Figure 1

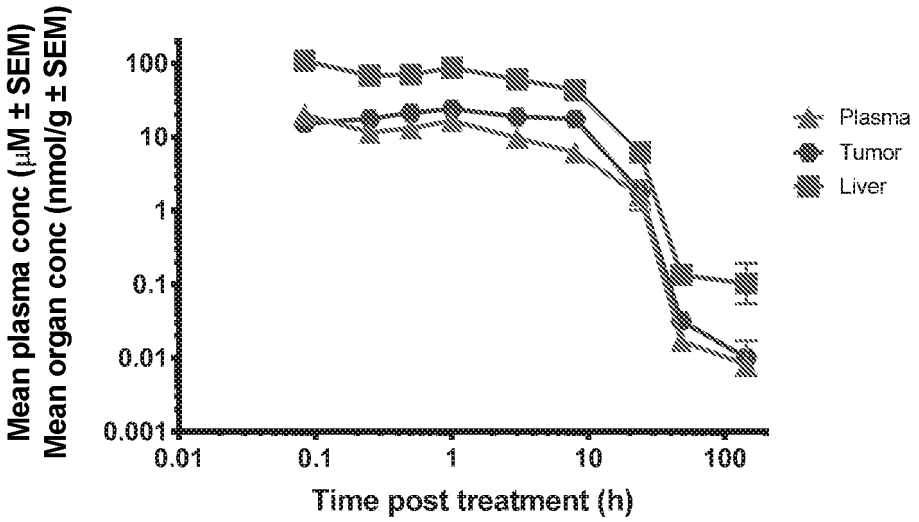


Figure 2

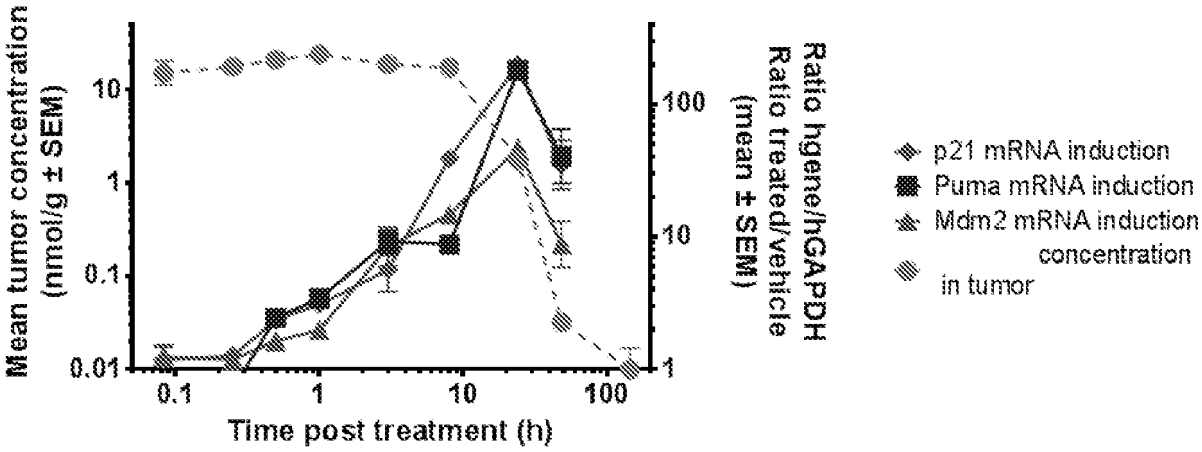


Figure 3

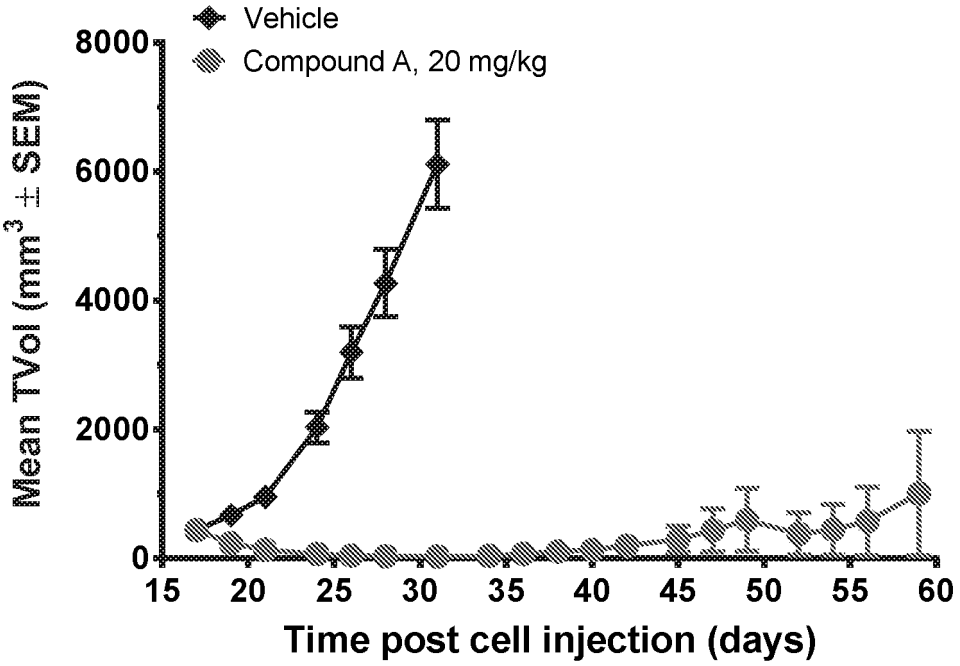


Figure 4

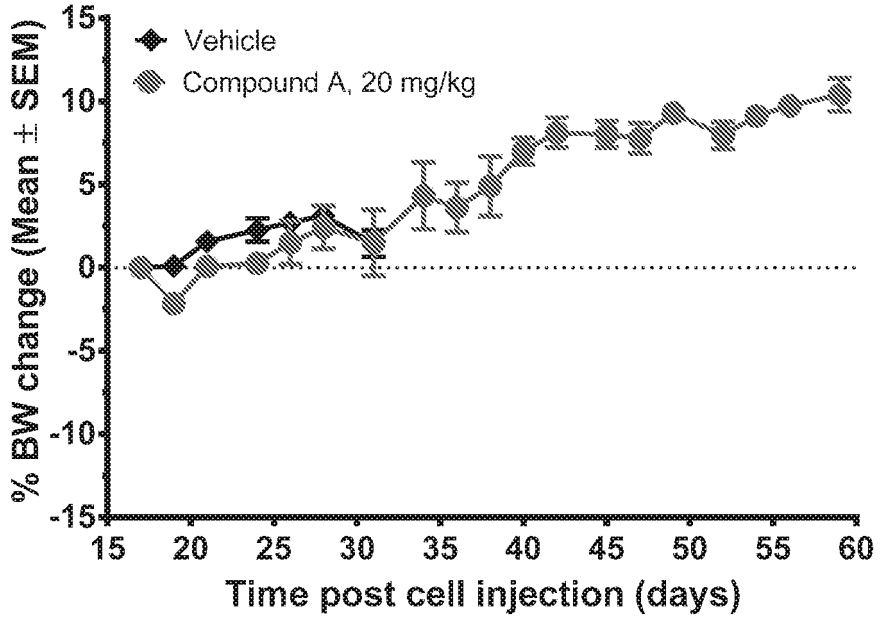


Figure 5

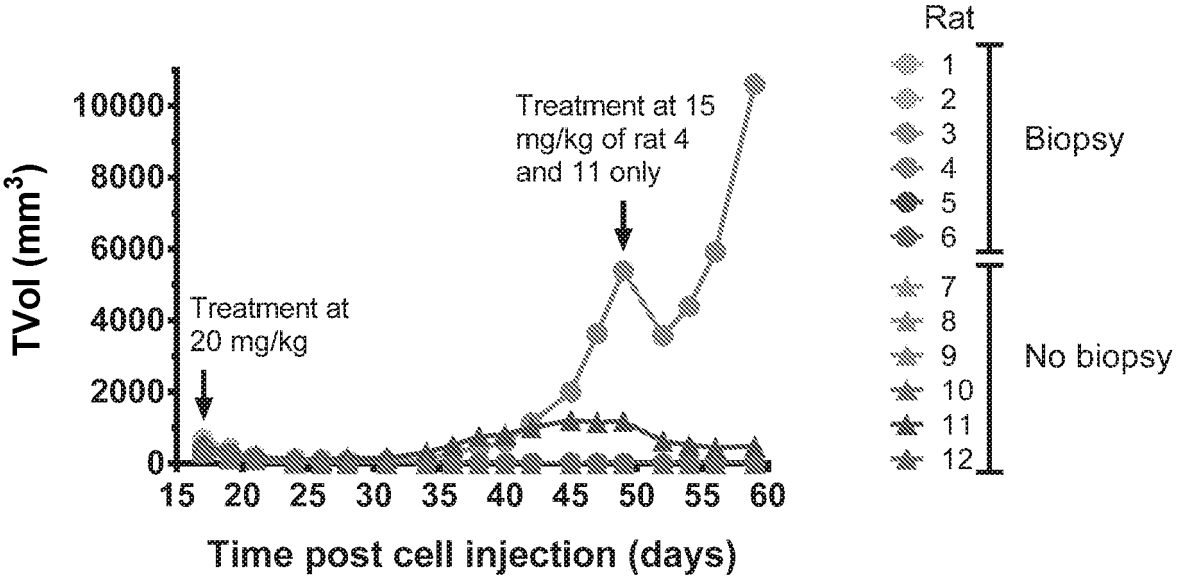
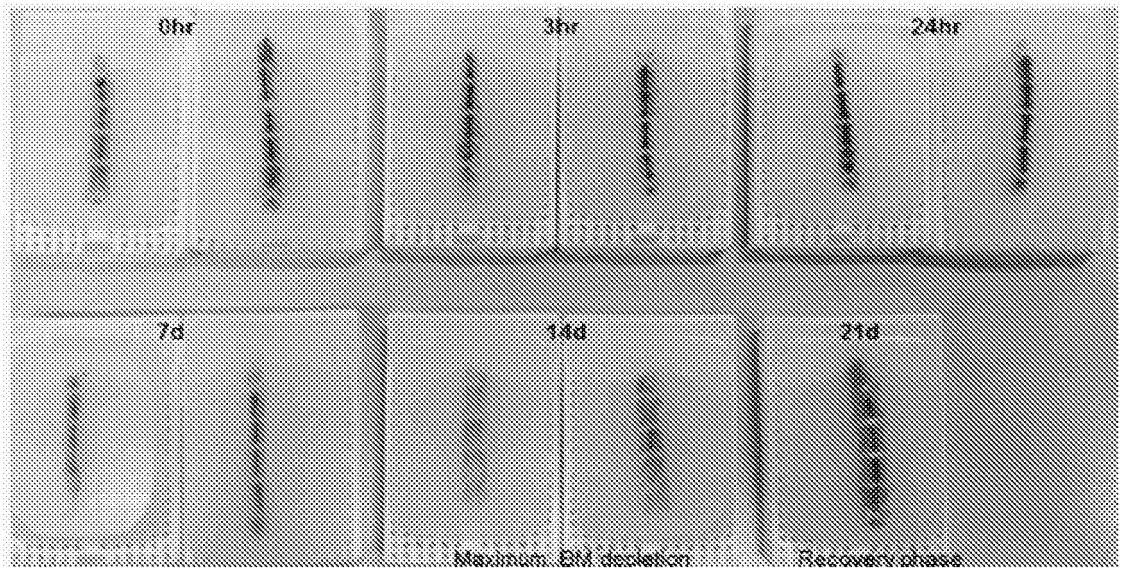

TVol (mm3)
10000
8000
6000
4000
2000
0
15 20 25 30 35 40 45 50 55 60
Time post cell injection (days)
Treatment at 20 mg/kg
Treatment at 15 mg/kg of rat 4 and 11 only
Rat
1
2
3
4
5
6
7
8
9
10
11
12
Biopsy
No biopsy

Figure 6

Sternum macroscopic image



Sternum microscopic image

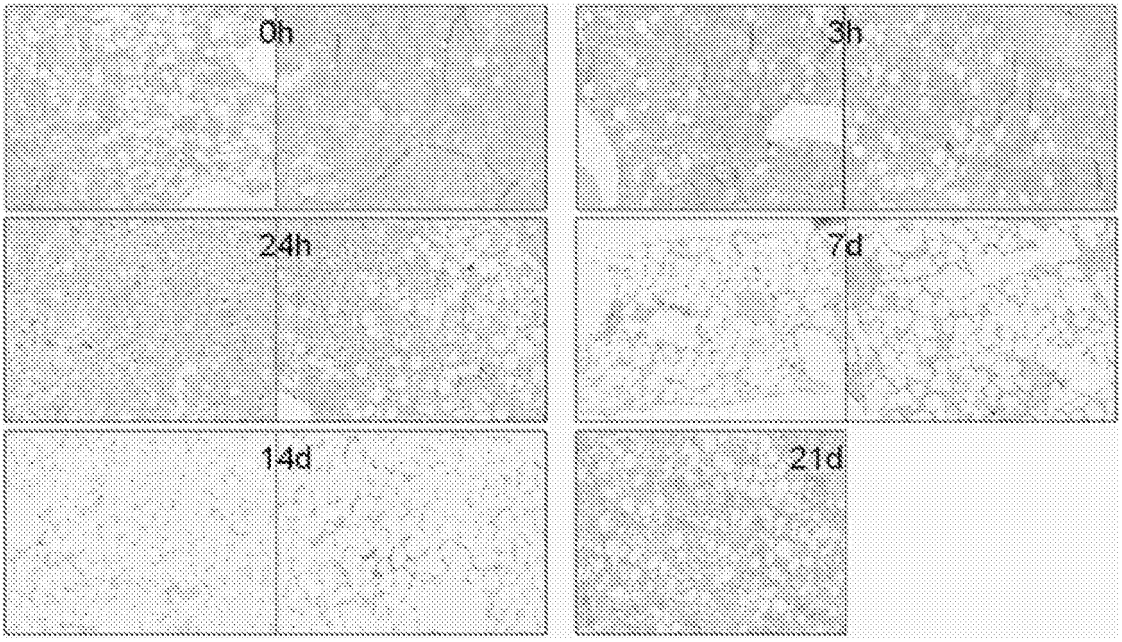


Figure 7

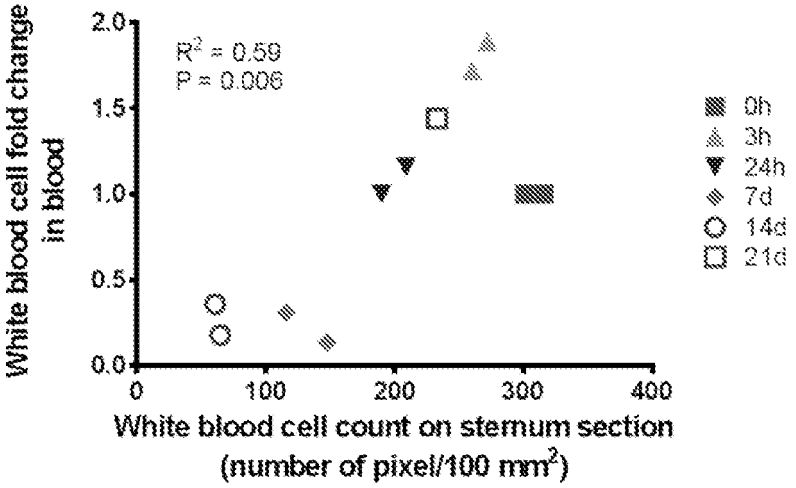


Figure 8

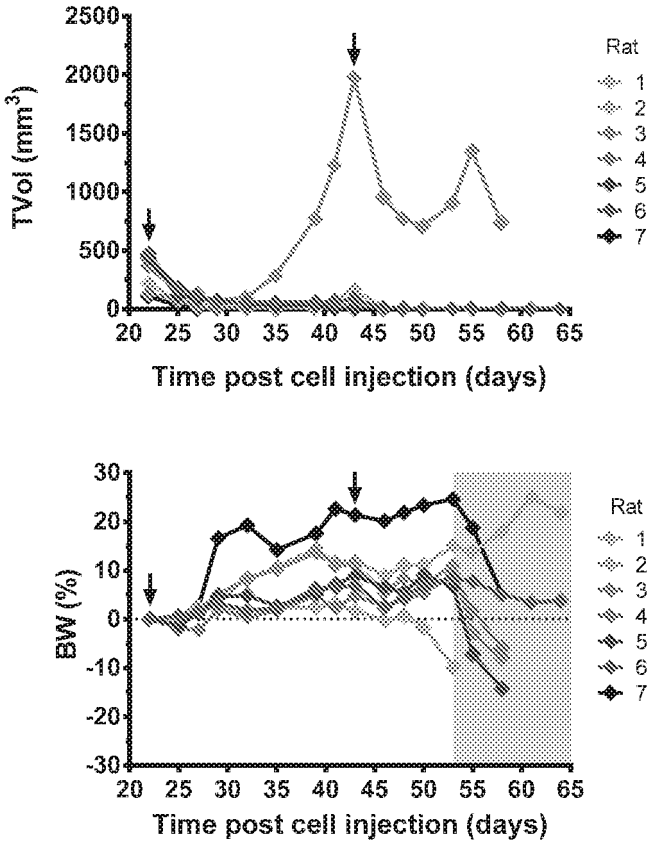


Figure 9

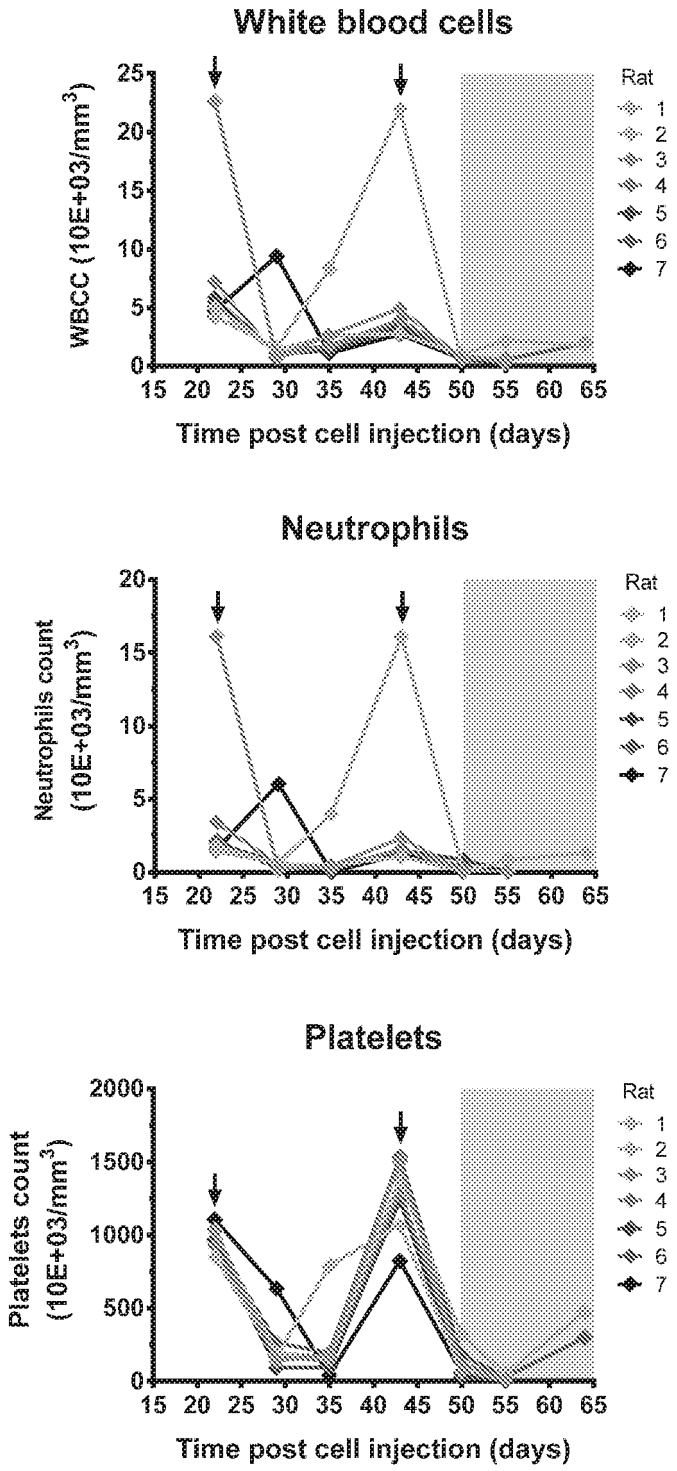

White blood cells
WBCC (10E+03/mm3)
25
20
15
10
5
0
15 20 25 30 35 40 45 50 55 60 65
Time post cell injection (days)
Rat
1
2
3
4
5
6
7
Neutrophils
Neutrophils count (10E+03/mm3)
20
15
10
5
0
15 20 25 30 35 40 45 50 55 60 65
Time post cell injection (days)
Rat
1
2
3
4
5
6
7
Platelets
Platelets count (10E+03/mm3)
2000
1500
1000
500
0
15 20 25 30 35 40 45 50 55 60 65
Time post cell injection (days)
Rat
1
2
3
4
5
6
7

Figure 10

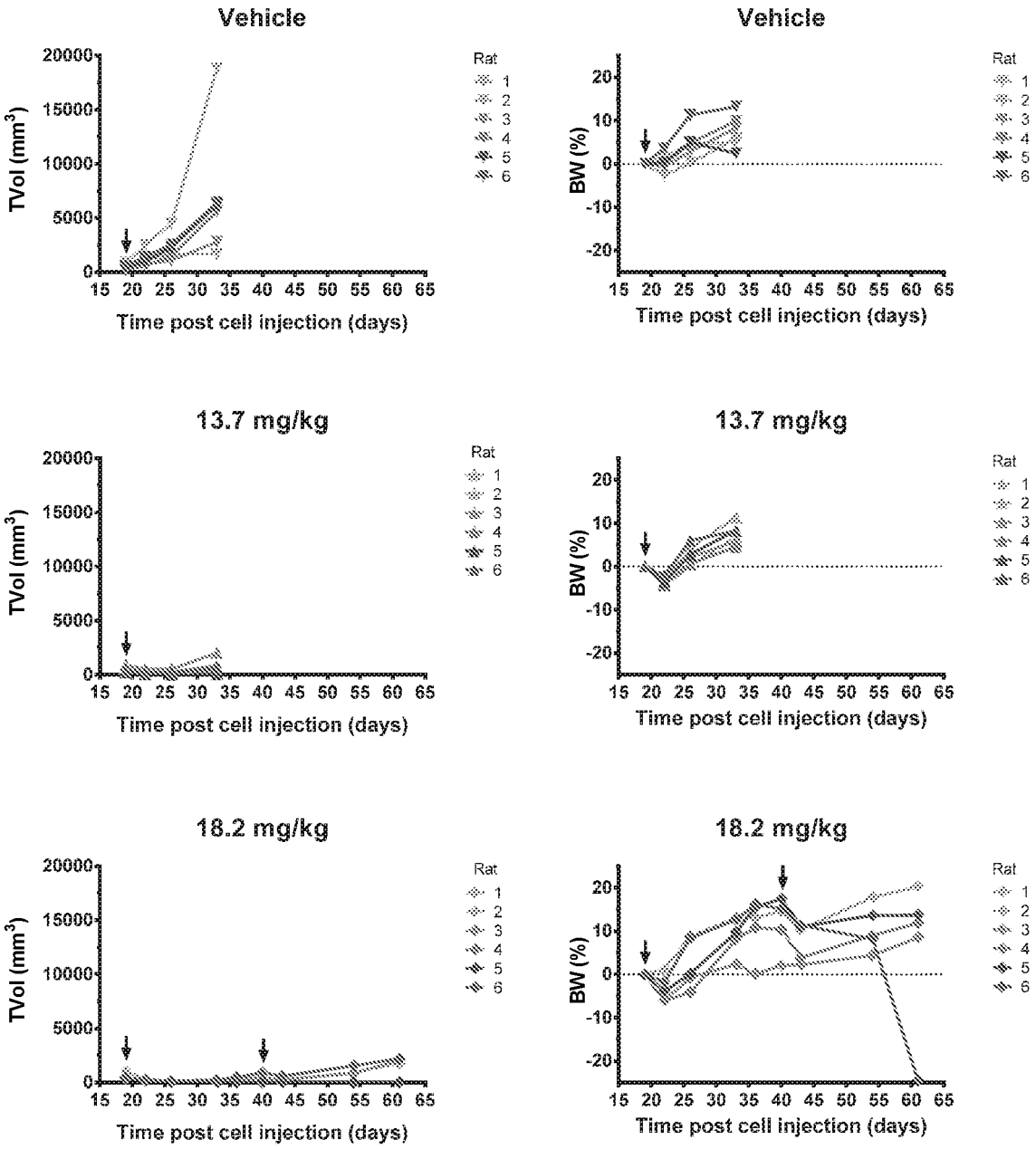

Vehicle
TVol (mm3)
Time post cell injection (days)
Rat
1
2
3
4
5
6
Vehicle
BW (%)
Time post cell injection (days)
13.7 mg/kg
TVol (mm3)
Time post cell injection (days)
13.7 mg/kg
BW (%)
Time post cell injection (days)
18.2 mg/kg
TVol (mm3)
Time post cell injection (days)
18.2 mg/kg
BW (%)
Time post cell injection (days)

Figure 11

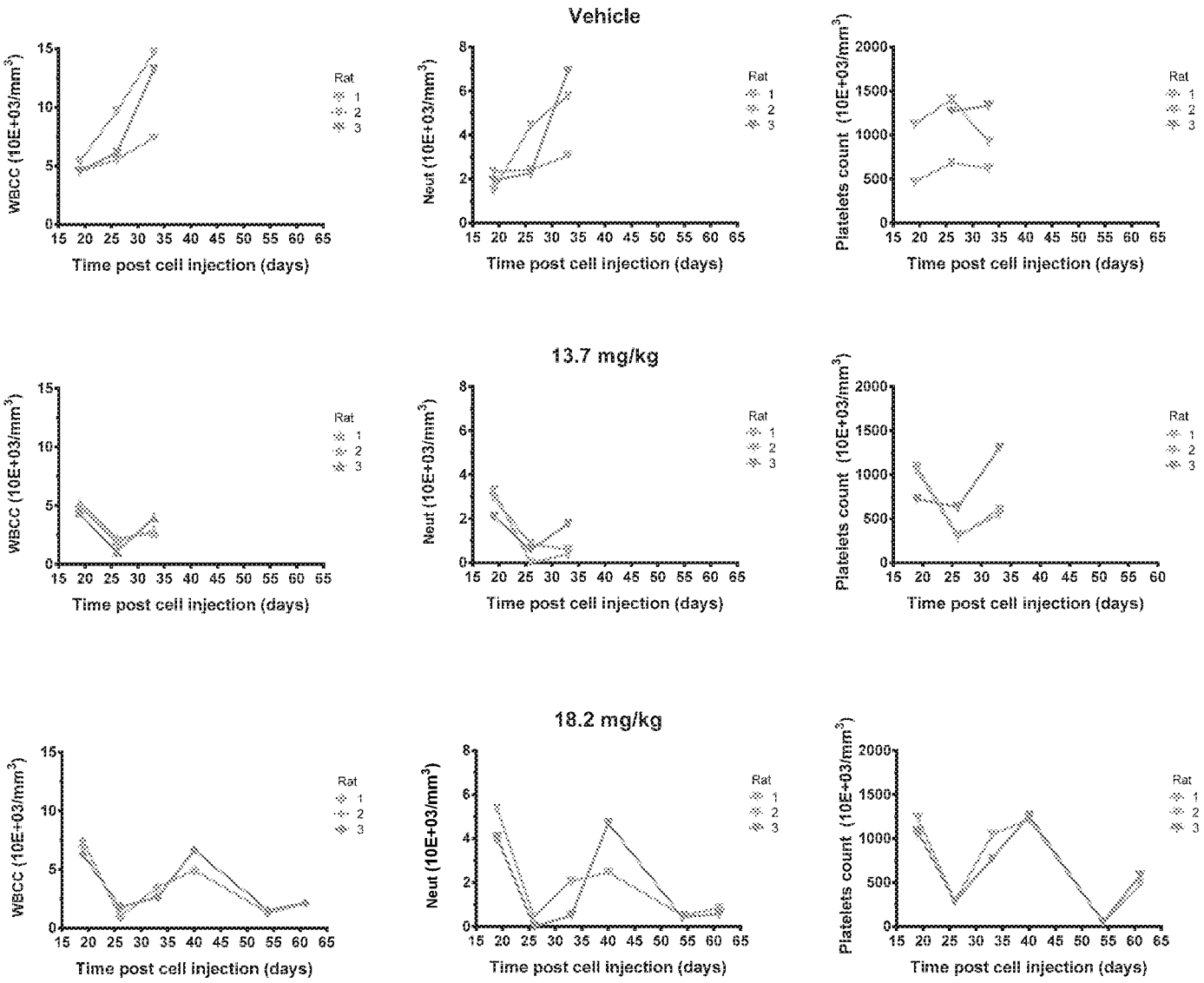

Vehicle
13.7 mg/kg
18.2 mg/kg
WBCC (10E+03/mm3)
Neut (10E+03/mm3)
Platelets count (10E+03/mm3)
Time post cell injection (days)
Rat
1
2
3

Figure 12

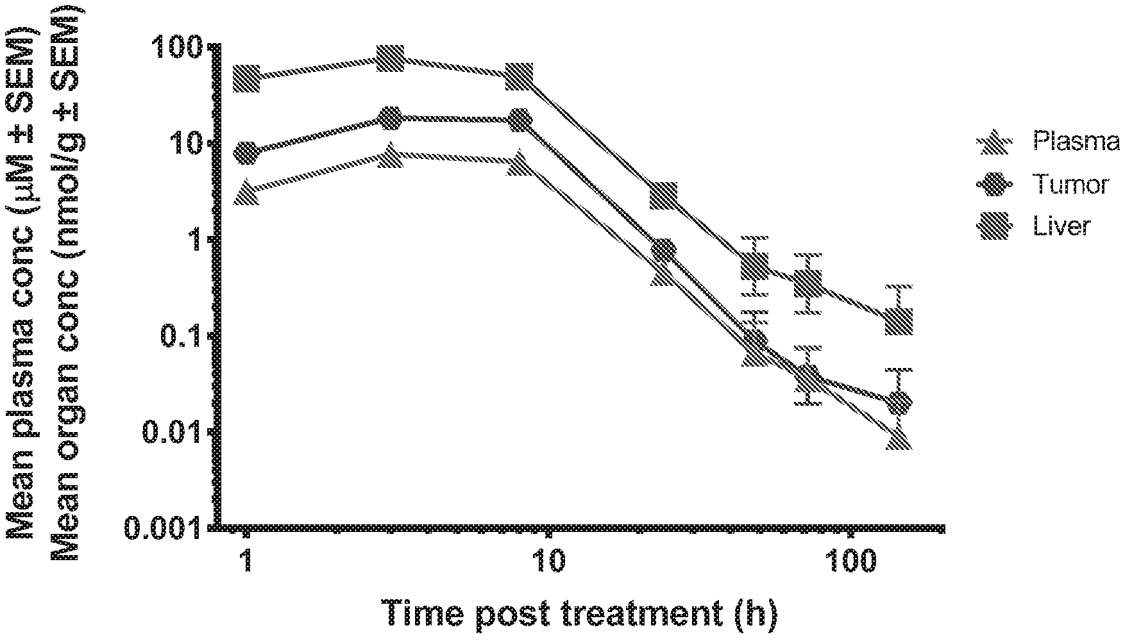


Figure 13

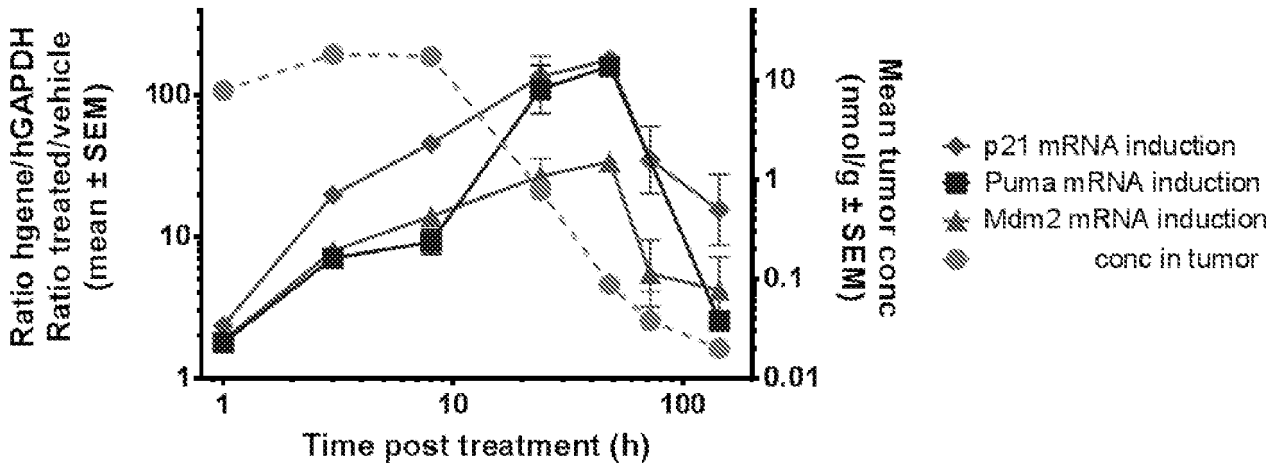


Figure 14

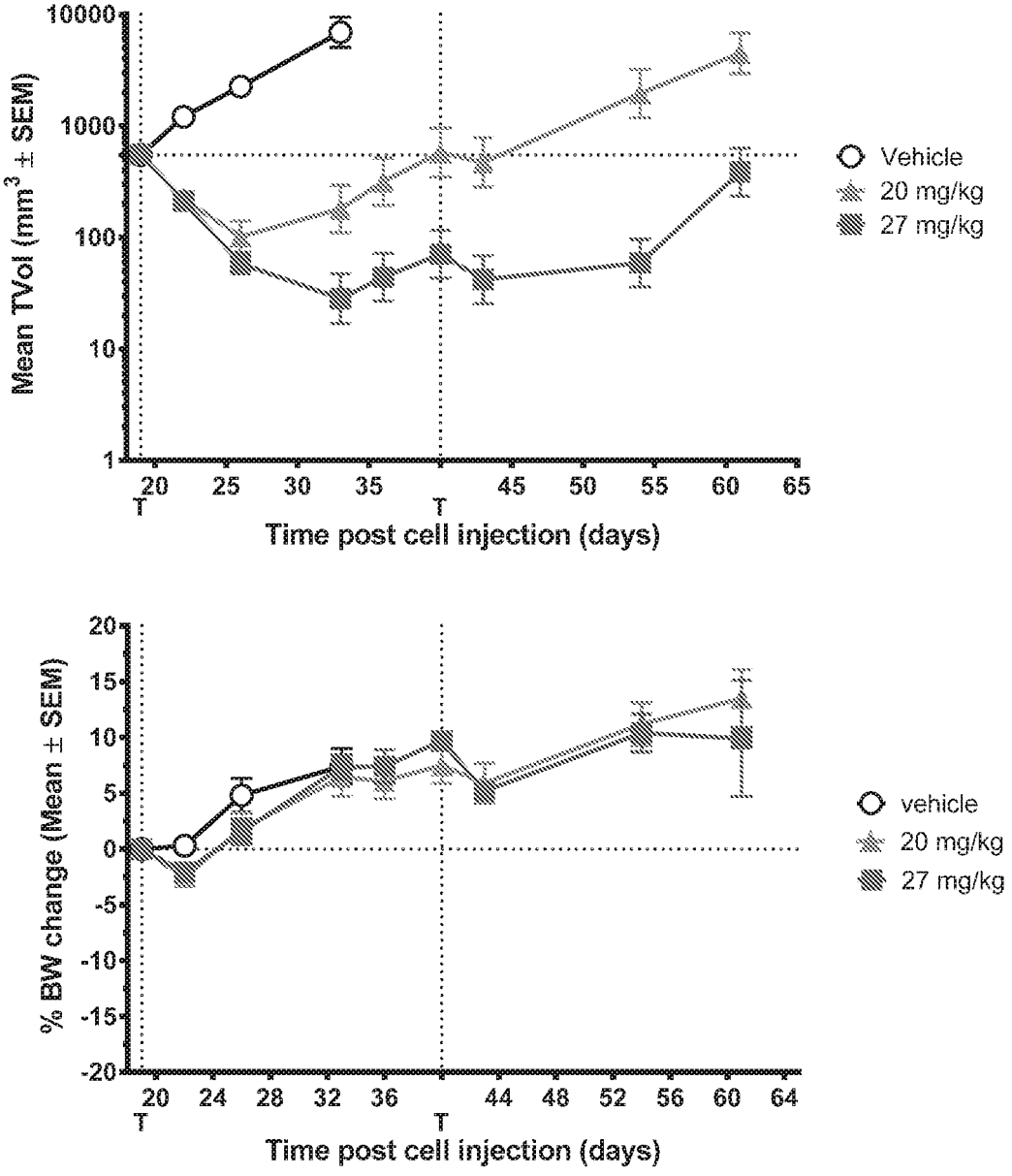

Mean TVol (mm3 ± SEM)
10000
1000
100
10
1
20
25
30
35
45
50
55
60
65
T
T
Time post cell injection (days)
Vehicle
20 mg/kg
27 mg/kg
% BW change (Mean ± SEM)
20
15
10
5
0
-5
-10
-15
-20
20
24
28
32
36
44
48
52
56
60
64
T
T
Time post cell injection (days)
vehicle
20 mg/kg
27 mg/kg

Figure 15

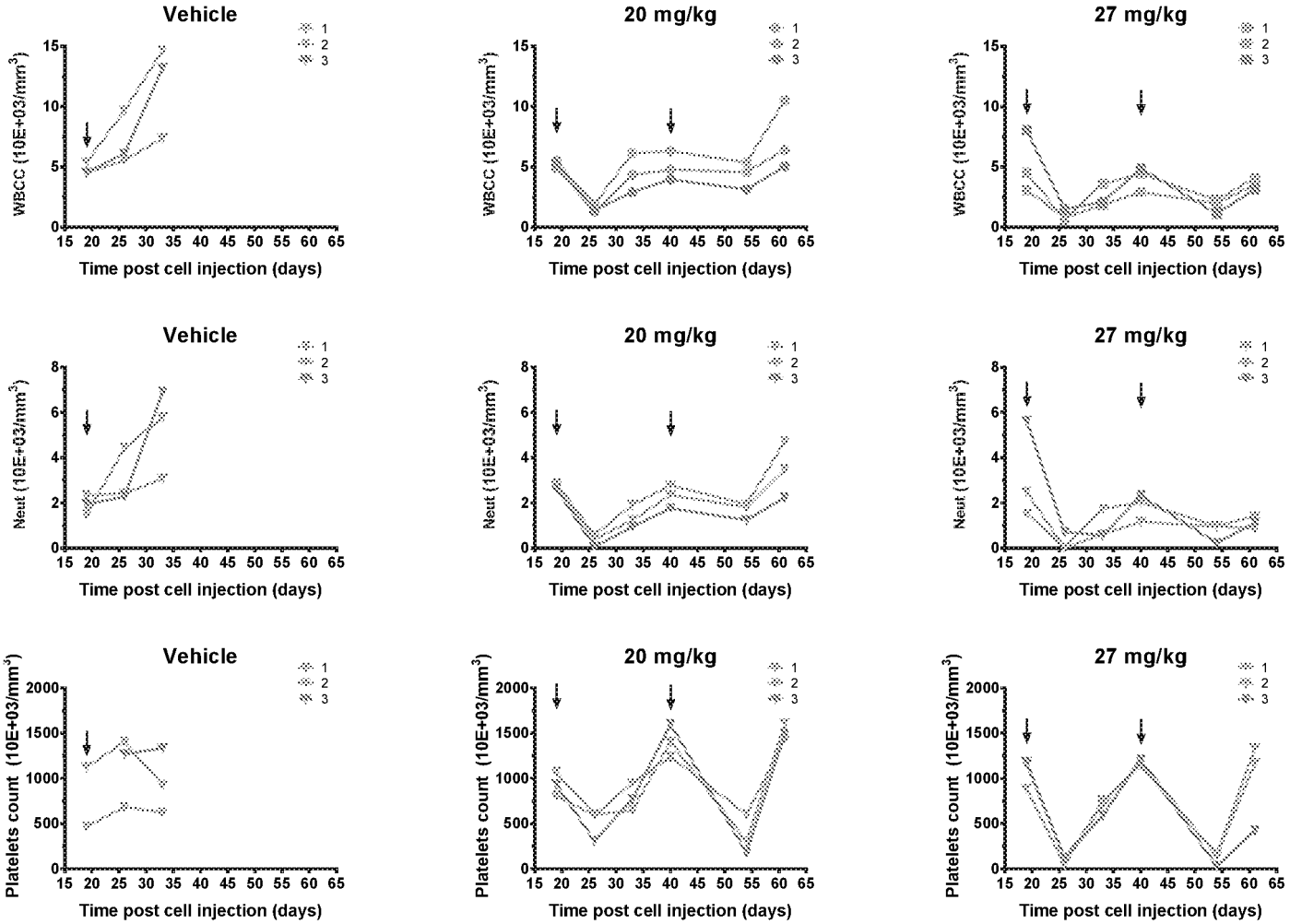

Vehicle
20 mg/kg
27 mg/kg
WBCC (10E+03/mm3)
Neut (10E+03/mm3)
Platelets count (10E+03/mm3)
Time post cell injection (days)
1
2
3

Figure 16

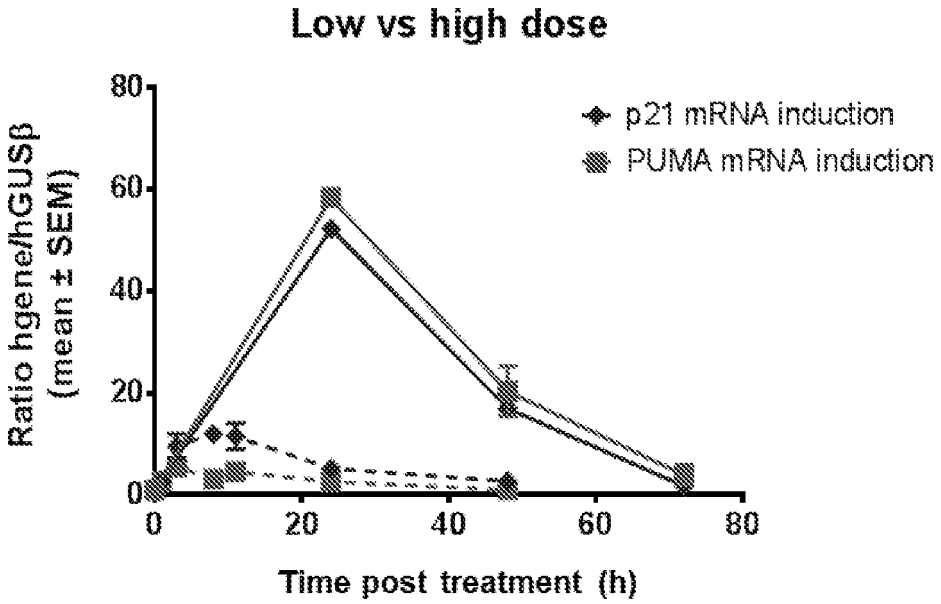
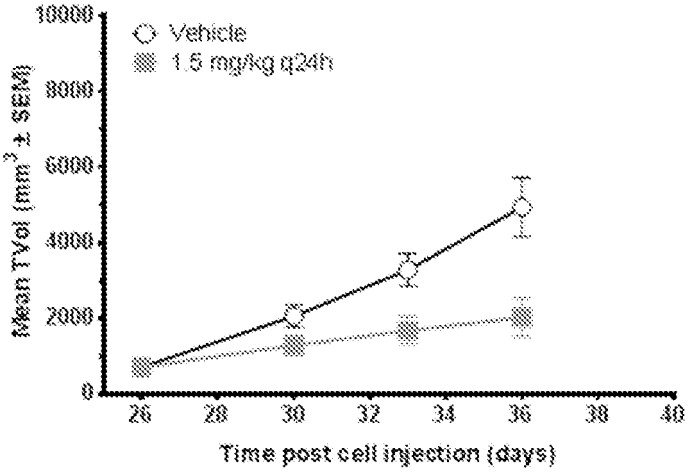
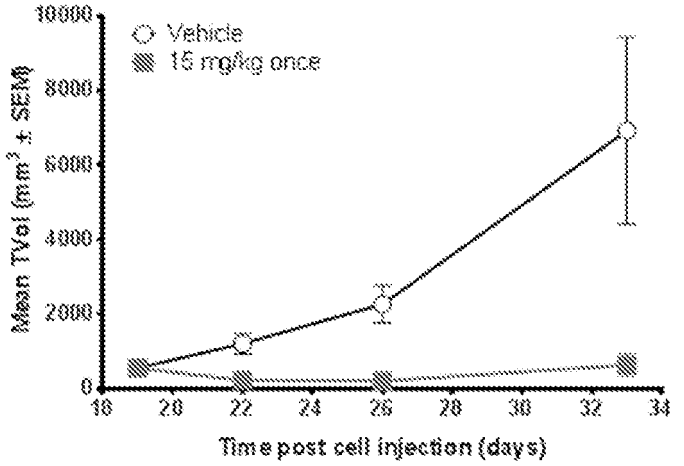

Low vs high dose
p21 mRNA induction
PUMA mRNA induction
Ratio hgene/hGUSβ
(mean ± SEM)
80
60
40
20
0
0
20
40
60
80
Time post treatment (h)

Figure 17


Vehicle
1.5 mg/kg q24h
Mean TVol (mm3 ± SEM)
Time post cell injection (days)


Vehicle
15 mg/kg once
Mean TVol (mm3 ± SEM)
Time post cell injection (days)

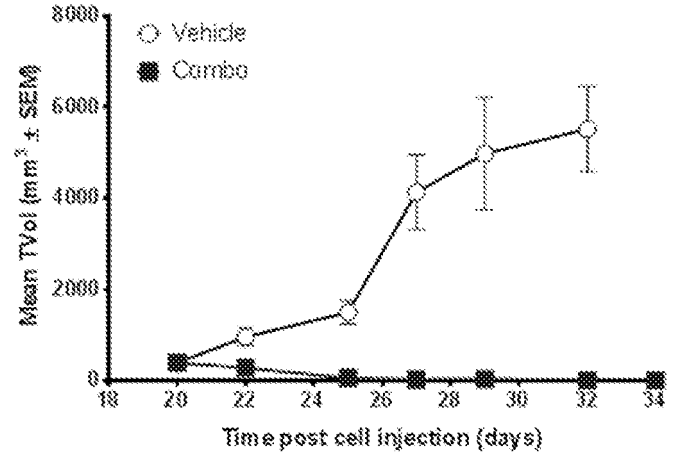
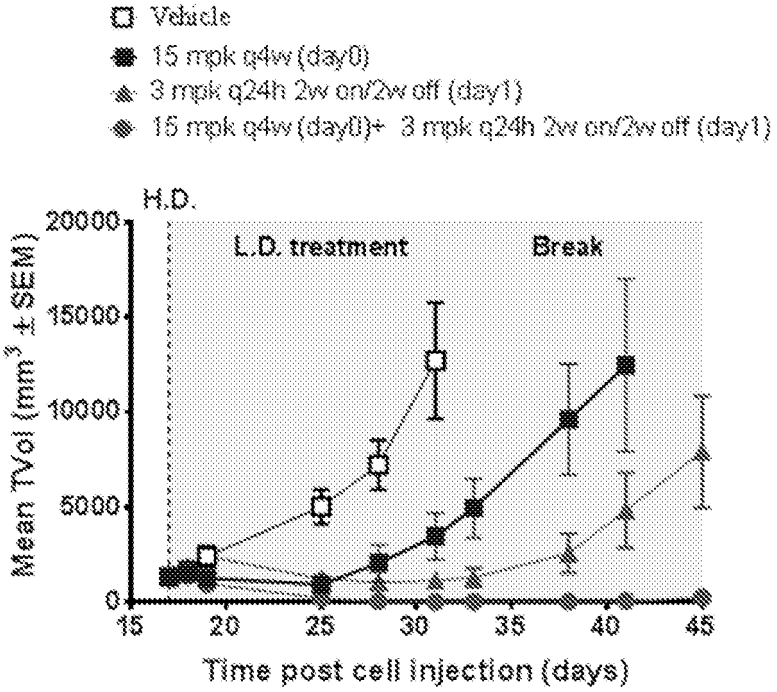

Vehicle
Combo
Mean TVol (mm3 ± SEM)
Time post cell injection (days)

Figure 18


Vehicle
15 mpk q4w (day0)
3 mpk q24h 2w on/2w off (day1)
15 mpk q4w (day0)+ 3 mpk q24h 2w on/2w off (day1)
H.D.
L.D. treatment
Break
Mean TVol (mm3 ± SEM)
20000
15000
10000
5000
0
15
20
25
30
35
40
45
Time post cell injection (days)

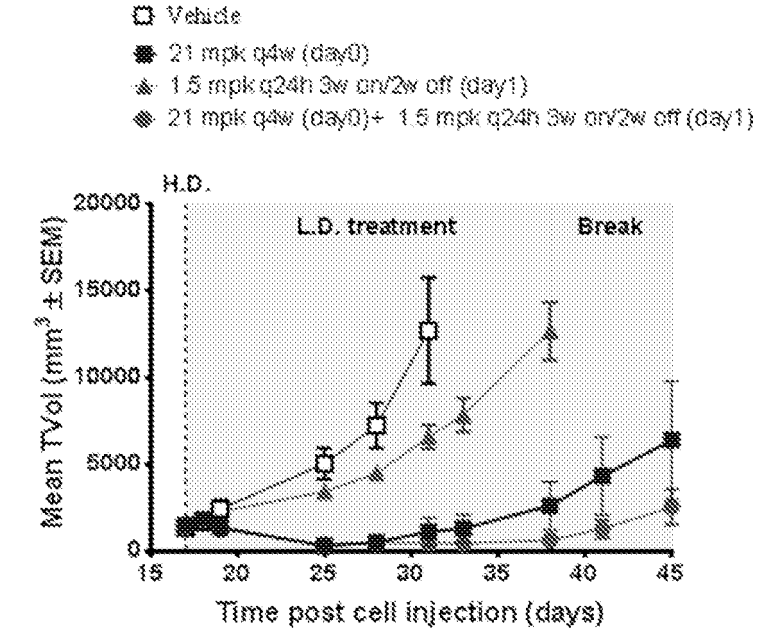
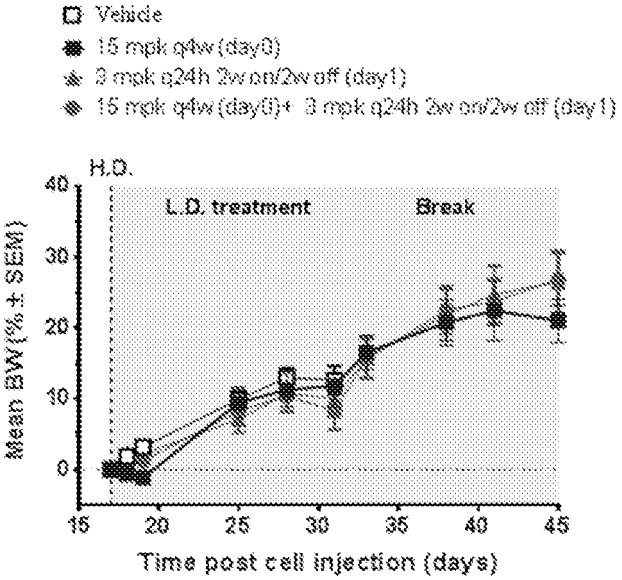

Vehicle
21 mpk q4w (day0)
1.5 mpk q24h 3w on/2w off (day1)
21 mpk q4w (day0)+ 1.5 mpk q24h 3w on/2w off (day1)
H.D.
L.D. treatment
Break
Mean TVol (mm3 ± SEM)
20000
15000
10000
5000
0
15
20
25
30
35
40
45
Time post cell injection (days)

Figure 19


Vehicle
15 mpk q4w (day0)
3 mpk q24h 2w on/2w off (day1)
15 mpk q4w (day0)+ 3 mpk q24h 2w on/2w off (day1)
H.D.
L.D. treatment
Break
Mean BW (% ± SEM)
Time post cell injection (days)

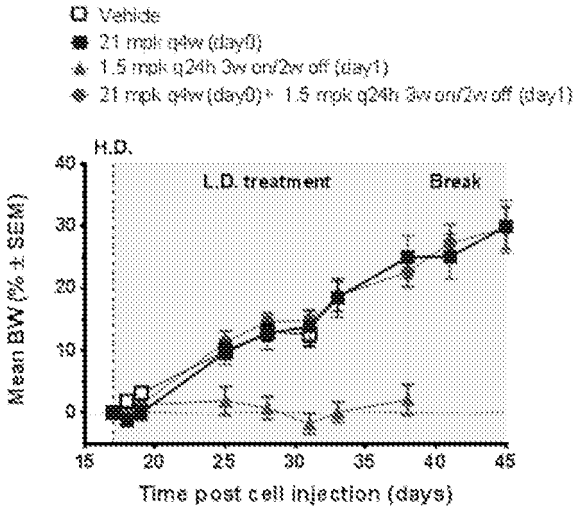

Vehicle
21 mpk q4w (day0)
1.5 mpk q24h 3w on/2w off (day1)
21 mpk q4w (day0)+ 1.5 mpk q24h 3w on/2w off (day1)
H.D.
L.D. treatment
Break
Mean BW (% ± SEM)
Time post cell injection (days)

Figure 20

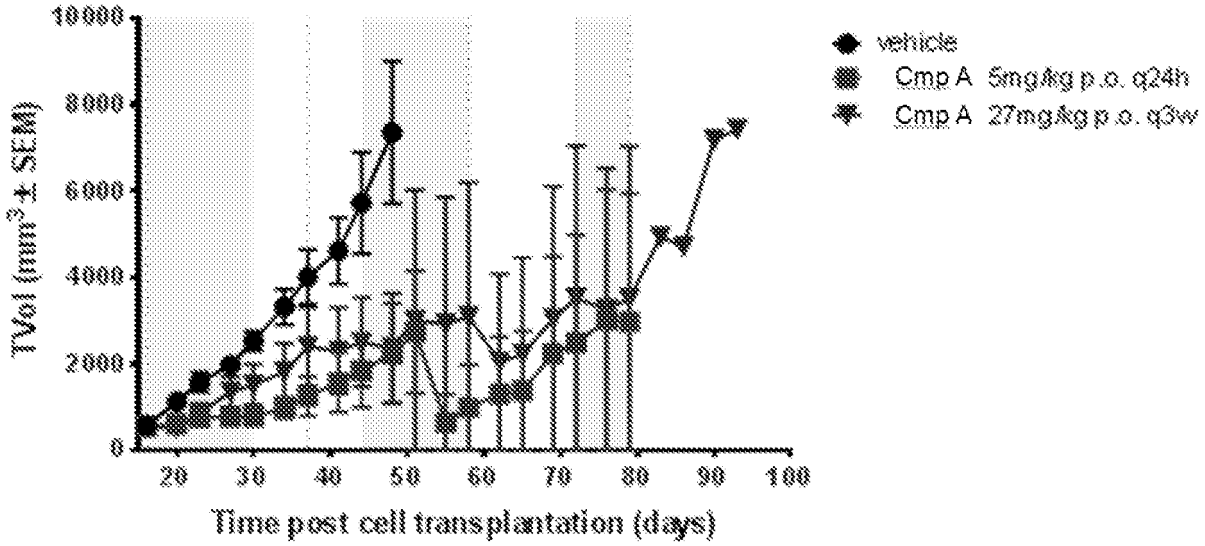


Figure 21

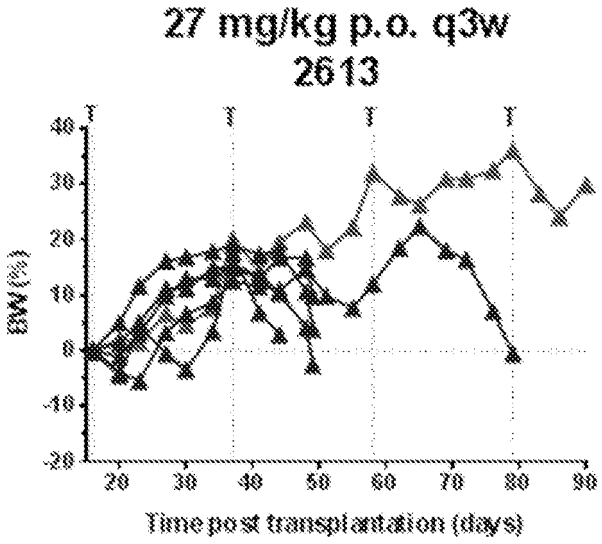
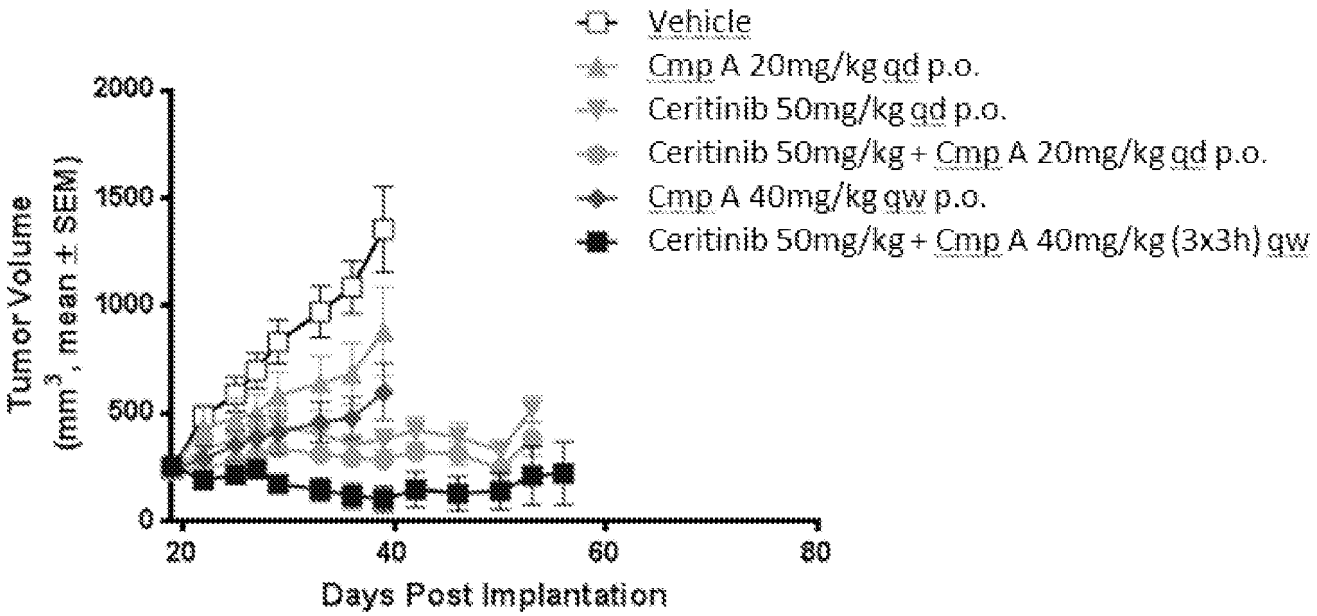


Figure 22


Vehicle
Cmp A 20mg/kg qd p.o.
Ceritinib 50mg/kg qd p.o.
Ceritinib 50mg/kg + Cmp A 20mg/kg qd p.o.
Cmp A 40mg/kg qw p.o.
Ceritinib 50mg/kg + Cmp A 40mg/kg (3x3h) qw
Tumor Volume
(mm3, mean + SEM)
2000
1500
1000
500
0
20
40
60
80
Days Post Implantation