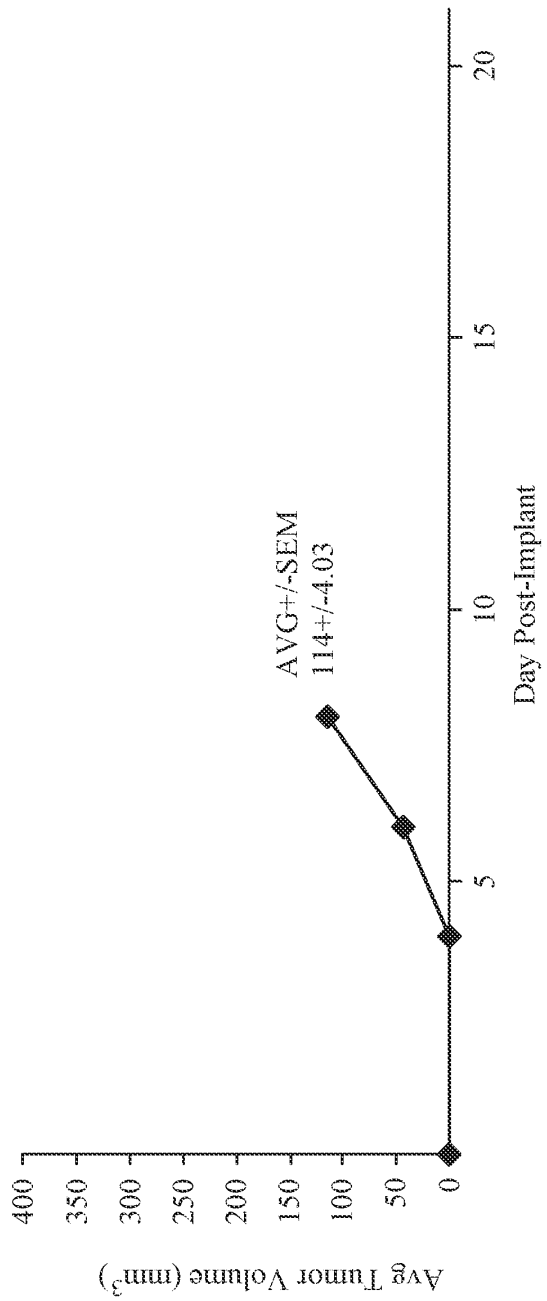
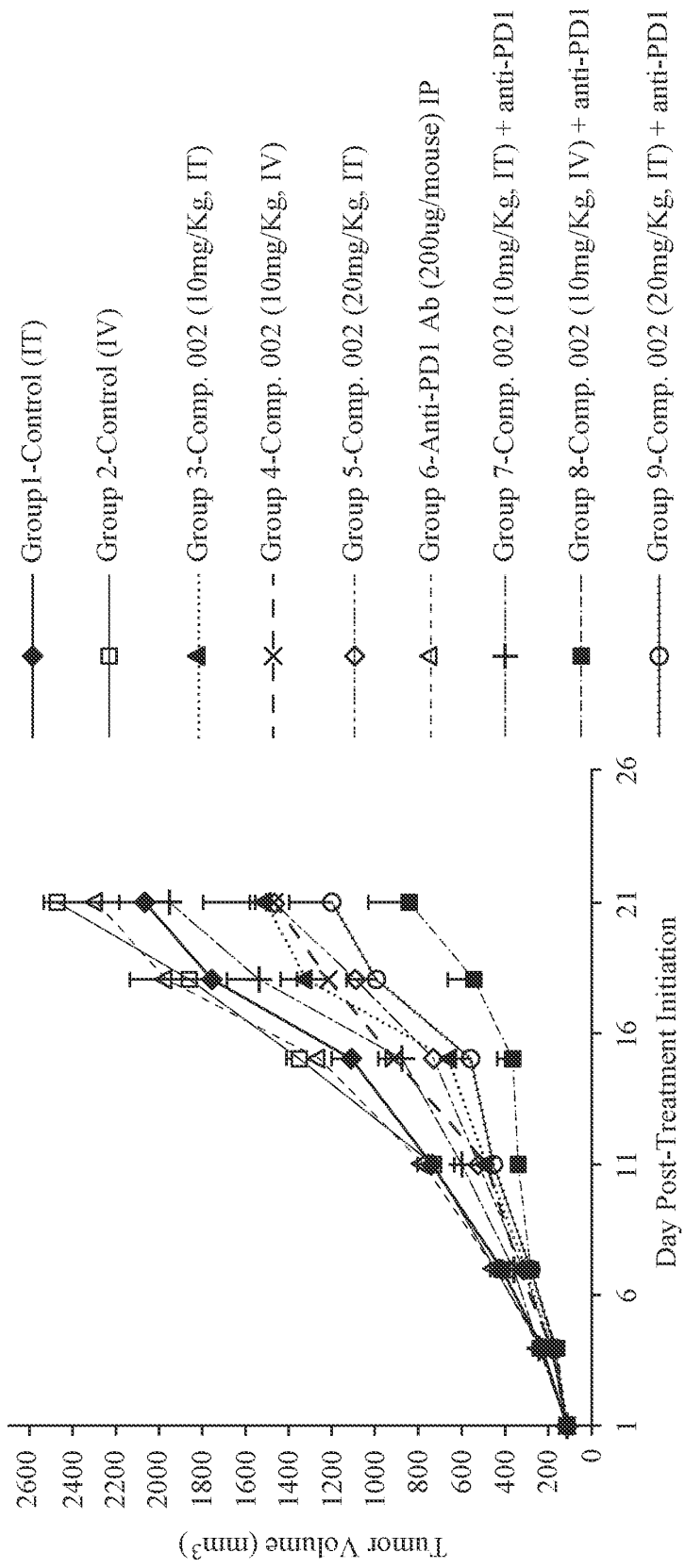

Avg Tumor Volume (mm3)
400
350
300
250
200
150
100
50
0
AVG+/-SEM
114+/-4.03
5
10
15
20
Day Post-Implant

FIG. 1



*Group 5:Comp. 002 15 mg/Kg IV (Day 1) >20 mg/Kg IT (on Day 4)

FIG. 2

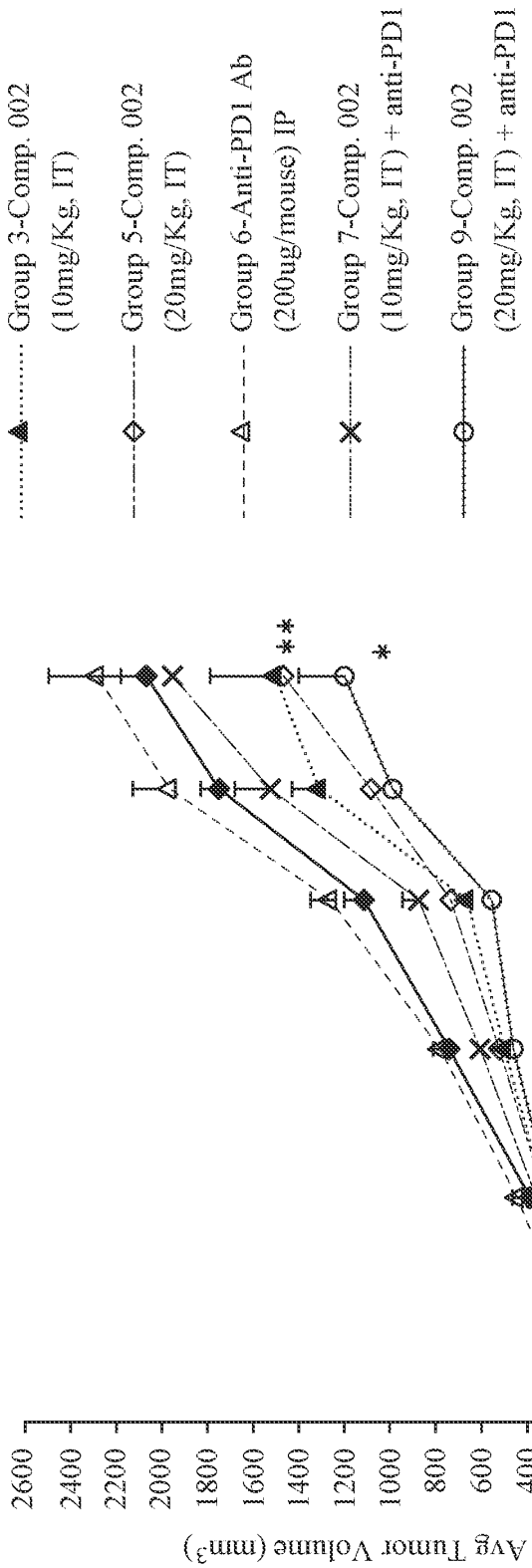

Group1-Control (IT)
Group 3-Comp. 002 (10mg/Kg, IT)
Group 5-Comp. 002 (20mg/Kg, IT)
Group 6-Anti-PD1 Ab (200ug/mouse) IP
Group 7-Comp. 002 (10mg/Kg, IT) + anti-PD1
Group 9-Comp. 002 (20mg/Kg, IT) + anti-PD1
* p<0.01 vs. Control GR1
** p<0.05 vs. GR1 and GR6
Avg Tumor Volume (mm3)
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
1
5
9
13
17
21
Day Post-Treatment Initiation
Group 5:Comp. 002 15 mg/Kg IV (Day 1) >20 mg/Kg IT (on Day 4)

FIG. 3A

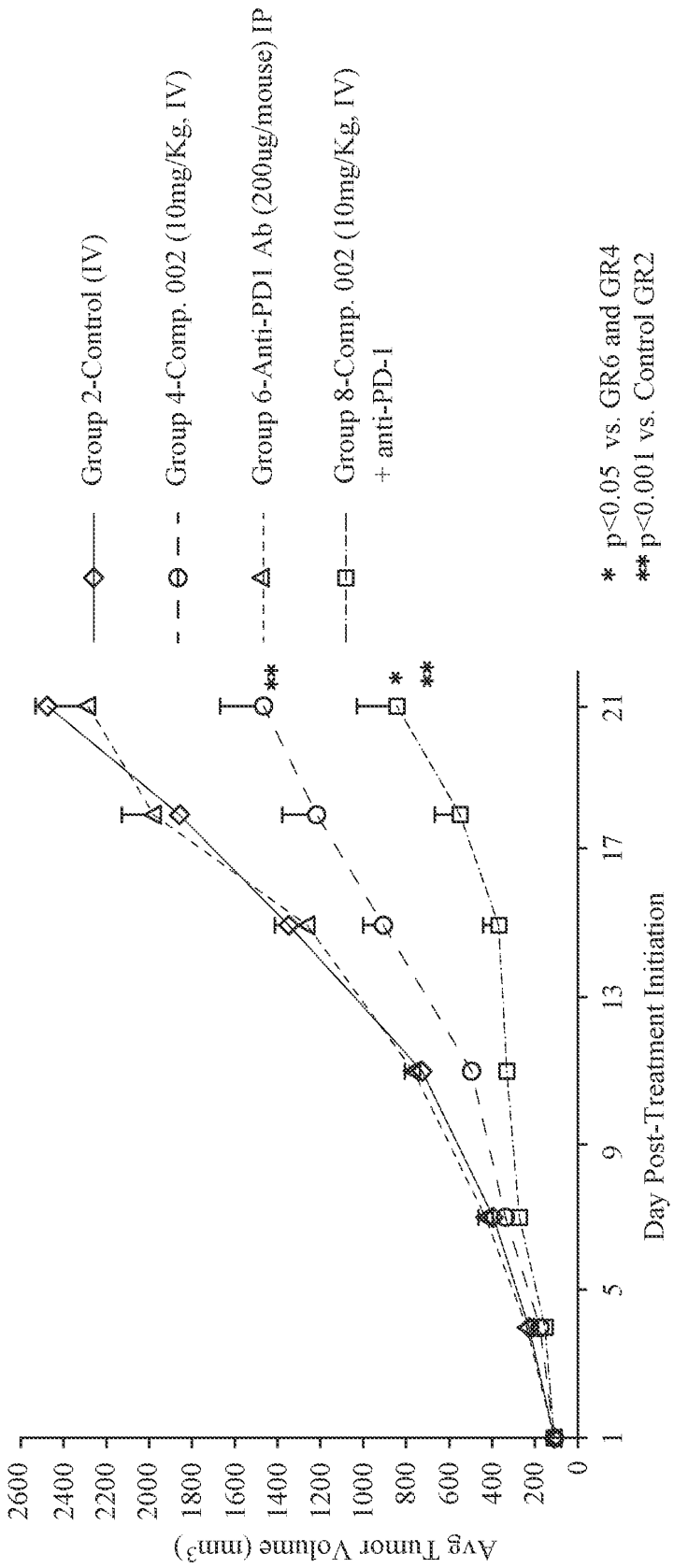

Group 2-Control (IV)
Group 4-Comp. 002 (10mg/Kg, IV)
Group 6-Anti-PD1 Ab (200ug/mouse) IP
Group 8-Comp. 002 (10mg/Kg, IV)
+ anti-PD-1
* p<0.05 vs. GR6 and GR4
** p<0.001 vs. Control GR2
Avg Tumor Volume (mm3)
Day Post-Treatment Initiation
0
200
400
600
800
1000
1200
1400
1600
1800
2000
2200
2400
2600
1
5
9
13
17
21

FIG. 3B

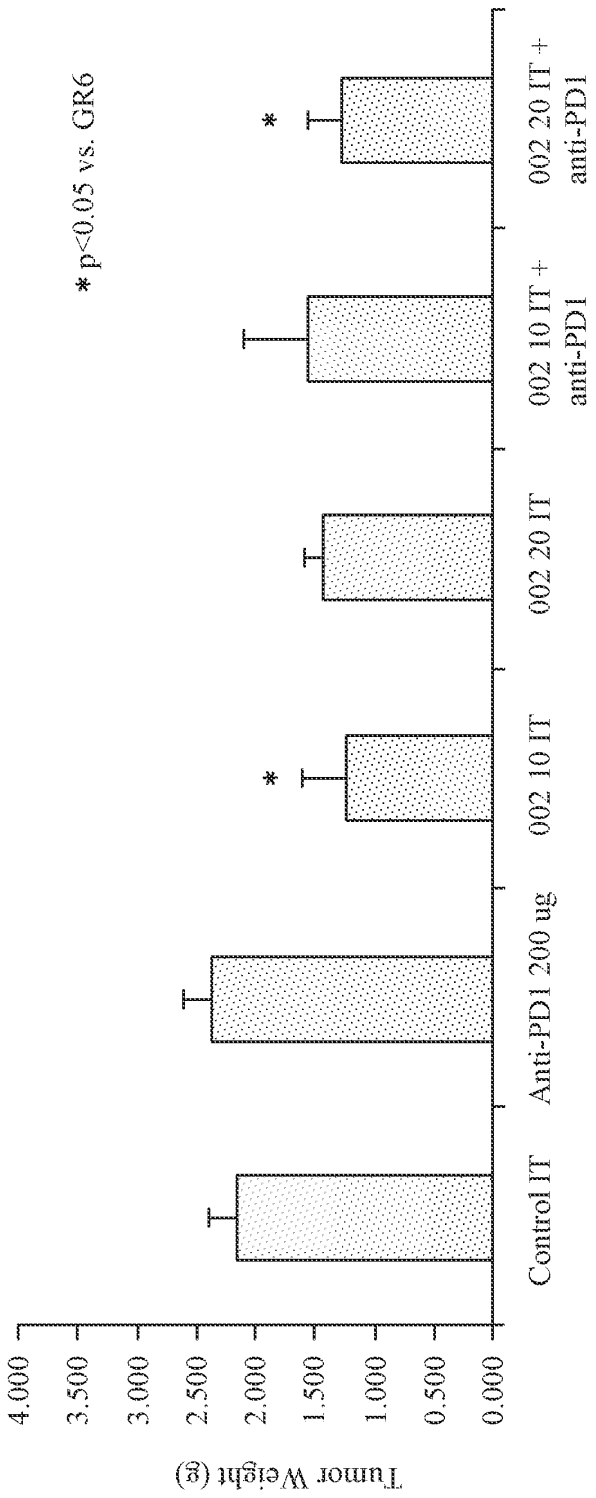

* p<0.05 vs. GR6
Tumor Weight (g)
4.000
3.500
3.000
2.500
2.000
1.500
1.000
0.500
0.000
*
*
Control IT
Anti-PD1 200 ug
002 10 IT
002 20 IT
002 10 IT + anti-PD1
002 20 IT + anti-PD1

FIG. 4A

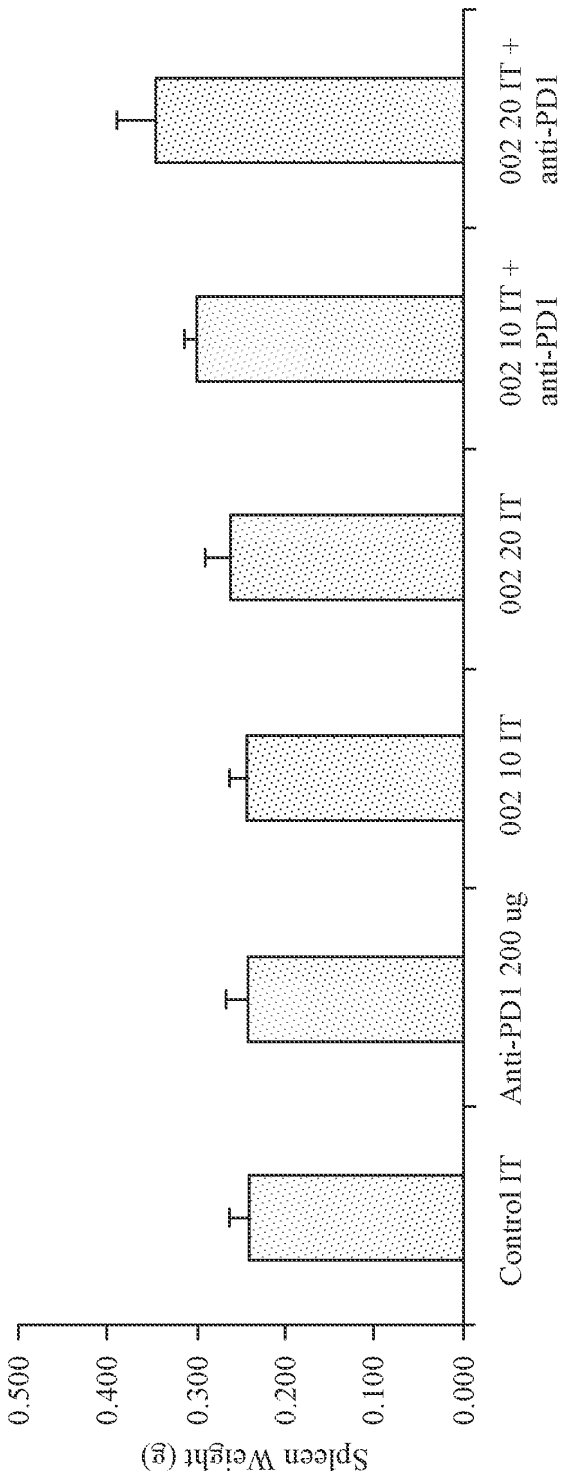

Spleen Weight (g)
0.500
0.400
0.300
0.200
0.100
0.000
Control IT
Anti-PD1 200 ug
002 10 IT
002 20 IT
002 10 IT + anti-PD1
002 20 IT + anti-PD1

FIG. 4B

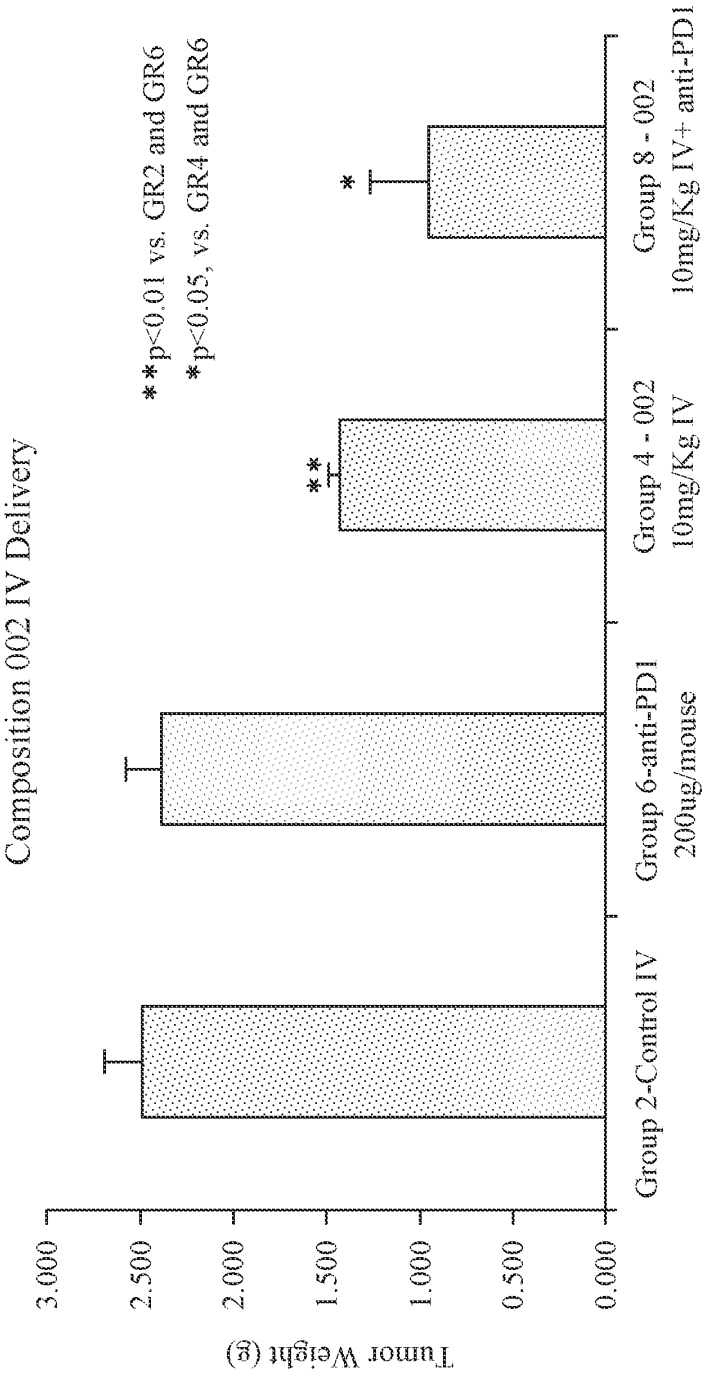

Composition 002 IV Delivery
**p<0.01 vs. GR2 and GR6
*p<0.05, vs. GR4 and GR6
Tumor Weight (g)
3.000
2.500
2.000
1.500
1.000
0.500
0.000
**
*
Group 2-Control IV
Group 6-anti-PD1
200ug/mouse
Group 4 - 002
10mg/Kg IV
Group 8 - 002
10mg/Kg IV+ anti-PD1

FIG. 5A

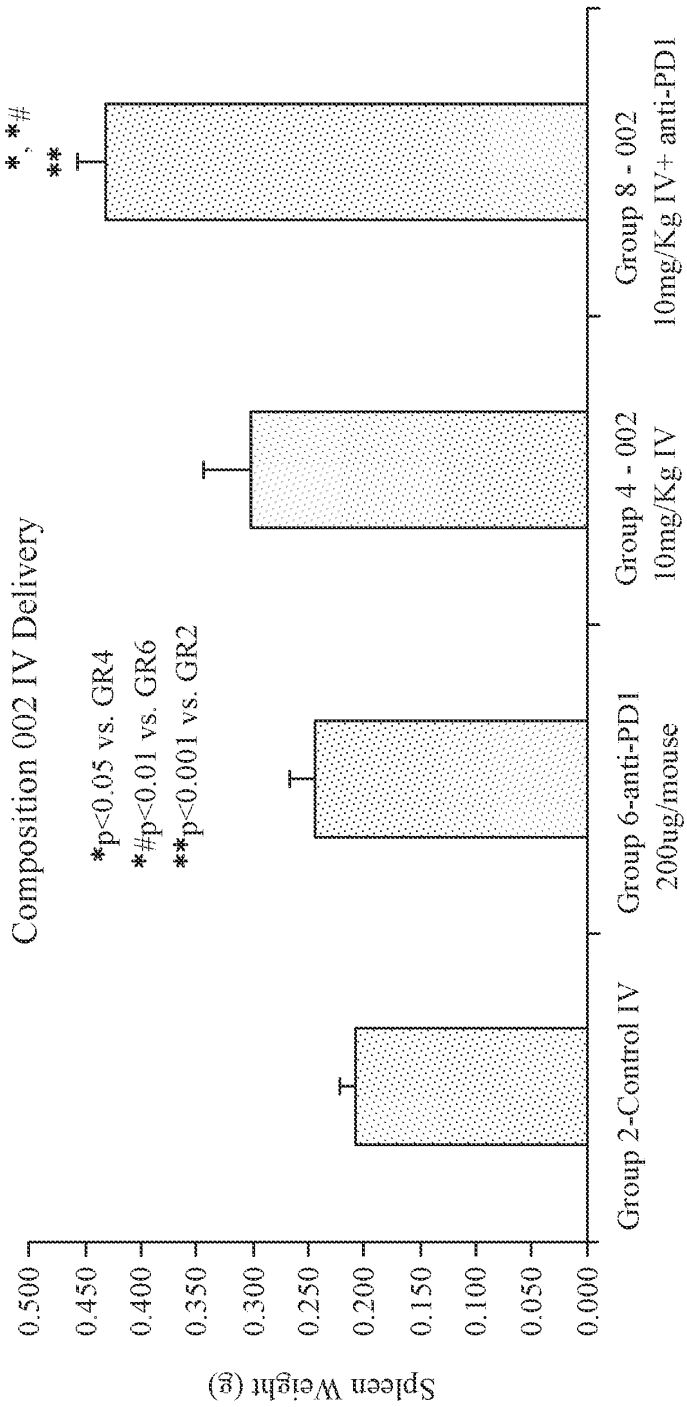

Composition 002 IV Delivery
*p<0.05 vs. GR4
*#p<0.01 vs. GR6
**p<0.001 vs. GR2
*, *#
**
Spleen Weight (g)
0.500
0.450
0.400
0.350
0.300
0.250
0.200
0.150
0.100
0.050
0.000
Group 2-Control IV
Group 6-anti-PD1
200ug/mouse
Group 4 - 002
10mg/Kg IV
Group 8 - 002
10mg/Kg IV+ anti-PD1

FIG. 5B

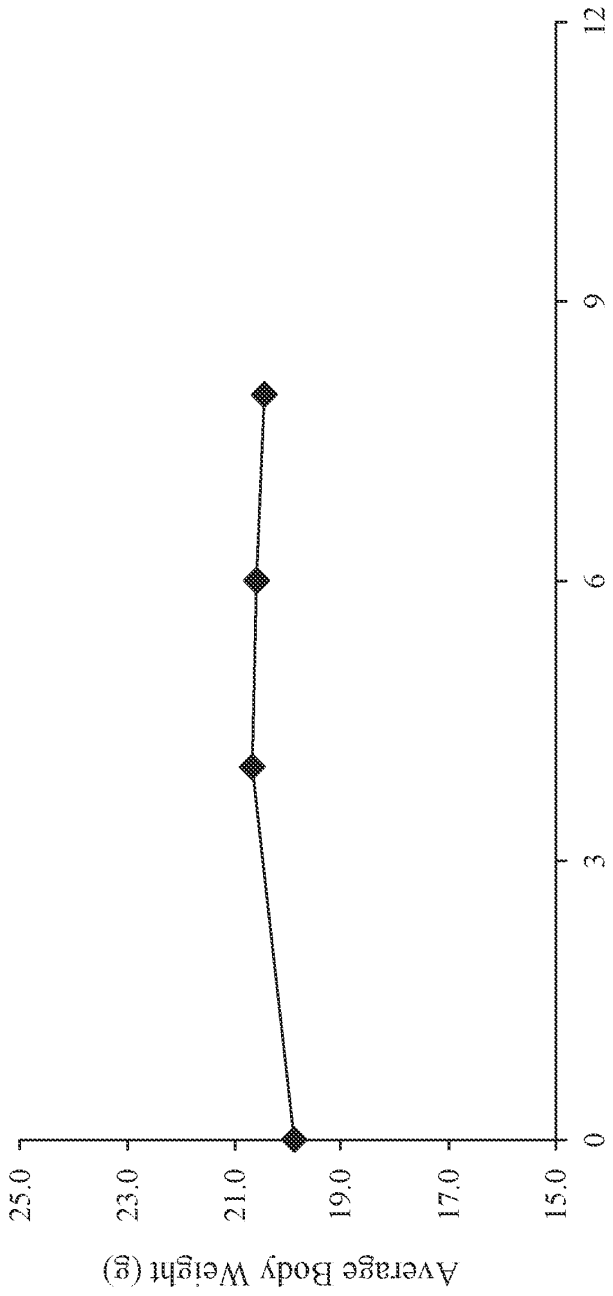

Average Body Weight (g)
25.0
23.0
21.0
19.0
17.0
15.0
0
3
6
9
12
Days Post-Implant

FIG. 6A

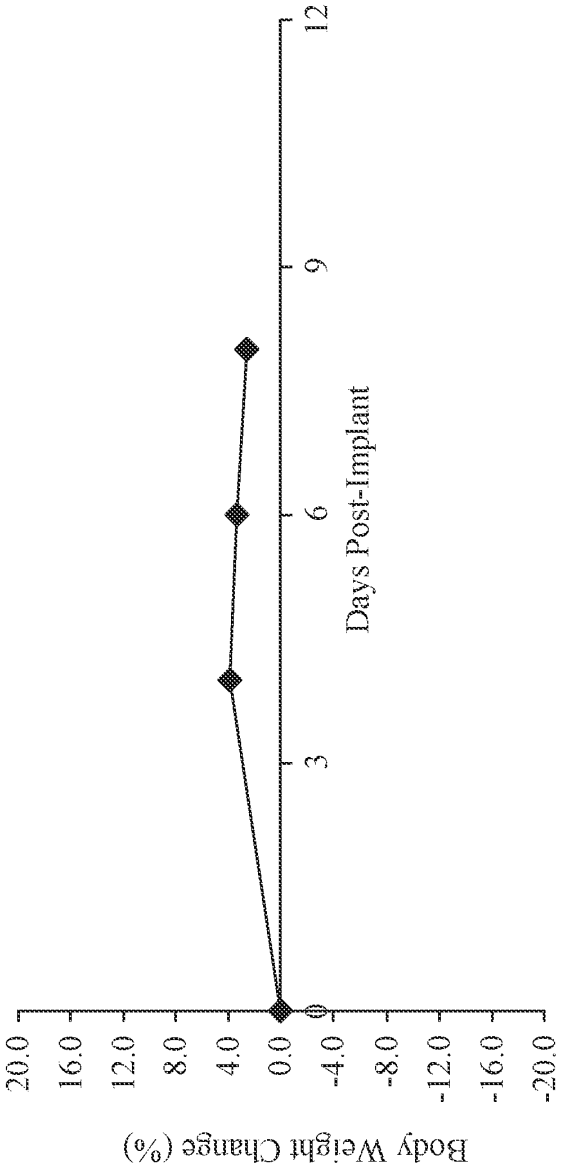

Body Weight Change (%)
20.0
16.0
12.0
8.0
4.0
0.0
-4.0
-8.0
-12.0
-16.0
-20.0
0
3
6
9
12
Days Post-Implant

FIG. 6B

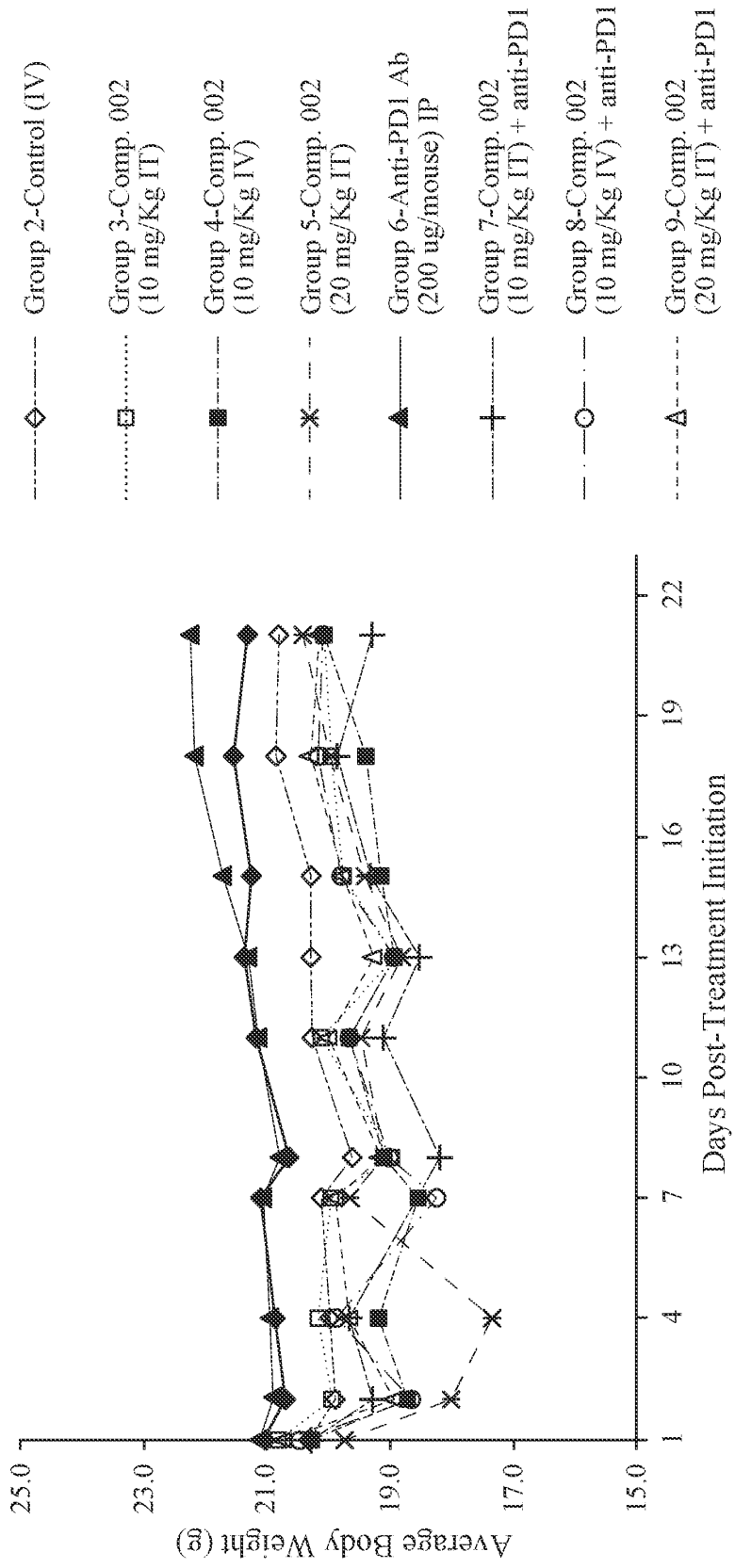

Group 1-Control (IT)
Group 2-Control (IV)
Group 3-Comp. 002 (10 mg/Kg IT)
Group 4-Comp. 002 (10 mg/Kg IV)
Group 5-Comp. 002 (20 mg/Kg IT)
Group 6-Anti-PD1 Ab (200 ug/mouse) IP
Group 7-Comp. 002 (10 mg/Kg IT) + anti-PD1
Group 8-Comp. 002 (10 mg/Kg IV) + anti-PD1
Group 9-Comp. 002 (20 mg/Kg IT) + anti-PD1
Average Body Weight (g)
25.0
23.0
21.0
19.0
17.0
15.0
1
4
7
10
13
16
19
22
Days Post-Treatment Initiation

FIG. 7A

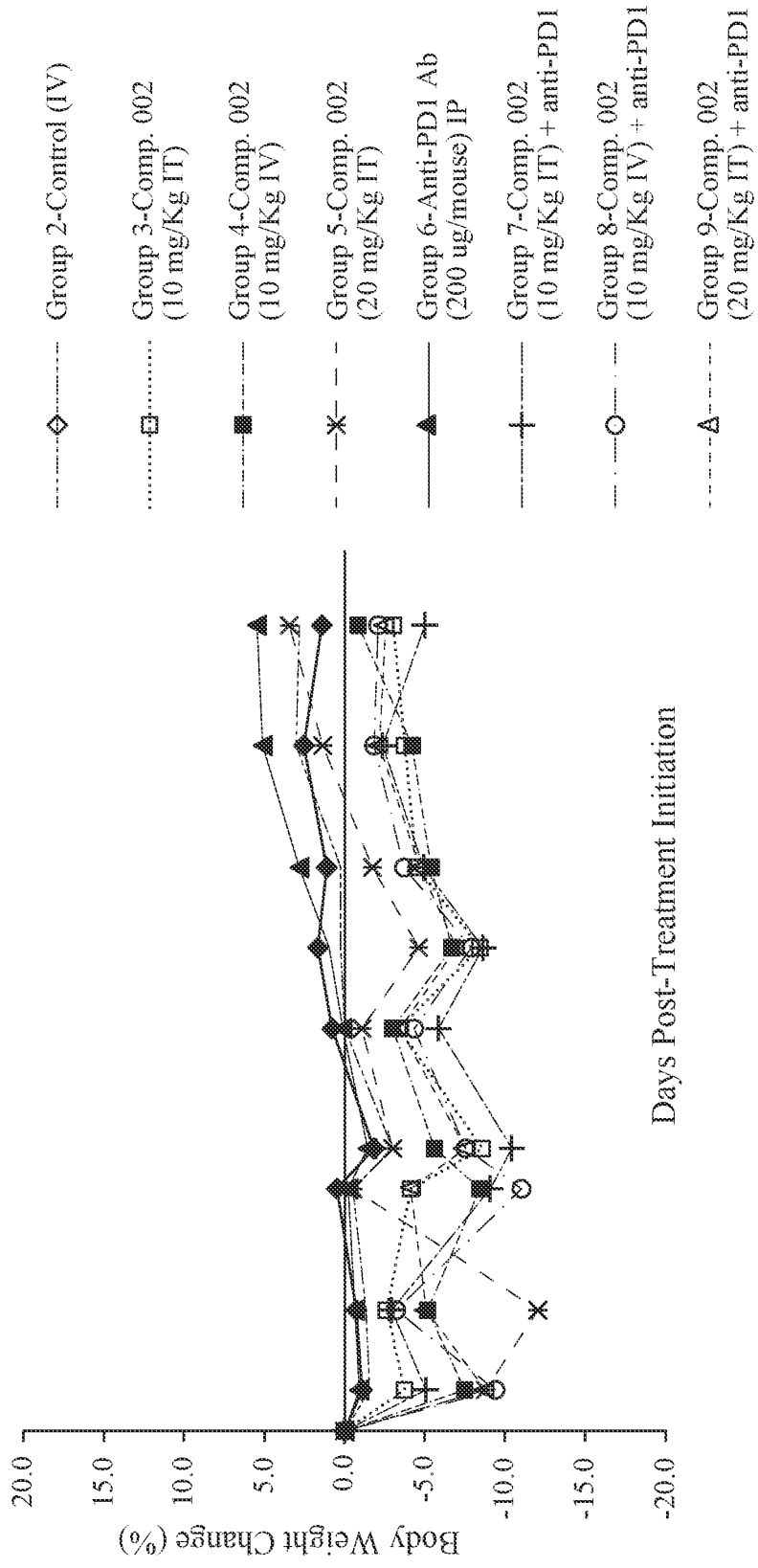

Group 1-Control (IT)
Group 2-Control (IV)
Group 3-Comp. 002 (10 mg/Kg IT)
Group 4-Comp. 002 (10 mg/Kg IV)
Group 5-Comp. 002 (20 mg/Kg IT)
Group 6-Anti-PD1 Ab (200 ug/mouse) IP
Group 7-Comp. 002 (10 mg/Kg IT) + anti-PD1
Group 8-Comp. 002 (10 mg/Kg IV) + anti-PD1
Group 9-Comp. 002 (20 mg/Kg IT) + anti-PD1
Body Weight Change (%)
20.0
15.0
10.0
5.0
0.0
-5.0
-10.0
-15.0
-20.0
Days Post-Treatment Initiation

FIG. 7B

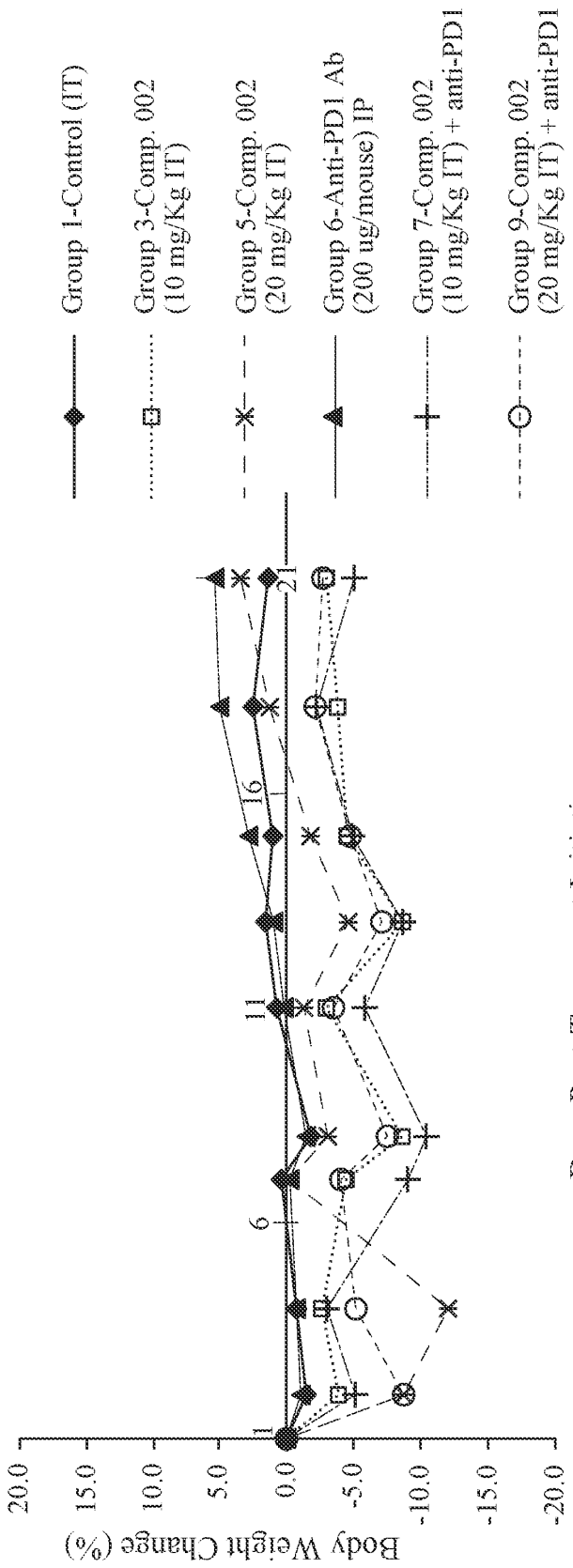

Group 1-Control (IT)
Group 3-Comp. 002 (10 mg/Kg IT)
Group 5-Comp. 002 (20 mg/Kg IT)
Group 6-Anti-PD1 Ab (200 ug/mouse) IP
Group 7-Comp. 002 (10 mg/Kg IT) + anti-PD1
Group 9-Comp. 002 (20 mg/Kg IT) + anti-PD1
Body Weight Change (%)
20.0
15.0
10.0
5.0
0.0
-5.0
-10.0
-15.0
-20.0
1
6
11
16
21
Days Post-Treatment Initiation

FIG. 8A

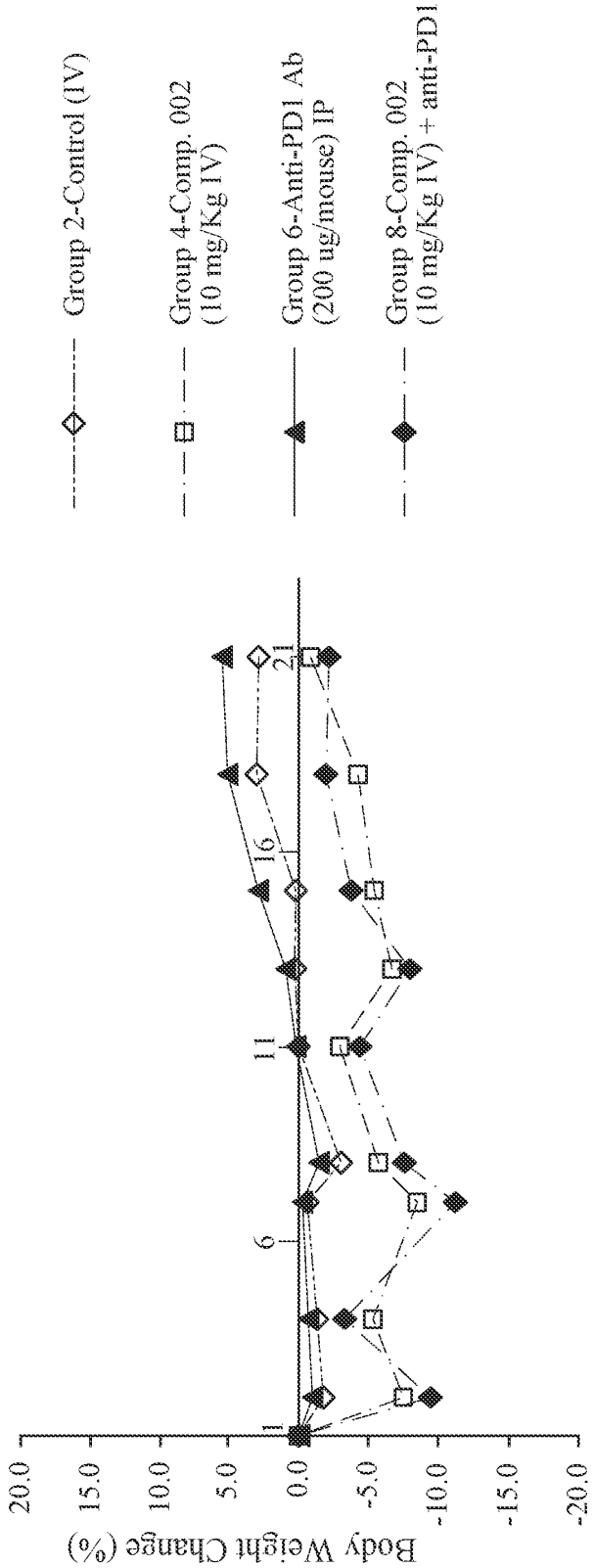

Group 2-Control (IV)
Group 4-Comp. 002 (10 mg/Kg IV)
Group 6-Anti-PD1 Ab (200 ug/mouse) IP
Group 8-Comp. 002 (10 mg/Kg IV) + anti-PD1
Body Weight Change (%)
20.0
15.0
10.0
5.0
0.0
-5.0
-10.0
-15.0
-20.0
1
6
11
16
21

FIG. 8B

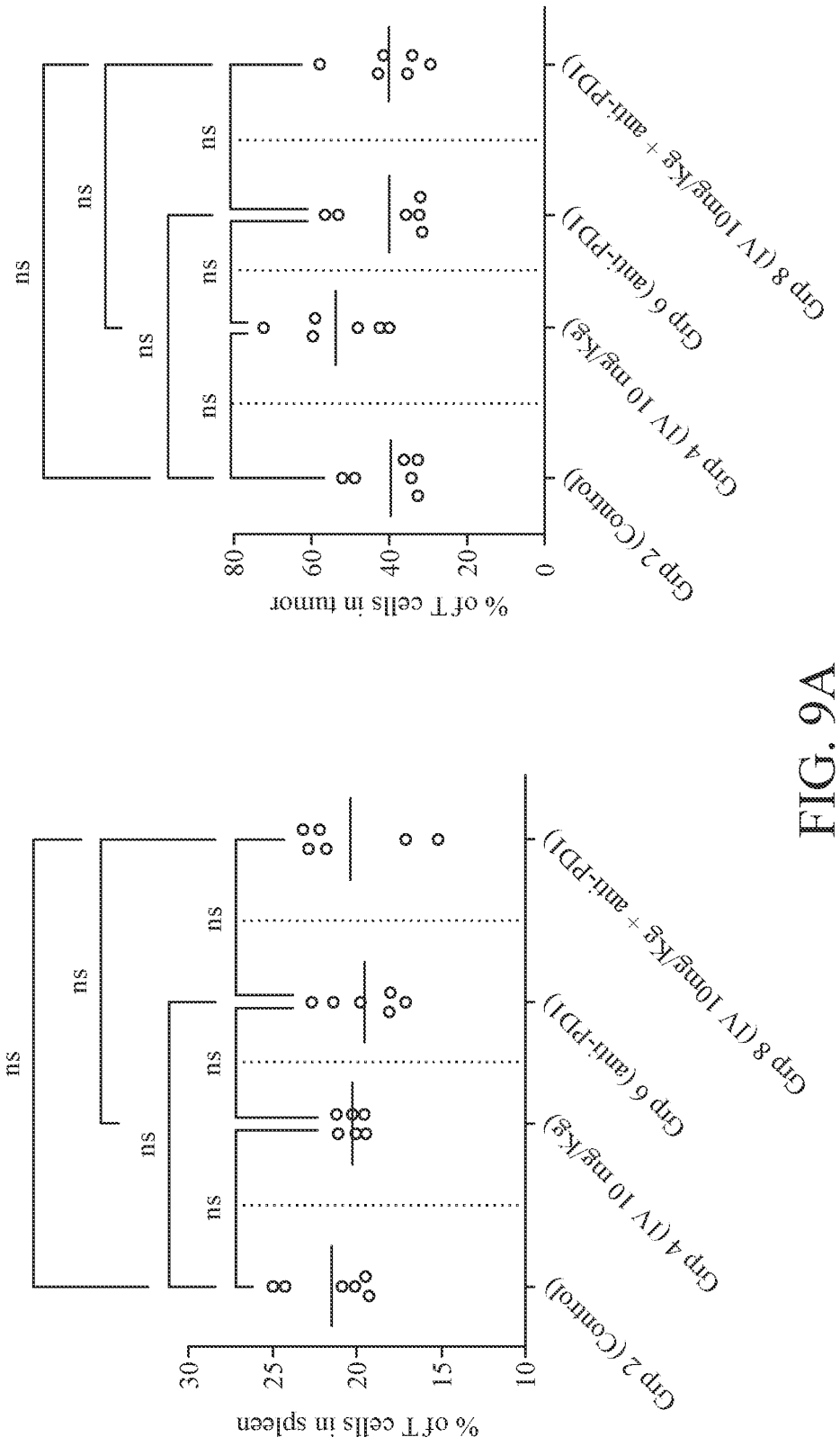

% of T cells in tumor
0
20
40
60
80
Grp 2 (Control)
Grp 4 (IV 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 8 (IV 10mg/Kg + anti-PD1)
ns
ns
ns
ns
% of T cells in spleen
10
15
20
25
30
Grp 2 (Control)
Grp 4 (IV 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 8 (IV 10mg/Kg + anti-PD1)
ns
ns
ns
ns

FIG. 9A

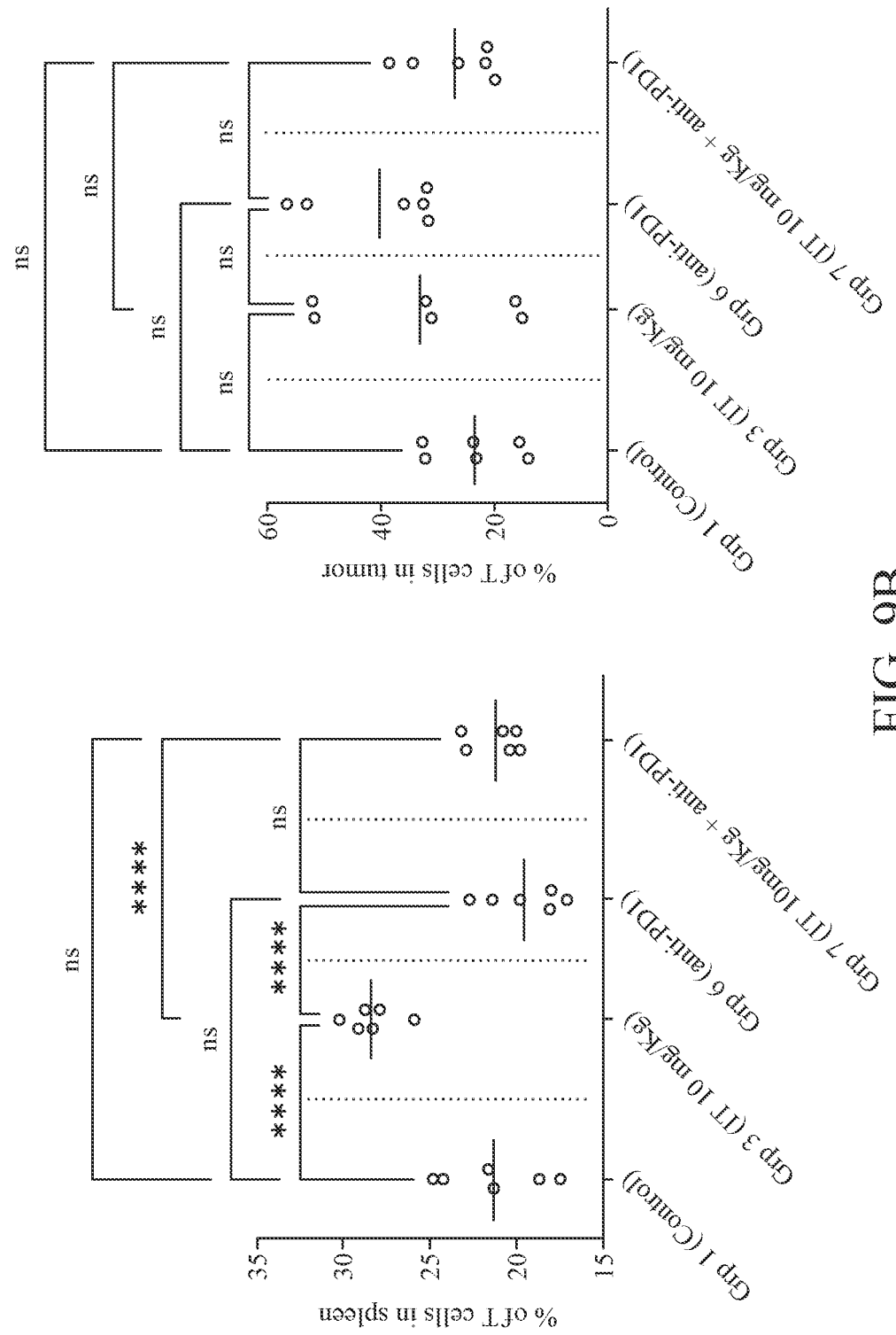

% of T cells in tumor
0
20
40
60
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 7 (IT 10 mg/Kg + anti-PD1)
ns
ns
ns
ns
% of T cells in spleen
15
20
25
30
35
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 7 (IT 10mg/Kg + anti-PD1)
****
****
****
ns
ns

FIG. 9B

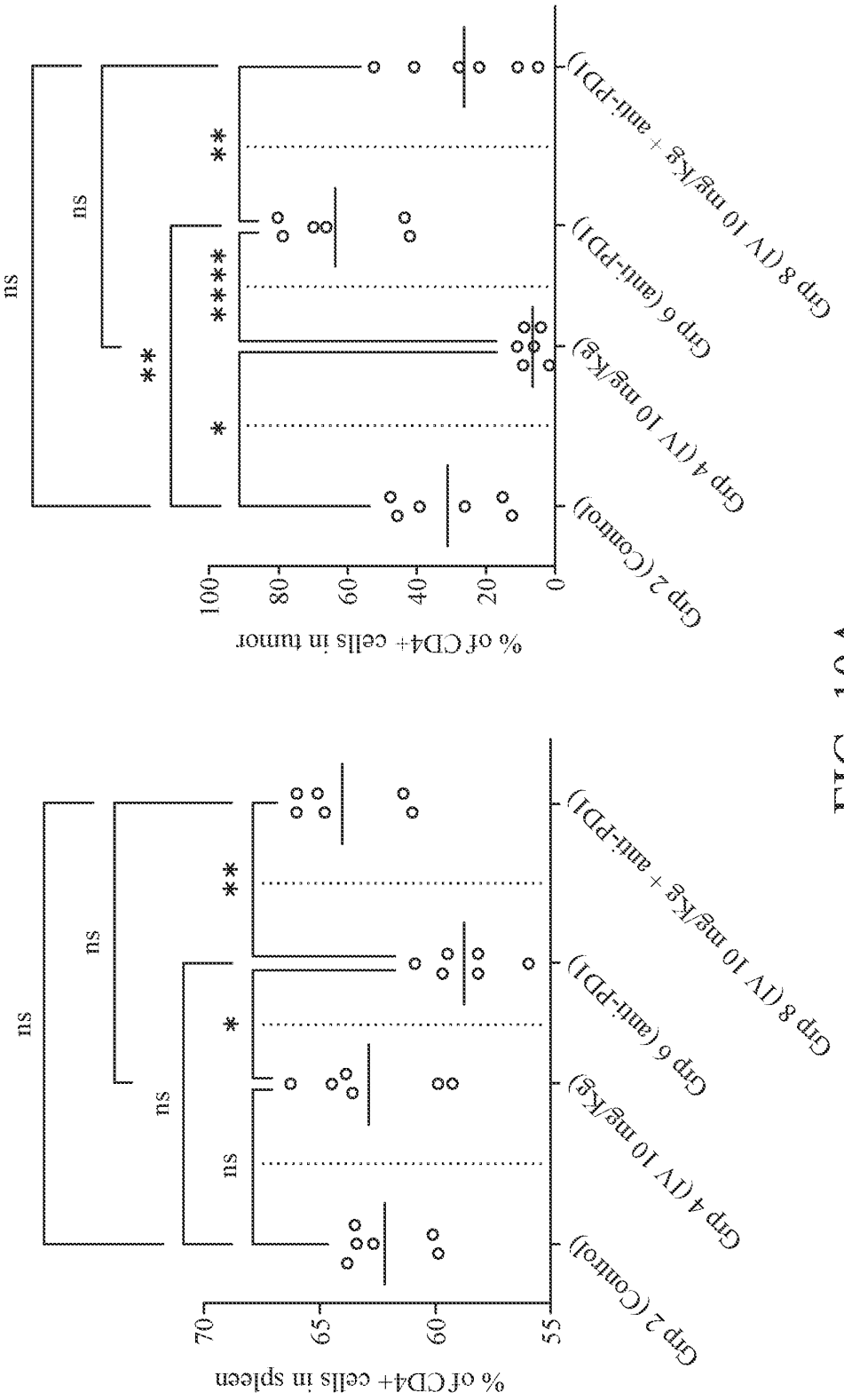

% of CD4+ cells in tumor
100
80
60
40
20
0
Grp 2 (Control)
Grp 4 (IV 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 8 (IV 10 mg/Kg + anti-PD1)
ns
ns
**
*
****
**
% of CD4+ cells in spleen
70
65
60
55
Grp 2 (Control)
Grp 4 (IV 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 8 (IV 10 mg/Kg + anti-PD1)
ns
ns
ns
*
**

FIG. 10A

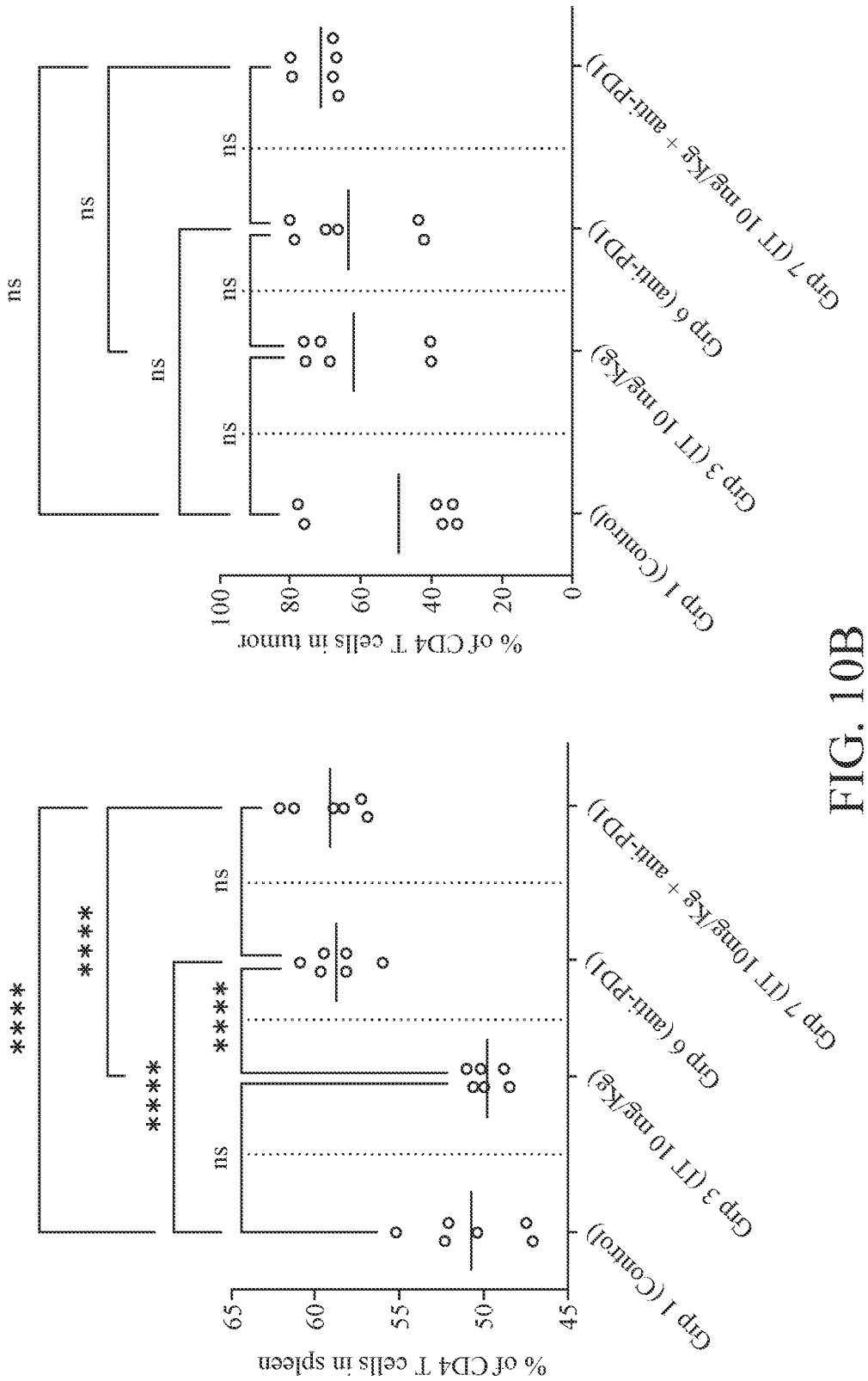

% of CD4 T cells in tumor
100
80
60
40
20
0
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 7 (IT 10mg/Kg + anti-PD1)
ns
ns
ns
ns
% of CD4 T cells in spleen
65
60
55
50
45
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 7 (IT 10mg/Kg + anti-PD1)
****
****
****
****
ns
ns

FIG. 10B

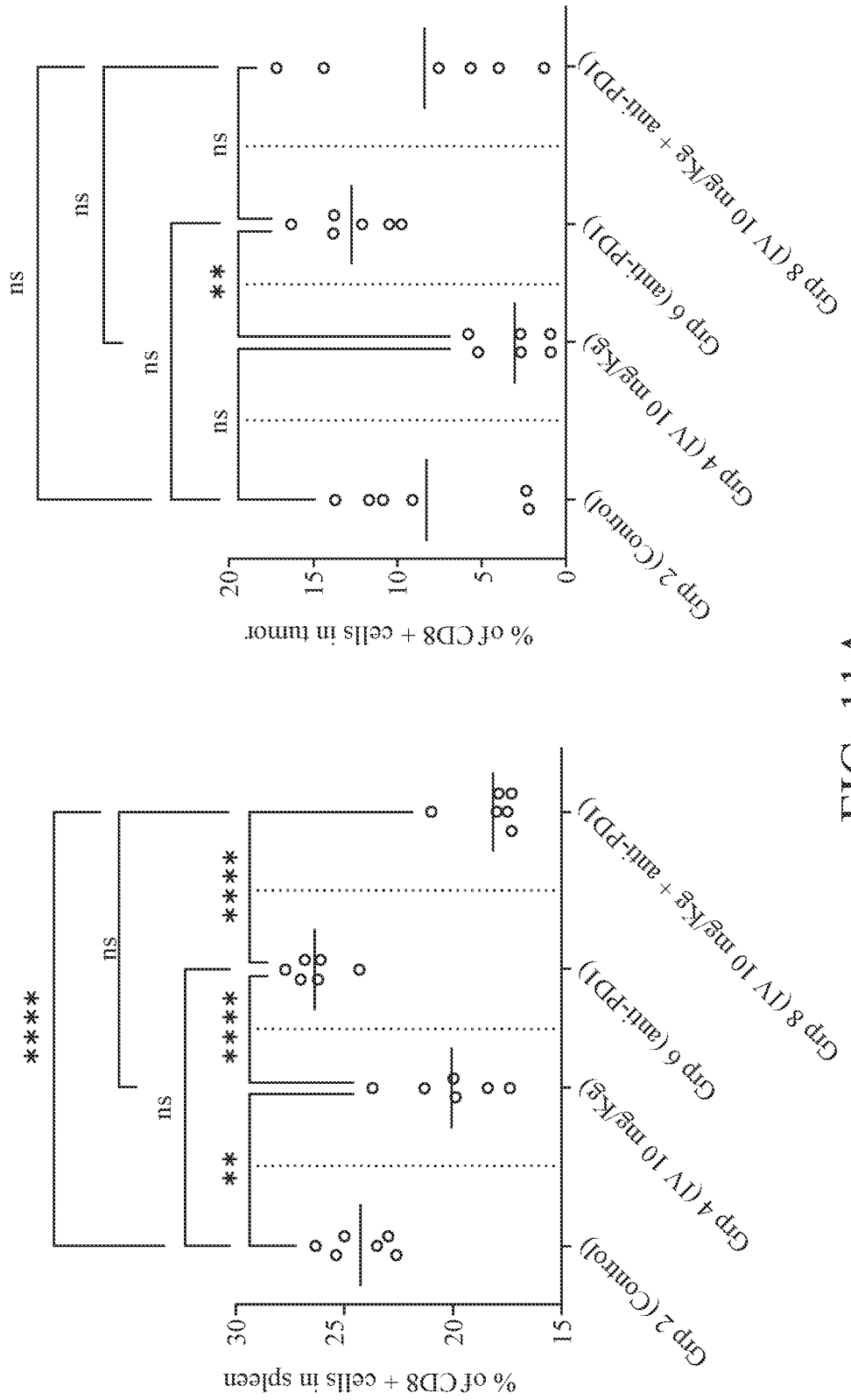

% of CD8 + cells in tumor
0
5
10
15
20
Grp 2 (Control)
Grp 4 (IV 10 mg/Kg)
Grp 6 (anti-PDL1)
Grp 8 (IV 10 mg/Kg + anti-PDL1)
ns
ns
ns
**
ns
% of CD8 + cells in spleen
15
20
25
30
Grp 2 (Control)
Grp 4 (IV 10 mg/Kg)
Grp 6 (anti-PDL1)
Grp 8 (IV 10 mg/Kg + anti-PDL1)
**
****
****
ns
****

FIG. 11A

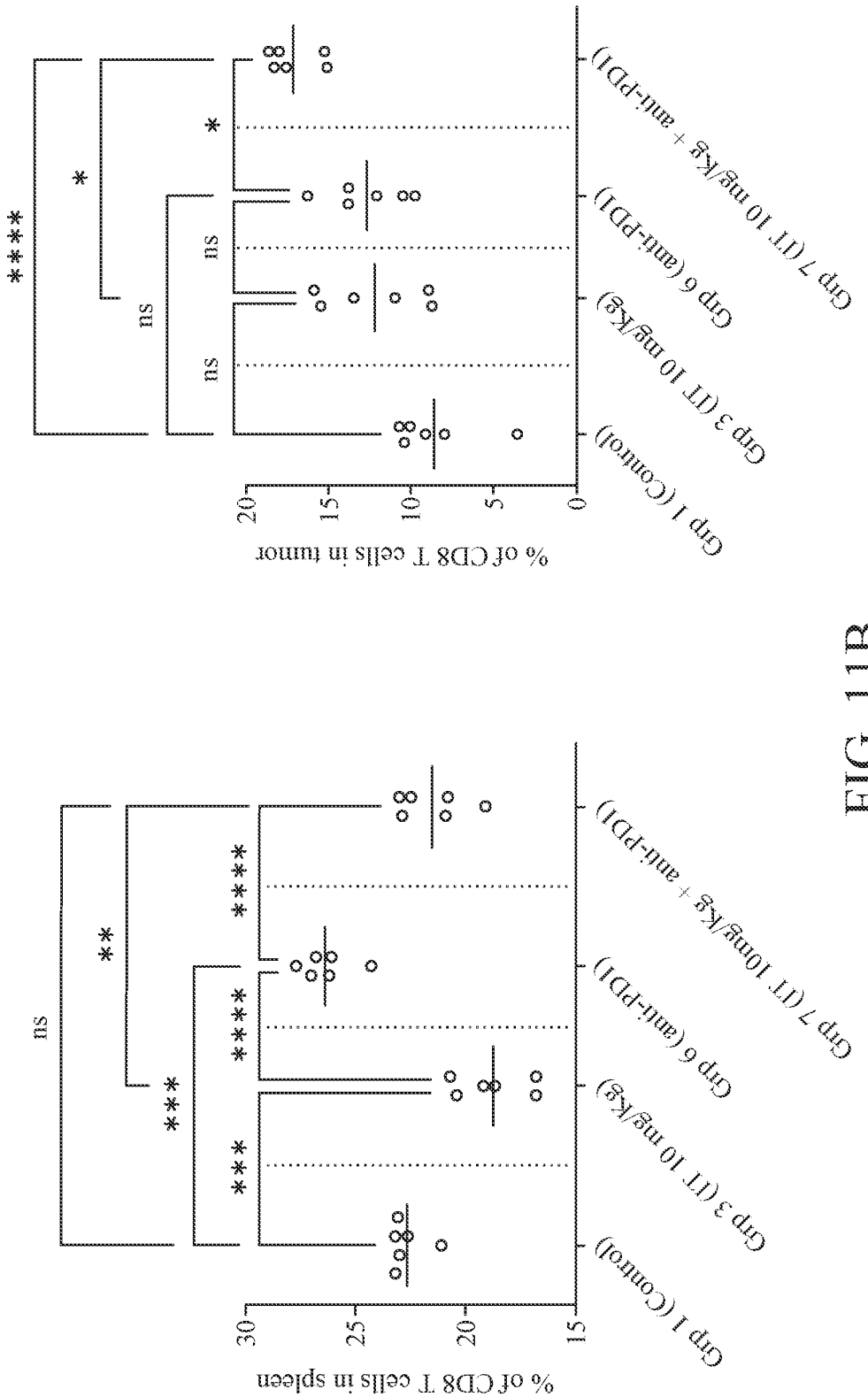

% of CD8 T cells in tumor
0
5
10
15
20
Grp 1 (Control)
Grp 3 (IT 10 mg/kg)
Grp 6 (anti-PD1)
Grp 7 (IT 10mg/kg + anti-PD1)
ns
ns
ns
*
*****
% of CD8 T cells in spleen
15
20
25
30
Grp 1 (Control)
Grp 3 (IT 10 mg/kg)
Grp 6 (anti-PD1)
Grp 7 (IT 10mg/kg + anti-PD1)
ns
**
***
*****
*****

FIG. 11B

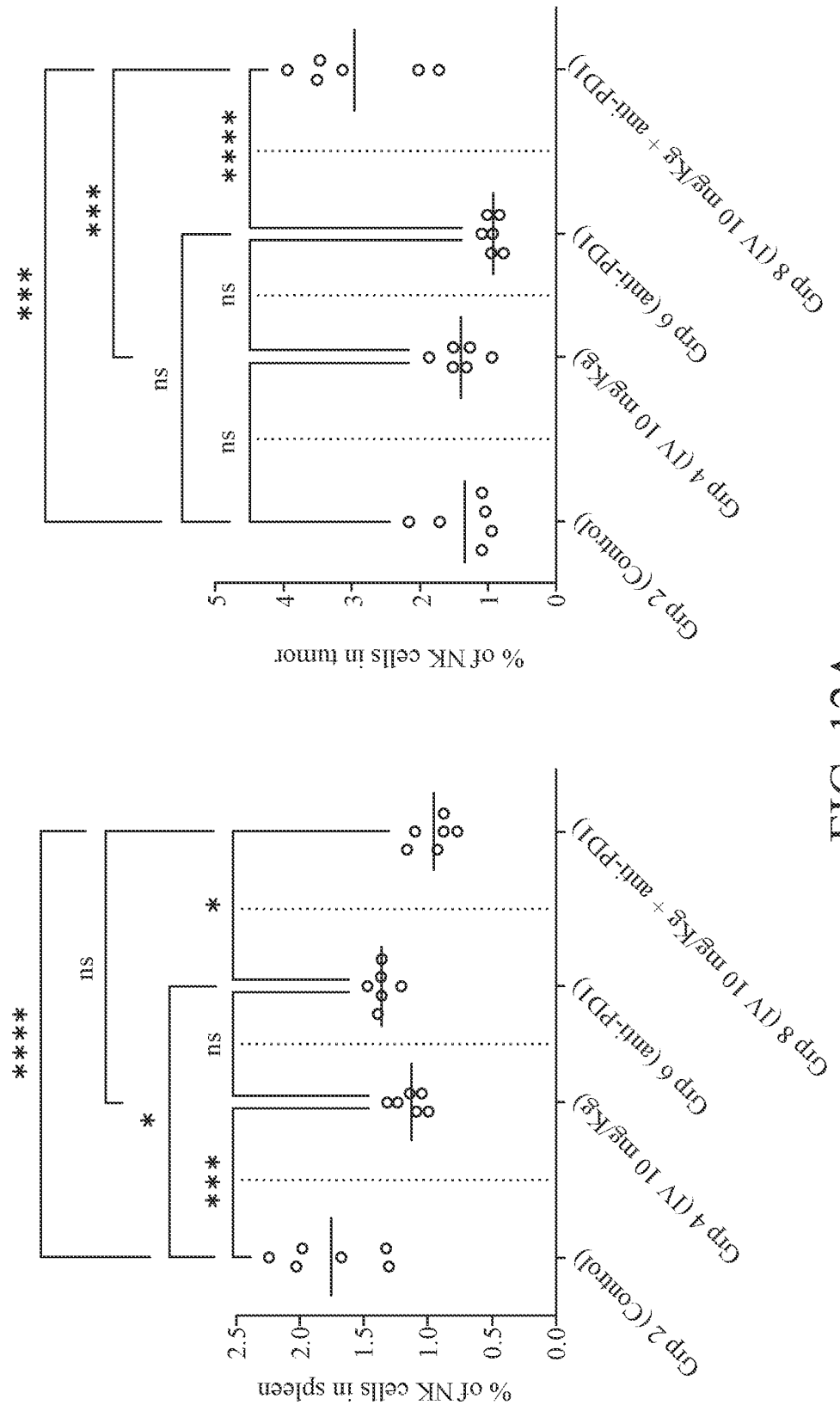

% of NK cells in tumor
0
1
2
3
4
5
Grp 2 (Control)
Grp 4 (IV 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 8 (IV 10 mg/Kg + anti-PD1)
ns
ns
***
***
****
% of NK cells in spleen
0.0
0.5
1.0
1.5
2.0
2.5
Grp 2 (Control)
Grp 4 (IV 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 8 (IV 10 mg/Kg + anti-PD1)
***
ns
*
*
ns
****

FIG. 12A

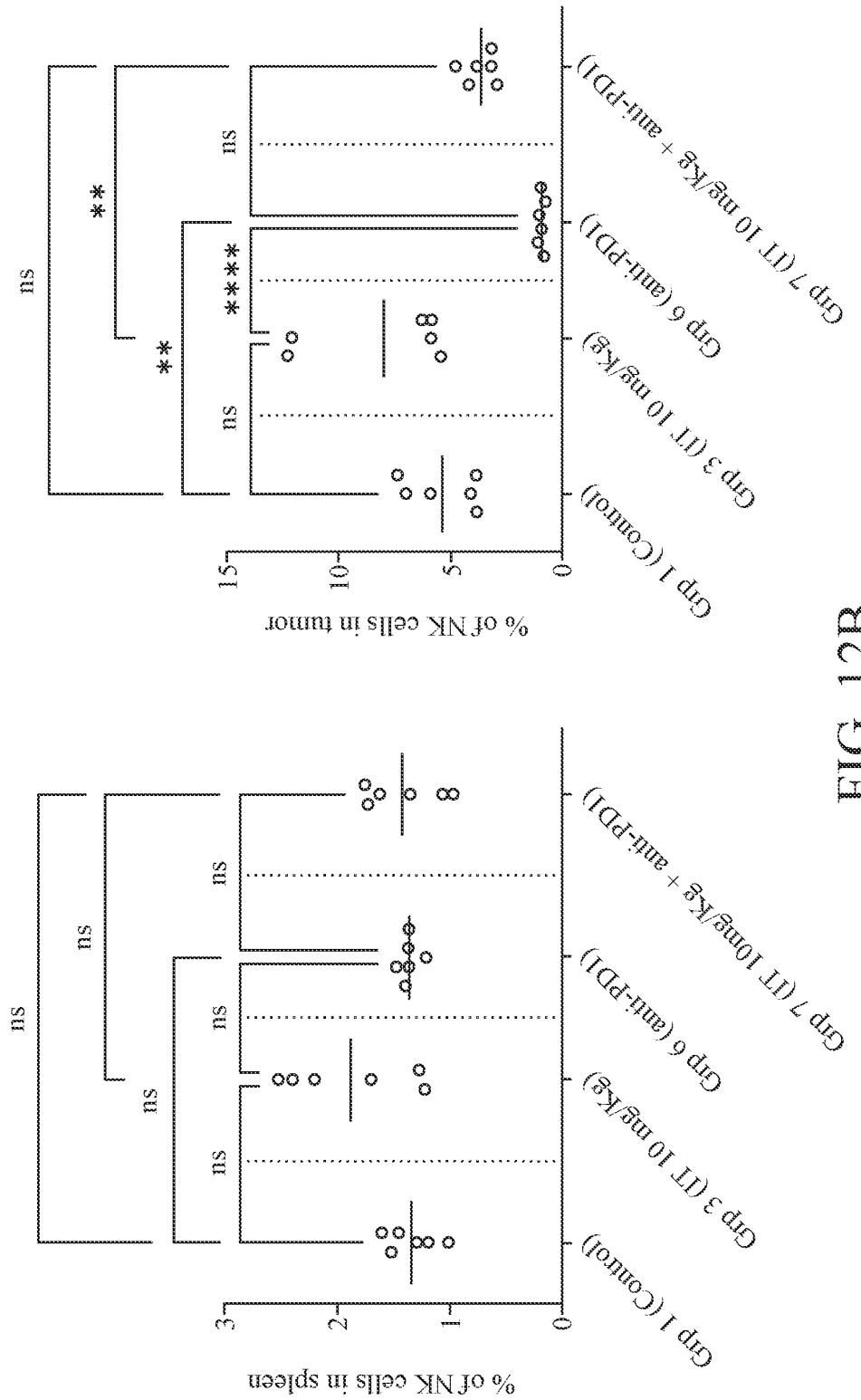

% of NK cells in tumor
0
5
10
15
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 7 (IT 10mg/Kg + anti-PD1)
ns
**
****
**
ns
% of NK cells in spleen
0
1
2
3
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 7 (IT 10mg/Kg + anti-PD1)
ns
ns
ns
ns

FIG. 12B

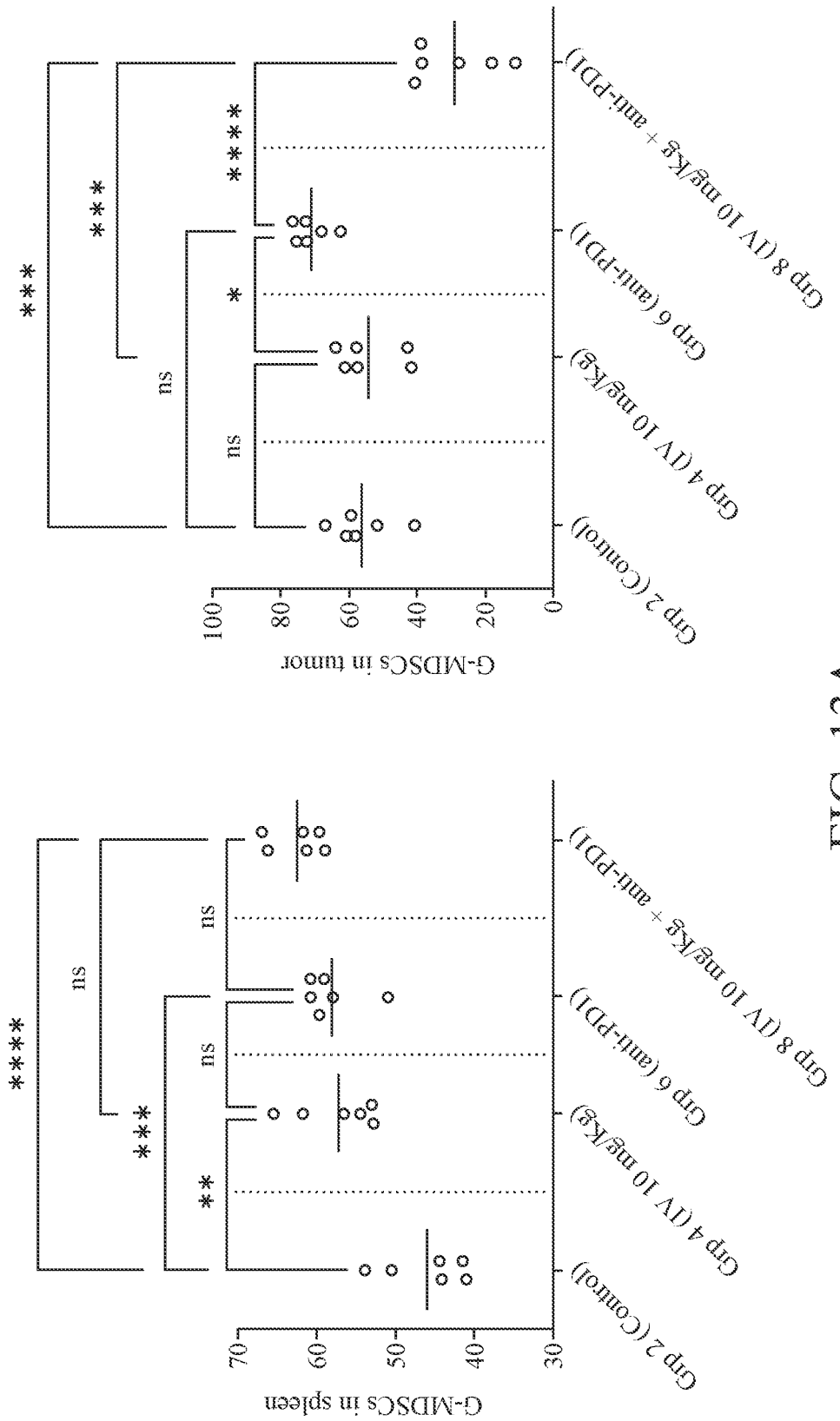

G-MDSCs in tumor
100
80
60
40
20
0
Grp 2 (Control)
Grp 4 (IV 10 mg/kg)
Grp 6 (anti-PD1)
Grp 8 (IV 10 mg/kg + anti-PD1)
ns
ns
*
****
***
***
G-MDSCs in spleen
70
60
50
40
30
Grp 2 (Control)
Grp 4 (IV 10 mg/kg)
Grp 6 (anti-PD1)
Grp 8 (IV 10 mg/kg + anti-PD1)
ns
ns
ns
**
***
****

FIG. 13A

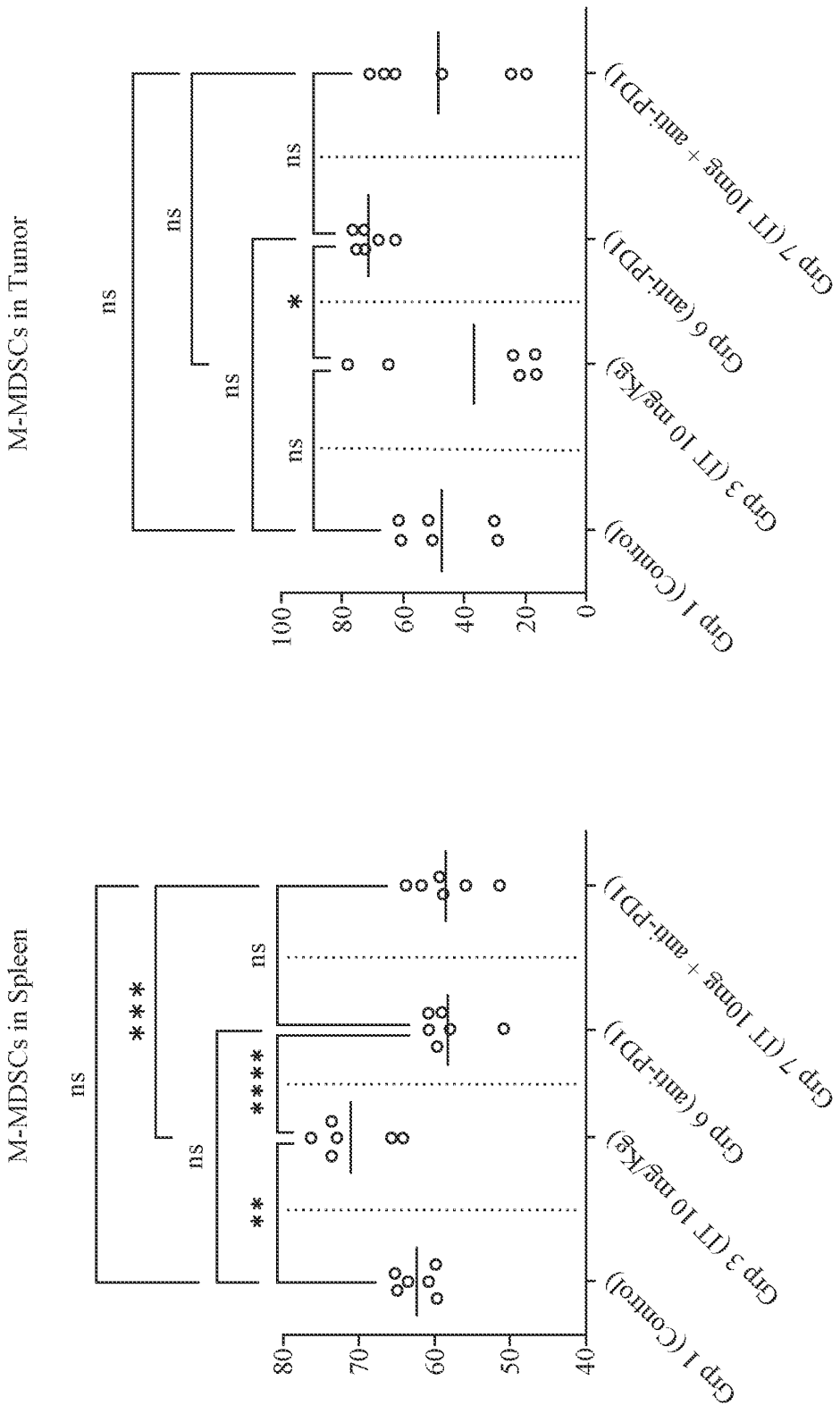

M-MDSCs in Tumor
100
80
60
40
20
0
ns
ns
ns
*
ns
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 7 (IT 10mg + anti-PD1)
M-MDSCs in Spleen
80
70
60
50
40
ns
***
ns
**
****
ns
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 7 (IT 10mg + anti-PD1)

FIG. 13B

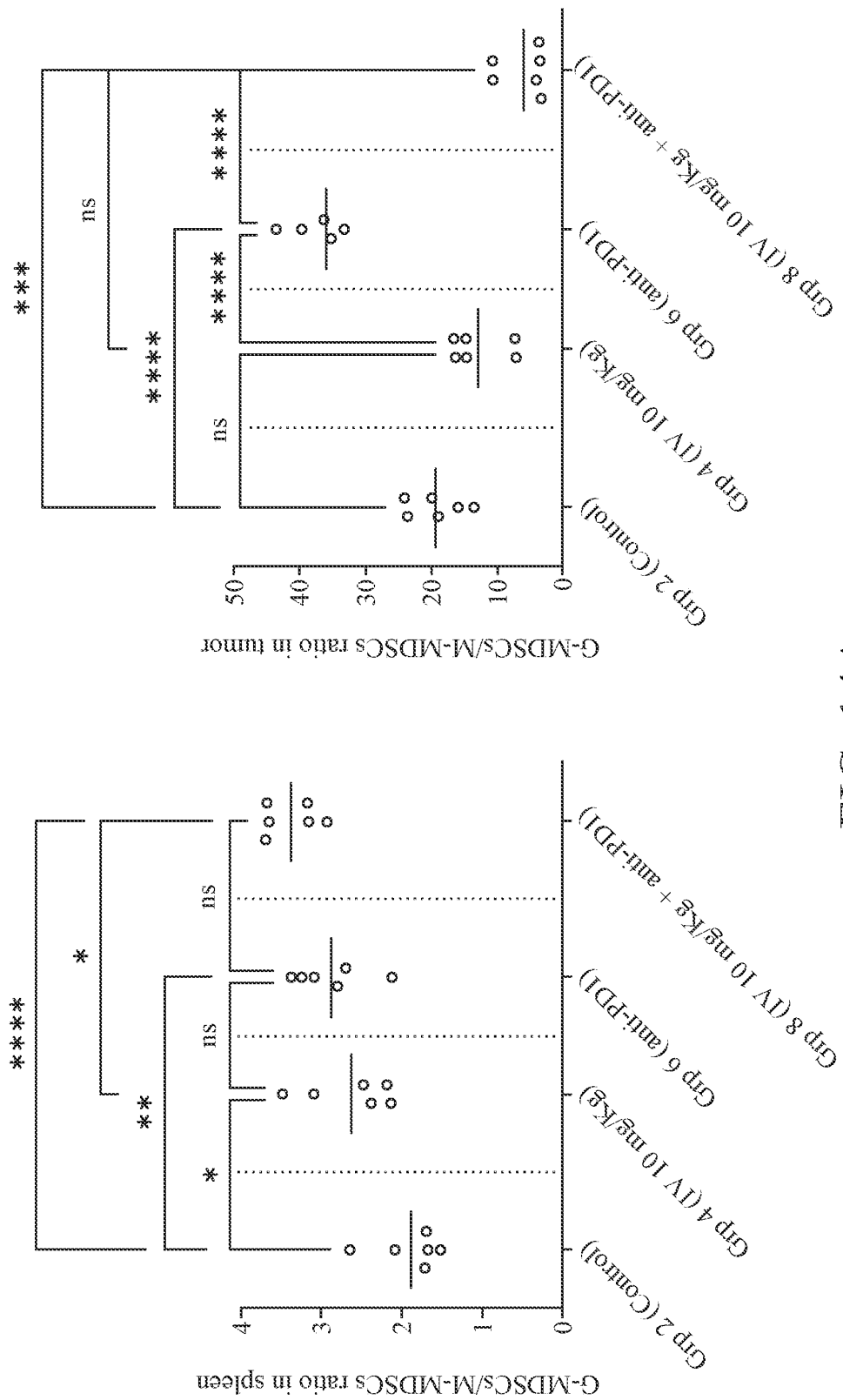

G-MDSCs/M-MDSCs ratio in tumor
0
10
20
30
40
50
Grp 2 (Control)
Grp 4 (IV 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 8 (IV 10 mg/Kg + anti-PD1)
ns
****
****
***
G-MDSCs/M-MDSCs ratio in spleen
0
1
2
3
4
Grp 2 (Control)
Grp 4 (IV 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 8 (IV 10 mg/Kg + anti-PD1)
ns
*
**
*
****

FIG. 14A

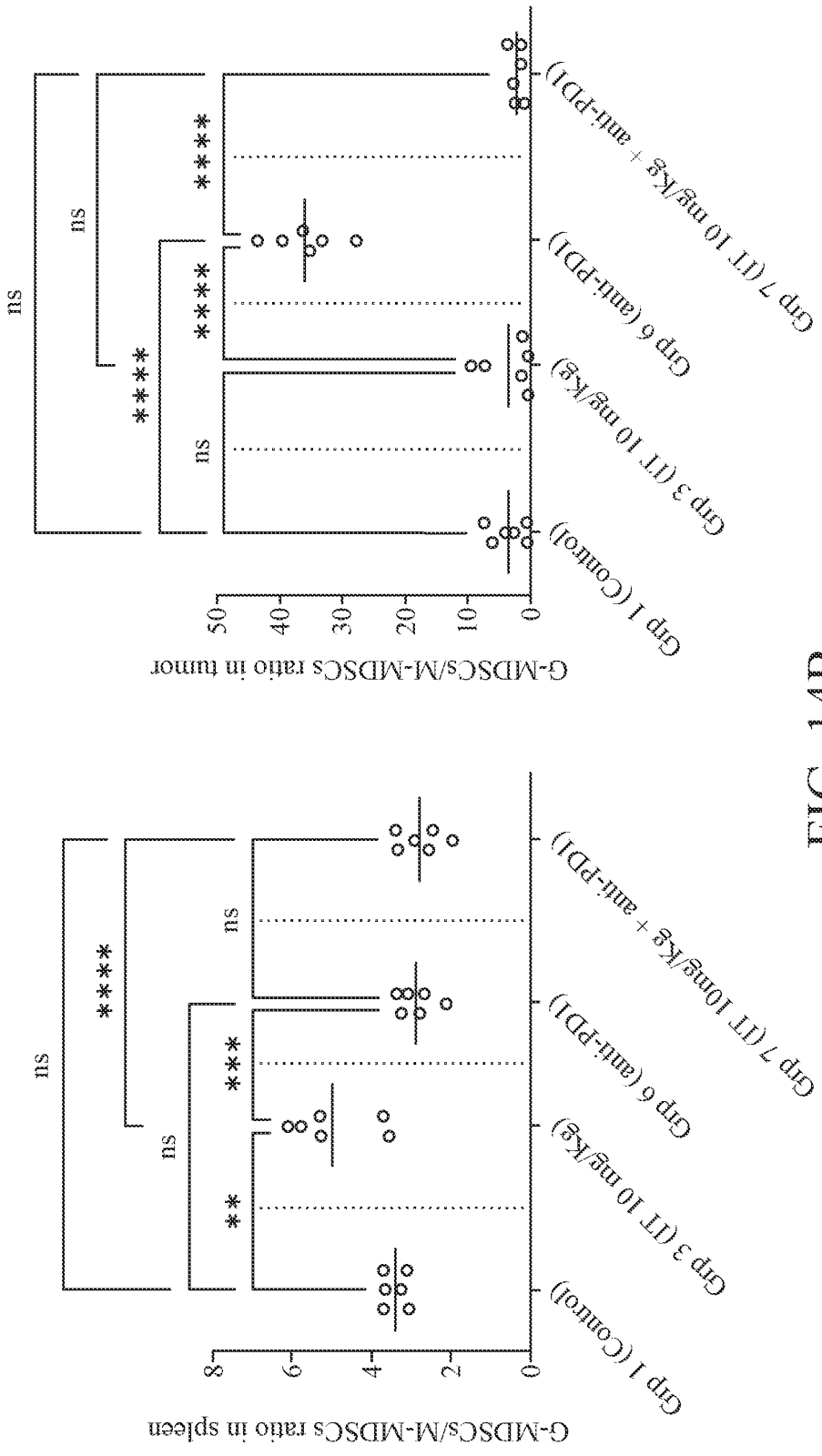

G-MDSCs/M-MDSCs ratio in tumor
0
10
20
30
40
50
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 7 (IT 10mg/Kg + anti-PD1)
ns
ns
****
****
G-MDSCs/M-MDSCs ratio in spleen
0
2
4
6
8
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 7 (IT 10mg/Kg + anti-PD1)
ns
ns
****
***
**

FIG. 14B

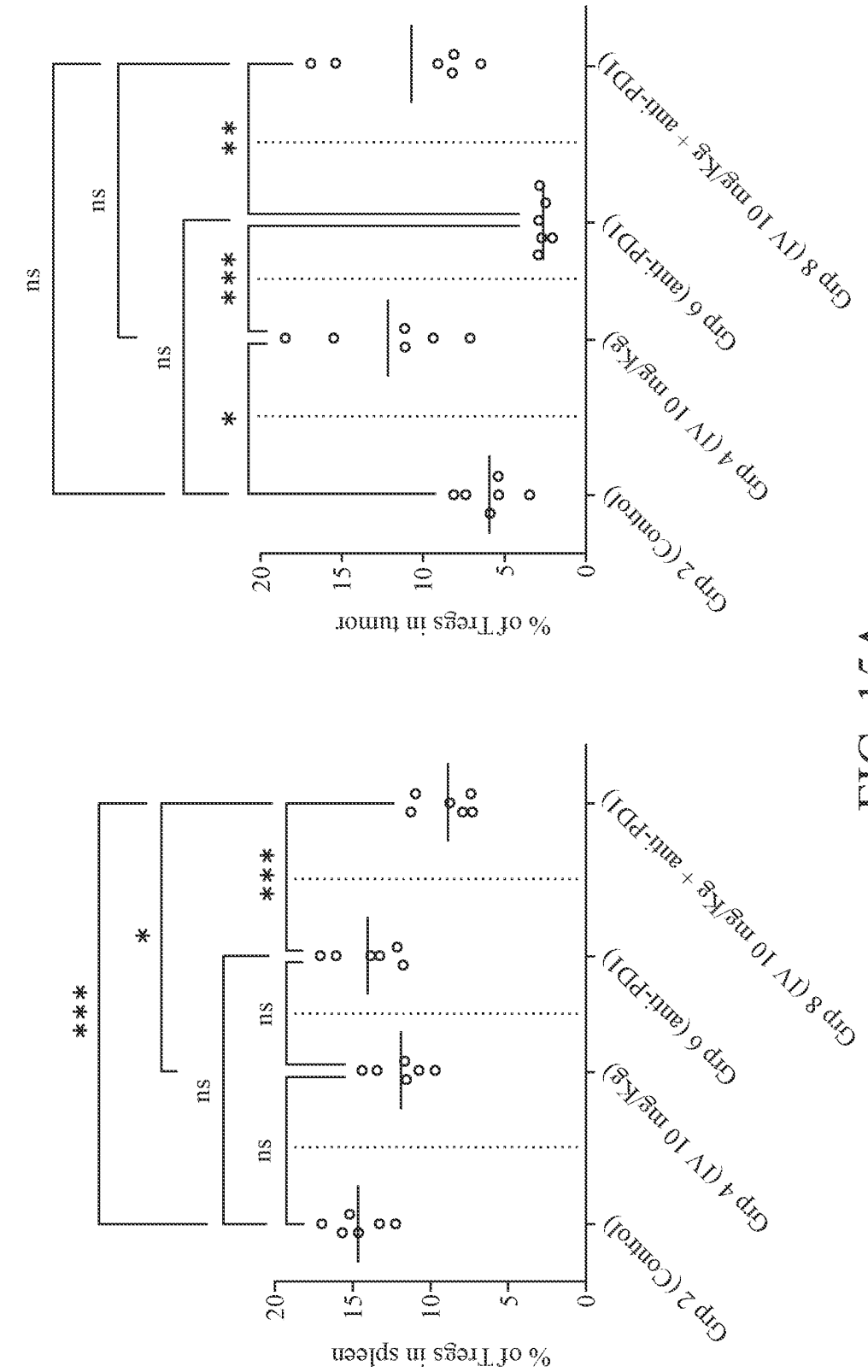

% of Tregs in tumor
0
5
10
15
20
Grp 2 (Control)
Grp 4 (IV 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 8 (IV 10 mg/Kg + anti-PD1)
ns
ns
ns
*
***
**
% of Tregs in spleen
0
5
10
15
20
Grp 2 (Control)
Grp 4 (IV 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 8 (IV 10 mg/Kg + anti-PD1)
ns
ns
ns
***
*
***

FIG. 15A

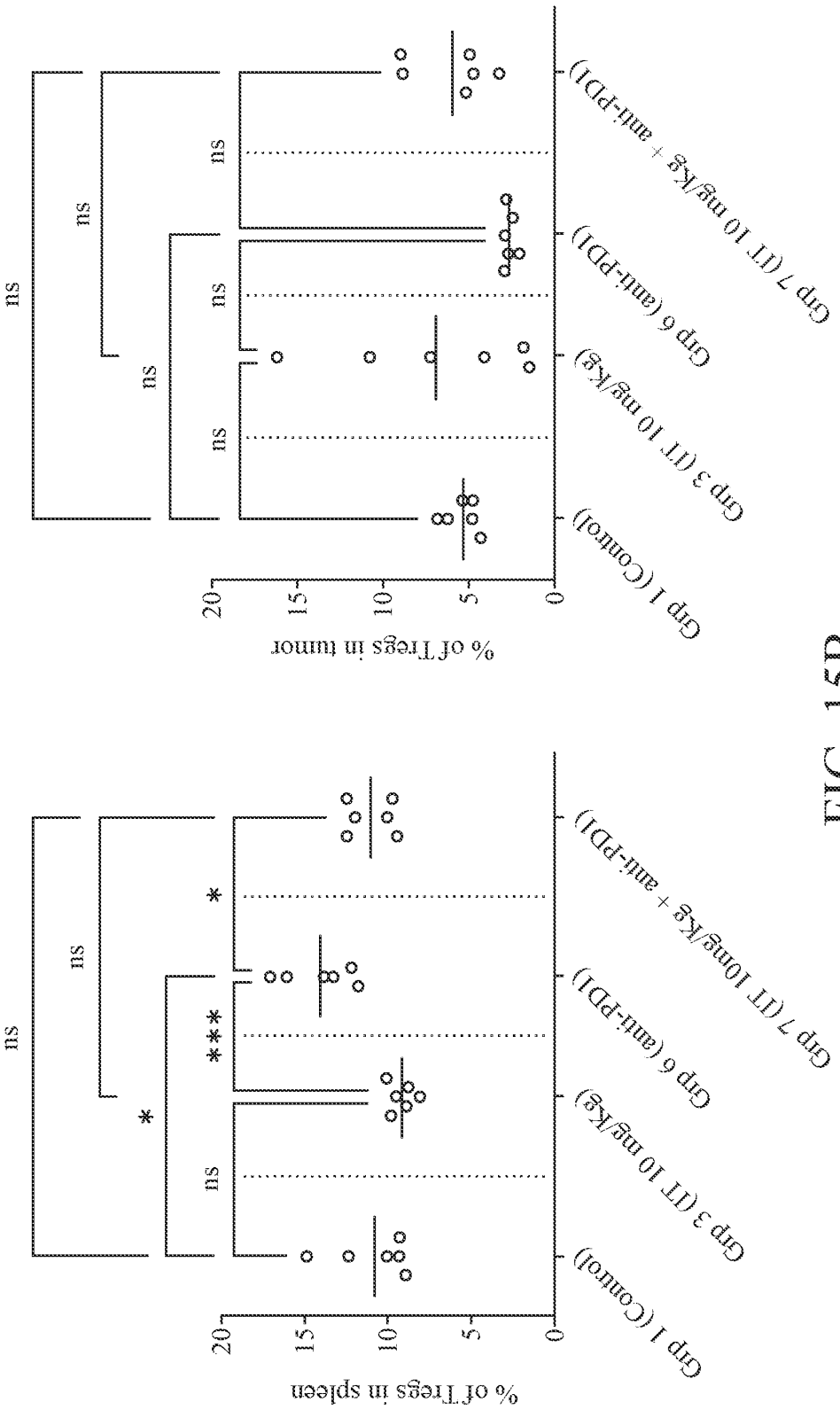

% of Tregs in spleen
% of Tregs in tumor
0
5
10
15
20
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 7 (IT 10mg/Kg + anti-PD1)
ns
*
***

FIG. 15B

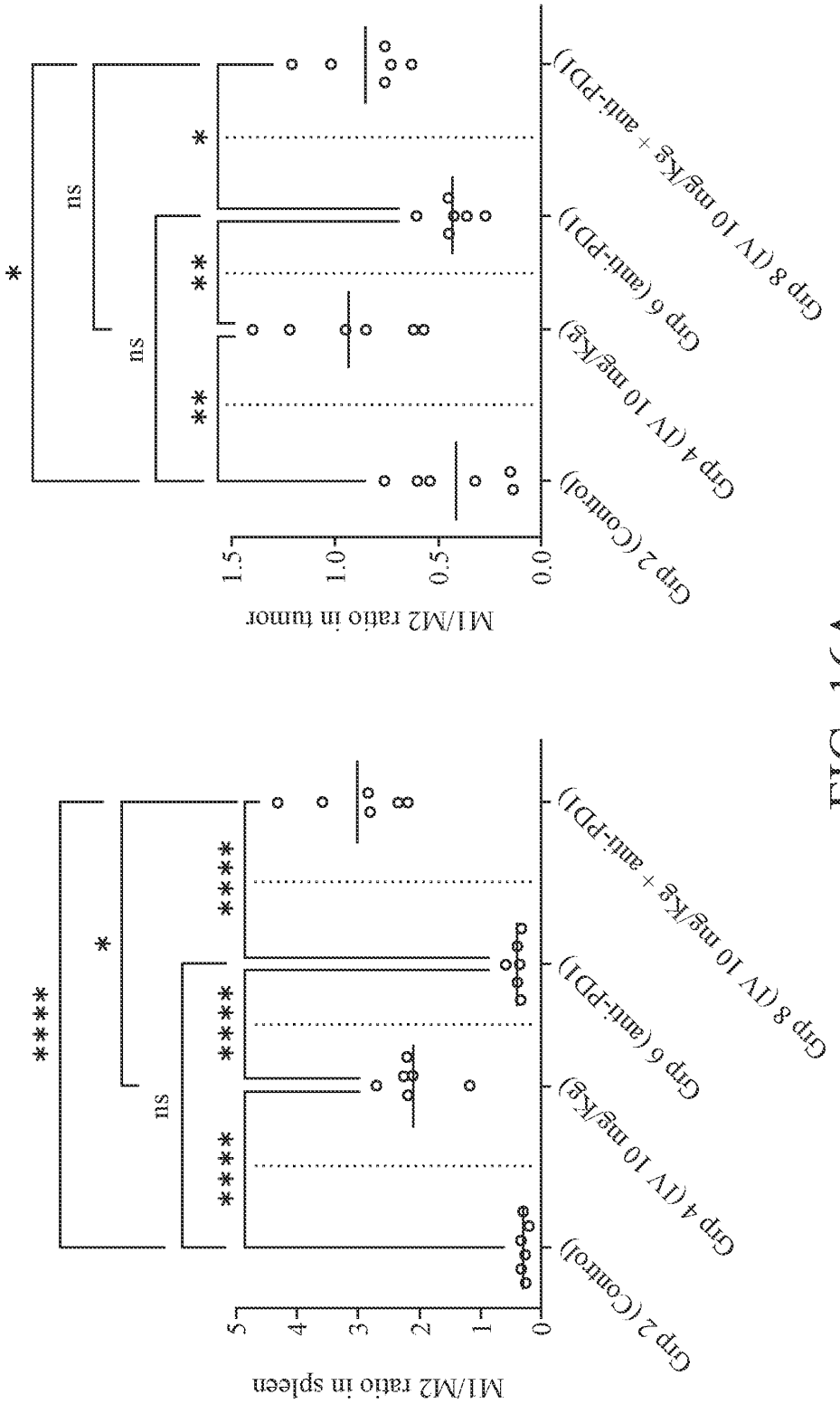

M1/M2 ratio in spleen
0
1
2
3
4
5
Grp 2 (Control)
Grp 4 (IV 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 8 (IV 10 mg/Kg + anti-PD1)
*****
ns
*
*****
*****
*****
M1/M2 ratio in tumor
0.0
0.5
1.0
1.5
Grp 2 (Control)
Grp 4 (IV 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 8 (IV 10 mg/Kg + anti-PD1)
*
ns
ns
**
**
**

FIG. 16A

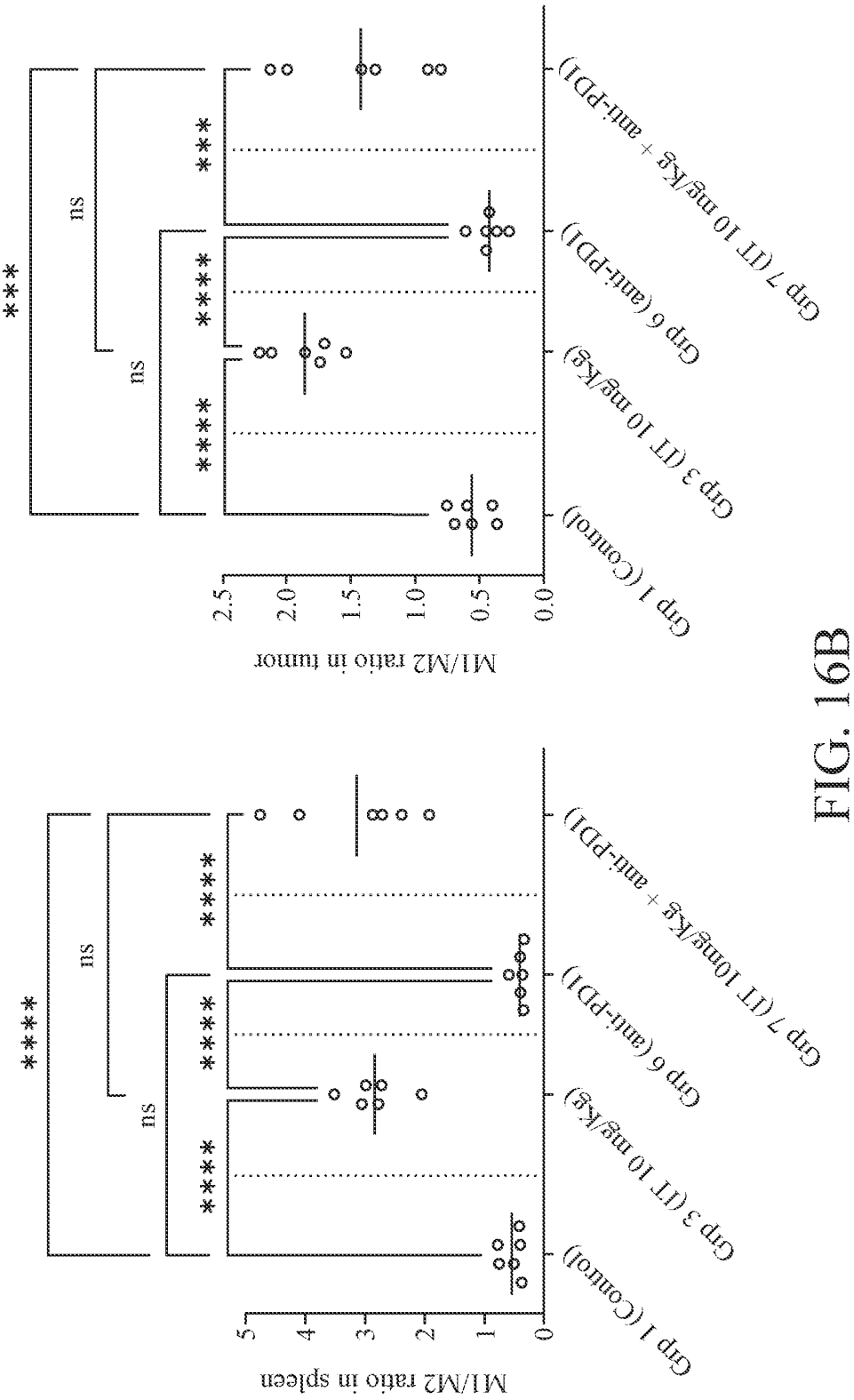

M1/M2 ratio in tumor
2.5
2.0
1.5
1.0
0.5
0.0
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 7 (IT 10mg/Kg + anti-PD1)
****
ns
ns
****
****
****
M1/M2 ratio in spleen
5
4
3
2
1
0
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 7 (IT 10mg/Kg + anti-PD1)
****
ns
ns
****
****
****

FIG. 16B

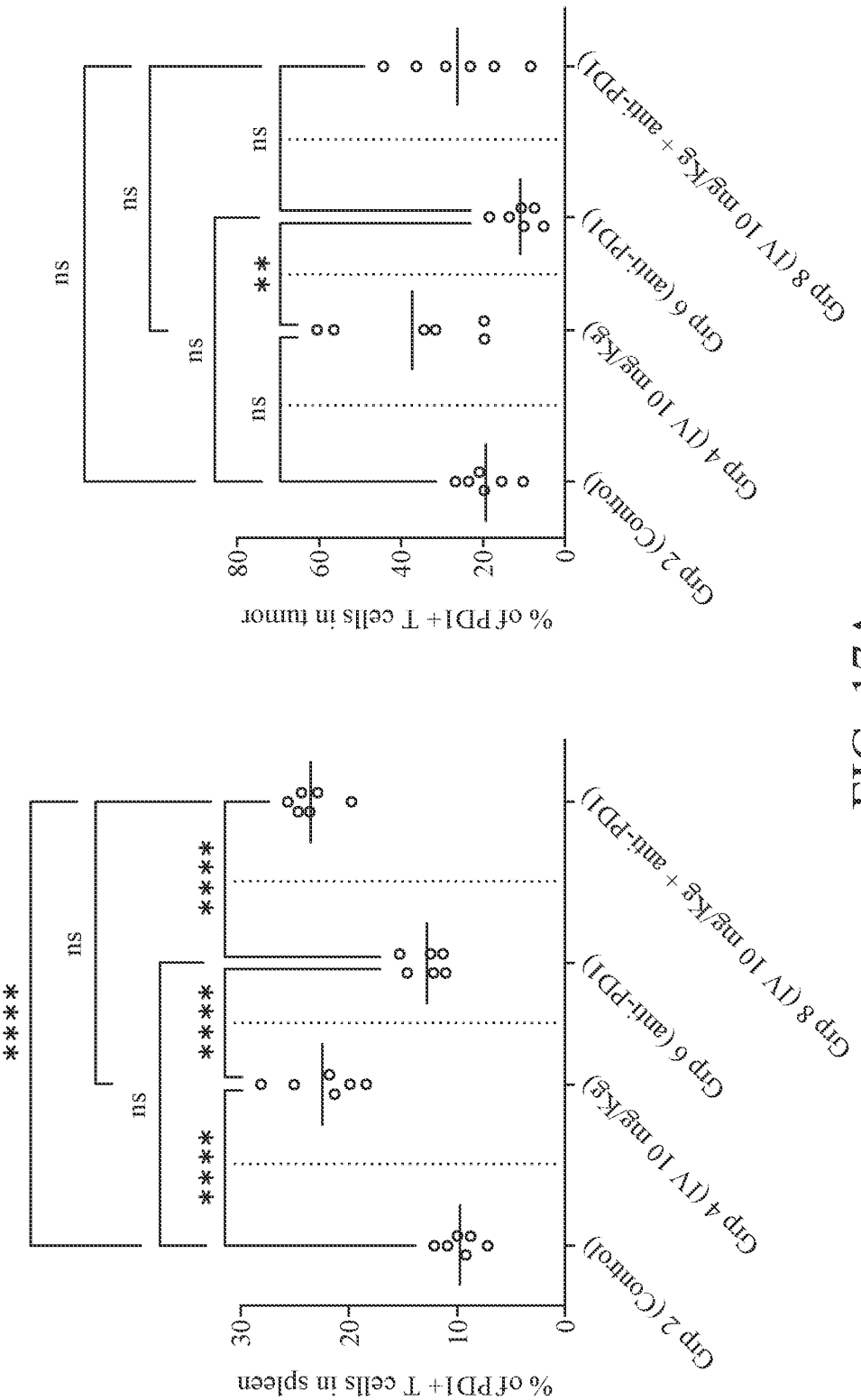

% of PD1+ T cells in tumor
0
20
40
60
80
Grp 2 (Control)
Grp 4 (IV 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 8 (IV 10 mg/Kg + anti-PD1)
ns
ns
ns
**
% of PD1+ T cells in spleen
0
10
20
30
Grp 2 (Control)
Grp 4 (IV 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 8 (IV 10 mg/Kg + anti-PD1)
****
****
****
****
ns
ns

FIG. 17A

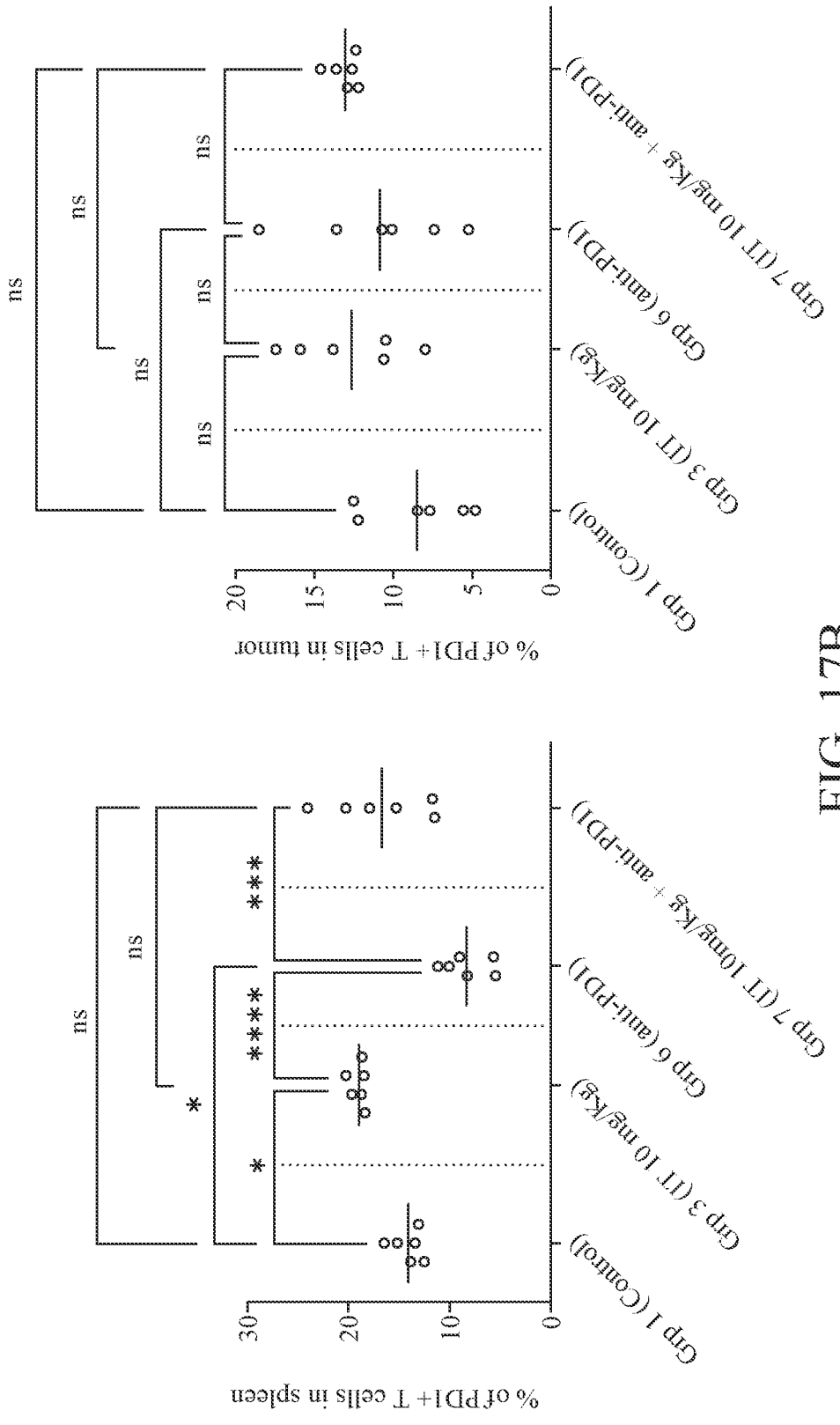

% of PD1+ T cells in tumor
0
5
10
15
20
ns
ns
ns
ns
ns
Grp 1 (Control)
Grp 3 (IT 10 mg/kg)
Grp 6 (anti-PD1)
Grp 7 (IT 10mg/kg + anti-PD1)
% of PD1+ T cells in spleen
0
10
20
30
ns
ns
*
*
****
****

FIG. 17B

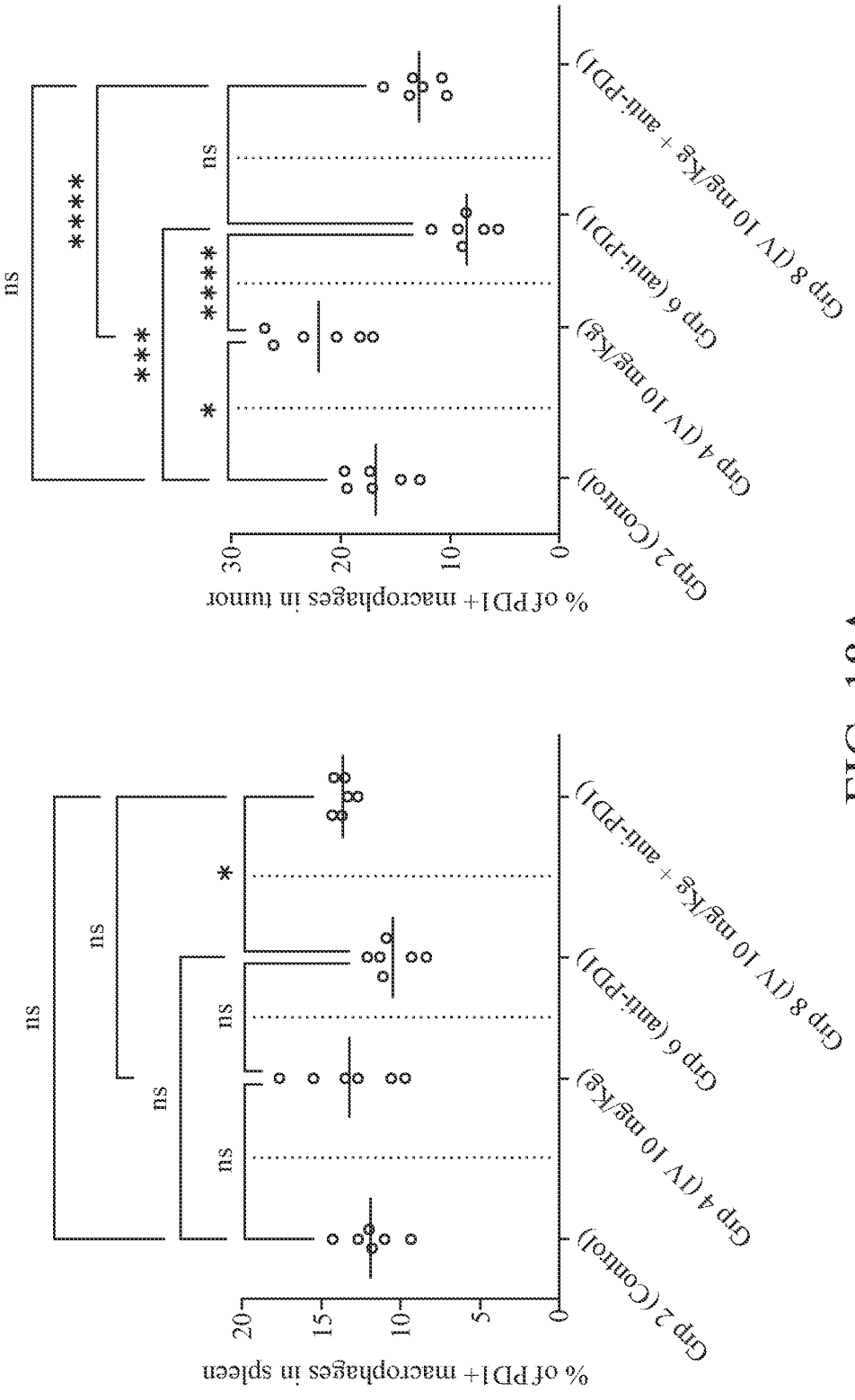

% of PD1+ macrophages in tumor
0
10
20
30
ns
****
***
****
*
Grp 2 (Control)
Grp 4 (IV 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 8 (IV 10 mg/Kg + anti-PD1)
% of PD1+ macrophages in spleen
0
5
10
15
20
ns
ns
ns
ns
*
Grp 2 (Control)
Grp 4 (IV 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 8 (IV 10 mg/Kg + anti-PD1)

FIG. 18A

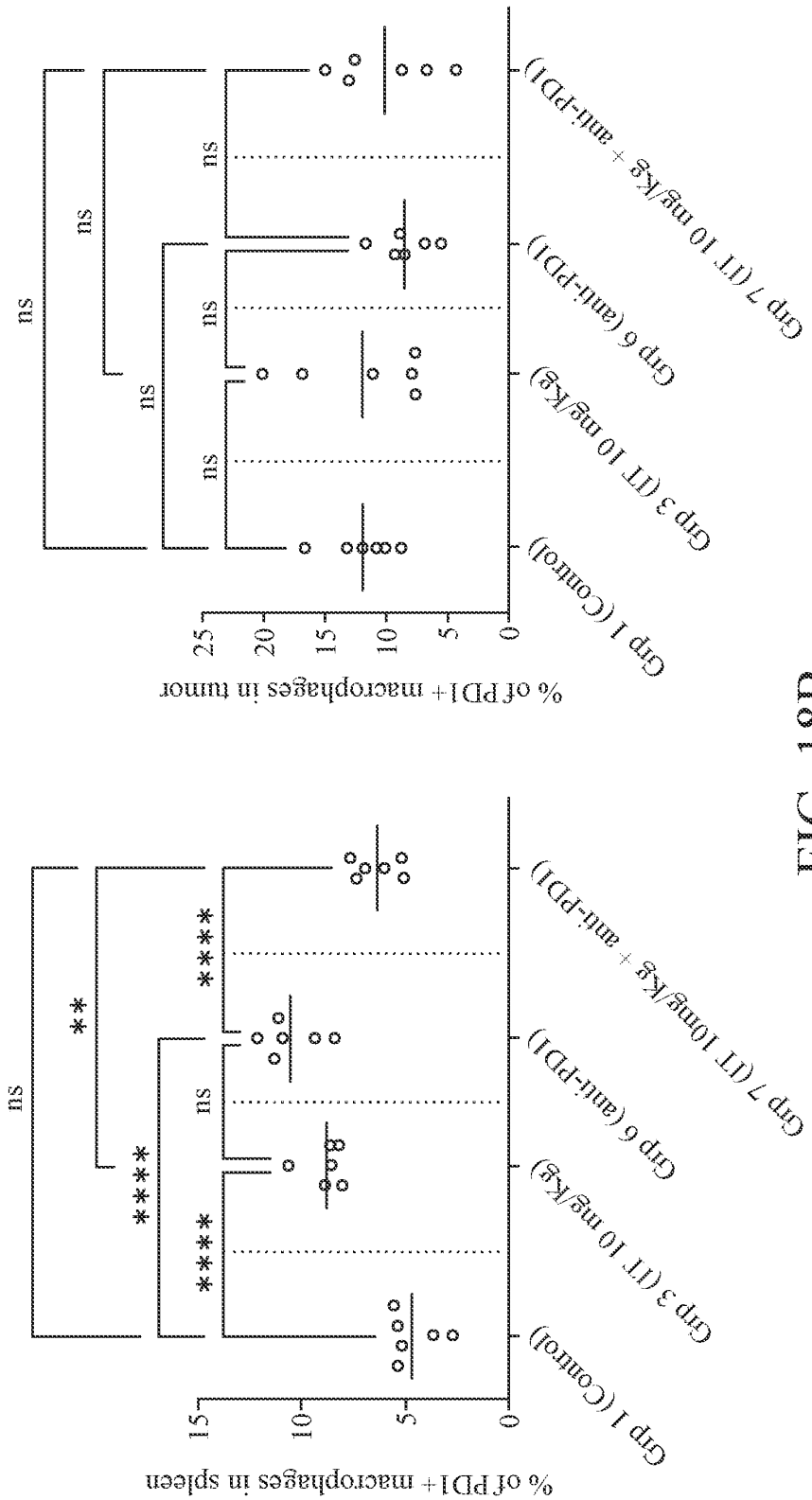

% of PD1+ macrophages in tumor
0
5
10
15
20
25
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 7 (IT 10mg/Kg + anti-PD1)
ns
ns
ns
ns
% of PD1+ macrophages in spleen
0
5
10
15
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 7 (IT 10mg/Kg + anti-PD1)
ns
**
****
****
ns

FIG. 18B

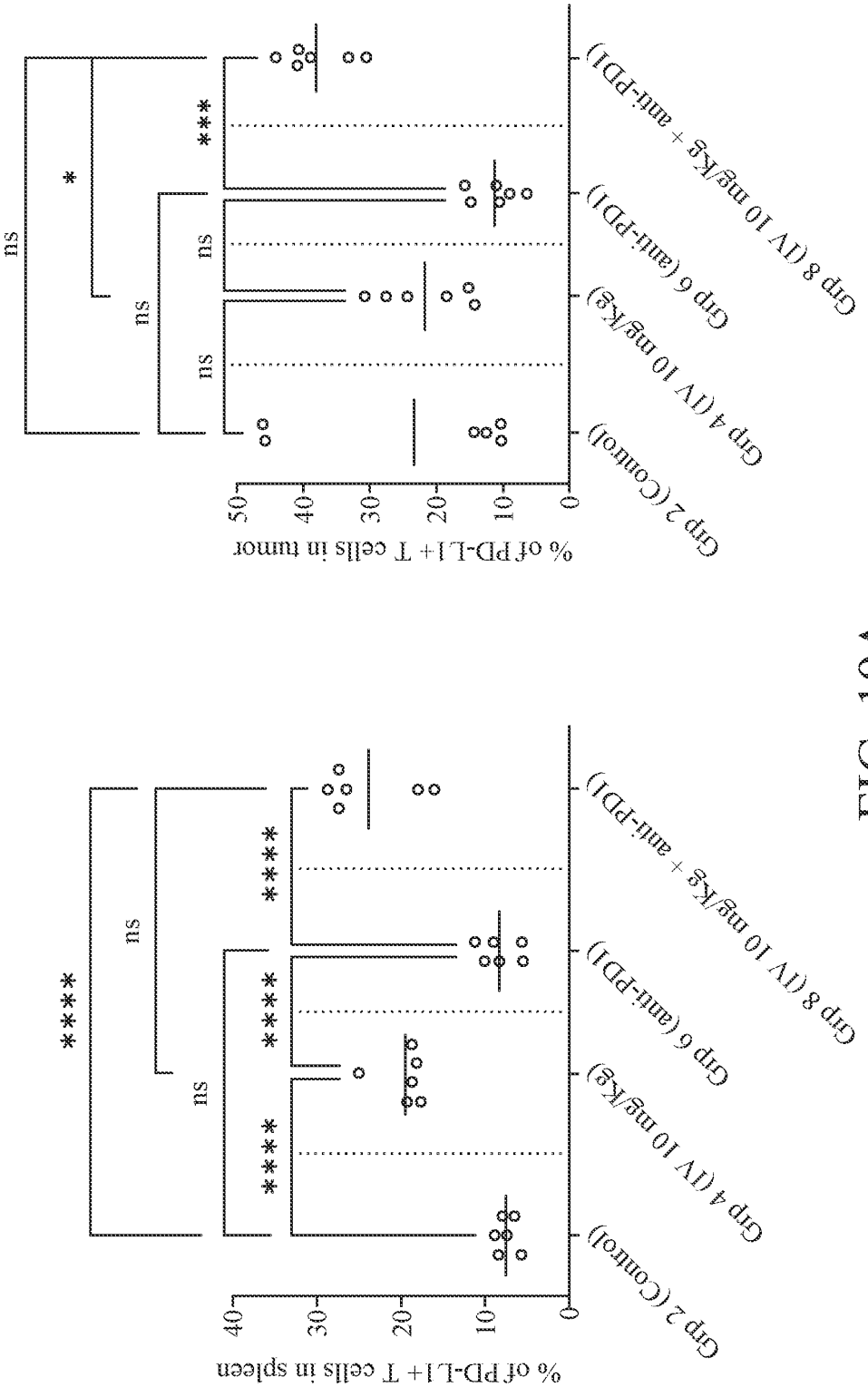

% of PD-L1+ T cells in tumor
0
10
20
30
40
50
Grp 2 (Control)
Grp 4 (IV 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 8 (IV 10 mg/Kg + anti-PD1)
ns
ns
ns
*
***
% of PD-L1+ T cells in spleen
0
10
20
30
40
Grp 2 (Control)
Grp 4 (IV 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 8 (IV 10 mg/Kg + anti-PD1)
ns
ns
****
****
****
****
****

FIG. 19A

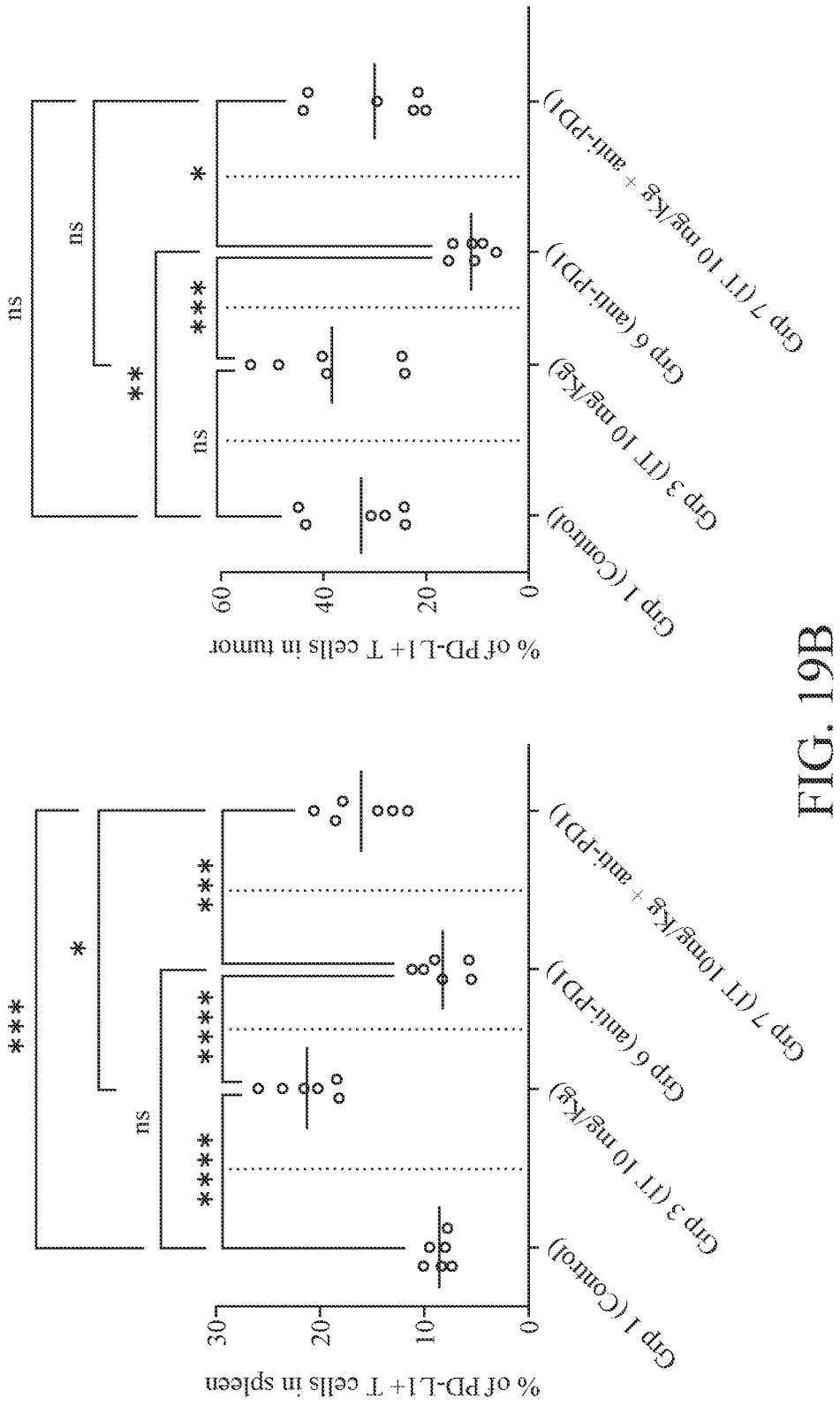

% of PD-L1+ T cells in tumor
0
20
40
60
ns
**
***
ns
*
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 7 (IT 10mg/Kg + anti-PD1)
% of PD-L1+ T cells in spleen
0
10
20
30
***
*
ns
****
****
***
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 7 (IT 10mg/Kg + anti-PD1)

FIG. 19B

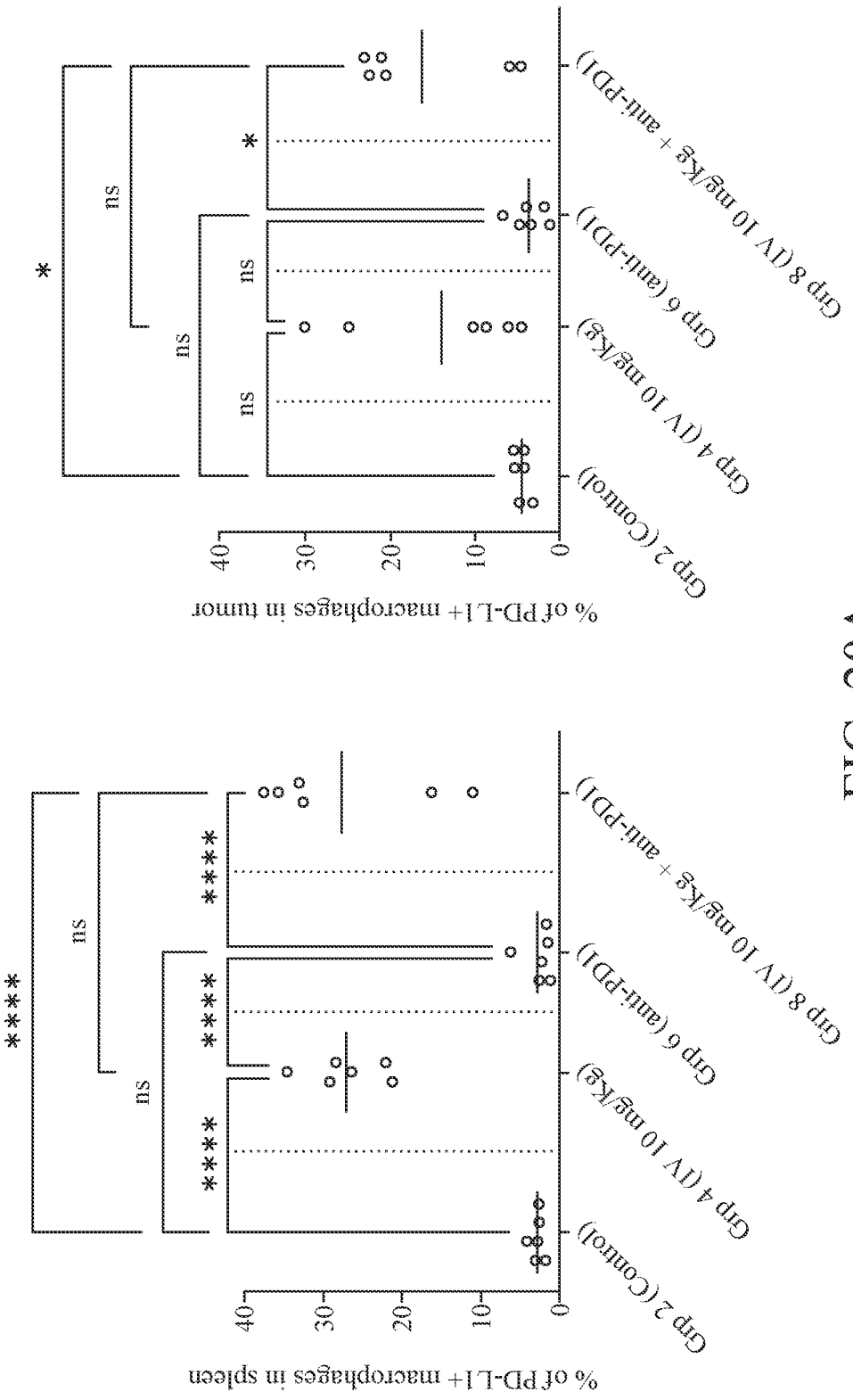
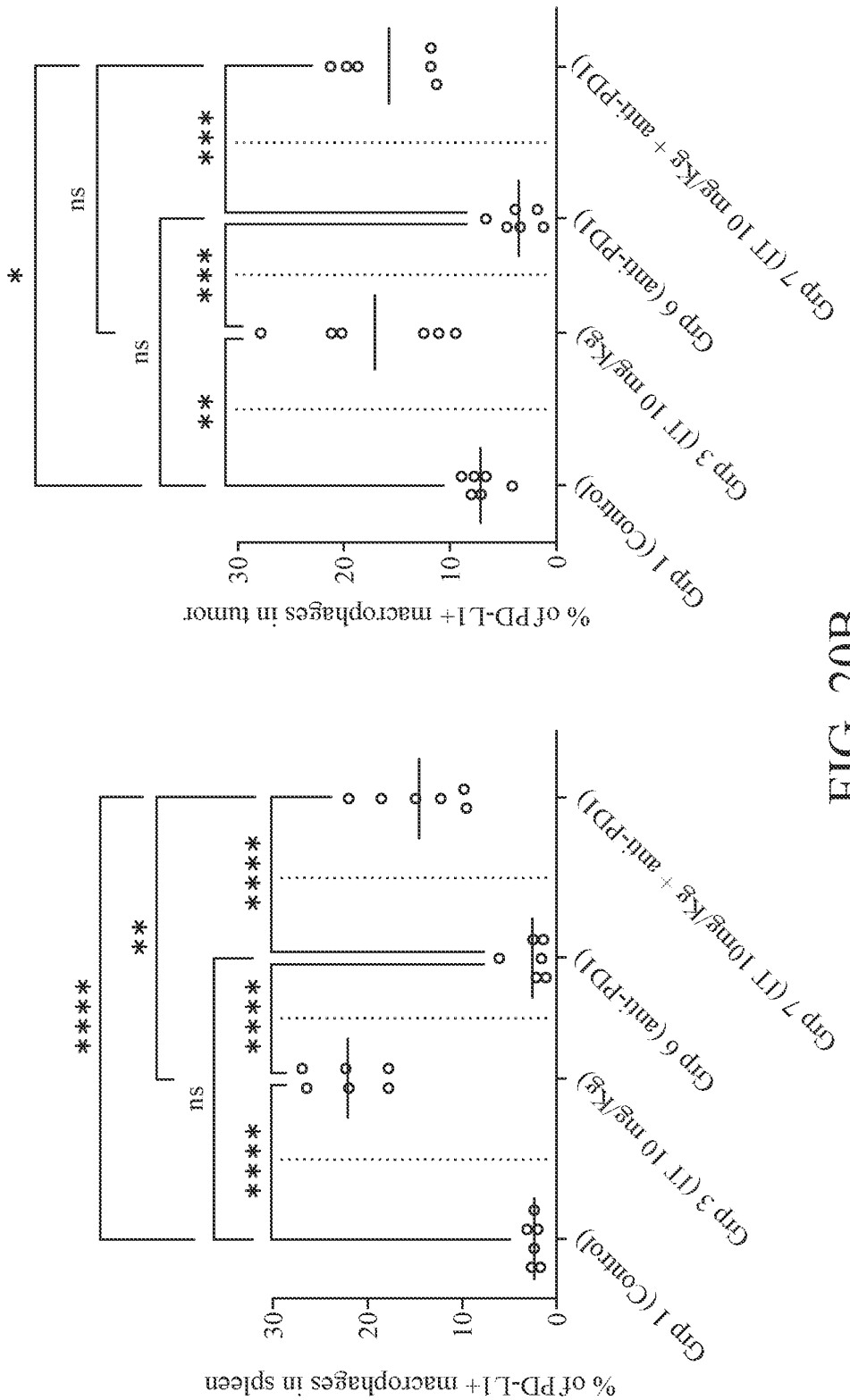

% of PD-L1+ macrophages in spleen
0
10
20
30
40
Grp 2 (Control)
Grp 4 (IV 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 8 (IV 10 mg/Kg + anti-PD1)
****
ns
****
****
****
% of PD-L1+ macrophages in tumor
0
10
20
30
40
Grp 2 (Control)
Grp 4 (IV 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 8 (IV 10 mg/Kg + anti-PD1)
*
ns
ns
ns
*

FIG. 20A


% of PD-L1+ macrophages in tumor
0
10
20
30
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 7 (IT 10mg/Kg + anti-PD1)
*
ns
ns
**
***
***

% of PD-L1+ macrophages in spleen
0
10
20
30
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 6 (anti-PD1)
Grp 7 (IT 10mg/Kg + anti-PD1)
****
**
ns
****
****
****

FIG. 20B

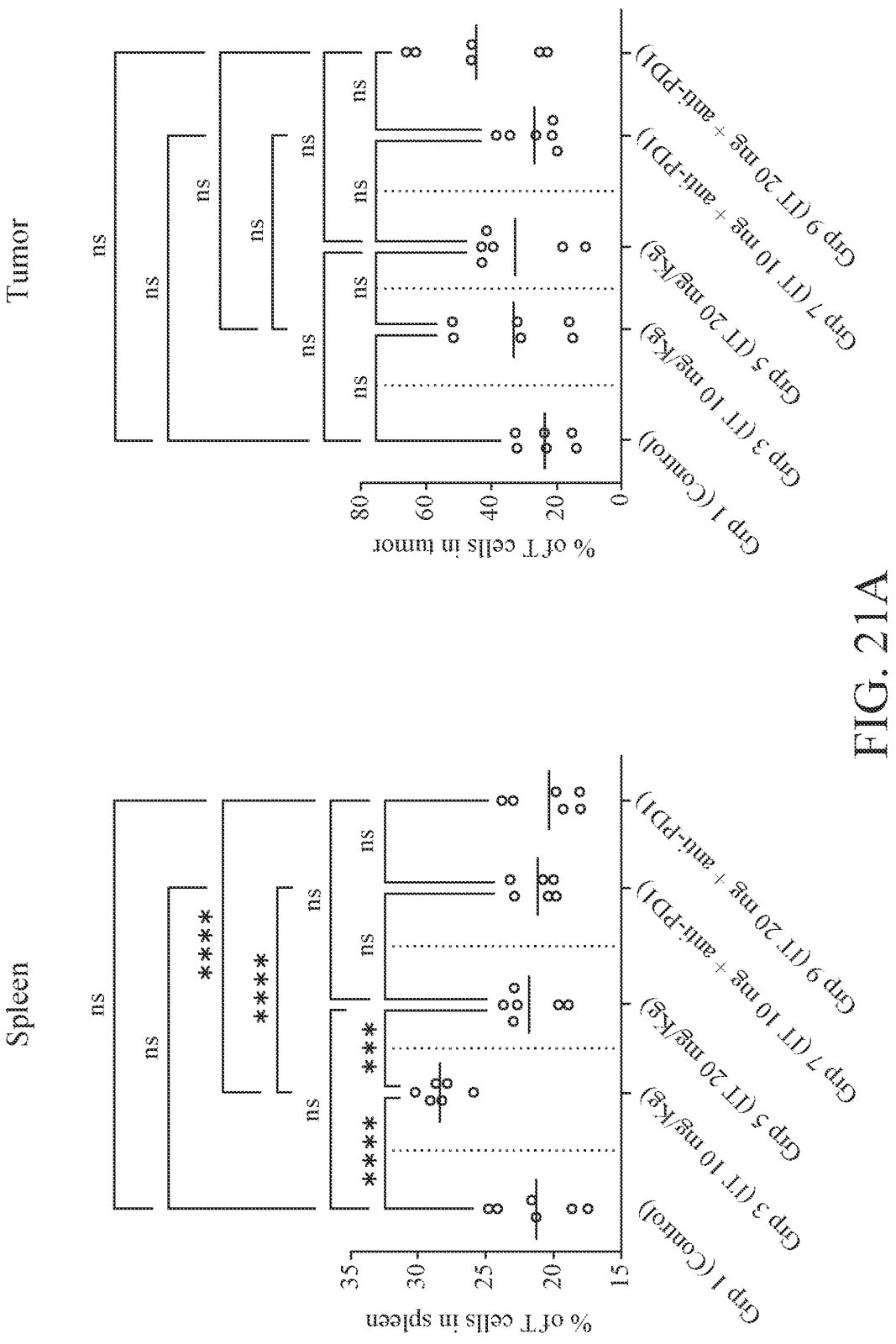

Tumor
% of T cells in tumor
0
20
40
60
80
ns
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 5 (IT 20 mg/Kg)
Grp 7 (IT 10 mg + anti-PD1)
Grp 9 (IT 20 mg + anti-PD1)
Spleen
% of T cells in spleen
15
20
25
30
35
****
ns
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 5 (IT 20 mg/Kg)
Grp 7 (IT 10 mg + anti-PD1)
Grp 9 (IT 20 mg + anti-PD1)

FIG. 21A

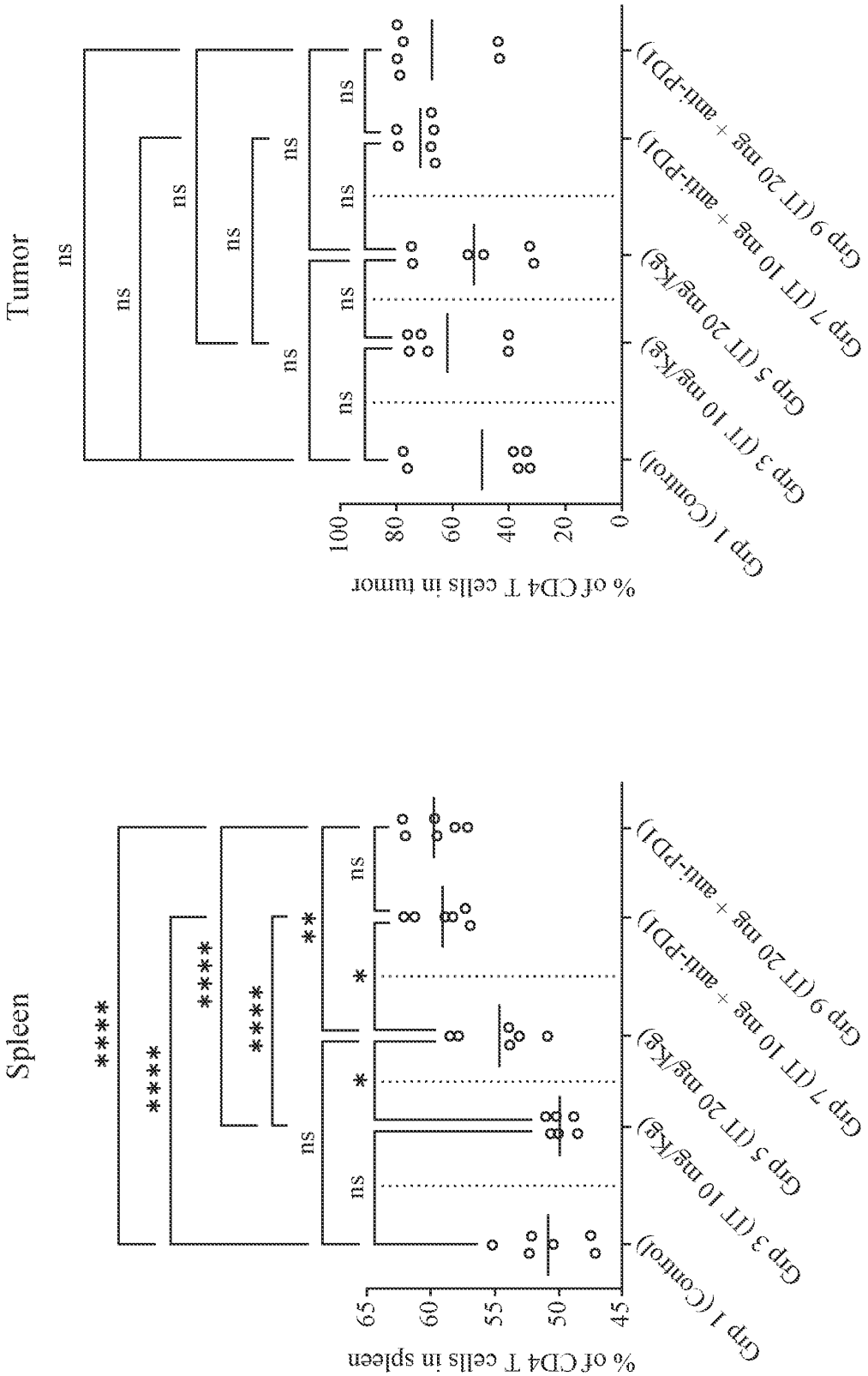

Spleen
% of CD4 T cells in spleen
65
60
55
50
45
****
****
****
****
**
*
*
ns
ns
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 5 (IT 20 mg/Kg)
Grp 7 (IT 10 mg + anti-PD1)
Grp 9 (IT 20 mg + anti-PD1)
Tumor
% of CD4 T cells in tumor
100
80
60
40
20
0
ns
ns
ns
ns
ns
ns
ns
ns
ns
ns
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 5 (IT 20 mg/Kg)
Grp 7 (IT 10 mg + anti-PD1)
Grp 9 (IT 20 mg + anti-PD1)

FIG. 21B

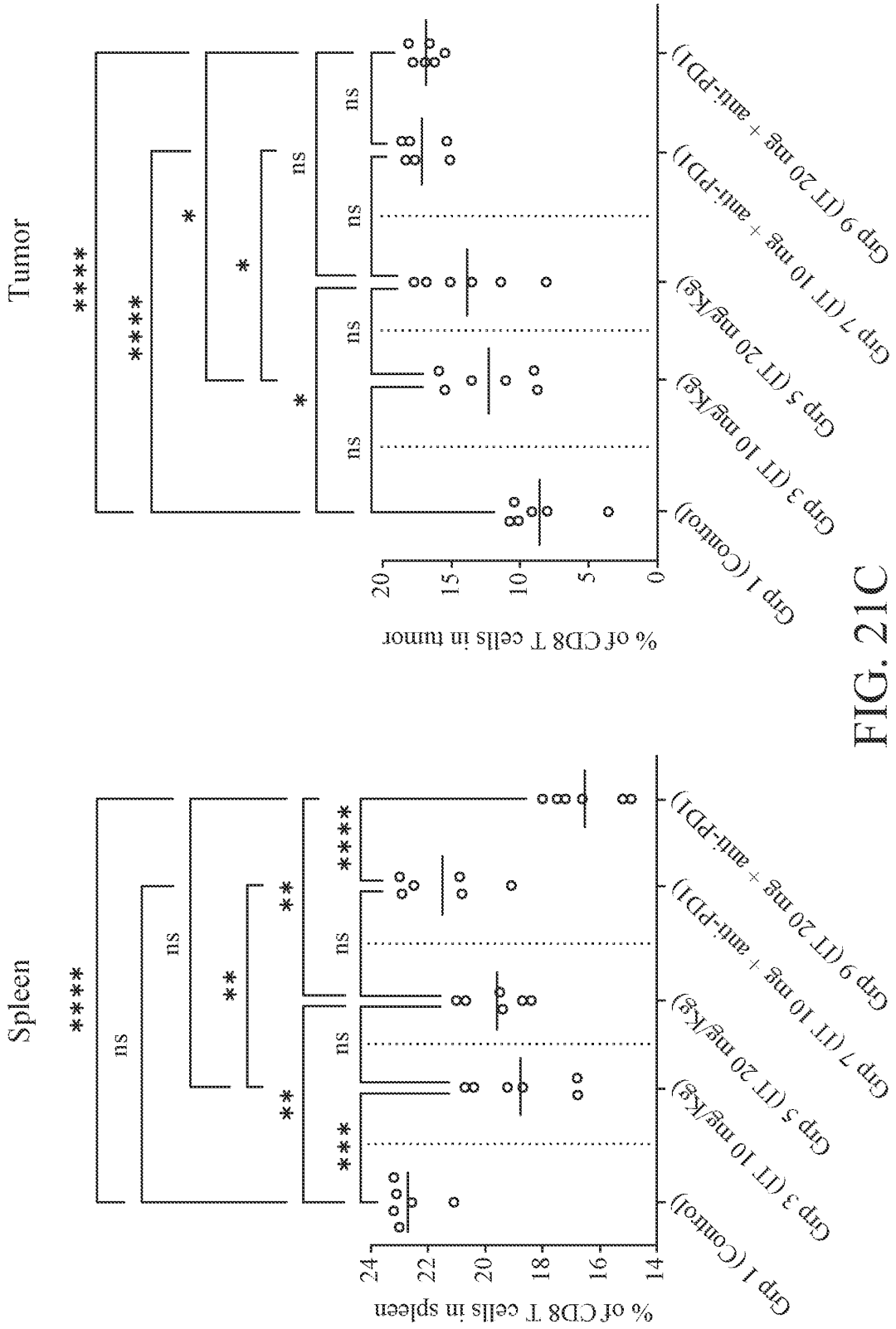

Tumor
% of CD8 T cells in tumor
20
15
10
5
0
****
****
*
*
*
ns
ns
ns
ns
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 5 (IT 20 mg/Kg)
Grp 7 (IT 10 mg + anti-PD1)
Grp 9 (IT 20 mg + anti-PD1)
Spleen
% of CD8 T cells in spleen
24
22
20
18
16
14
****
ns
**
**
***
**
****
ns
ns
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 5 (IT 20 mg/Kg)
Grp 7 (IT 10 mg + anti-PD1)
Grp 9 (IT 20 mg + anti-PD1)

FIG. 21C

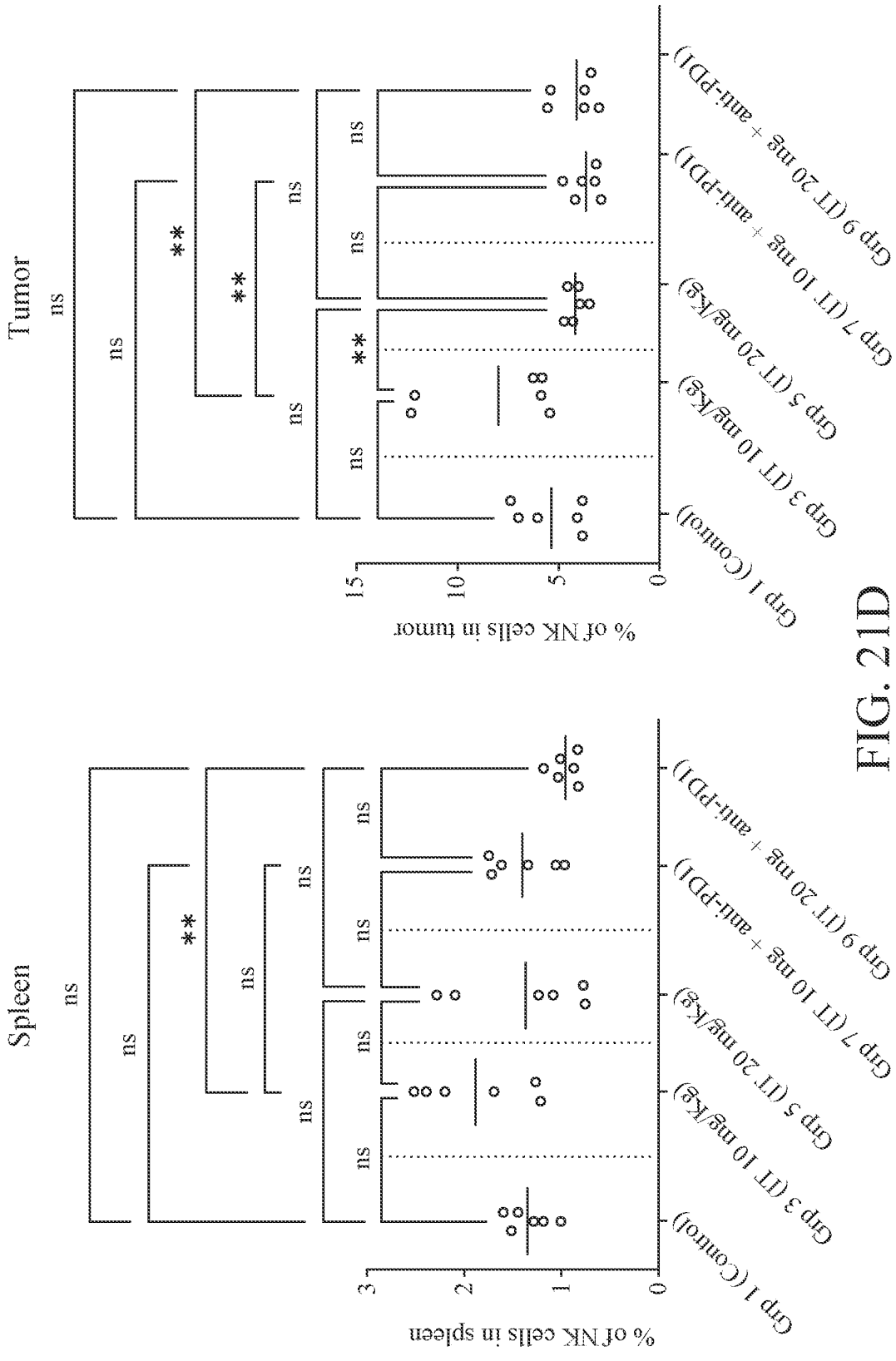

Tumor
% of NK cells in tumor
0
5
10
15
ns
**
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 5 (IT 20 mg/Kg)
Grp 7 (IT 10 mg + anti-PD1)
Grp 9 (IT 20 mg + anti-PD1)
Spleen
% of NK cells in spleen
0
1
2
3

FIG. 21D

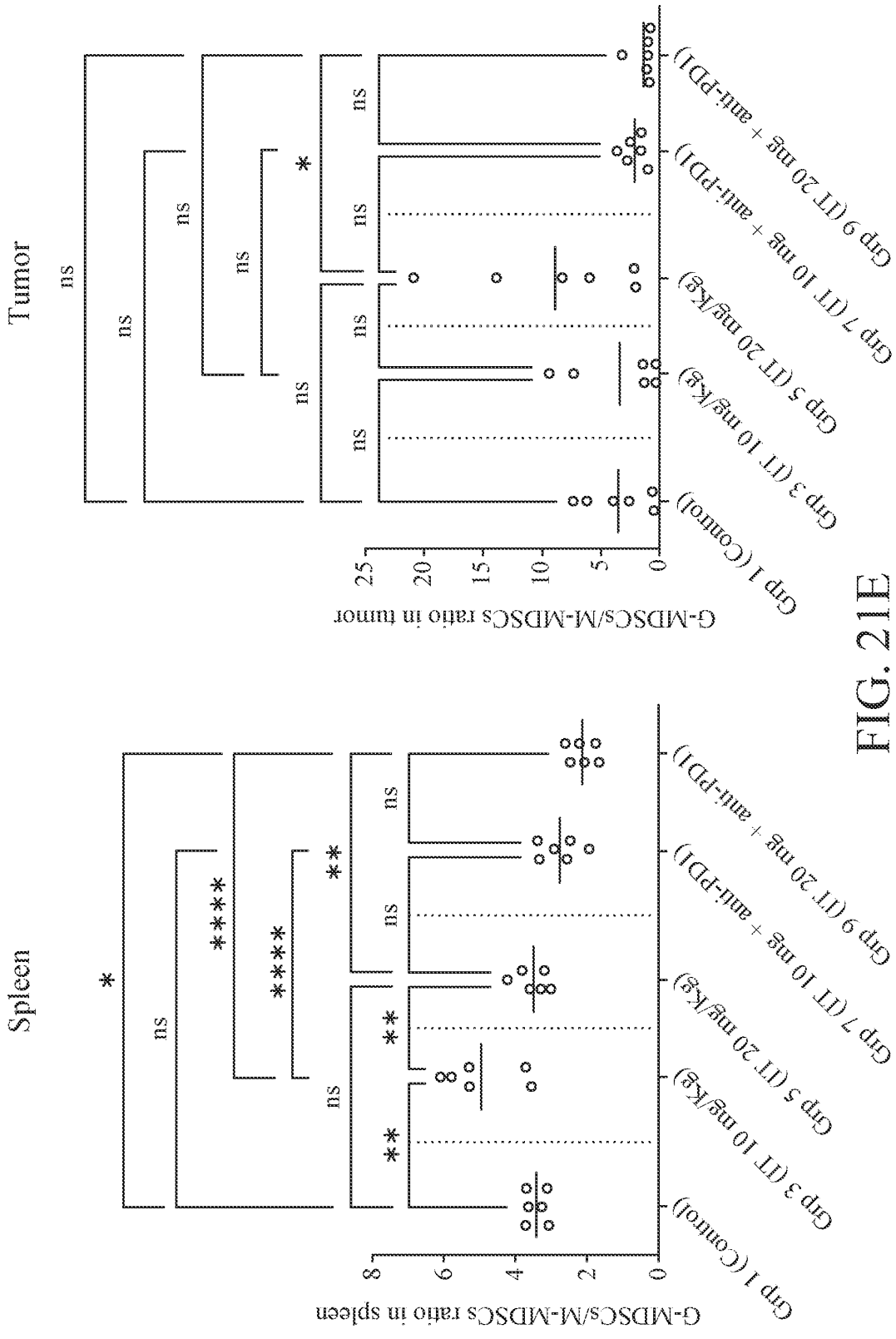

Tumor
G-MDSCs/M-MDSCs ratio in tumor
0
5
10
15
20
25
ns
ns
ns
*
ns
ns
ns
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 5 (IT 20 mg/Kg)
Grp 7 (IT 10 mg + anti-PD1)
Grp 9 (IT 20 mg + anti-PD1)
Spleen
G-MDSCs/M-MDSCs ratio in spleen
0
2
4
6
8
*
ns
****
****
**
**
**
ns
ns
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 5 (IT 20 mg/Kg)
Grp 7 (IT 10 mg + anti-PD1)
Grp 9 (IT 20 mg + anti-PD1)

FIG. 21E

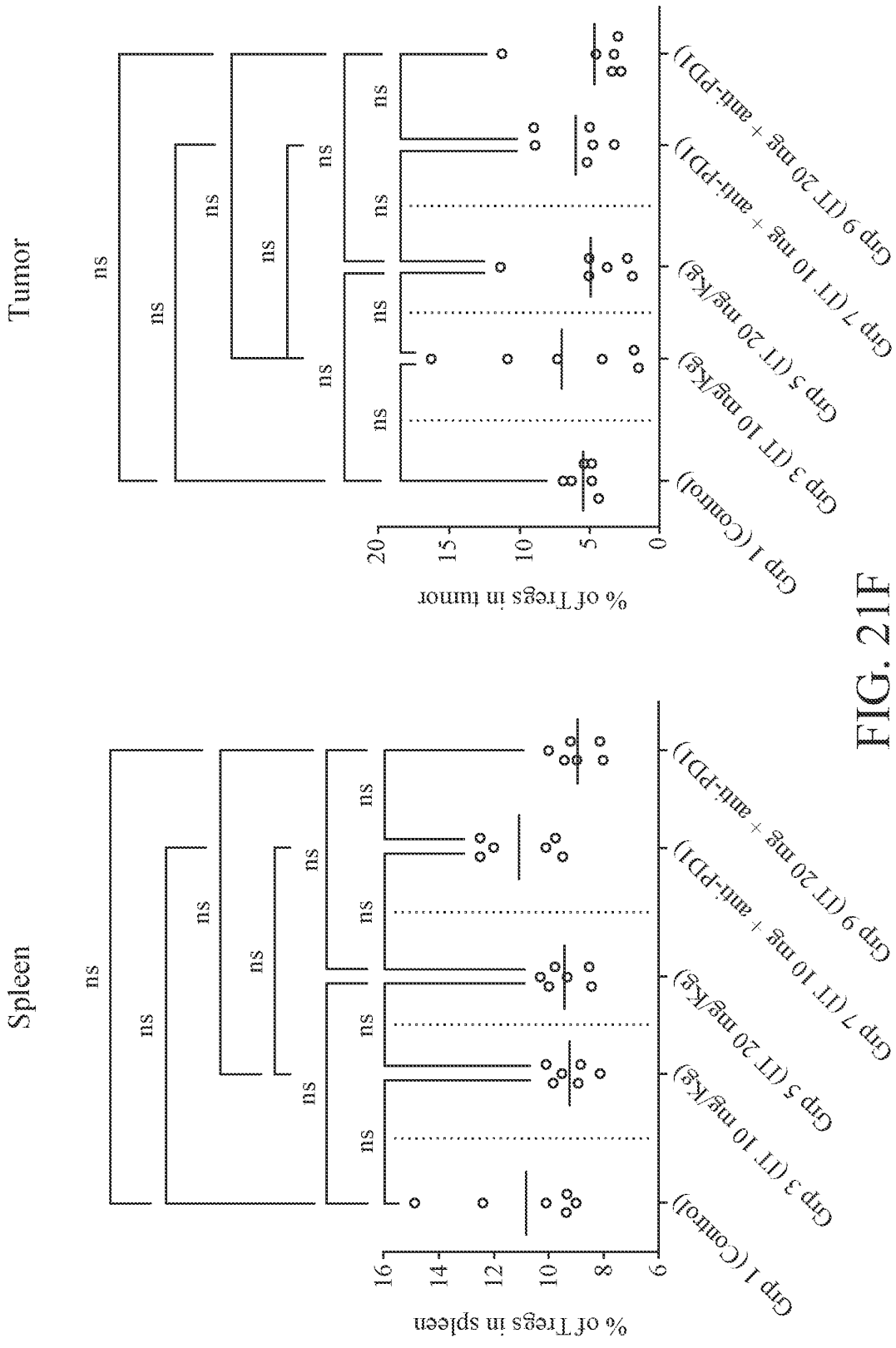

Tumor
% of Tregs in tumor
0
5
10
15
20
ns
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 5 (IT 20 mg/Kg)
Grp 7 (IT 10 mg + anti-PD1)
Grp 9 (IT 20 mg + anti-PD1)
Spleen
% of Tregs in spleen
6
8
10
12
14
16

FIG. 21F

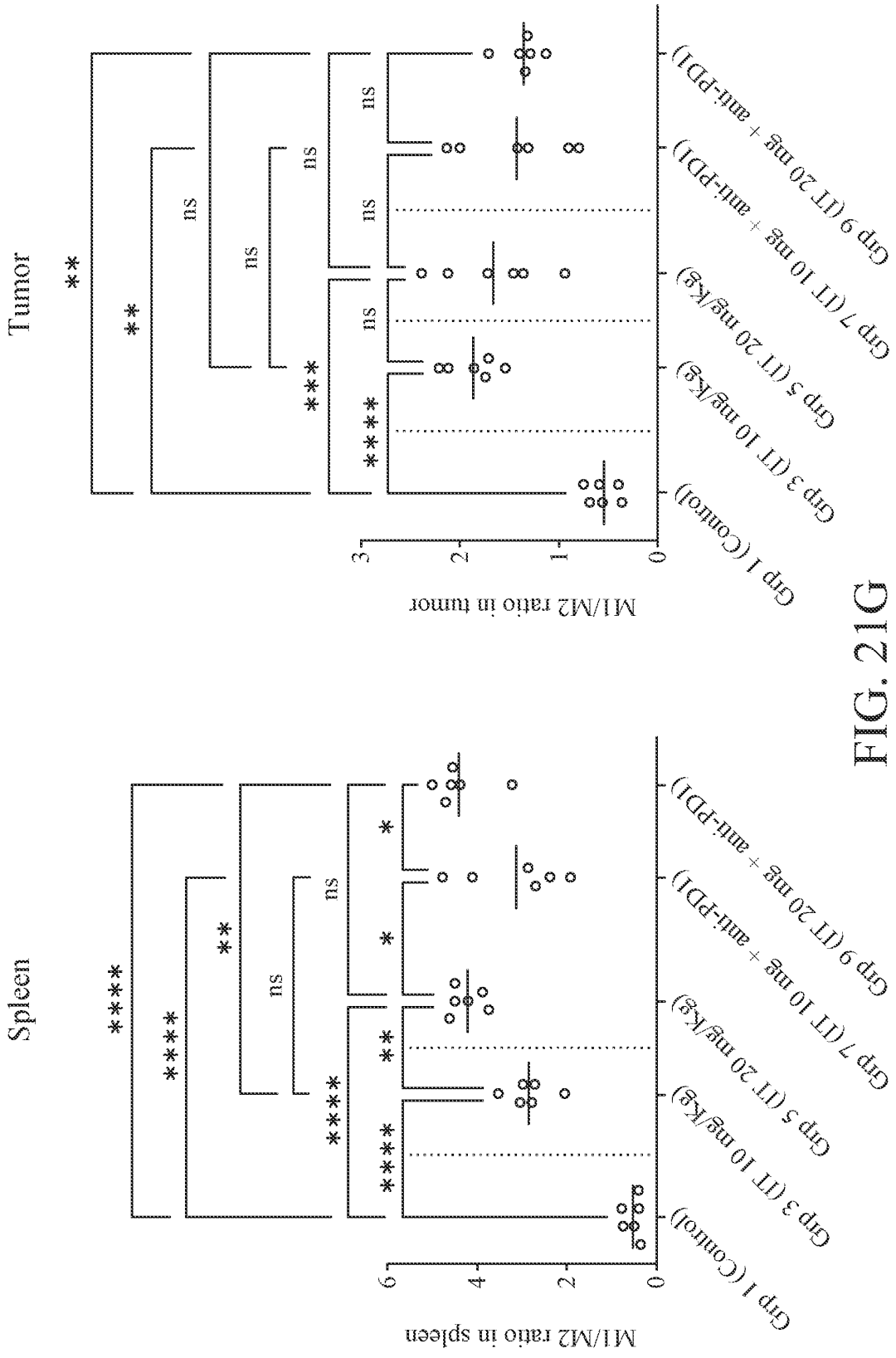

Tumor
M1/M2 ratio in tumor
0
1
2
3
ns
ns
ns
ns
ns
**
**
***
****
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 5 (IT 20 mg/Kg)
Grp 7 (IT 10 mg + anti-PD1)
Grp 9 (IT 20 mg + anti-PD1)
Spleen
M1/M2 ratio in spleen
0
2
4
6
ns
*
*
**
****
****
****
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 5 (IT 20 mg/Kg)
Grp 7 (IT 10 mg + anti-PD1)
Grp 9 (IT 20 mg + anti-PD1)

FIG. 21G

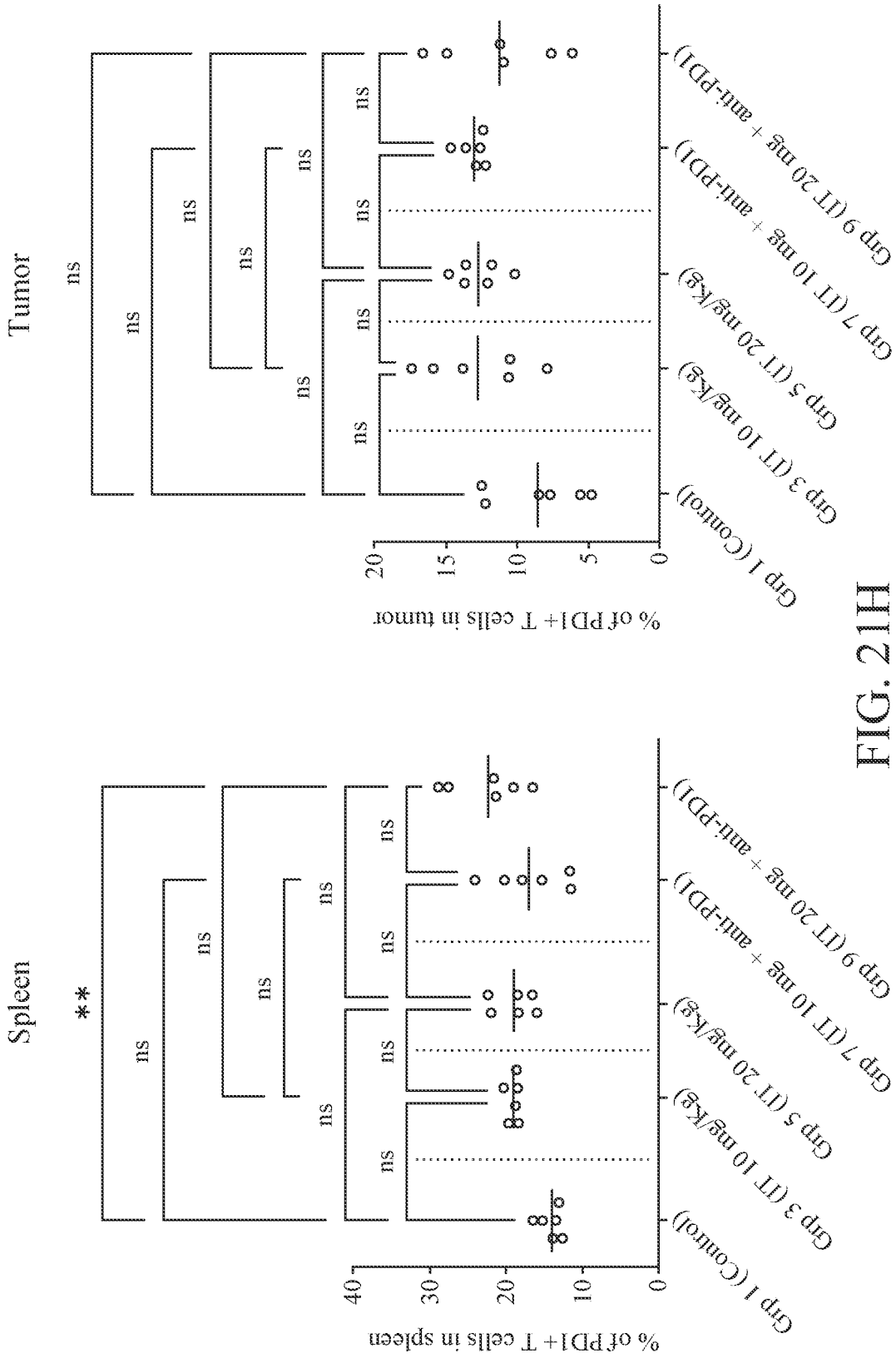

Tumor
% of PD1+ T cells in tumor
0
5
10
15
20
ns
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 5 (IT 20 mg/Kg)
Grp 7 (IT 10 mg + anti-PD1)
Grp 9 (IT 20 mg + anti-PD1)
Spleen
% of PD1+ T cells in spleen
0
10
20
30
40
**
ns
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 5 (IT 20 mg/Kg)
Grp 7 (IT 10 mg + anti-PD1)
Grp 9 (IT 20 mg + anti-PD1)

FIG. 21H

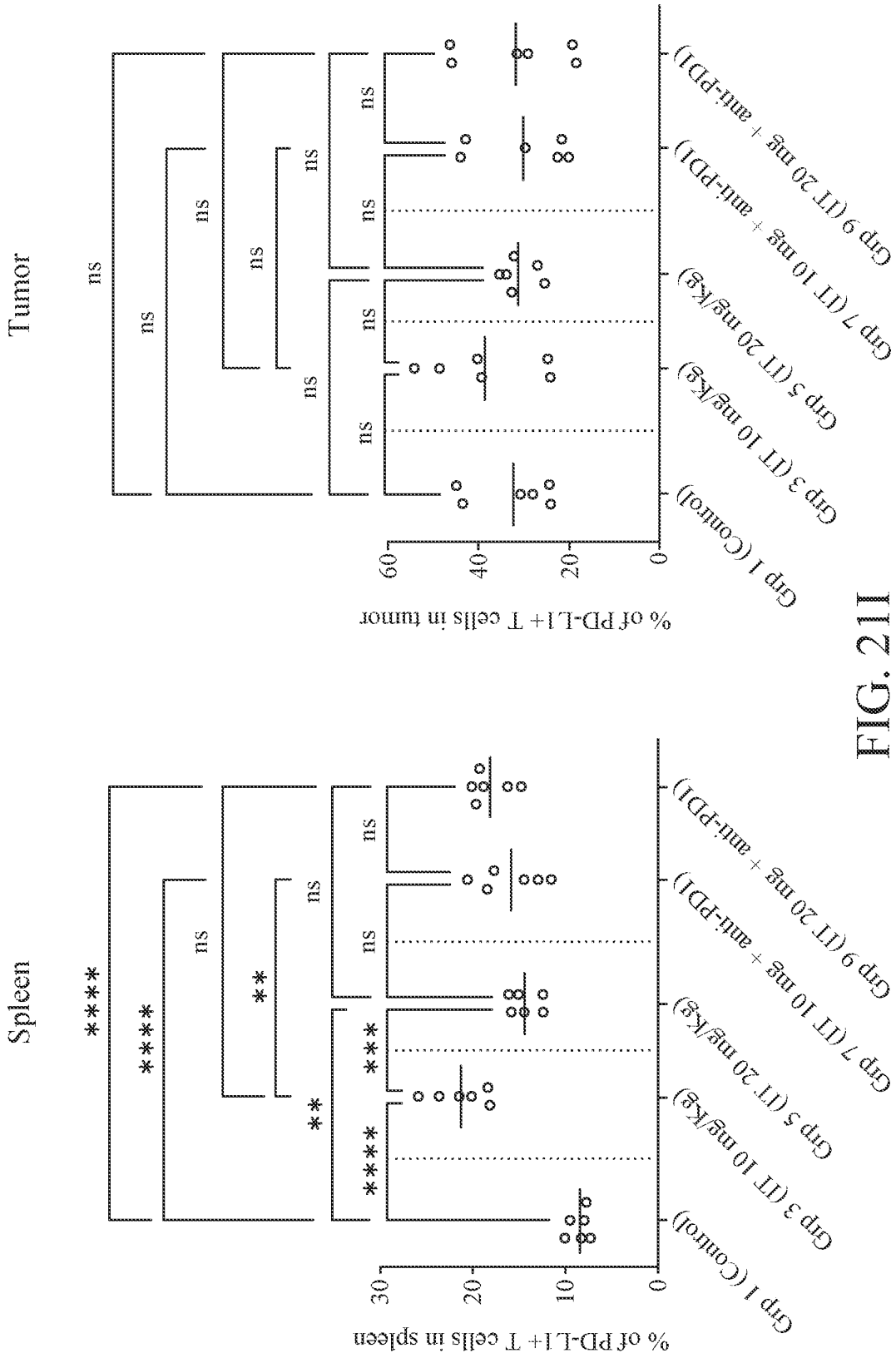

Tumor
% of PD-L1+ T cells in tumor
0
20
40
60
ns
ns
ns
ns
ns
ns
ns
ns
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 5 (IT 20 mg/Kg)
Grp 7 (IT 10 mg + anti-PD1)
Grp 9 (IT 20 mg + anti-PD1)
Spleen
% of PD-L1+ T cells in spleen
0
10
20
30
****
****
ns
**
**
****
***
ns
ns
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 5 (IT 20 mg/Kg)
Grp 7 (IT 10 mg + anti-PD1)
Grp 9 (IT 20 mg + anti-PD1)

FIG. 21I

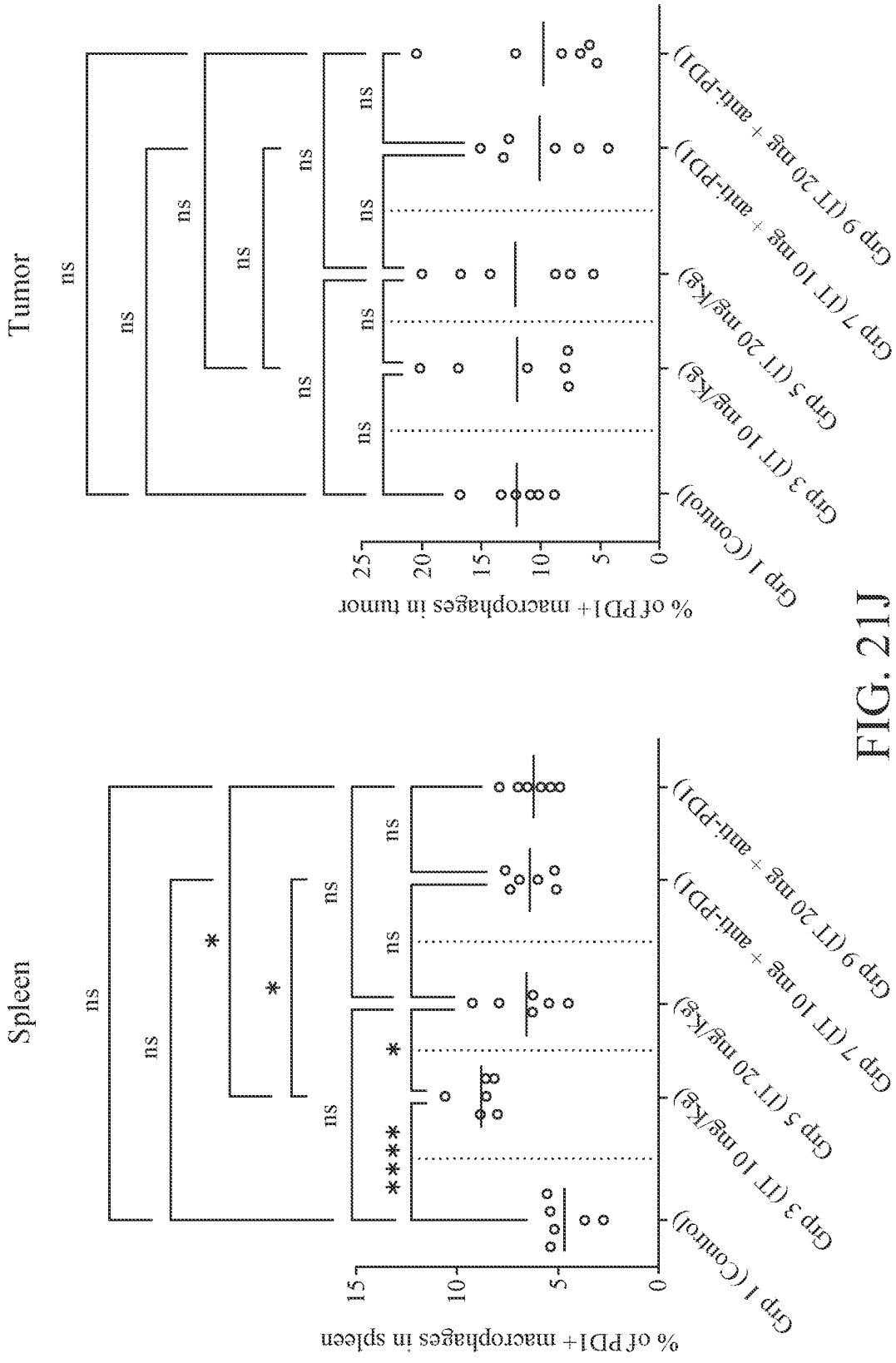

Tumor
% of PD1+ macrophages in tumor
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 5 (IT 20 mg/Kg)
Grp 7 (IT 10 mg/Kg + anti-PD1)
Grp 9 (IT 20 mg/Kg + anti-PD1)
ns
Spleen
% of PD1+ macrophages in spleen
****
*

FIG. 21J

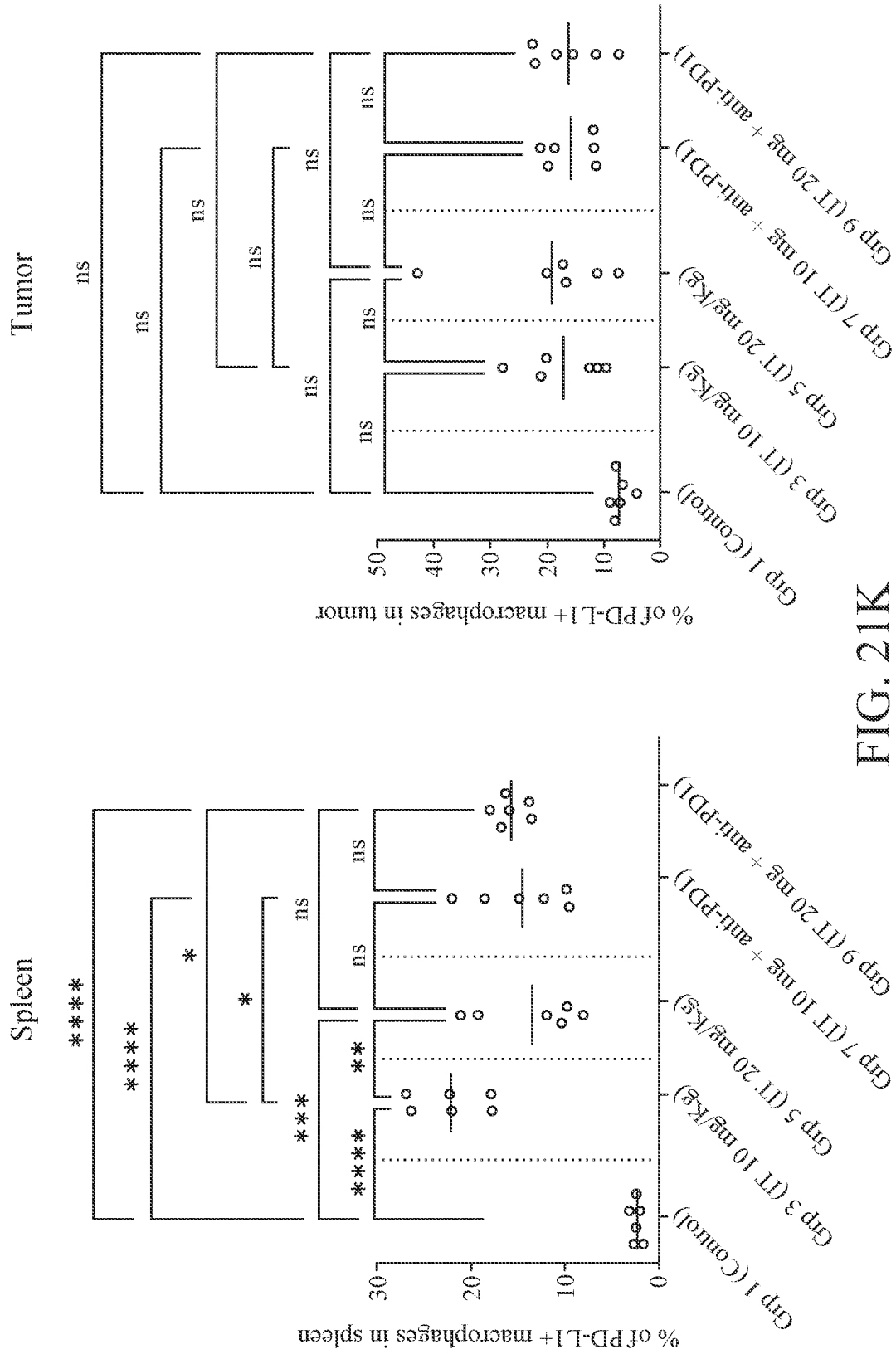

Tumor
% of PD-L1+ macrophages in tumor
0
10
20
30
40
50
ns
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 5 (IT 20 mg/Kg)
Grp 7 (IT 10 mg + anti-PD1)
Grp 9 (IT 20 mg + anti-PD1)
Spleen
% of PD-L1+ macrophages in spleen
0
10
20
30
****
****
*
*
***
****
**
ns
ns
ns
Grp 1 (Control)
Grp 3 (IT 10 mg/Kg)
Grp 5 (IT 20 mg/Kg)
Grp 7 (IT 10 mg + anti-PD1)
Grp 9 (IT 20 mg + anti-PD1)

FIG. 21K

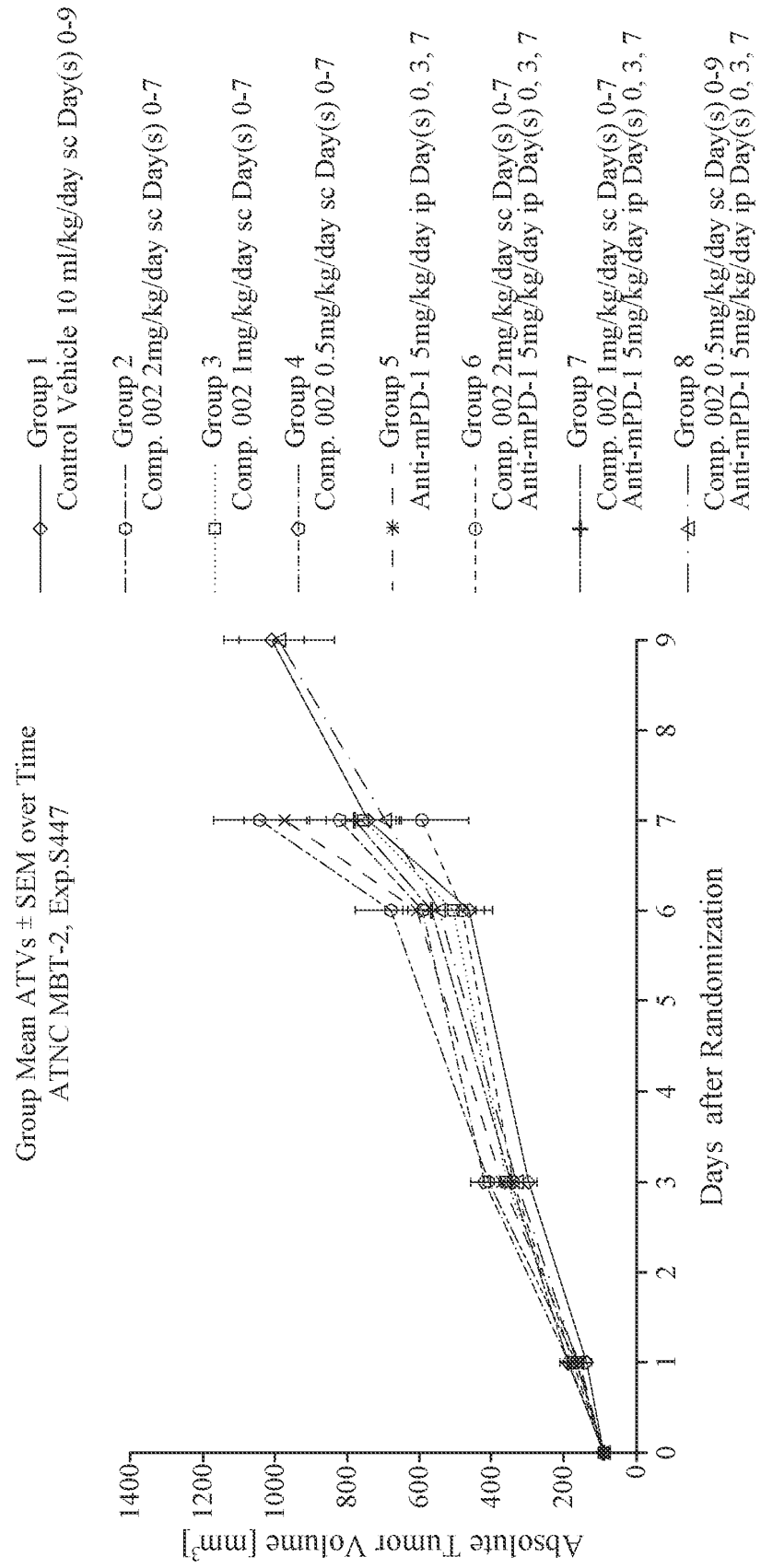

Group Mean ATVs ± SEM over Time
ATNC MBT-2, Exp.S447
Absolute Tumor Volume [mm³]
1400
1200
1000
800
600
400
200
0
0
1
2
3
4
5
6
7
8
9
Days after Randomization
Group 1
Control Vehicle 10 ml/kg/day sc Day(s) 0-9
Group 2
Comp. 002 2mg/kg/day sc Day(s) 0-7
Group 3
Comp. 002 1mg/kg/day sc Day(s) 0-7
Group 4
Comp. 002 0.5mg/kg/day sc Day(s) 0-7
Group 5
Anti-mPD-1 5mg/kg/day ip Day(s) 0, 3, 7
Group 6
Comp. 002 2mg/kg/day sc Day(s) 0-7
Anti-mPD-1 5mg/kg/day ip Day(s) 0, 3, 7
Group 7
Comp. 002 1mg/kg/day sc Day(s) 0-7
Anti-mPD-1 5mg/kg/day ip Day(s) 0, 3, 7
Group 8
Comp. 002 0.5mg/kg/day sc Day(s) 0-9
Anti-mPD-1 5mg/kg/day ip Day(s) 0, 3, 7

FIG. 22A

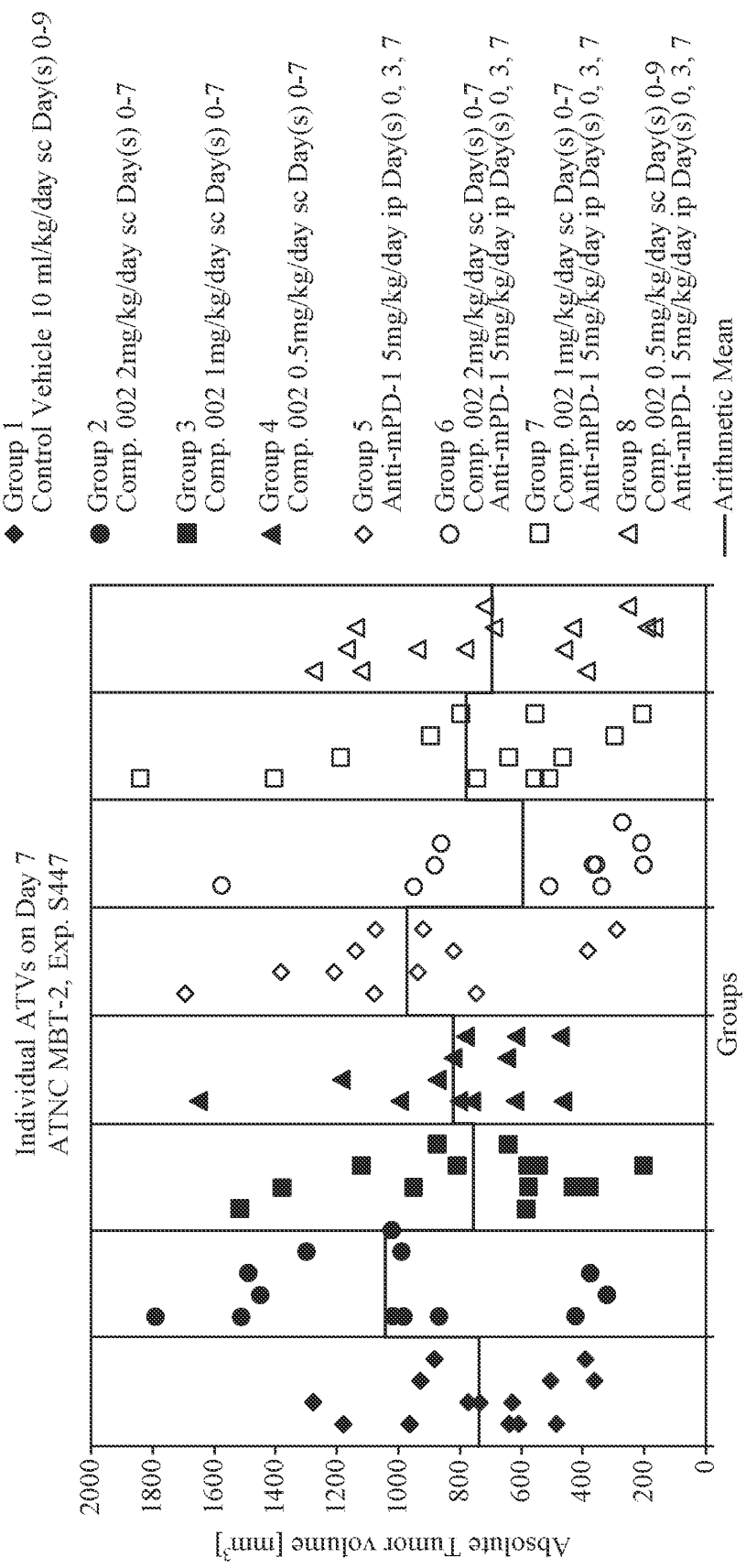

Individual ATVs on Day 7
ATNC MBT-2, Exp. S447
Absolute Tumor volume [mm³]
2000
1800
1600
1400
1200
1000
800
600
400
200
0
Groups
Group 1
Control Vehicle 10 ml/kg/day sc Day(s) 0-9
Group 2
Comp. 002 2mg/kg/day sc Day(s) 0-7
Group 3
Comp. 002 1mg/kg/day sc Day(s) 0-7
Group 4
Comp. 002 0.5mg/kg/day sc Day(s) 0-7
Group 5
Anti-mPD-1 5mg/kg/day ip Day(s) 0, 3, 7
Group 6
Comp. 002 2mg/kg/day sc Day(s) 0-7
Anti-mPD-1 5mg/kg/day ip Day(s) 0, 3, 7
Group 7
Comp. 002 1mg/kg/day sc Day(s) 0-7
Anti-mPD-1 5mg/kg/day ip Day(s) 0, 3, 7
Group 8
Comp. 002 0.5mg/kg/day sc Day(s) 0-9
Anti-mPD-1 5mg/kg/day ip Day(s) 0, 3, 7
Arithmetic Mean

FIG. 22B

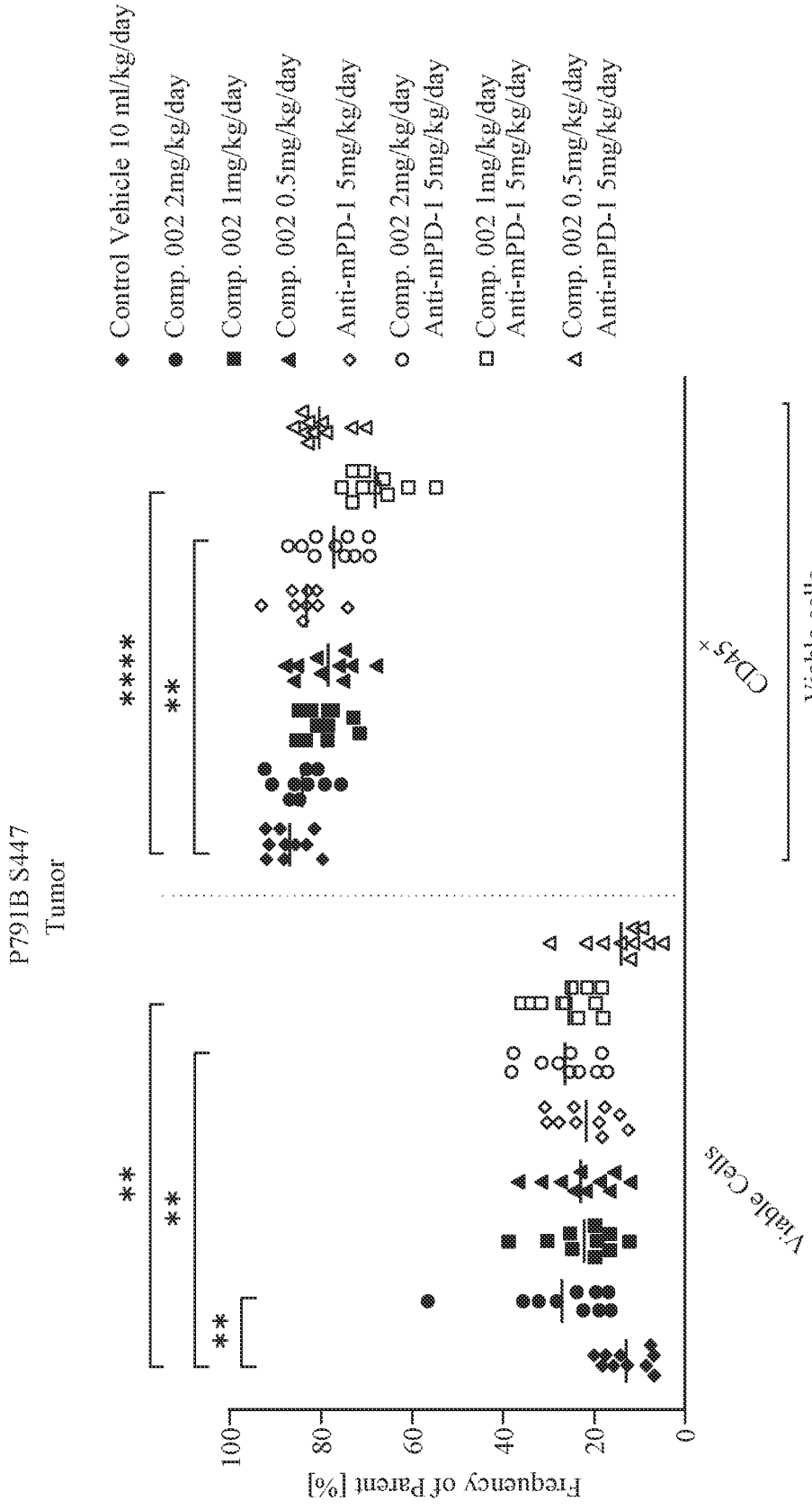

P791B S447
Tumor
Control Vehicle 10 ml/kg/day
Comp. 002 2mg/kg/day
Comp. 002 1mg/kg/day
Comp. 002 0.5mg/kg/day
Anti-mPD-1 5mg/kg/day
Comp. 002 2mg/kg/day Anti-mPD-1 5mg/kg/day
Comp. 002 1mg/kg/day Anti-mPD-1 5mg/kg/day
Comp. 002 0.5mg/kg/day Anti-mPD-1 5mg/kg/day
Frequency of Parent [%]
100
80
60
40
20
0
Viable Cells
CD45+
Viable cells
**
**
**
**
****

FIG. 23A

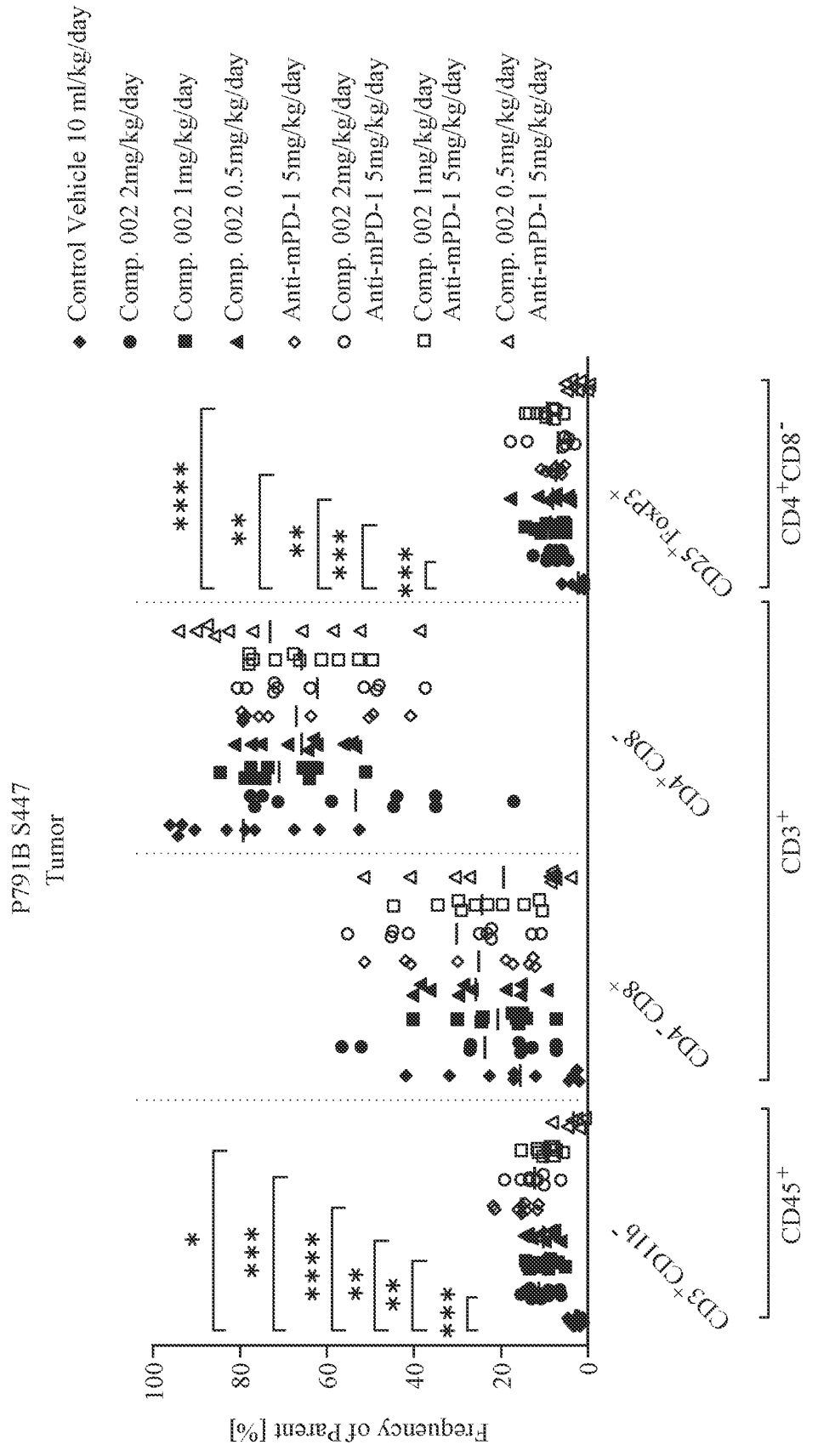

Control Vehicle 10 ml/kg/day
Comp. 002 2mg/kg/day
Comp. 002 1mg/kg/day
Comp. 002 0.5mg/kg/day
Anti-mPD-1 5mg/kg/day
Comp. 002 2mg/kg/day Anti-mPD-1 5mg/kg/day
Comp. 002 1mg/kg/day Anti-mPD-1 5mg/kg/day
Comp. 002 0.5mg/kg/day Anti-mPD-1 5mg/kg/day
P791B S447
Tumor
Frequency of Parent [%]
100
80
60
40
20
0
CD3+CD11b-
CD45+
CD4-CD8+
CD4+CD8-
CD3+
CD4+CD8-
CD25+FoxP3+
CD4+CD8-

FIG. 23B

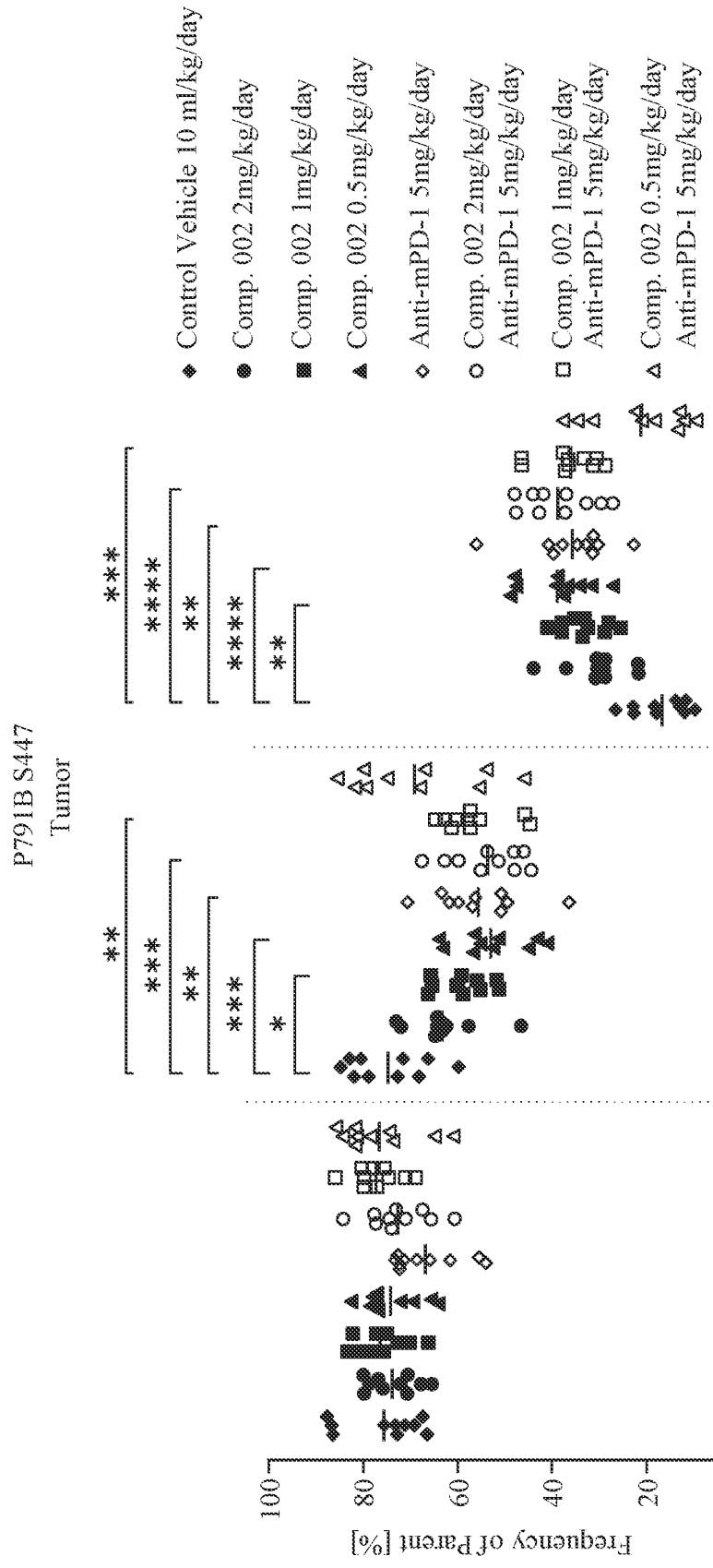

P791B S447
Tumor
Frequency of Parent [%]
100
80
60
40
20
0
CD3-CD11b+
CD45+
gMDSC
mMDSC
CD3-CD11b+
Control Vehicle 10 ml/kg/day
Comp. 002 2mg/kg/day
Comp. 002 1mg/kg/day
Comp. 002 0.5mg/kg/day
Anti-mPD-1 5mg/kg/day
Comp. 002 2mg/kg/day Anti-mPD-1 5mg/kg/day
Comp. 002 1mg/kg/day Anti-mPD-1 5mg/kg/day
Comp. 002 0.5mg/kg/day Anti-mPD-1 5mg/kg/day

FIG. 23C

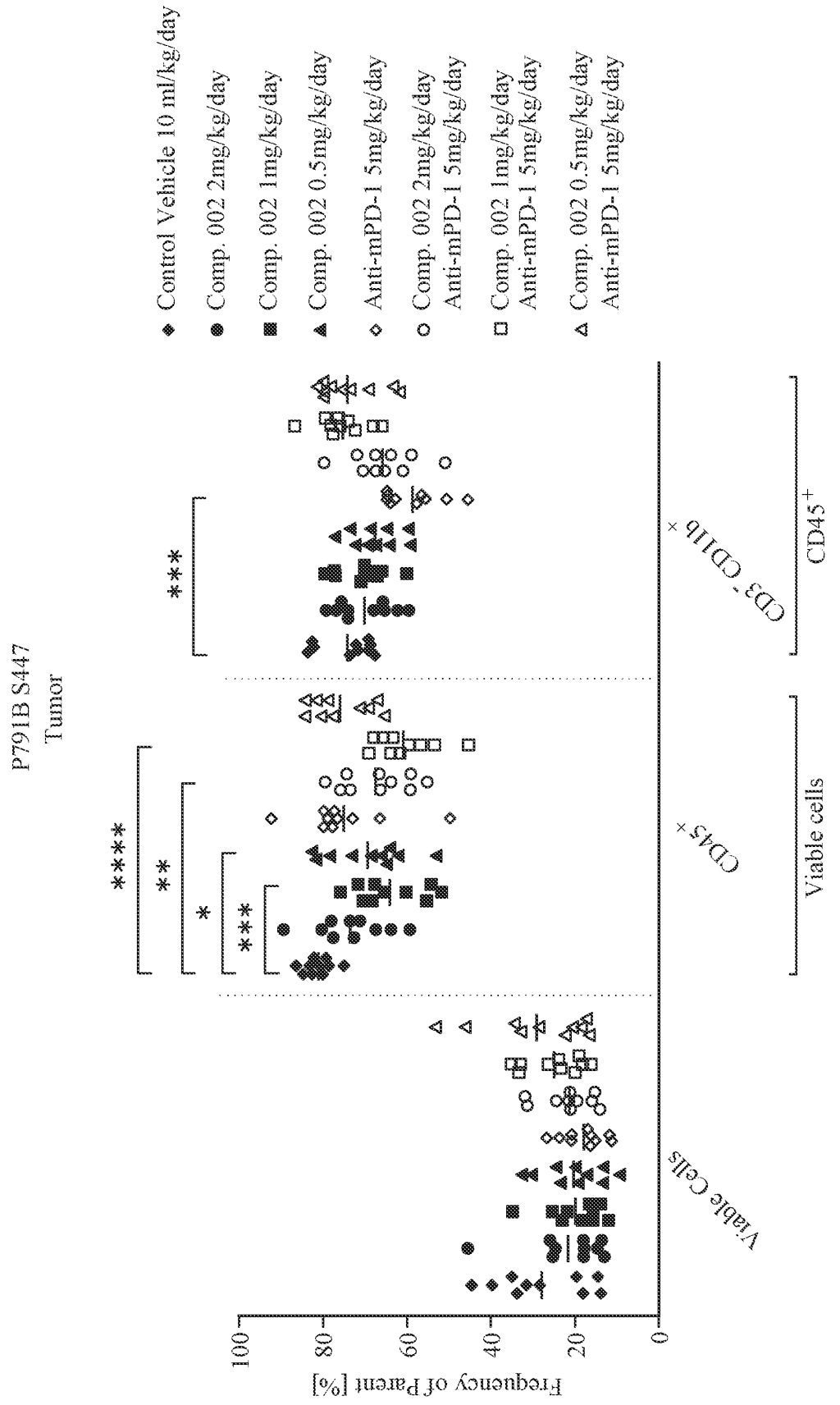

P791B S447
Tumor
Control Vehicle 10 ml/kg/day
Comp. 002 2mg/kg/day
Comp. 002 1mg/kg/day
Comp. 002 0.5mg/kg/day
Anti-mPD-1 5mg/kg/day
Comp. 002 2mg/kg/day Anti-mPD-1 5mg/kg/day
Comp. 002 1mg/kg/day Anti-mPD-1 5mg/kg/day
Comp. 002 0.5mg/kg/day Anti-mPD-1 5mg/kg/day
Frequency of Parent [%]
100
80
60
40
20
0
Viable cells
CD45+
Viable cells
CD45+
CD3- CD11b+
CD3- CD11b+
****
**
*
***
***

FIG. 23D

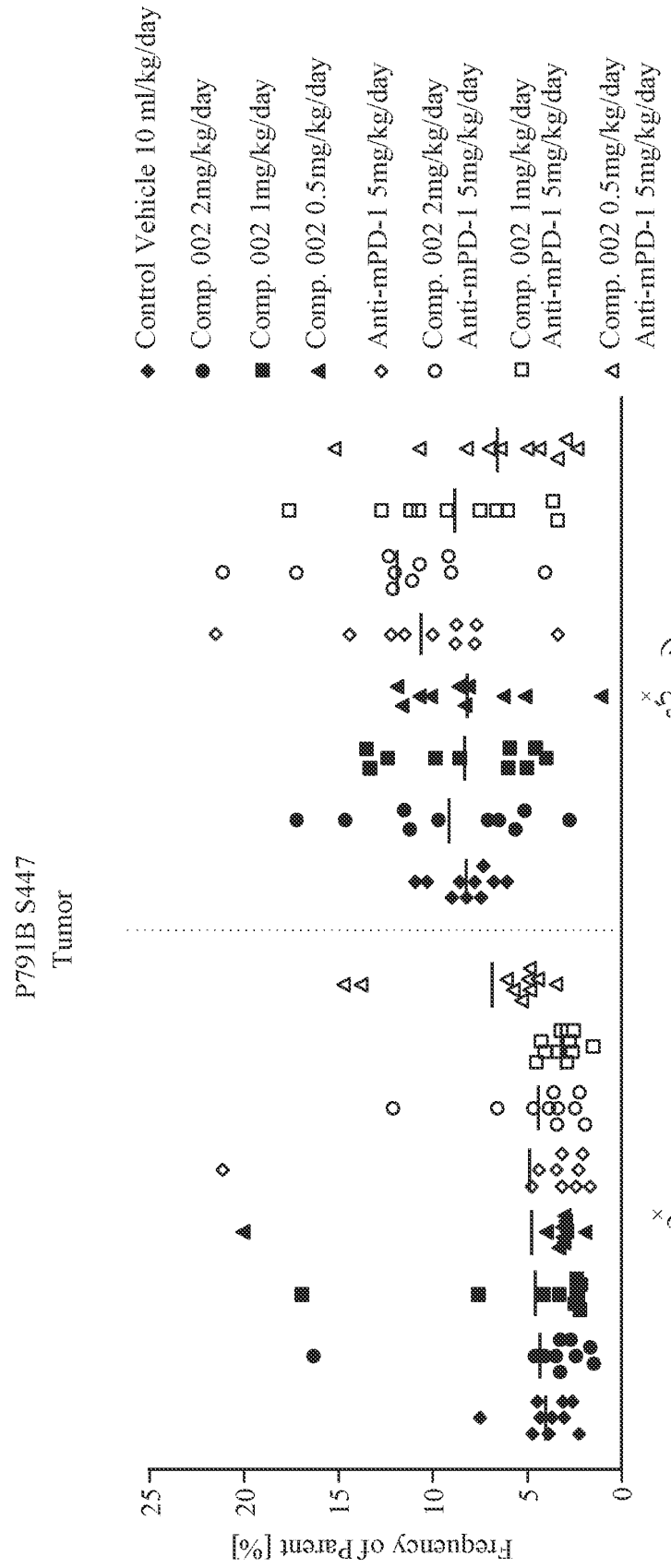

P791B S447
Tumor
Frequency of Parent [%]
25
20
15
10
5
0
CD3⁻CD11b⁺
CD49⁺
CD49⁺
CD335⁺
(NK cells)
Control Vehicle 10 ml/kg/day
Comp. 002 2mg/kg/day
Comp. 002 1mg/kg/day
Comp. 002 0.5mg/kg/day
Anti-mPD-1 5mg/kg/day
Comp. 002 2mg/kg/day
Anti-mPD-1 5mg/kg/day
Comp. 002 1mg/kg/day
Anti-mPD-1 5mg/kg/day
Comp. 002 0.5mg/kg/day
Anti-mPD-1 5mg/kg/day

FIG. 23E

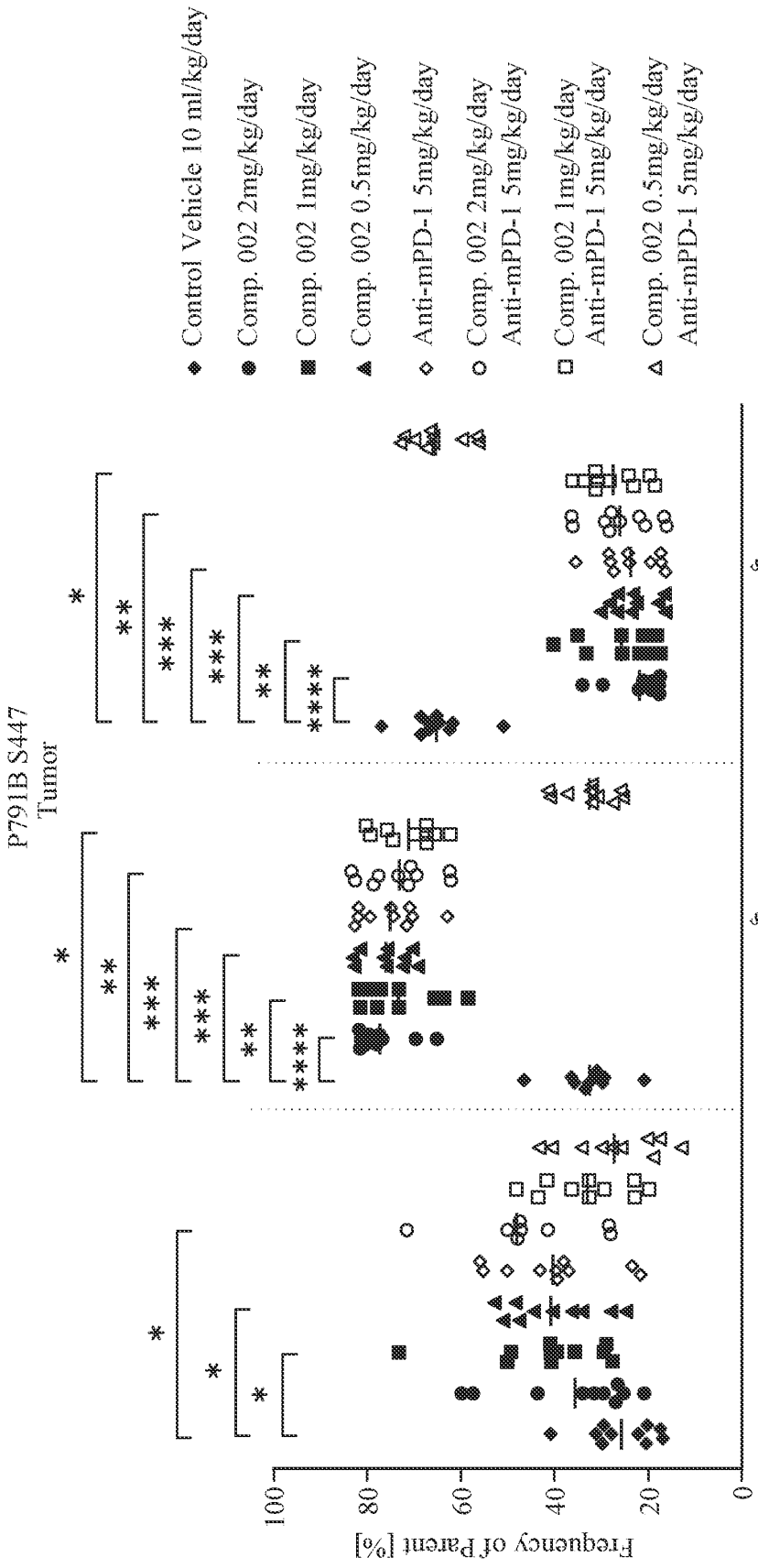

Control Vehicle 10 ml/kg/day
Comp. 002 2mg/kg/day
Comp. 002 1mg/kg/day
Comp. 002 0.5mg/kg/day
Anti-mPD-1 5mg/kg/day
Comp. 002 2mg/kg/day Anti-mPD-1 5mg/kg/day
Comp. 002 1mg/kg/day Anti-mPD-1 5mg/kg/day
Comp. 002 0.5mg/kg/day Anti-mPD-1 5mg/kg/day
P791B S447 Tumor
Frequency of Parent [%]
M1 Macrophages
M2 Macrophages
F4/80+
CD3-CD11b+
F4/80+

FIG. 23F

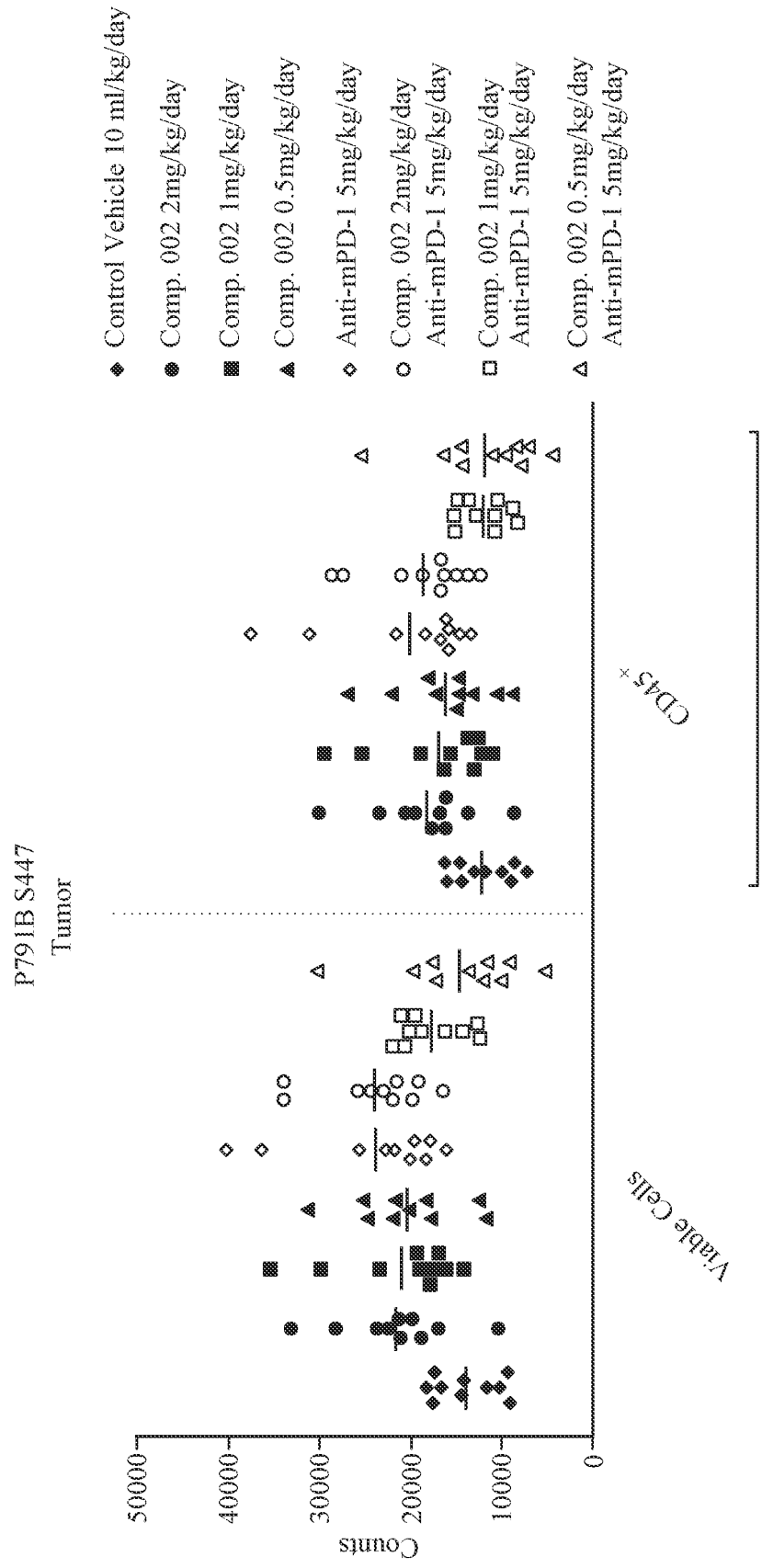

Control Vehicle 10 ml/kg/day
Comp. 002 2mg/kg/day
Comp. 002 1mg/kg/day
Comp. 002 0.5mg/kg/day
Anti-mPD-1 5mg/kg/day
Comp. 002 2mg/kg/day Anti-mPD-1 5mg/kg/day
Comp. 002 1mg/kg/day Anti-mPD-1 5mg/kg/day
Comp. 002 0.5mg/kg/day Anti-mPD-1 5mg/kg/day
P791B S447
Tumor
Counts
50000
40000
30000
20000
10000
0
Viable Cells
CD45+
Viable cells

FIG. 24A

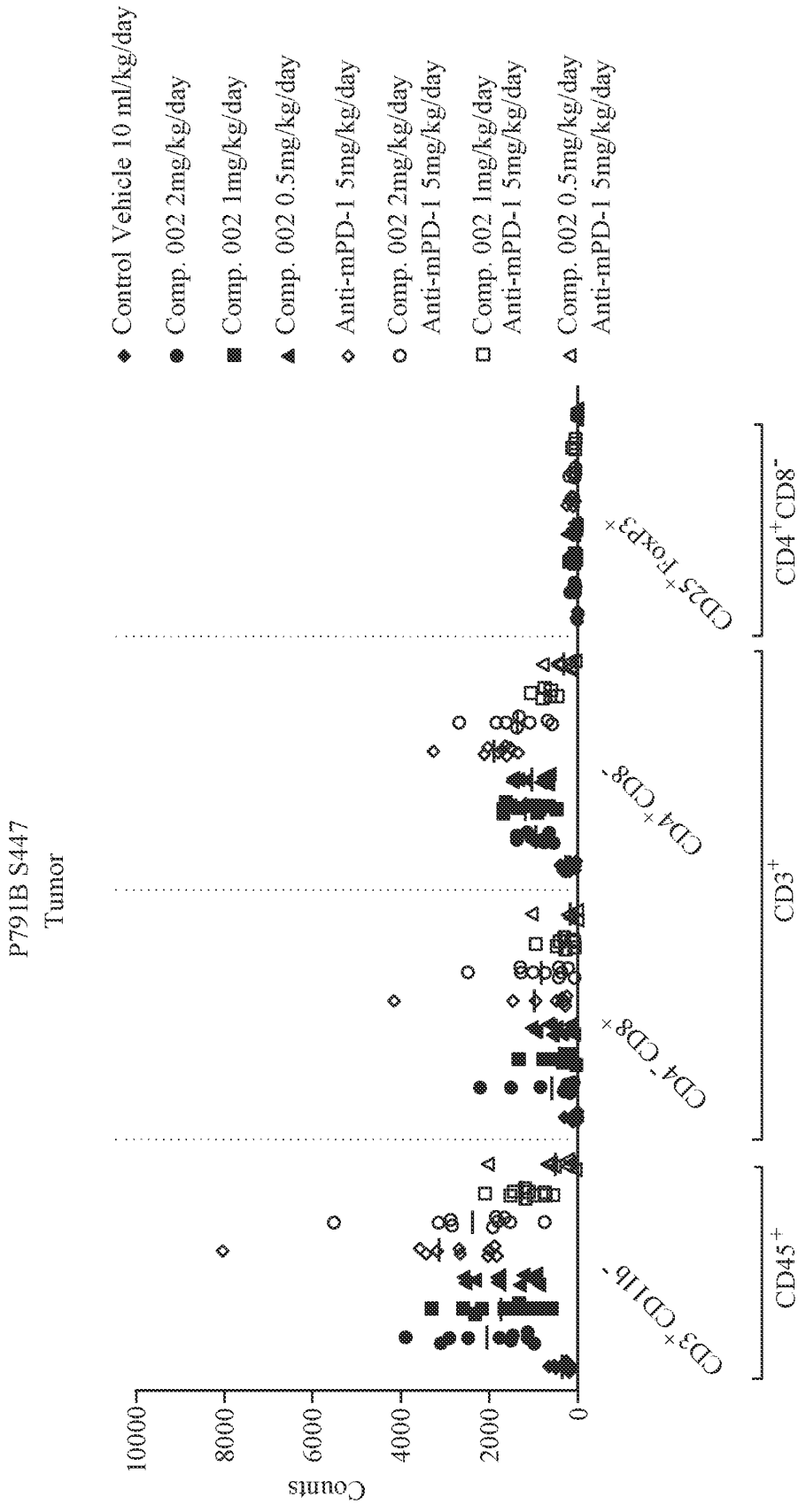

P791B S447
Tumor
Counts
10000
8000
6000
4000
2000
0
Control Vehicle 10 ml/kg/day
Comp. 002 2mg/kg/day
Comp. 002 1mg/kg/day
Comp. 002 0.5mg/kg/day
Anti-mPD-1 5mg/kg/day
Comp. 002 2mg/kg/day Anti-mPD-1 5mg/kg/day
Comp. 002 1mg/kg/day Anti-mPD-1 5mg/kg/day
Comp. 002 0.5mg/kg/day Anti-mPD-1 5mg/kg/day
CD3+CD11b-
CD4-CD8+
CD4+CD8-
CD25+FoxP3+
CD45+
CD3+

FIG. 24B

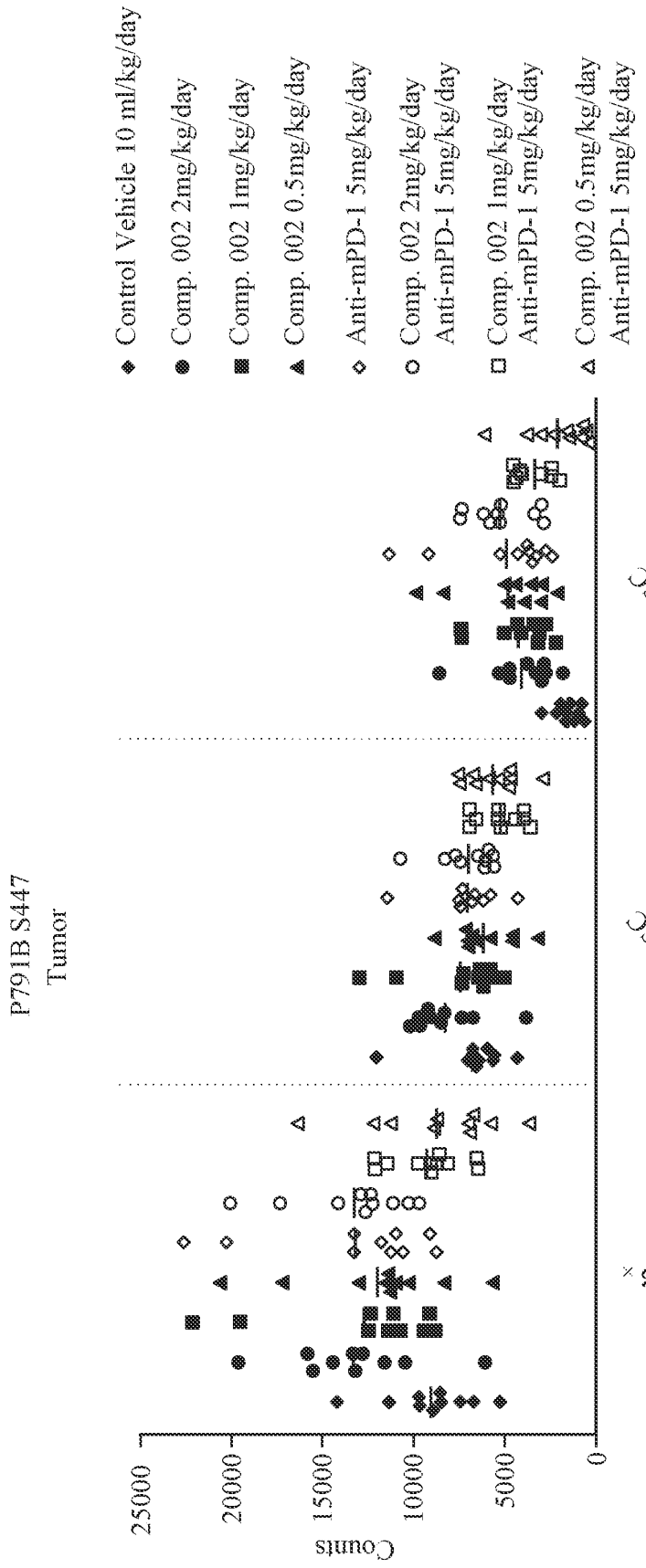

Control Vehicle 10 ml/kg/day
Comp. 002 2mg/kg/day
Comp. 002 1mg/kg/day
Comp. 002 0.5mg/kg/day
Anti-mPD-1 5mg/kg/day
Comp. 002 2mg/kg/day Anti-mPD-1 5mg/kg/day
Comp. 002 1mg/kg/day Anti-mPD-1 5mg/kg/day
Comp. 002 0.5mg/kg/day Anti-mPD-1 5mg/kg/day
P791B S447
Tumor
Counts
25000
20000
15000
10000
5000
0
CD3-CD11b+
CD45+
gMDSC
mMDSC
CD3-CD11b+

FIG. 24C

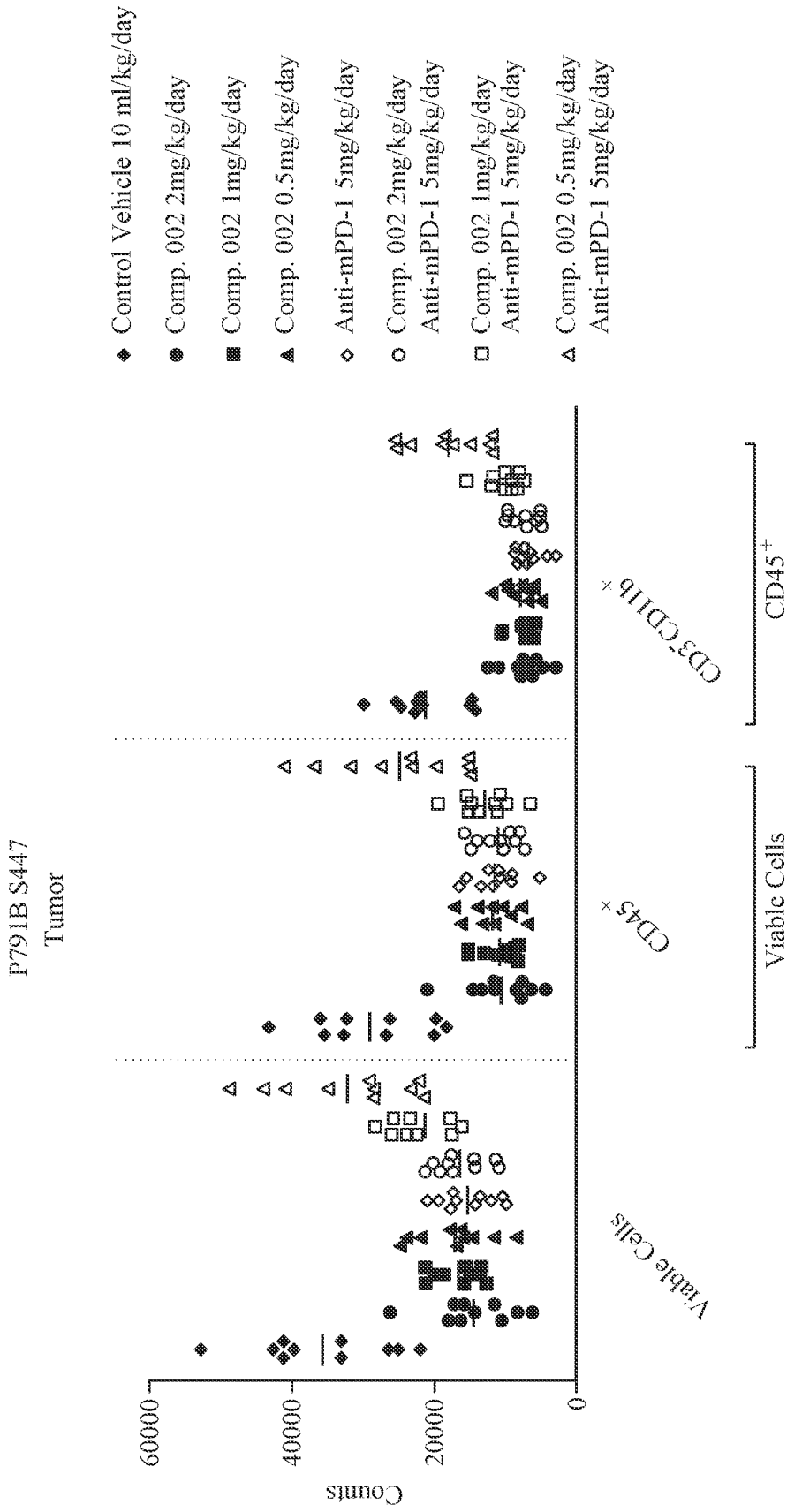

Control Vehicle 10 ml/kg/day
Comp. 002 2mg/kg/day
Comp. 002 1mg/kg/day
Comp. 002 0.5mg/kg/day
Anti-mPD-1 5mg/kg/day
Comp. 002 2mg/kg/day Anti-mPD-1 5mg/kg/day
Comp. 002 1mg/kg/day Anti-mPD-1 5mg/kg/day
Comp. 002 0.5mg/kg/day Anti-mPD-1 5mg/kg/day
P791B S447 Tumor
Counts
60000
40000
20000
0
Viable Cells
CD45+
CD3-CD11b+
Viable Cells
CD45+

FIG. 24D

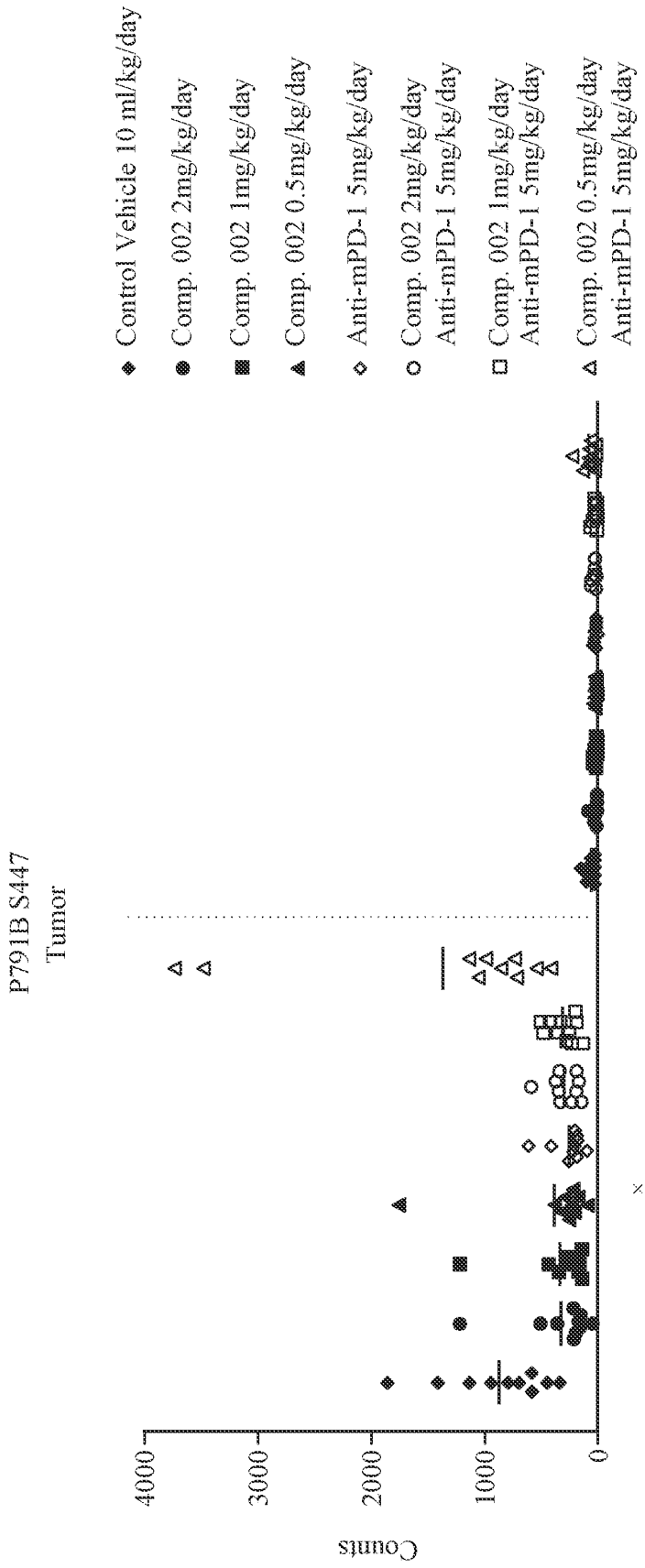

P791B S447
Tumor
Control Vehicle 10 ml/kg/day
Comp. 002 2mg/kg/day
Comp. 002 1mg/kg/day
Comp. 002 0.5mg/kg/day
Anti-mPD-1 5mg/kg/day
Comp. 002 2mg/kg/day Anti-mPD-1 5mg/kg/day
Comp. 002 1mg/kg/day Anti-mPD-1 5mg/kg/day
Comp. 002 0.5mg/kg/day Anti-mPD-1 5mg/kg/day
Counts
4000
3000
2000
1000
0
CD3-CD11b+
CD49+
NK-cells
CD49-

FIG. 24E

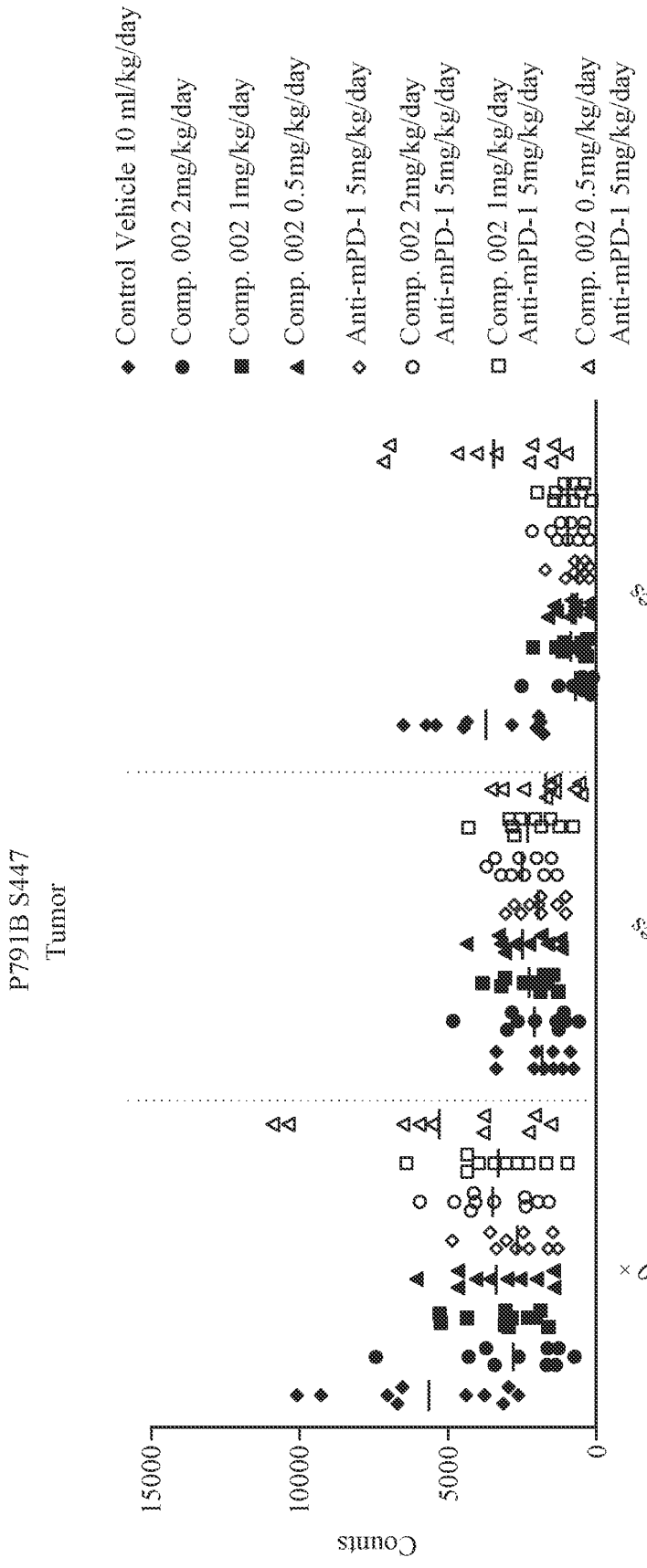

Control Vehicle 10 ml/kg/day
Comp. 002 2mg/kg/day
Comp. 002 1mg/kg/day
Comp. 002 0.5mg/kg/day
Anti-mPD-1 5mg/kg/day
Comp. 002 2mg/kg/day Anti-mPD-1 5mg/kg/day
Comp. 002 1mg/kg/day Anti-mPD-1 5mg/kg/day
Comp. 002 0.5mg/kg/day Anti-mPD-1 5mg/kg/day
P791B S447
Tumor
Counts
15000
10000
5000
0
F4/80+
M1 Macrophages
M2 Macrophages
CD3-CD11b+
F4/80+

FIG. 24F

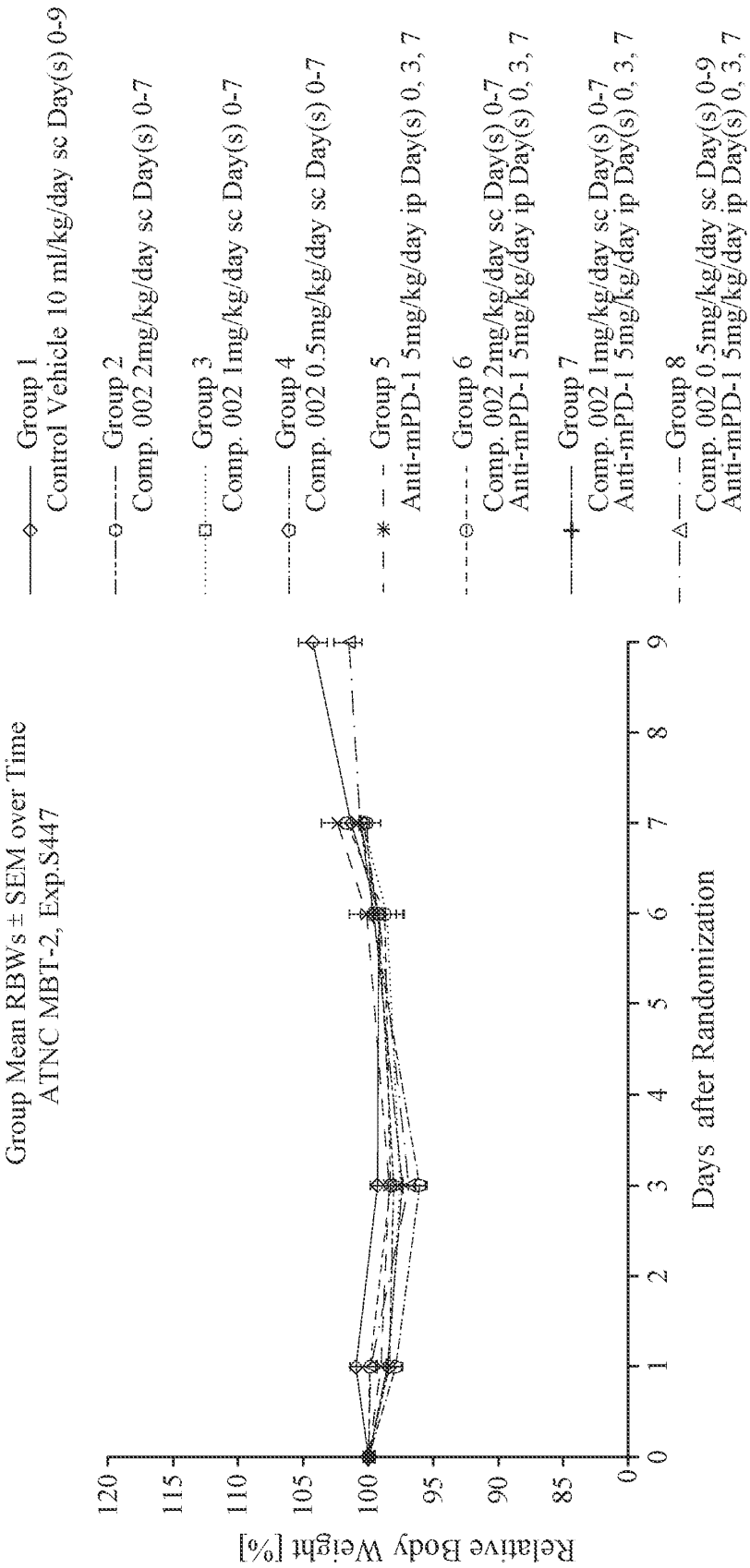

Group Mean RBWs ± SEM over Time
ATNC MBT-2, Exp.S447
Relative Body Weight [%]
120
115
110
105
100
95
90
85
0
1
2
3
4
5
6
7
8
9
Days after Randomization
Group 1
Control Vehicle 10 ml/kg/day sc Day(s) 0-9
Group 2
Comp. 002 2mg/kg/day sc Day(s) 0-7
Group 3
Comp. 002 1mg/kg/day sc Day(s) 0-7
Group 4
Comp. 002 0.5mg/kg/day sc Day(s) 0-7
Group 5
Anti-mPD-1 5mg/kg/day ip Day(s) 0, 3, 7
Group 6
Comp. 002 2mg/kg/day sc Day(s) 0-7
Anti-mPD-1 5mg/kg/day ip Day(s) 0, 3, 7
Group 7
Comp. 002 1mg/kg/day sc Day(s) 0-7
Anti-mPD-1 5mg/kg/day ip Day(s) 0, 3, 7
Group 8
Comp. 002 0.5mg/kg/day sc Day(s) 0-9
Anti-mPD-1 5mg/kg/day ip Day(s) 0, 3, 7

FIG. 25

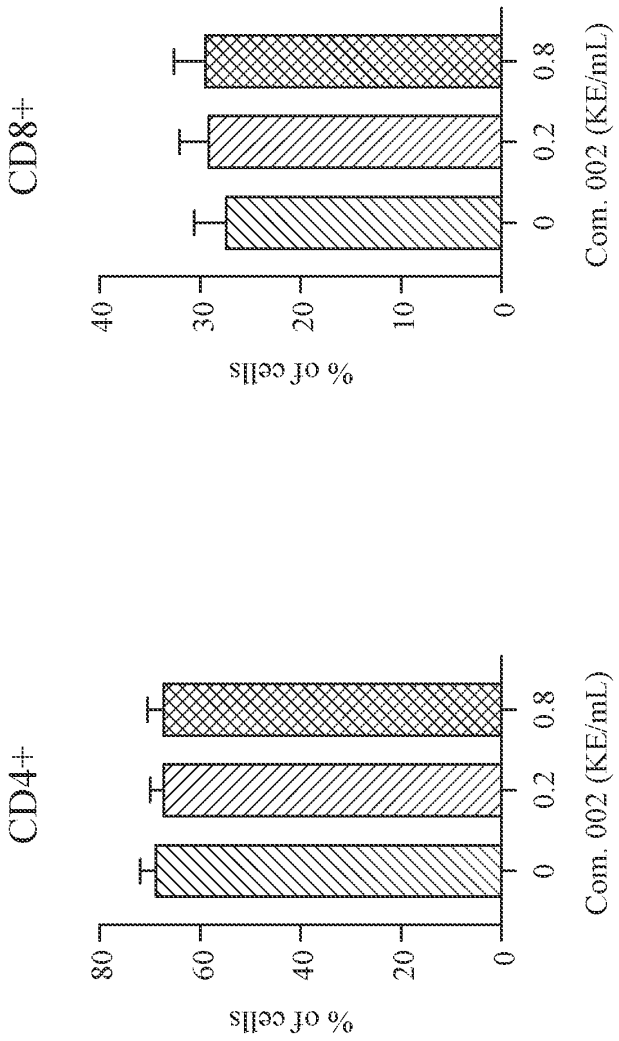

CD8+
% of cells
0
10
20
30
40
0
0.2
0.8
Com. 002 (KE/mL)
CD4+
% of cells
0
20
40
60
80
0
0.2
0.8
Com. 002 (KE/mL)

FIG. 26

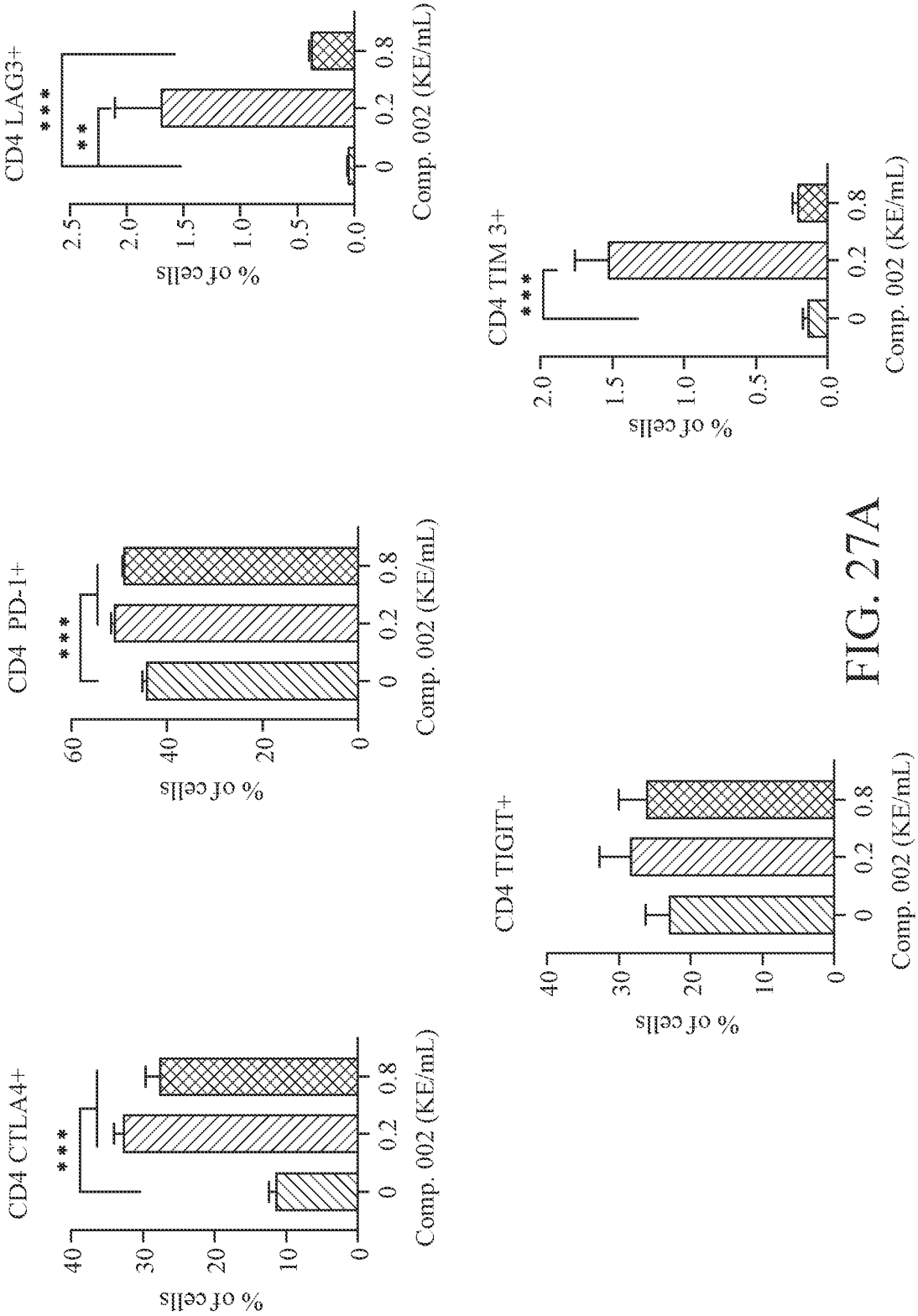

CD4 LAG3+
***
**
% of cells
2.5
2.0
1.5
1.0
0.5
0.0
0
0.2
0.8
Comp. 002 (KE/mL)
CD4 TIM 3+
***
% of cells
2.0
1.5
1.0
0.5
0.0
0
0.2
0.8
Comp. 002 (KE/mL)
CD4 PD-1+
***
% of cells
60
40
20
0
0
0.2
0.8
Comp. 002 (KE/mL)
CD4 TIGIT+
% of cells
40
30
20
10
0
0
0.2
0.8
Comp. 002 (KE/mL)
CD4 CTLA4+
***
% of cells
40
30
20
10
0
0
0.2
0.8
Comp. 002 (KE/mL)

FIG. 27A

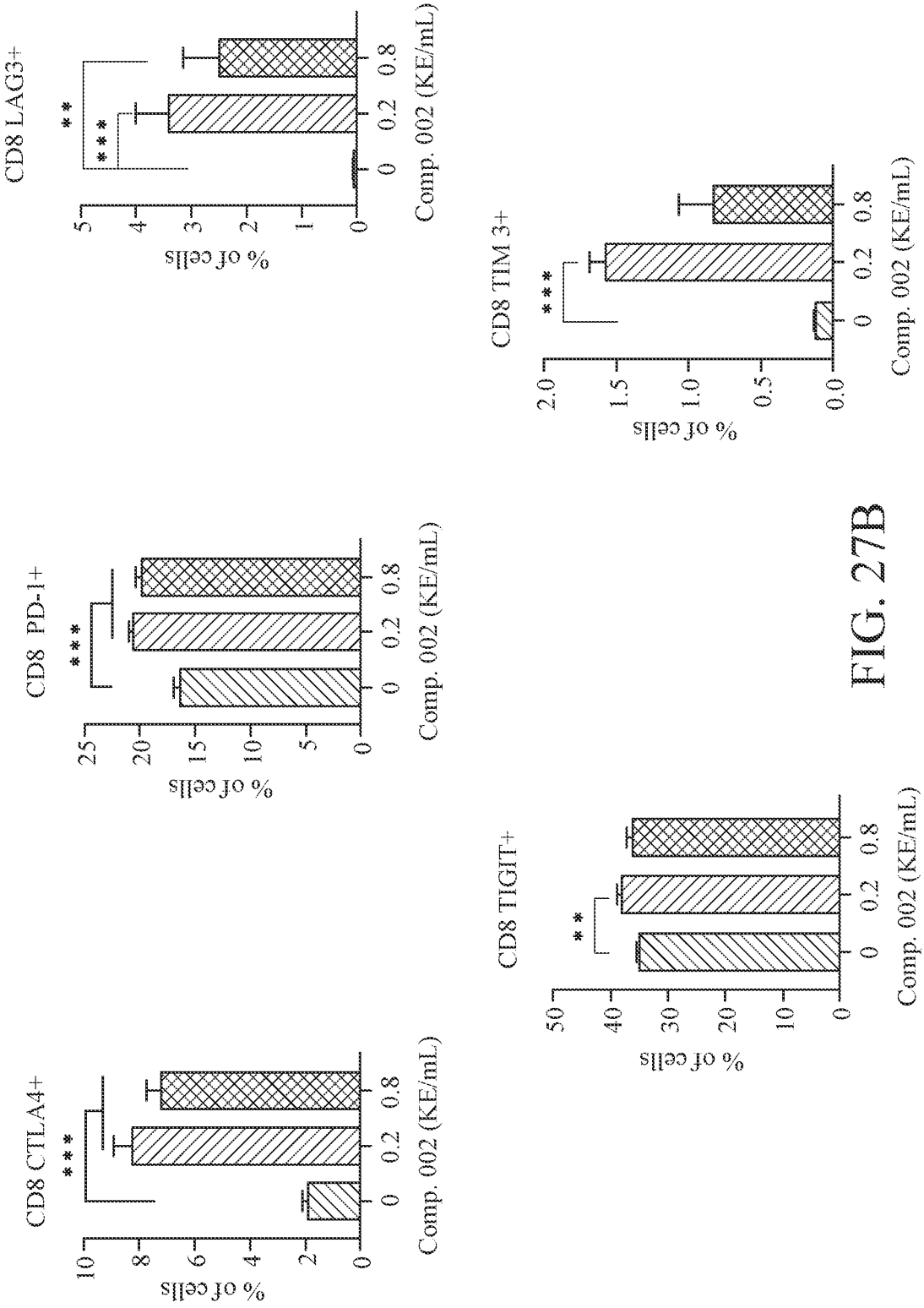

CD8 CTLA4+
% of cells
Comp. 002 (KE/mL)
CD8 PD-1+
% of cells
Comp. 002 (KE/mL)
CD8 LAG3+
% of cells
Comp. 002 (KE/mL)
CD8 TIGIT+
% of cells
Comp. 002 (KE/mL)
CD8 TIM 3+
% of cells
Comp. 002 (KE/mL)

FIG. 27B

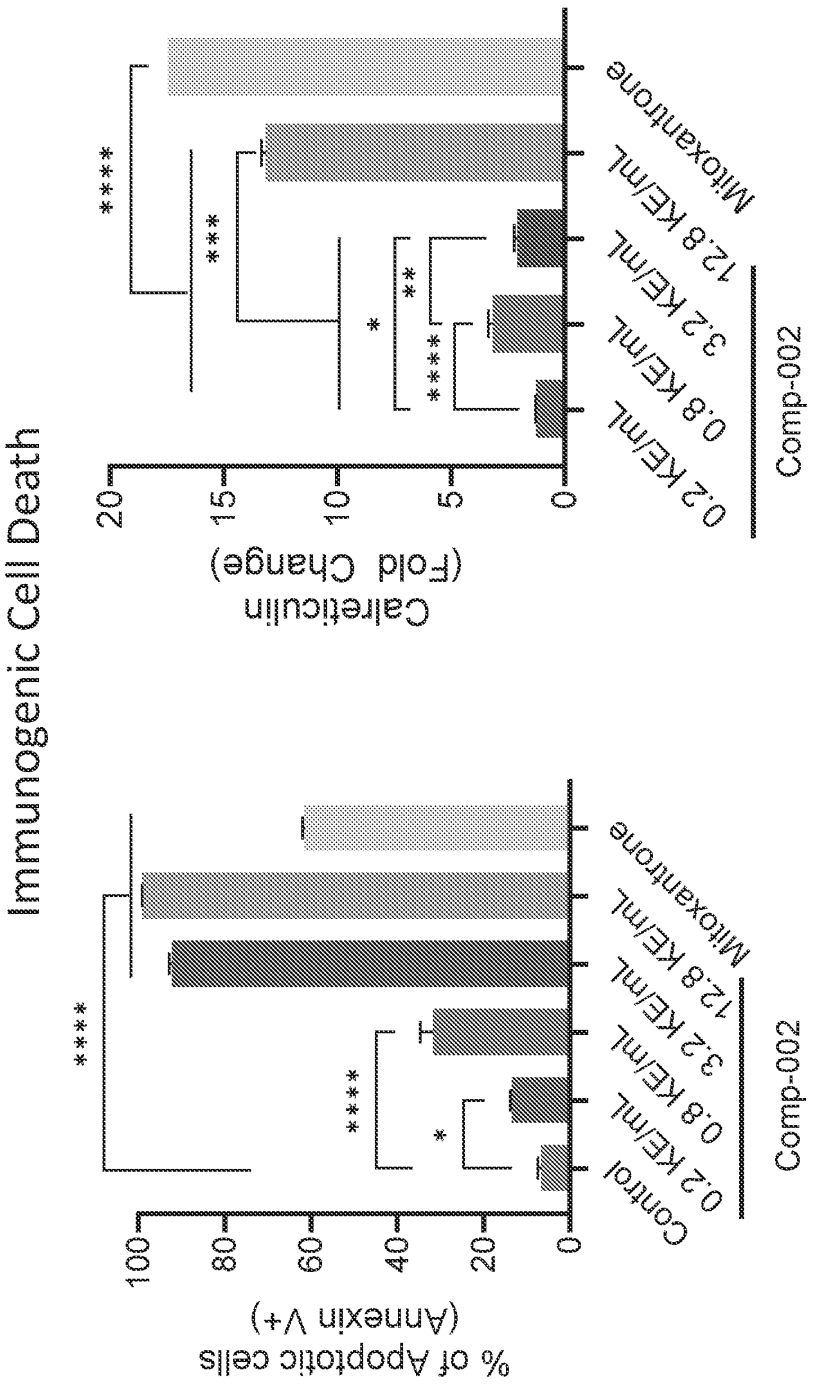


FIG. 28A

FIG. 28B

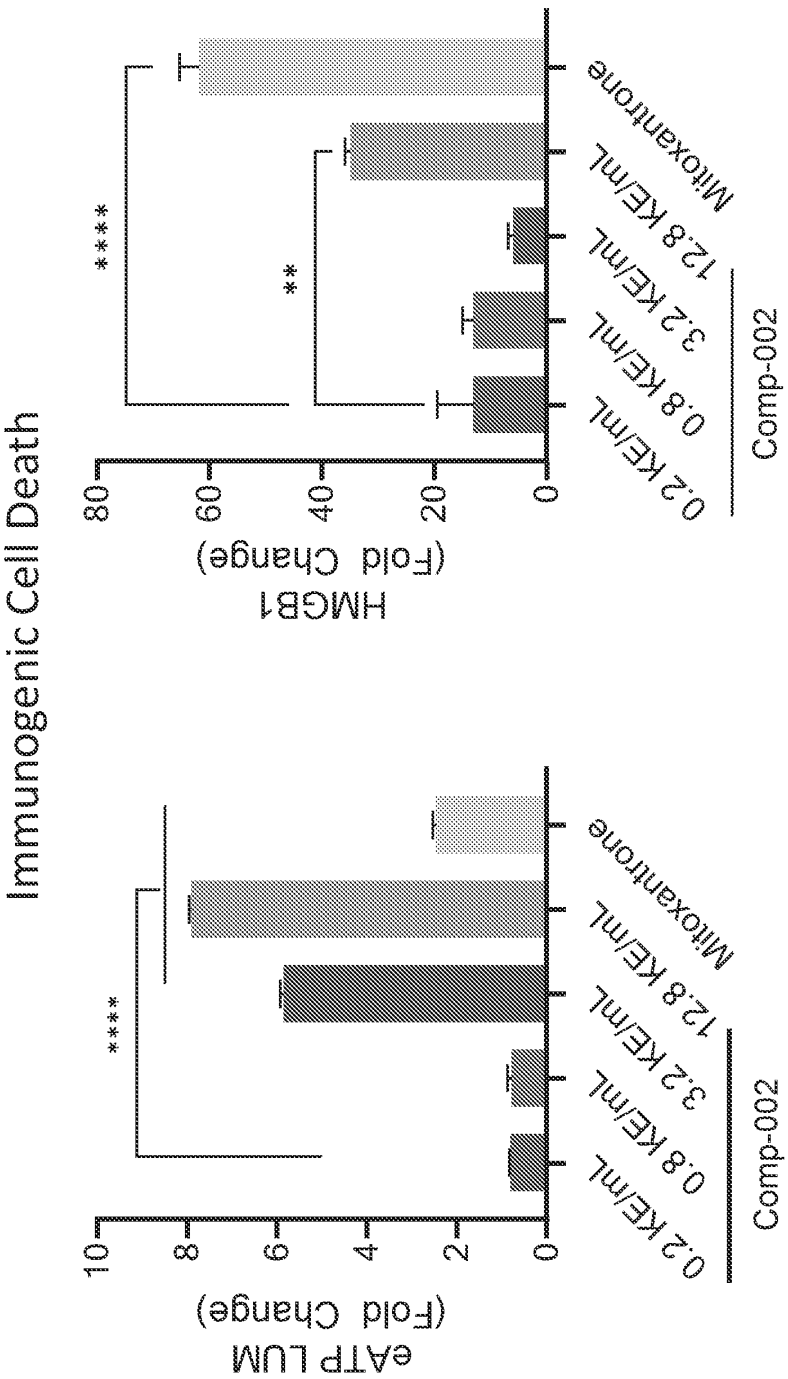


FIG. 28C

FIG. 28D

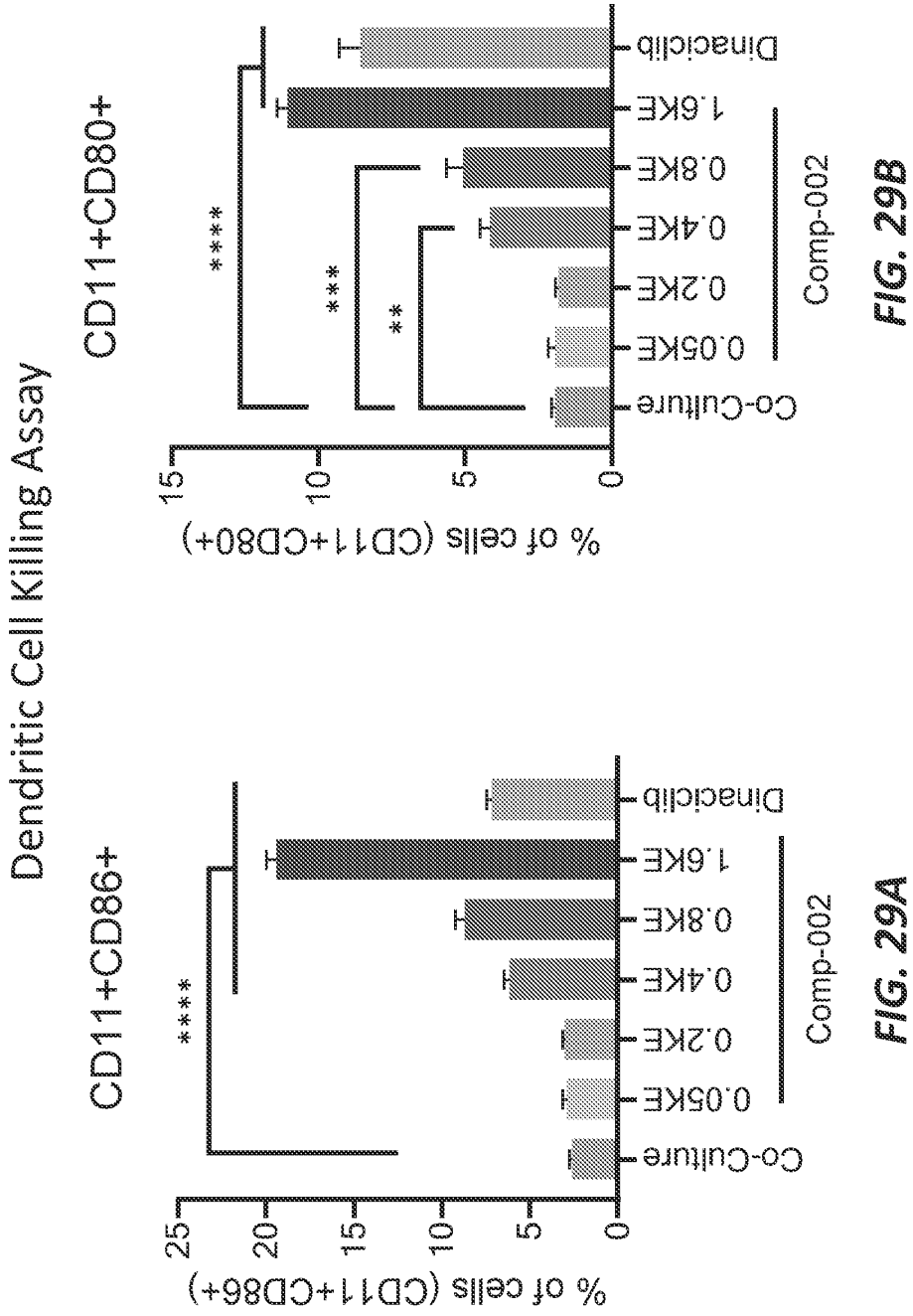


FIG. 29A

FIG. 29B

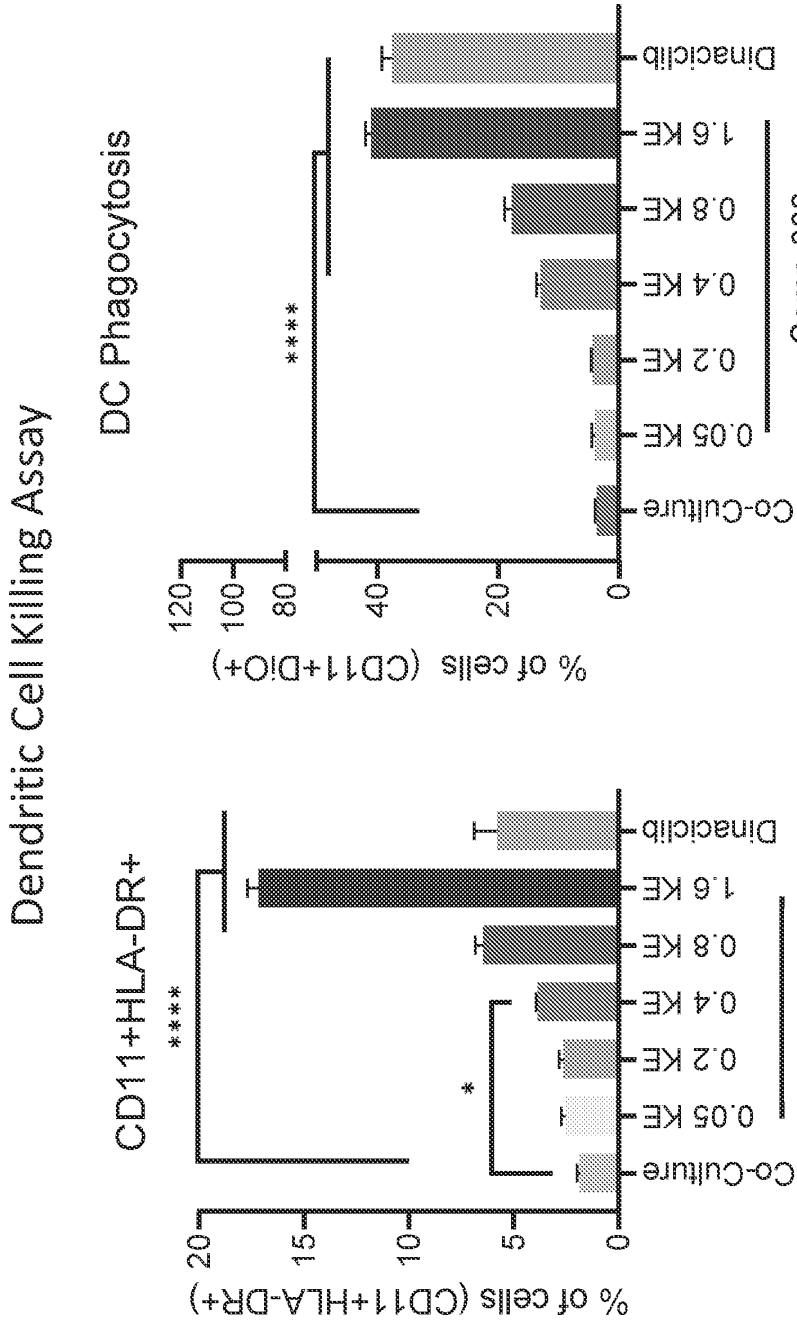


FIG. 29C

FIG. 29D

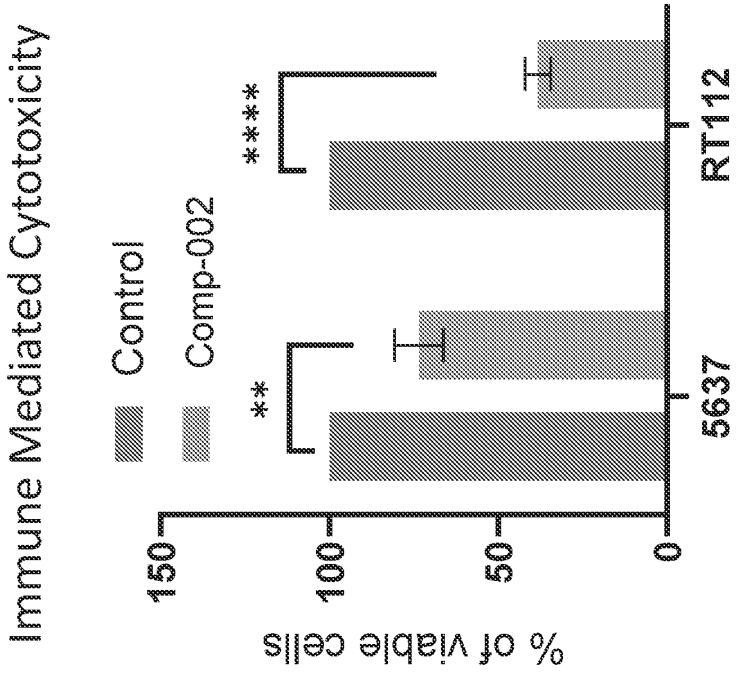


FIG. 30B

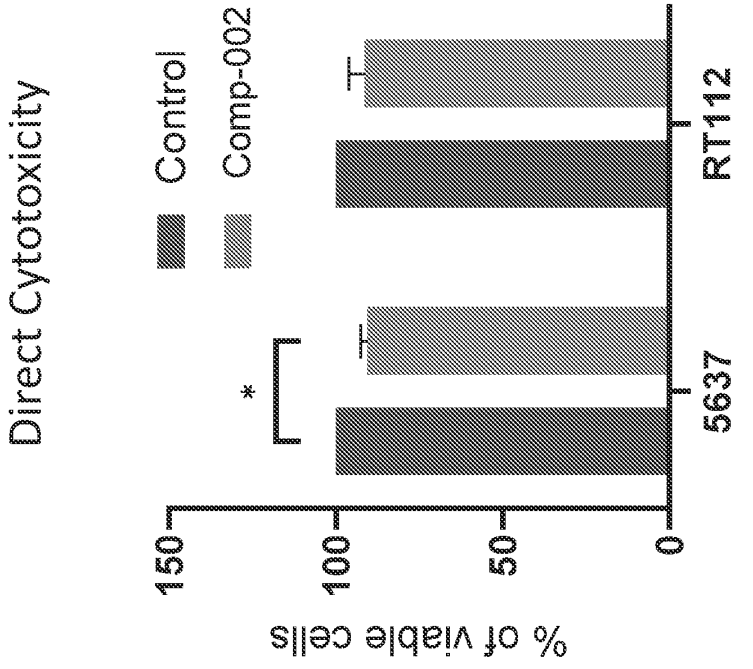


FIG. 30A

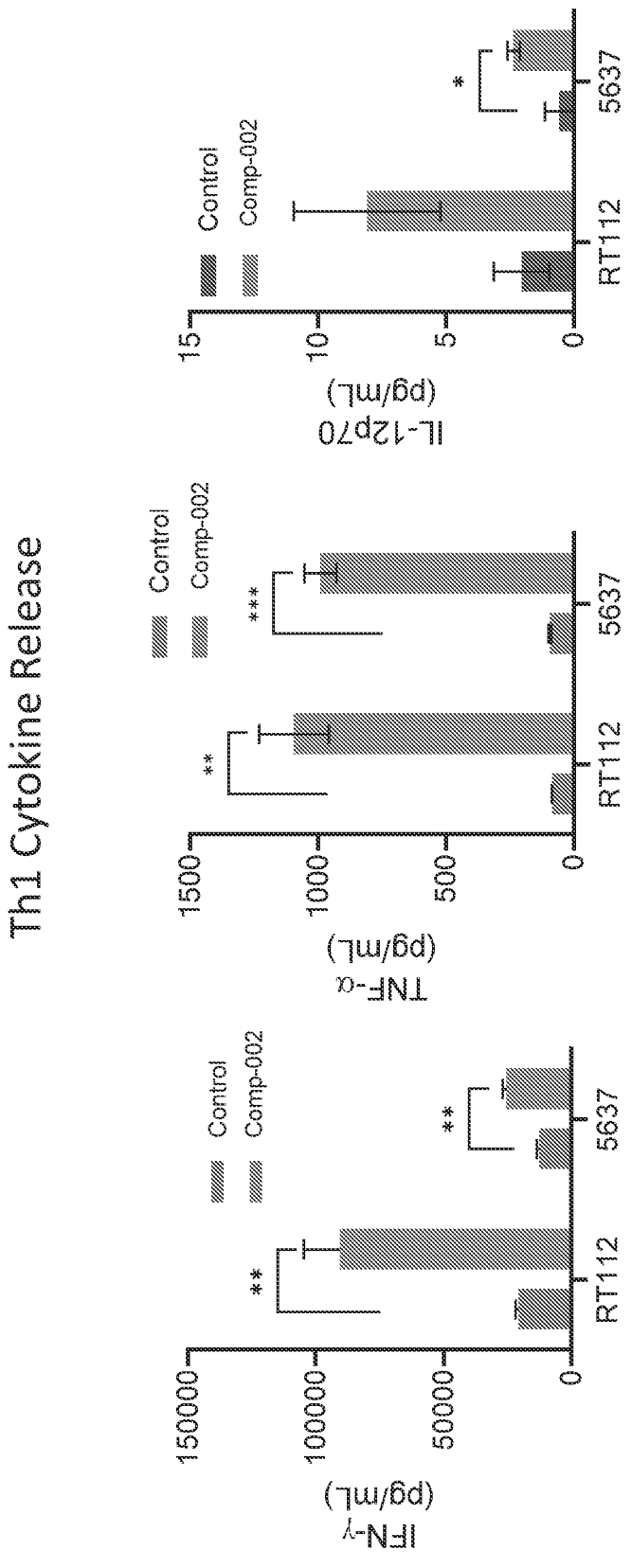

Th1 Cytokine Release
IFN-γ (pg/mL)
150000
100000
50000
0
Control
Comp-002
**
RT112
5637
TNF-α (pg/mL)
1500
1000
500
0
Control
Comp-002
**
***
RT112
5637
IL-12p70 (pg/mL)
15
10
5
0
Control
Comp-002
*
RT112
5637

FIG. 31A

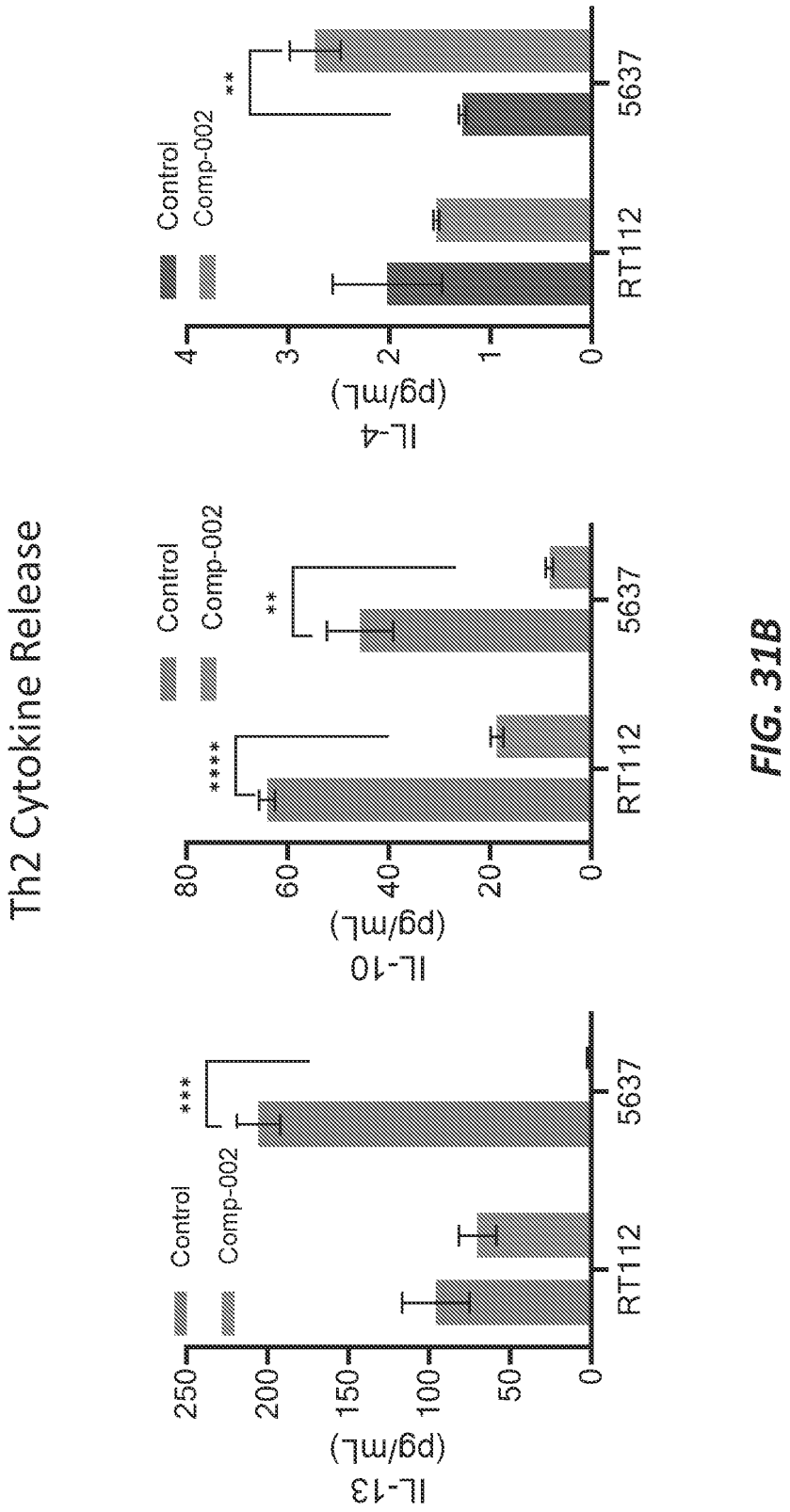

Th2 Cytokine Release
IL-13 (pg/mL)
IL-10 (pg/mL)
IL-4 (pg/mL)
Control
Comp-002
RT112
5637
***
****
**
**
0
50
100
150
200
250
0
20
40
60
80
0
1
2
3
4

FIG. 31B

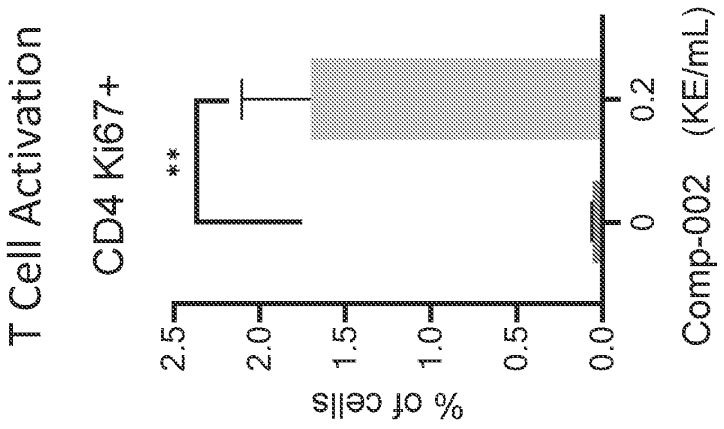

T Cell Activation
CD4 Ki67+
**
% of cells
2.5
2.0
1.5
1.0
0.5
0.0
0
0.2
Comp-002 (KE/mL)

FIG. 32A

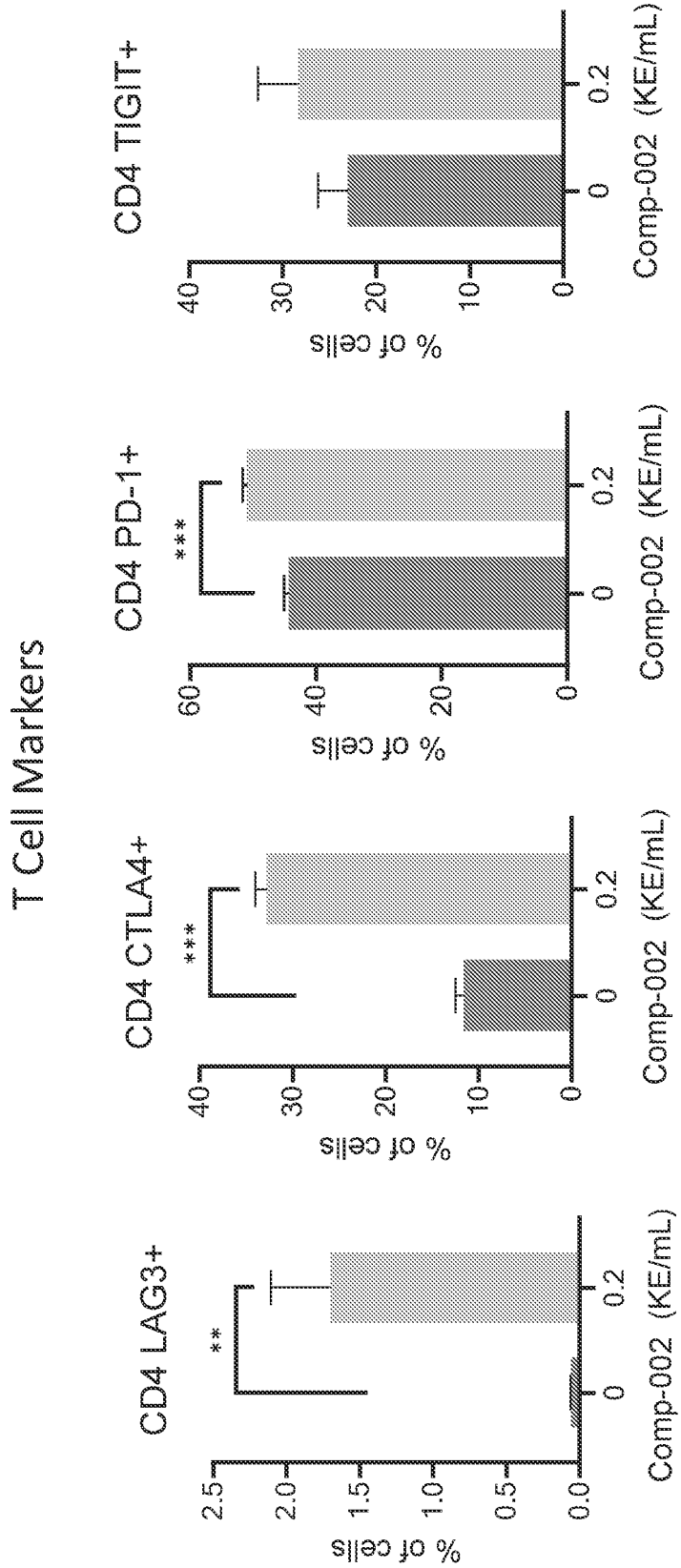


FIG. 32B FIG. 32C FIG. 32D FIG. 32E

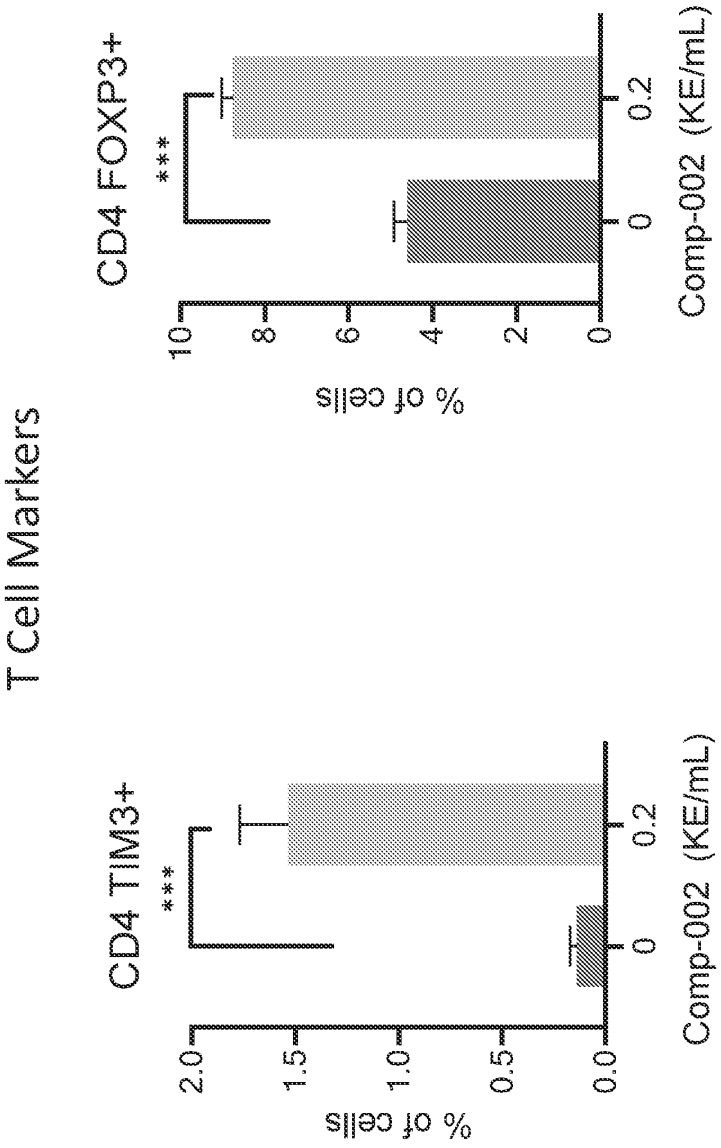


FIG. 32F

FIG. 32G

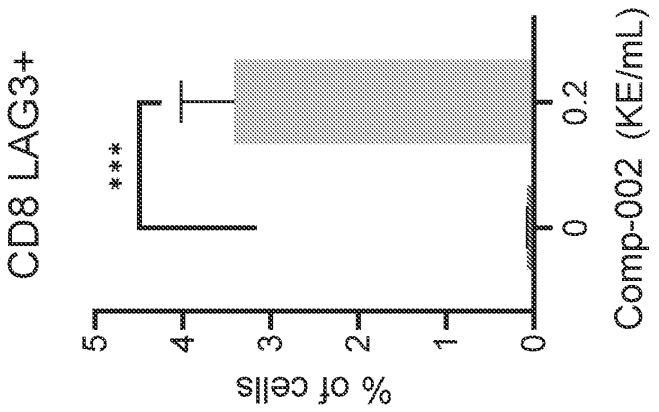


FIG. 32J

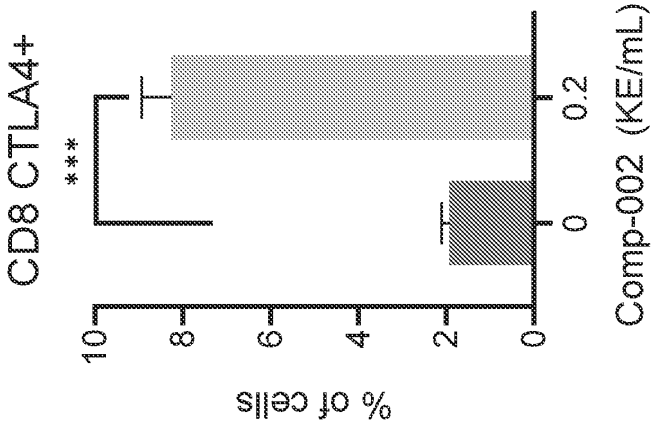


FIG. 32I

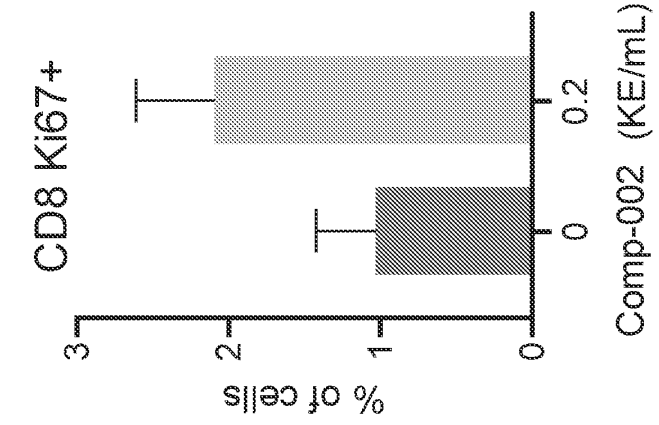


FIG. 32H

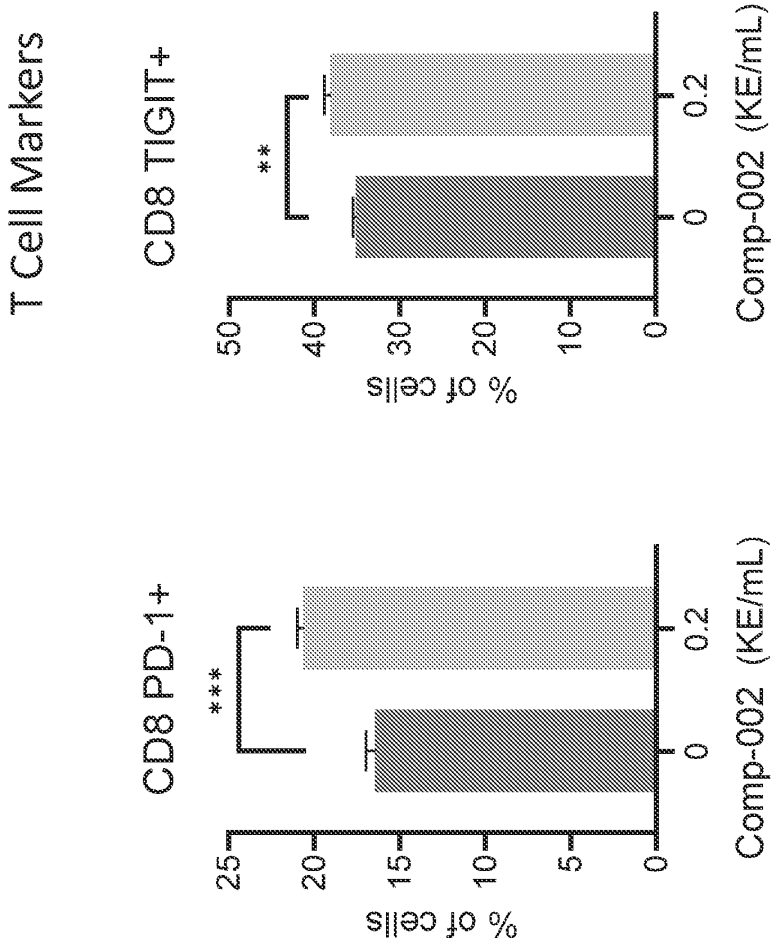


FIG. 32K

FIG. 32L

FIG. 32M

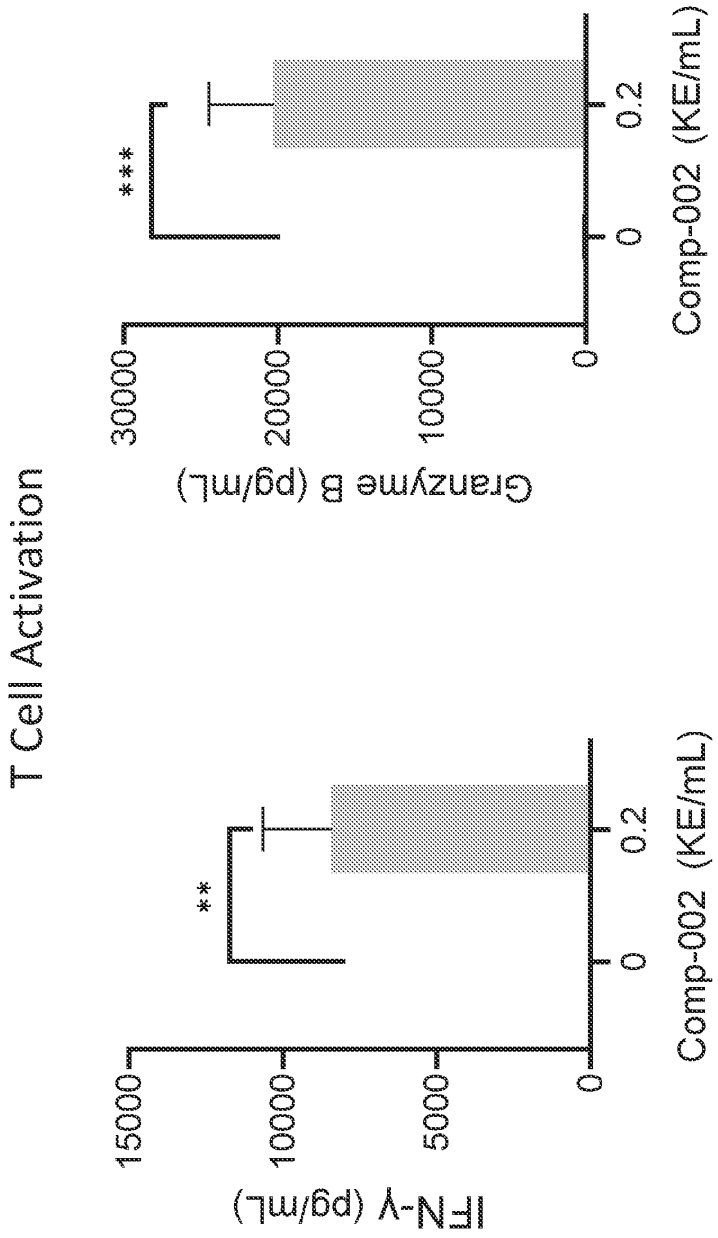


FIG. 33A

FIG. 33B

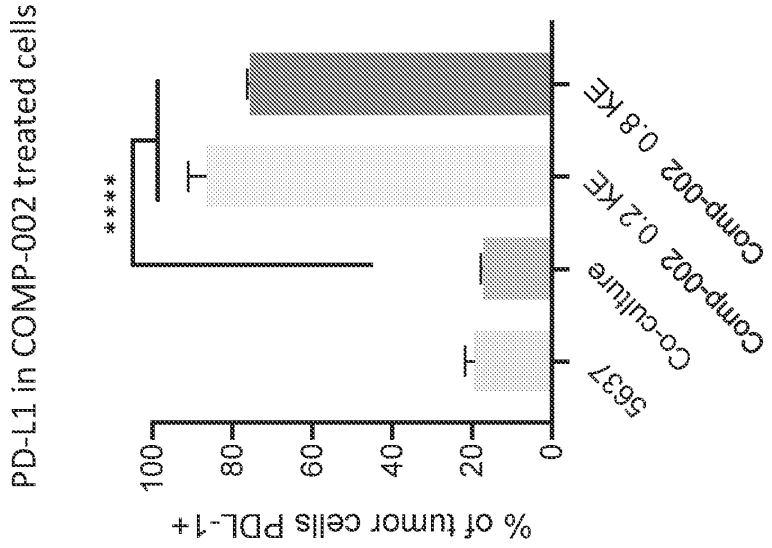

PD-L1 in COMP-002 treated cells
% of tumor cells PDL-1+
100
80
60
40
20
0
****
5637
Co-culture
Comp-002 0.2 KE
Comp-002 0.8 KE

FIG. 34

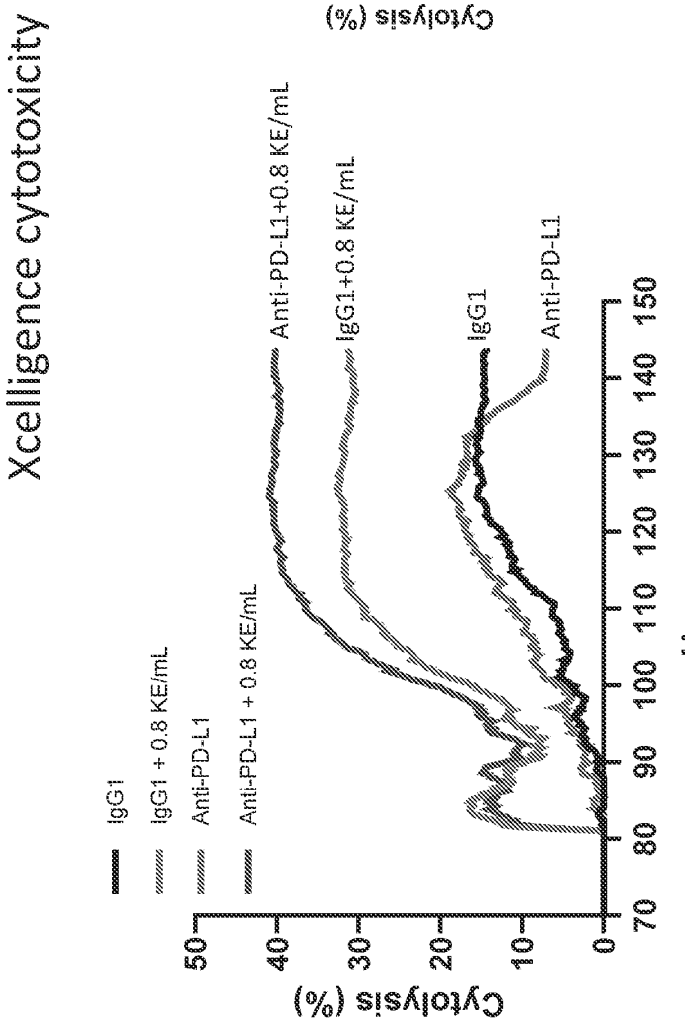


FIG. 35A

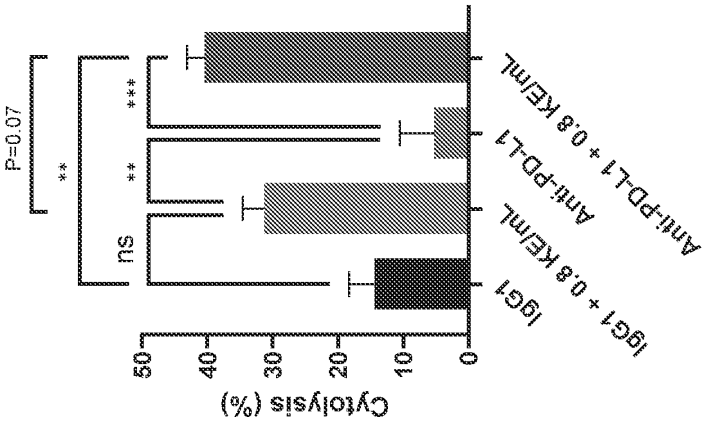


FIG. 35B

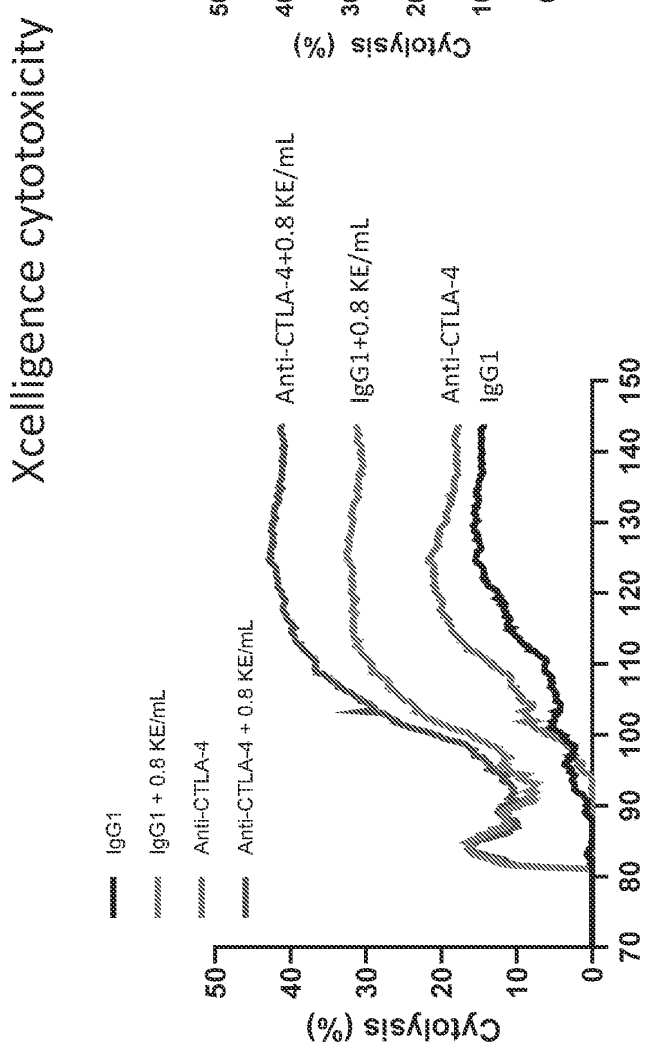


FIG. 35C

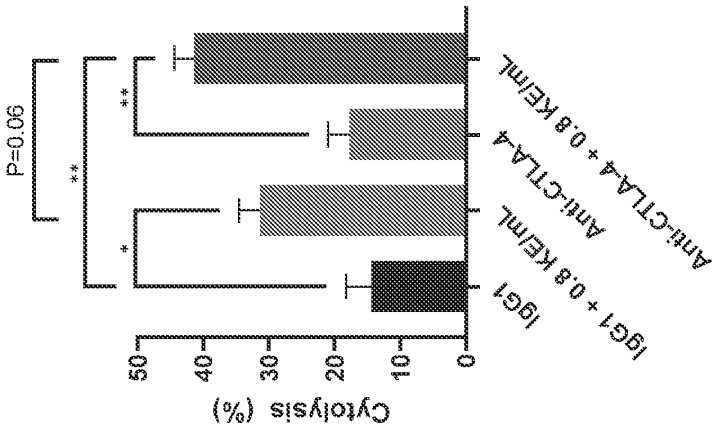


FIG. 35D

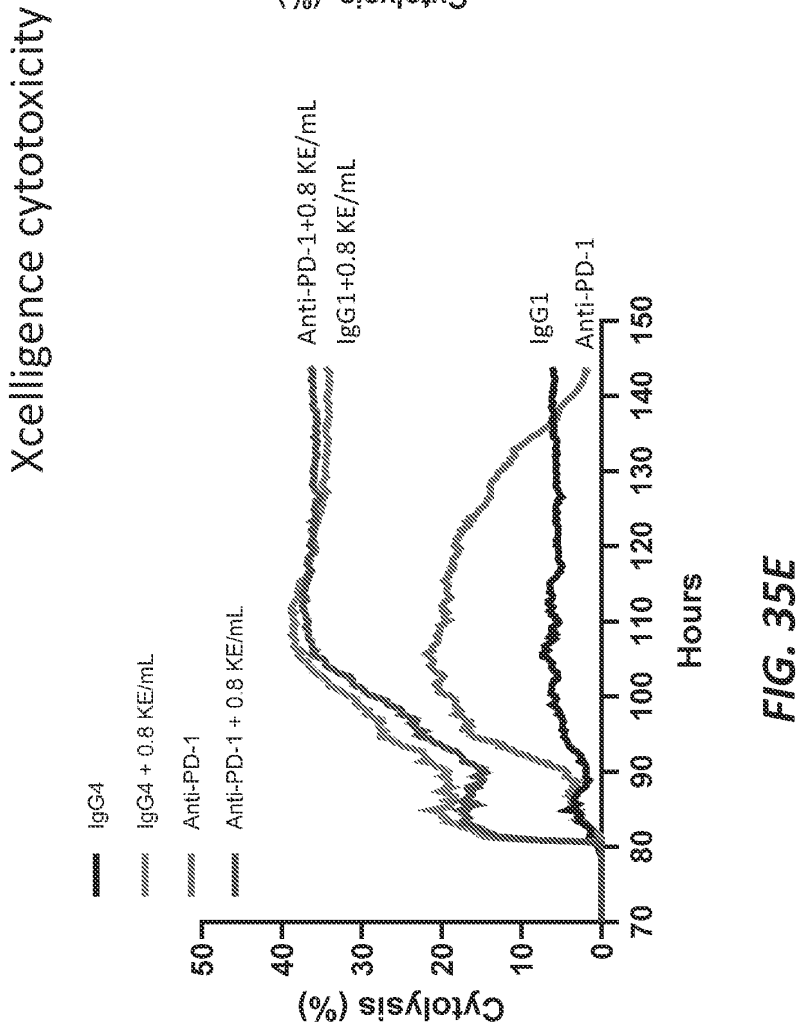


FIG. 35E

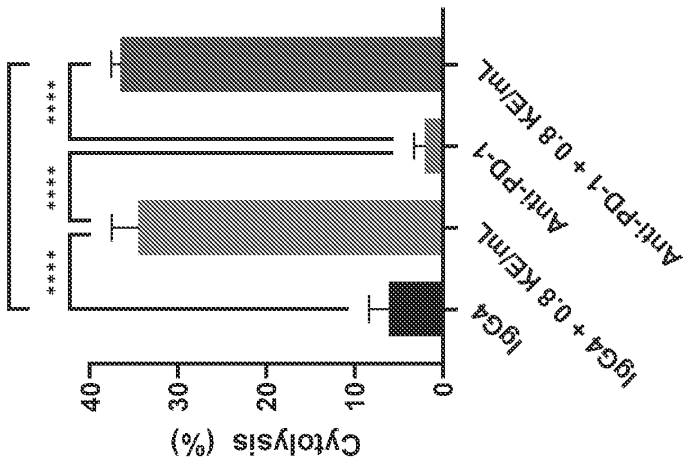


FIG. 35F

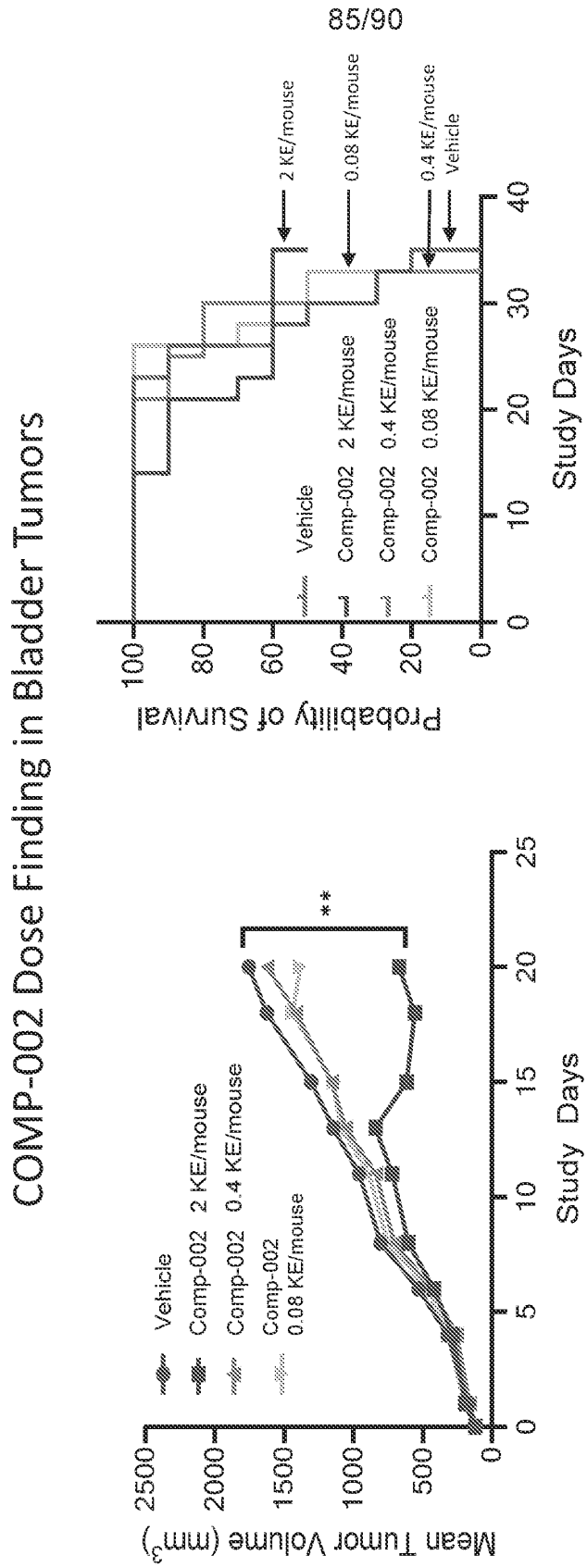


FIG. 36A

FIG. 36B

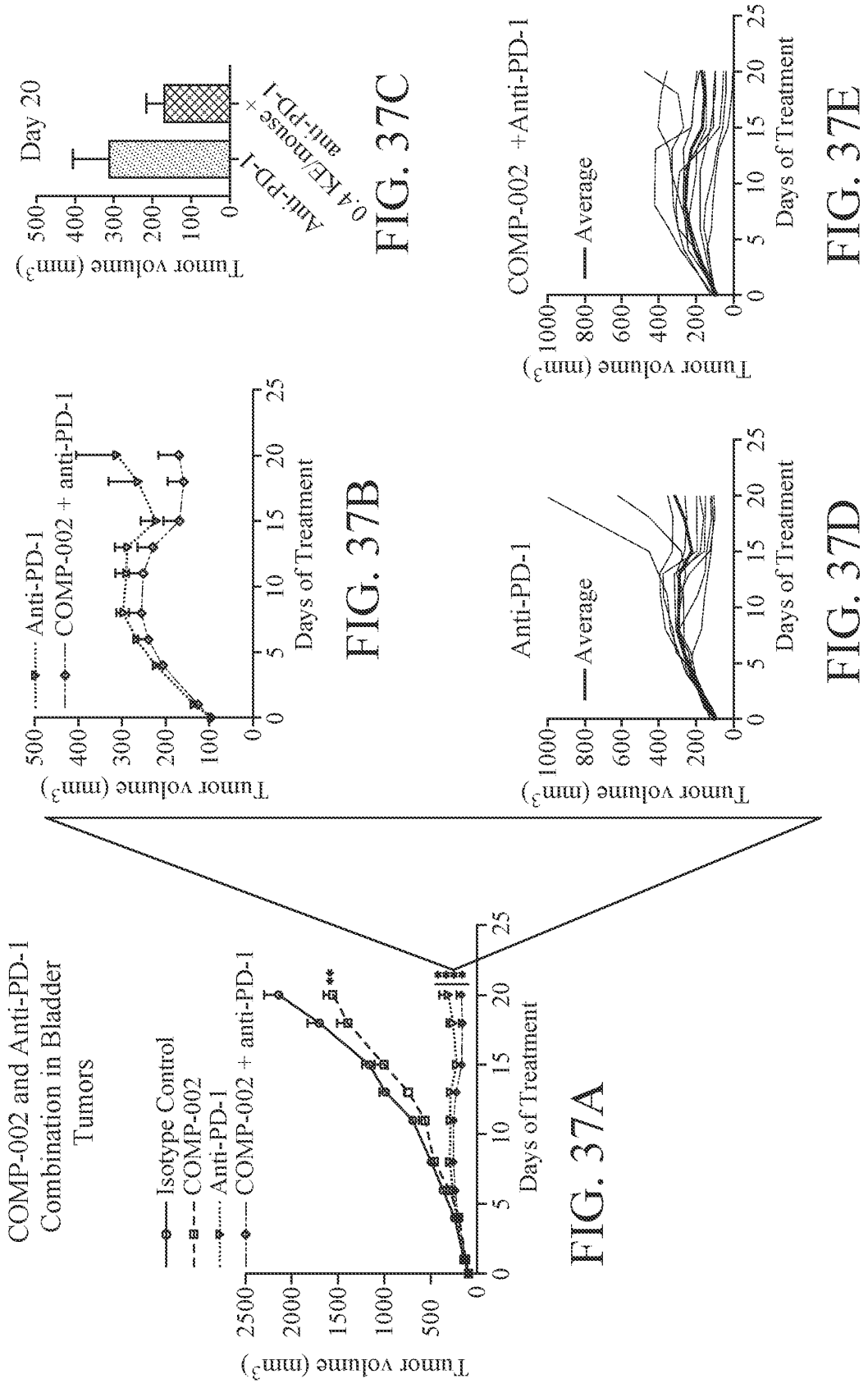


FIG. 37A

FIG. 37B

FIG. 37C

FIG. 37D

FIG. 37E

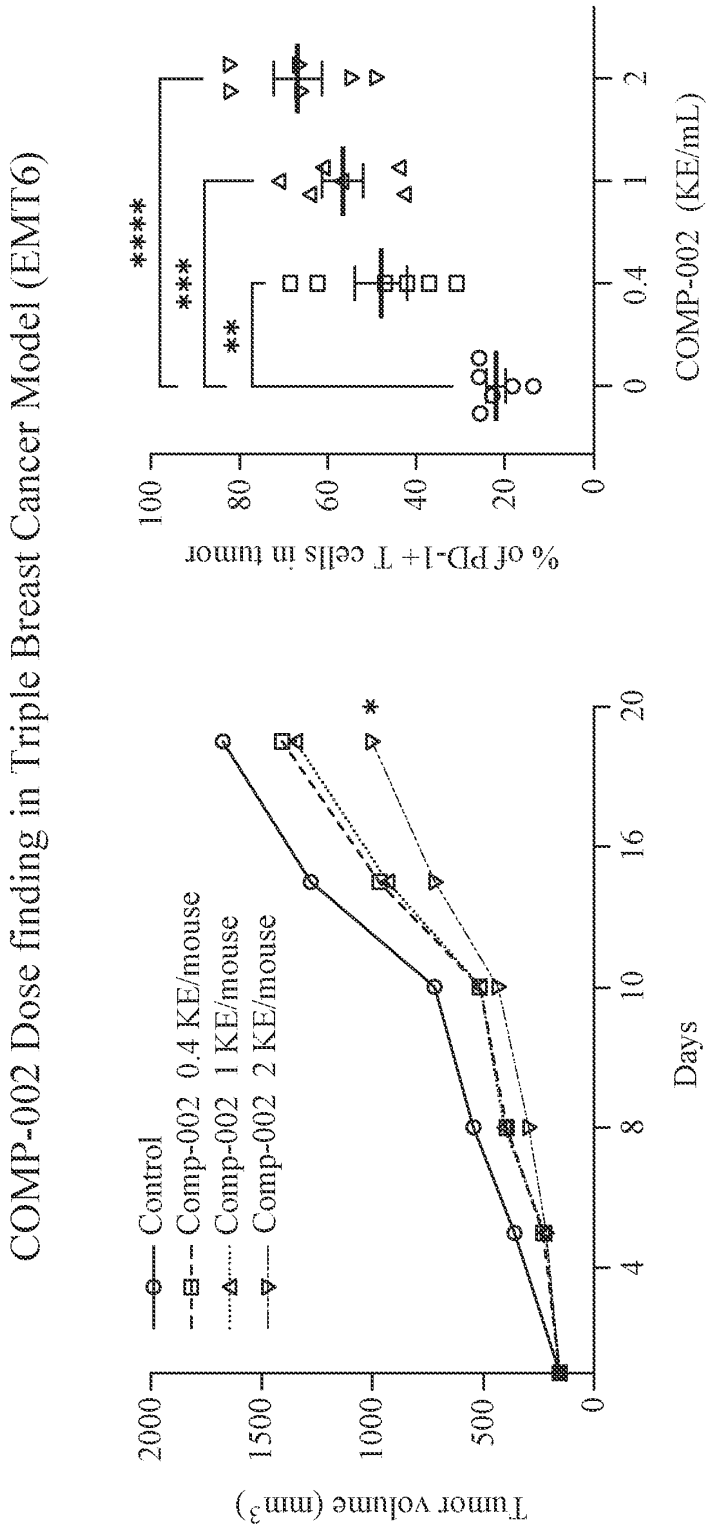


FIG. 38A

FIG. 38B

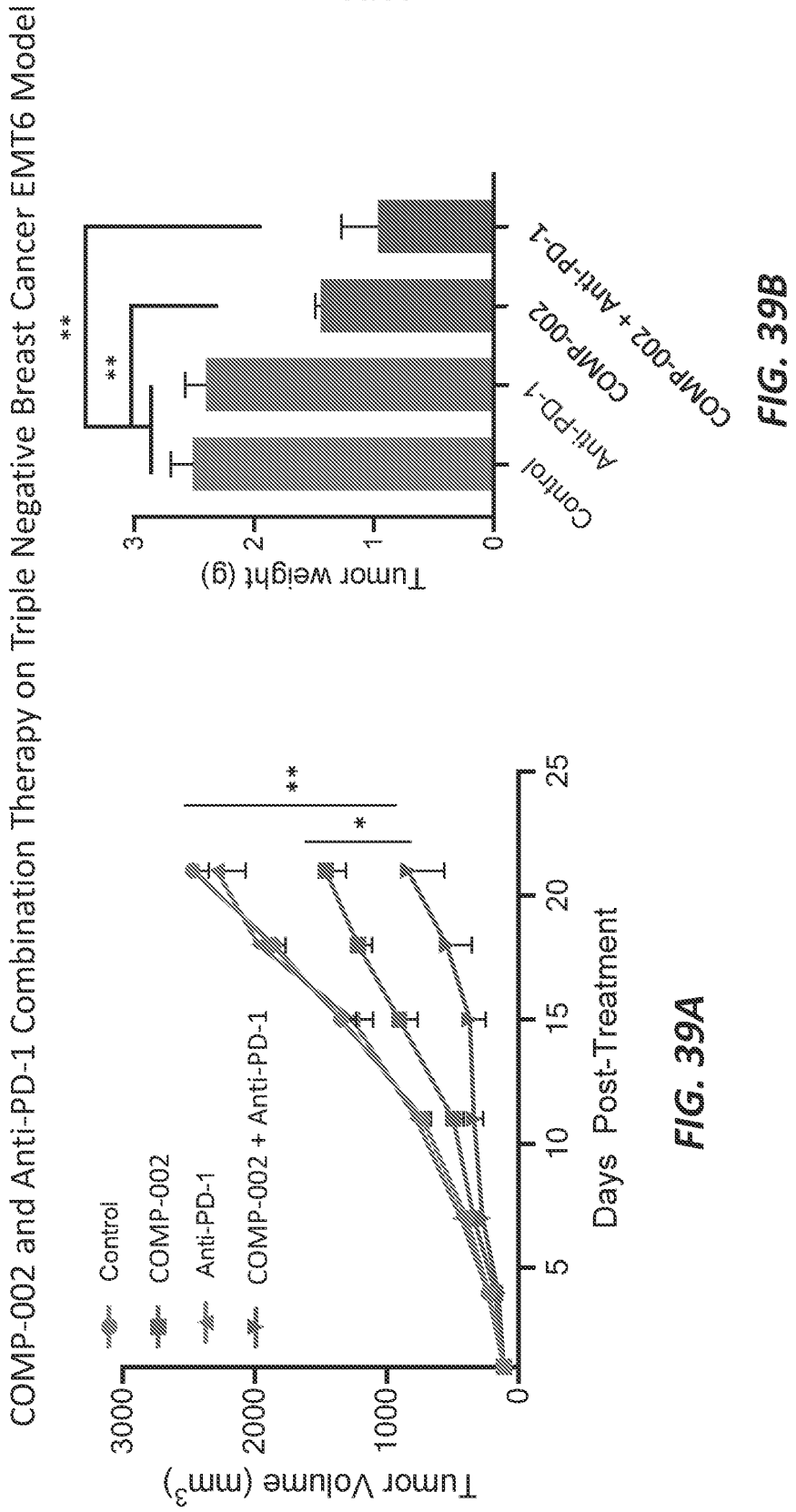


FIG. 39A

FIG. 39B

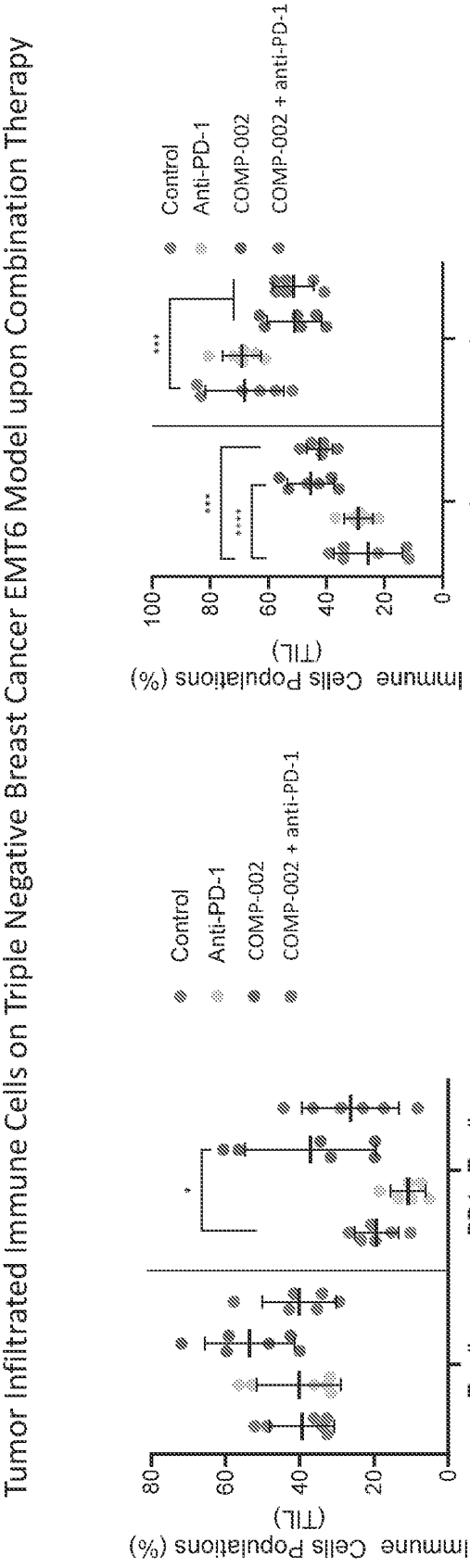


FIG. 40A

FIG. 40B

FIG. 40C

FIG. 40D