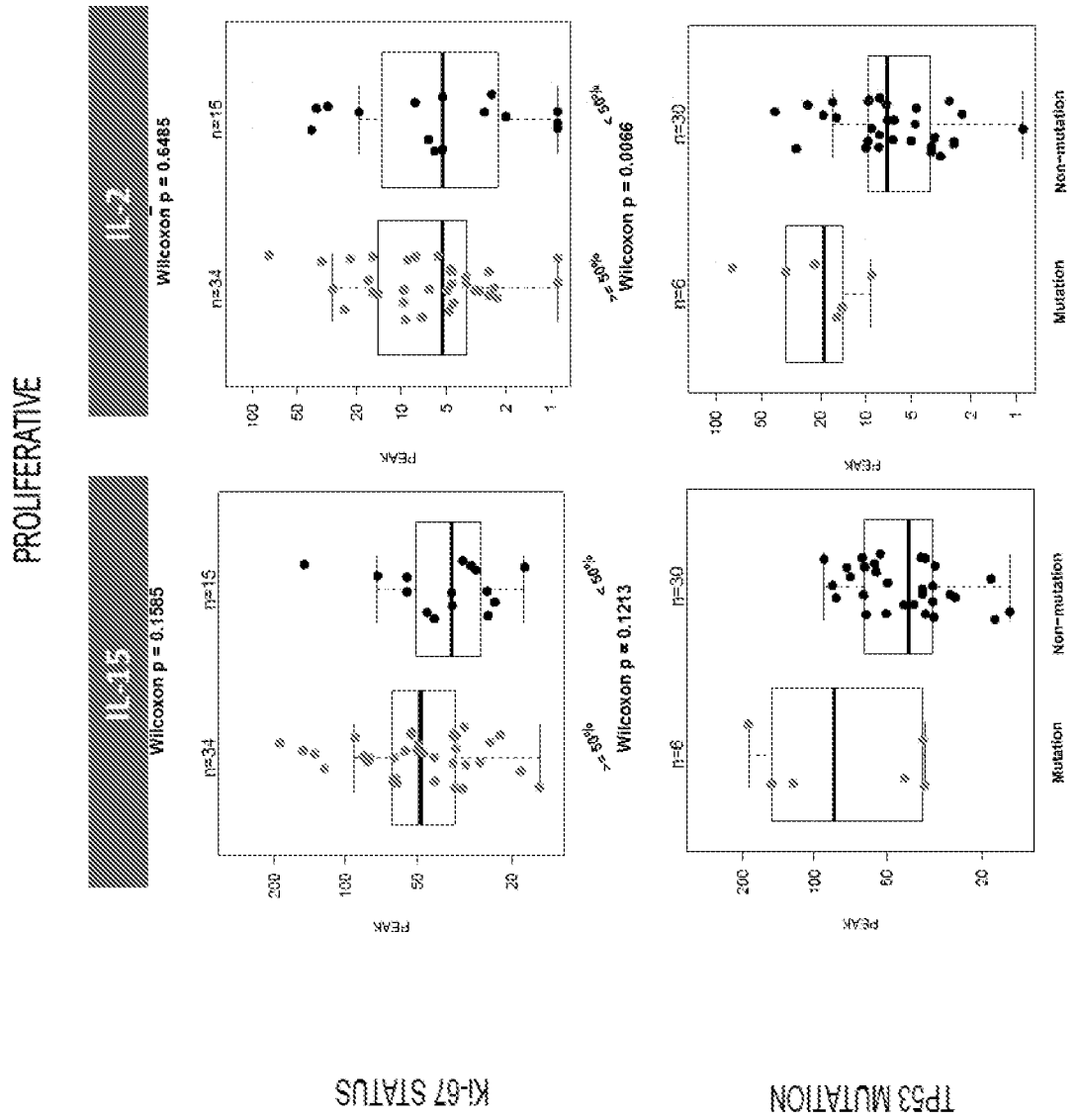

PROLIFERATIVE
IL-15
IL-2
Wilcoxon p = 0.1585
Wilcoxon p = 0.6485
Wilcoxon p = 0.1213
Wilcoxon p = 0.0066
n=34
n=16
n=6
n=30
PEAK
Mutation
Non-mutation
KI-67 STATUS
TP53 MUTATION

FIG. 1A

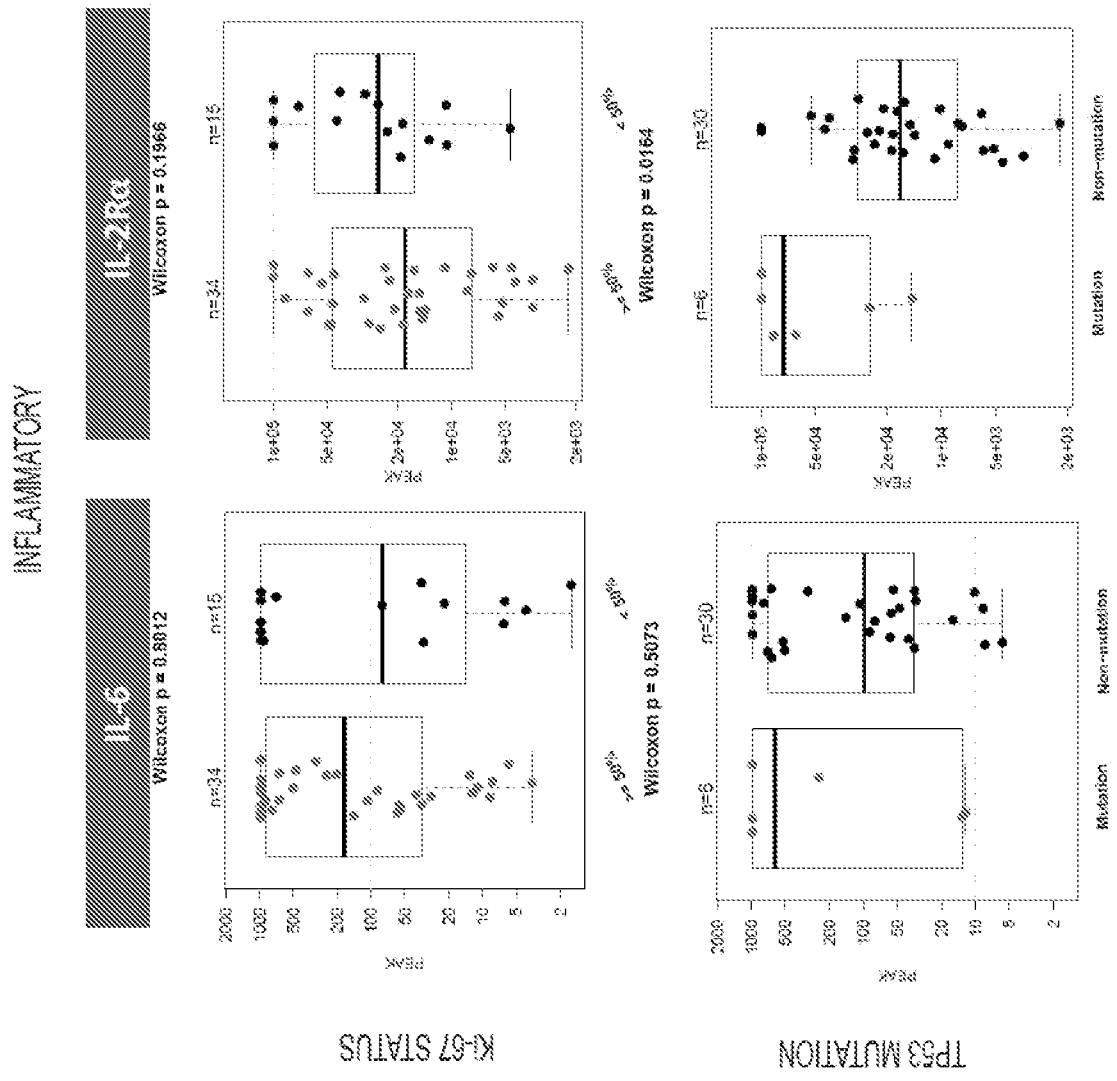

INFLAMMATORY
IL6
Wilcoxon p = 0.8812
IL2Ra
Wilcoxon p = 0.1966
Wilcoxon p = 0.5073
Wilcoxon p = 0.6164
Ki-67 STATUS
TP53 MUTATION
PEAK
n=34
n=15
n=6
n=30
Mutation
Non-mutation

FIG. 1B

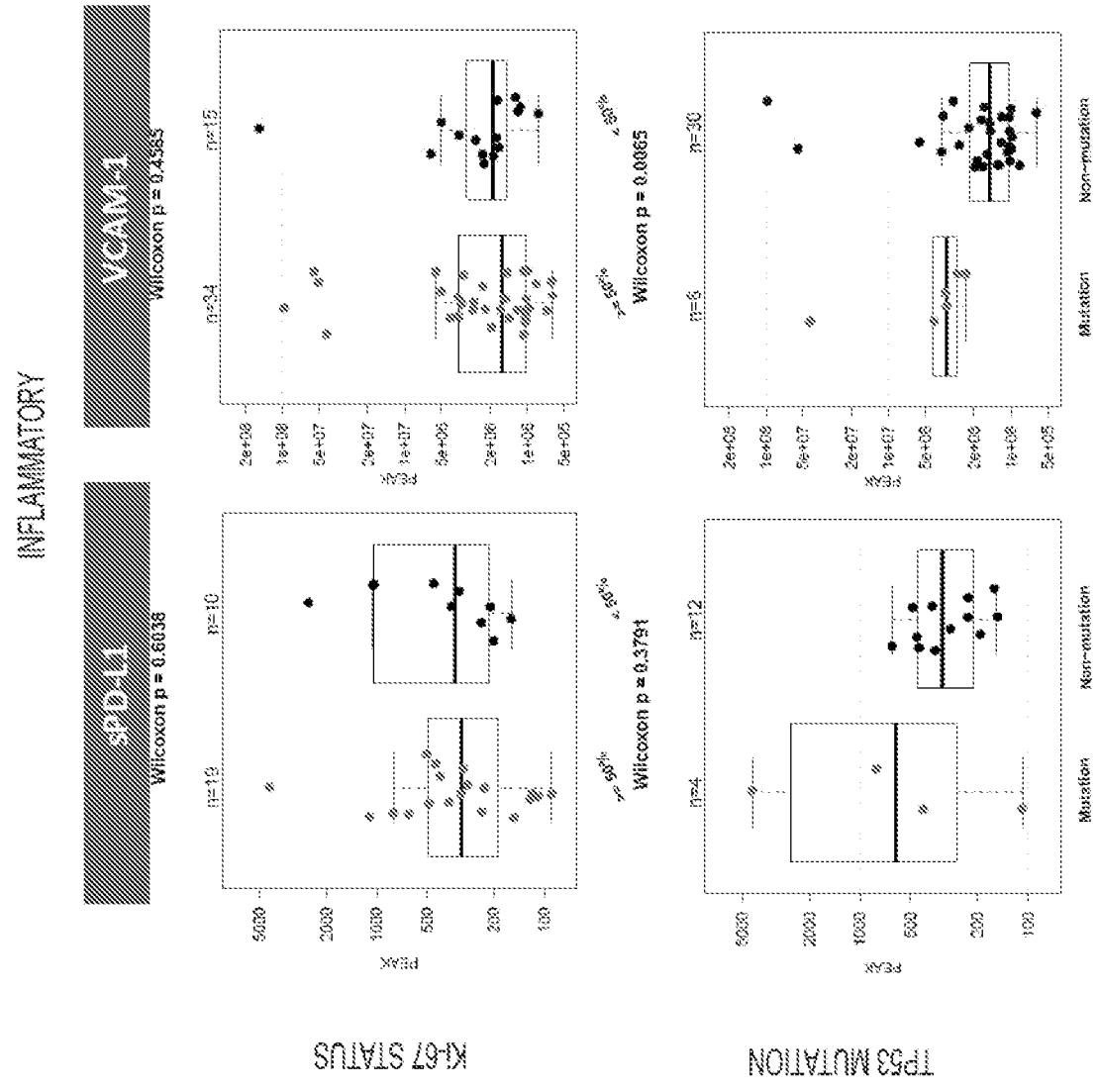

INFLAMMATORY
SPP1
Wilcoxon p = 0.6038
VCAM1
Wilcoxon p = 0.4585
Ki-67 STATUS
n=19
n=10
n=34
n=15
PEAK
Wilcoxon p = 0.3791
Wilcoxon p = 0.0065
TP53 MUTATION
n=4
n=12
n=6
n=30
Mutation
Non-mutation

FIG. 1C

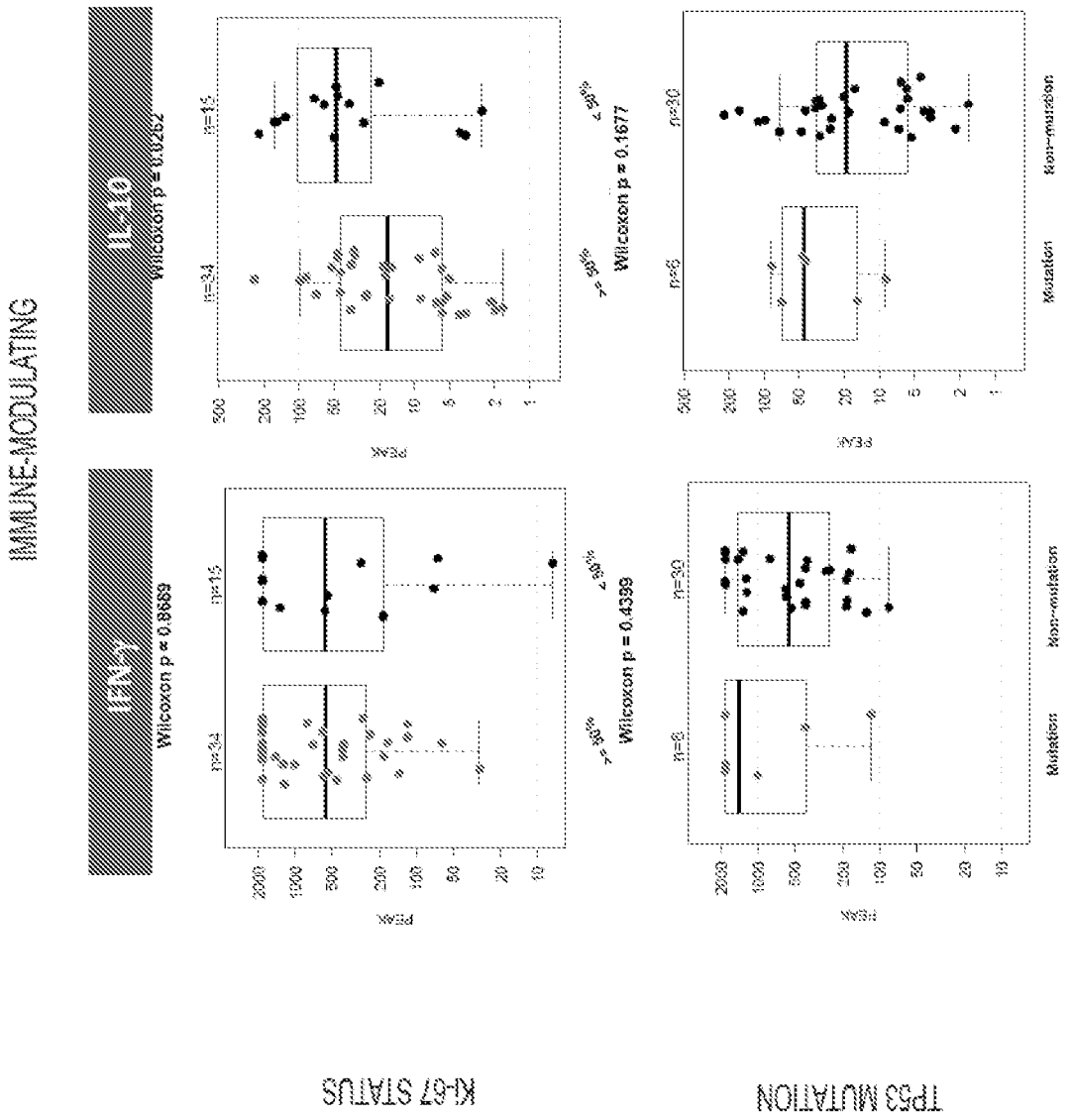

IMMUNE-MODULATING
IFN-γ
Wilcoxon p = 0.8689
IL-10
Wilcoxon p = 0.0262
Wilcoxon p = 0.4399
Wilcoxon p = 0.1677
PEAK
Mutation
Non-mutation
Ki-67 STATUS
TP53 MUTATION

FIG. 1D

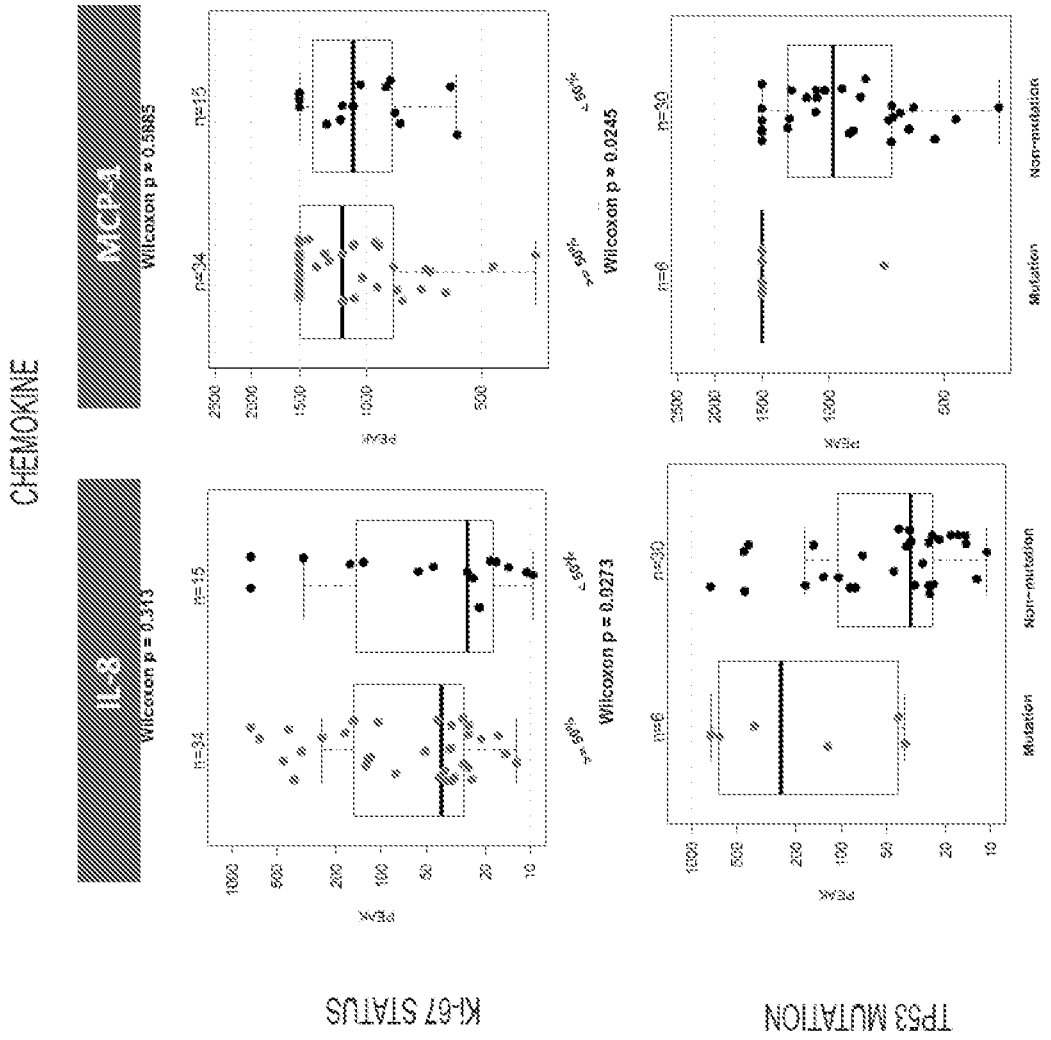

CHEMOKINE
IL-8
Wilcoxon p = 0.313
MCP-1
Wilcoxon p = 0.5885
Wilcoxon p = 0.0273
Wilcoxon p = 0.0245
n=34
n=15
n=6
n=30
PE/M
Mutation
Non-mutation
Ki-67 STATUS
TP53 MUTATION

FIG. 1E

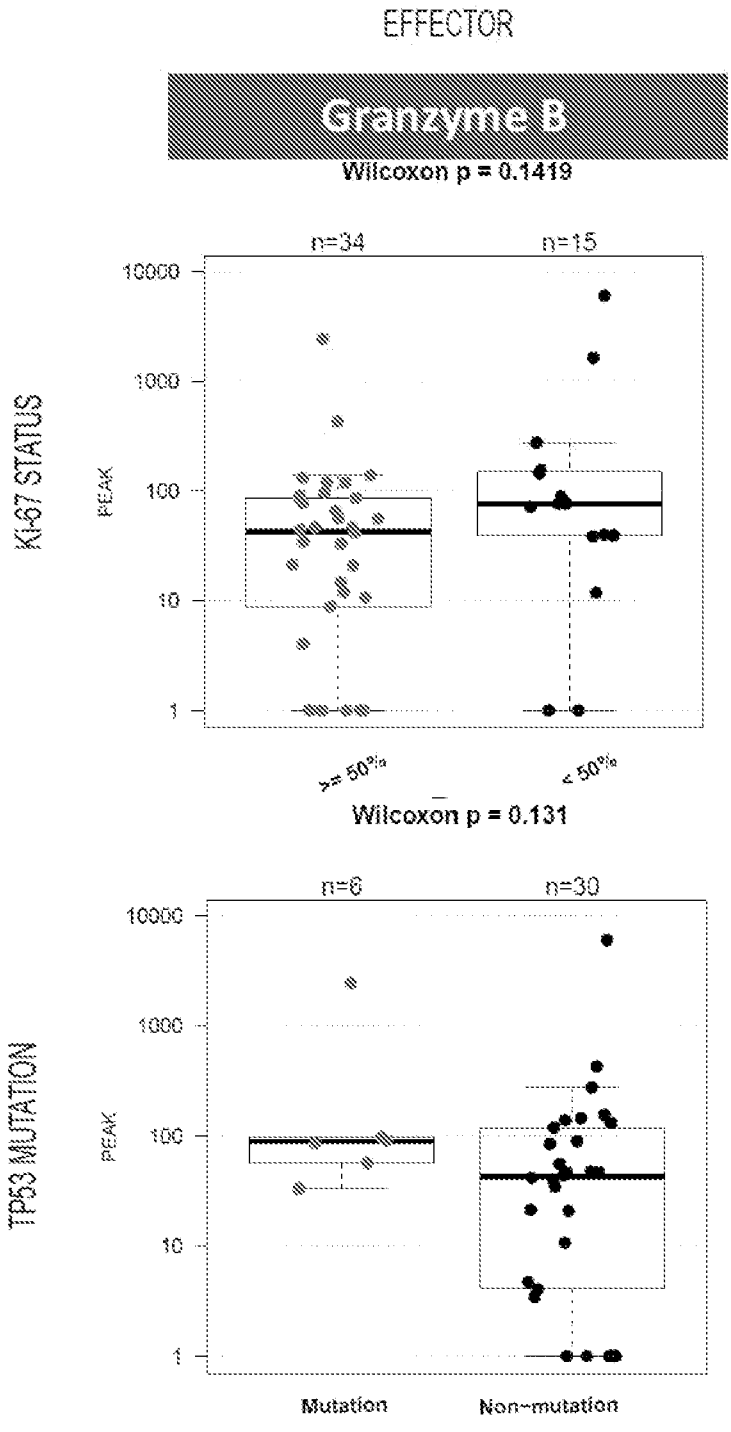

EFFECTOR
Granzyme B
Wilcoxon p = 0.1419
n=34
n=15
KI-67 STATUS
PEAK
10000
1000
100
10
1
>= 50%
< 50%
Wilcoxon p = 0.131
n=6
n=30
TP53 MUTATION
PEAK
10000
1000
100
10
1
Mutation
Non-mutation

FIG. 1F

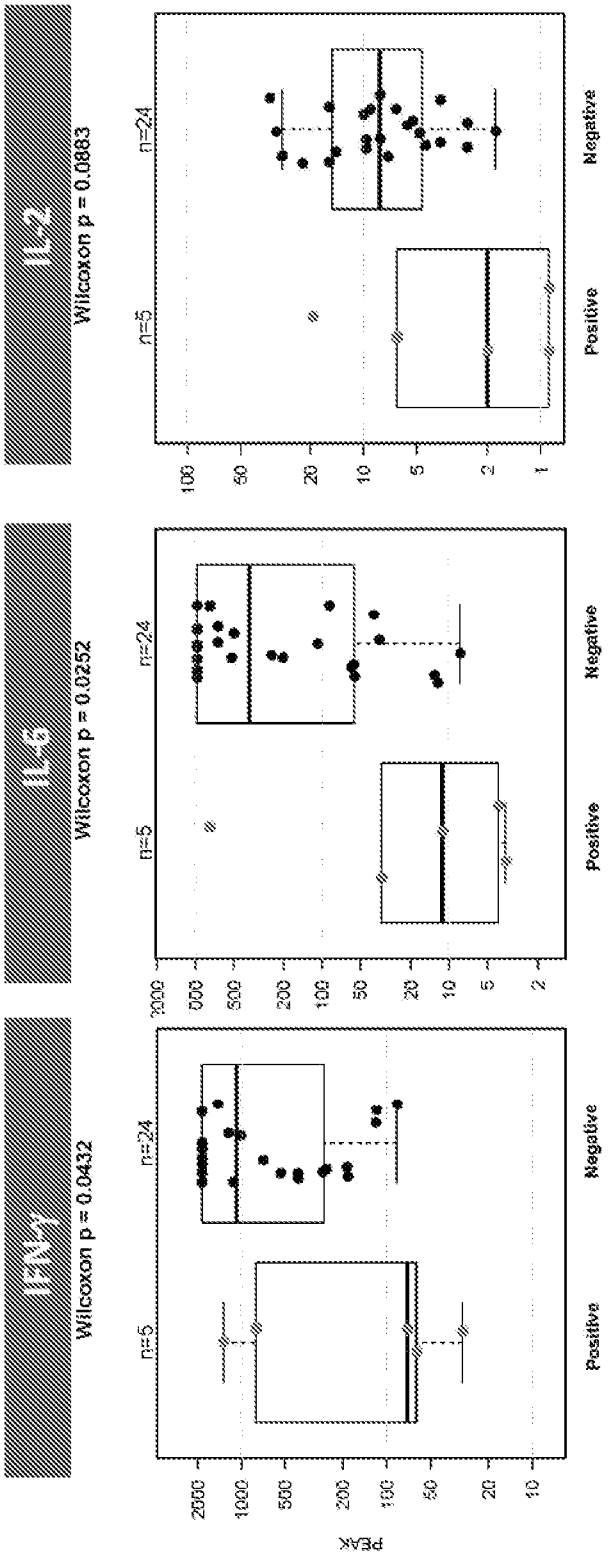

IFNγ
Wilcoxon p = 0.0432
n=5
n=24
Positive
Negative
PEAK
2000
1000
500
200
100
50
20
10
IL-6
Wilcoxon p = 0.0252
n=5
n=24
Positive
Negative
1000
500
200
100
50
20
10
5
2
IL-2
Wilcoxon p = 0.0883
n=5
n=24
Positive
Negative
100
50
20
10
5
2
1

FIG. 2A

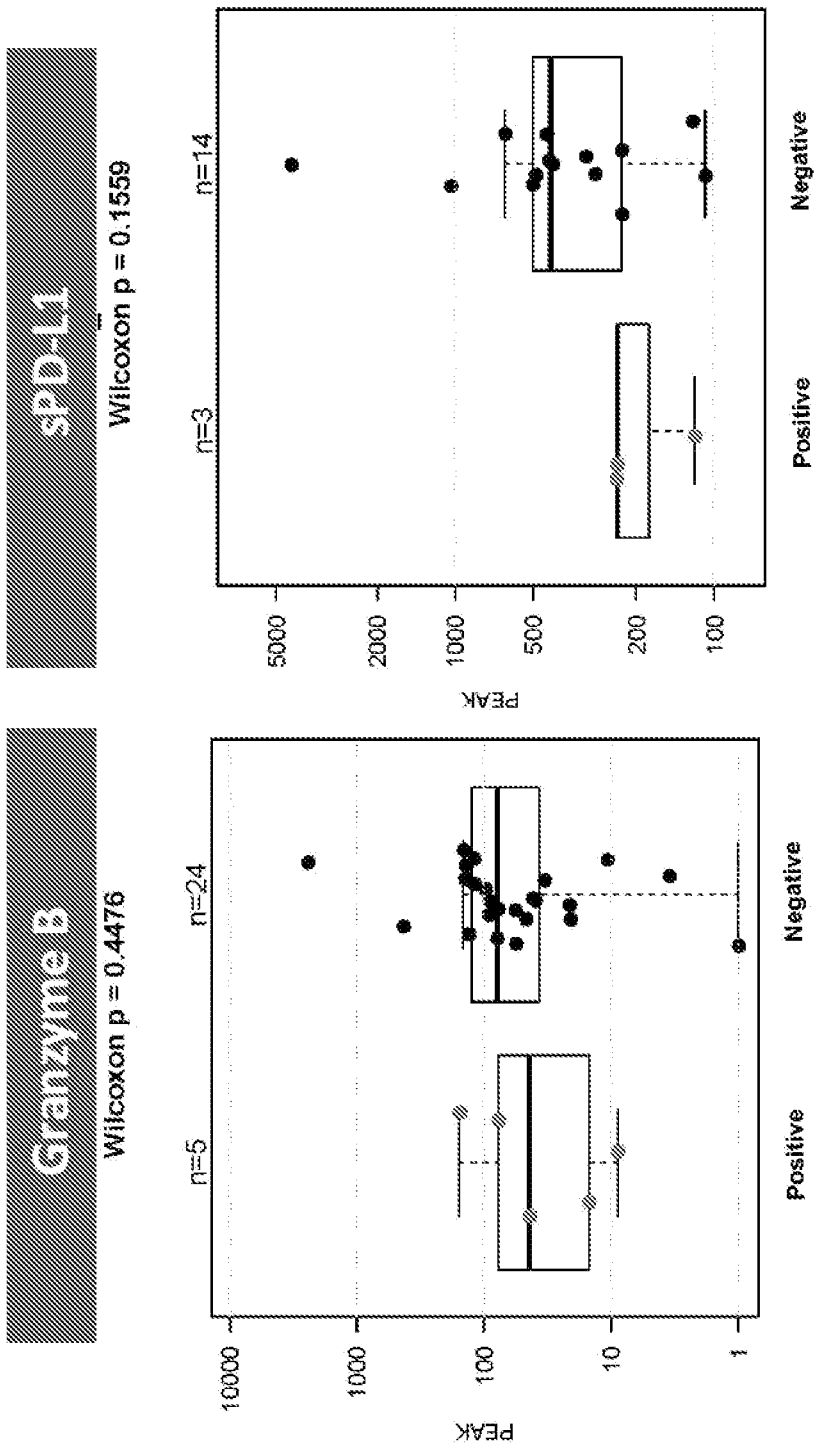

Granzyme B
Wilcoxon p = 0.4476
n=5
n=24
PEAK
10000
1000
100
10
1
Positive
Negative
sPD-L1
Wilcoxon p = 0.1559
n=3
n=14
PEAK
5000
2000
1000
500
200
100
Positive
Negative

FIG. 2B

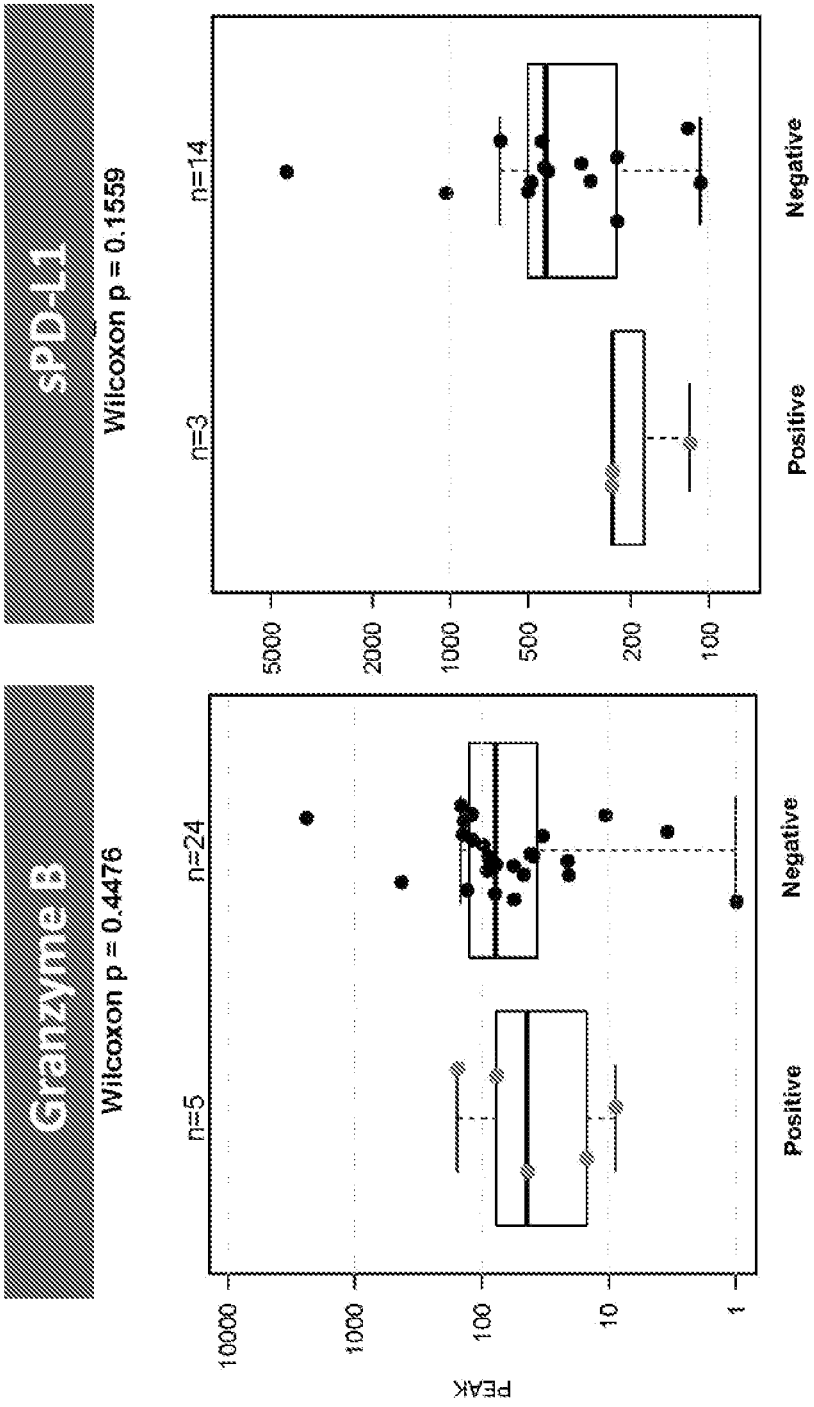

Granzyme B
Wilcoxon p = 0.4476
n=5
n=24
sPD-L1
Wilcoxon p = 0.1559
n=3
n=14
PEAK
10000
1000
100
10
1
5000
2000
1000
500
200
100
Positive
Negative
Positive
Negative

FIG. 2C

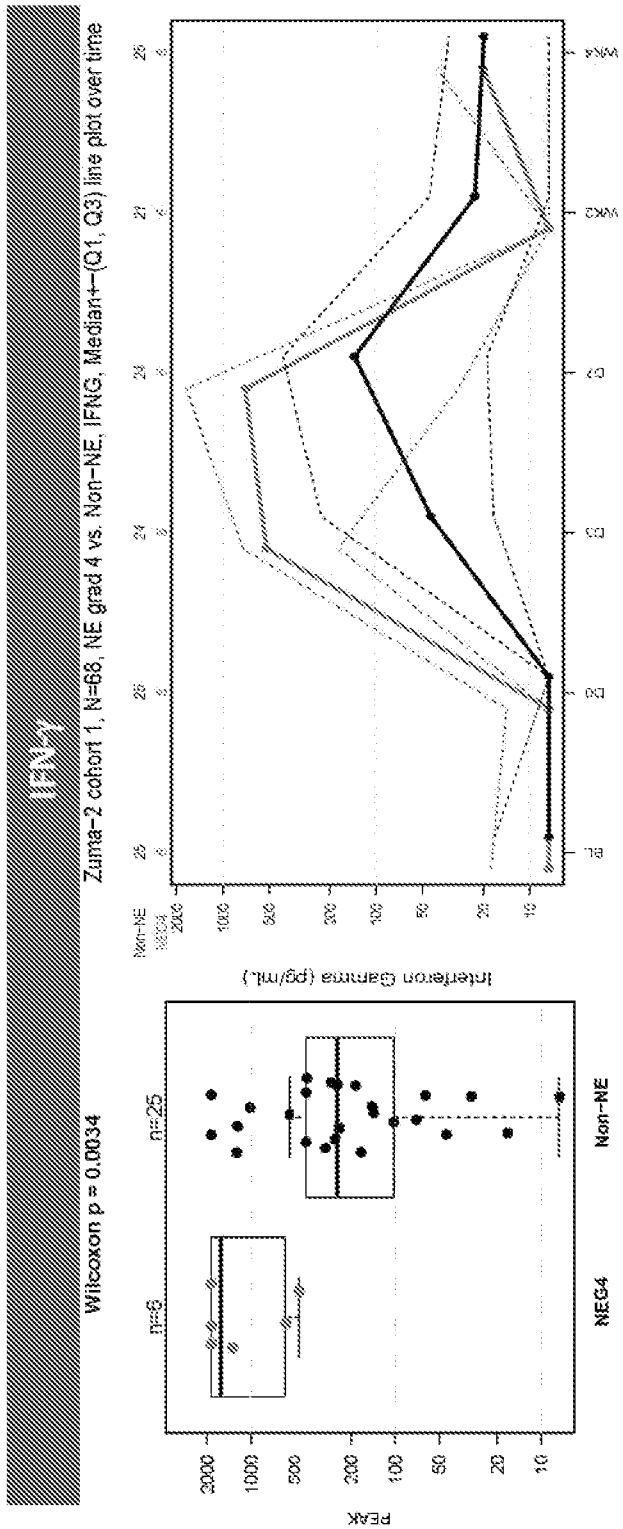

IFN17
Zuma-2 cohort 1, N=68, NE grad 4 vs. Non-NE, IFNG, Median+-(Q1, Q3) line plot over time
Interferon Gamma (pg/mL)
Non-NE
NEG4
C1
C2
C3
EOT
Wilcoxon p = 0.0034
n=6
n=25
PEAK
NEG4
Non-NE

FIG. 2D

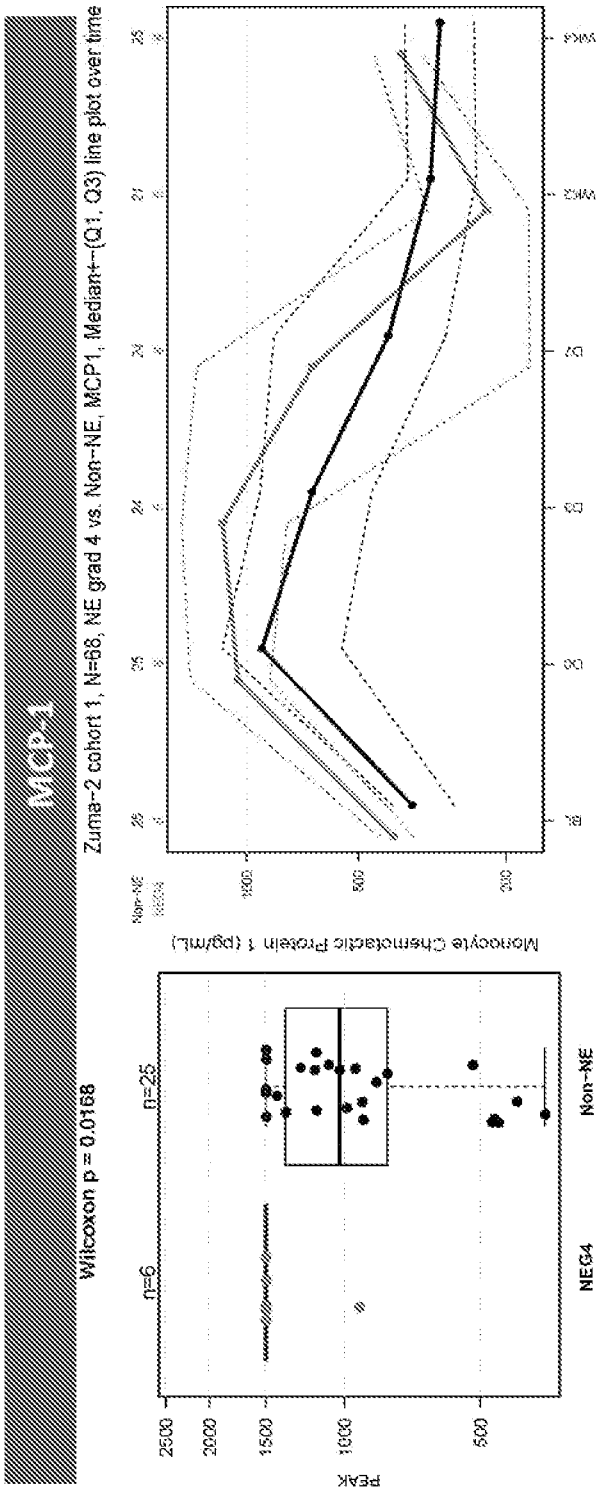

MCP-1
Wilcoxon p = 0.0168
n=6
n=25
PEAK
2500
2000
1500
1000
500
NEG4
Non-NE
Zuma-2 cohort 1, N=68, NE grad 4 vs. Non-NE, MCP1, Median+-(Q1, Q3) line plot over time
Monocyte Chemotactic Protein 1 (pg/mL)
Non-NE
NEG4
1500
500
-200
BL
C2D1
C2D8
C2D15
C3D1
W4
W8
W12
W24

FIG. 2E

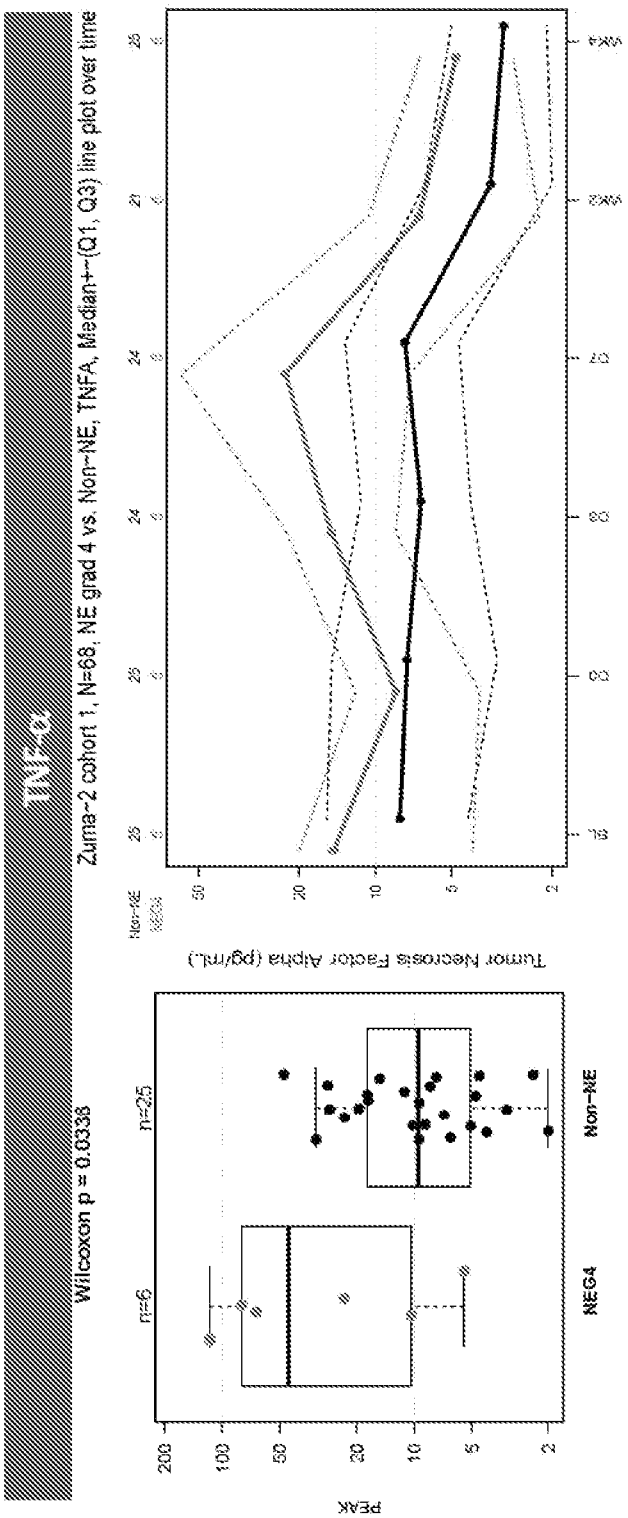

TNF-α
Zuma-2 cohort 1, N=68, NE grad 4 vs. Non-NE, TNFA, Median+-(Q1, Q3) line plot over time
Wilcoxon p = 0.0338
PEAK
n=6
n=25
NEG4
Non-NE
Tumor Necrosis Factor Alpha (pg/mL)
Non-NE
n=25
Wk1
Wk2
Wk4

FIG. 2F

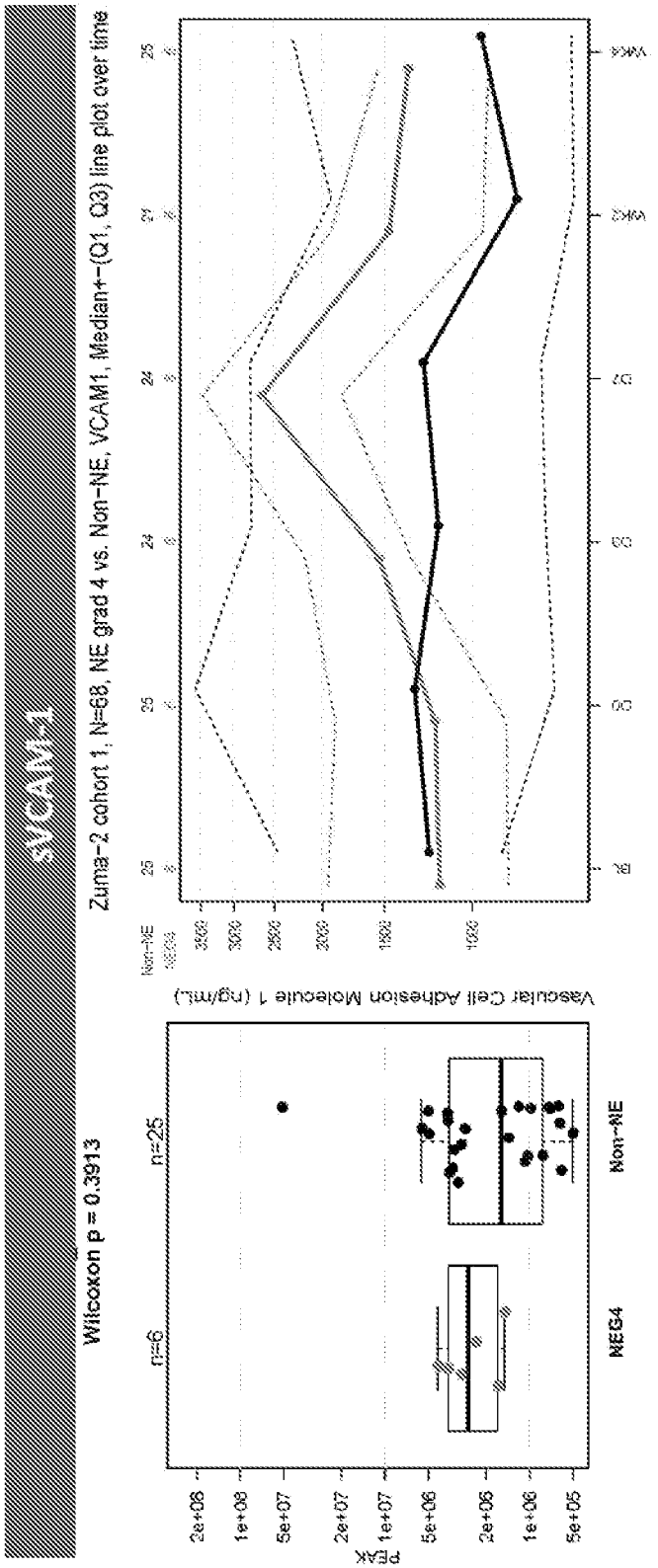

sVCAM-1
Zuma-2 cohort 1, N=68, NE grad 4 vs. Non-NE, VCAM1, Median+-(Q1, Q3) line plot over time
Vascular Cell Adhesion Molecule 1 (ng/mL)
Wilcoxon p = 0.3913
n=6
n=25
PEAK
NEG4
Non-NE

FIG. 2G

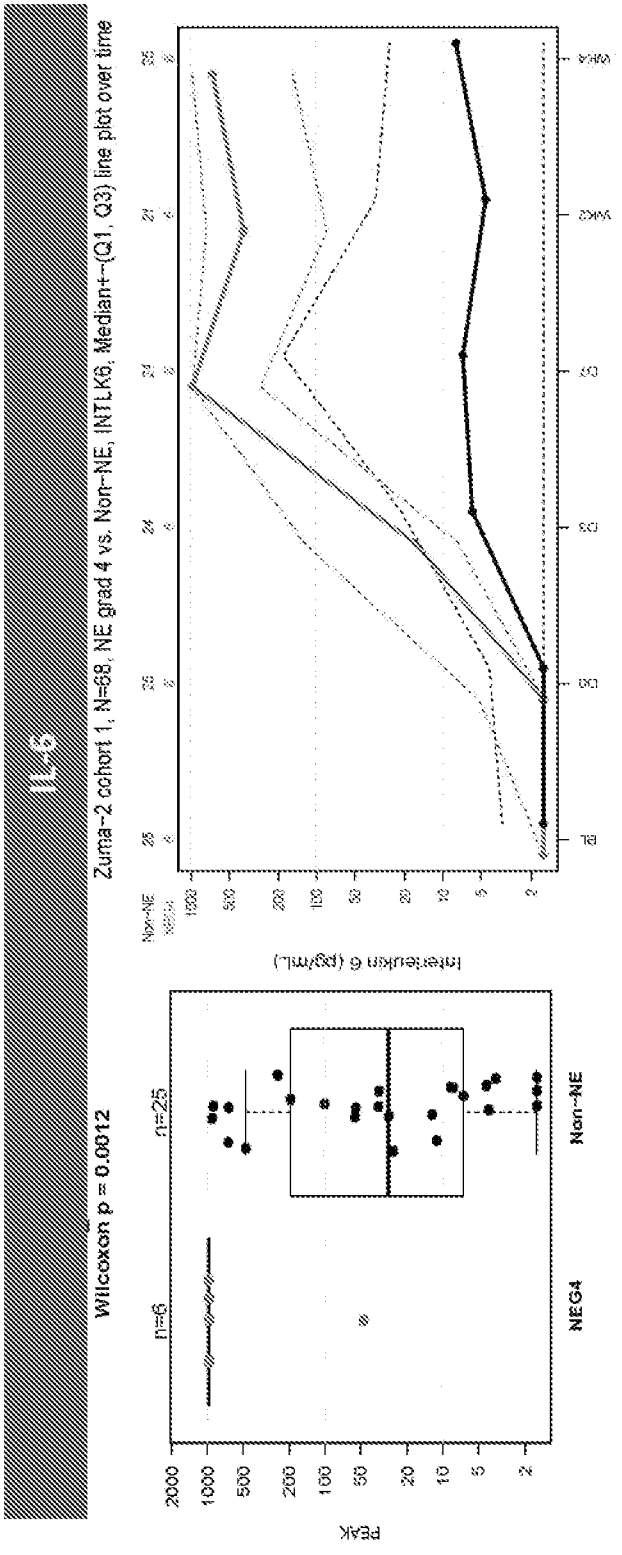

IL-6
Zuma-2 cohort 1, N=68, NE grad 4 vs. Non-NE, INTLK6, Median+-(Q1, Q3) line plot over time
Wilcoxon p = 0.0012
n=6
n=25
NEG4
Non-NE
PEAK
Interleukin 6 (pg/mL)
Non-NE
NEG4
Wk2

FIG. 2H

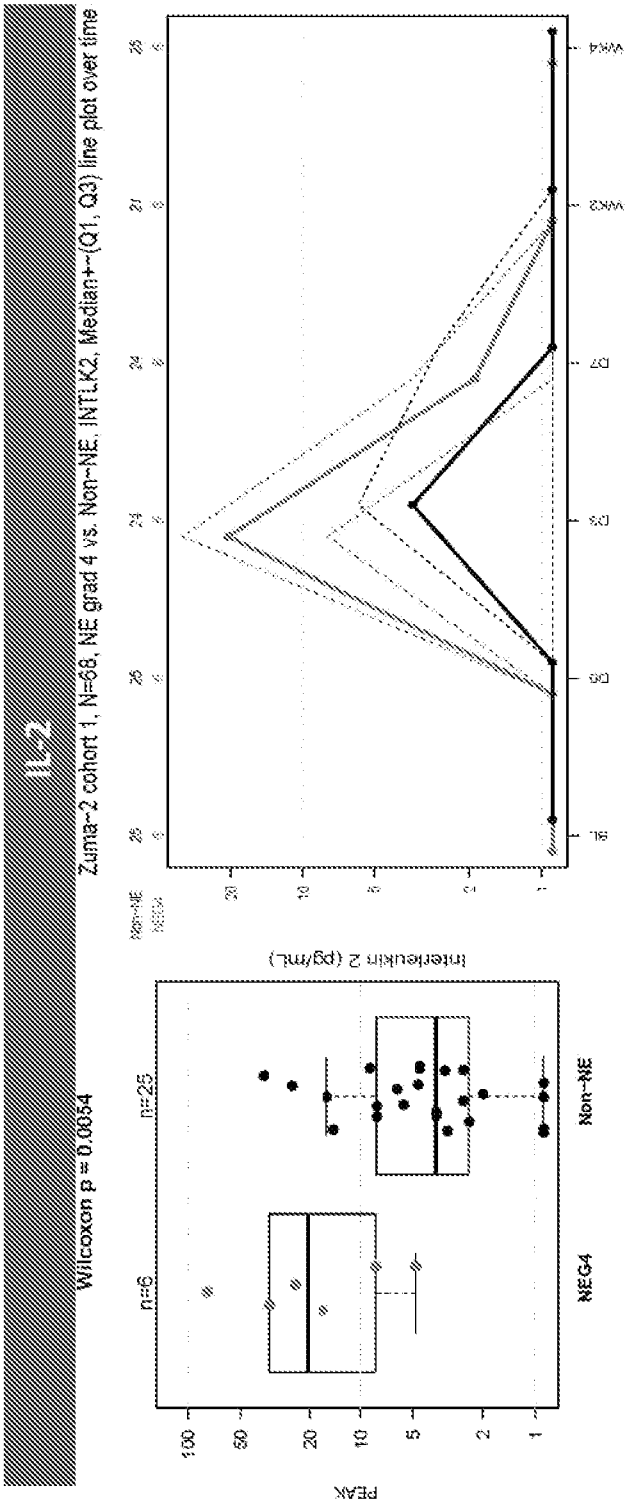

IL-2
Zuma-2 cohort 1, N=68, NE grad 4 vs. Non-NE, INTLK2, Median+-(Q1, Q3) line plot over time
Wilcoxon p = 0.0054
n=6
n=25
NEG4
Non-NE
PEAK
100
50
20
10
5
2
1
interleukin 2 (pg/mL)
Non-NE
BL
D8
D15
D22
D29
WK2
WK4

FIG. 2I

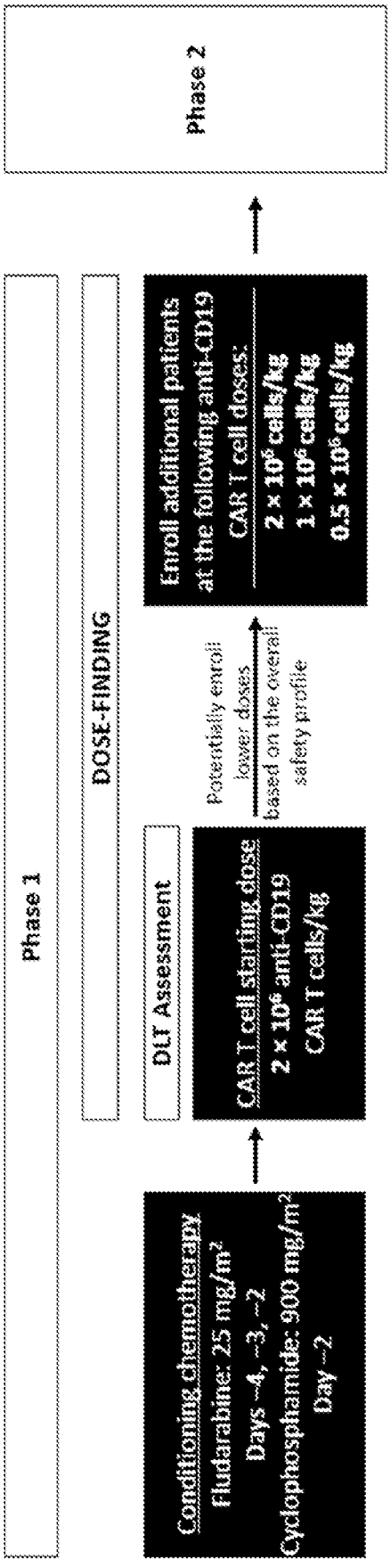

Phase 1
DOSE-FINDING
DLT Assessment
Conditioning chemotherapy
Fludarabine: 25 mg/m²
Days −4, −3, −2
Cyclophosphamide: 900 mg/m²
Day −2
CAR T cell starting dose
2 × 10⁶ anti-CD19
CAR T cells/kg
Potentially enroll lower doses based on the overall safety profile
Enroll additional patients at the following anti-CD19 CAR T cell doses:
2 × 10⁶ cells/kg
1 × 10⁶ cells/kg
0.5 × 10⁶ cells/kg
Phase 2

FIG. 3

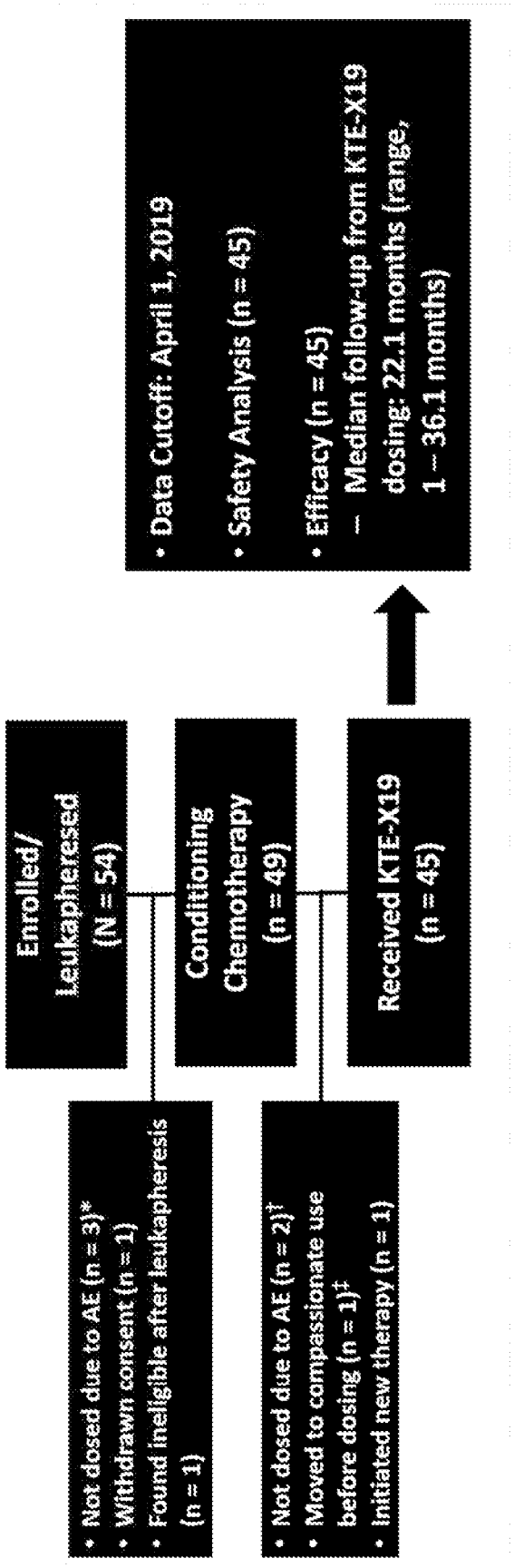

Enrolled/ Leukapheresed (N = 54)
Conditioning Chemotherapy (n = 49)
Received KTE-X19 (n = 45)
• Not dosed due to AE (n = 3)*
• Withdrawn consent (n = 1)
• Found ineligible after leukapheresis (n = 1)
• Not dosed due to AE (n = 2)†
• Moved to compassionate use before dosing (n = 1)‡
• Initiated new therapy (n = 1)
• Data Cutoff: April 1, 2019
• Safety Analysis (n = 45)
• Efficacy (n = 45)
– Median follow-up from KTE-X19 dosing: 22.1 months (range, 1 – 36.1 months)

FIG. 4

FIG. 5

Evaluable Patients
Responding Patients
ORR (95% CI)
Overall 46 31 0.69 (0.53, 0.82)
Prior Therapy
1 8 6 0.83 (0.36, 1.00)
2 9 6 0.67 (0.30, 0.93)
3 18 8 0.50 (0.23, 0.77)
≥ 4 15 11 0.73 (0.45, 0.92)
Philadelphia Chromosome
Yes 8 8 1.00 (0.63, 1.00)
No 37 23 0.62 (0.45, 0.78)
Sex
Male 22 17 0.77 (0.55, 0.92)
Female 23 14 0.61 (0.39, 0.80)
Percent Blasts in BM at Screening
5 1 1 1.00 (0.03, 1.00)
>5 - ≤25 5 5 1.00 (0.48, 1.00)
>25 - ≤50 10 7 0.70 (0.35, 0.93)
>50 - ≤75 10 7 0.70 (0.35, 0.93)
>75 - 100 18 10 0.56 (0.31, 0.78)
Prior SCT
Yes 13 10 0.77 (0.46, 0.95)
No 33 21 0.64 (0.47, 0.81)
Prior Blinatumomab
Yes 21 15 0.67 (0.43, 0.85)
No 24 16 0.70 (0.48, 0.85)
Prior Inotuzumab
Yes 6 3 0.50 (0.12, 0.88)
No 39 28 0.72 (0.56, 0.85)
Relapsed/Refractory Group
First relapse ≤ 12 months 2 2 1.00 (0.16, 1.00)
Primary refractory 16 9 0.56 (0.30, 0.80)
Relapsed/refractory post SCT 13 10 0.77 (0.46, 0.95)
Relapsed/refractory after ≥ 2 lines of prior therapy 14 10 0.71 (0.42, 0.92)
0.0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0
Objective Response Rate

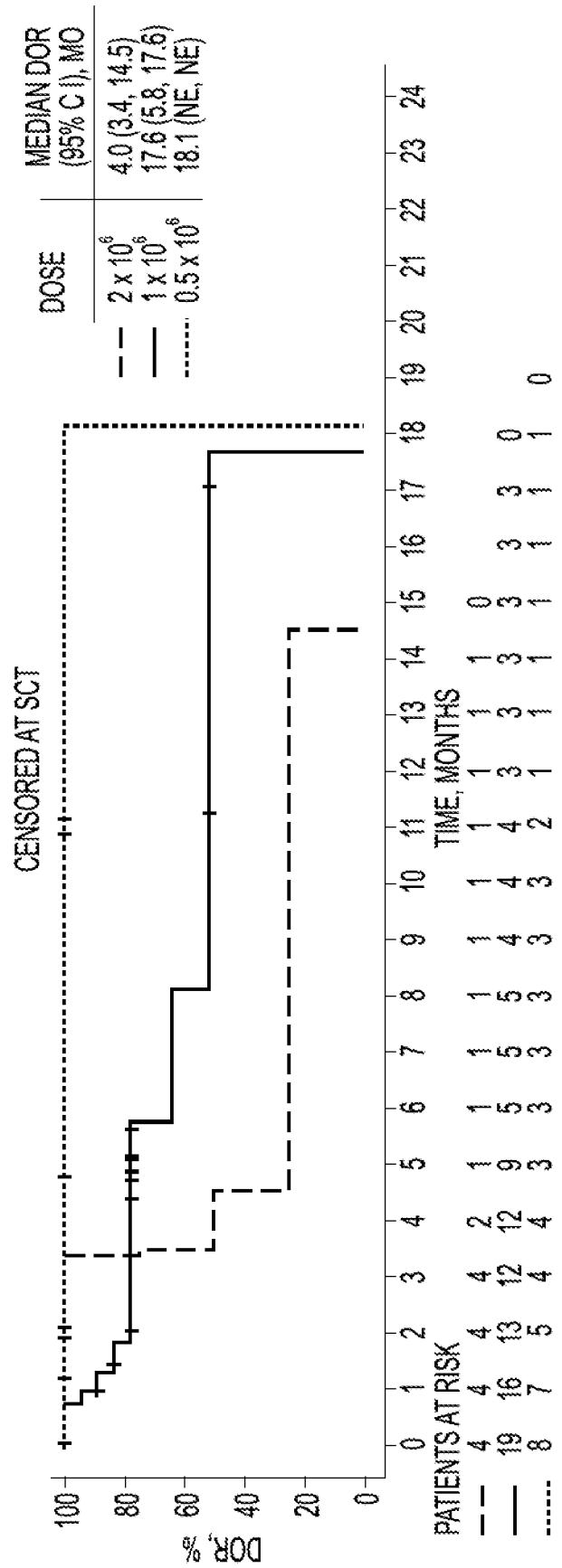

DOSE
MEDIAN DOR (95% CI), MO
2 x 10^6 4.0 (3.4, 14.5)
1 x 10^6 17.6 (5.8, 17.6)
0.5 x 10^6 18.1 (NE, NE)
CENSORED AT SCT
DOR, %
100
80
60
40
20
0
TIME, MONTHS
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24
PATIENTS AT RISK
4 4 4 4 2 1 1 1 1 1 1 1 1 1 1 0
19 16 13 12 12 9 5 5 5 4 4 4 3 3 3 3 3 3 1 0
8 7 5 4 4 3 3 3 3 3 3 2 1 1 1 1 1 1 1

FIG. 6A

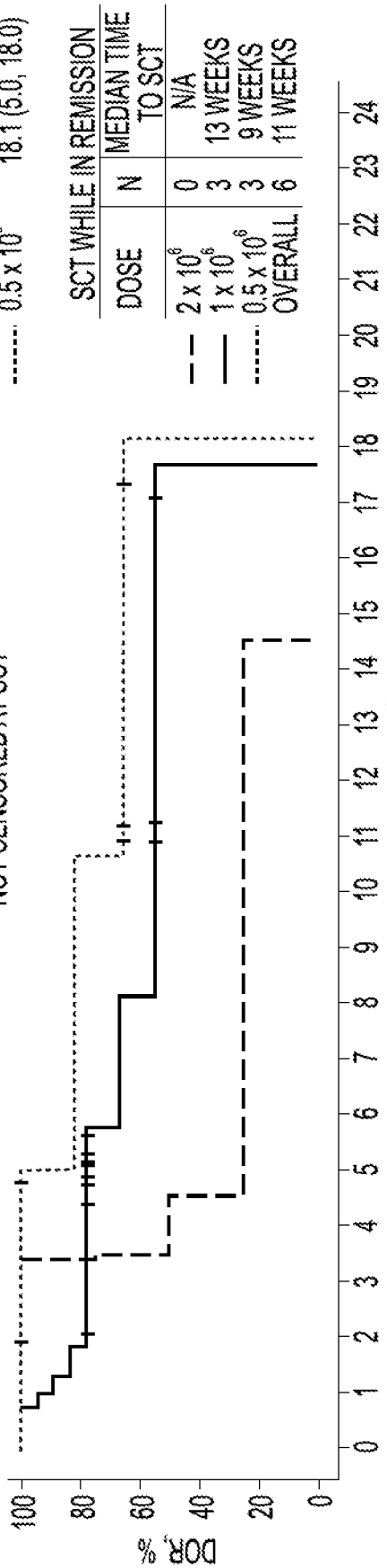

DOSE
MEDIAN DOR (95% CI), MO
2 x 10^6 4.0 (3.4, 14.5)
1 x 10^6 17.6 (5.8, 17.6)
0.5 x 10^6 18.1 (5.0, 18.0)
SCT WHILE IN REMISSION
DOSE
N
MEDIAN TIME TO SCT
2 x 10^6 0 N/A
1 x 10^6 3 13 WEEKS
0.5 x 10^6 3 9 WEEKS
OVERALL 6 11 WEEKS
NOT CENSORED AT SCT
DOR, %
100
80
60
40
20
0
TIME, MONTHS
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24
PATIENTS AT RISK
4 4 4 4 2 1 1 1 1 1 1 1 1 1 1 0 3 3 3 0
19 17 15 14 14 11 6 6 5 5 5 4 3 2 2 2 2 2 2 1 0
8 8 8 7 7 5 5 5 5 5 3 2 2 2 2 2 2 1 1 0

FIG. 6B

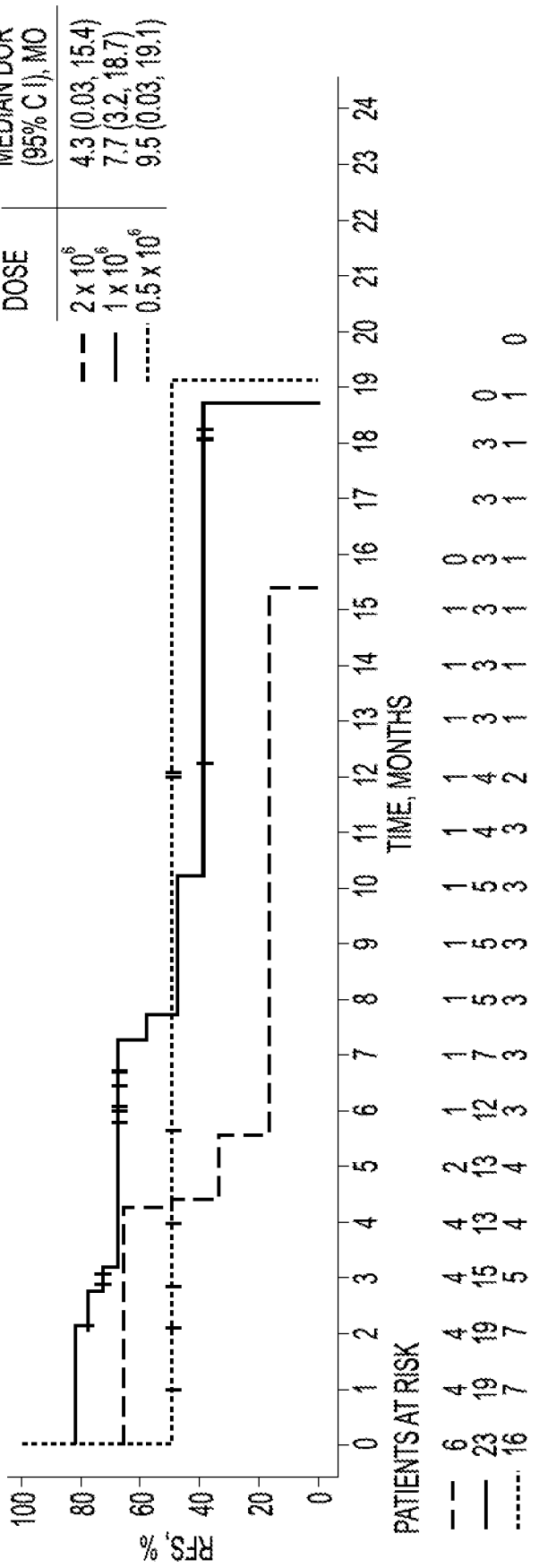

DOSE
MEDIAN DOR (95% CI), MO
2 x 10^6 4.3 (0.03, 15.4)
1 x 10^6 7.7 (3.2, 18.7)
0.5 x 10^6 9.5 (0.03, 19.1)
RFS, %
100
80
60
40
20
0
TIME, MONTHS
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24
PATIENTS AT RISK
6 4 4 4 4 2 1 1 1 1 1 1 1 1 1 1 0
23 19 19 15 13 13 12 7 5 5 4 4 3 3 3 3 3 3 1
16 7 7 5 4 4 3 3 3 3 3 3 2 1 1 1 1 1 0

FIG. 6C

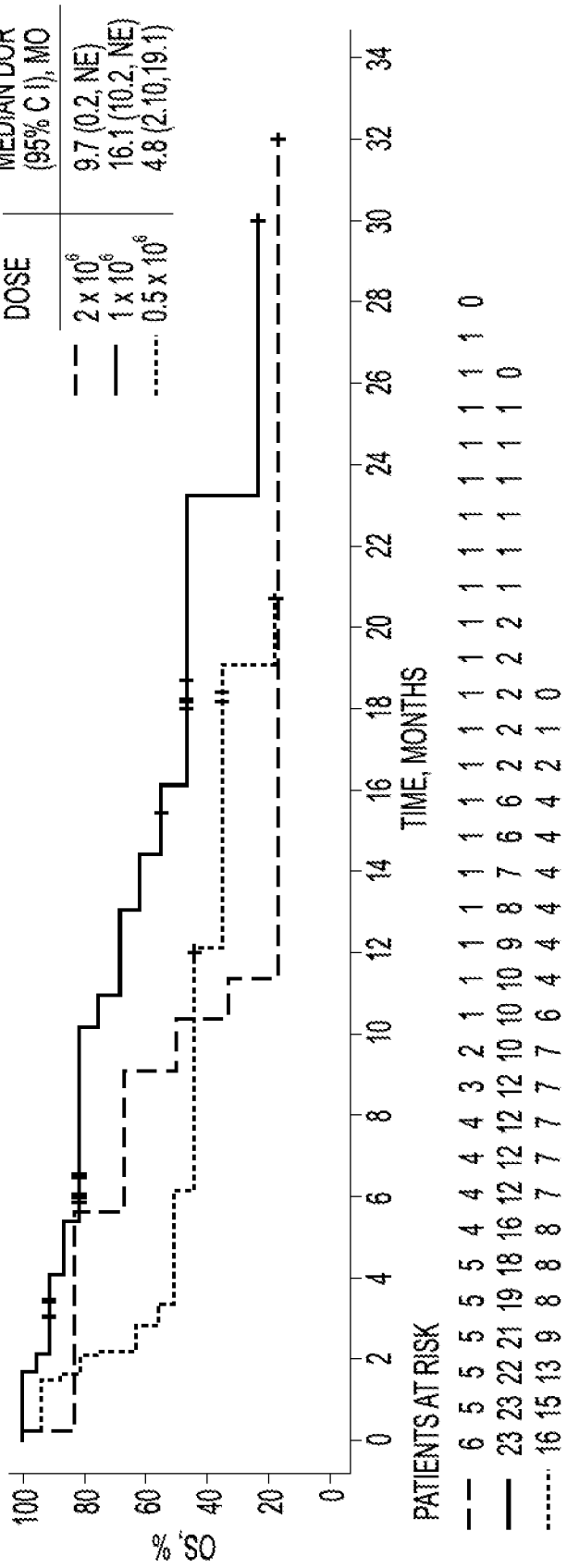

DOSE
MEDIAN DOR (95% CI), MO
2 x 10^6 9.7 (0.2, NE)
1 x 10^6 16.1 (10.2, NE)
0.5 x 10^6 4.8 (2.10,19.1)
OS, %
100
80
60
40
20
0
0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32 34
TIME, MONTHS
PATIENTS AT RISK
6 5 5 5 5 5 4 4 4 4 4 3 2 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 0
23 23 22 21 19 18 16 12 12 12 12 7 7 7 7 7 7 7 6 4 4 4 4 4 4 4 4 4 4 2 2 2 2 2 2 2 1 1 1 1 1 1 1 1 1 1 0
16 15 13 9 8 8 8 8 7 7 7 7 7 7 7 6 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 0

FIG. 6D

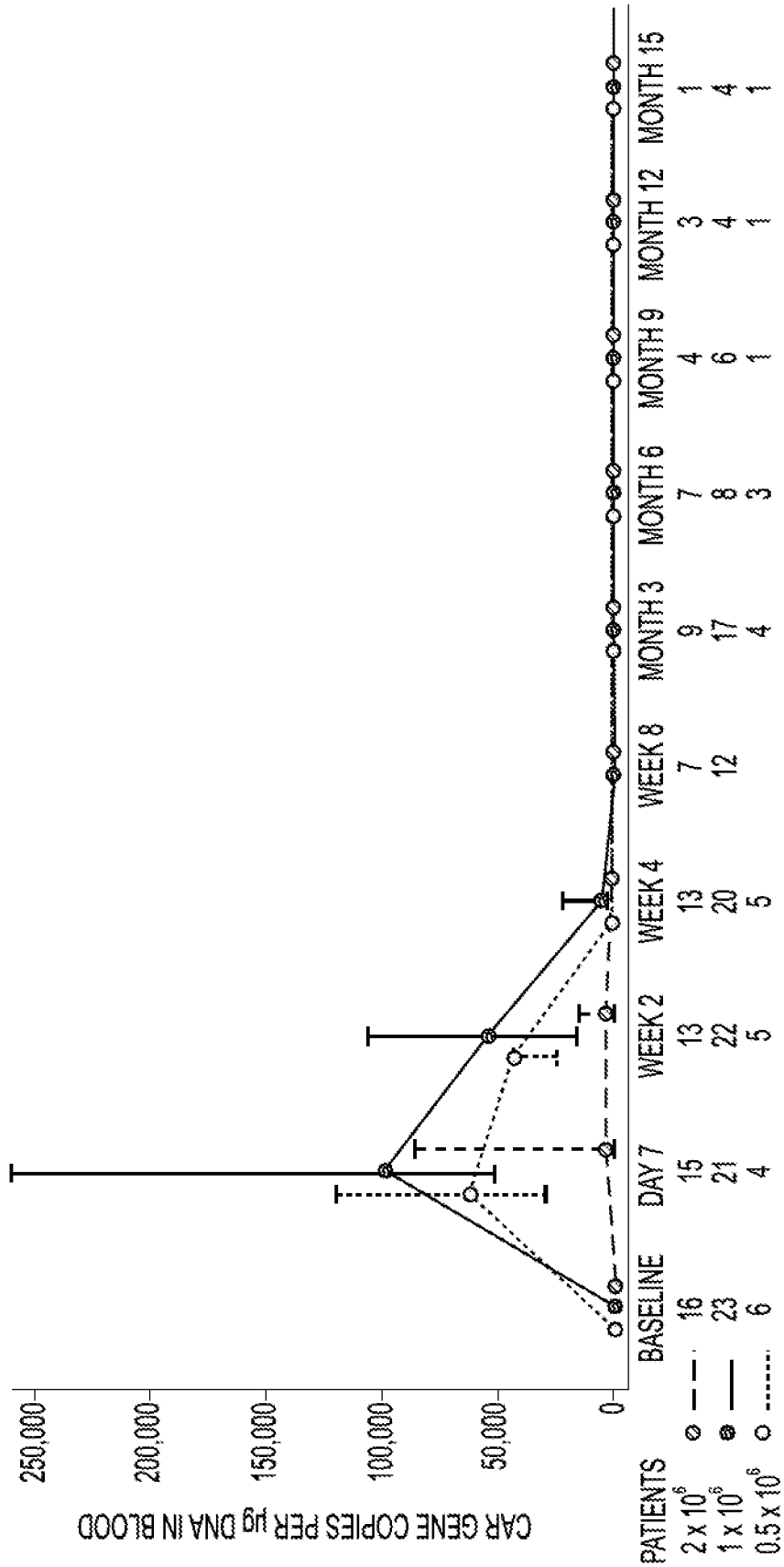

CAR GENE COPIES PER µg DNA IN BLOOD
250,000
200,000
150,000
100,000
50,000
0
PATIENTS
2 x 10^5 16
1 x 10^5 23
0.5 x 10^5 6
BASELINE
DAY 7 15 21 4
WEEK 2 13 22 5
WEEK 4 13 20 5
WEEK 8 7 12
MONTH 3 9 17 4
MONTH 6 7 8 3
MONTH 9 4 6 1
MONTH 12 3 4 1
MONTH 15 1 4 1

FIG. 7A

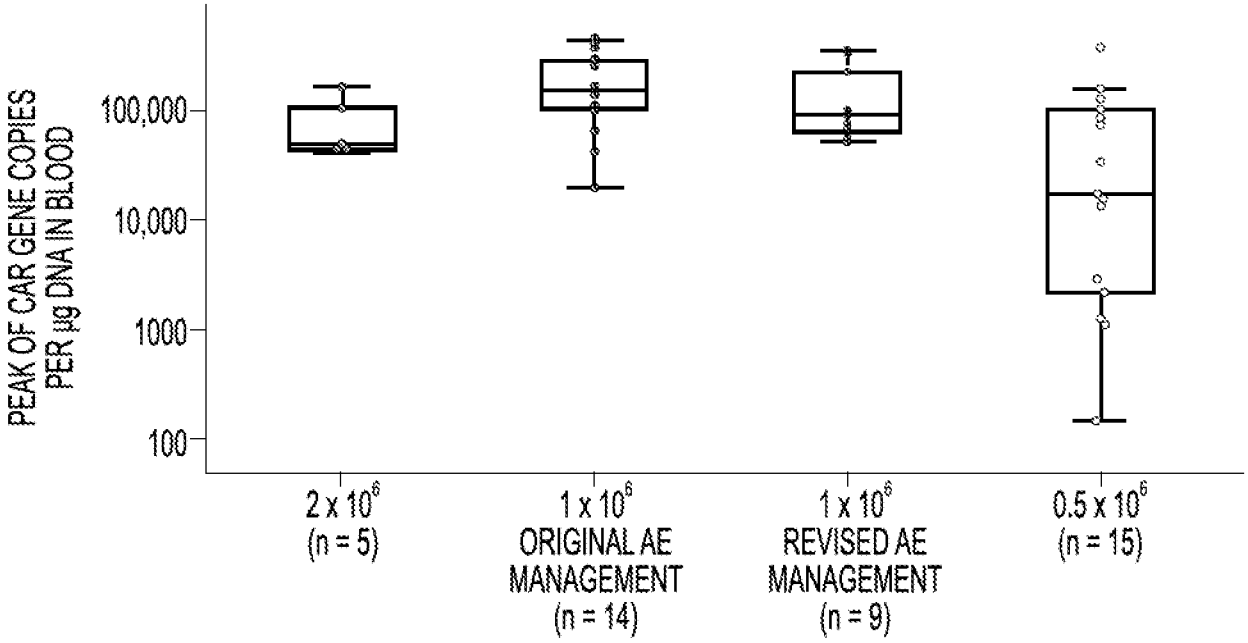

PEAK OF CAR GENE COPIES PER µg DNA IN BLOOD
100,000
10,000
1000
100
2 x 10^6 (n = 5)
1 x 10^6 ORIGINAL AE MANAGEMENT (n = 14)
1 x 10^6 REVISED AE MANAGEMENT (n = 9)
0.5 x 10^6 (n = 15)

FIG. 7B

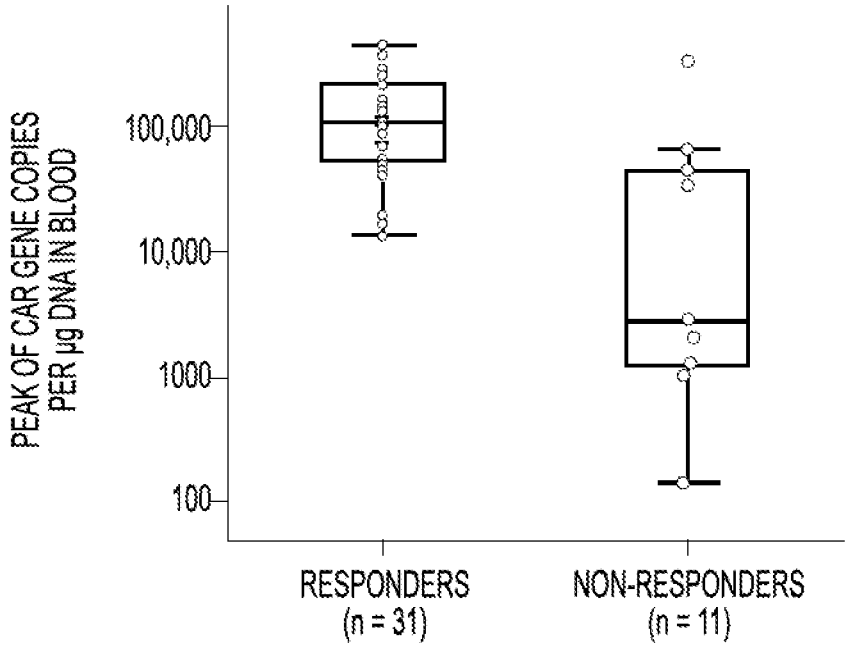

PEAK OF CAR GENE COPIES PER µg DNA IN BLOOD
100,000
10,000
1000
100
RESPONDERS (n = 31)
NON-RESPONDERS (n = 11)

FIG. 7C

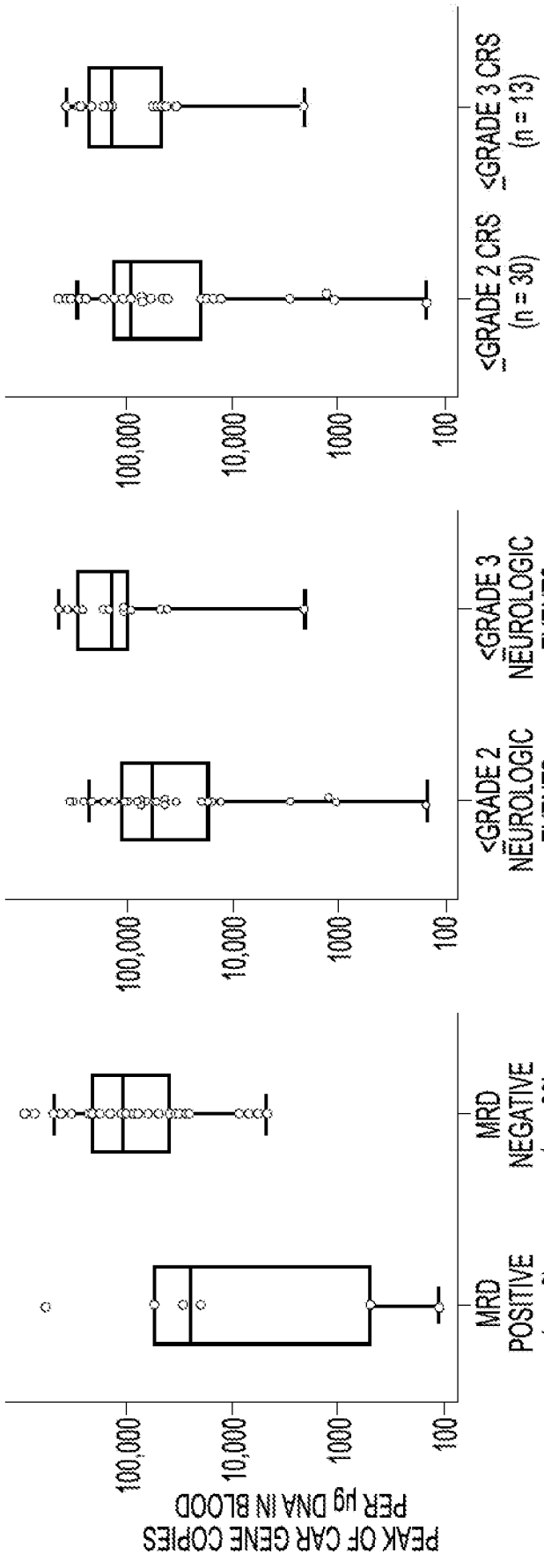
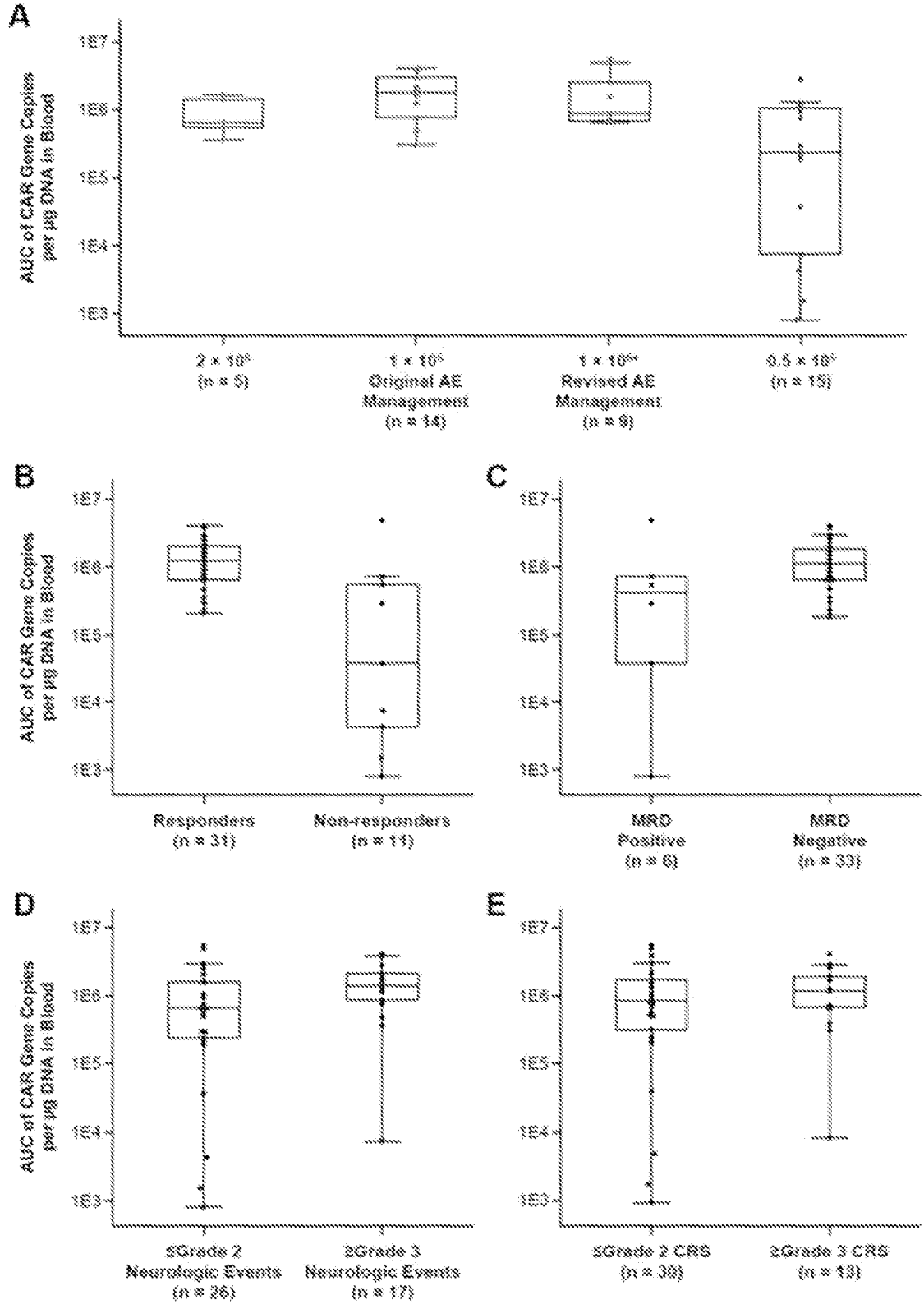


FIG. 7D

FIG. 7E

FIG. 7F

FIG. 8


A
AUC of CAR Gene Copies per µg DNA in Blood
1E7
1E6
1E5
1E4
1E3
2 × 10^6 (n = 5)
1 × 10^6 Original AE Management (n = 14)
1 × 10^6 Revised AE Management (n = 9)
0.5 × 10^6 (n = 15)
B
AUC of CAR Gene Copies per µg DNA in Blood
Responders (n = 31)
Non-responders (n = 11)
C
MRD Positive (n = 6)
MRD Negative (n = 33)
D
AUC of CAR Gene Copies per µg DNA in Blood
≤Grade 2 Neurologic Events (n = 26)
≥Grade 3 Neurologic Events (n = 17)
E
≤Grade 2 CRS (n = 30)
≥Grade 3 CRS (n = 13)

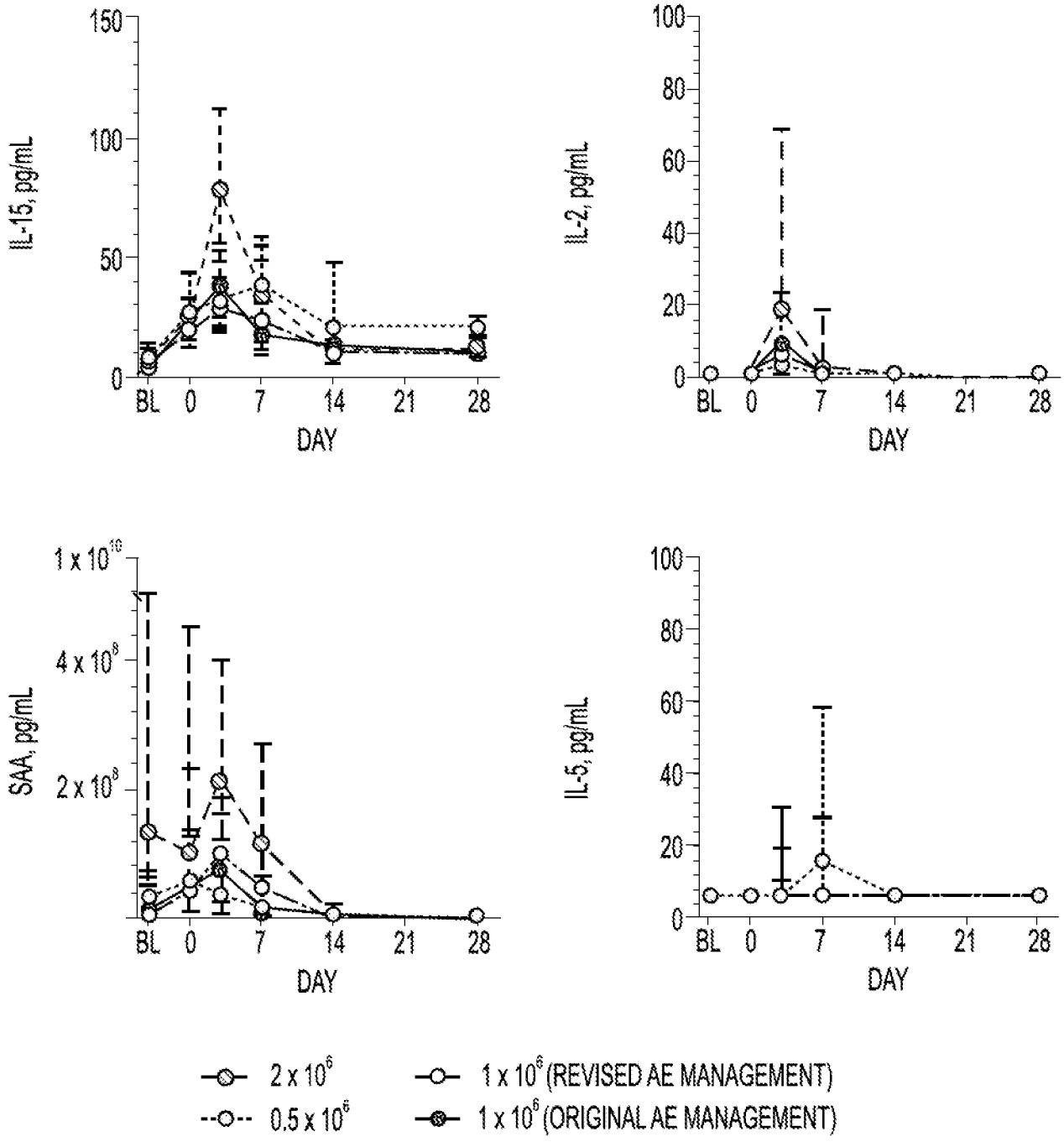

IL-15, pg/mL
150
100
50
0
BL 0 7 14 21 28
DAY
IL-2, pg/mL
100
80
60
40
20
0
BL 0 7 14 21 28
DAY
SAA, pg/mL
1 x 10^10
4 x 10^9
2 x 10^9
BL 0 7 14 21 28
DAY
IL-5, pg/mL
100
80
60
40
20
0
BL 0 7 14 21 28
DAY
2 x 10^6
0.5 x 10^6
1 x 10^6 (REVISED AE MANAGEMENT)
1 x 10^6 (ORIGINAL AE MANAGEMENT)

FIG. 9A

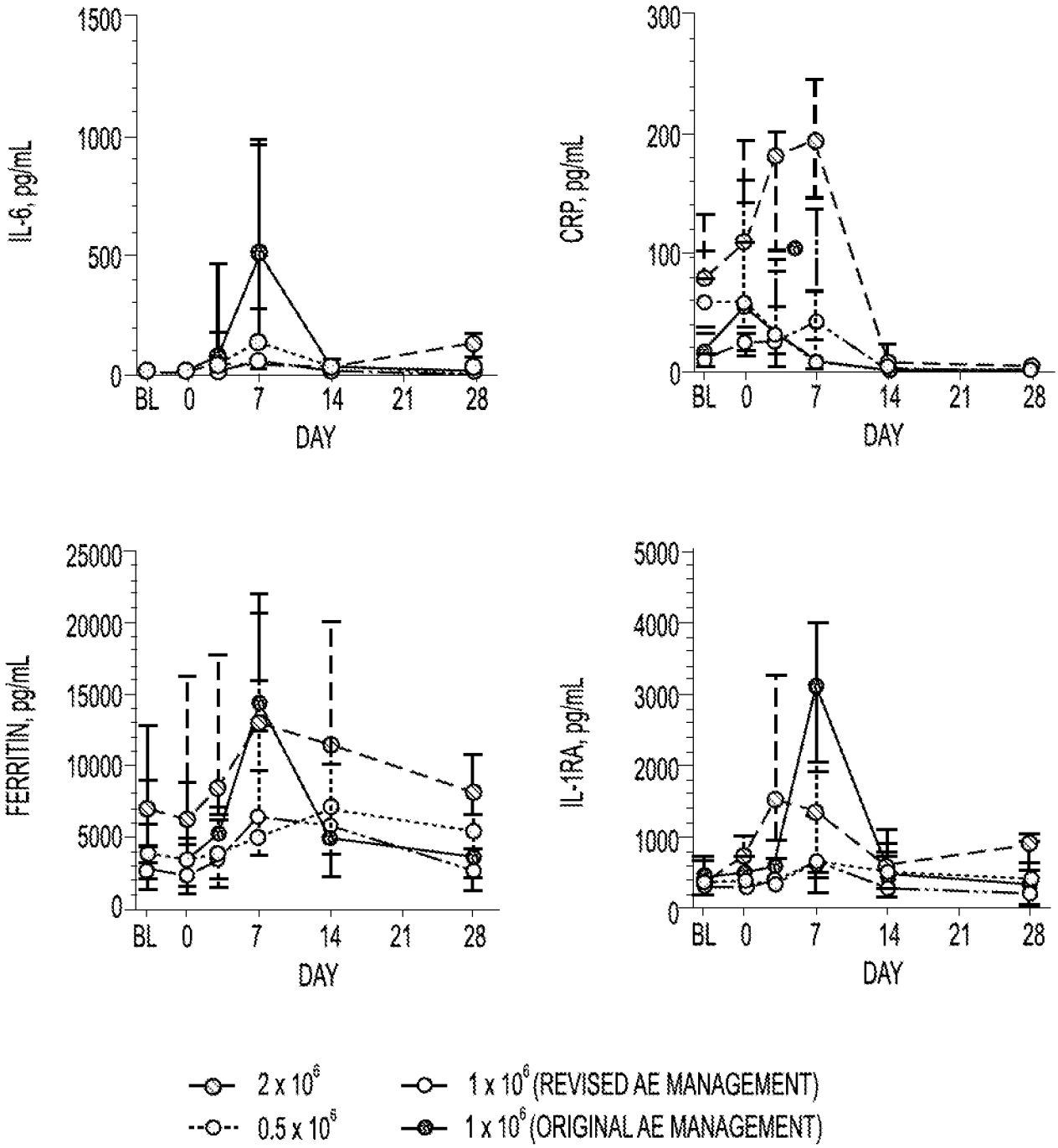

IL-6, pg/mL
1500
1000
500
0
BL 0 7 14 21 28
DAY
CRP, pg/mL
300
200
100
0
BL 0 7 14 21 28
DAY
FERRITIN, pg/mL
25000
20000
15000
10000
5000
0
BL 0 7 14 21 28
DAY
IL-1RA, pg/mL
5000
4000
3000
2000
1000
0
BL 0 7 14 21 28
DAY
2 x 10^6
0.5 x 10^6
1 x 10^6 (REVISED AE MANAGEMENT)
1 x 10^6 (ORIGINAL AE MANAGEMENT)

FIG. 9B

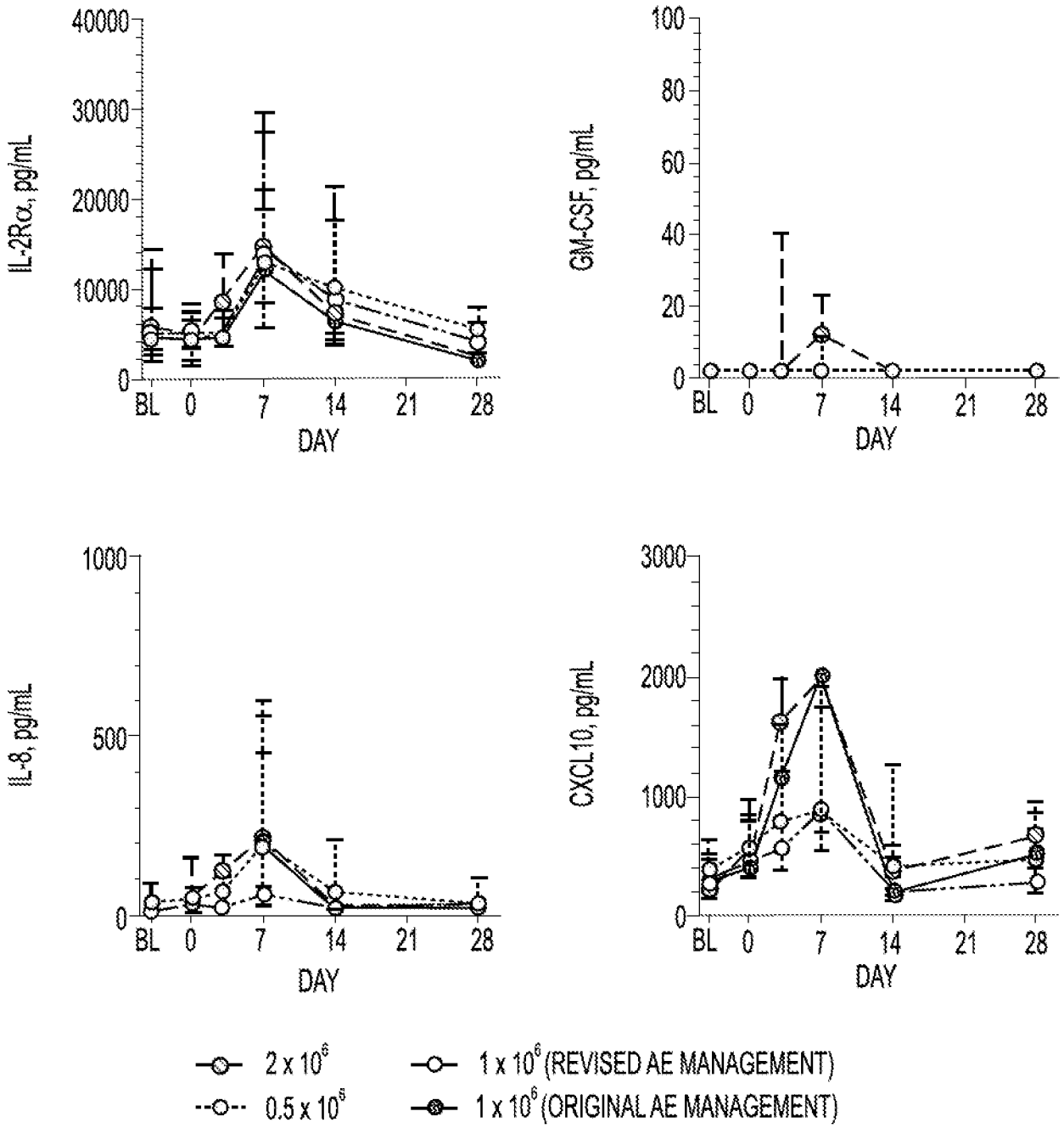

IL-2Rα, pg/mL
40000
30000
20000
10000
0
BL 0 7 14 21 28
DAY
GM-CSF, pg/mL
100
80
60
40
20
0
BL 0 7 14 21 28
DAY
IL-8, pg/mL
1000
500
0
BL 0 7 14 21 28
DAY
CXCL10, pg/mL
3000
2000
1000
0
BL 0 7 14 21 28
DAY
2 x 10^6
0.5 x 10^6
1 x 10^6 (REVISED AE MANAGEMENT)
1 x 10^6 (ORIGINAL AE MANAGEMENT)

FIG. 9C

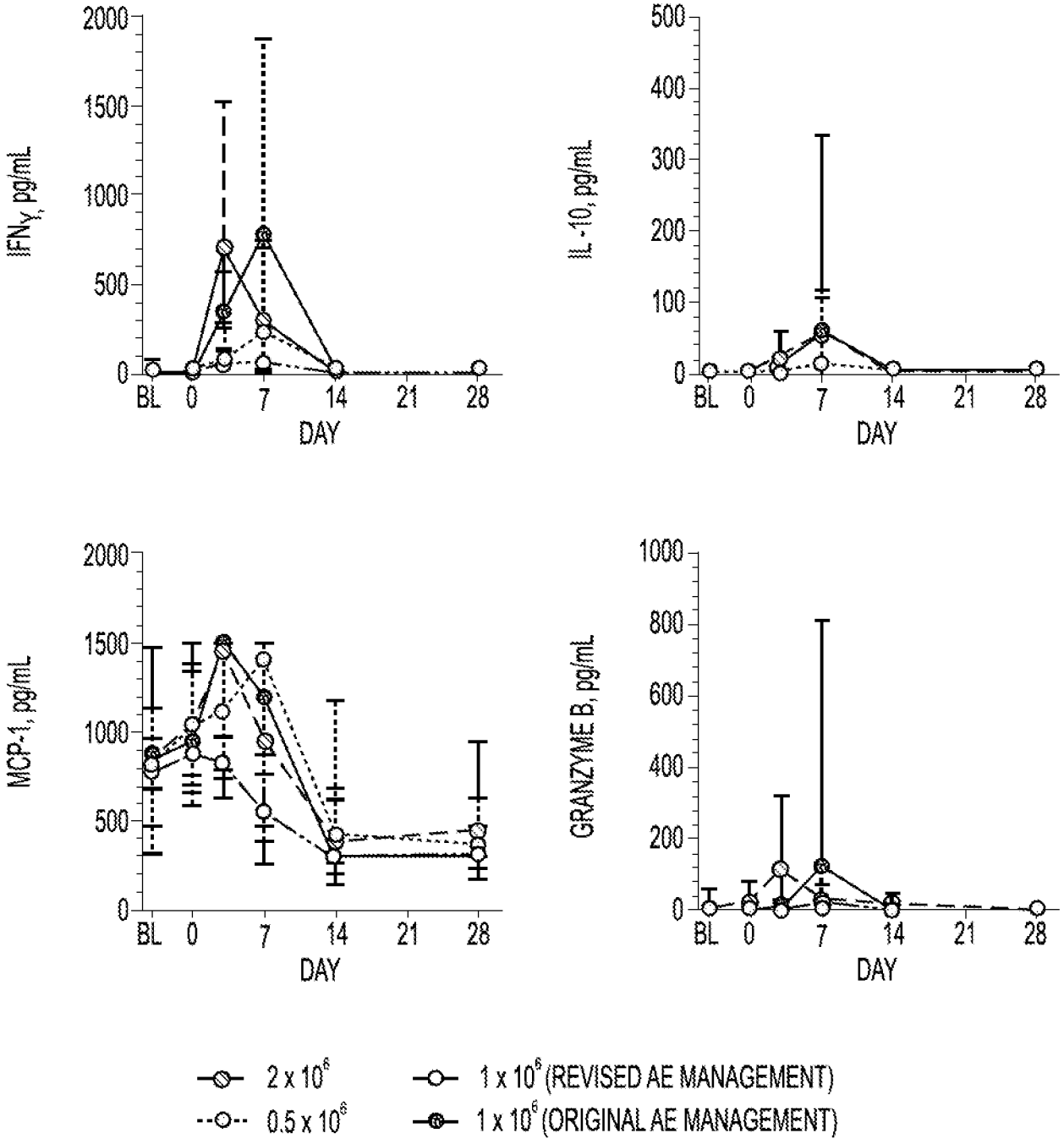

IFNγ, pg/mL
2000
1500
1000
500
0
BL 0 7 14 21 28
DAY
IL-10, pg/mL
500
400
300
200
100
0
BL 0 7 14 21 28
DAY
MCP-1, pg/mL
2000
1500
1000
500
0
BL 0 7 14 21 28
DAY
GRANZYME B, pg/mL
1000
800
600
400
200
0
BL 0 7 14 21 28
DAY
2 x 10^6
0.5 x 10^6
1 x 10^6 (REVISED AE MANAGEMENT)
1 x 10^6 (ORIGINAL AE MANAGEMENT)

FIG. 9D

FIG. 10

	2×10^8 cells/kg (n = 6)		1×10^8 cells/kg Original AE Management (n = 14)		1×10^8 cells/kg Revised AE Management (n = 8)		0.5×10^8 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* – 14,625.5
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	495.8 – 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	N/A	N/A	N/A	N/A	107.4	236.6	86.9	153.8
Range					69.7 – 196.0	120.5 – 1137.0	86.9 – 86.9	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

FIG. 11

Function	Peak Value - Median (range)	Cytokine Release Syndrome			Neurologic Events		
		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
Immune-modulating	GM-CSF, pg/mL	7.3 (1.9* – 112.5)	1.9* (1.9* – 239.7)	0.6038	5.7 (1.9* – 239.7)	1.9* (1.9* – 197.8)	0.5088

	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
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

FIG. 12

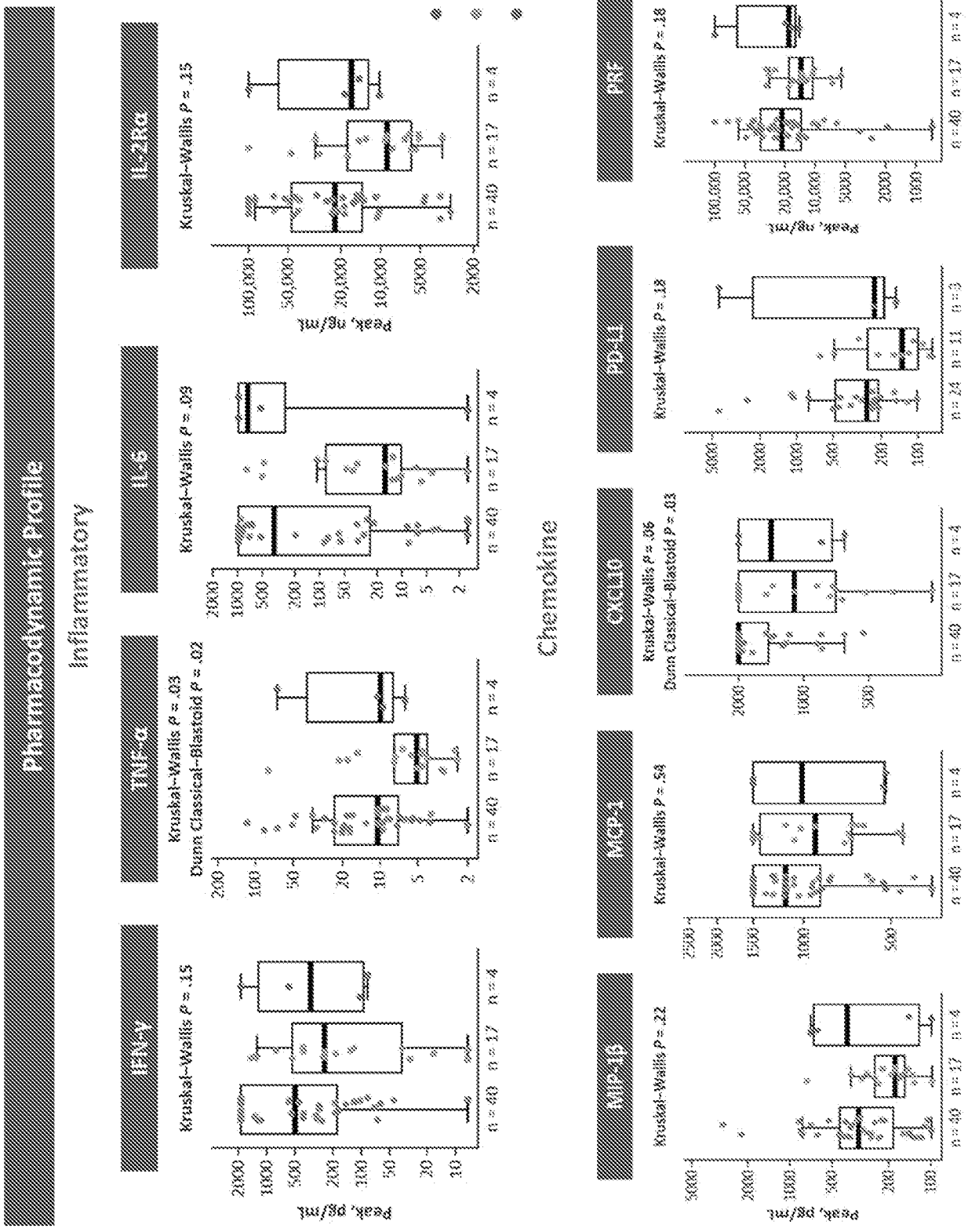

Pharmacodynamic Profile
Inflammatory
IFN-γ
TNF-α
IL-6
IL-2Rα
Kruskal–Wallis P = .15
Kruskal–Wallis P = .03
Dunn Classical–Blastoid P = .02
Kruskal–Wallis P = .09
Kruskal–Wallis P = .15
Peak, pg/mL
Peak, ng/mL
n = 40 n = 17 n = 4
Classical
Blastoid
Pleomorphic
Chemokine
MIP-1β
MCP-1
eotaxin
IP-10
PF4
Kruskal–Wallis P = .22
Kruskal–Wallis P = .54
Kruskal–Wallis P = .06
Dunn Classical–Blastoid P = .03
Kruskal–Wallis P = .18
Kruskal–Wallis P = .18
n = 24 n = 11 n = 3

FIG. 13

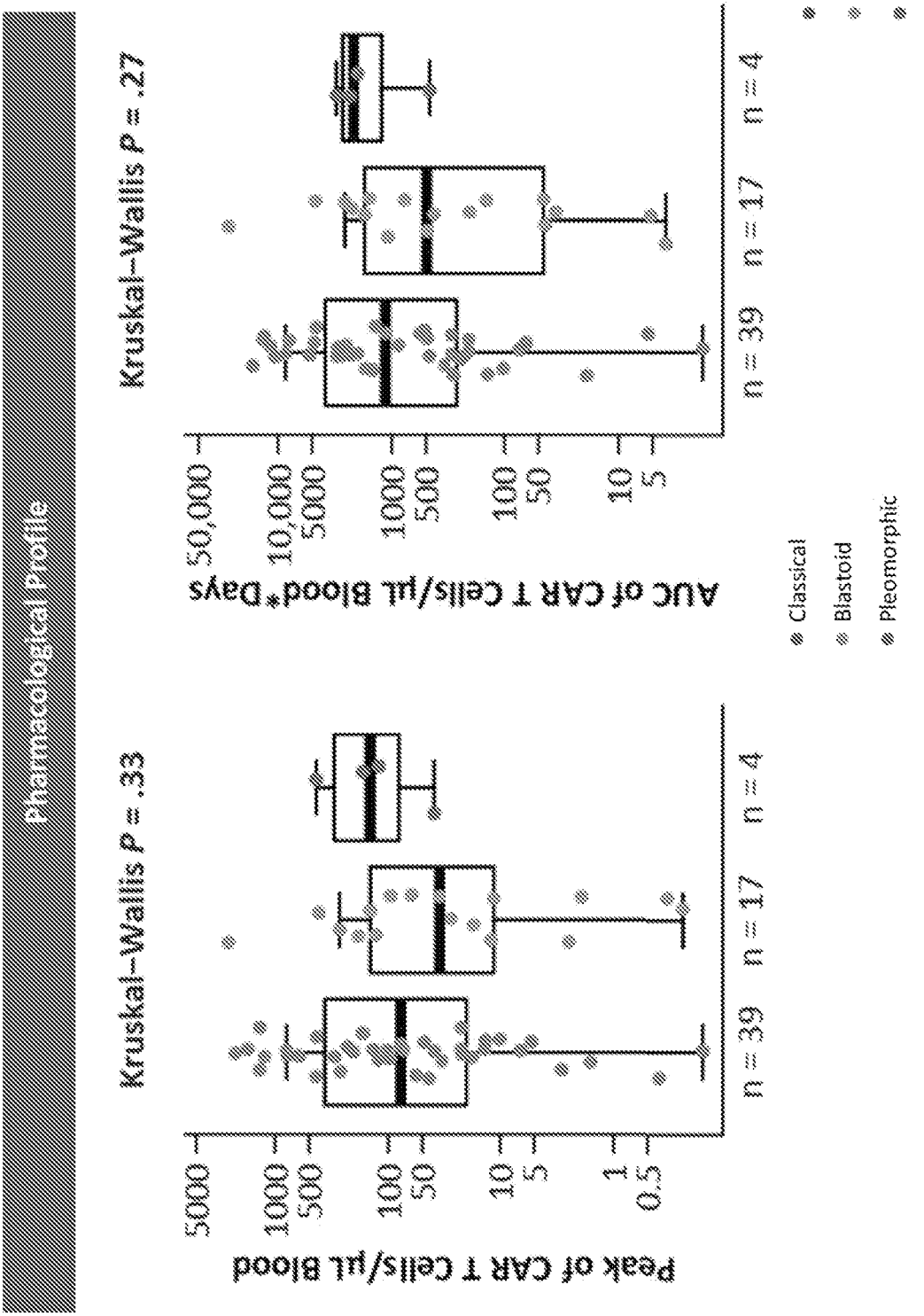

Pharmacological Profile
Kruskal–Wallis P = .33
Kruskal–Wallis P = .27
Peak of CAR T Cells/μL Blood
AUC of CAR T Cells/μL Blood*Days
5000
1000
500
100
50
10
5
1
0.5
50,000
10,000
5000
1000
500
100
50
10
5
n = 39
n = 17
n = 4
Classical
Blastoid
Pleomorphic

FIG. 14

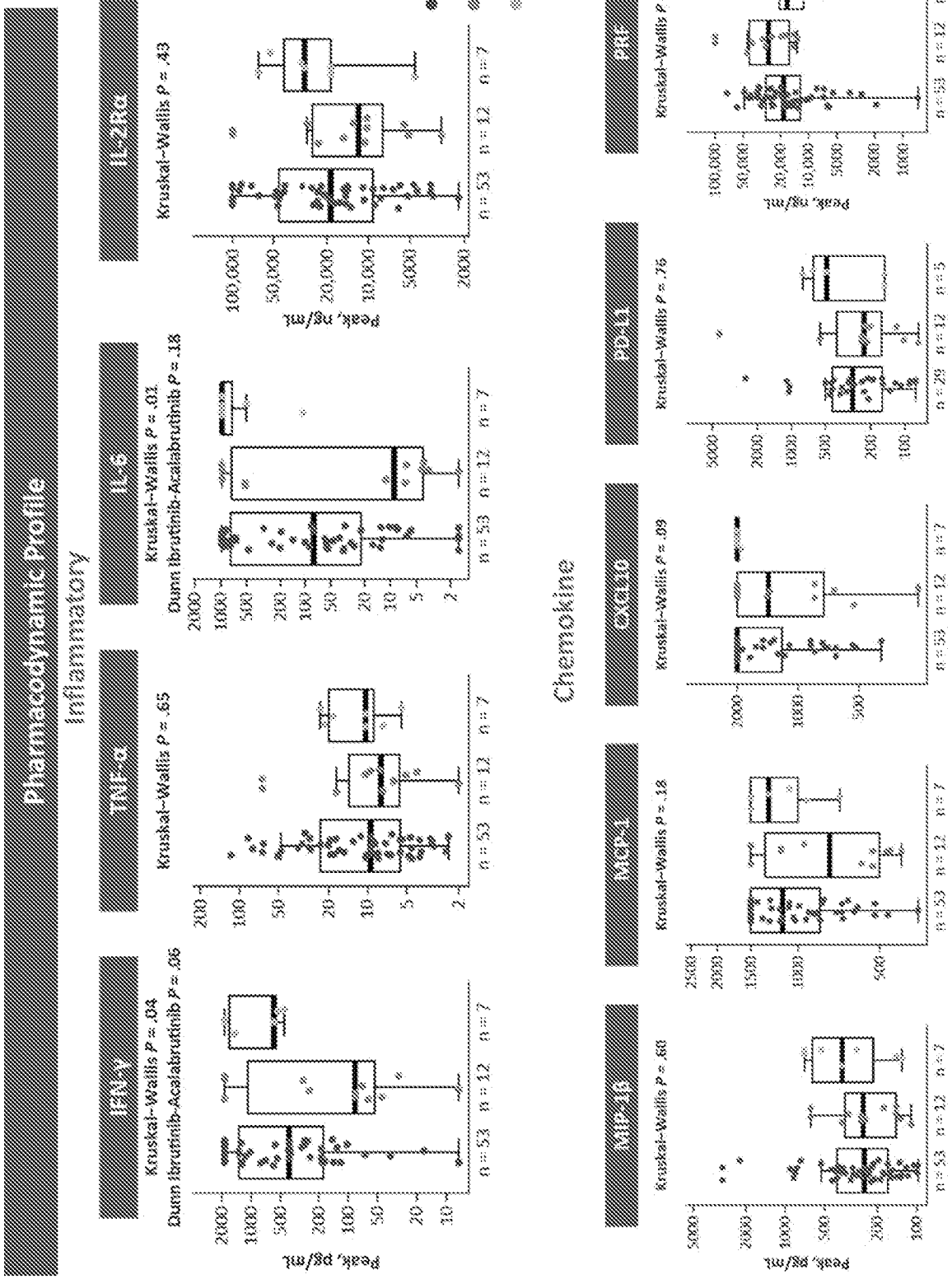

Pharmacodynamic Profile
Inflammatory
IFN-γ
TNF-α
IL-6
IL-2Rα
Kruskal–Wallis P = .04
Dunn Ibrutinib-Acalabrutinib P = .06
Kruskal–Wallis P = .65
Kruskal–Wallis P = .01
Dunn Ibrutinib-Acalabrutinib P = .18
Kruskal–Wallis P = .43
Peak, pg/mL
n = 53 n = 12 n = 7
Ibrutinib
Acalabrutinib
Both
Chemokine
MIP-1β
MCP-1
Eotaxin
PD-L1
PIF
Kruskal–Wallis P = .60
Kruskal–Wallis P = .18
Kruskal–Wallis P = .09
Kruskal–Wallis P = .76
Kruskal–Wallis P = .14

FIG. 15

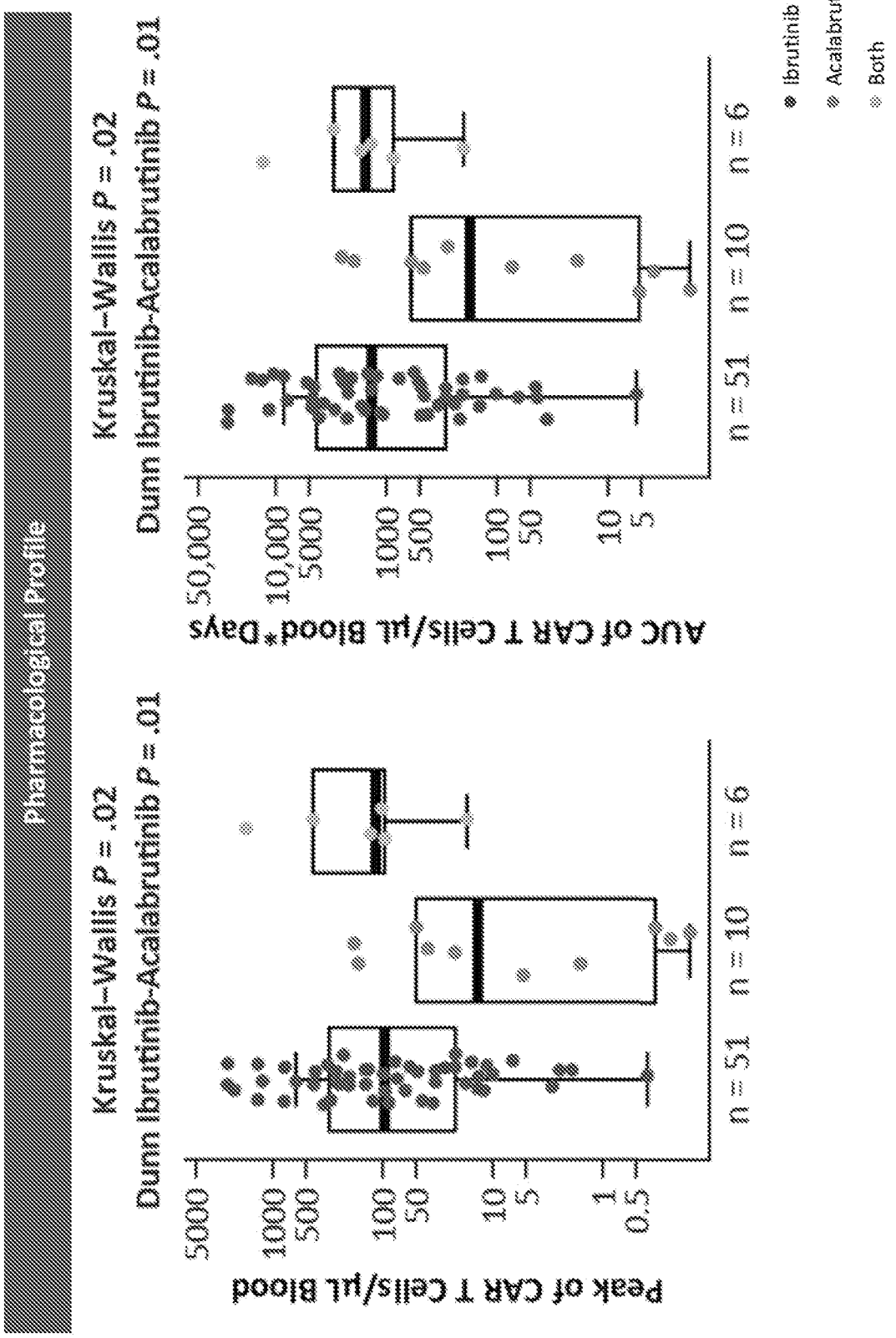

Pharmacological Profile
Kruskal–Wallis P = .02
Dunn Ibrutinib-Acalabrutinib P = .01
Peak of CAR T Cells/μL Blood
5000
1000
500
100
50
10
5
1
0.5
n = 51
n = 10
n = 6
Kruskal–Wallis P = .02
Dunn Ibrutinib-Acalabrutinib P = .01
AUC of CAR T Cells/μL Blood*Days
50,000
10,000
5000
1000
500
100
50
10
5
n = 51
n = 10
n = 6
Ibrutinib
Acalabrutinib
Both

FIG. 16

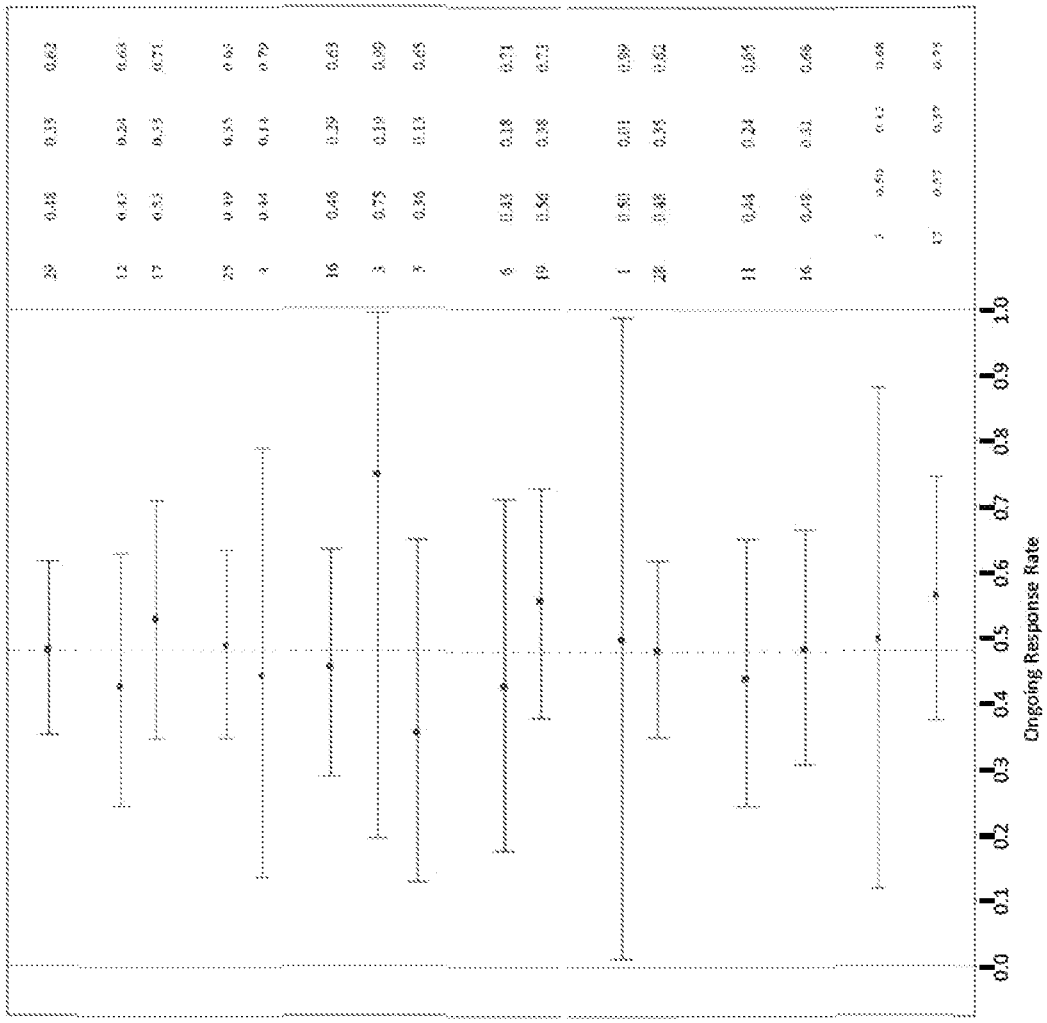

n
Resp. rate
LCI
UCI
Overall (N = 60)
Age at baseline
< 65 Years (n = 28)
≥ 65 Years (n = 32)
Sex
Male (n = 51)
Female (n = 9)
Morphological characteristics
Classical (n = 35)
Pleomorphic (n = 4)
Blastoid (n = 14)
Ki-67 proliferation index
< 50% (n = 14)
≥ 50% (n = 34)
Disease stage
I-II (n = 2)
III-IV (n = 58)
s-MIPI score
Low risk (n = 25)
Intermediate or high risk (n = 33)
TP53 mutation
Mutation detected (n = 6)
Mutation undetected (n = 30)
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
Ongoing Response Rate

FIG. 17A

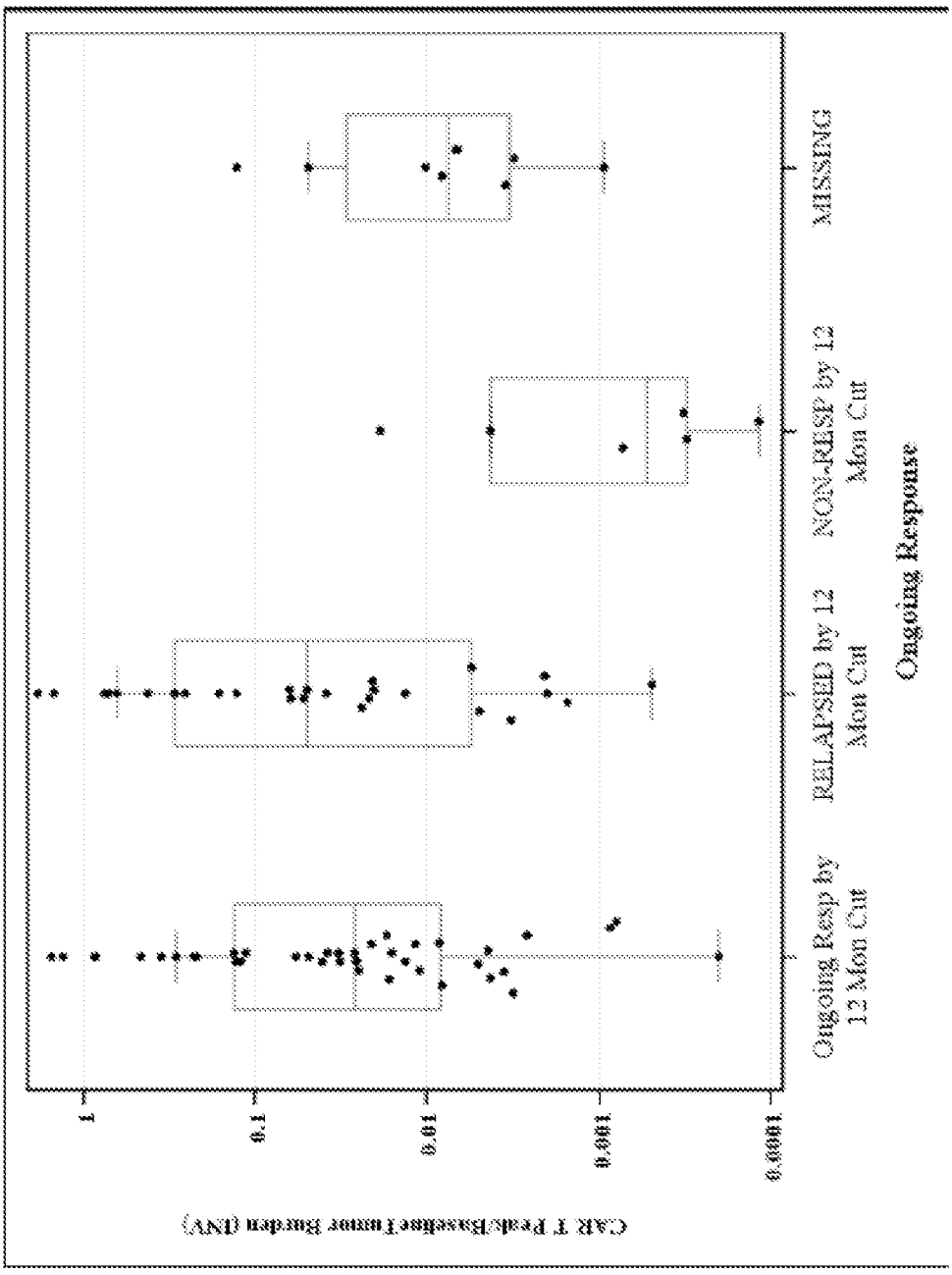
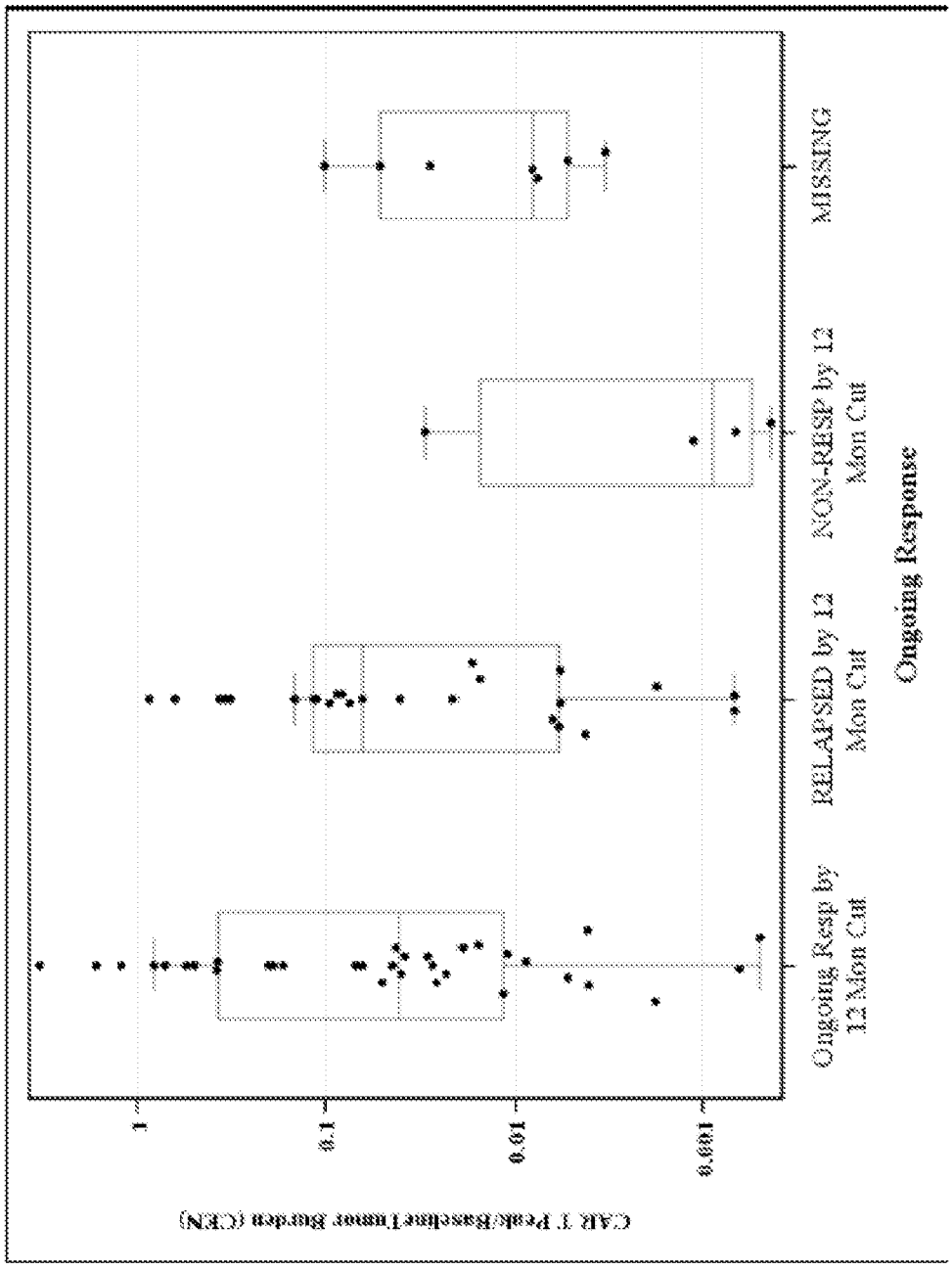

CAR T Peak/Baseline Tumor Burden (INV)
1
0.1
0.01
0.001
0.0001
Ongoing Resp by 12 Mon Cut
RELAPSED by 12 Mon Cut
NON-RESP by 12 Mon Cut
MISSING
Ongoing Response

FIG. 17B


CAR T Peak/BaselineTumor Burden (CEN)
1
0.1
0.01
0.001
Ongoing Resp by 12 Mon Cut
RELAPSED by 12 Mon Cut
NON-RESP by 12 Mon Cut
MISSING
Ongoing Response