**Figure 1**

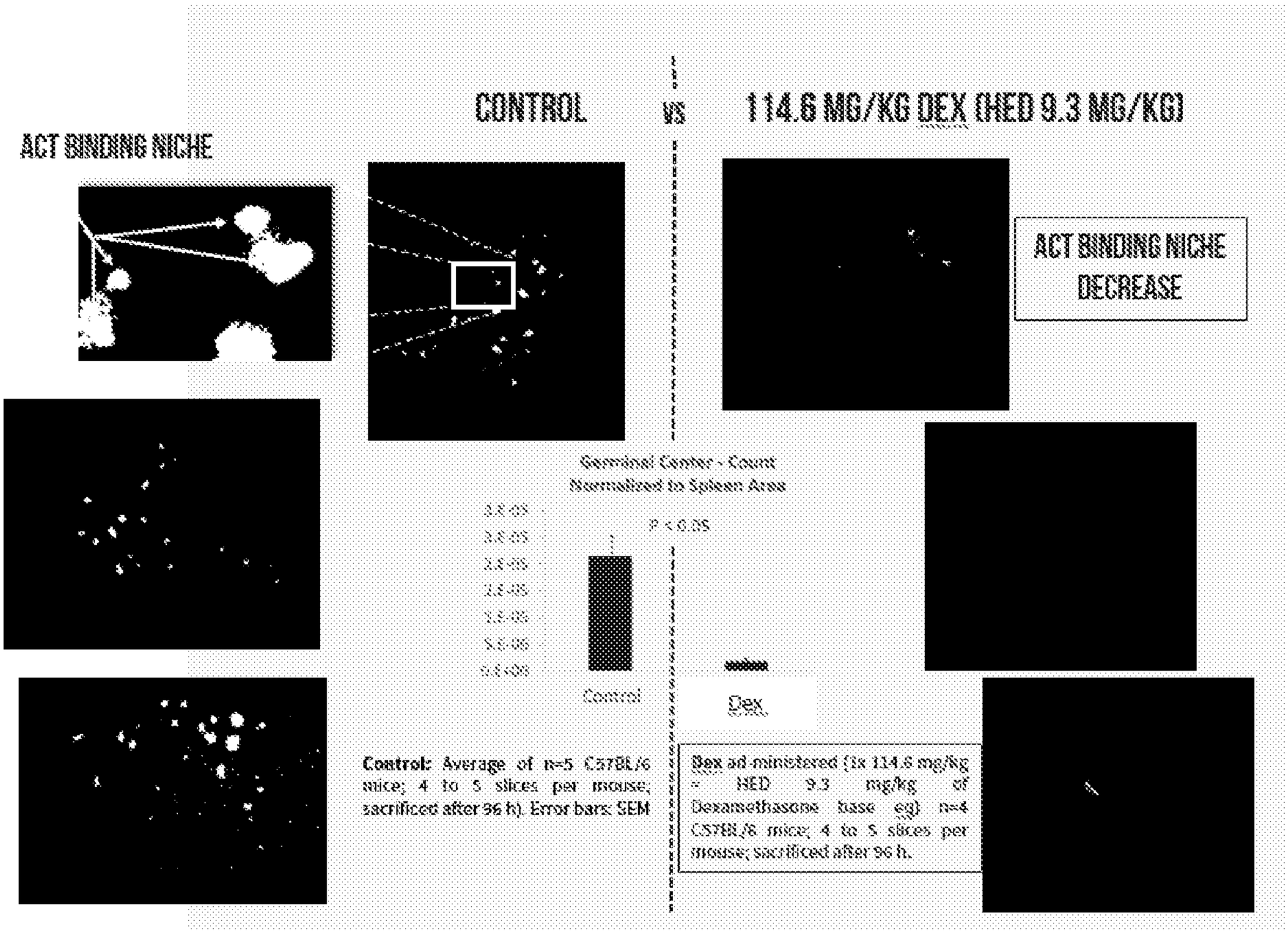

CONTROL
vs
114.6 MG/KG DEX (HED 9.3 MG/KG)
ACT BINDING NICHE
ACT BINDING NICHE DECREASE
Germinal Center - Count
Normalized to Spleen Area
P < 0.05
Control
Dex
Control: Average of n=5 C57BL/6 mice; 4 to 5 slices per mouse; sacrificed after 96 h). Error bars: SEM
Dex administered (1x 114.6 mg/kg = HED 9.3 mg/kg of Dexamethasone base eq) n=4 C57BL/6 mice; 4 to 5 slices per mouse; sacrificed after 96 h.

**Figure 2**

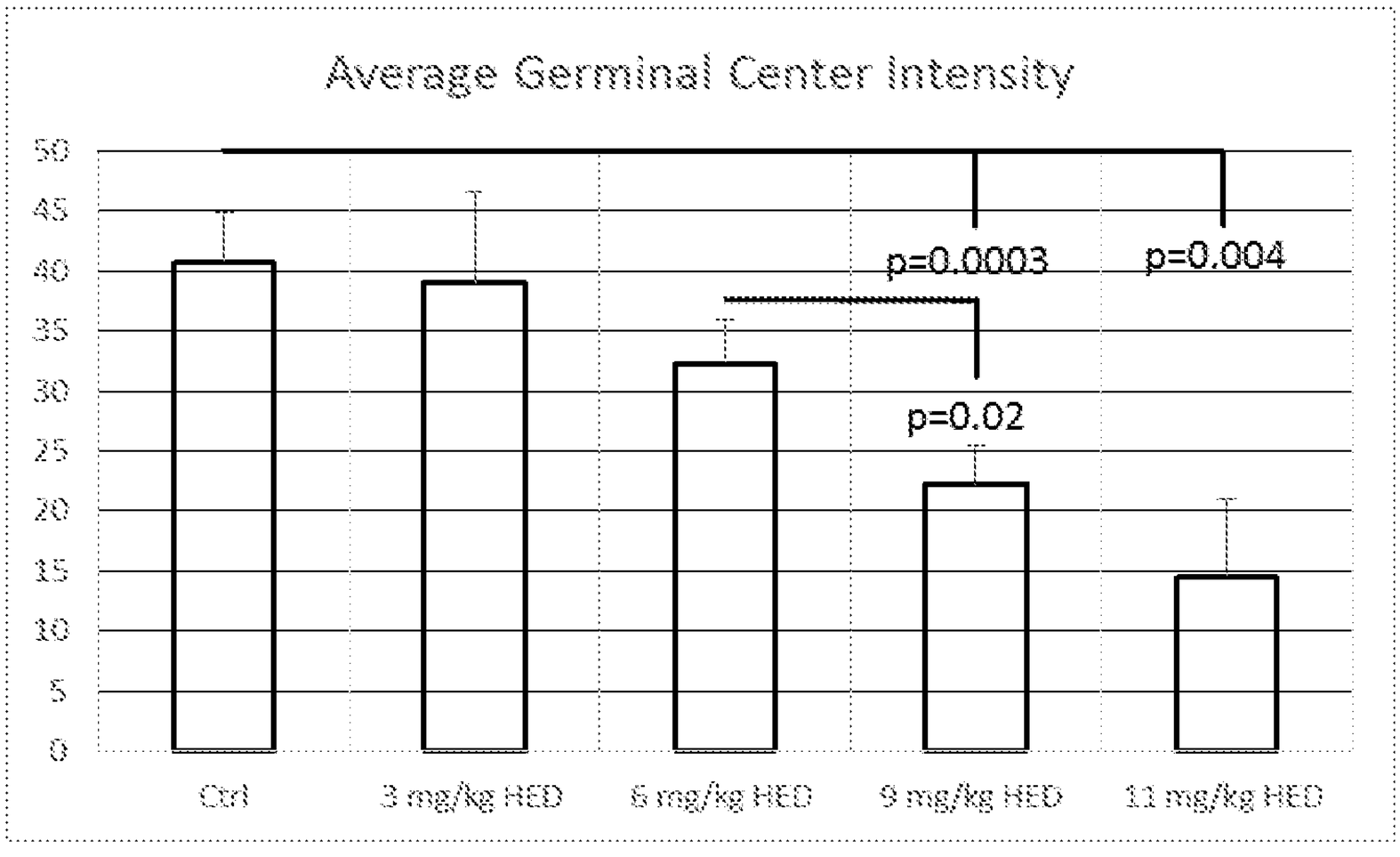
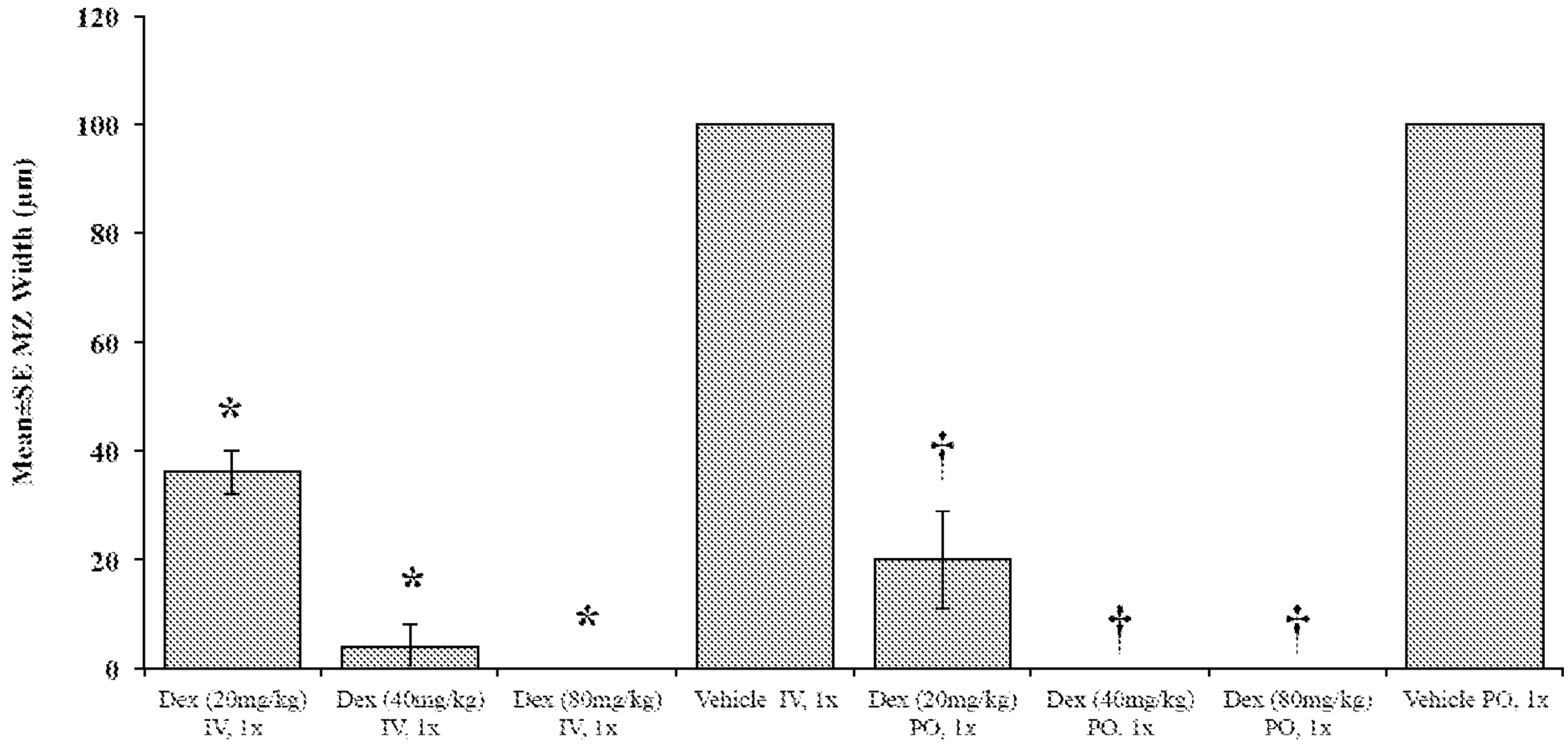

Average Germinal Center Intensity
50
45
40
35
30
25
20
15
10
5
0
p=0.0003
p=0.004
p=0.02
Ctrl
3 mg/kg HED
6 mg/kg HED
9 mg/kg HED
11 mg/kg HED

**Figure 3**



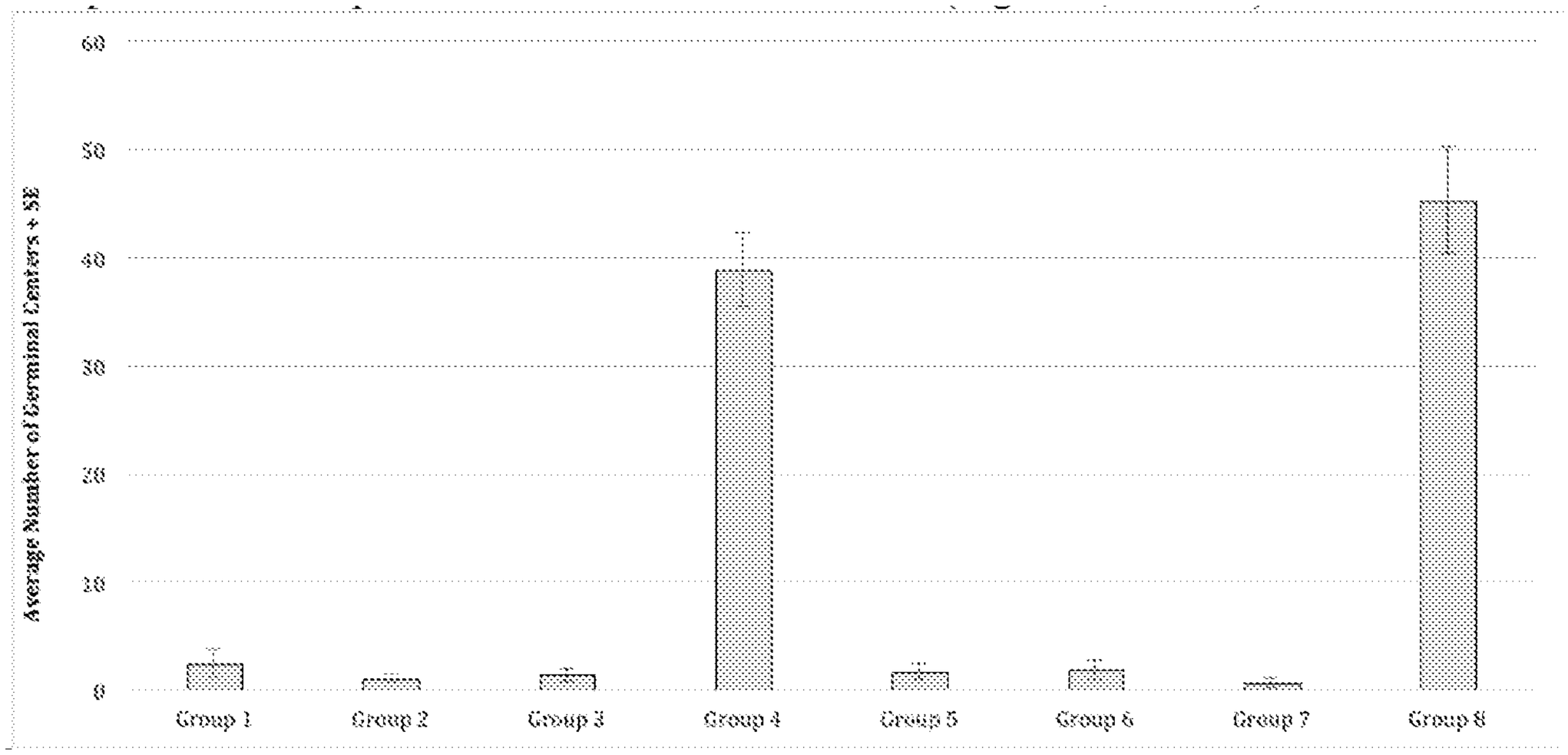

$n = 5$/group

*$p < 0.05$ ANOVA (Dunnett's post-hoc) vs. Vehicle IV

†$p < 0.05$ ANOVA (Dunnett's post-hoc) vs. Vehicle PO

‡$p < 0.05$ Student's *t*-test vs. Vehicle IV

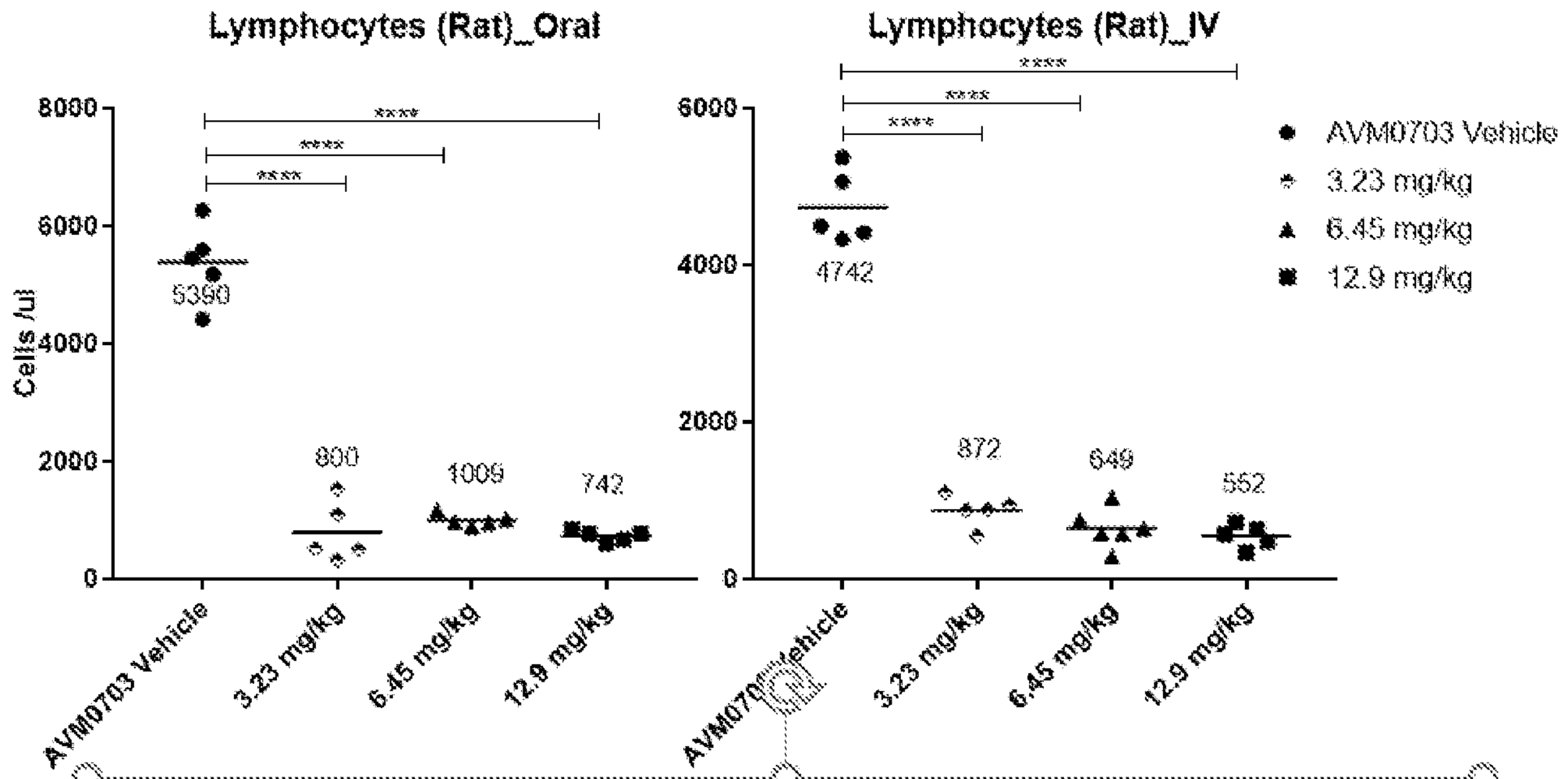
**Figure 4**




Groups 1-4 IV : 1 = 20 mg/kg, 2 = 40 mg/kg, 3 = 80 mg/kg, 4 = Placebo

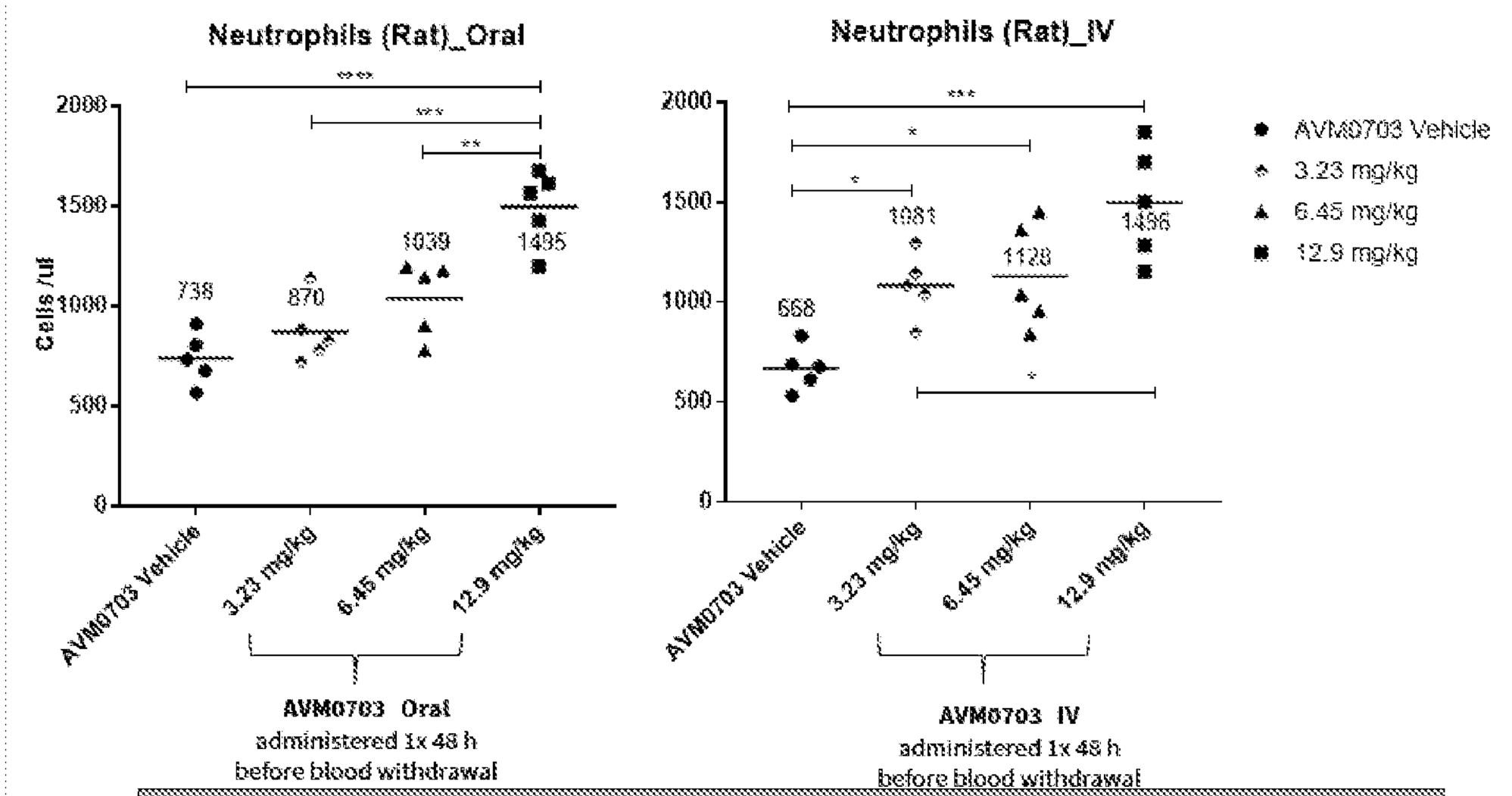
Groups 5-9 PO : 5 = 20 mg/kg, 6 = 40 mg/kg, 7 = 80 mg/kg, 8 = Placebo

**Figure 5**




AVM0703 was administered 48 hours before blood withdrawal. Note, significant lymphodepletion at all doses vs controls in rats whether IV (left) or oral dosing (right). Doses are shown as HED (human equivalent dose).

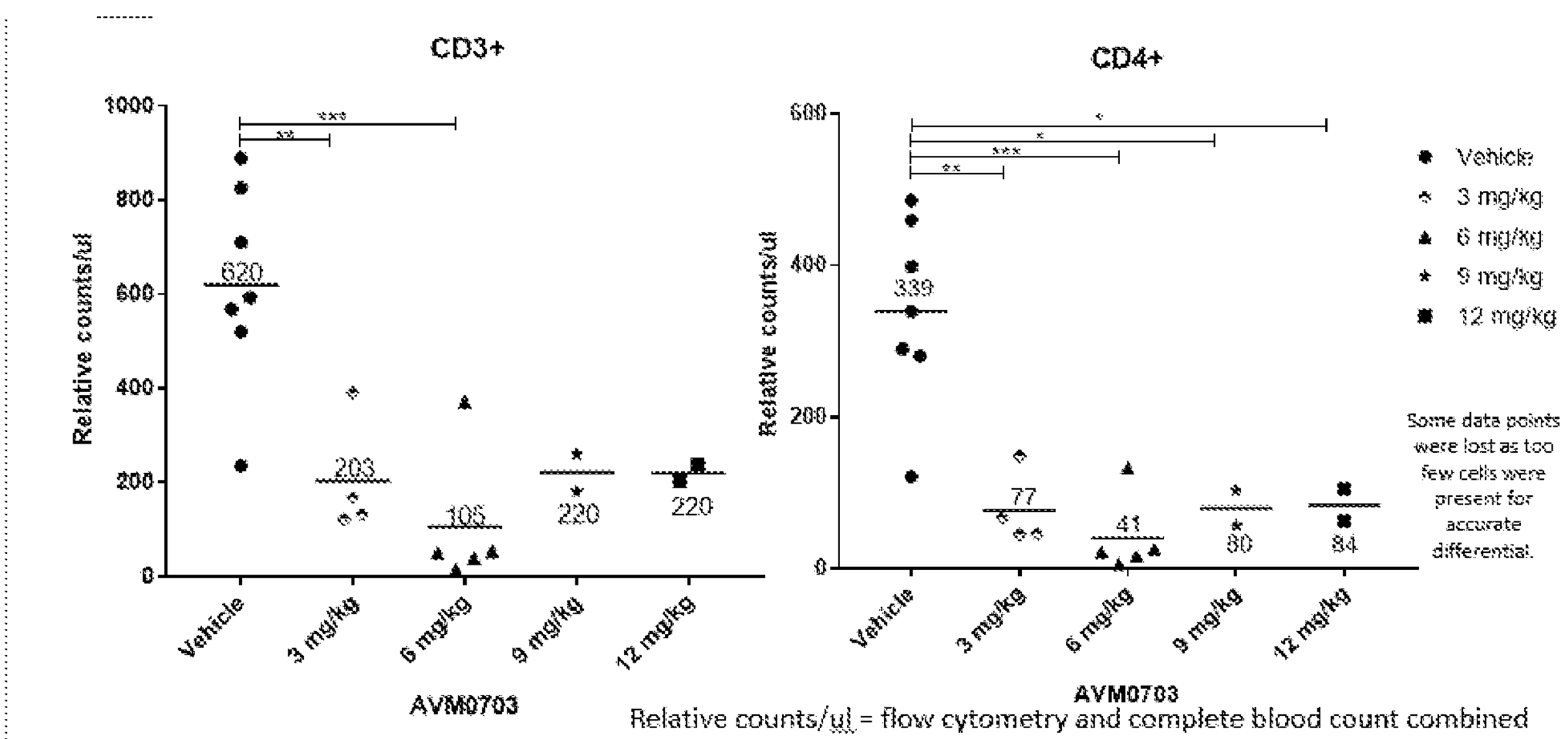
**Figure 6**




AVM0703 has a lymphodepletion profile that is neutrophil sparing. Note, AVM0703 does not adversely effect neutrophils.

Doses are shown as HED (human equivalent dose).

**Figure 7**

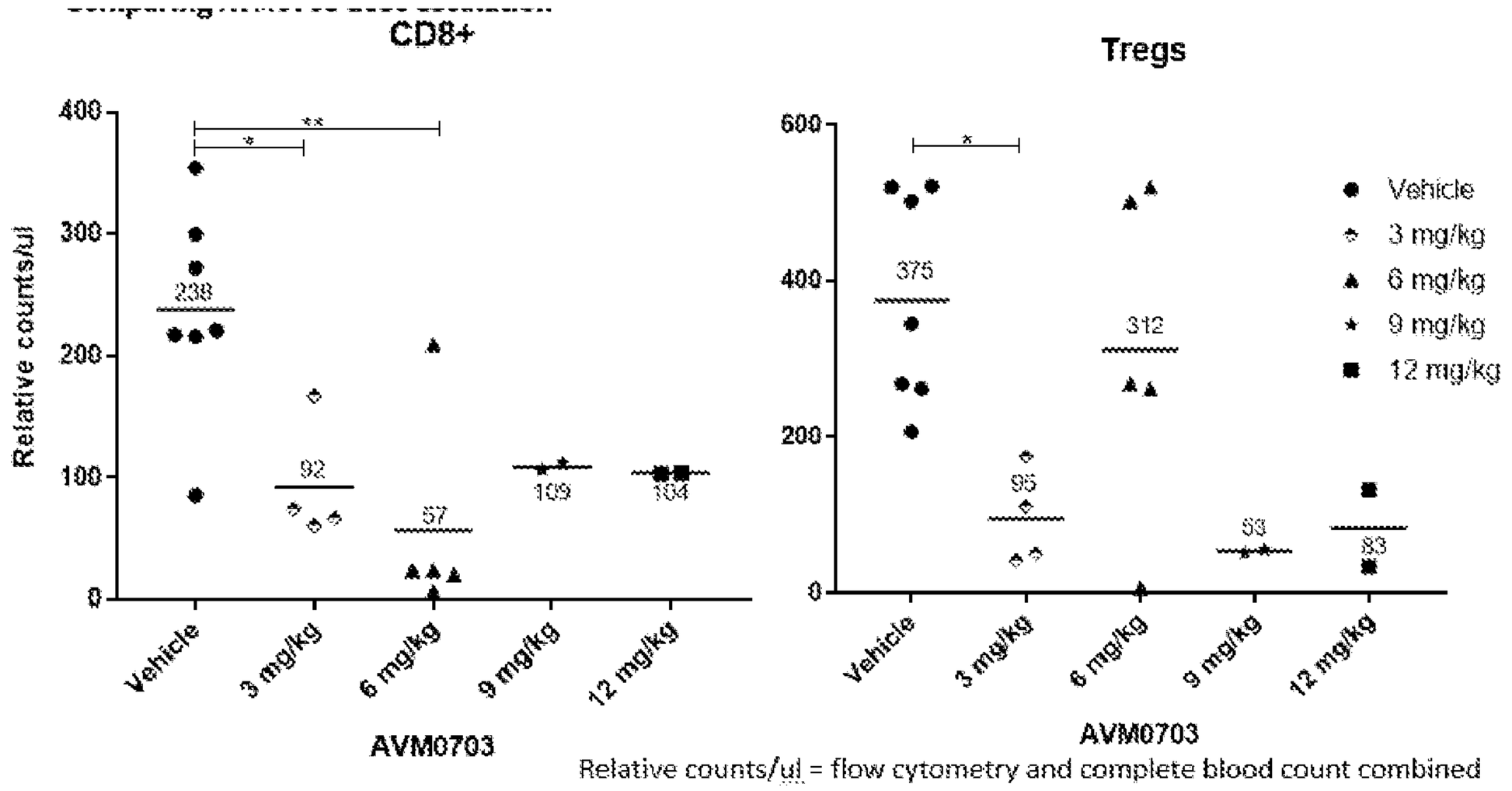



Relative counts/ul = flow cytometry and complete blood count combined

Compared to control, in the 12 mg/kg group:
1. 65% reduction in CD3+ cells
2. 75% reduction in CD4+ cells

A one-way ANOVA followed by post-hoc Tukey's test was incorporated to determine statistical significance between the treatment groups.
*p < 0.05
**p< 0.01
***p<0.001

**Figure 8**




Relative counts/ul = flow cytometry and complete blood count combined

Compared to control, in the 12 mg/kg group:

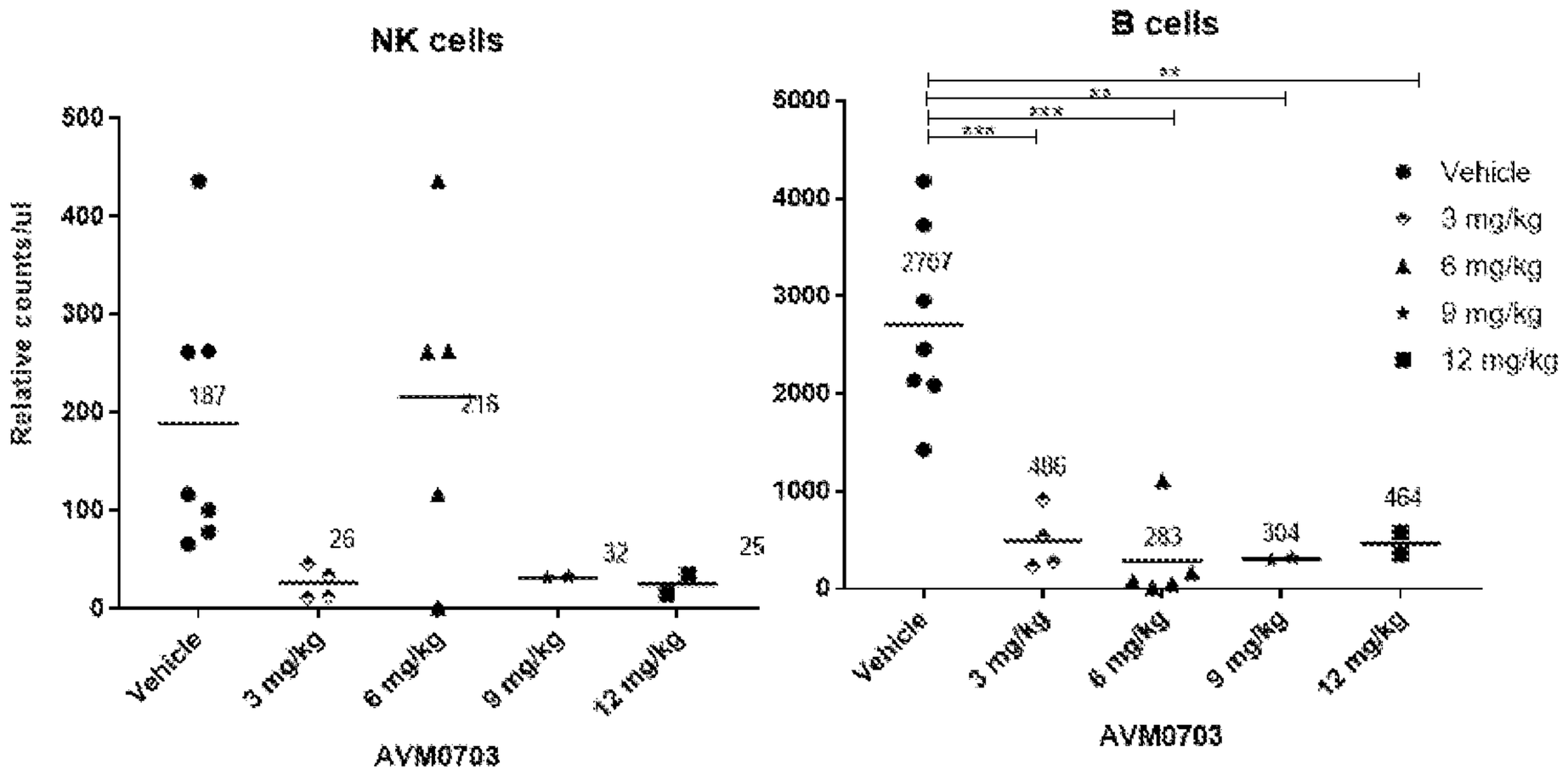
1. 56% reduction in CD8+ cells
2. 78% reduction in mouse treg

A one-way ANOVA followed by post-hoc Tukey's test was incorporated to determine statistical significance between the treatment groups.

*$p < 0.05$

**$p < 0.01$

**Figure 9**



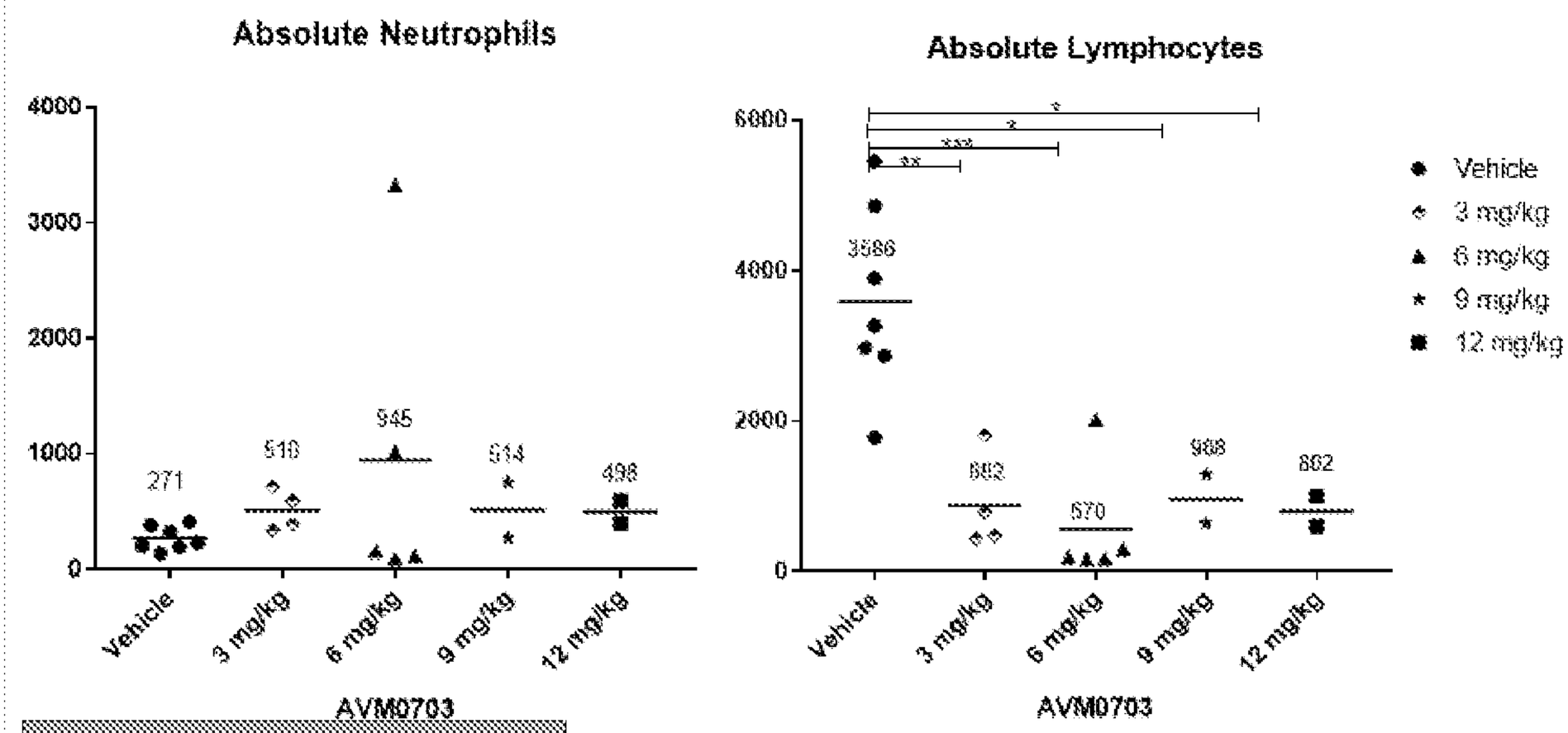

Relative counts/ul = flow cytometry and complete blood count combined

Compared to control in the 12 mg/kg groups:
1. 87% reduction in NK cells
2. 99% reduction in B cells

A one-way ANOVA followed by post-hoc Tukey's test was incorporated to determine statistical significance between the treatment groups

*p < 0.05
**p< 0.01
***p<0.001

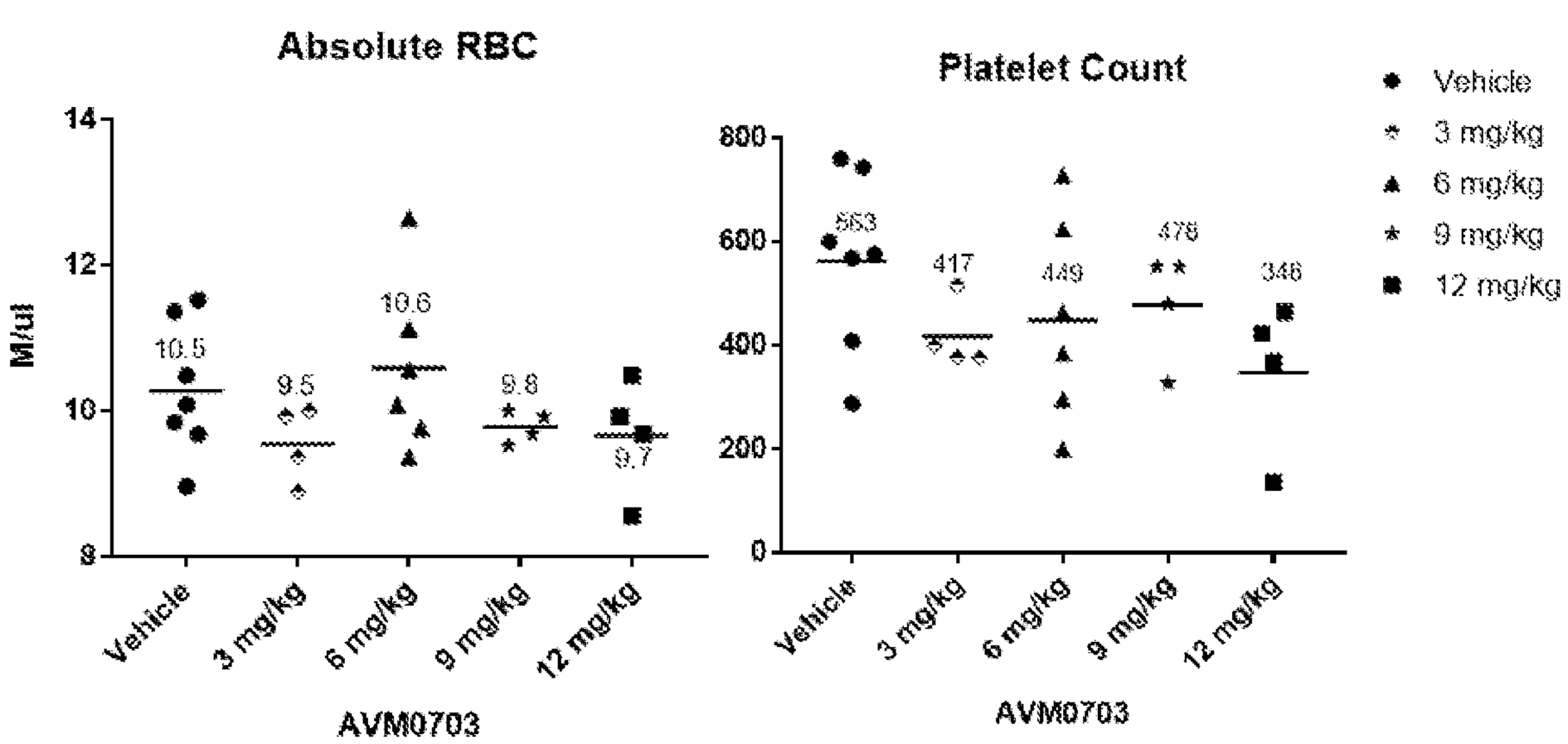
**Figure 10**




AVM0703 does not affect neutrophils, eliminates the need for transfusion and therefore provides a safer non-toxic alternative to chemo pre-conditioning

Cells/ul = absolute numbers obtained from CBC
A one-way ANOVA followed by post-hoc Tukey's test was incorporated to determine statistical significance between the treatment groups
*$p < 0.05$
**$p< 0.01$
***$p<0.001$

**Figure 11**




AVM0703 does not affect RBC or platelets, eliminates the need for transfusion and therefore provides a safer, non-toxic alternative to chemo preconditioning

Cells/ul = absolute numbers obtained from CBC
Platelet count measured by CBC - many samples had clumping

**Figure 12**

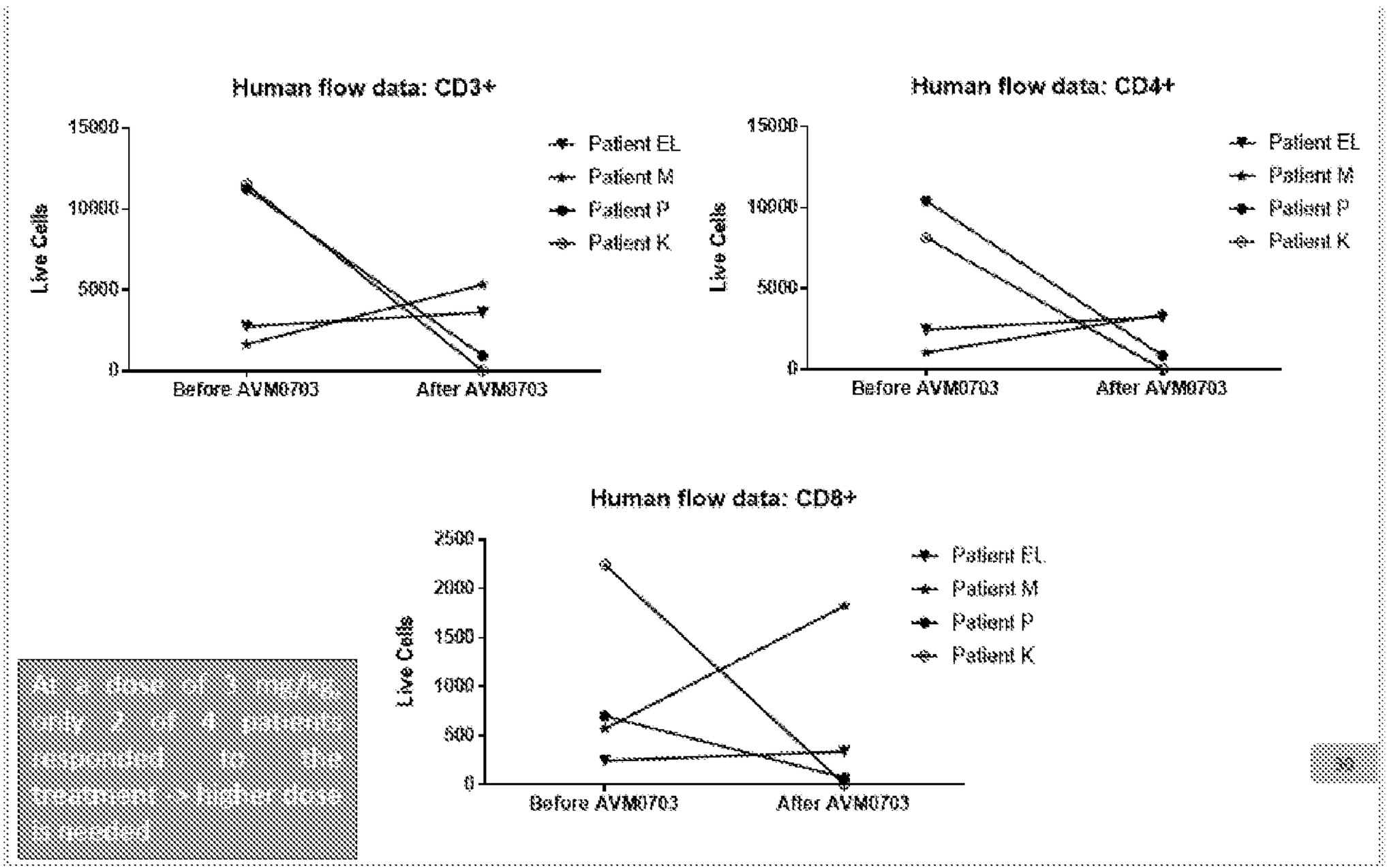
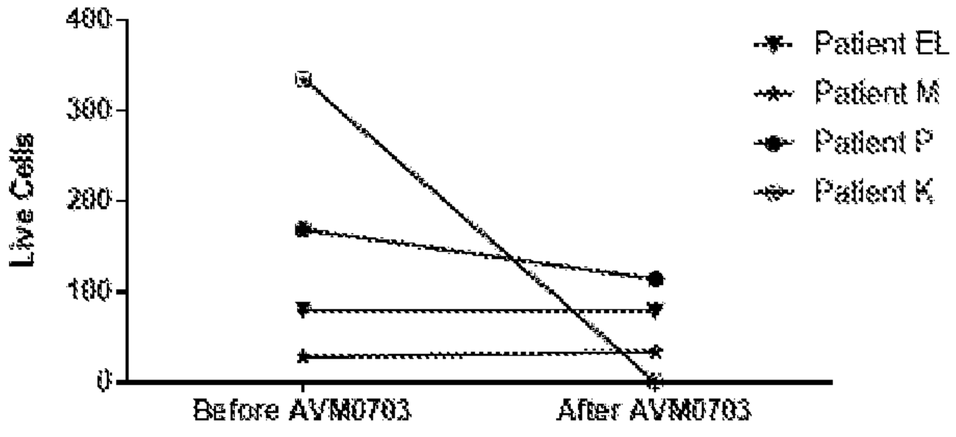
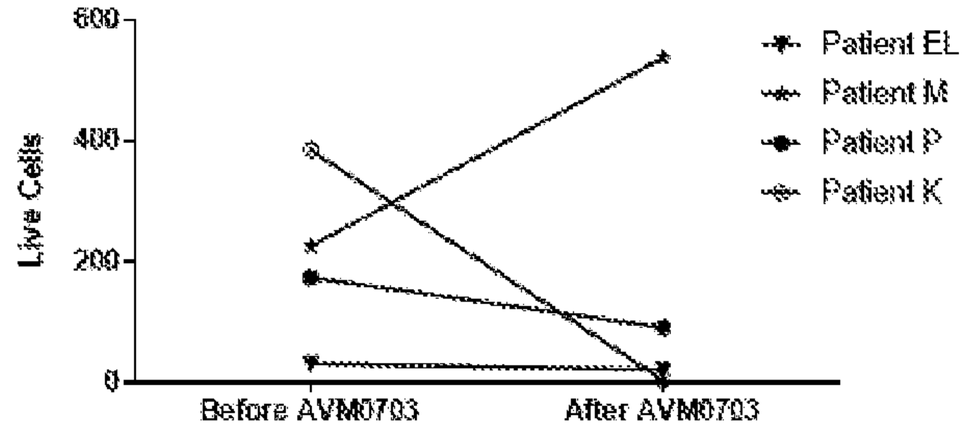

Human flow data: CD3+
Live Cells
15000
10000
5000
0
Before AVM0703
After AVM0703
Patient EL
Patient M
Patient P
Patient K
Human flow data: CD4+
Live Cells
15000
10000
5000
0
Before AVM0703
After AVM0703
Patient EL
Patient M
Patient P
Patient K
Human flow data: CD8+
Live Cells
2500
2000
1500
1000
500
0
Before AVM0703
After AVM0703
Patient EL
Patient M
Patient P
Patient K
At a dose of 3 mg/kg only 2 of 4 patients responded to the treatment - higher dose is needed

**Figure 13**

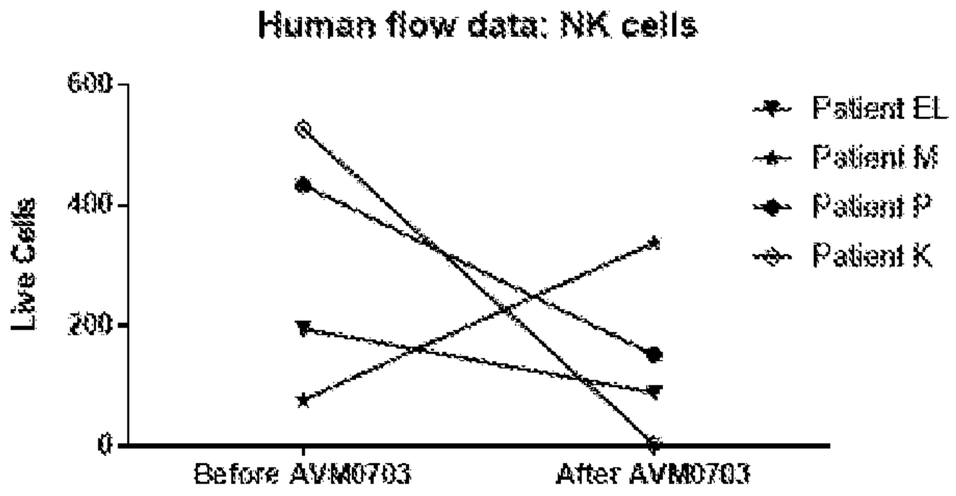


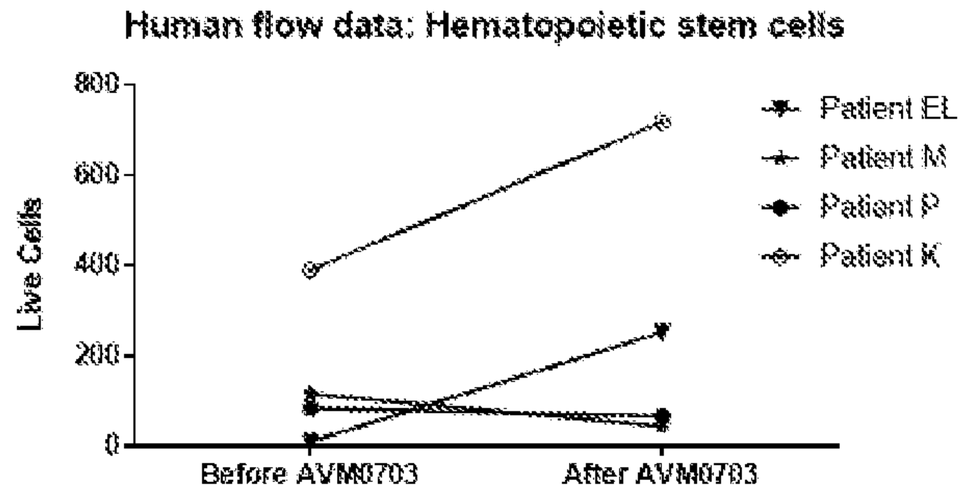




At a dose of 3 mg/kg, only 1 of 4 patients responded to the treatment => higher dose is needed

At a dose of 3 mg/kg, only 1 of 4 patients responded to the treatment => higher dose is needed

**Figure 14**




At a dose of 3 mg/kg, only 3 of 4 patients responded to the treatment -> higher dose to proceed

At a dose of 3 mg/kg, no adverse effect on HSC is seen

32

**Figure 15**

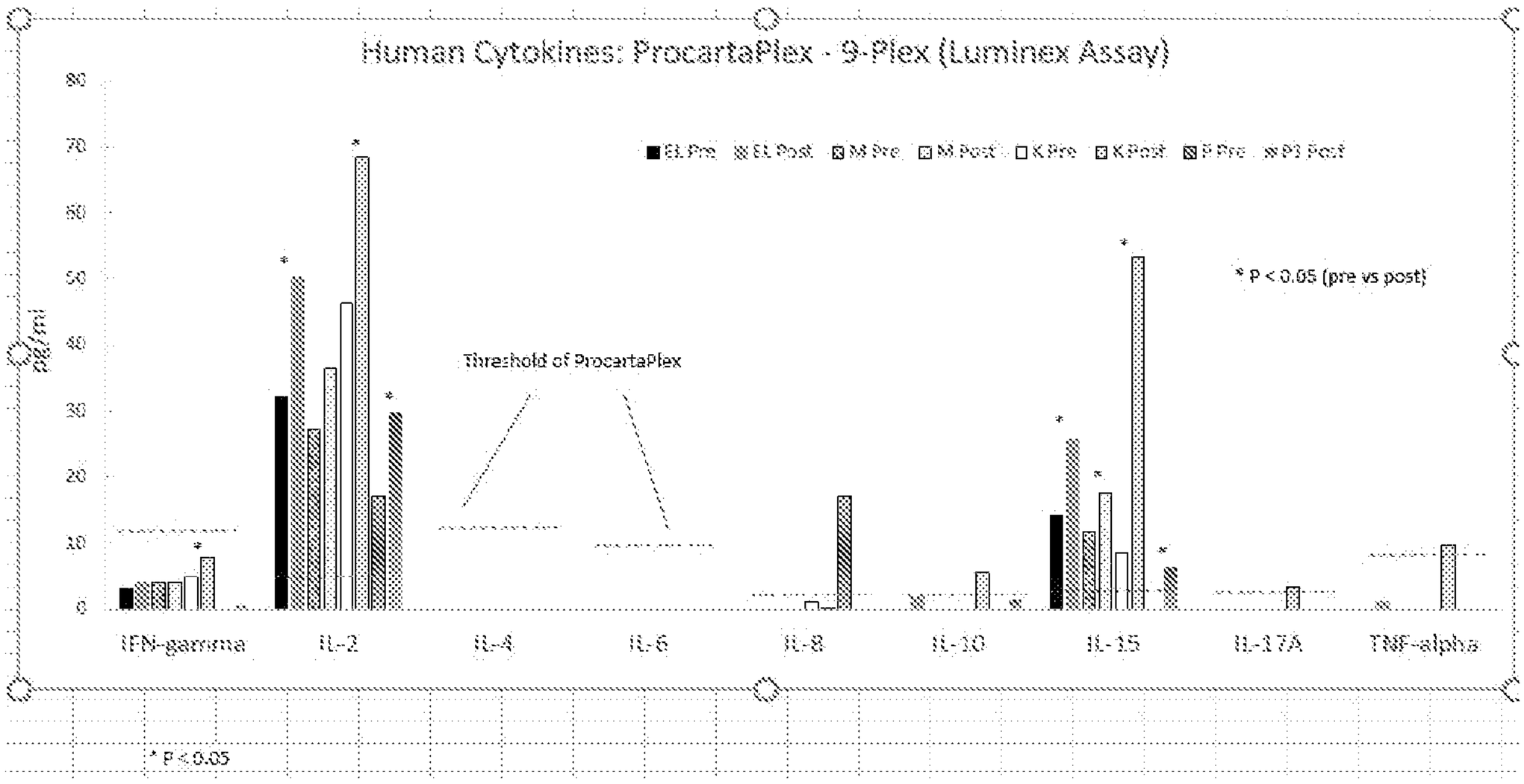

Human Cytokines: ProcartaPlex - 9-Plex (Luminex Assay)
EL Pre
EL Post
M Pre
M Post
K Pre
K Post
P Pre
P3 Post
pg/ml
80
70
60
50
40
30
20
10
0
Threshold of ProcartaPlex
* P < 0.05 (pre vs post)
IFN-gamma
IL-2
IL-4
IL-6
IL-8
IL-10
IL-15
IL-17A
TNF-alpha
* P < 0.05

**Figure 16**

**3 mg/kg oral dexamethasone base increases human Bone Marrow CFU-F per ml 48 hours later compared to 31 historical controls aspirated using the same Marrow Cellutions needle as for Patients M & P.**

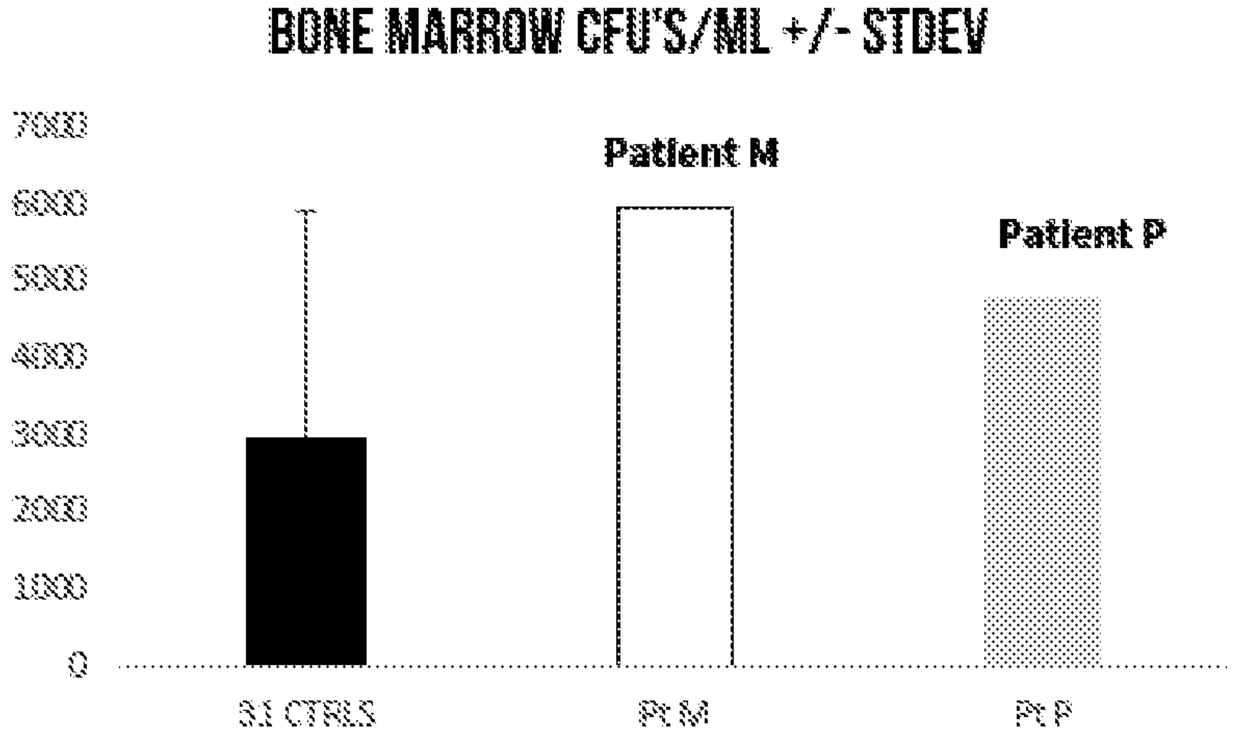


**Figure 17**

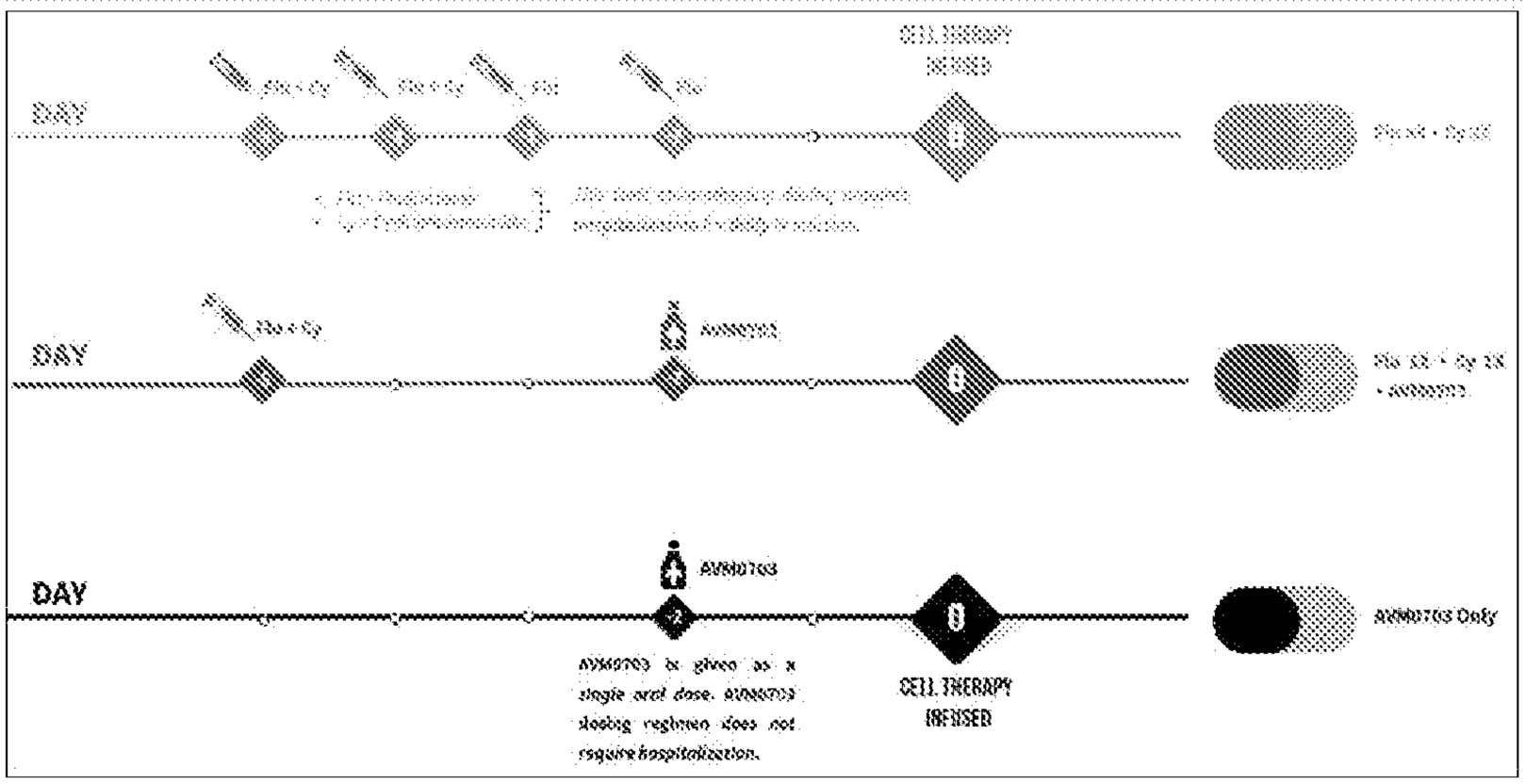

DAY
DAY
AUTOLOGOUS T CELL THERAPY INFUSED
AUTOLOGOUS T CELL THERAPY INFUSED
AUTOLOGOUS T CELL THERAPY INFUSED

**Figure 18**

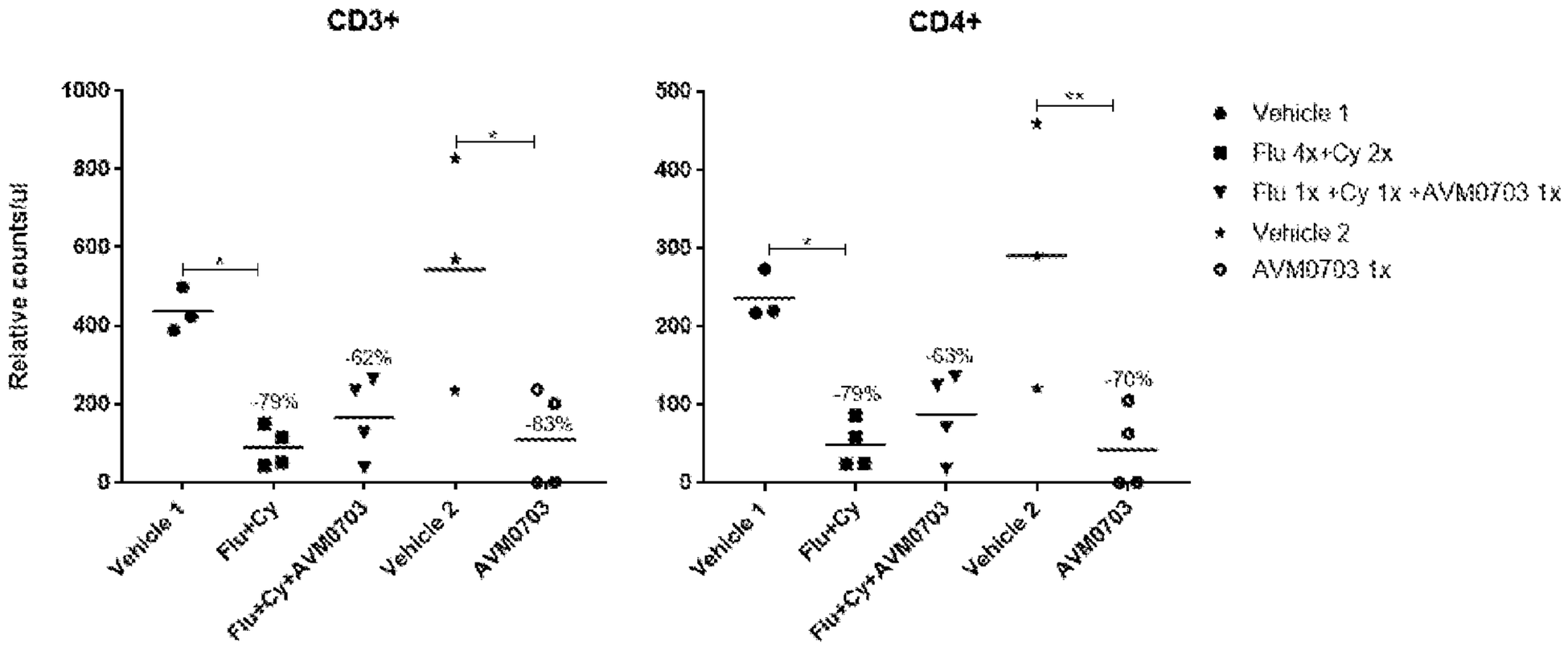

CD3+
CD4+
Relative counts/µl
1000
800
600
400
200
0
500
400
300
200
100
0
-79%
-62%
-83%
-79%
-63%
-70%
Vehicle 1
Flu+Cy
Flu+Cy+AVM0703
Vehicle 2
AVM0703
Vehicle 1
Flu 4x+Cy 2x
Flu 1x +Cy 1x +AVM0703 1x
Vehicle 2
AVM0703 1x

**Figure 19**

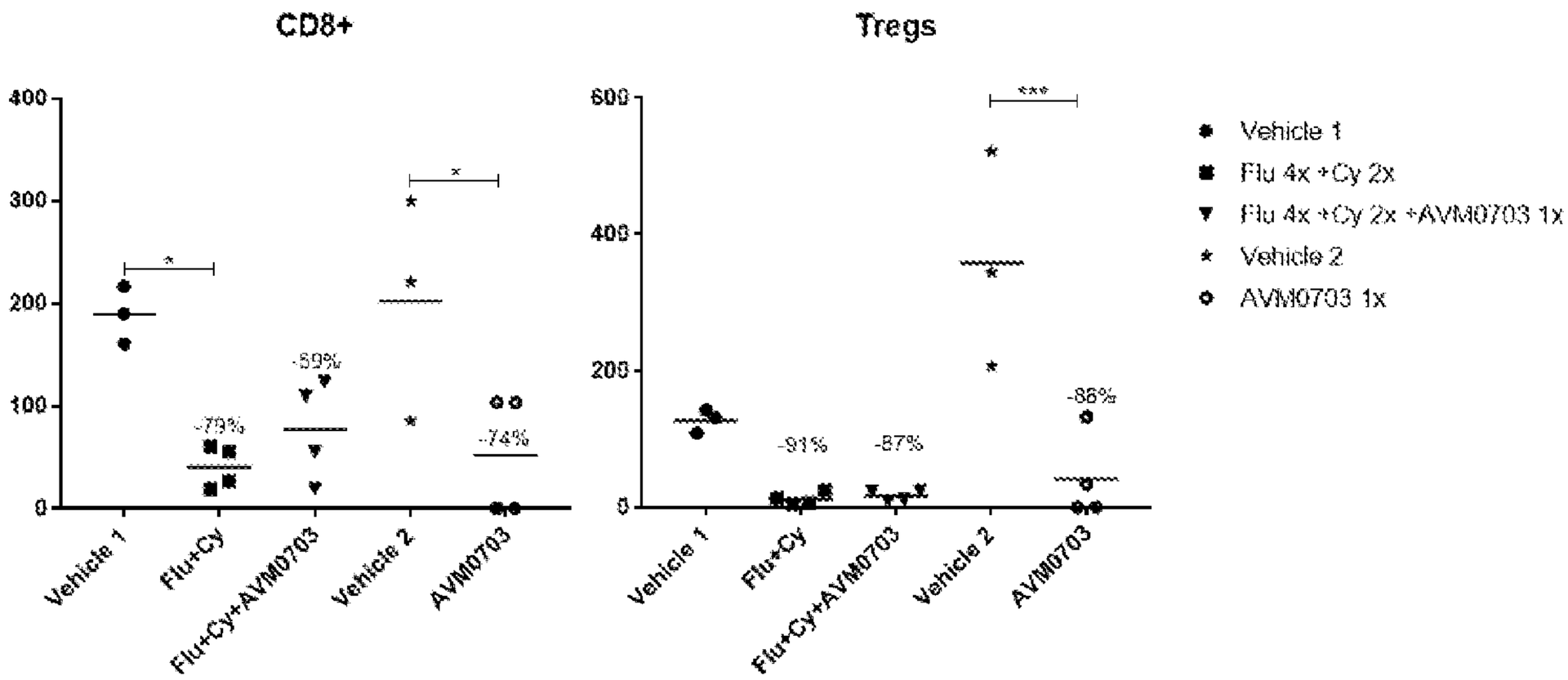

CD8+
Tregs
400
300
200
100
0
600
400
200
0
*
*
*
***
-79%
-59%
-74%
-91%
-87%
-86%
Vehicle 1
Flu+Cy
Flu+Cy+AVM0703
Vehicle 2
AVM0703
Vehicle 1
Flu 4x +Cy 2x
Flu 4x +Cy 2x +AVM0703 1x
Vehicle 2
AVM0703 1x

**Figure 20**

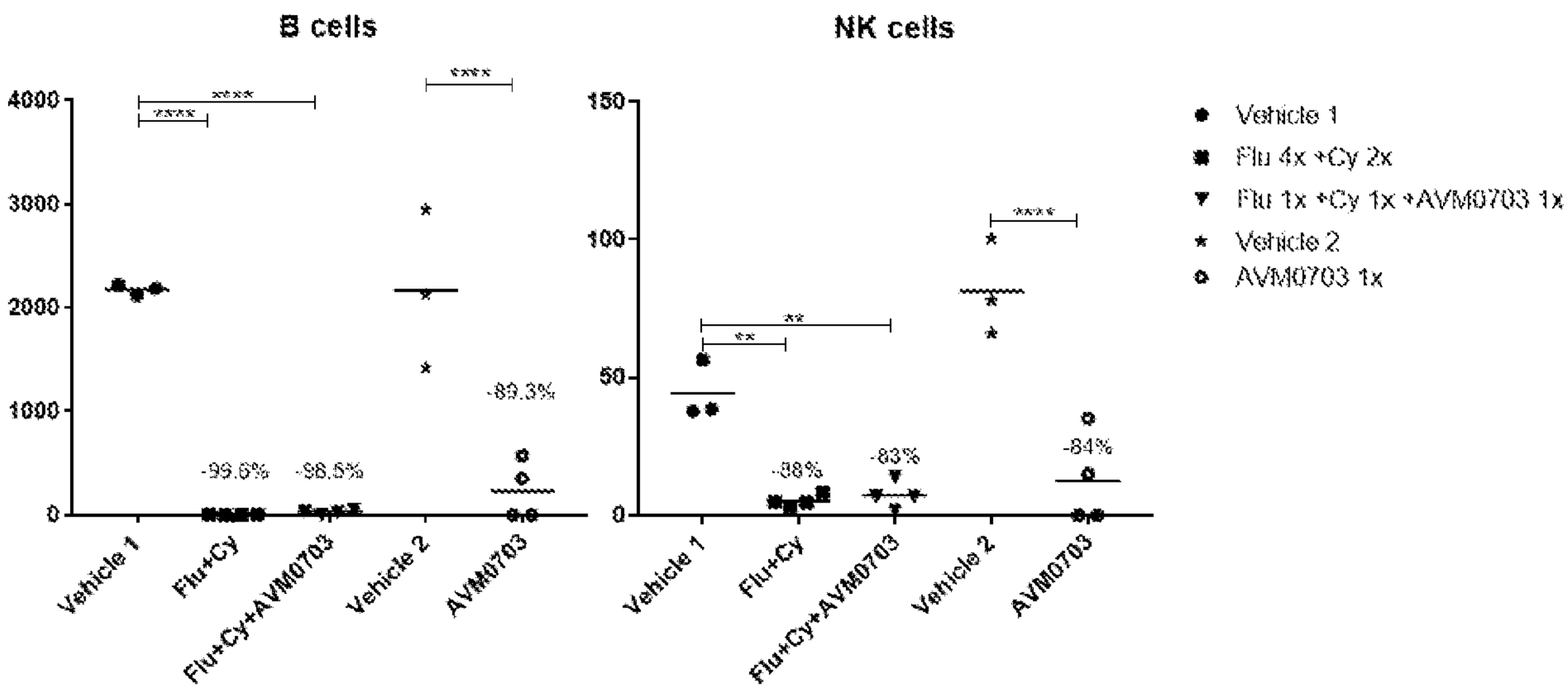

B cells
NK cells
Vehicle 1
Flu 4x +Cy 2x
Flu 1x +Cy 1x +AVM0703 1x
Vehicle 2
AVM0703 1x
4000
3000
2000
1000
0
150
100
50
0
****
**
-99.6%
-98.5%
-89.3%
-88%
-83%
-84%
Vehicle 1
Flu+Cy
Flu+Cy+AVM0703
Vehicle 2
AVM0703

**Figure 21**

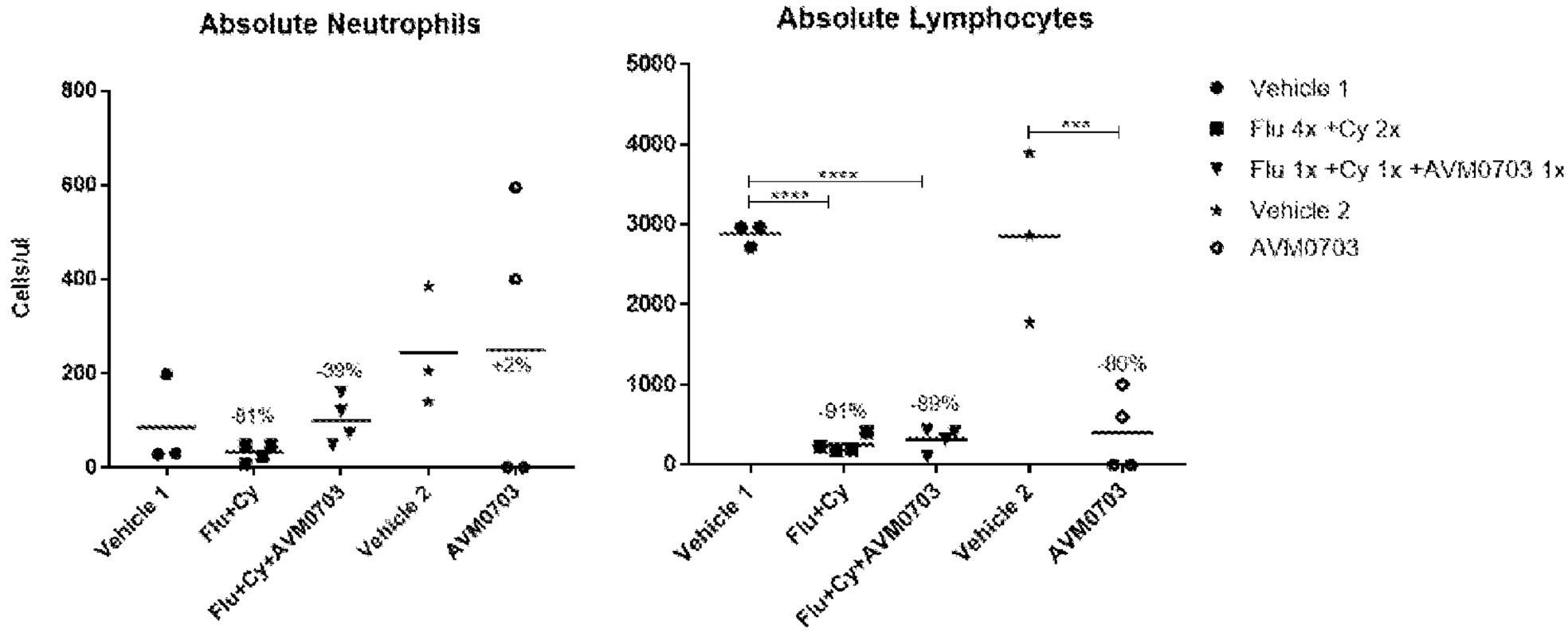

Absolute Neutrophils
Cells/ul
800
600
400
200
0
-91%
-39%
+2%
Vehicle 1
Flu+Cy
Flu+Cy+AVM0703
Vehicle 2
AVM0703
Absolute Lymphocytes
5000
4000
3000
2000
1000
0
****
****
***
-91%
-89%
-86%
Vehicle 1
Flu+Cy
Flu+Cy+AVM0703
Vehicle 2
AVM0703
Vehicle 1
Flu 4x +Cy 2x
Flu 1x +Cy 1x +AVM0703 1x
Vehicle 2
AVM0703

**Figure 22**

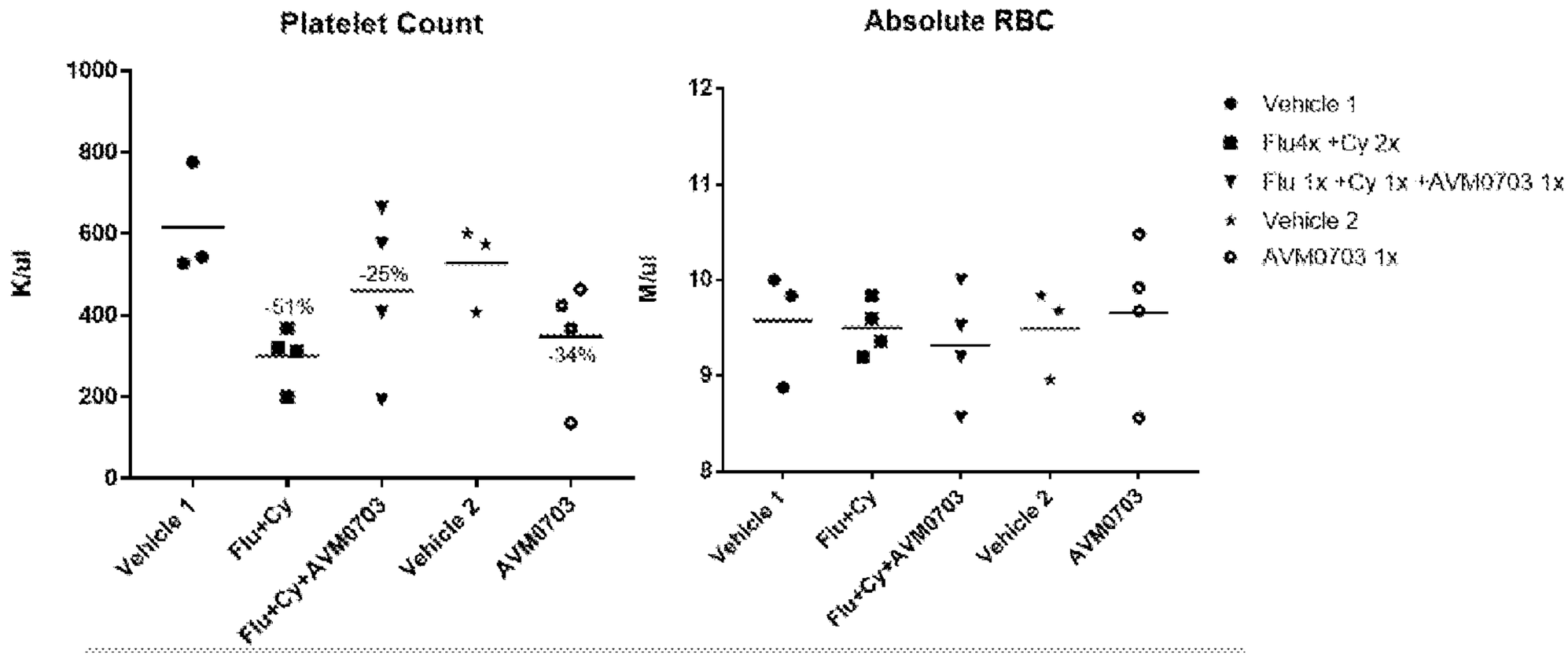
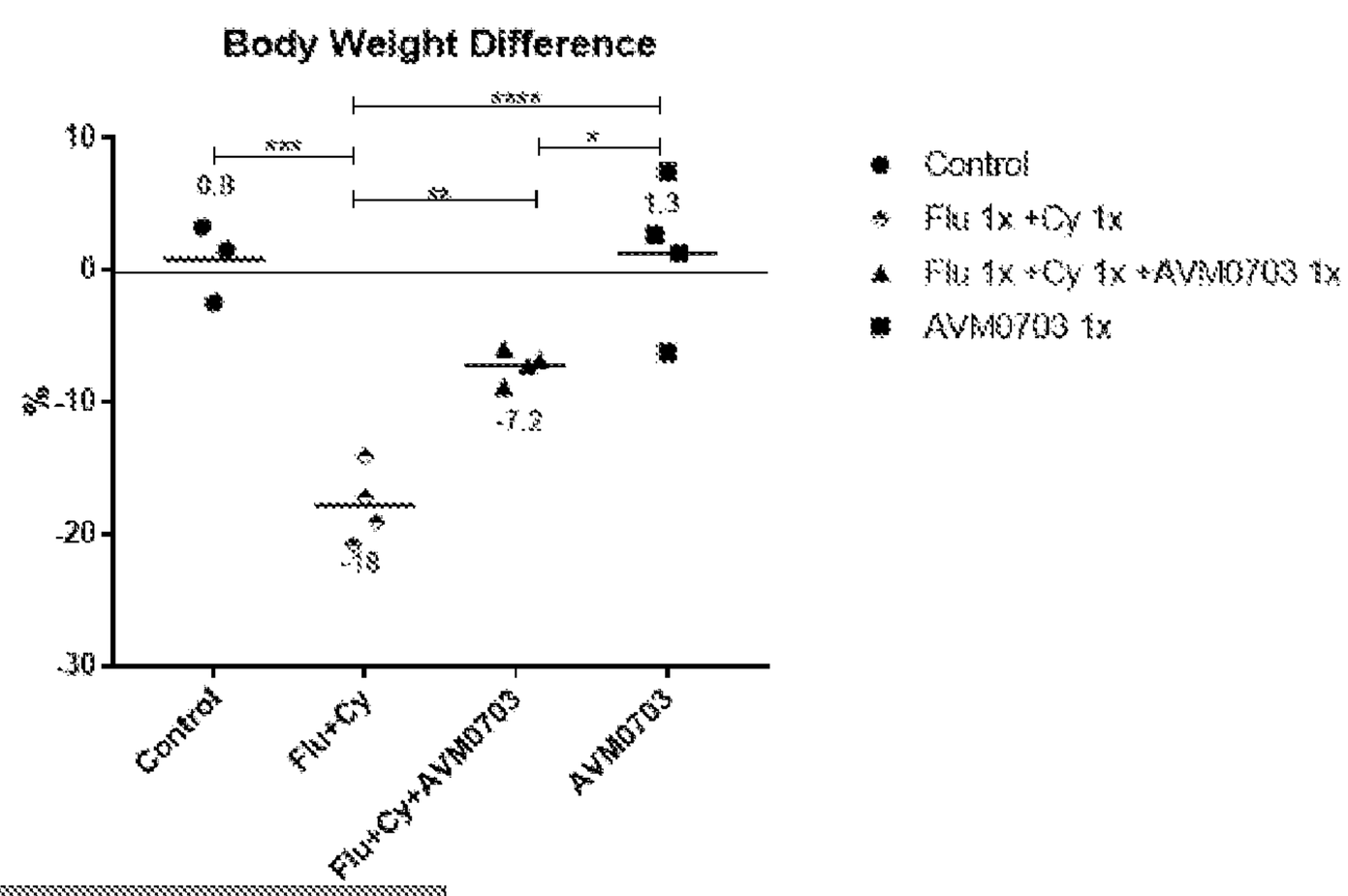

Platelet Count
K/ul
1000
800
600
400
200
0
-51%
-25%
-34%
Vehicle 1
Flu+Cy
Flu+Cy+AVM0703
Vehicle 2
AVM0703
Absolute RBC
M/ul
12
11
10
9
8
Vehicle 1
Flu+Cy
Flu+Cy+AVM0703
Vehicle 2
AVM0703
Vehicle 1
Flu4x +Cy 2x
Flu 1x +Cy 1x +AVM0703 1x
Vehicle 2
AVM0703 1x

**Figure 23**




AVM0703 groups is not associated with body weight loss unlike chemo groups.
Preconditioning with AVM0703 will provide a similar lymphodepletion effect as chemo but have no associated toxicity.