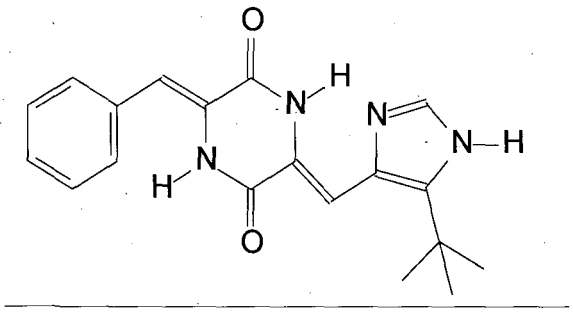
O
N
H
N
H
N
N
H
O

Fig. 1

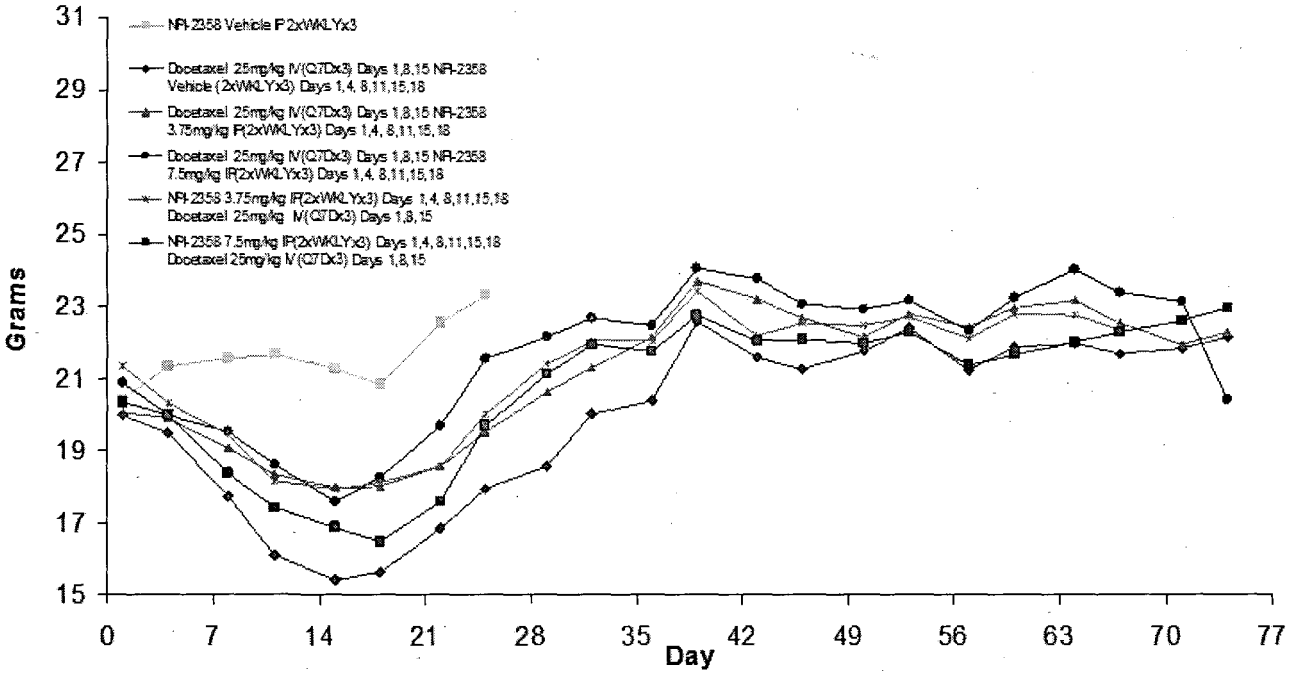
NPI-2358 Vehicle IP 2xWKLYx3
Docetaxel 25mg/kg IV(Q7Dx3) Days 1,8,15 NPI-2358 Vehicle (2xWKLYx3) Days 1,4, 8,11,15,18
Docetaxel 25mg/kg IV(Q7Dx3) Days 1,8,15 NPI-2358 3.75mg/kg IP(2xWKLYx3) Days 1,4, 8,11,15,18
Docetaxel 25mg/kg IV(Q7Dx3) Days 1,8,15 NPI-2358 7.5mg/kg IP(2xWKLYx3) Days 1,4, 8,11,15,18
NPI-2358 3.75mg/kg IP(2xWKLYx3) Days 1,4, 8,11,15,18 Docetaxel 25mg/kg IV(Q7Dx3) Days 1,8,15
NPI-2358 7.5mg/kg IP(2xWKLYx3) Days 1,4, 8,11,15,18 Docetaxel 25mg/kg IV(Q7Dx3) Days 1,8,15
Grams
31
29
27
25
23
21
19
17
15
0
7
14
21
28
35
42
49
56
63
70
77
Day

Fig. 2

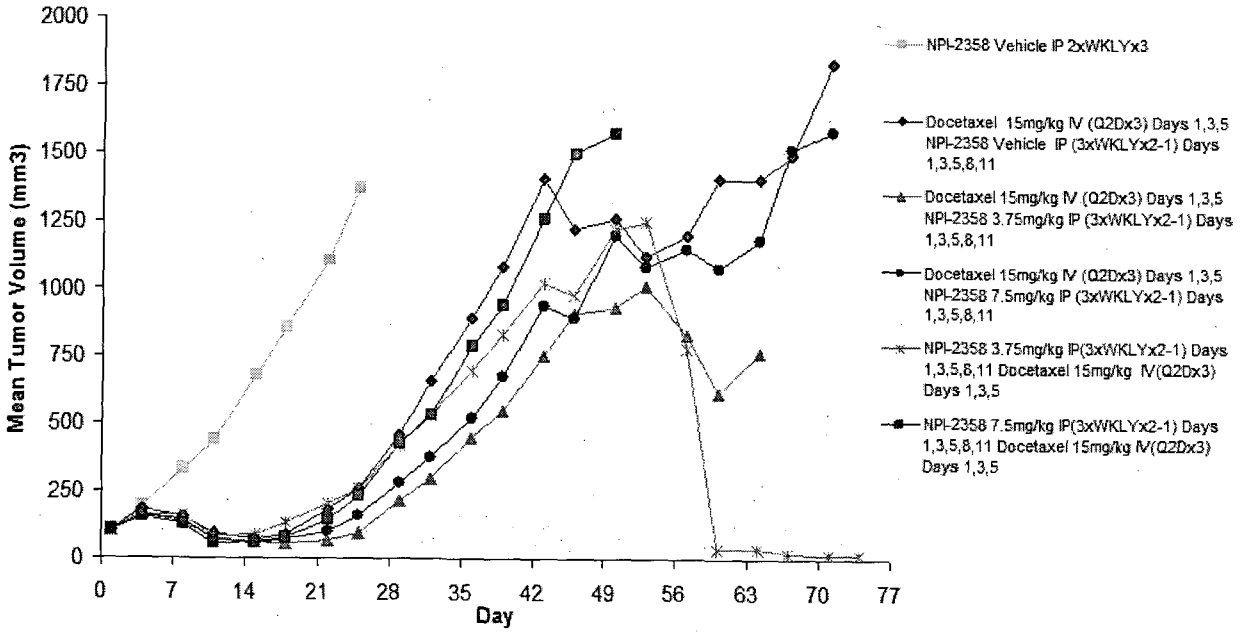
Mean Tumor Volume (mm3)
2000
1750
1500
1250
1000
750
500
250
0
0 7 14 21 28 35 42 49 56 63 70 77
Day
NPI-2358 Vehicle IP 2xWKLYx3
Docetaxel 15mg/kg IV (Q2Dx3) Days 1,3,5 NPI-2358 Vehicle IP (3xWKLYx2-1) Days 1,3,5,8,11
Docetaxel 15mg/kg IV (Q2Dx3) Days 1,3,5 NPI-2358 3.75mg/kg IP (3xWKLYx2-1) Days 1,3,5,8,11
Docetaxel 15mg/kg IV (Q2Dx3) Days 1,3,5 NPI-2358 7.5mg/kg IP (3xWKLYx2-1) Days 1,3,5,8,11
NPI-2358 3.75mg/kg IP(3xWKLYx2-1) Days 1,3,5,8,11 Docetaxel 15mg/kg IV(Q2Dx3) Days 1,3,5
NPI-2358 7.5mg/kg IP(3xWKLYx2-1) Days 1,3,5,8,11 Docetaxel 15mg/kg IV(Q2Dx3) Days 1,3,5

Fig. 3

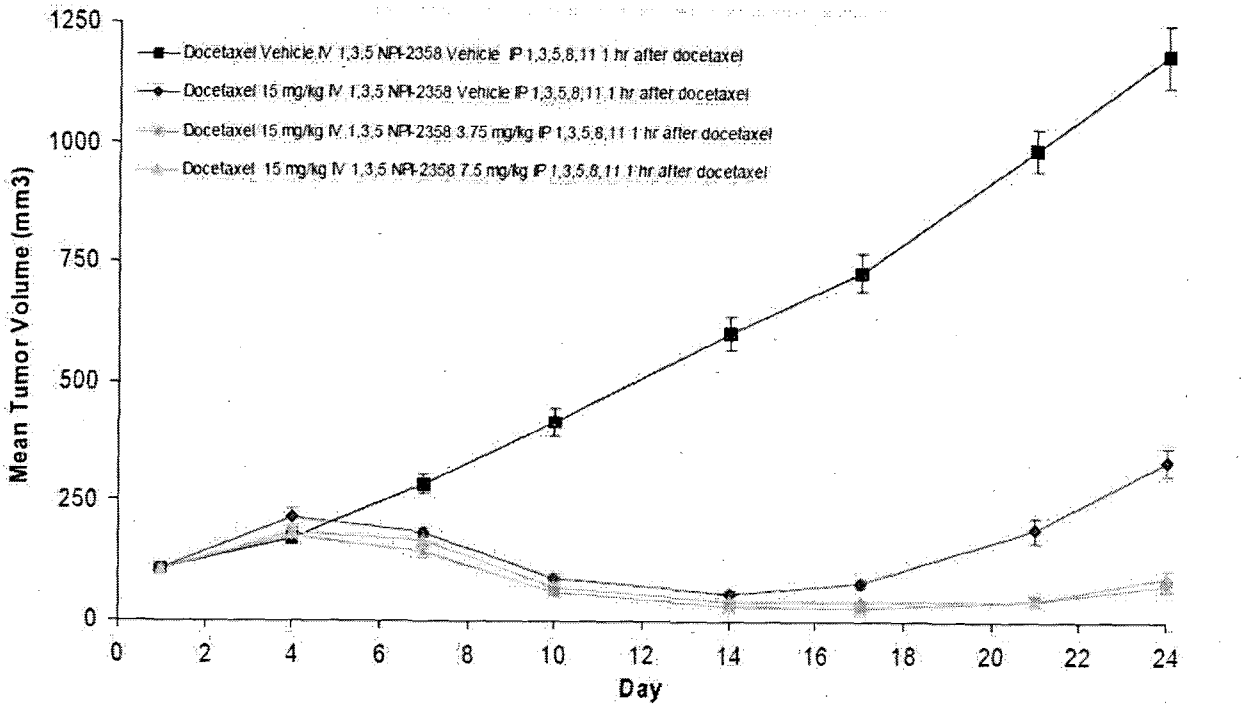
Mean Tumor Volume (mm3)
1250
1000
750
500
250
0
0 2 4 6 8 10 12 14 16 18 20 22 24
Day
Docetaxel Vehicle IV 1,3,5 NPI-2358 Vehicle IP 1,3,5,8,11 1 hr after docetaxel
Docetaxel 15 mg/kg IV 1,3,5 NPI-2358 Vehicle IP 1,3,5,8,11 1 hr after docetaxel
Docetaxel 15 mg/kg IV 1,3,5 NPI-2358 3.75 mg/kg IP 1,3,5,8,11 1 hr after docetaxel
Docetaxel 15 mg/kg IV 1,3,5 NPI-2358 7.5 mg/kg IP 1,3,5,8,11 1 hr after docetaxel

Fig. 4A

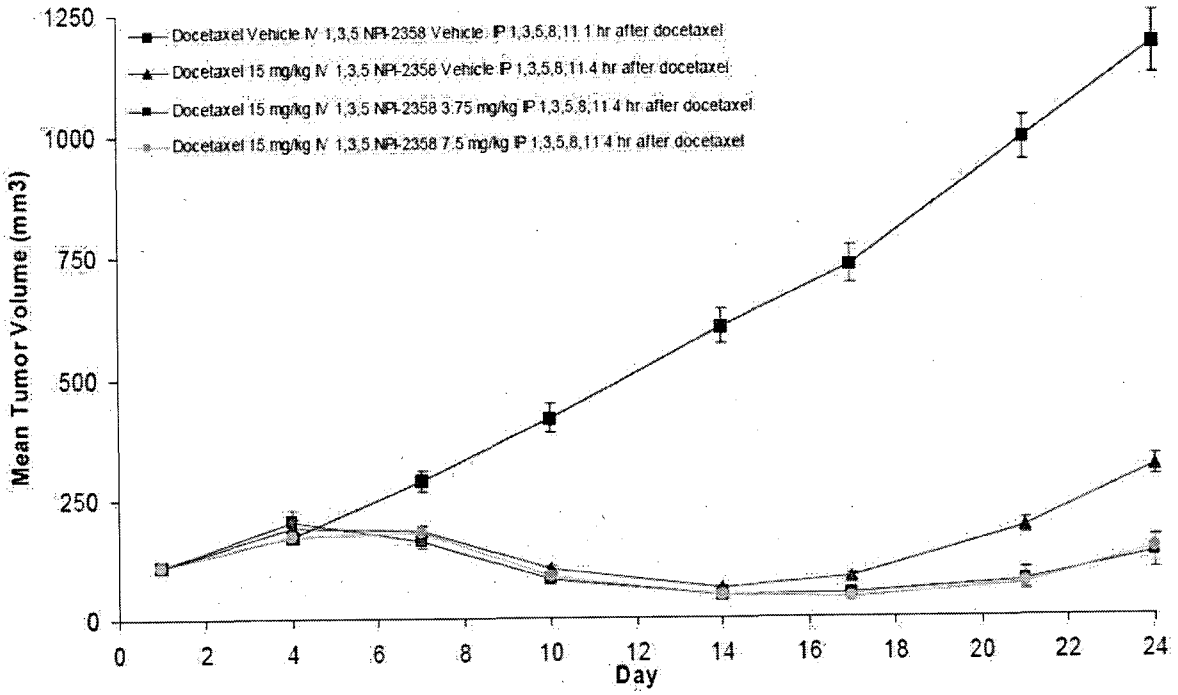
Docetaxel Vehicle IV 1,3,5 NPI-2358 Vehicle IP 1,3,5,8,11 1 hr after docetaxel
Docetaxel 15 mg/kg IV 1,3,5 NPI-2358 Vehicle IP 1,3,5,8,11 4 hr after docetaxel
Docetaxel 15 mg/kg IV 1,3,5 NPI-2358 3.75 mg/kg IP 1,3,5,8,11 4 hr after docetaxel
Docetaxel 15 mg/kg IV 1,3,5 NPI-2358 7.5 mg/kg IP 1,3,5,8,11 4 hr after docetaxel
Mean Tumor Volume (mm3)
Day
0
250
500
750
1000
1250
0
2
4
6
8
10
12
14
16
18
20
22
24

Fig. 4B

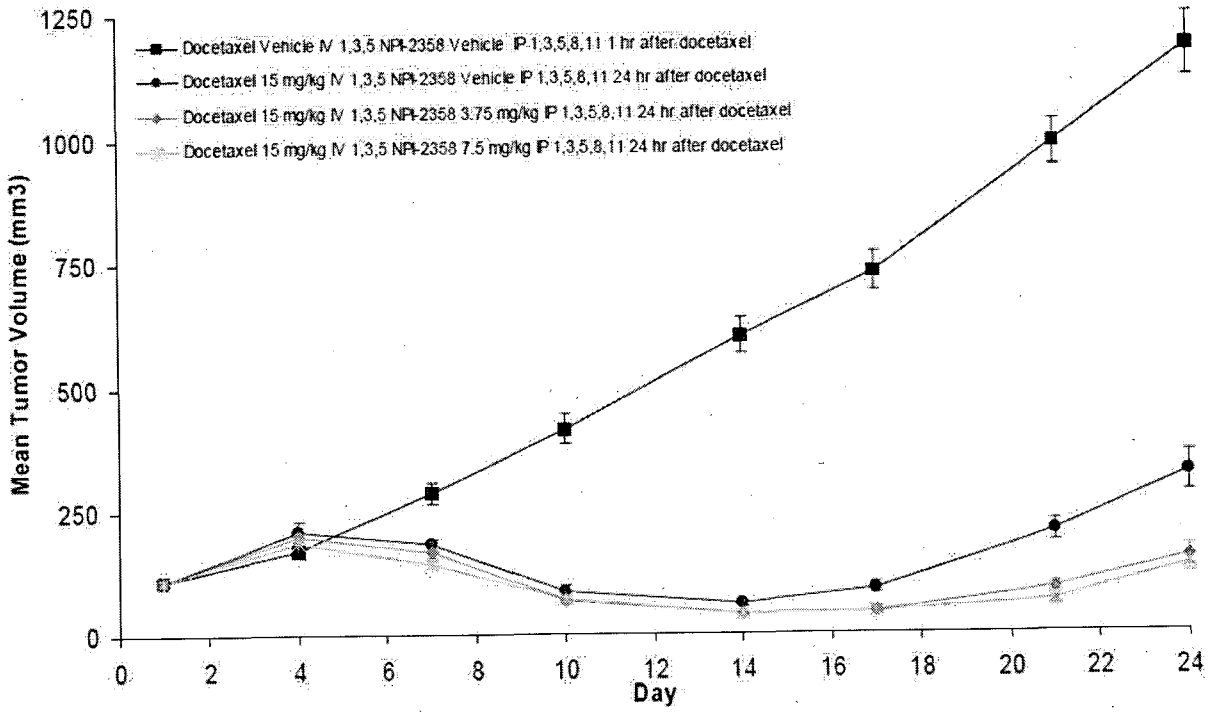
Docetaxel Vehicle IV 1,3,5 NPI-2358 Vehicle IP 1,3,5,8,11 1 hr after docetaxel
Docetaxel 15 mg/kg IV 1,3,5 NPI-2358 Vehicle IP 1,3,5,8,11 24 hr after docetaxel
Docetaxel 15 mg/kg IV 1,3,5 NPI-2358 3.75 mg/kg IP 1,3,5,8,11 24 hr after docetaxel
Docetaxel 15 mg/kg IV 1,3,5 NPI-2358 7.5 mg/kg IP 1,3,5,8,11 24 hr after docetaxel
Mean Tumor Volume (mm3)
Day
0
250
500
750
1000
1250
0
2
4
6
8
10
12
14
16
18
20
22
24

Fig. 4C

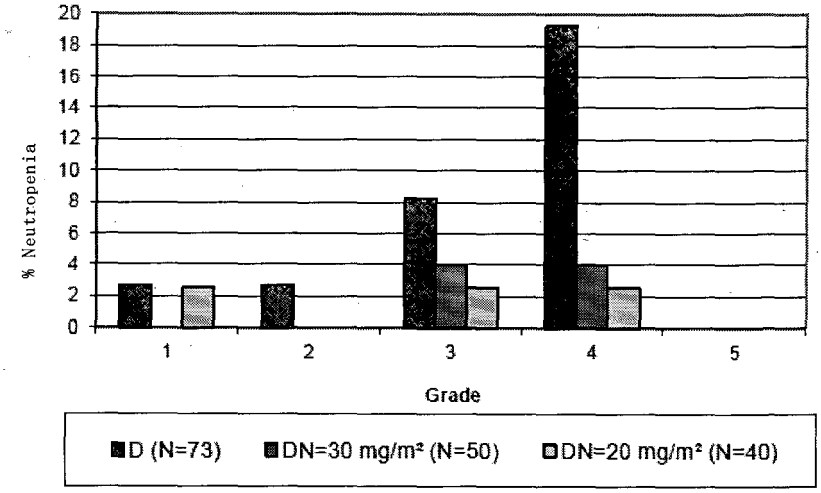
% Neutropenia
20
18
16
14
12
10
8
6
4
2
0
1
2
3
4
5
Grade
D (N=73)
DN=30 mg/m² (N=50)
DN=20 mg/m² (N=40)

Fig. 5

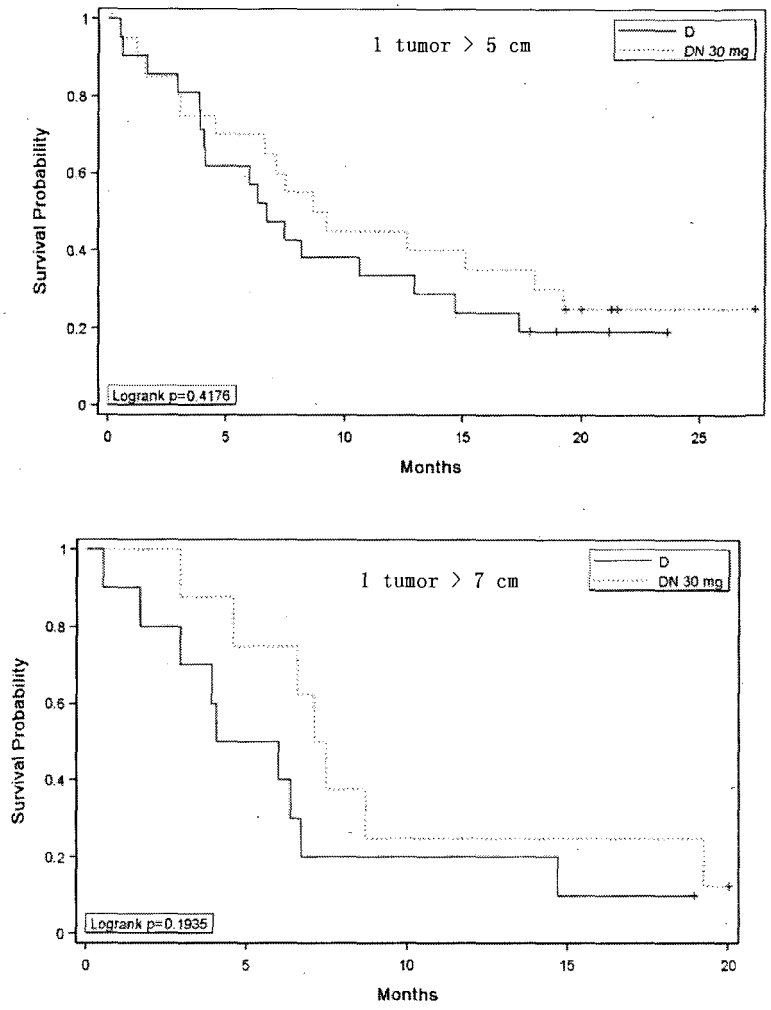
1 tumor > 5 cm
D
DN 30 mg
Survival Probability
Logrank p=0.4176
Months
1 tumor > 7 cm
D
DN 30 mg
Survival Probability
Logrank p=0.1935
Months

Fig. 6