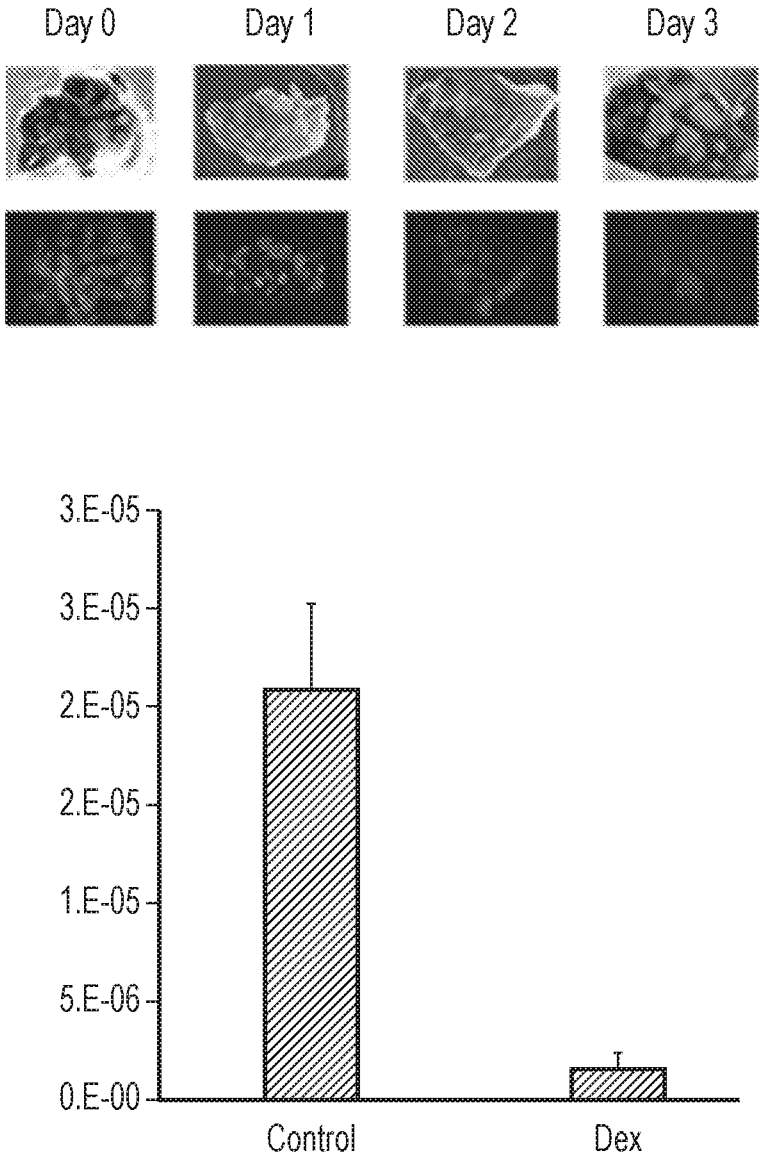

Day 0
Day 1
Day 2
Day 3
3.E-05
3.E-05
2.E-05
2.E-05
1.E-05
5.E-06
0.E-00
Control
Dex

FIG. 1

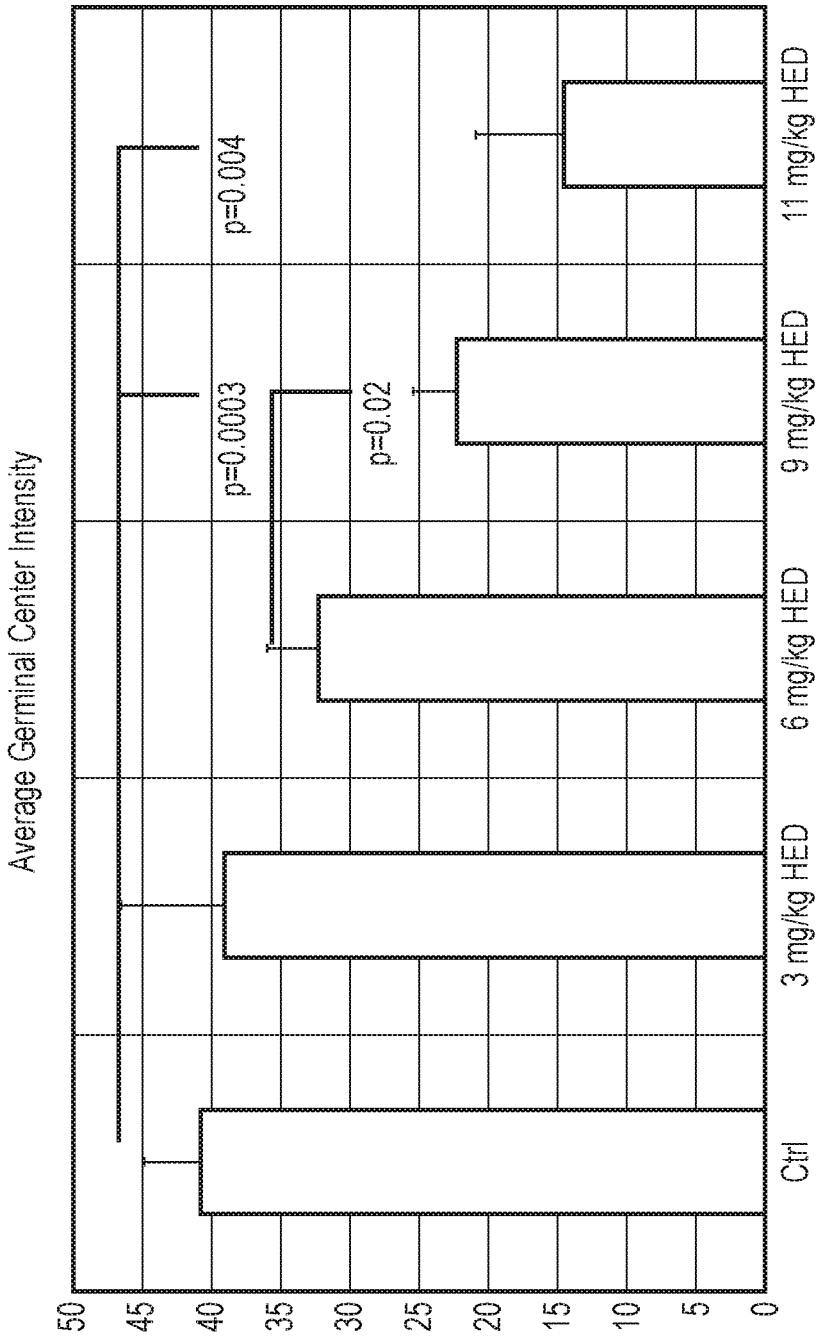

Average Germinal Center Intensity
50
45
40
35
30
25
20
15
10
5
0
Ctrl
3 mg/kg HED
6 mg/kg HED
9 mg/kg HED
11 mg/kg HED
p=0.004
p=0.0003
p=0.02

FIG. 2

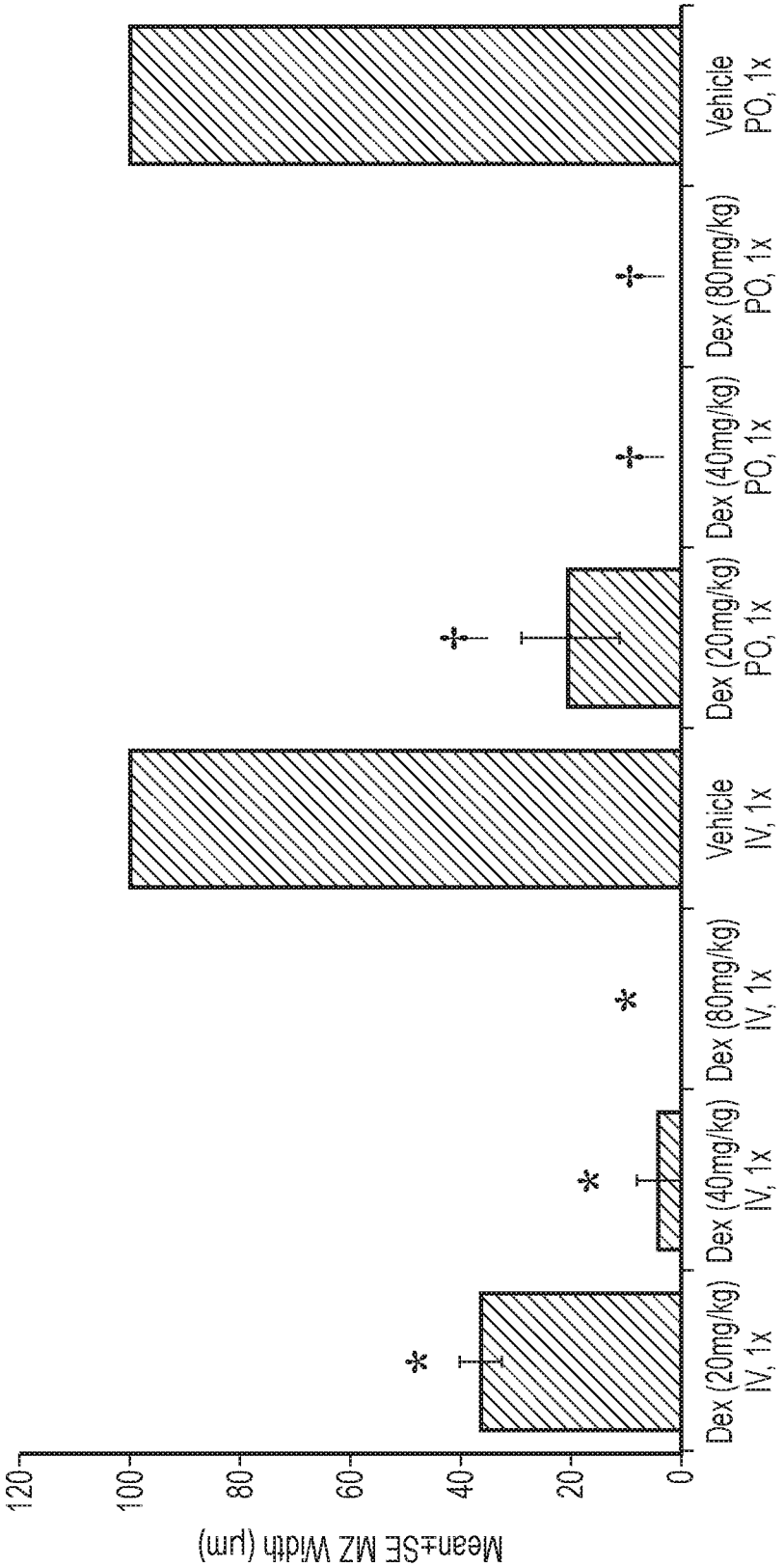

Mean±SE MZ Width (µm)
0
20
40
60
80
100
120
*
*
*
Dex (20mg/kg) IV, 1x
Dex (40mg/kg) IV, 1x
Dex (80mg/kg) IV, 1x
Vehicle IV, 1x
Dex (20mg/kg) PO, 1x
Dex (40mg/kg) PO, 1x
Dex (80mg/kg) PO, 1x
Vehicle PO, 1x

FIG. 3

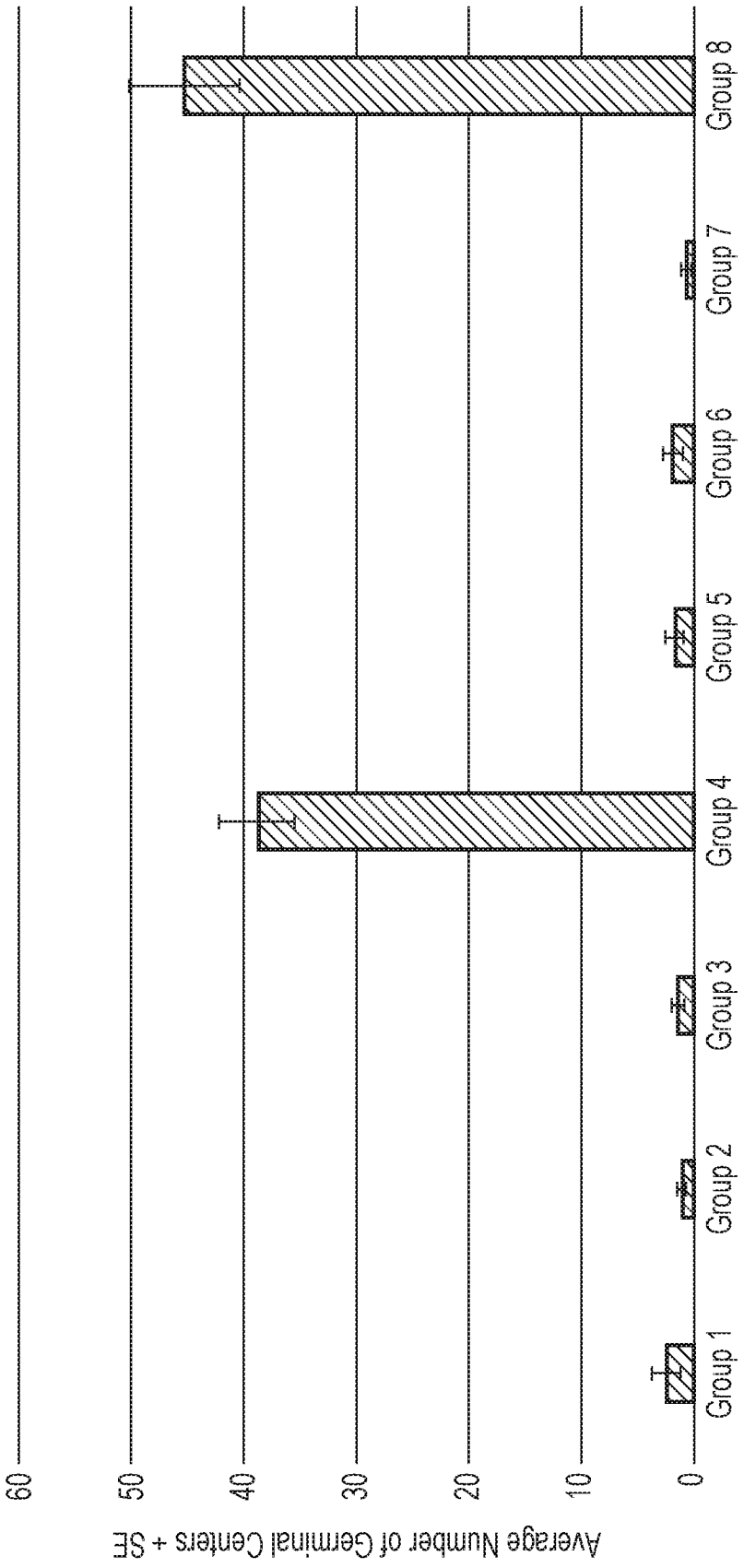
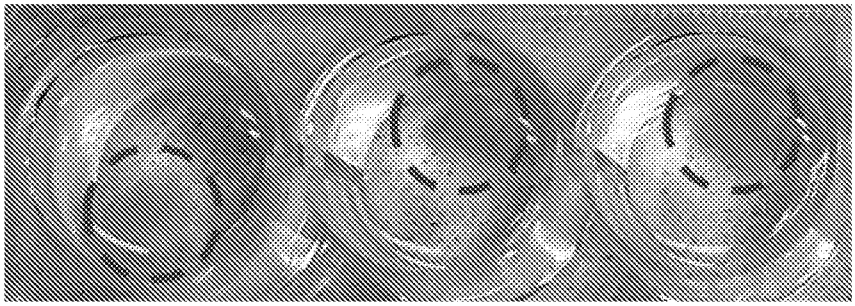
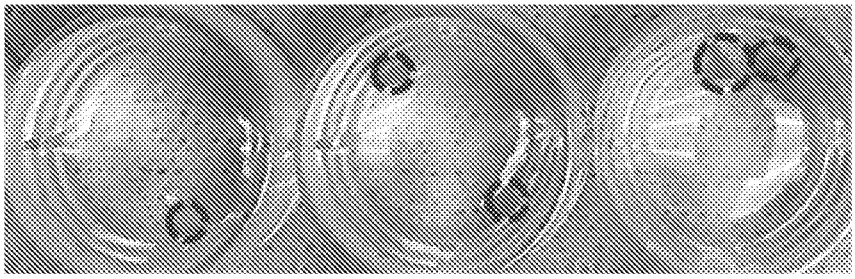

Average Number of Germinal Centers + SE
60
50
40
30
20
10
0
Group 1
Group 2
Group 3
Group 4
Group 5
Group 6
Group 7
Group 8

FIG. 4

Thymus: Placebo x 1 treatment group



Thymus: 6 mg/kg AVM0703 x 1 treatment group



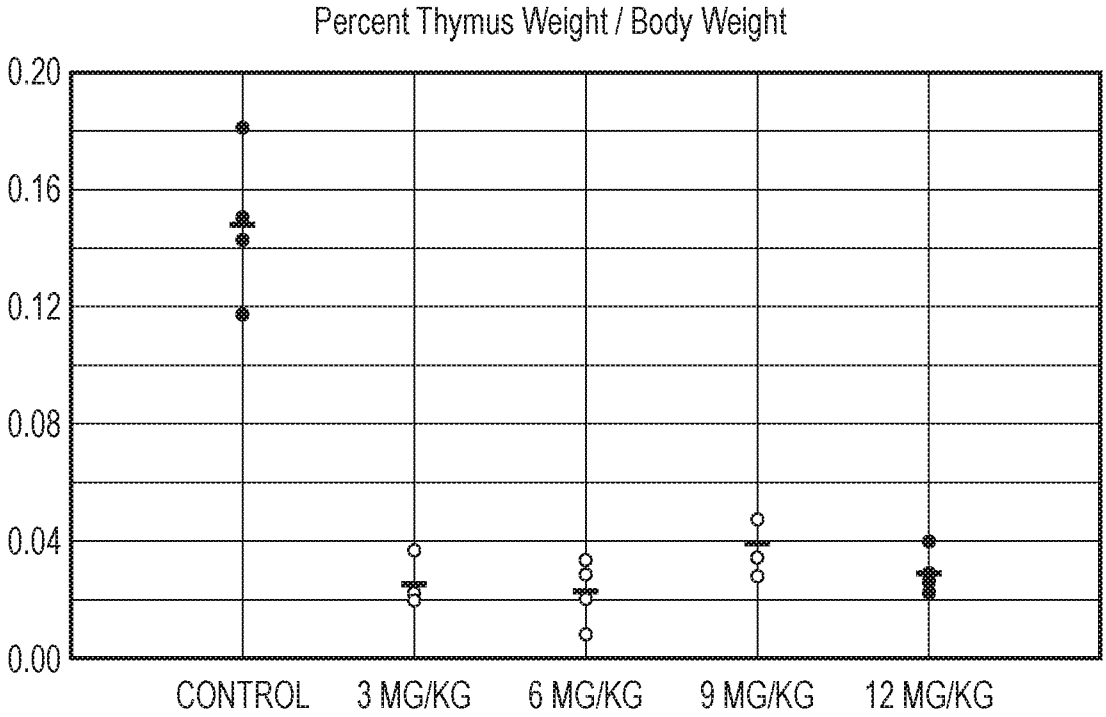


FIG. 5

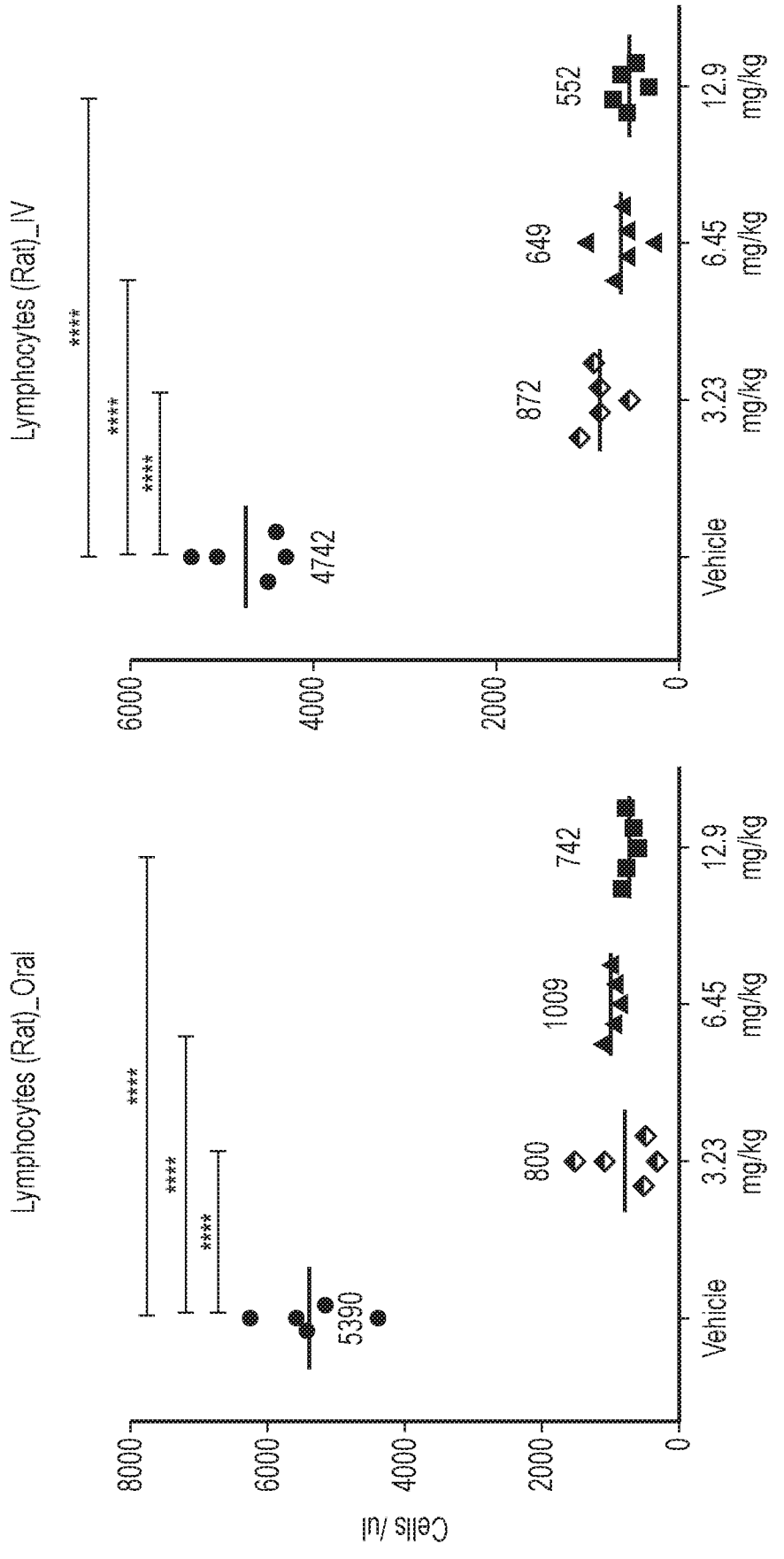

Lymphocytes (Rat)_Oral
Cells /ul
8000
6000
4000
2000
0
****
****
****
5390
800
1009
742
Vehicle
3.23 mg/kg
6.45 mg/kg
12.9 mg/kg
Lymphocytes (Rat)_IV
6000
4000
2000
0
****
****
****
4742
872
649
552
Vehicle
3.23 mg/kg
6.45 mg/kg
12.9 mg/kg
AVM0703 Vehicle
6.45 mg/kg
3.23 mg/kg
12.9 mg/kg

FIG. 6

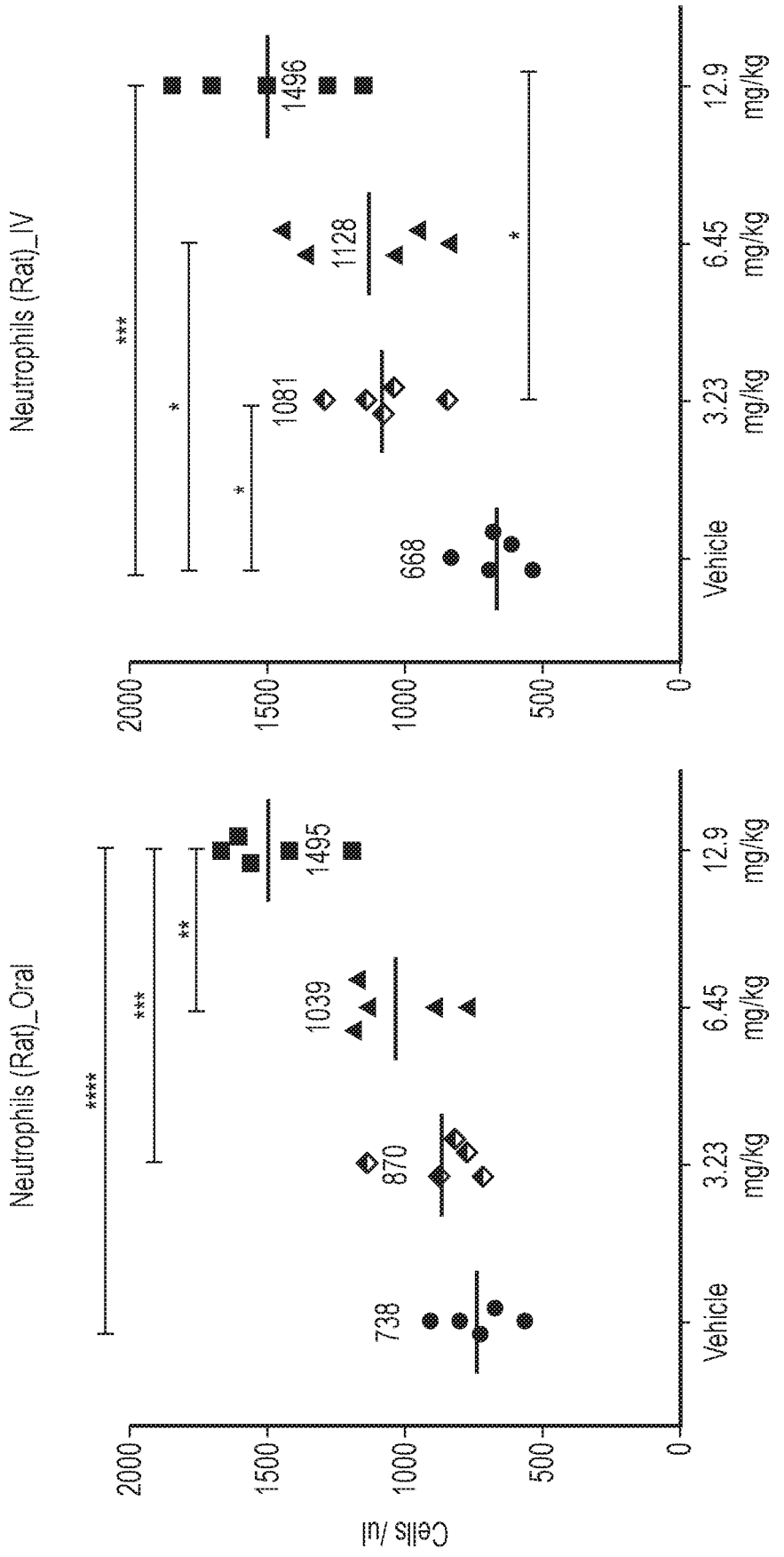

Neutrophils (Rat)_Oral
Neutrophils (Rat)_IV
Cells /ul
2000
1500
1000
500
0
Vehicle
3.23 mg/kg
6.45 mg/kg
12.9 mg/kg
738
870
1039
1495
668
1081
1128
1496
****
***
**
*
AVM0703 Vehicle
3.23 mg/kg
6.45 mg/kg
12.9 mg/kg

FIG. 7

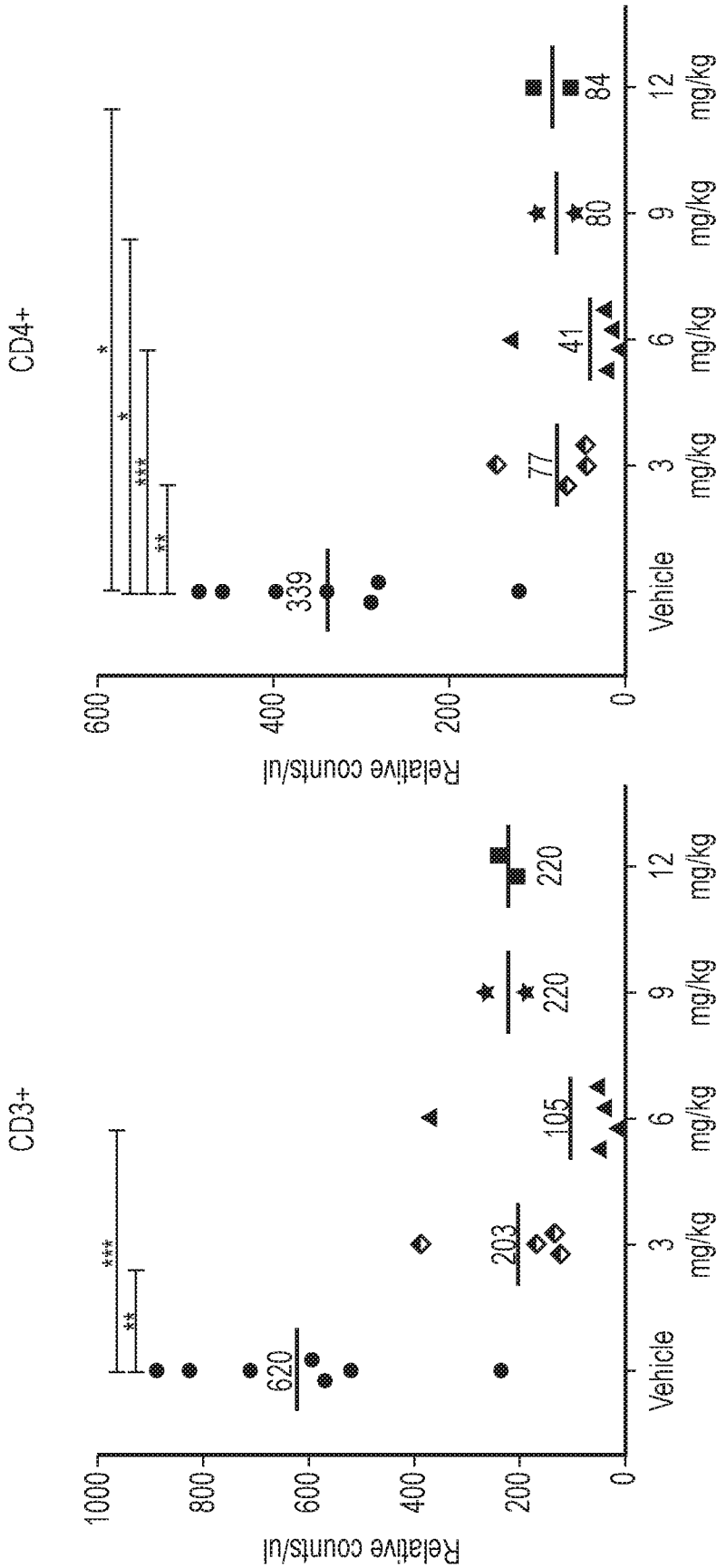

CD3+
CD4+
Relative counts/ul
1000
800
600
400
200
0
Vehicle
3 mg/kg
6 mg/kg
9 mg/kg
12 mg/kg
620
203
105
220
220
77
339
41
80
84
**
***
*
Some data points were lost as too few cells were present for accurate differential.

FIG. 8

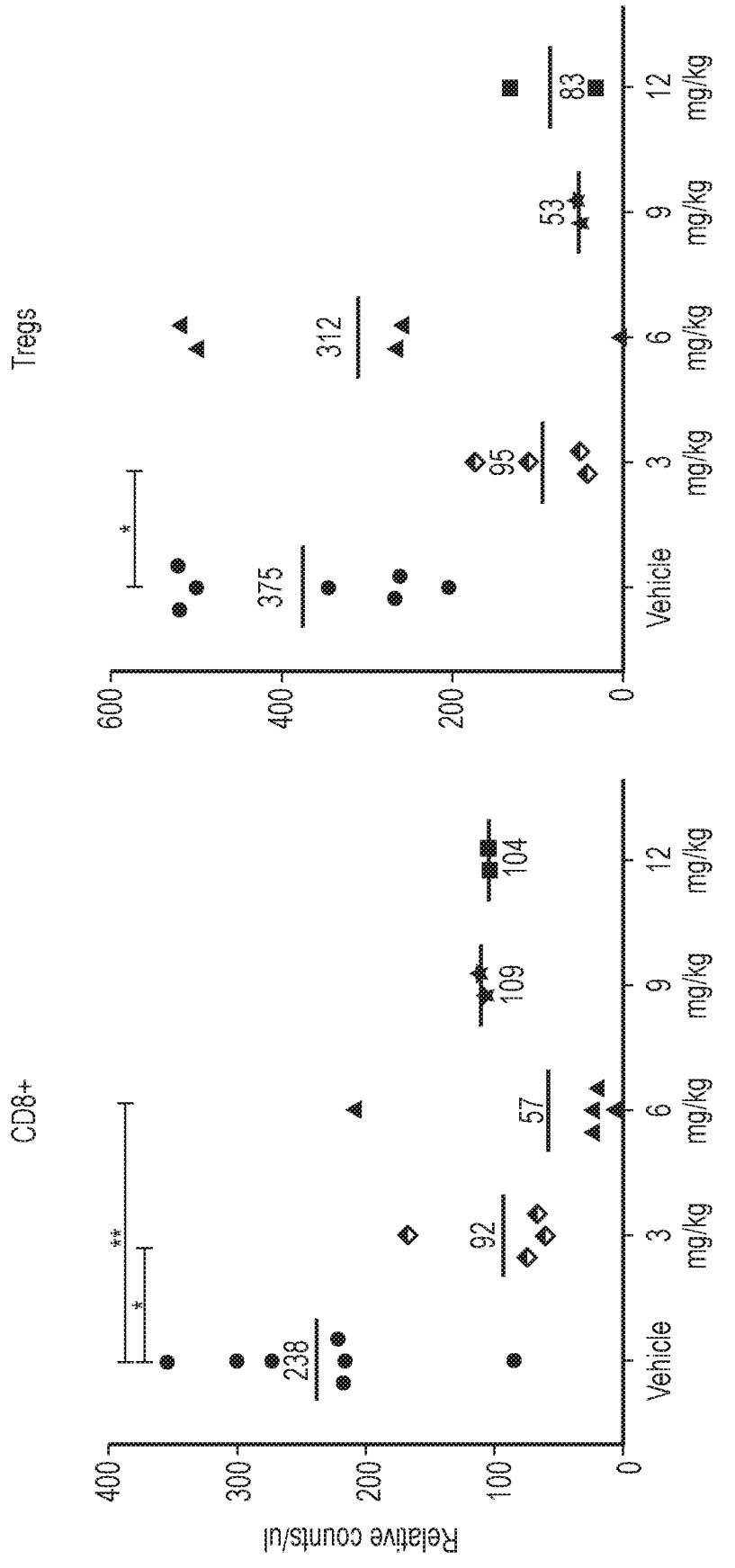

CD8+
Tregs
Relative counts/ul
400
300
200
100
0
600
400
200
0
Vehicle
3 mg/kg
6 mg/kg
9 mg/kg
12 mg/kg
238
92
57
109
104
375
312
95
53
83
*
**
Vehicle
6 mg/kg
12 mg/kg
3 mg/kg
9 mg/kg

FIG. 9

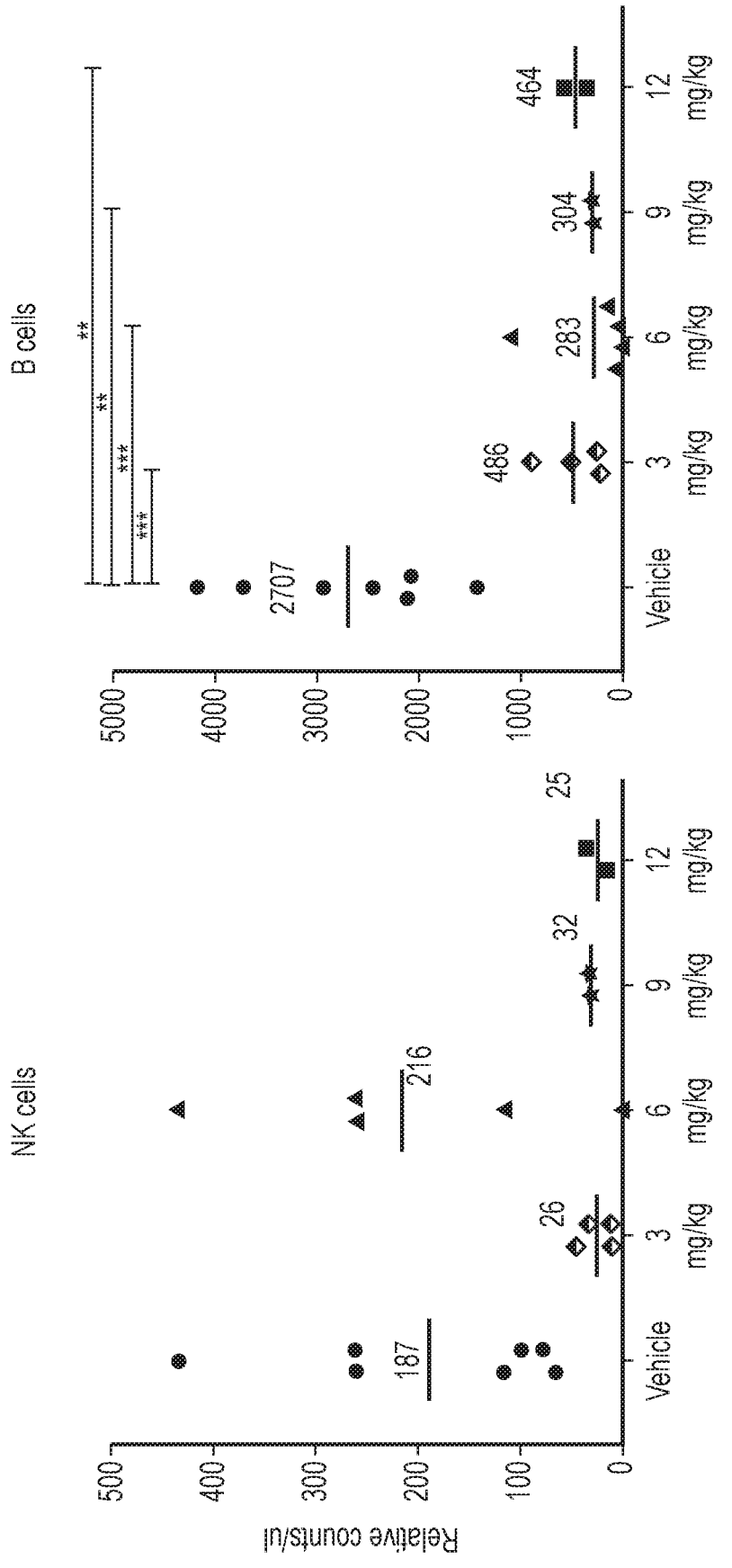

NK cells
B cells
Relative counts/ul
500
400
300
200
100
0
5000
4000
3000
2000
1000
0
187
216
26
32
25
2707
486
283
304
464
**
**
***
***
Vehicle
3 mg/kg
6 mg/kg
9 mg/kg
12 mg/kg
Vehicle
6 mg/kg
12 mg/kg
3 mg/kg
9 mg/kg

FIG. 10

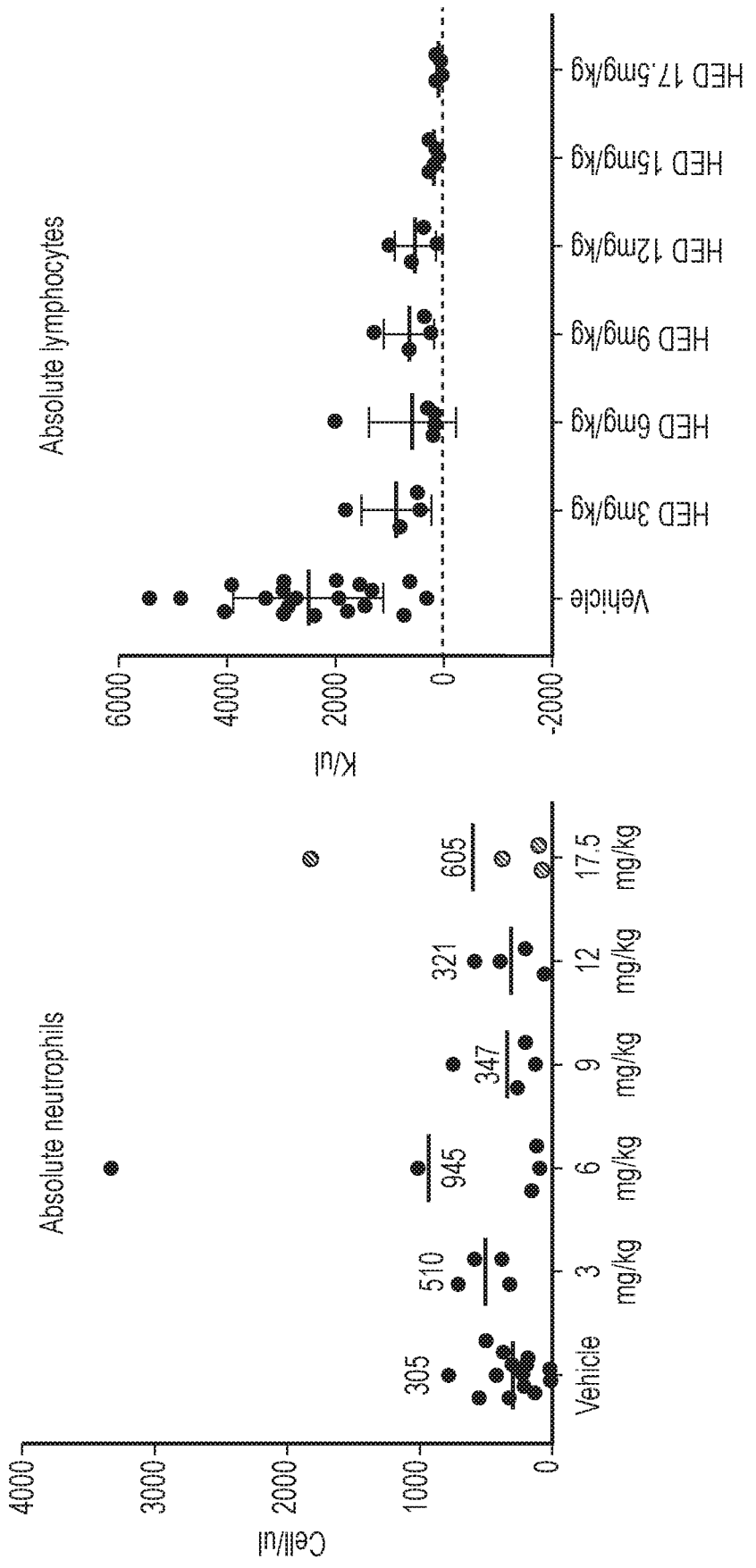

Absolute neutrophils
Cell/ul
4000
3000
2000
1000
0
Vehicle
3 mg/kg
6 mg/kg
9 mg/kg
12 mg/kg
17.5 mg/kg
305
510
945
347
321
605
Absolute lymphocytes
K/ul
6000
4000
2000
0
-2000
Vehicle
HED 3mg/kg
HED 6mg/kg
HED 9mg/kg
HED 12mg/kg
HED 15mg/kg
HED 17.5mg/kg

FIG. 11

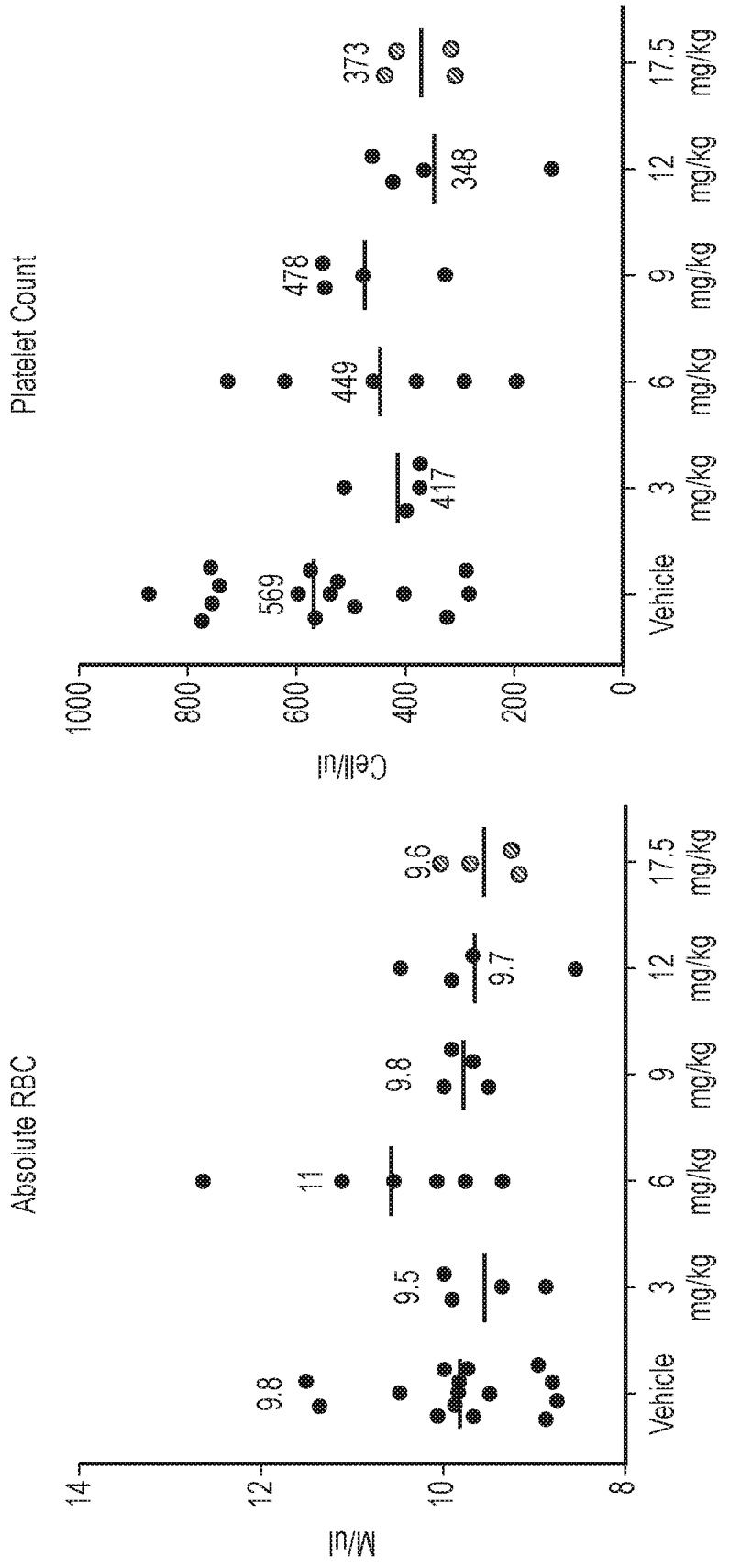

Platelet Count
Cell/uL
1000
800
600
400
200
0
569
417
449
478
348
373
Vehicle
3 mg/kg
6 mg/kg
9 mg/kg
12 mg/kg
17.5 mg/kg
Absolute RBC
M/uL
14
12
10
8
9.8
11
9.5
9.8
9.7
9.6

FIG. 12

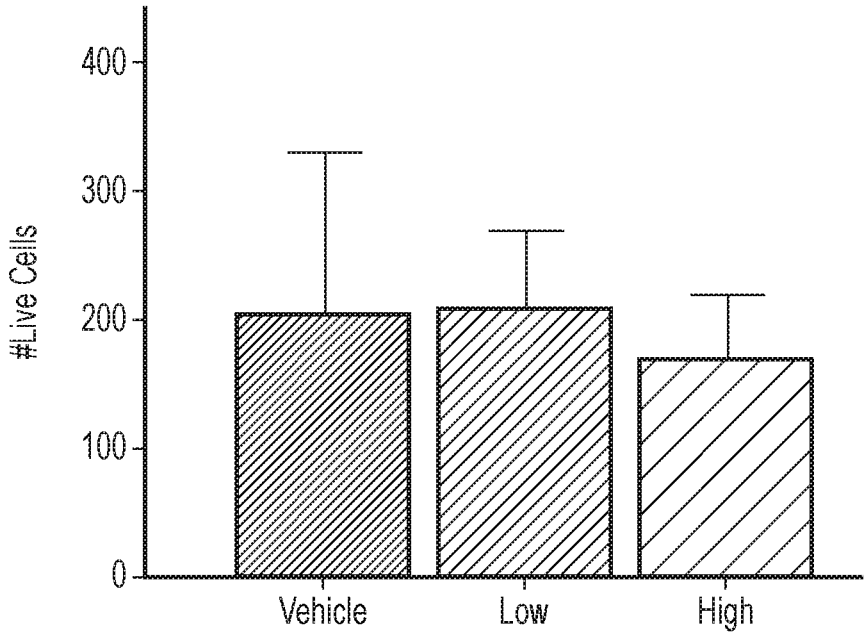


FIG. 13

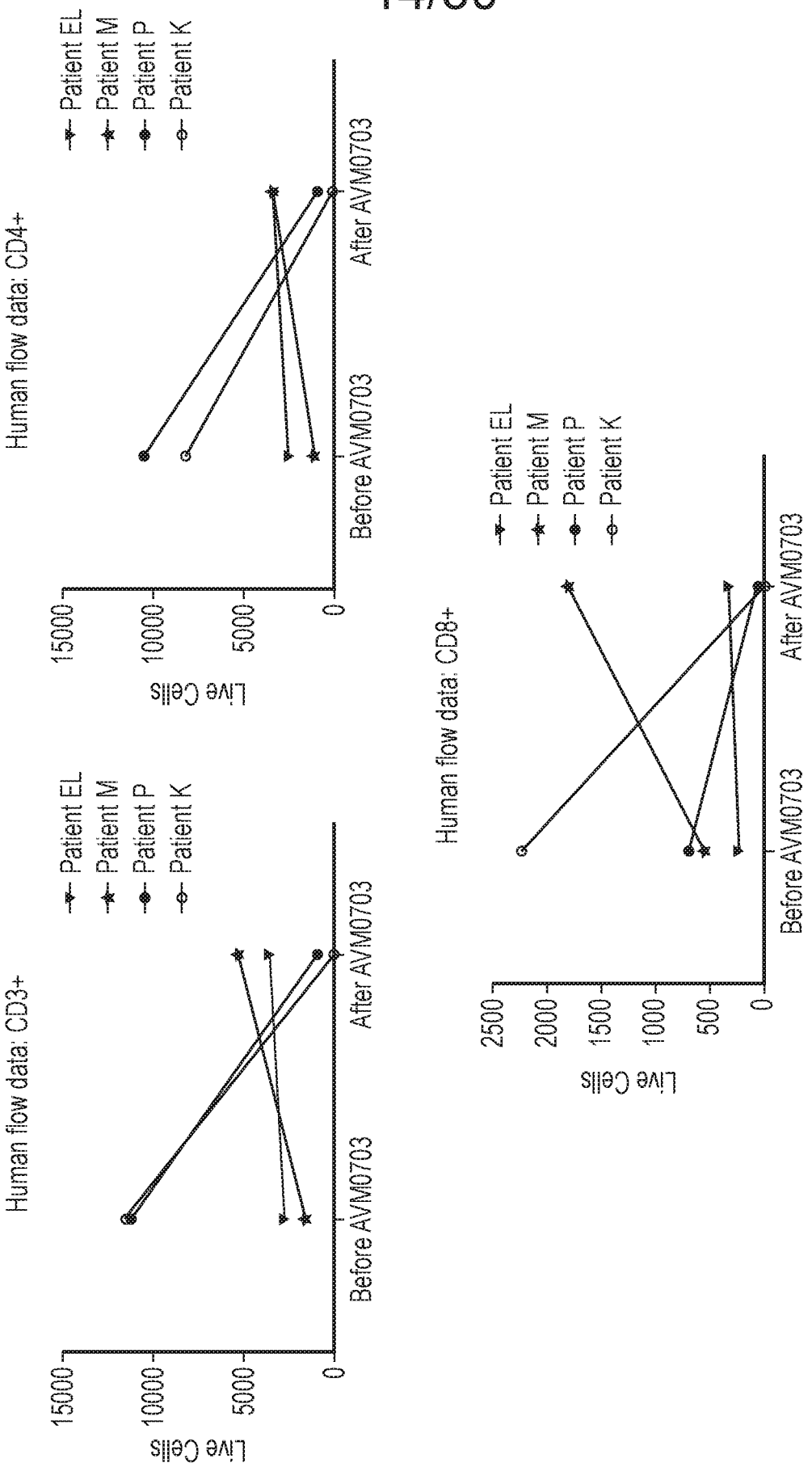

Human flow data: CD4+
Patient EL
Patient M
Patient P
Patient K
Live Cells
15000
10000
5000
0
Before AVM0703
After AVM0703
Human flow data: CD3+
Patient EL
Patient M
Patient P
Patient K
Live Cells
15000
10000
5000
0
Before AVM0703
After AVM0703
Human flow data: CD8+
Patient EL
Patient M
Patient P
Patient K
Live Cells
2500
2000
1500
1000
500
0
Before AVM0703
After AVM0703

FIG. 14

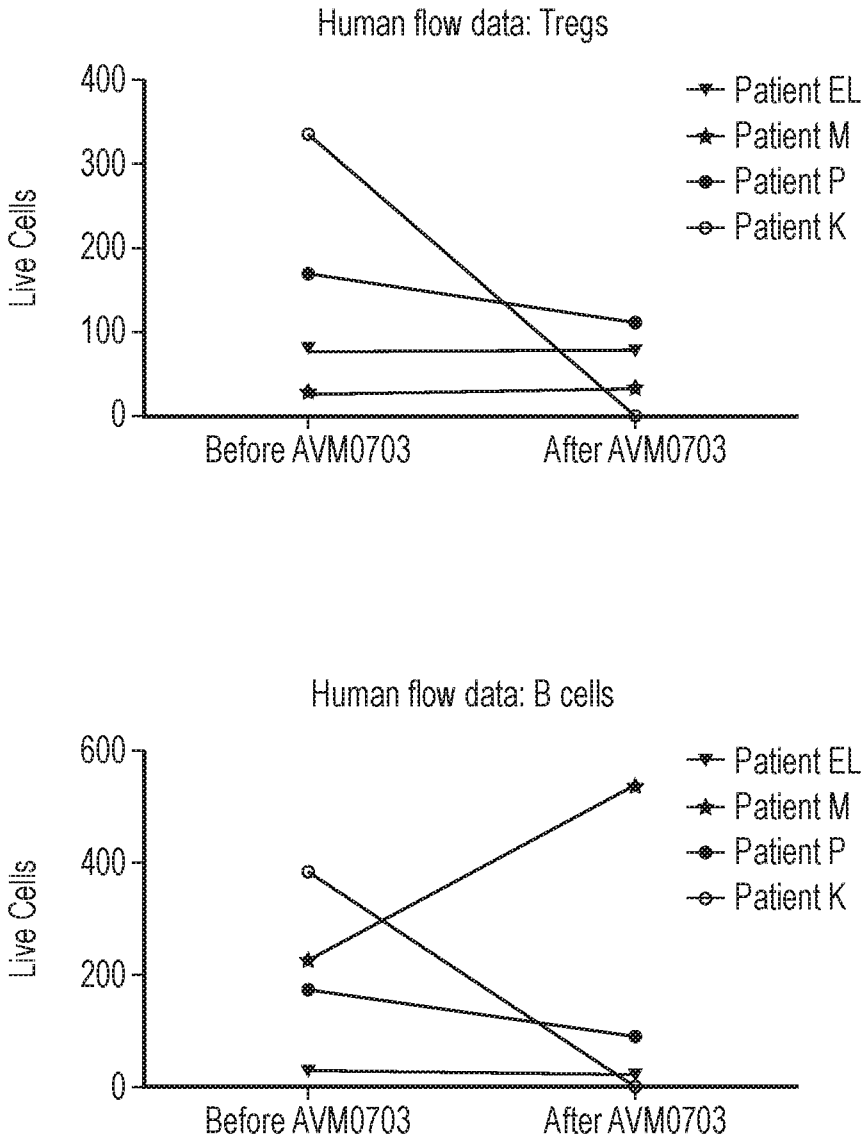

Human flow data: Tregs
Live Cells
400
300
200
100
0
Before AVM0703
After AVM0703
Patient EL
Patient M
Patient P
Patient K
Human flow data: B cells
Live Cells
600
400
200
0
Before AVM0703
After AVM0703
Patient EL
Patient M
Patient P
Patient K

FIG. 15

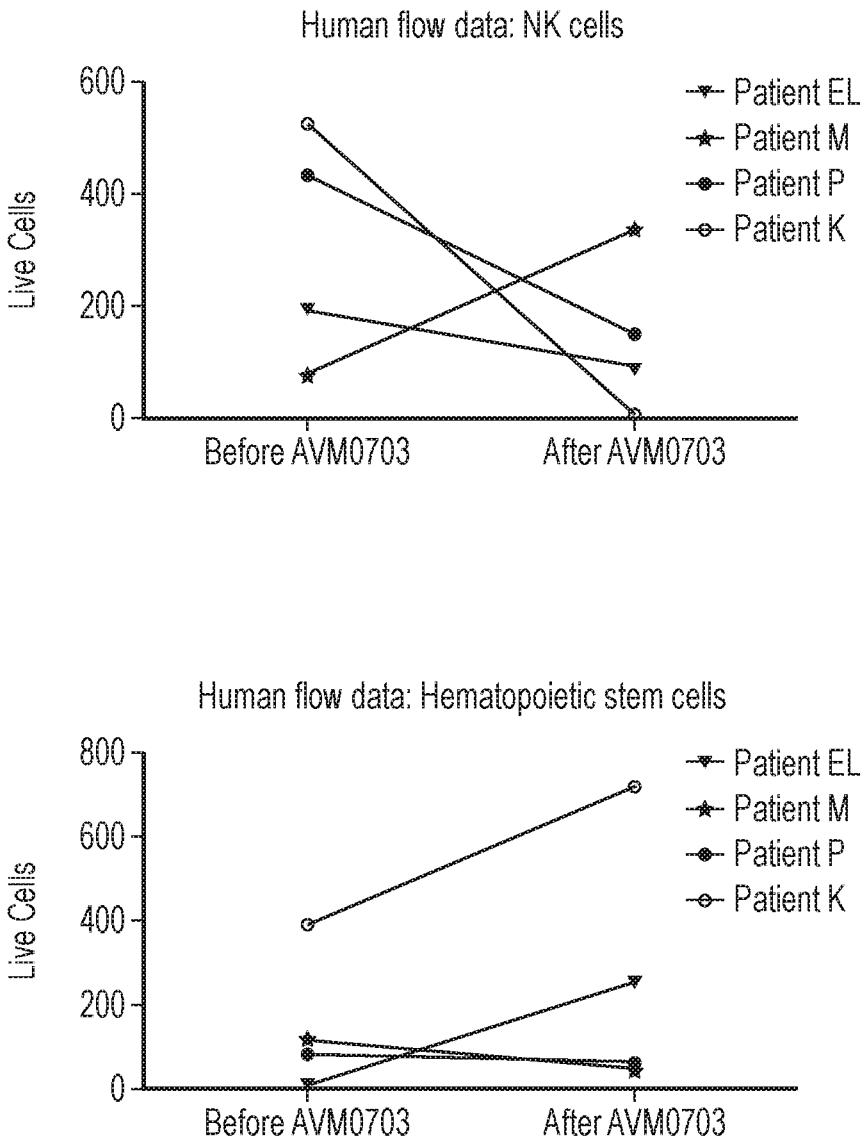

Human flow data: NK cells
Live Cells
600
400
200
0
Before AVM0703
After AVM0703
Patient EL
Patient M
Patient P
Patient K
Human flow data: Hematopoietic stem cells
Live Cells
800
600
400
200
0
Before AVM0703
After AVM0703
Patient EL
Patient M
Patient P
Patient K

FIG. 16

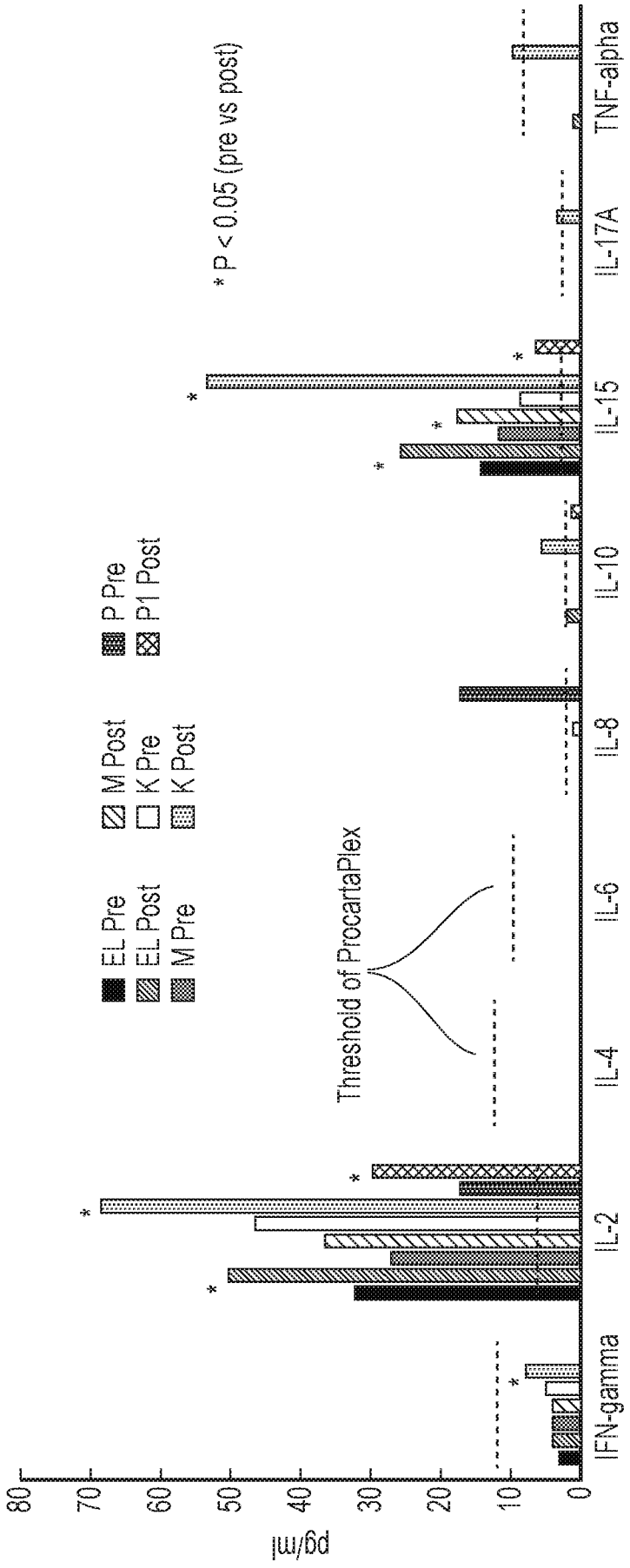

* P < 0.05 (pre vs post)
EL Pre
EL Post
M Pre
M Post
K Pre
K Post
P Pre
P1 Post
Threshold of ProcartaPlex
IFN-gamma
IL-2
IL-4
IL-6
IL-8
IL-10
IL-15
IL-17A
TNF-alpha
pg/ml
0
10
20
30
40
50
60
70
80

FIG. 17

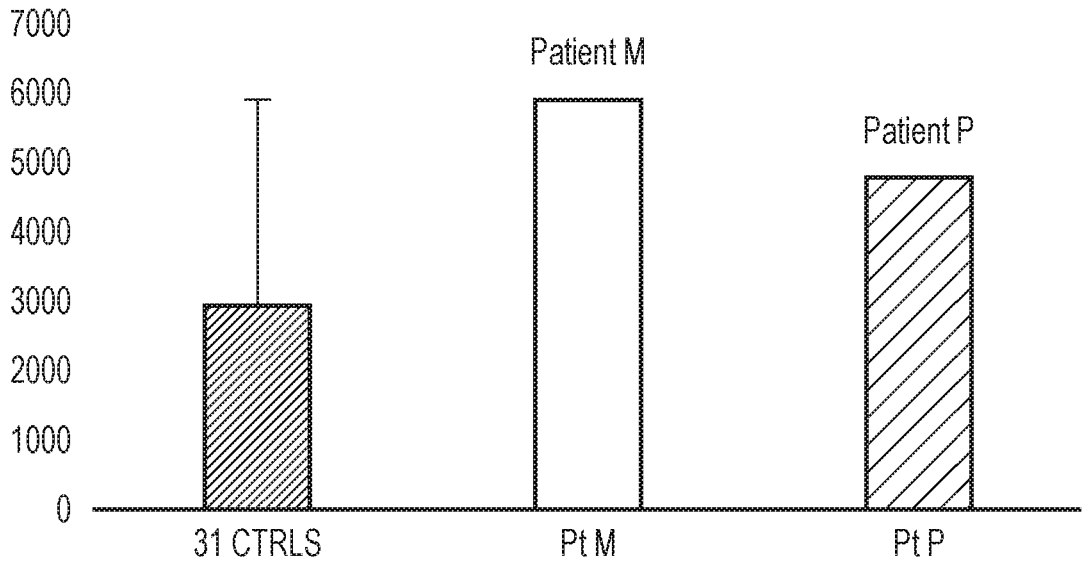

7000
6000
5000
4000
3000
2000
1000
0
Patient M
Patient P
31 CTRLS
Pt M
Pt P

FIG. 18

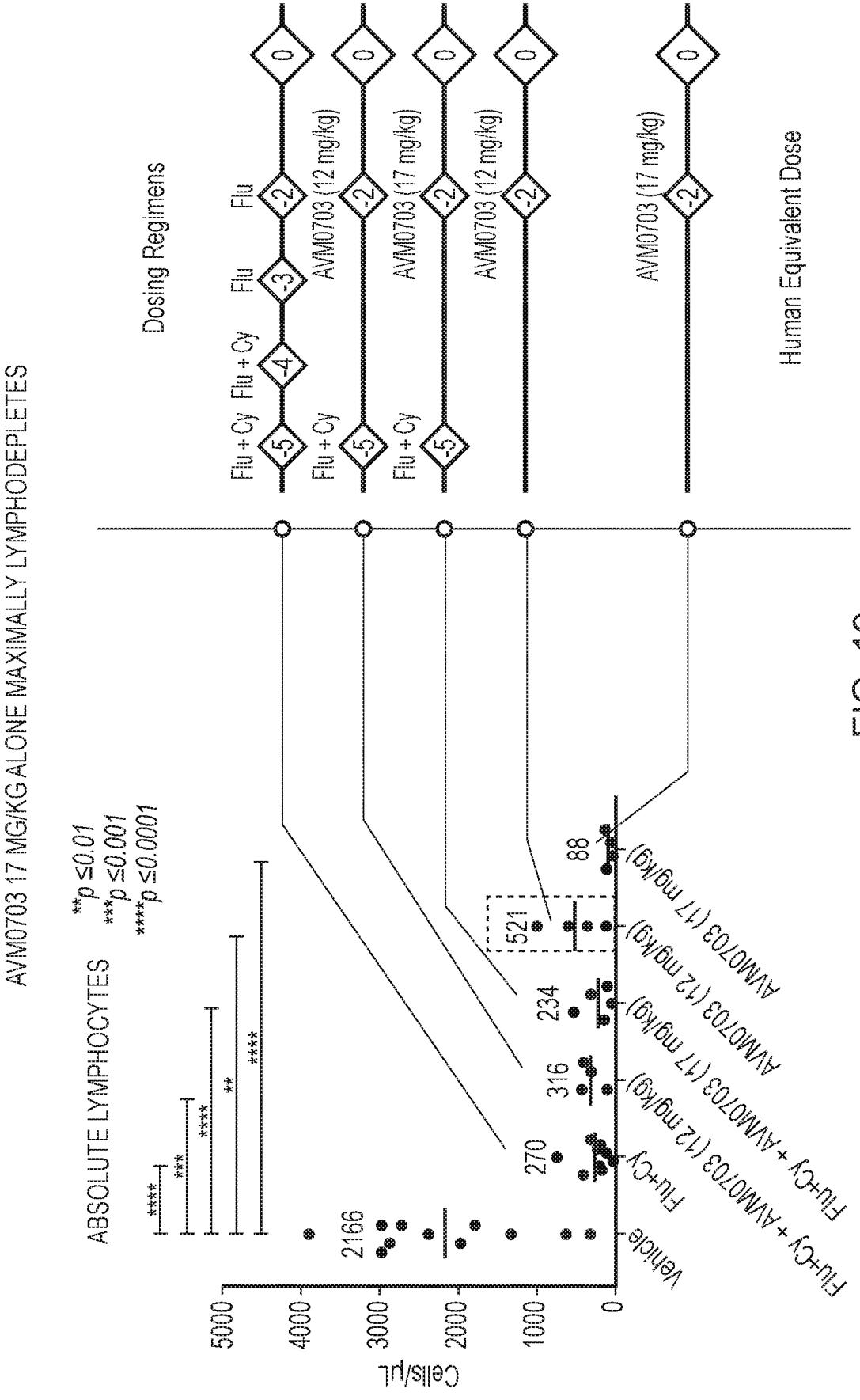

AVM0703 17 MG/KG ALONE MAXIMALLY LYMPHODEPLETES
Dosing Regimens
Human Equivalent Dose
Flu + Cy
Flu
AVM0703 (12 mg/kg)
AVM0703 (17 mg/kg)
-5
-4
-3
-2
0
ABSOLUTE LYMPHOCYTES
**p ≤0.01
***p ≤0.001
****p ≤0.0001
Cells/µL
5000
4000
3000
2000
1000
0
2166
270
316
234
521
88
Vehicle
Flu+Cy
Flu+Cy + AVM0703 (12 mg/kg)
Flu+Cy + AVM0703 (17 mg/kg)
AVM0703 (12 mg/kg)
AVM0703 (17 mg/kg)

FIG. 19

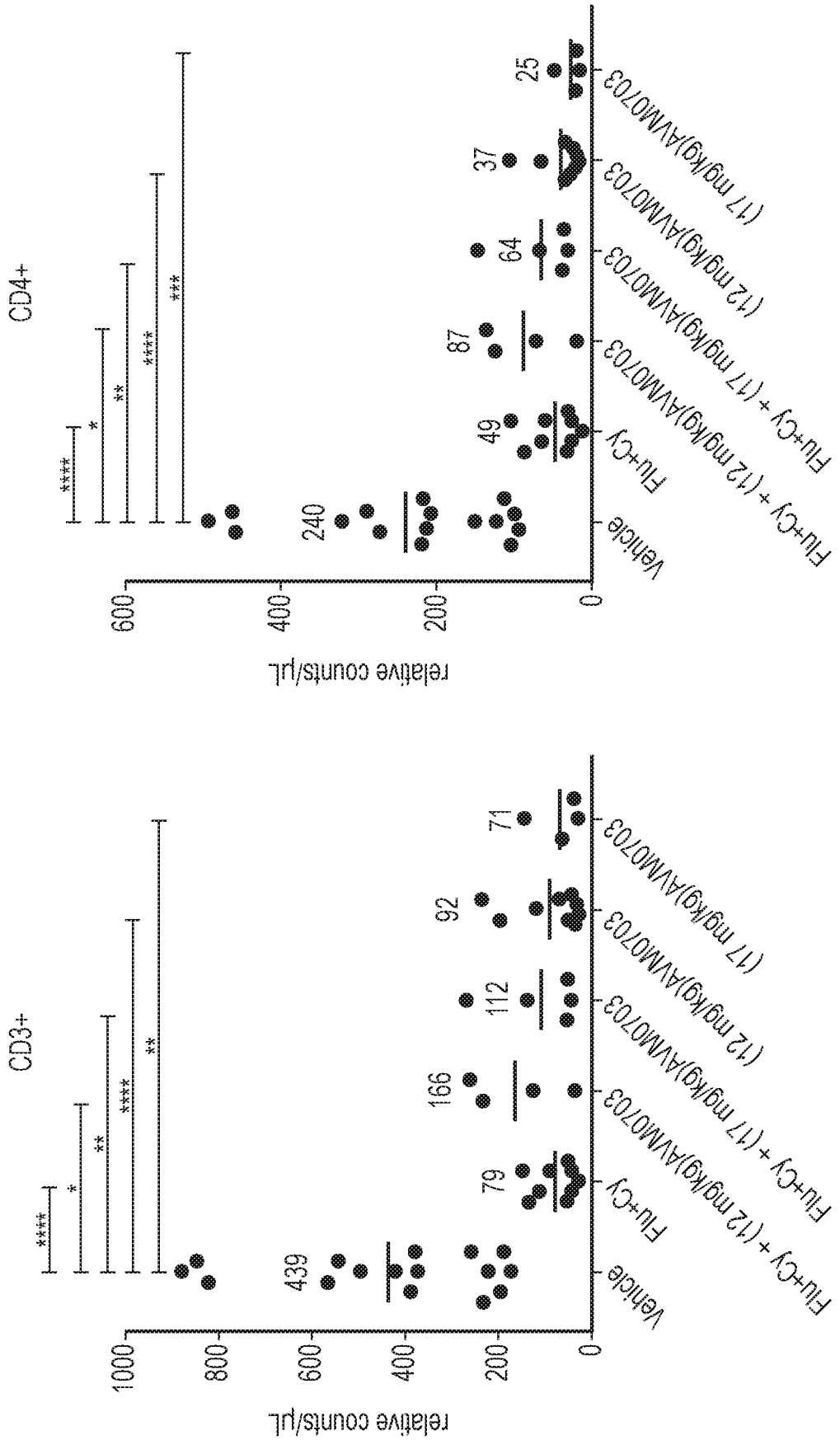

CD3+
relative counts/µL
1000
800
600
400
200
0
****
*
**
****
**
439
79
166
112
92
71
Vehicle
Flu+Cy
Flu+Cy + (12 mg/kg)AVM0703
Flu+Cy + (17 mg/kg)AVM0703
(12 mg/kg)AVM0703
(17 mg/kg)AVM0703
CD4+
relative counts/µL
600
400
200
0
****
*
**
****
***
240
49
87
64
37
25
Vehicle
Flu+Cy
Flu+Cy + (12 mg/kg)AVM0703
Flu+Cy + (17 mg/kg)AVM0703
(12 mg/kg)AVM0703
(17 mg/kg)AVM0703

FIG. 20

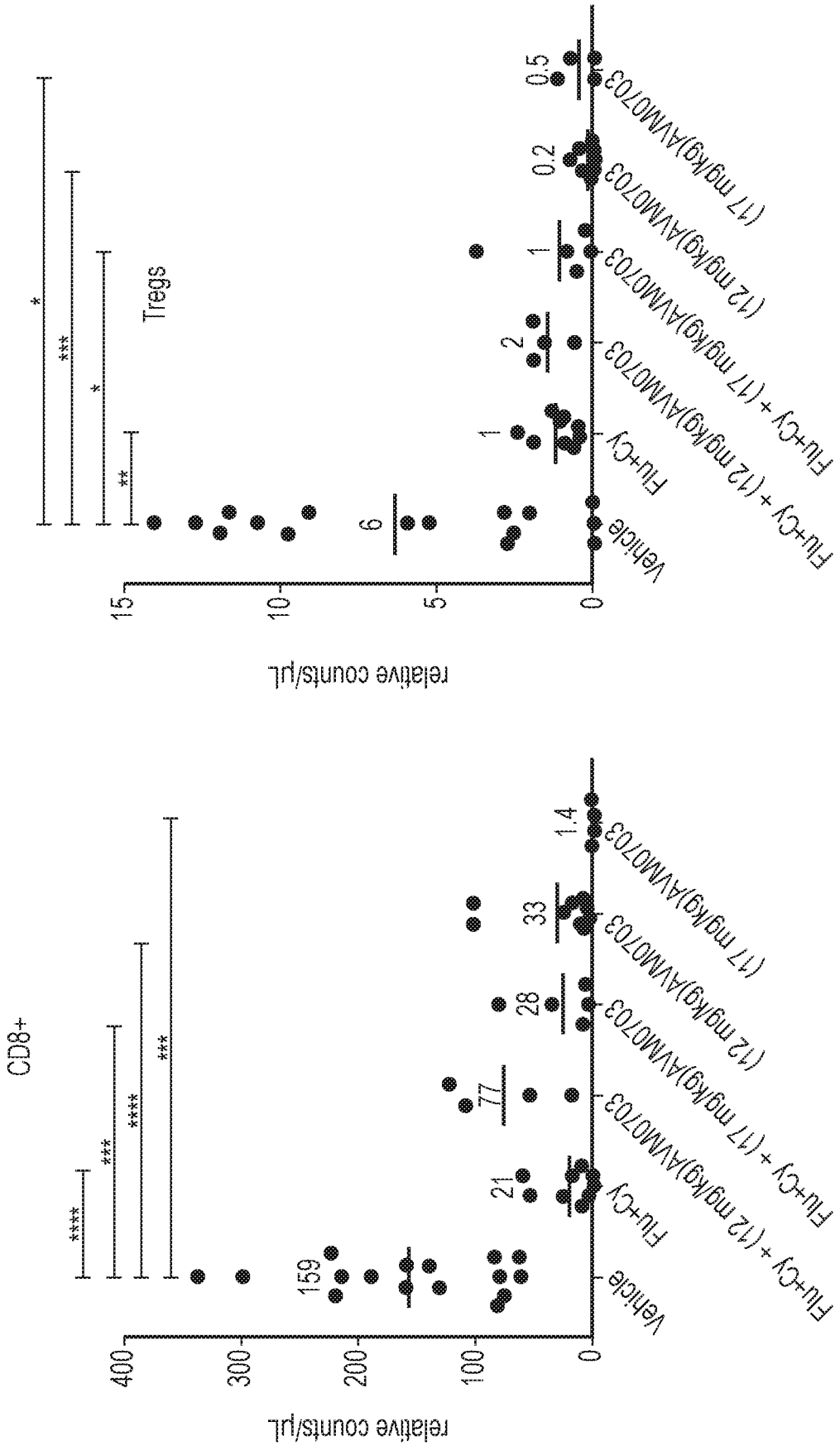

Tregs
relative counts/µL
15
10
5
0
Vehicle
Flu+Cy
Flu+Cy + (12 mg/kg)AVM0703
Flu+Cy + (17 mg/kg)AVM0703
(12 mg/kg)AVM0703
(17 mg/kg)AVM0703
0.5
0.2
1
2
1
6
*
***
*
**
CD8+
relative counts/µL
400
300
200
100
0
Vehicle
Flu+Cy
Flu+Cy + (12 mg/kg)AVM0703
Flu+Cy + (17 mg/kg)AVM0703
(12 mg/kg)AVM0703
(17 mg/kg)AVM0703
1.4
33
28
77
21
159
****
***
****
***

FIG. 21

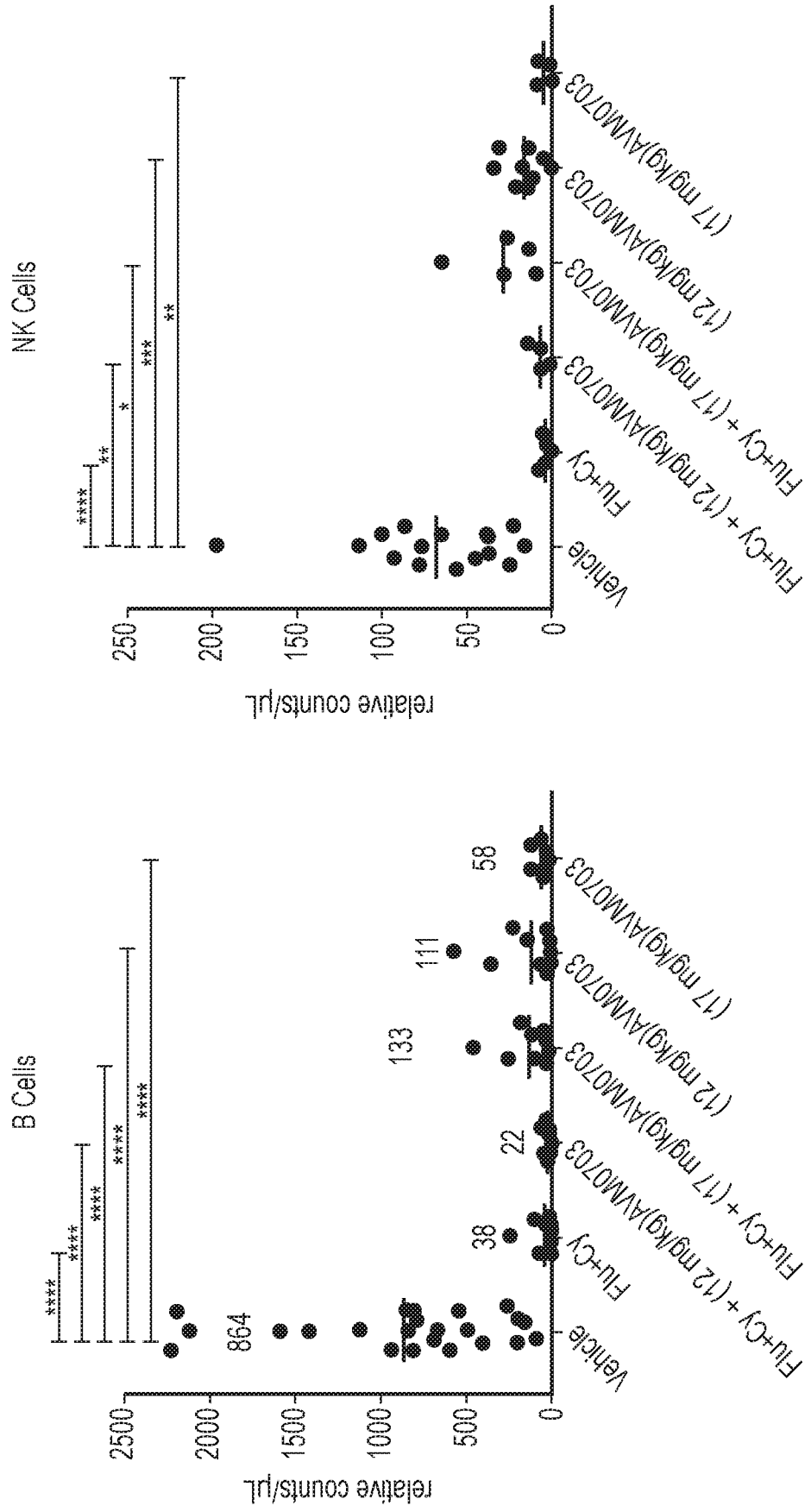

NK Cells
relative counts/µL
250
200
150
100
50
0
****
**
*
***
**
Vehicle
Flu+Cy
Flu+Cy + (12 mg/kg)AVM0703
Flu+Cy + (17 mg/kg)AVM0703
(12 mg/kg)AVM0703
(17 mg/kg)AVM0703
B Cells
relative counts/µL
2500
2000
1500
1000
500
0
****
****
****
****
****
864
38
133
22
111
58
Vehicle
Flu+Cy
Flu+Cy + (12 mg/kg)AVM0703
Flu+Cy + (17 mg/kg)AVM0703
(12 mg/kg)AVM0703
(17 mg/kg)AVM0703

FIG. 22

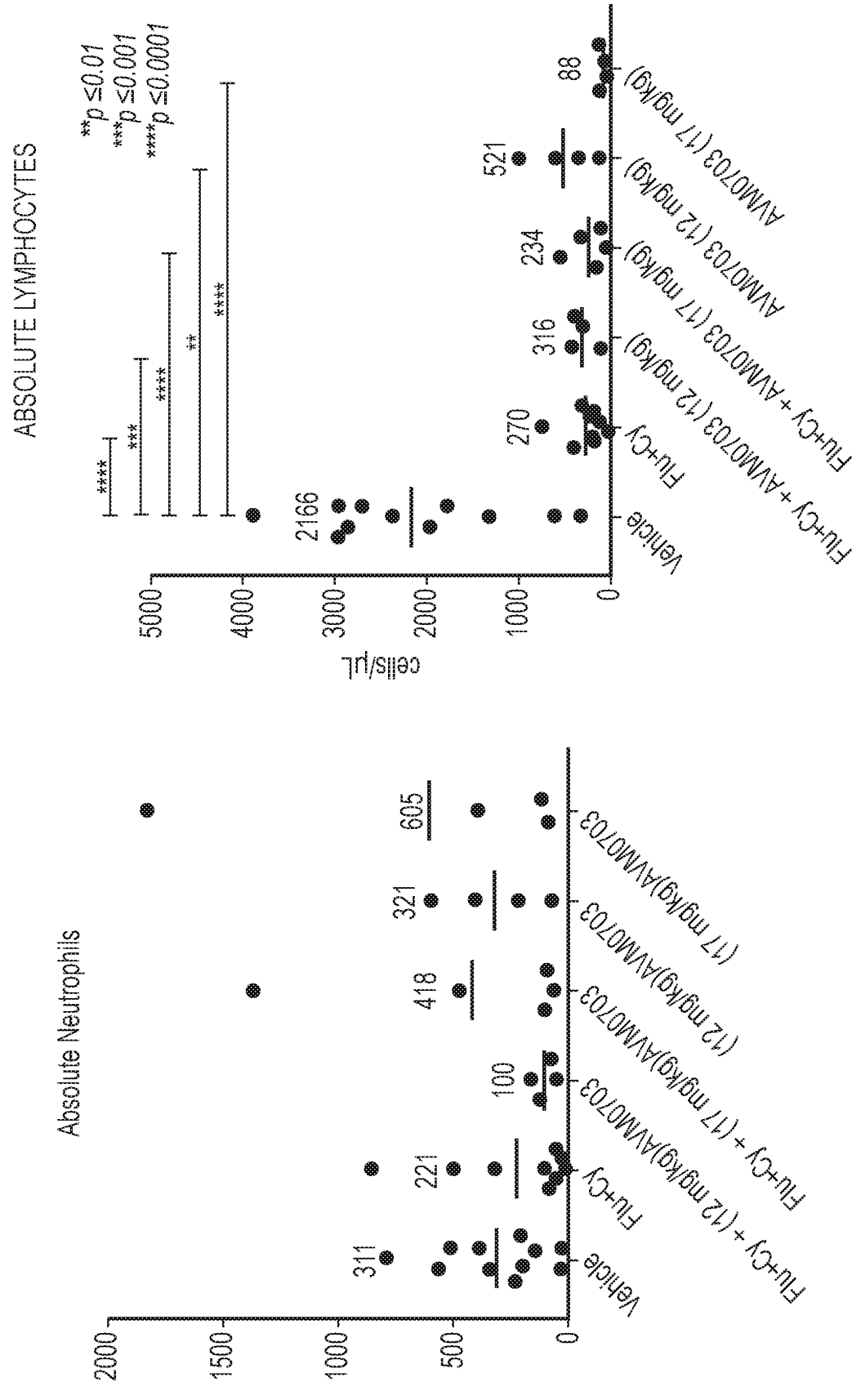

ABSOLUTE LYMPHOCYTES
**p ≤0.01
***p ≤0.001
****p ≤0.0001
cells/µL
5000
4000
3000
2000
1000
0
2166
270
316
234
521
88
Vehicle
Flu+Cy
Flu+Cy + AVM0703 (12 mg/kg)
Flu+Cy + AVM0703 (17 mg/kg)
AVM0703 (12 mg/kg)
AVM0703 (17 mg/kg)
Absolute Neutrophils
2000
1500
1000
500
0
311
221
100
418
321
605
Vehicle
Flu+Cy
Flu+Cy + (12 mg/kg)AVM0703
Flu+Cy + (17 mg/kg)AVM0703
(12 mg/kg)AVM0703
(17 mg/kg)AVM0703

FIG. 23

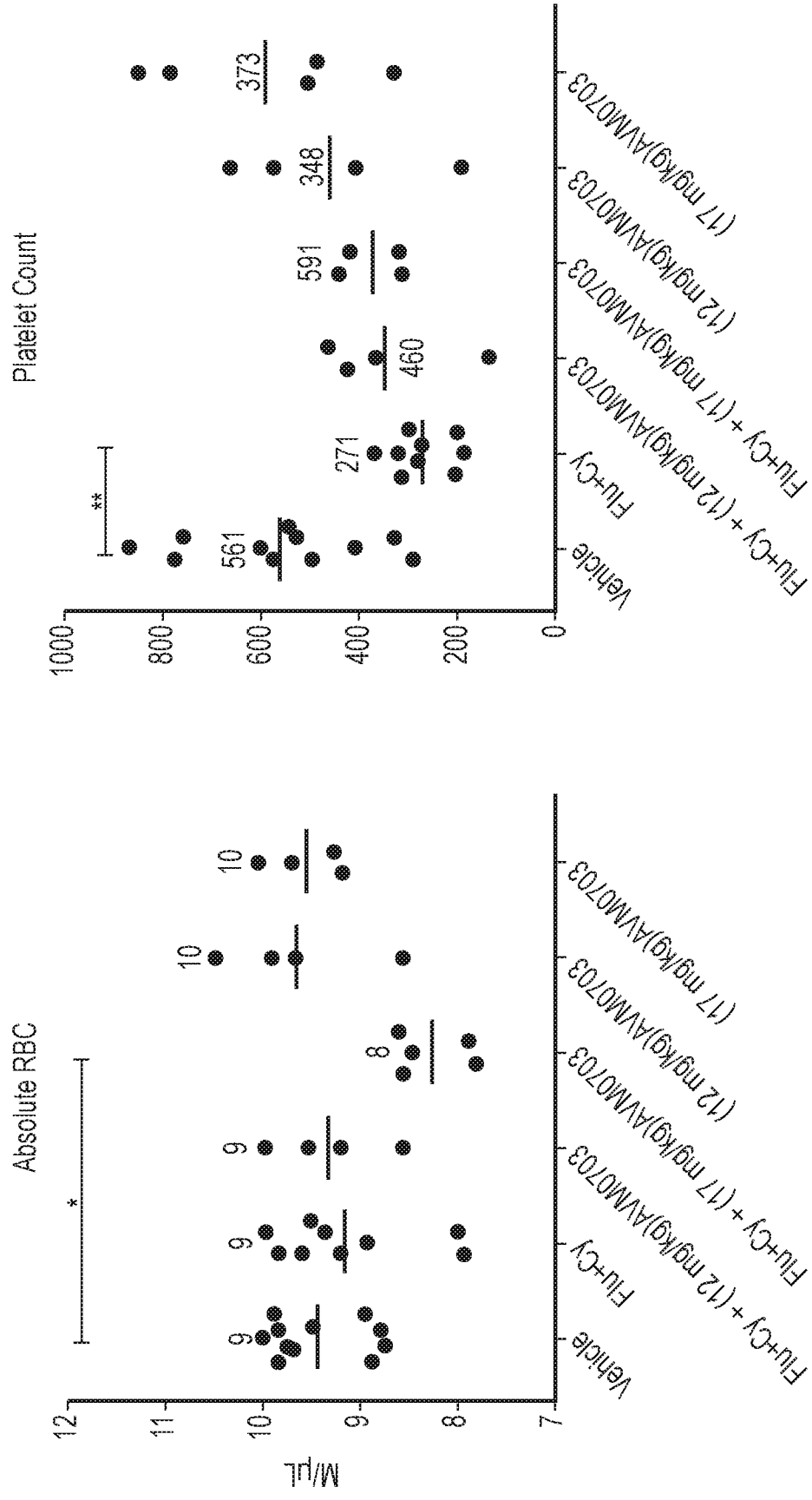

Absolute RBC
M/μL
12
11
10
9
8
7
*
9
9
9
10
10
8
Platelet Count
1000
800
600
400
200
0
**
561
271
591
460
348
373
Vehicle
Flu+Cy
Flu+Cy + (12 mg/kg)AVM0703
Flu+Cy + (17 mg/kg)AVM0703
(12 mg/kg)AVM0703
(17 mg/kg)AVM0703

FIG. 24

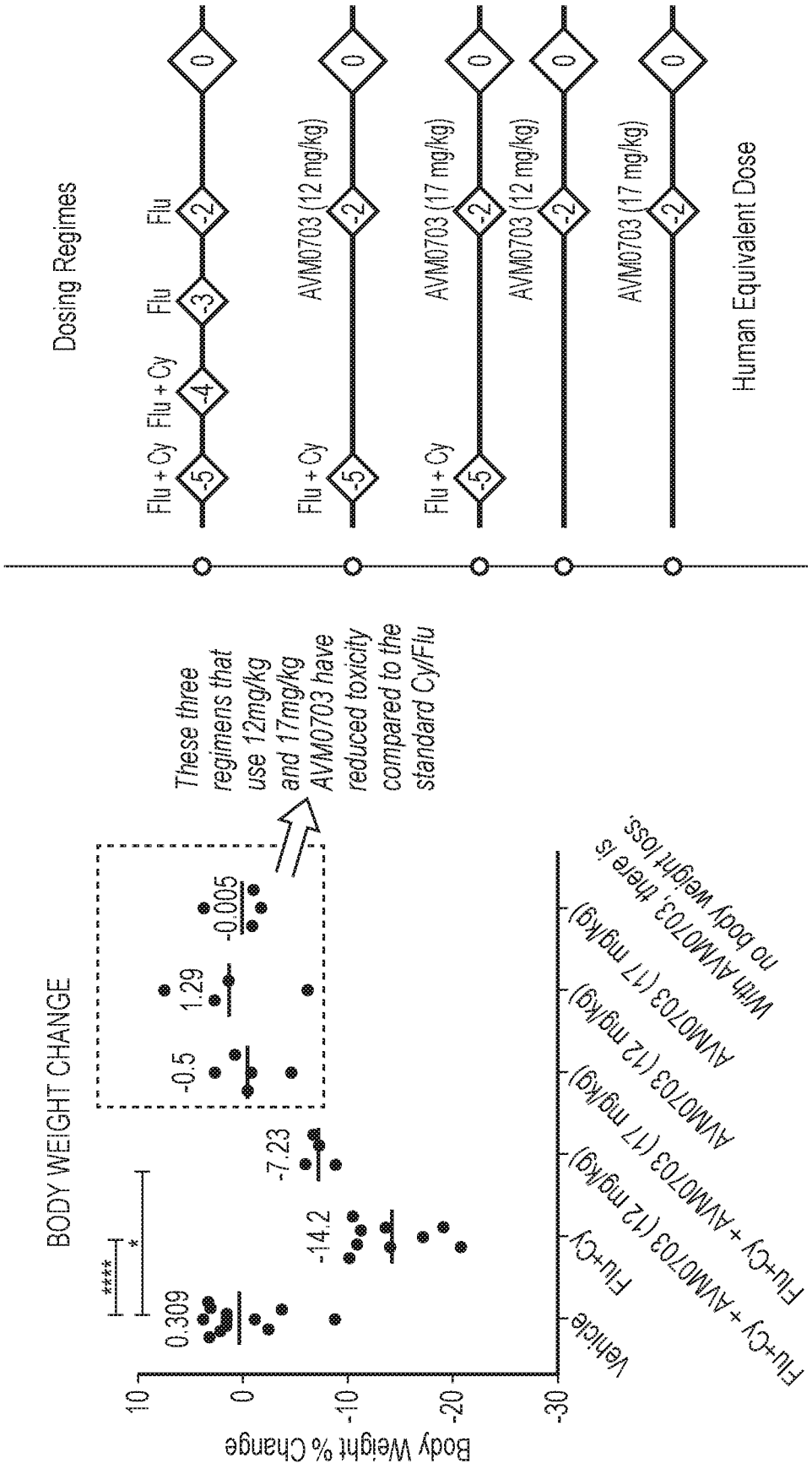

Dosing Regimes
Flu + Cy
Flu + Cy
Flu
Flu
AVM0703 (12 mg/kg)
AVM0703 (17 mg/kg)
AVM0703 (12 mg/kg)
AVM0703 (17 mg/kg)
Human Equivalent Dose
These three regimens that use 12mg/kg and 17mg/kg AVM0703 have reduced toxicity compared to the standard Cy/Flu
BODY WEIGHT CHANGE
****
*
0.309
-14.2
-7.23
-0.5
1.29
-0.005
Body Weight % Change
10
0
-10
-20
-30
Vehicle
Flu+Cy
Flu+Cy + AVM0703 (12 mg/kg)
Flu+Cy + AVM0703 (17 mg/kg)
AVM0703 (12 mg/kg)
AVM0703 (17 mg/kg)
With AVM0703, there is no body weight loss.

FIG. 25

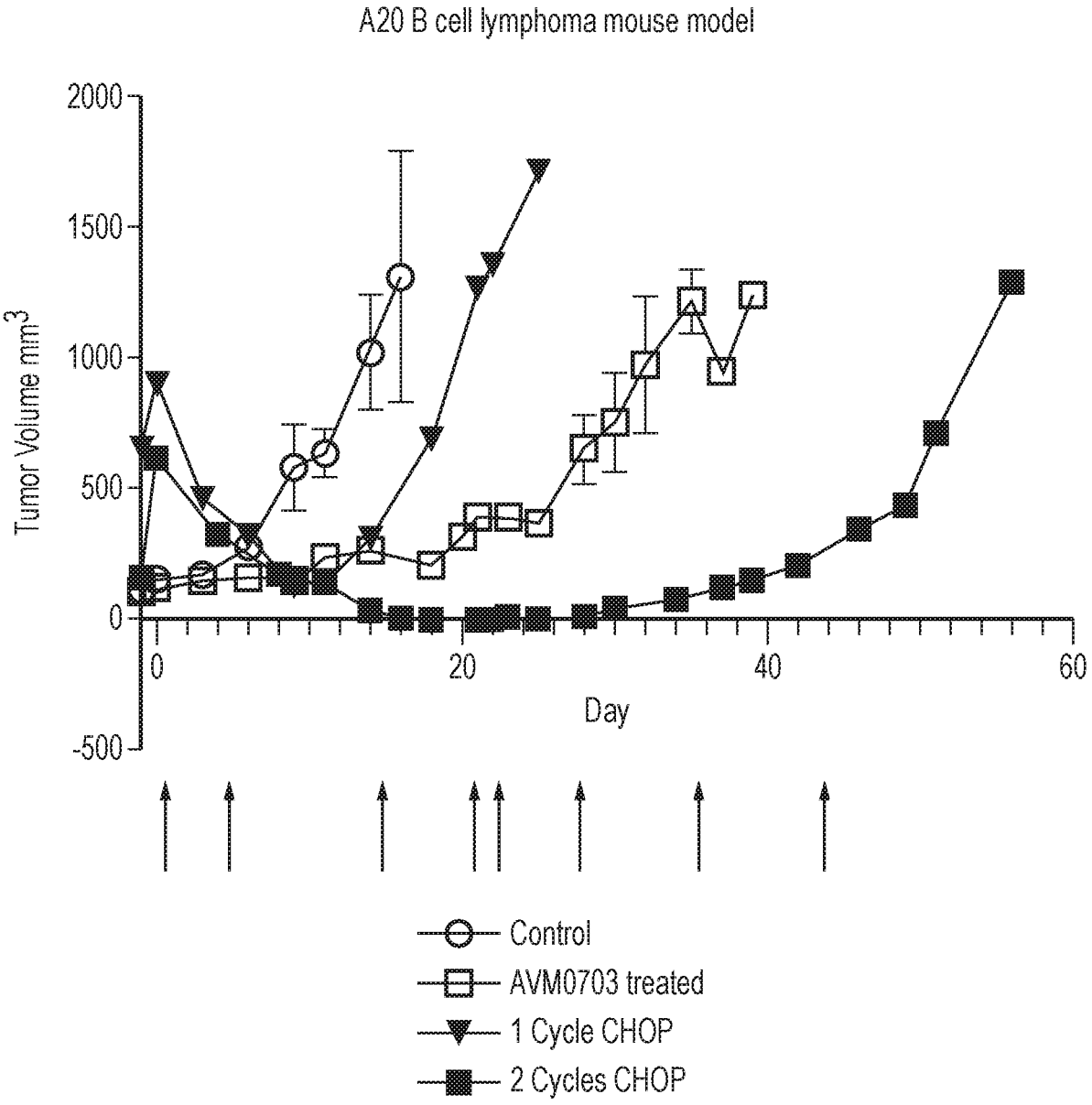

A20 B cell lymphoma mouse model
Tumor Volume mm3
2000
1500
1000
500
0
-500
0
20
40
60
Day
Control
AVM0703 treated
1 Cycle CHOP
2 Cycles CHOP

FIG. 26

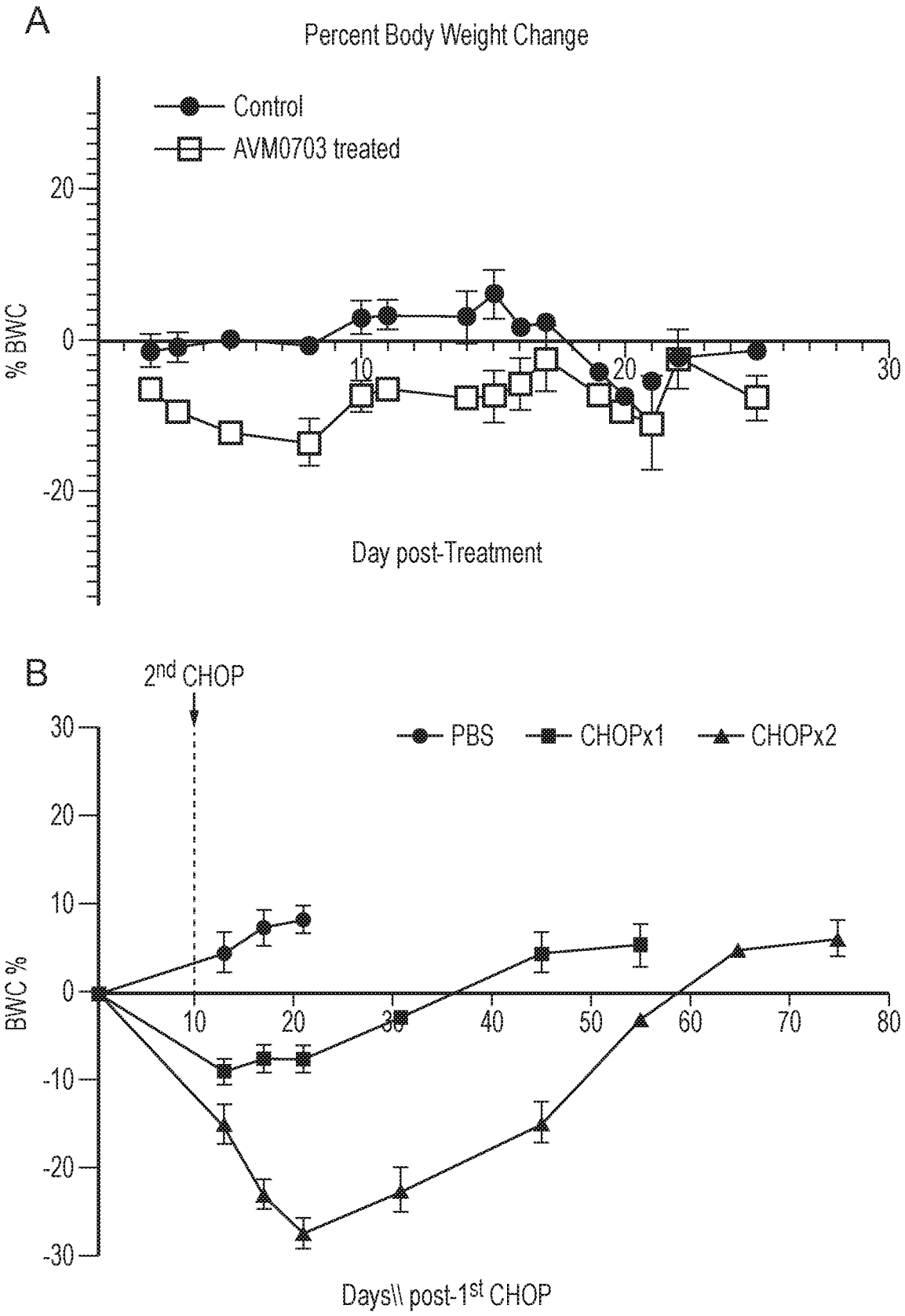

A
Percent Body Weight Change
Control
AVM0703 treated
% BWC
20
0
-20
10
20
30
Day post-Treatment
B
2nd CHOP
PBS
CHOPx1
CHOPx2
BWC %
30
20
10
0
-10
-20
-30
10
20
30
40
50
60
70
80
Days\\ post-1st CHOP

FIG. 27

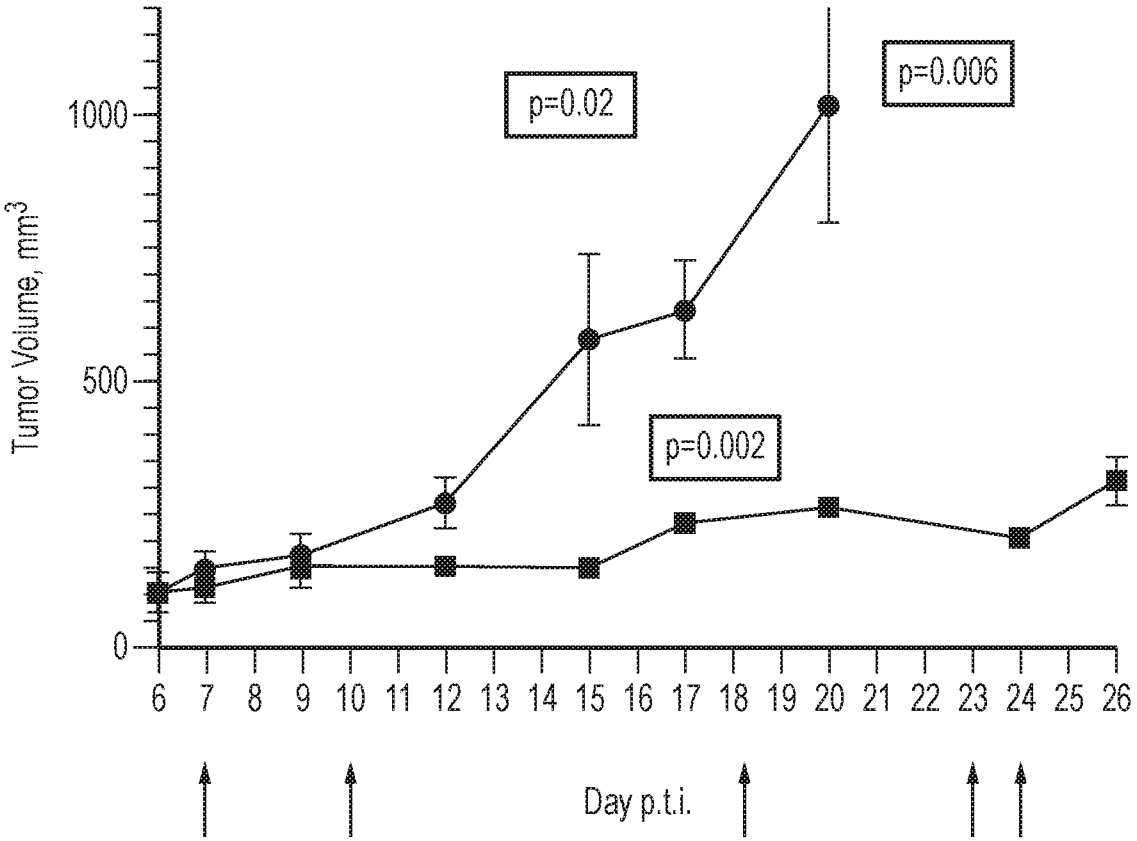

p=0.02
p=0.006
p=0.002
Tumor Volume, mm3
1000
500
0
6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26
Day p.t.i.

FIG. 28

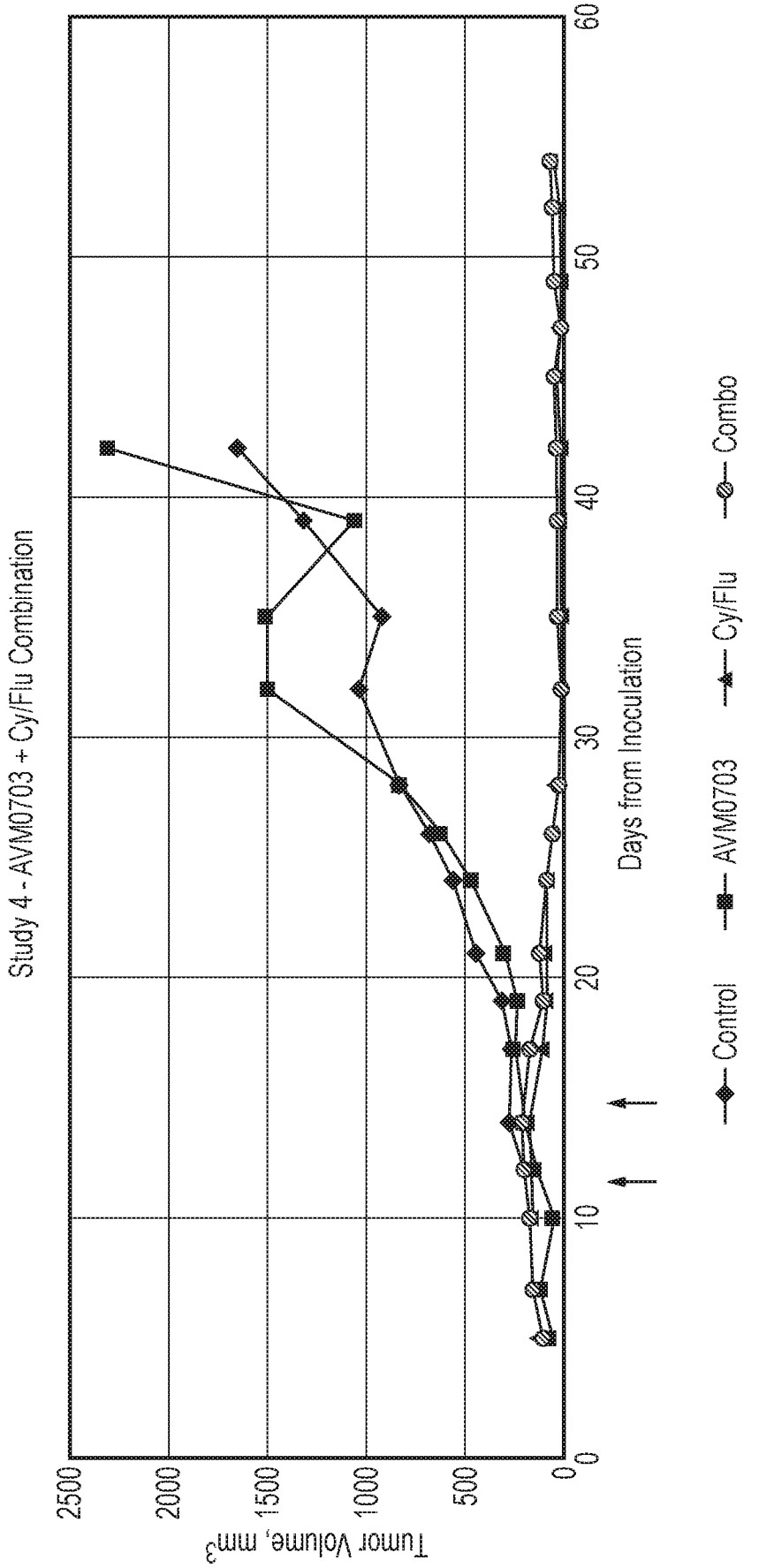

Study 4 - AVM0703 + Cy/Flu Combination
Tumor Volume, mm3
2500
2000
1500
1000
500
0
0
10
20
30
40
50
60
Days from Inoculation
Control
AVM0703
Cy/Flu
Combo

FIG. 29

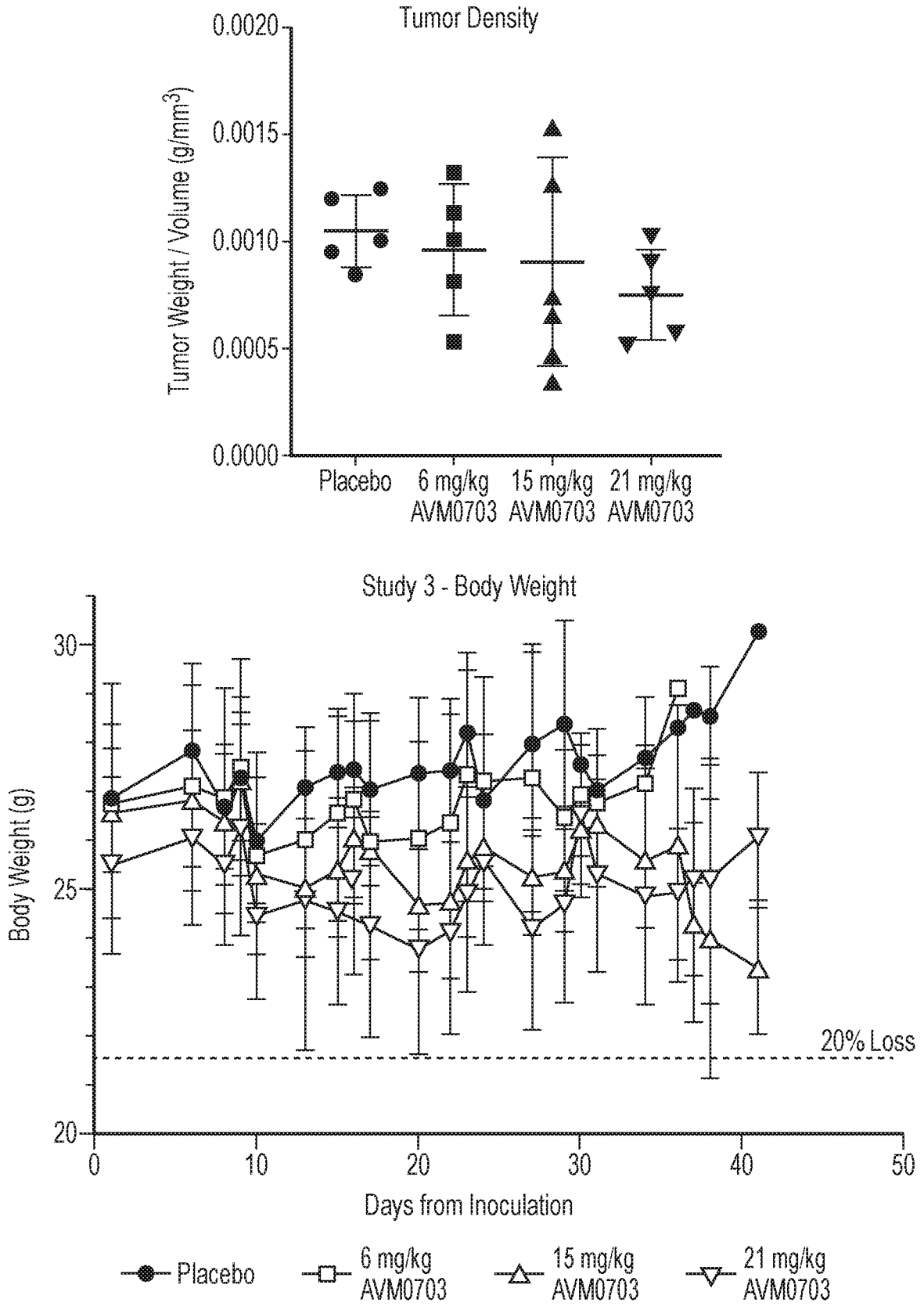

Tumor Density
Tumor Weight / Volume (g/mm3)
0.0020
0.0015
0.0010
0.0005
0.0000
Placebo
6 mg/kg AVM0703
15 mg/kg AVM0703
21 mg/kg AVM0703
Study 3 - Body Weight
Body Weight (g)
30
25
20
0
10
20
30
40
50
Days from Inoculation
20% Loss
Placebo
6 mg/kg AVM0703
15 mg/kg AVM0703
21 mg/kg AVM0703

FIG. 30