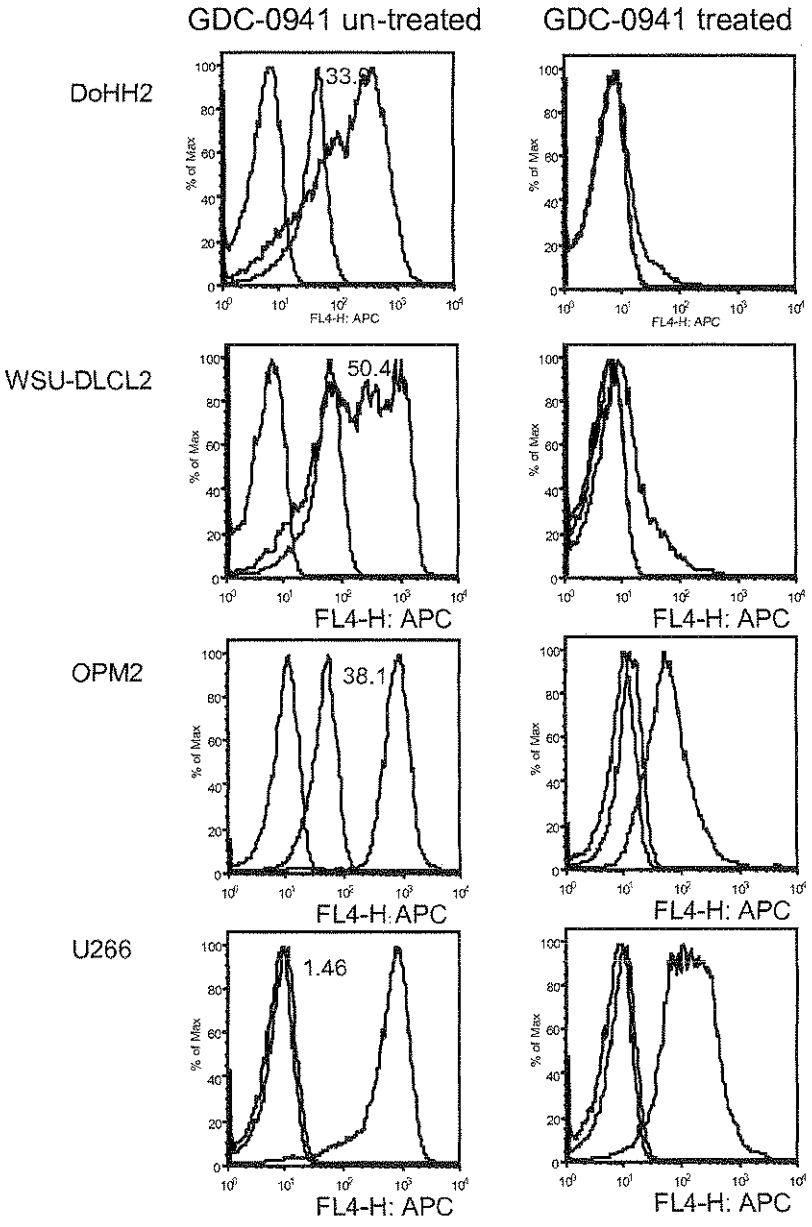
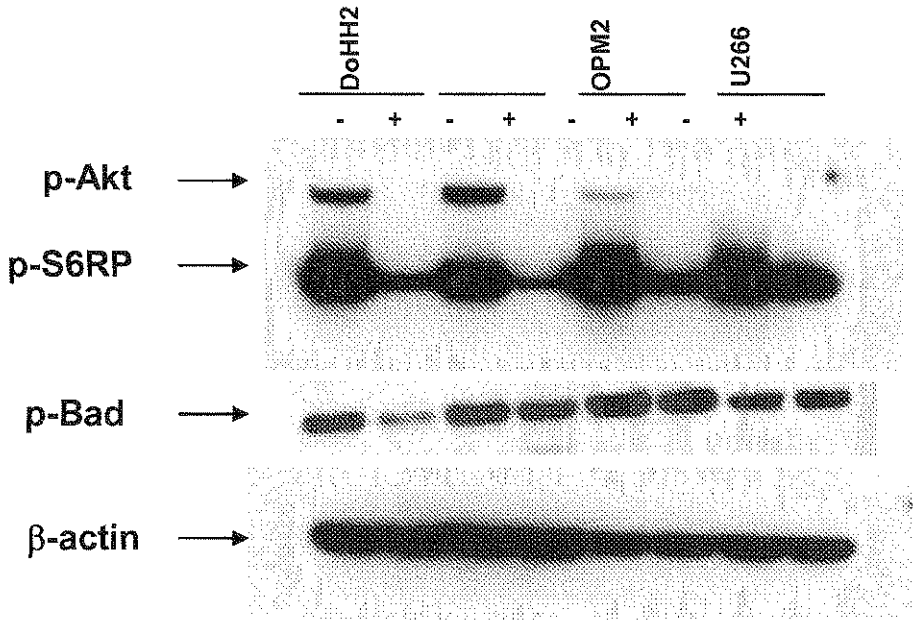

GDC-0941 un-treated
GDC-0941 treated
DoHH2
WSU-DLCL2
OPM2
U266
33.9
50.4
38.1
1.46
% of Max
FL4-H: APC
Rabbit IgG Alexa Fluor-647
p-Akt Alexa Fluor-647 (MFI indicated)
p-S6RP Alexa Fluor-647
GDC-0941 5 uM 4hrs

Figure 1



p-Akt, clone 193H12
p-Bad, clone 185D10
p-S6RP, clone D57.2.2E
Same clones used for WB and FACS

Figure 2

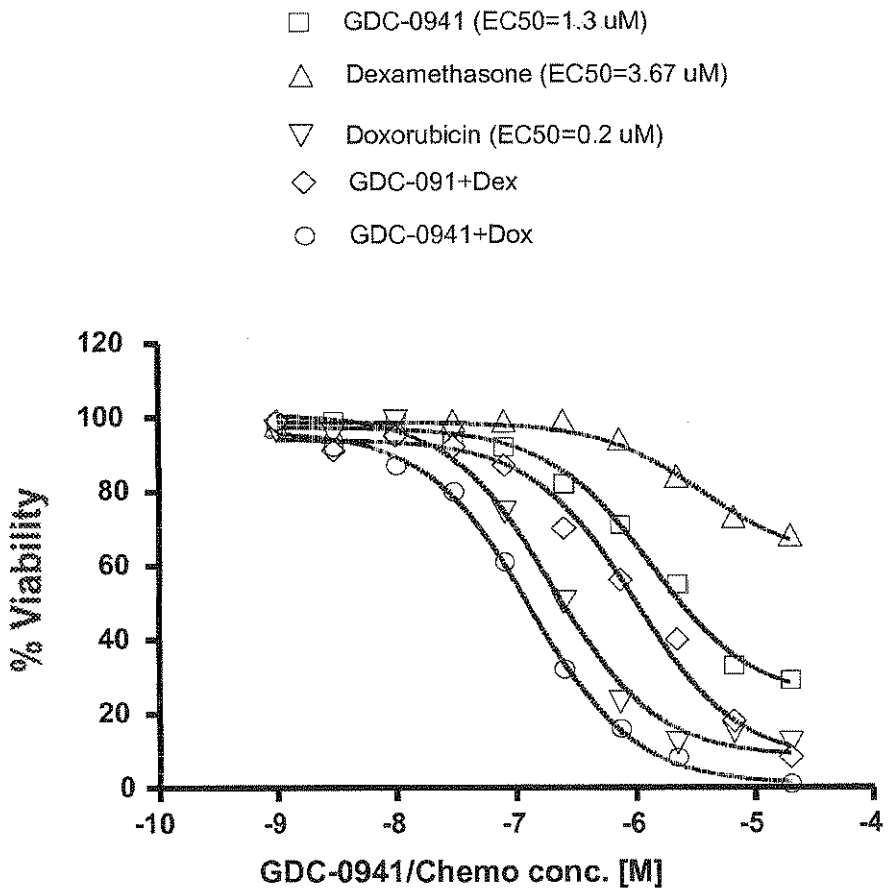

GDC-0941 (EC50=1.3 uM)
Dexamethasone (EC50=3.67 uM)
Doxorubicin (EC50=0.2 uM)
GDC-091+Dex
GDC-0941+Dox
% Viability
120
100
80
60
40
20
0
-10
-9
-8
-7
-6
-5
-4
GDC-0941/Chemo conc. [M]

Figure 3

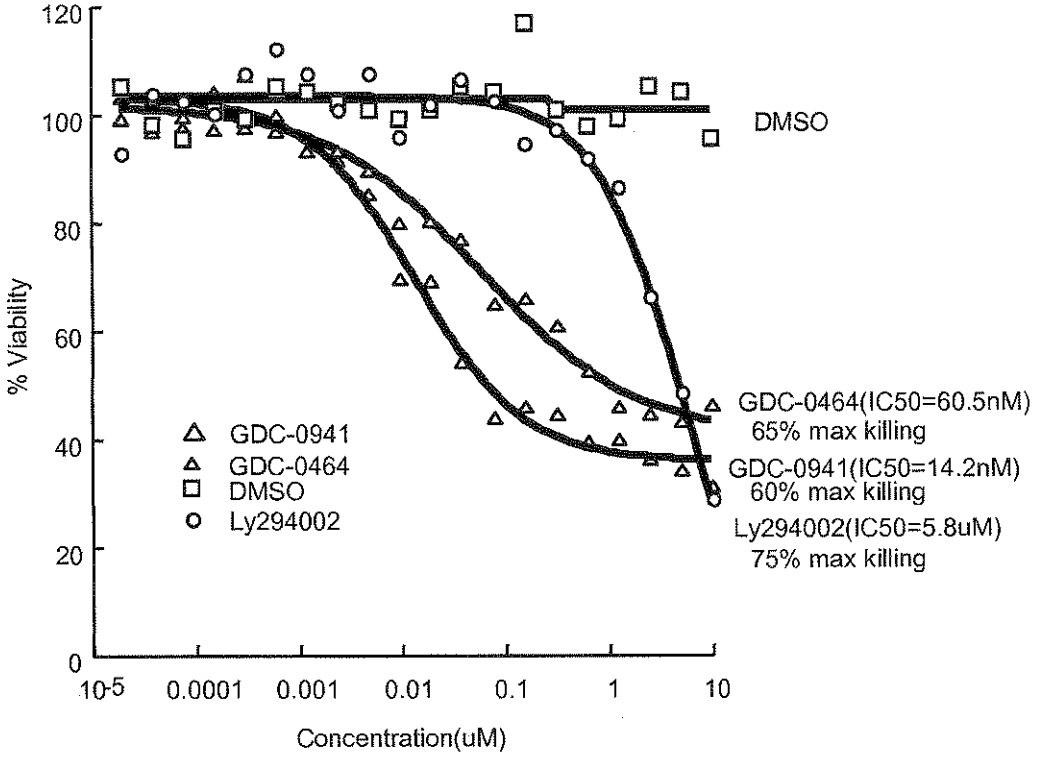

120
100
80
60
40
20
0
% Viability
10-5
0.0001
0.001
0.01
0.1
1
10
Concentration(uM)
GDC-0941
GDC-0464
DMSO
Ly294002
DMSO
GDC-0464(IC50=60.5nM)
65% max killing
GDC-0941(IC50=14.2nM)
60% max killing
Ly294002(IC50=5.8uM)
75% max killing

Figure 4

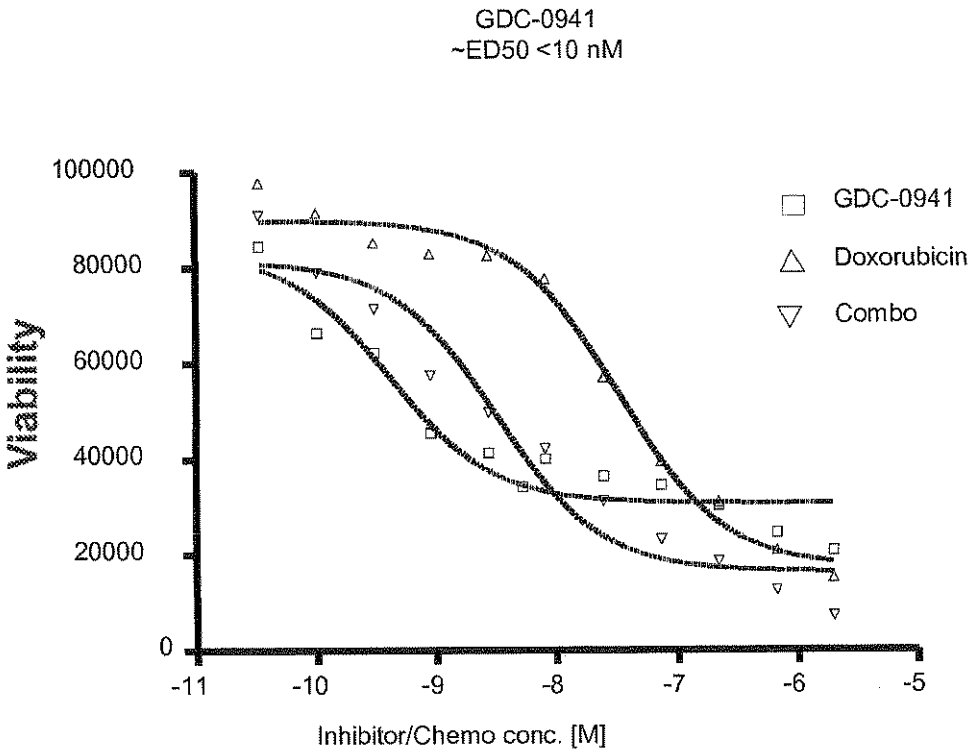

GDC-0941
~ED50 <10 nM
100000
80000
60000
40000
20000
0
Viability
-11
-10
-9
-8
-7
-6
-5
Inhibitor/Chemo conc. [M]
GDC-0941
Doxorubicin
Combo

Figure 5

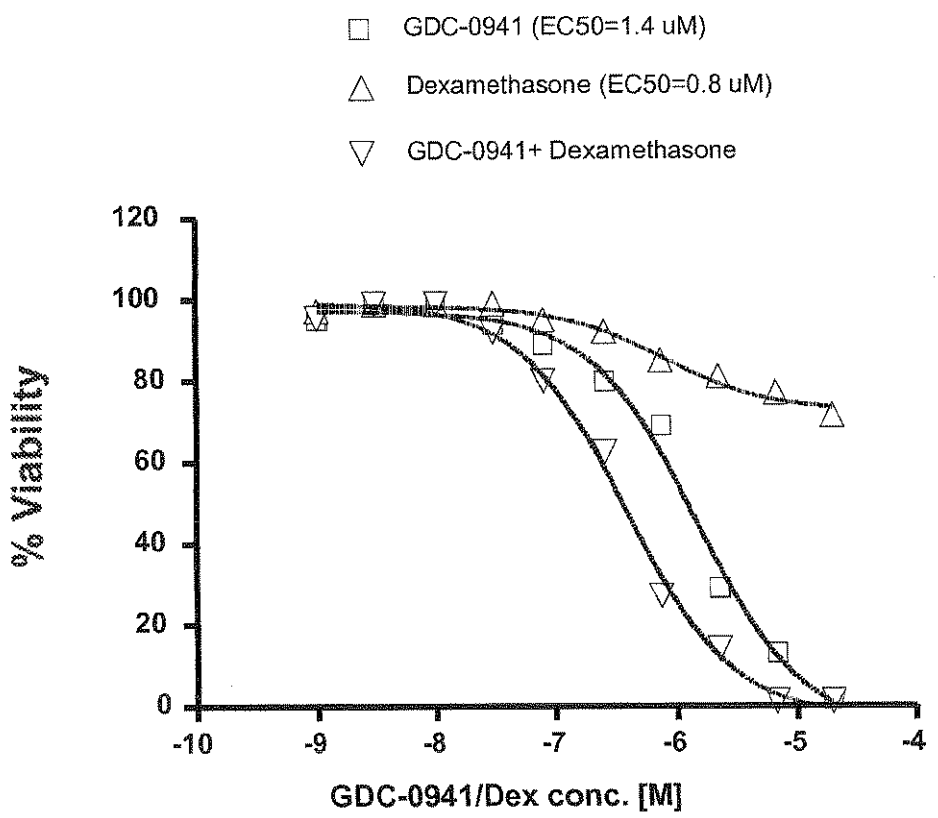

GDC-0941 (EC50=1.4 uM)
Dexamethasone (EC50=0.8 uM)
GDC-0941+ Dexamethasone
% Viability
120
100
80
60
40
20
0
-10
-9
-8
-7
-6
-5
-4
GDC-0941/Dex conc. [M]

Figure 6

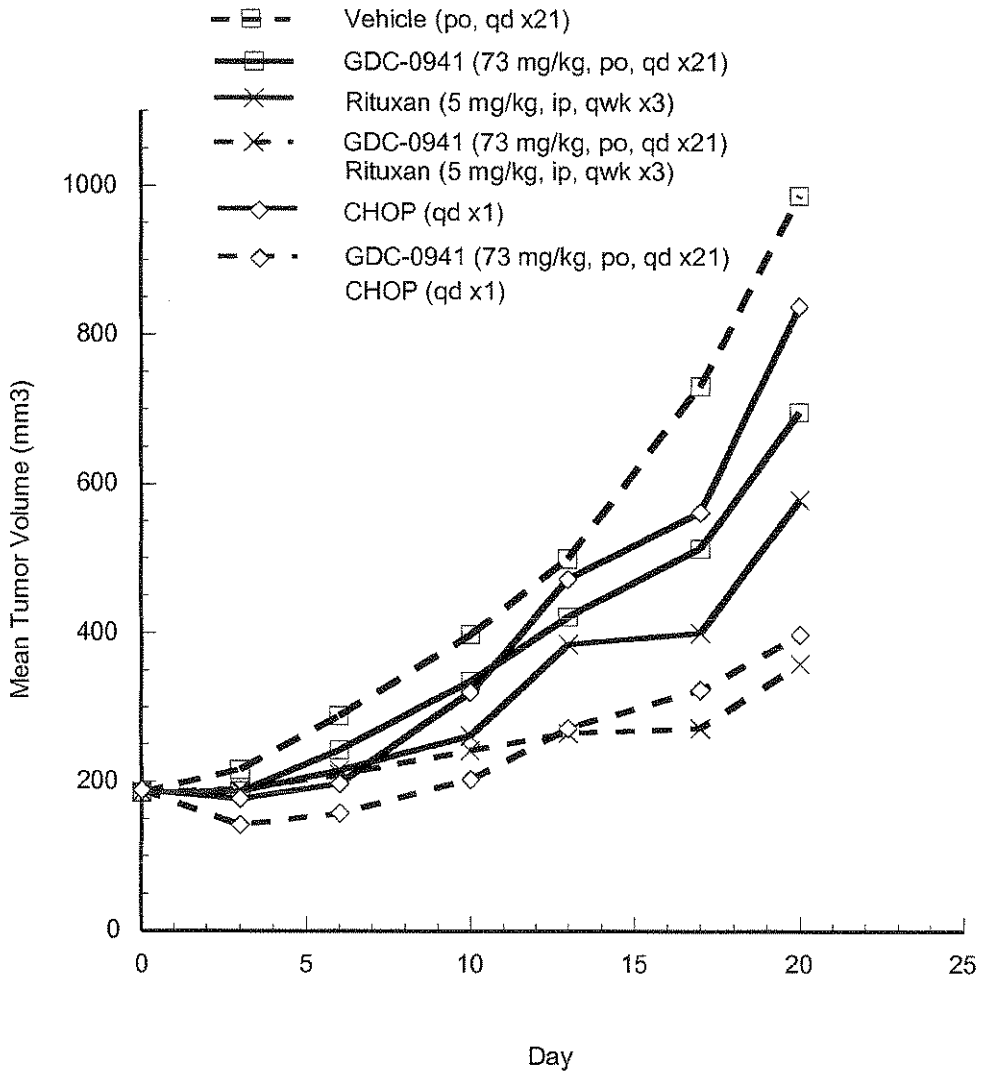

Vehicle (po, qd x21)
GDC-0941 (73 mg/kg, po, qd x21)
Rituxan (5 mg/kg, ip, qwk x3)
GDC-0941 (73 mg/kg, po, qd x21)
Rituxan (5 mg/kg, ip, qwk x3)
CHOP (qd x1)
GDC-0941 (73 mg/kg, po, qd x21)
CHOP (qd x1)
Mean Tumor Volume (mm3)
1000
800
600
400
200
0
0
5
10
15
20
25
Day

Figure 7

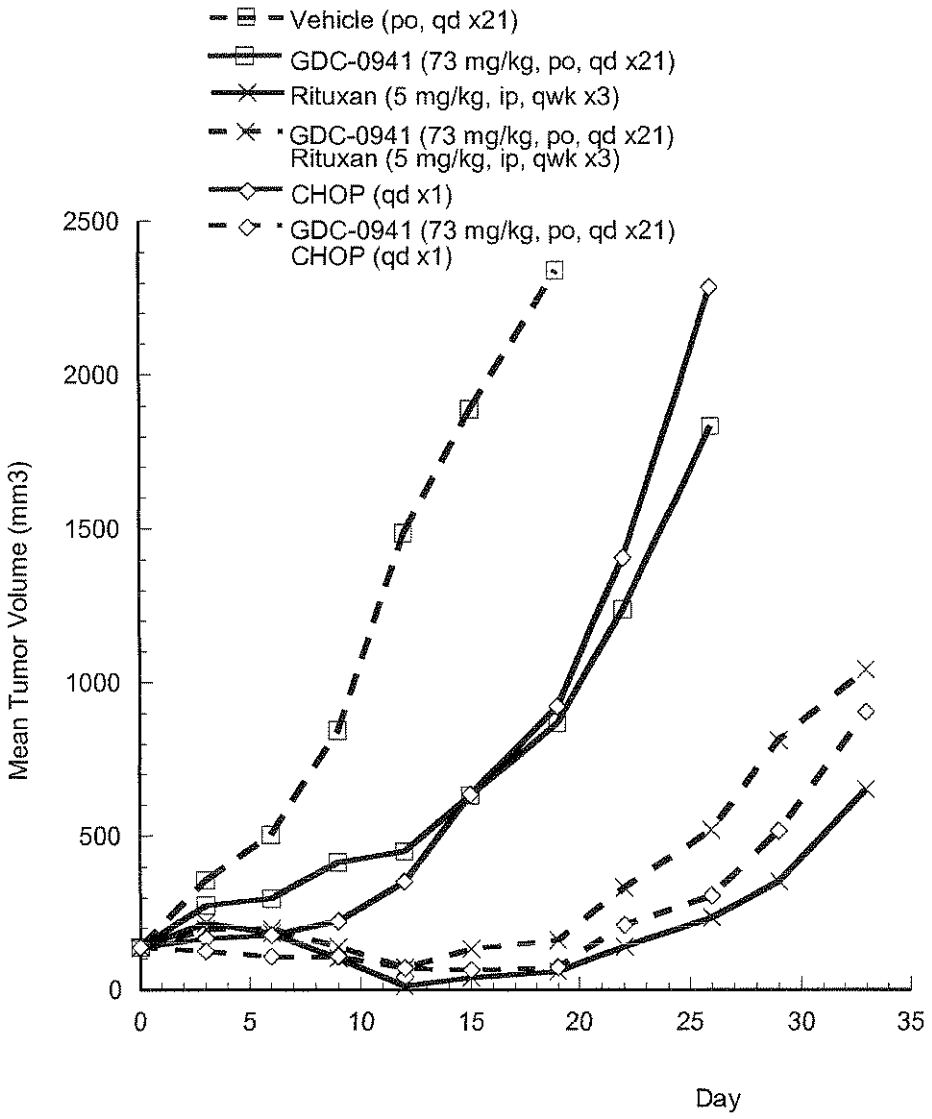

Vehicle (po, qd x21)
GDC-0941 (73 mg/kg, po, qd x21)
Rituxan (5 mg/kg, ip, qwk x3)
GDC-0941 (73 mg/kg, po, qd x21)
Rituxan (5 mg/kg, ip, qwk x3)
CHOP (qd x1)
GDC-0941 (73 mg/kg, po, qd x21)
CHOP (qd x1)
Mean Tumor Volume (mm3)
2500
2000
1500
1000
500
0
0
5
10
15
20
25
30
35
Day

Figure 8

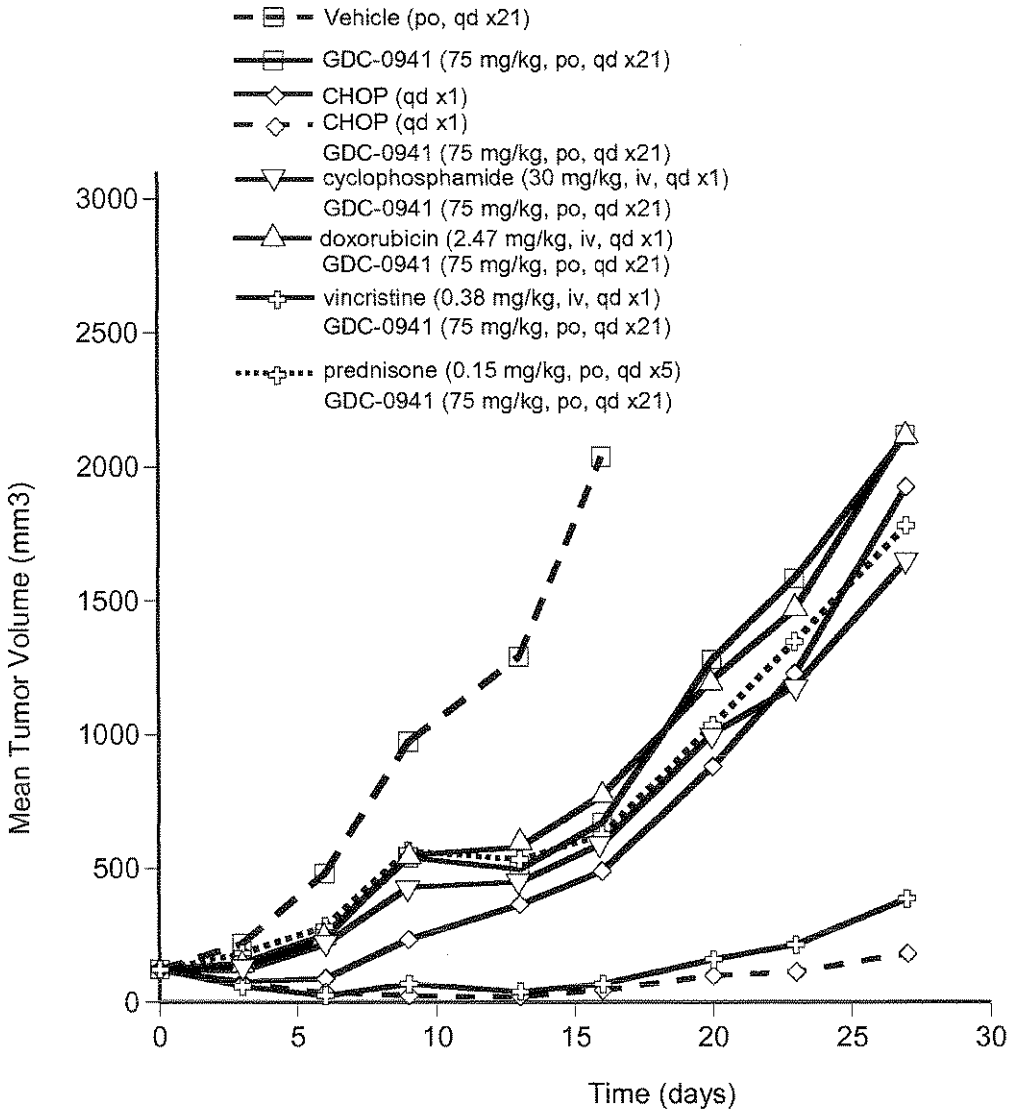

Vehicle (po, qd x21)
GDC-0941 (75 mg/kg, po, qd x21)
CHOP (qd x1)
CHOP (qd x1)
GDC-0941 (75 mg/kg, po, qd x21)
cyclophosphamide (30 mg/kg, iv, qd x1)
GDC-0941 (75 mg/kg, po, qd x21)
doxorubicin (2.47 mg/kg, iv, qd x1)
GDC-0941 (75 mg/kg, po, qd x21)
vincristine (0.38 mg/kg, iv, qd x1)
GDC-0941 (75 mg/kg, po, qd x21)
prednisone (0.15 mg/kg, po, qd x5)
GDC-0941 (75 mg/kg, po, qd x21)
Mean Tumor Volume (mm3)
3000
2500
2000
1500
1000
500
0
0
5
10
15
20
25
30
Time (days)

Figure 9

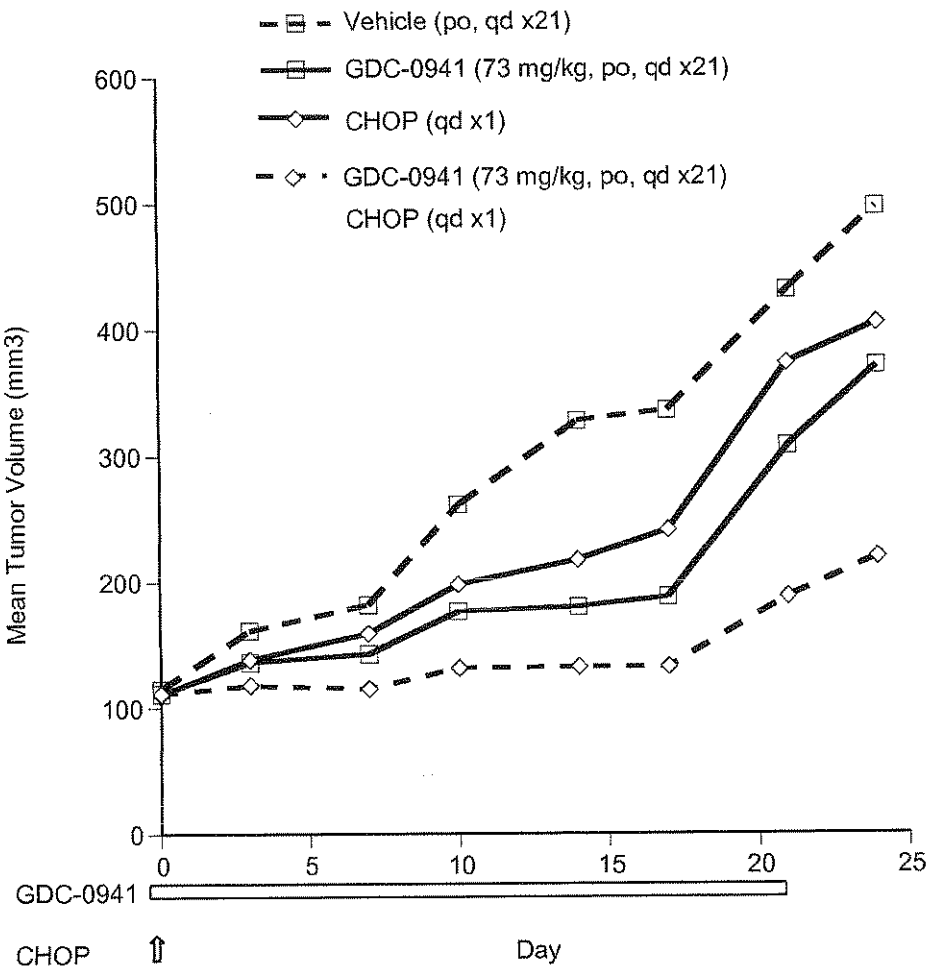

Vehicle (po, qd x21)
GDC-0941 (73 mg/kg, po, qd x21)
CHOP (qd x1)
GDC-0941 (73 mg/kg, po, qd x21)
CHOP (qd x1)
Mean Tumor Volume (mm3)
600
500
400
300
200
100
0
0
5
10
15
20
25
GDC-0941
CHOP
Day

Figure 10

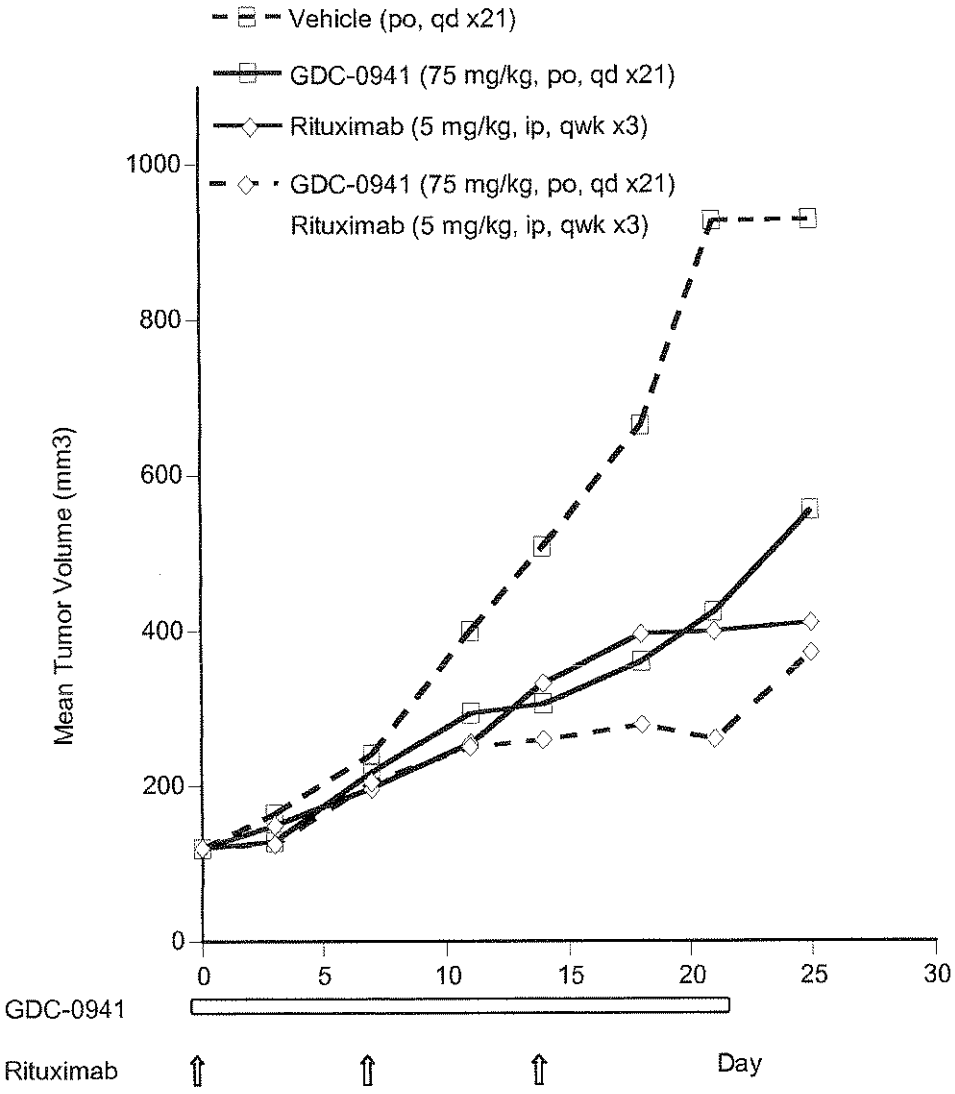

Vehicle (po, qd x21)
GDC-0941 (75 mg/kg, po, qd x21)
Rituximab (5 mg/kg, ip, qwk x3)
GDC-0941 (75 mg/kg, po, qd x21)
Rituximab (5 mg/kg, ip, qwk x3)
Mean Tumor Volume (mm3)
1000
800
600
400
200
0
0
5
10
15
20
25
30
GDC-0941
Rituximab
Day

Figure 11

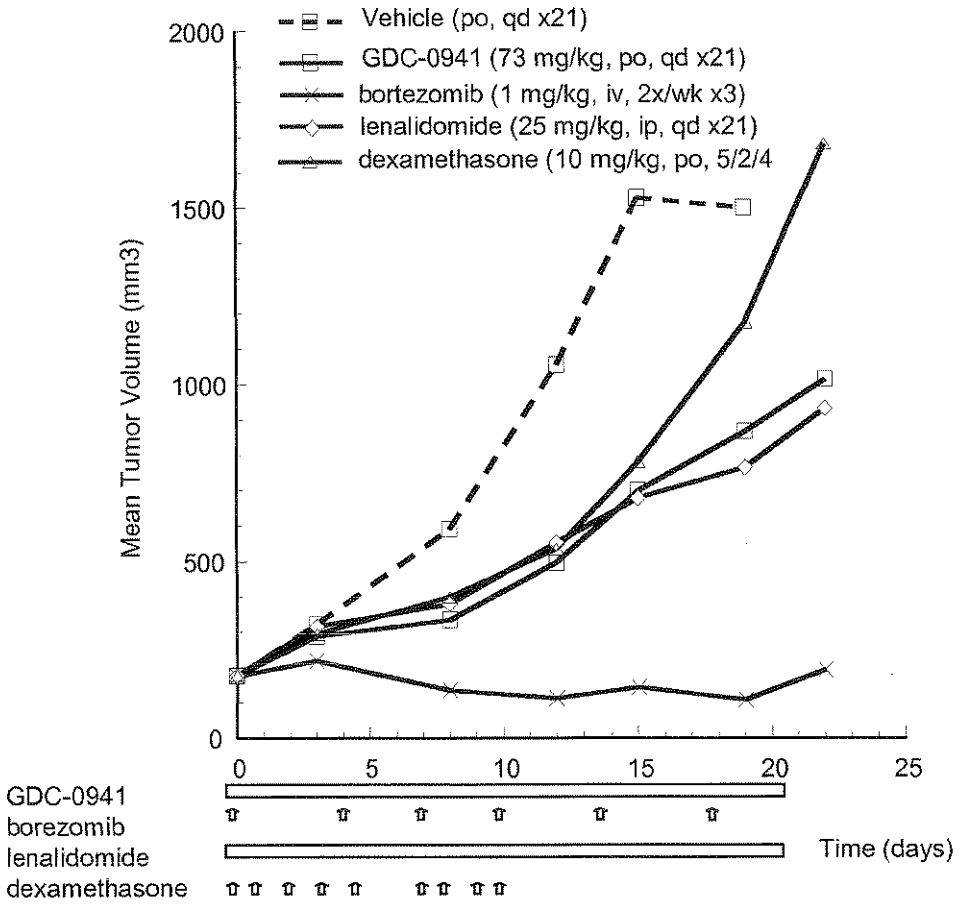

Vehicle (po, qd x21)
GDC-0941 (73 mg/kg, po, qd x21)
bortezomib (1 mg/kg, iv, 2x/wk x3)
lenalidomide (25 mg/kg, ip, qd x21)
dexamethasone (10 mg/kg, po, 5/2/4
Mean Tumor Volume (mm3)
2000
1500
1000
500
0
0
5
10
15
20
25
GDC-0941
borezomib
lenalidomide
dexamethasone
Time (days)

Figure 12

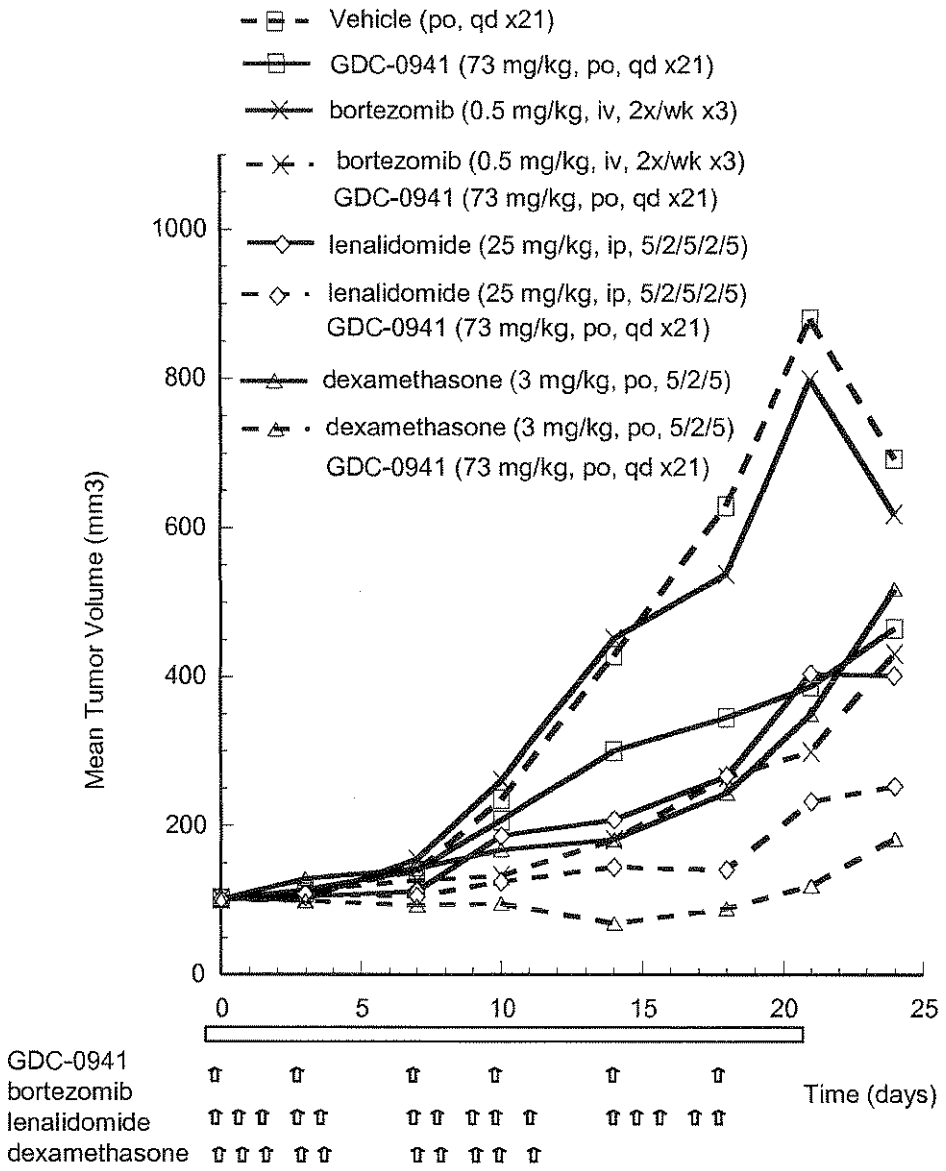

Vehicle (po, qd x21)
GDC-0941 (73 mg/kg, po, qd x21)
bortezomib (0.5 mg/kg, iv, 2x/wk x3)
bortezomib (0.5 mg/kg, iv, 2x/wk x3)
GDC-0941 (73 mg/kg, po, qd x21)
lenalidomide (25 mg/kg, ip, 5/2/5/2/5)
lenalidomide (25 mg/kg, ip, 5/2/5/2/5)
GDC-0941 (73 mg/kg, po, qd x21)
dexamethasone (3 mg/kg, po, 5/2/5)
dexamethasone (3 mg/kg, po, 5/2/5)
GDC-0941 (73 mg/kg, po, qd x21)
Mean Tumor Volume (mm3)
1000
800
600
400
200
0
0
5
10
15
20
25
Time (days)
GDC-0941
bortezomib
lenalidomide
dexamethasone

Figure 13

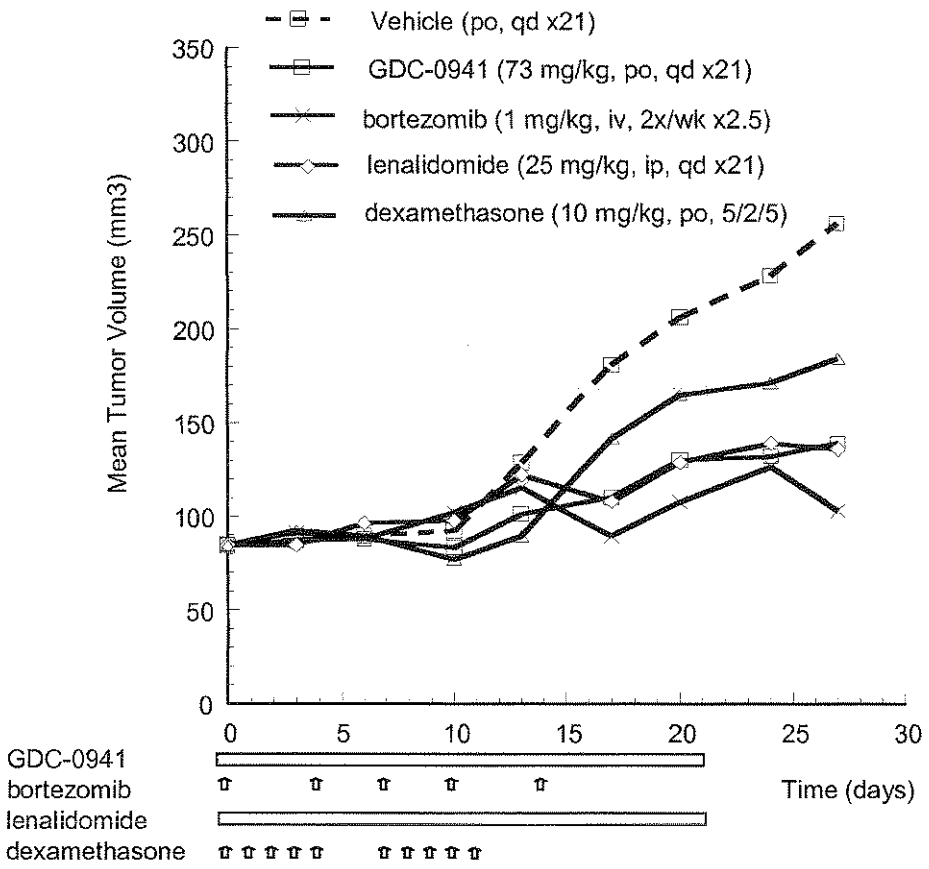

Vehicle (po, qd x21)
GDC-0941 (73 mg/kg, po, qd x21)
bortezomib (1 mg/kg, iv, 2x/wk x2.5)
lenalidomide (25 mg/kg, ip, qd x21)
dexamethasone (10 mg/kg, po, 5/2/5)
Mean Tumor Volume (mm3)
350
300
250
200
150
100
50
0
0
5
10
15
20
25
30
GDC-0941
bortezomib
lenalidomide
dexamethasone
Time (days)

Figure 14

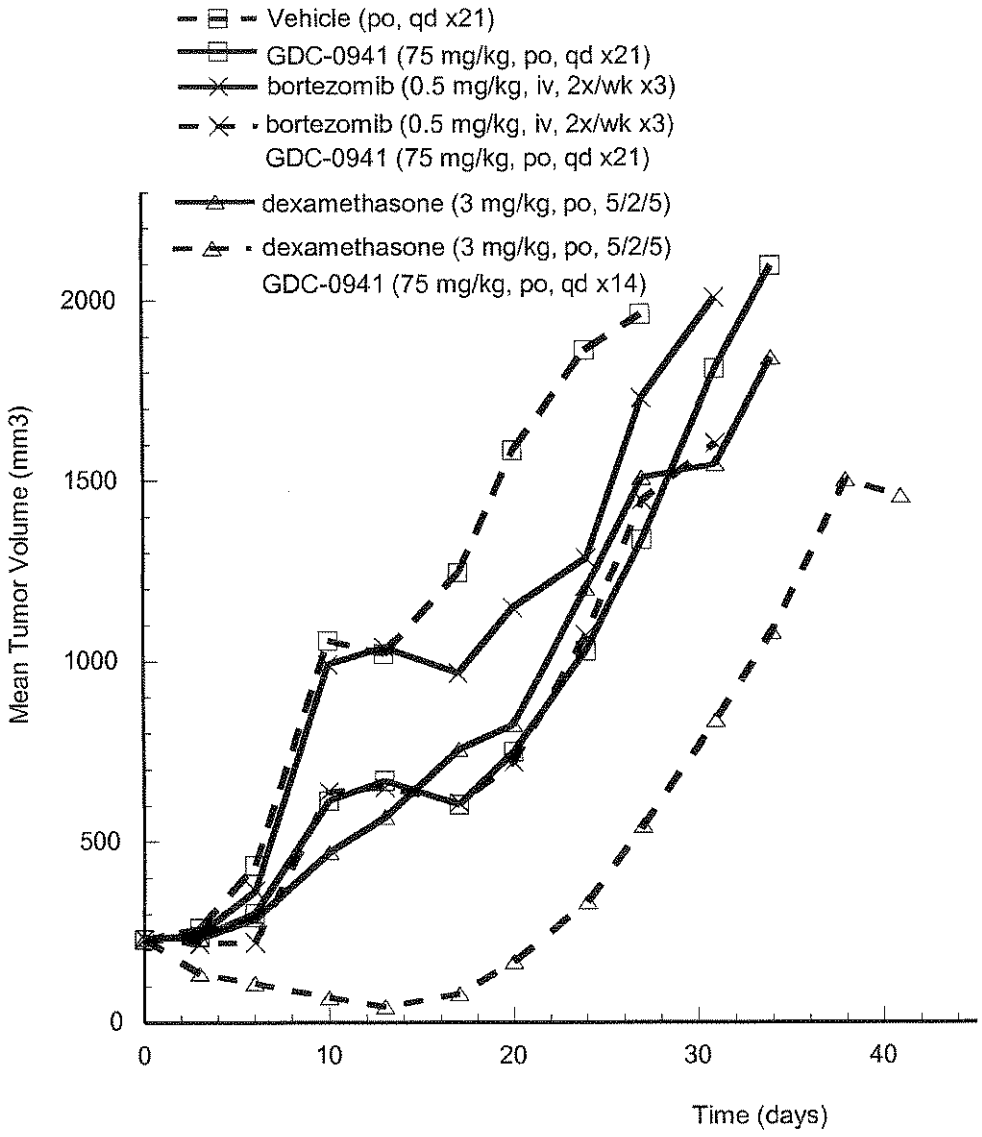

Vehicle (po, qd x21)
GDC-0941 (75 mg/kg, po, qd x21)
bortezomib (0.5 mg/kg, iv, 2x/wk x3)
bortezomib (0.5 mg/kg, iv, 2x/wk x3)
GDC-0941 (75 mg/kg, po, qd x21)
dexamethasone (3 mg/kg, po, 5/2/5)
dexamethasone (3 mg/kg, po, 5/2/5)
GDC-0941 (75 mg/kg, po, qd x14)
Mean Tumor Volume (mm3)
2000
1500
1000
500
0
0
10
20
30
40
Time (days)

Figure 15

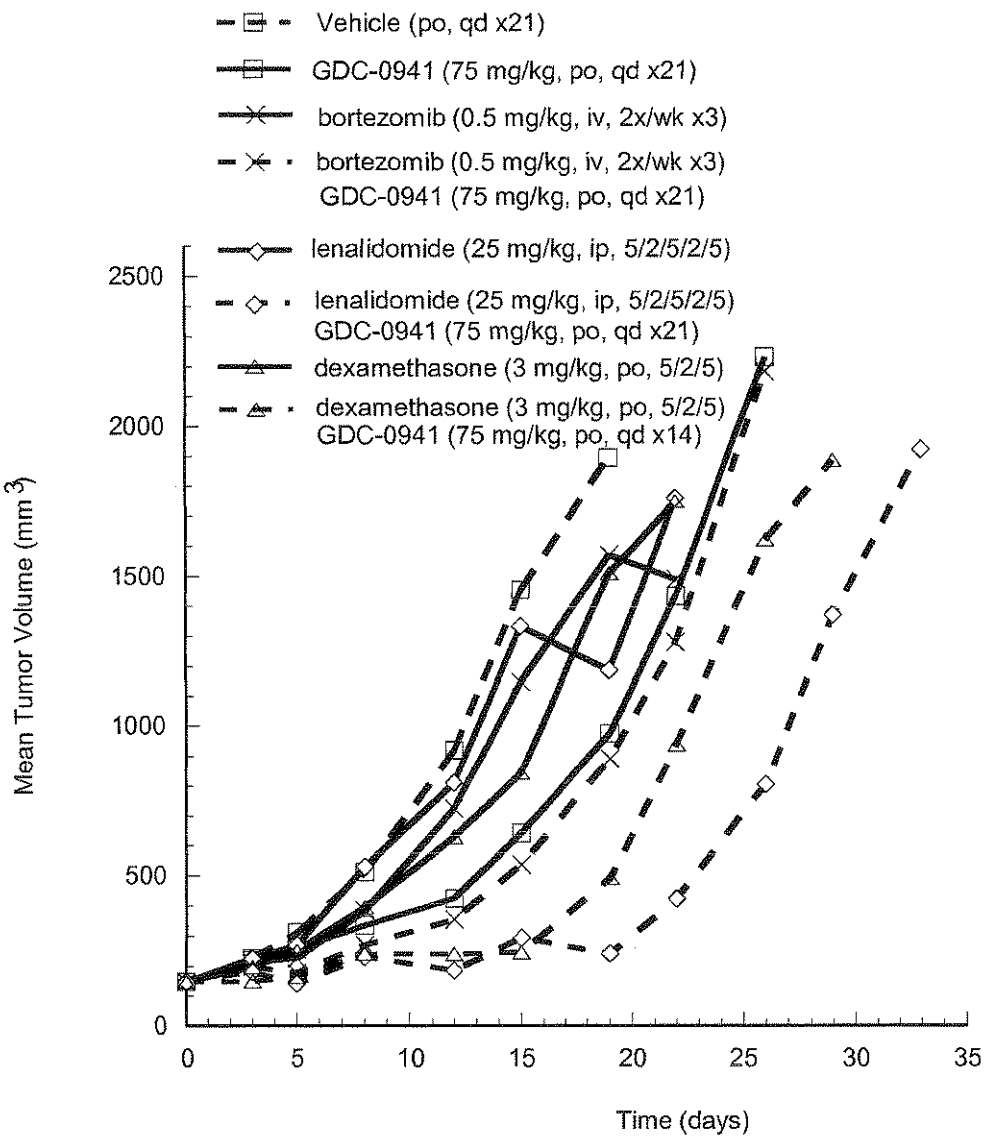

Vehicle (po, qd x21)
GDC-0941 (75 mg/kg, po, qd x21)
bortezomib (0.5 mg/kg, iv, 2x/wk x3)
bortezomib (0.5 mg/kg, iv, 2x/wk x3)
GDC-0941 (75 mg/kg, po, qd x21)
lenalidomide (25 mg/kg, ip, 5/2/5/2/5)
lenalidomide (25 mg/kg, ip, 5/2/5/2/5)
GDC-0941 (75 mg/kg, po, qd x21)
dexamethasone (3 mg/kg, po, 5/2/5)
dexamethasone (3 mg/kg, po, 5/2/5)
GDC-0941 (75 mg/kg, po, qd x14)
Mean Tumor Volume (mm3)
2500
2000
1500
1000
500
0
0
5
10
15
20
25
30
35
Time (days)

Figure 16

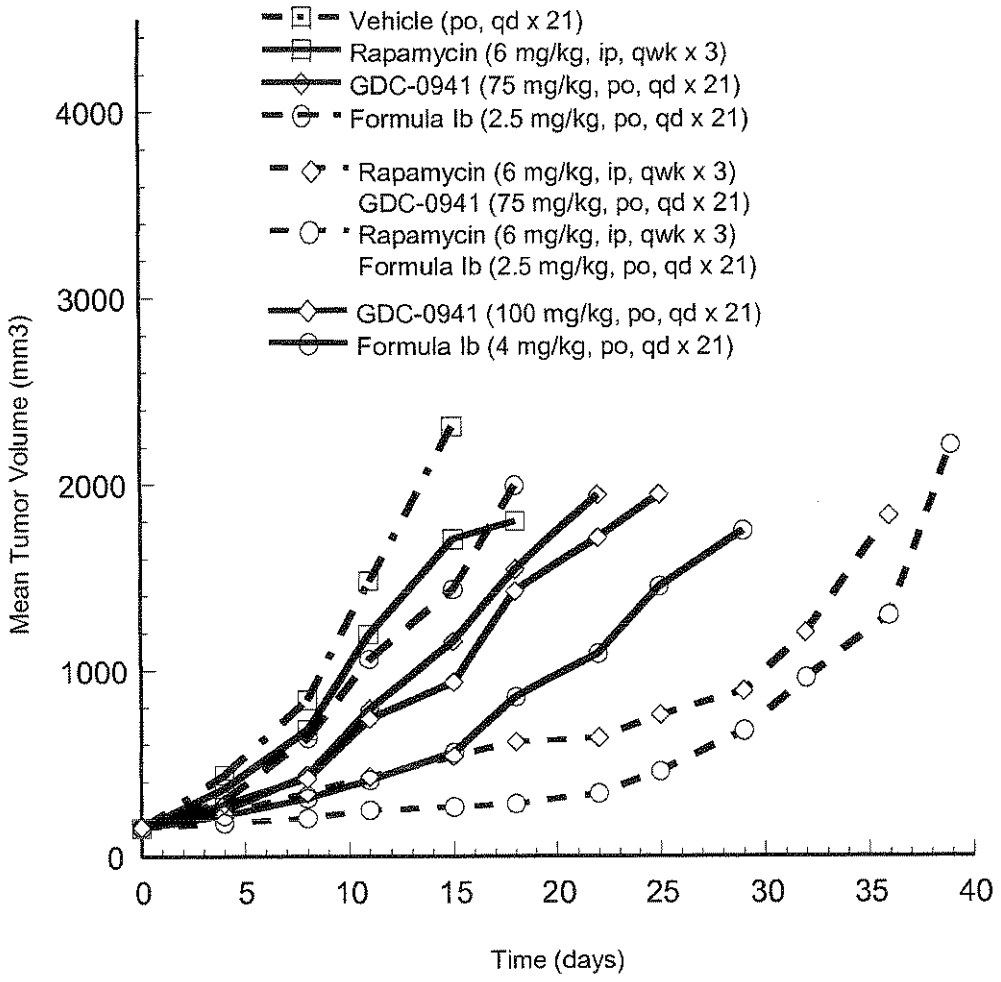

Vehicle (po, qd x 21)
Rapamycin (6 mg/kg, ip, qwk x 3)
GDC-0941 (75 mg/kg, po, qd x 21)
Formula Ib (2.5 mg/kg, po, qd x 21)
Rapamycin (6 mg/kg, ip, qwk x 3)
GDC-0941 (75 mg/kg, po, qd x 21)
Rapamycin (6 mg/kg, ip, qwk x 3)
Formula Ib (2.5 mg/kg, po, qd x 21)
GDC-0941 (100 mg/kg, po, qd x 21)
Formula Ib (4 mg/kg, po, qd x 21)
Mean Tumor Volume (mm3)
0
1000
2000
3000
4000
0
5
10
15
20
25
30
35
40
Time (days)

Figure 17

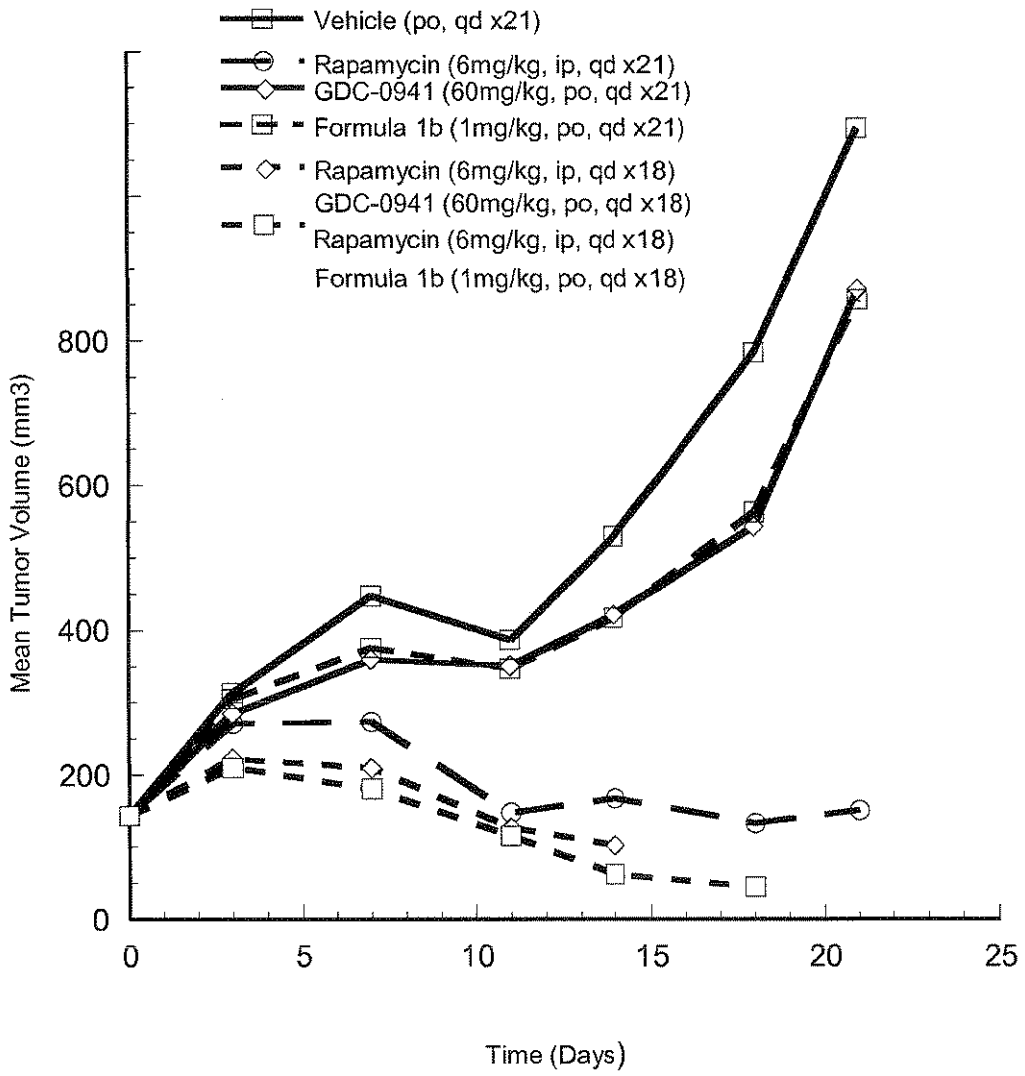

Vehicle (po, qd x21)
Rapamycin (6mg/kg, ip, qd x21)
GDC-0941 (60mg/kg, po, qd x21)
Formula 1b (1mg/kg, po, qd x21)
Rapamycin (6mg/kg, ip, qd x18)
GDC-0941 (60mg/kg, po, qd x18)
Rapamycin (6mg/kg, ip, qd x18)
Formula 1b (1mg/kg, po, qd x18)
Mean Tumor Volume (mm3)
0
200
400
600
800
0
5
10
15
20
25
Time (Days)

Figure 18