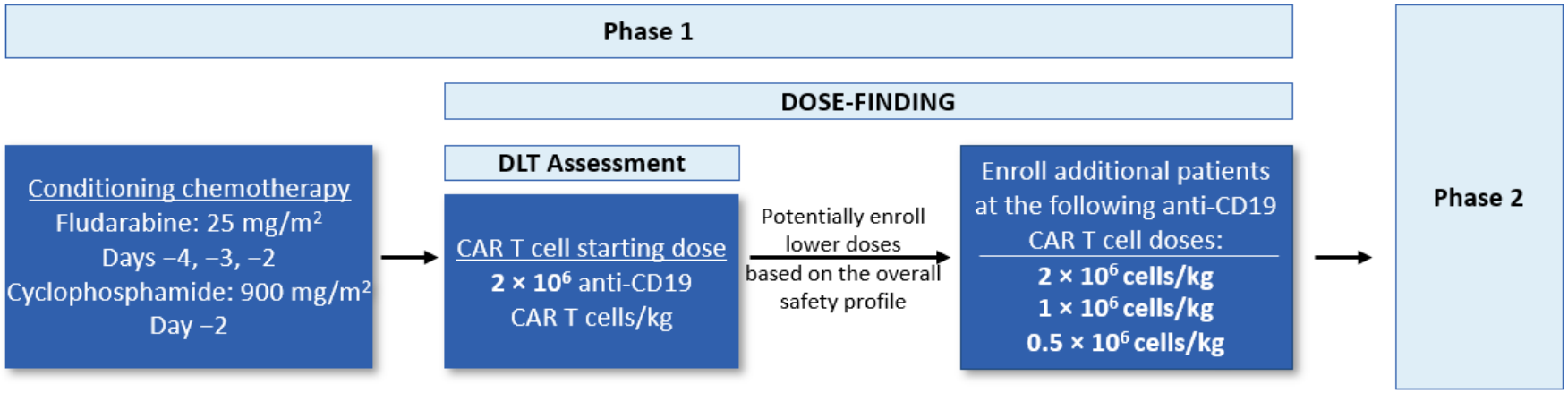
Supplemental Table 13. Product characteristics

Median characteristic (range)	2×10^6 (n = 6)	1×10^6 Original AE Management (n = 14)	1×10^6 Revised AE Management (n = 9)	0.5×10^6 (n = 16)
T-cell subsets, %				
Naïve	32.9 (16.4-60.5)	41.1 (9.9-73.2)	30.2 (0.1-65.0)	33.1 (12.5-80.9)
Central memory	34.5 (15.1-42.7)	21.9 (14.6-40.7)	19.3 (3.2-36.3)	18.0 (3.0-48.2)
Effector	8.9 (3.7-13.4)	8.9 (4.5-41.6)	14.5 (2.4-20.9)	14.3 (2.4-38.1)
Effector memory	20.7 (15.5-52.4)	18.4 (4.8-60.0)	19.9 (3.9-94.3)	22.6 (1.0-45.3)
CD4, %	44.7 (33.9-58.8)	47.6 (21.9-76.8)	56.8 (41.0-93.7)	58.8 (28.5-85.9)
CD8, %	55.4 (41.2-66.2)	49.0 (23.2-78.1)	43.3 (6.3-59.0)	41.2 (14.1-71.4)
CD4/CD8 ratio	0.8 (0.5-1.4)	1.0 (0.3-3.3)	1.4 (0.7-14.9)	1.4 (0.4-6.1)
IFNγ production in co-culture (pg/mL)*	7944.0 (1679.5-11214.4)	9980.5 (3025.0-37921.9)	10317.3 (5255.0-45235.7)	9059.5 (1040.6-27859.1)
Transduction, %	55.9 (44.0-72.0)	53.1 (31.8-77.6)	62.0 (20.0-82.0)	71.7 (19.0-81.0)
Viability, %	90.4 (88.8-93.9)	92.7 (88.2-96.7)	87.0 (75.0-97.0)	89.0 (82.0-96.4)

* Co-culture experiments were performed using Toledo cells mixed in a 1:1 ratio with KTE-X19 product cells. IFNγ was measured in cell culture media 24 h post-incubation using a qualified ELISA.

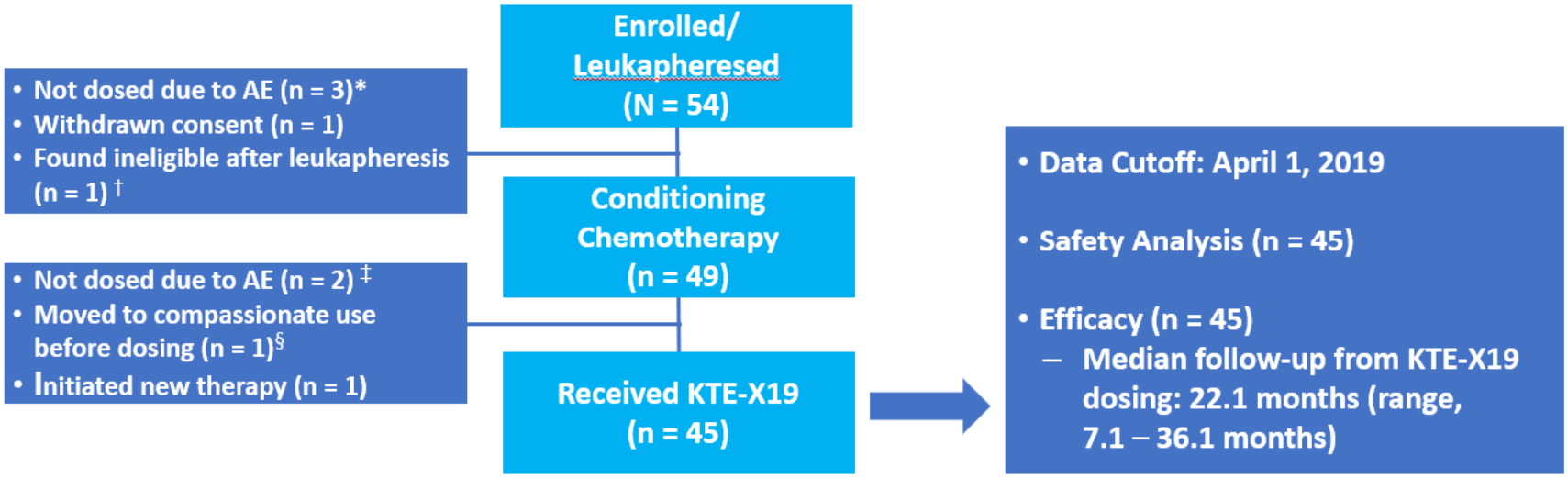
AE, adverse event; IFNγ, interferon gamma.

Supplemental Figure 1. ZUMA-3 Study Design



CAR, chimeric antigen receptor; DLT, dose-limiting toxicity.

Supplemental Figure 2. ZUMA-3 CONSORT Diagram



* AEs were grade 3 pulmonary mass (n = 1), grade 1 subdural hematoma (n = 1), and grade 3 febrile neutropenia (n = 1).

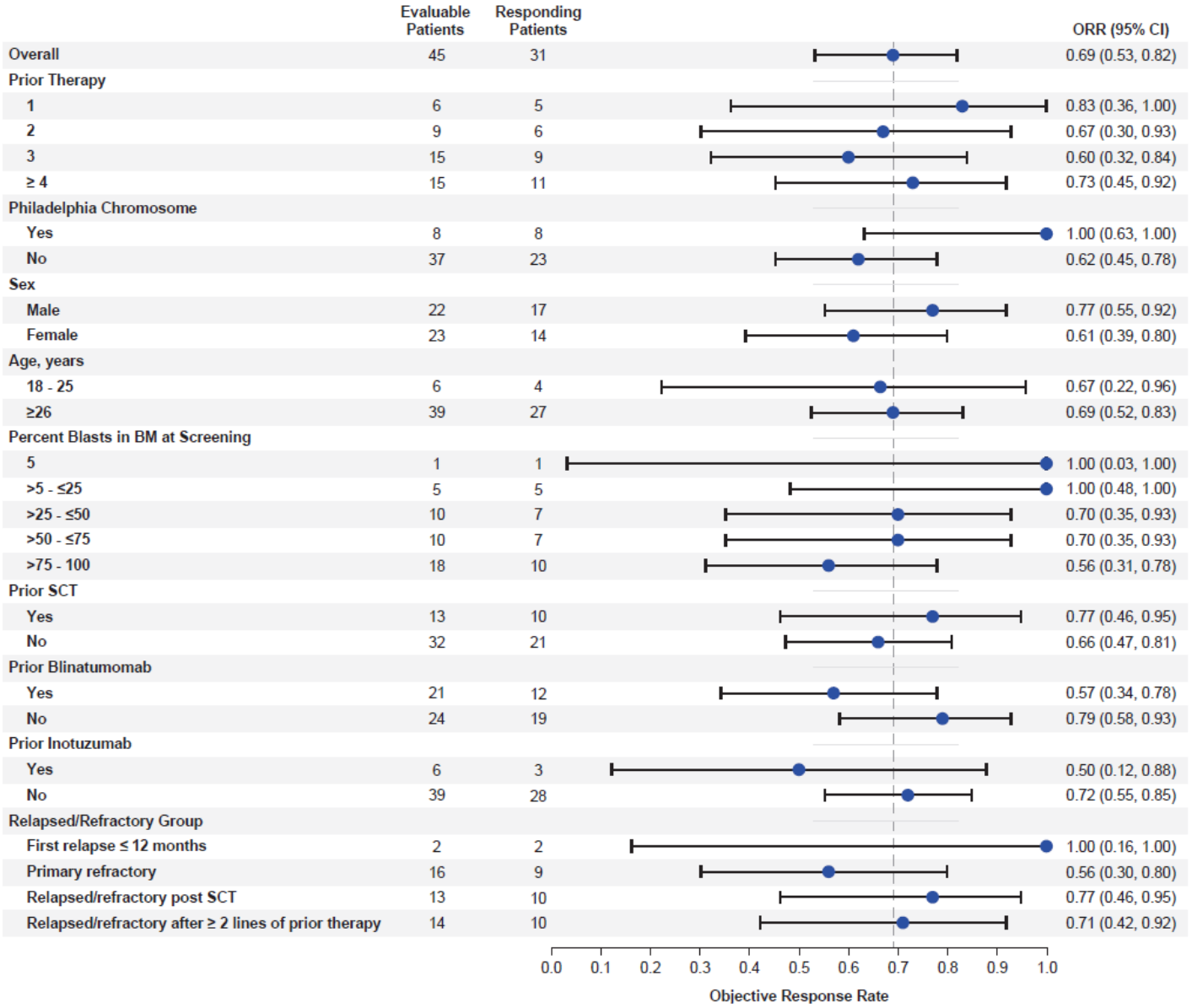
† Due to central nervous system abnormality (brain lesion).

‡ AEs were grade 4 sepsis (n = 1) and grade 5 sepsis (n = 1).

§ One patient did receive KTE-X19 under compassionate use due to deep vein thrombosis, a study exclusion criterion.

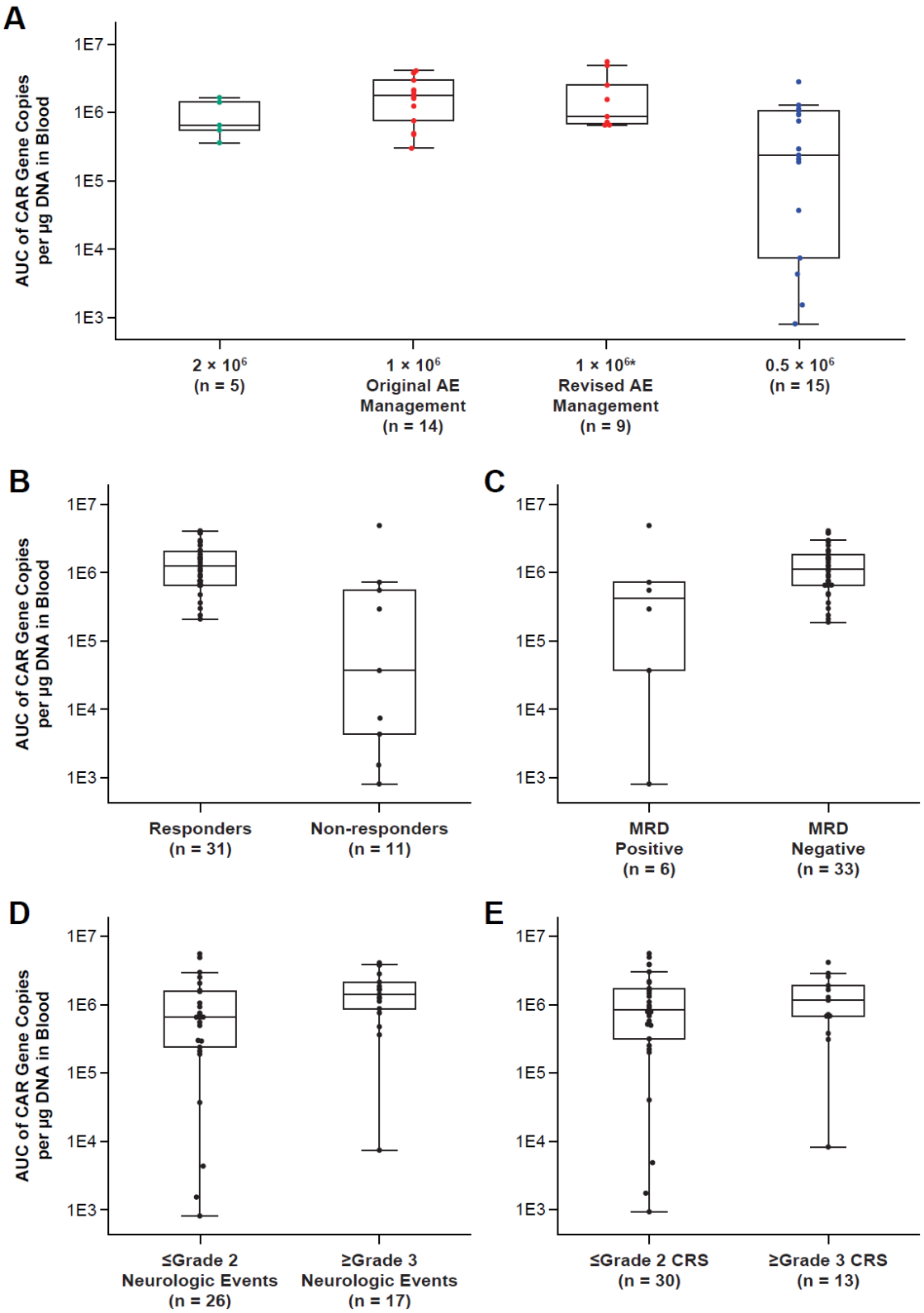
AE, adverse event.

Supplemental Figure 3. Subgroup analysis of complete response rate



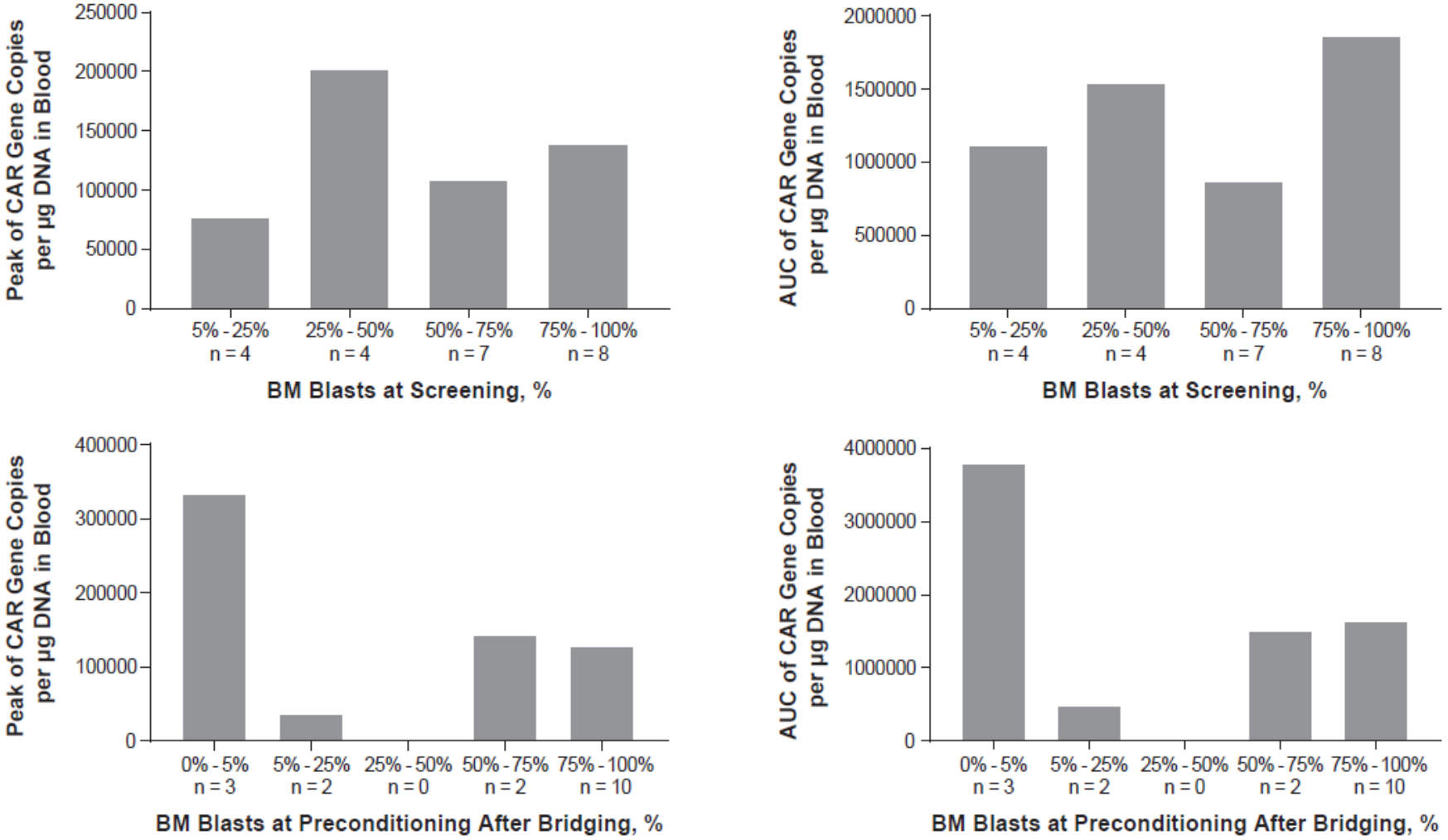
BM, bone marrow; ORR, overall remission rate; SCT, stem cell transplant.

Supplemental Figure 4. CAR T-cell area under the curve associations with response, minimal residual disease, and toxicity



AE, adverse event; AUC, area under the curve; CAR, chimeric antigen receptor; CRS, cytokine release syndrome; MRD, minimal residual disease.

Supplemental Figure 5. Median peak and AUC of CAR gene copies in blood by quartile of percent bone marrow blasts at screening or preconditioning after bridging



AUC, area under the curve; BM, bone marrow; CAR, chimeric antigen receptor.

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