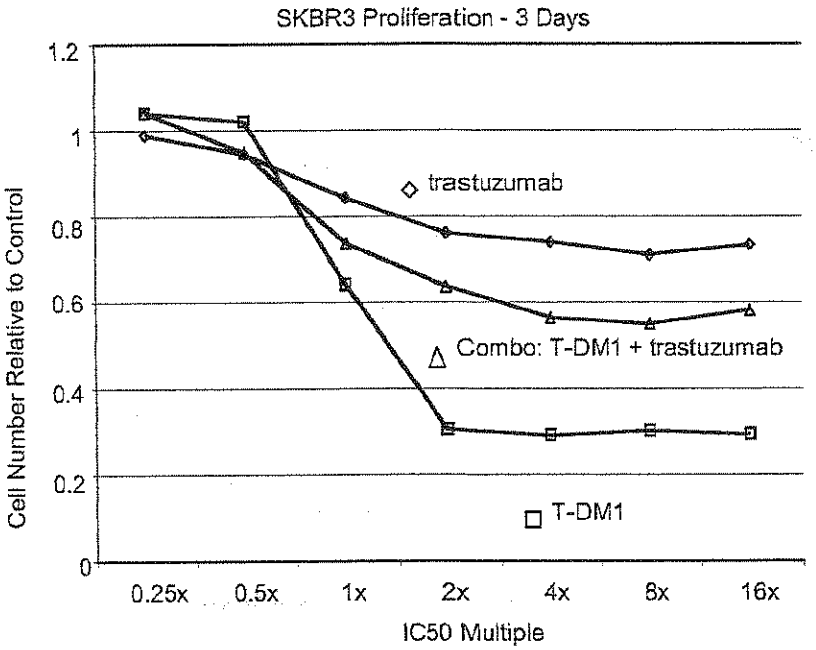



**Figure 1**

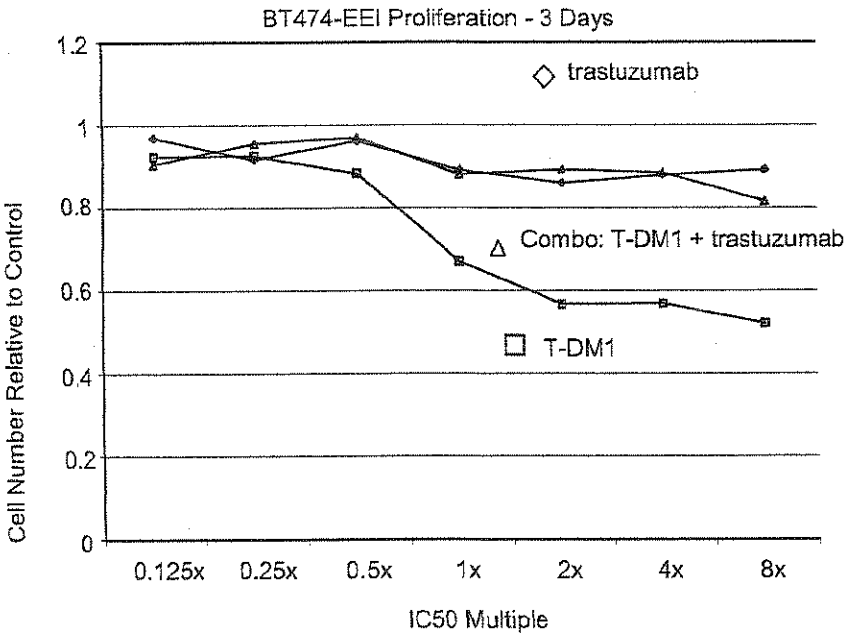



**Figure 2**

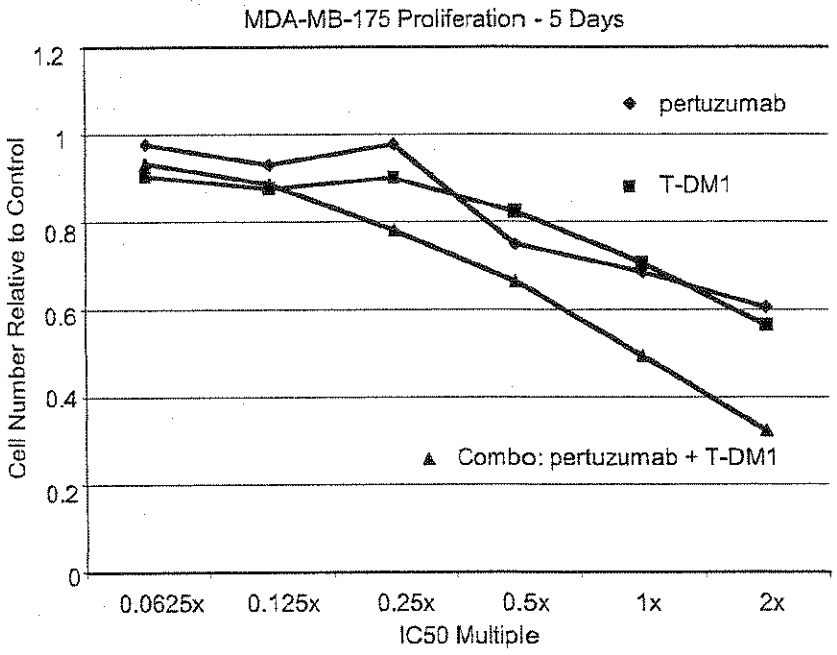



**Figure 3**

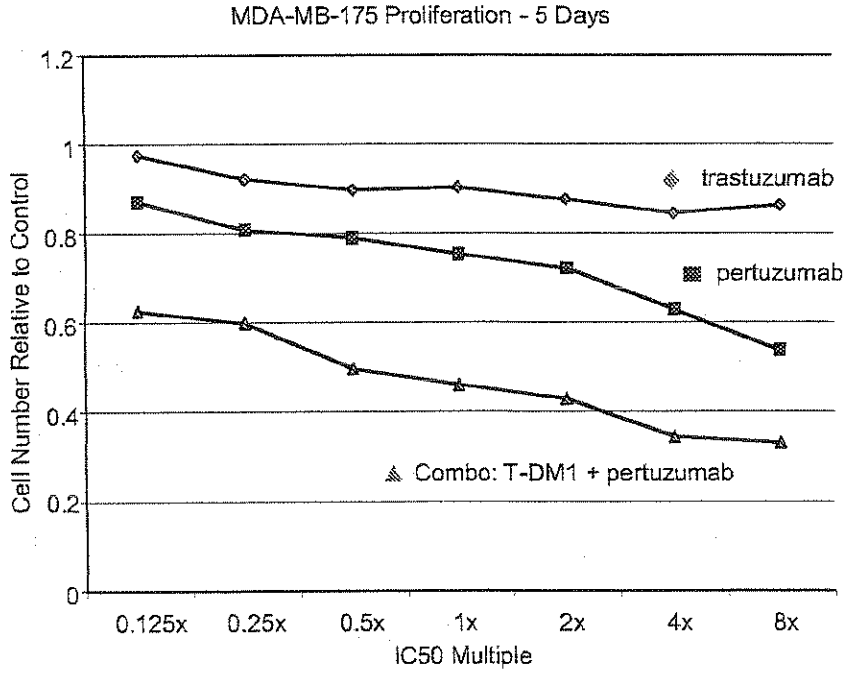



**Figure 3a**

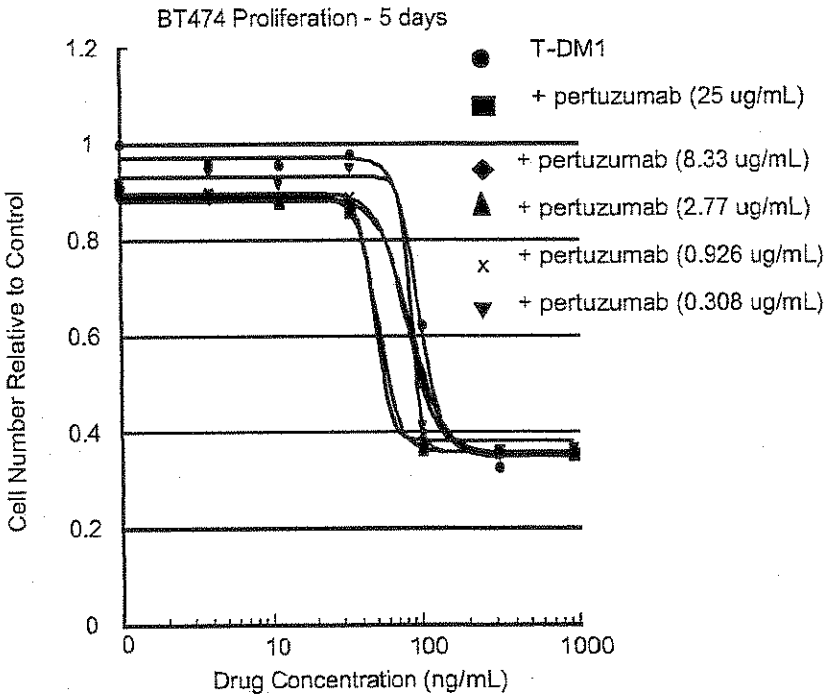



**Figure 4**

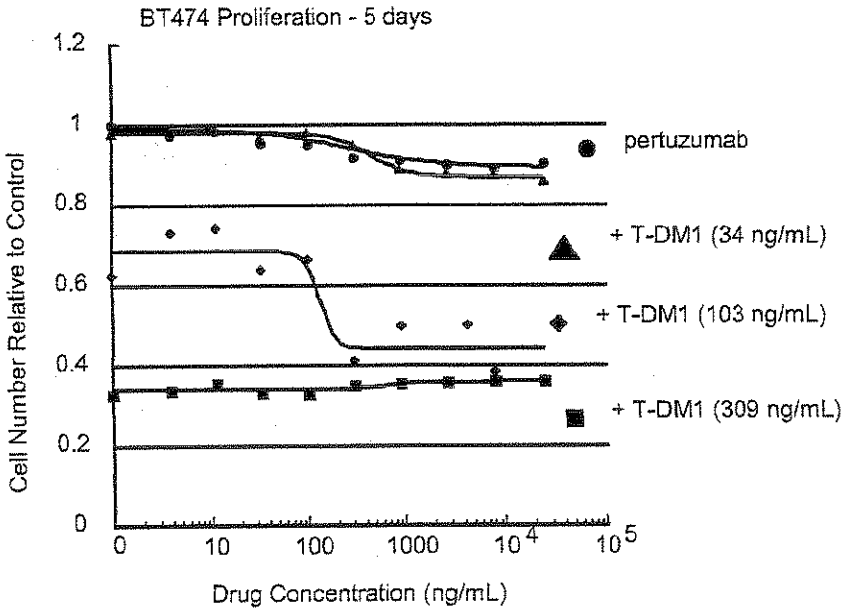



**Figure 5**

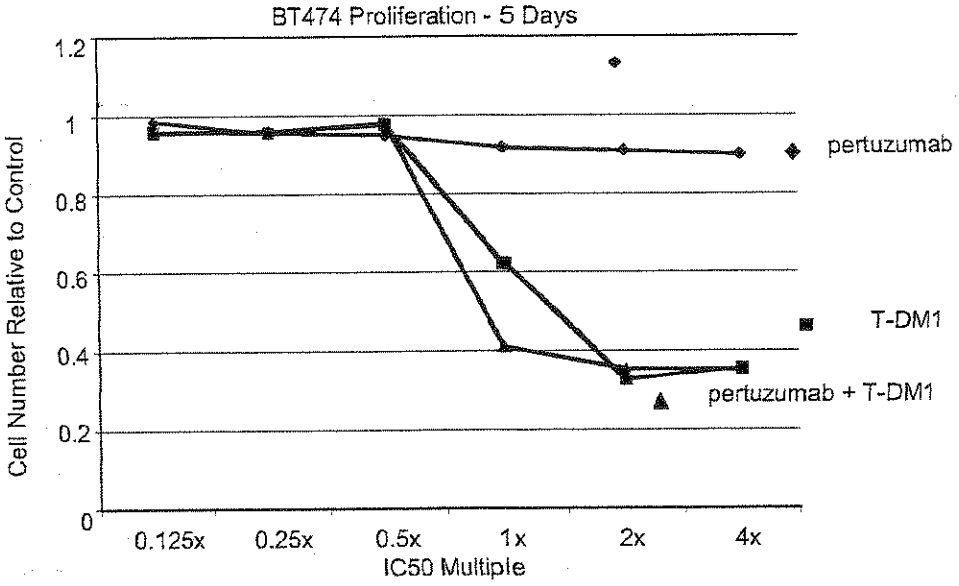



**Figure 6**

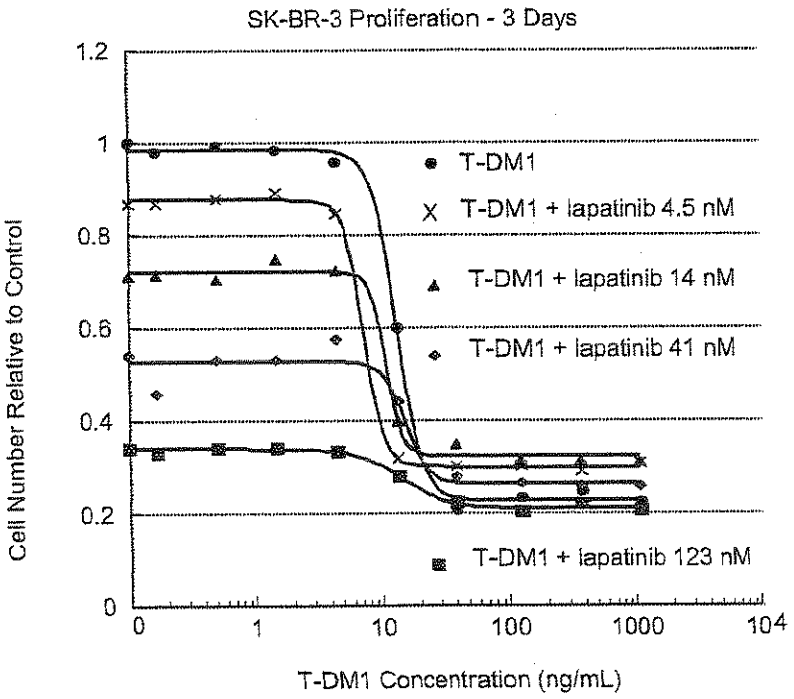



**Figure 7**

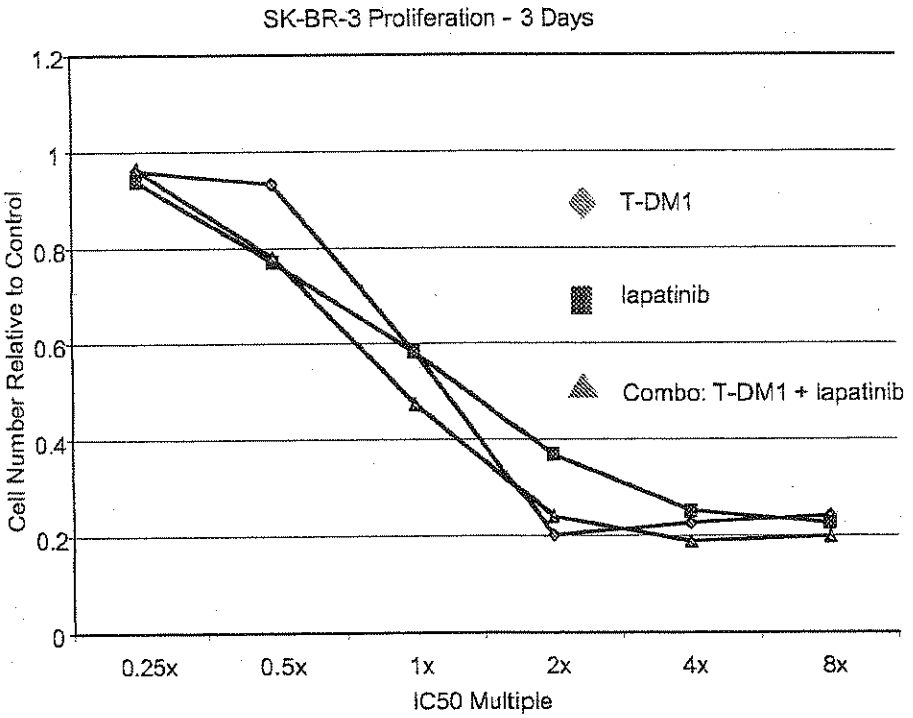



**Figure 7a**

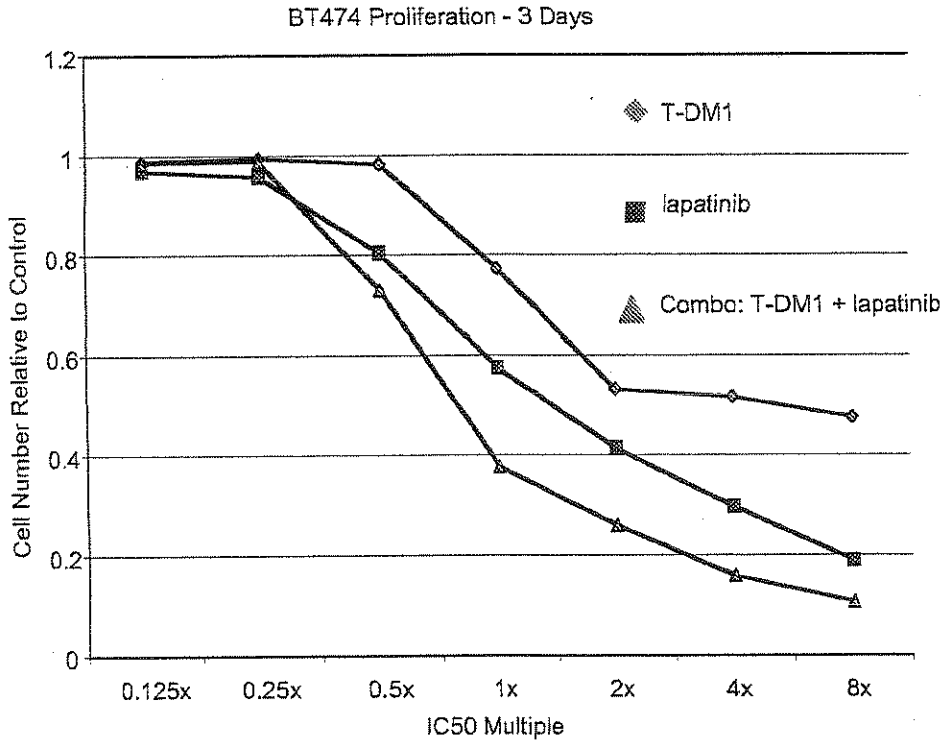



**Figure 8a**

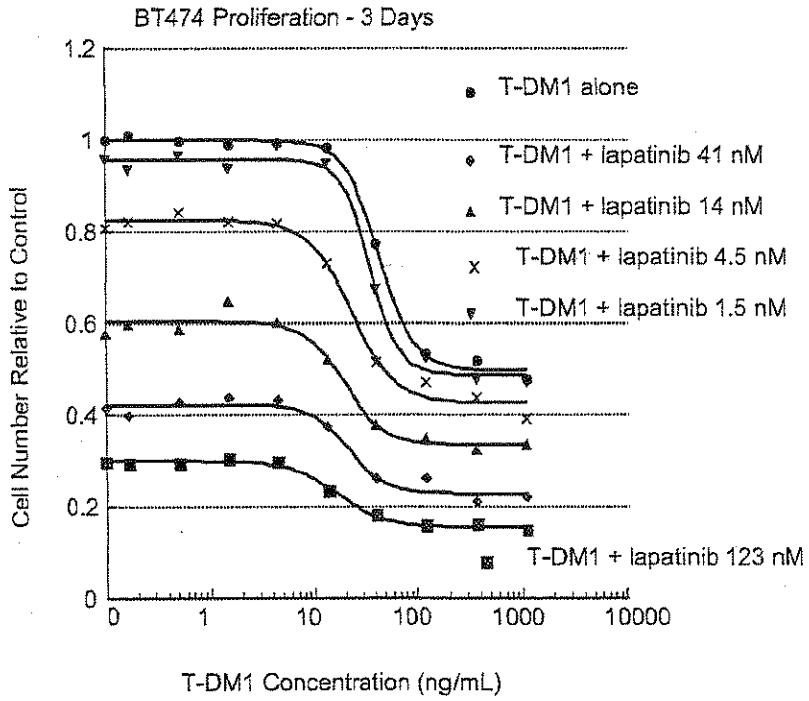



**Figure 8**

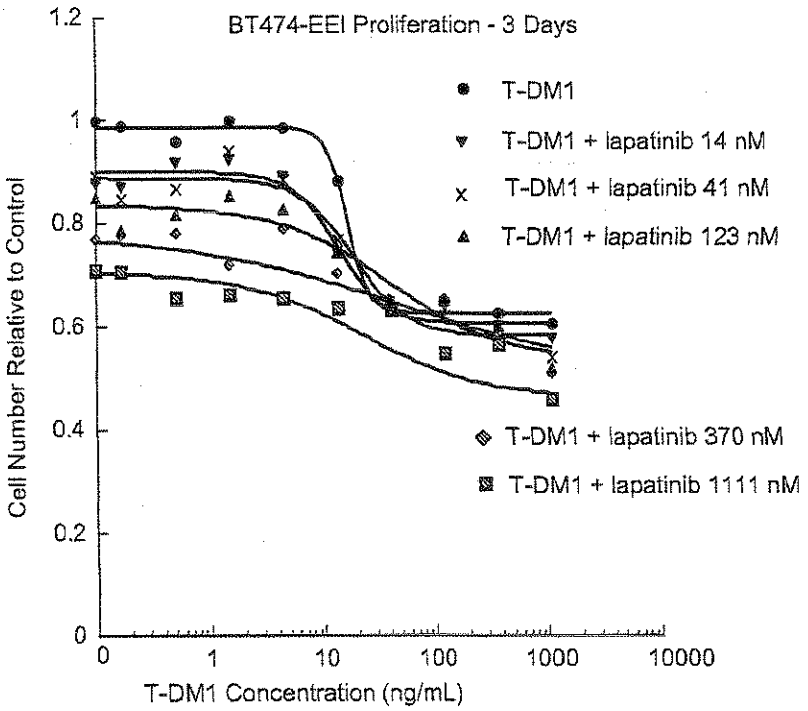



**Figure 9**

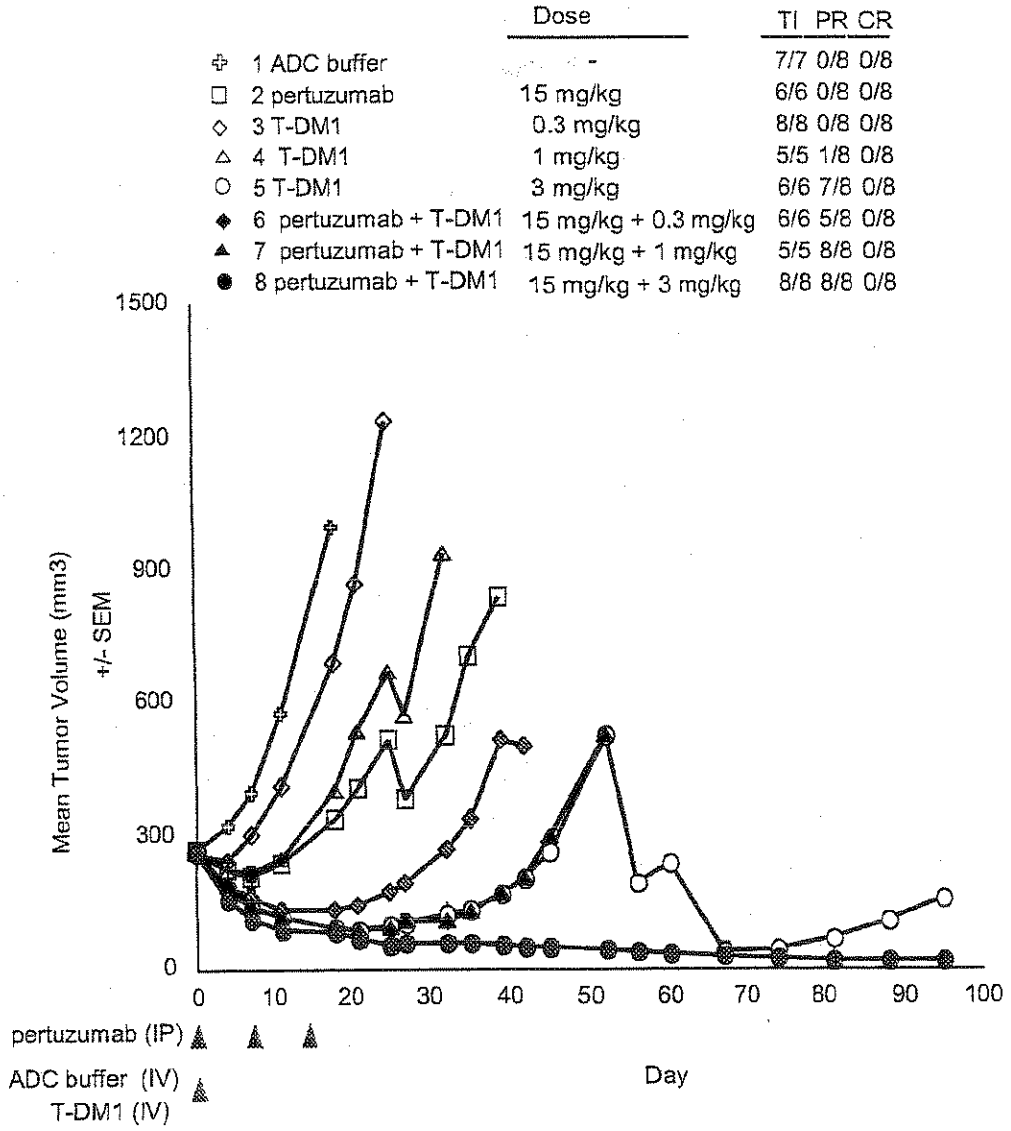

Dose
TI PR CR
1 ADC buffer - 7/7 0/8 0/8
2 pertuzumab 15 mg/kg 6/6 0/8 0/8
3 T-DM1 0.3 mg/kg 8/8 0/8 0/8
4 T-DM1 1 mg/kg 5/5 1/8 0/8
5 T-DM1 3 mg/kg 6/6 7/8 0/8
6 pertuzumab + T-DM1 15 mg/kg + 0.3 mg/kg 6/6 5/8 0/8
7 pertuzumab + T-DM1 15 mg/kg + 1 mg/kg 5/5 8/8 0/8
8 pertuzumab + T-DM1 15 mg/kg + 3 mg/kg 8/8 8/8 0/8
Mean Tumor Volume (mm3)
+/- SEM
1500
1200
900
600
300
0
0 10 20 30 40 50 60 70 80 90 100
Day
pertuzumab (IP)
ADC buffer (IV)
T-DM1 (IV)

**Figure 10**

| | | Dose | TI | PR | CR |
|---|---|---|---|---|---|
| ⊠ | 1 ADC buffer | — | 9/9 | 0/9 | 0/9 |
| ○ | 2 5-FU | 100 mg/kg | 8/8 | 0/9 | 0/9 |
| ◇ | 3 pertuzumab | 40 mg/kg | 9/9 | 0/9 | 0/9 |
| △ | 4 B20-4.1 | 5 mg/kg | 8/8 | 0/9 | 0/9 |
| ▩ | 5 T-DM1 | 5 mg/kg | 8/8 | 9/9 | 0/9 |
| ● | 6 5-FU + T-DM1 | 100 mg/kg + 5 mg/kg | 5/5 | 9/9 | 0/9 |
| ◆ | 7 pertuzumab + T-DM1 | 40 mg/kg + 5 mg/kg | 9/9 | 9/9 | 0/9 |
| ▲ | 8 B20-4.1 + T-DM1 | 5 mg/kg + 5 mg/kg | 6/6 | 6/9 | 0/9 |
| ✣ | 9 B20-4.1 + pertuzumab | 5 mg/kg + 40 mg/kg | 9/9 | 1/9 | 0/8 |

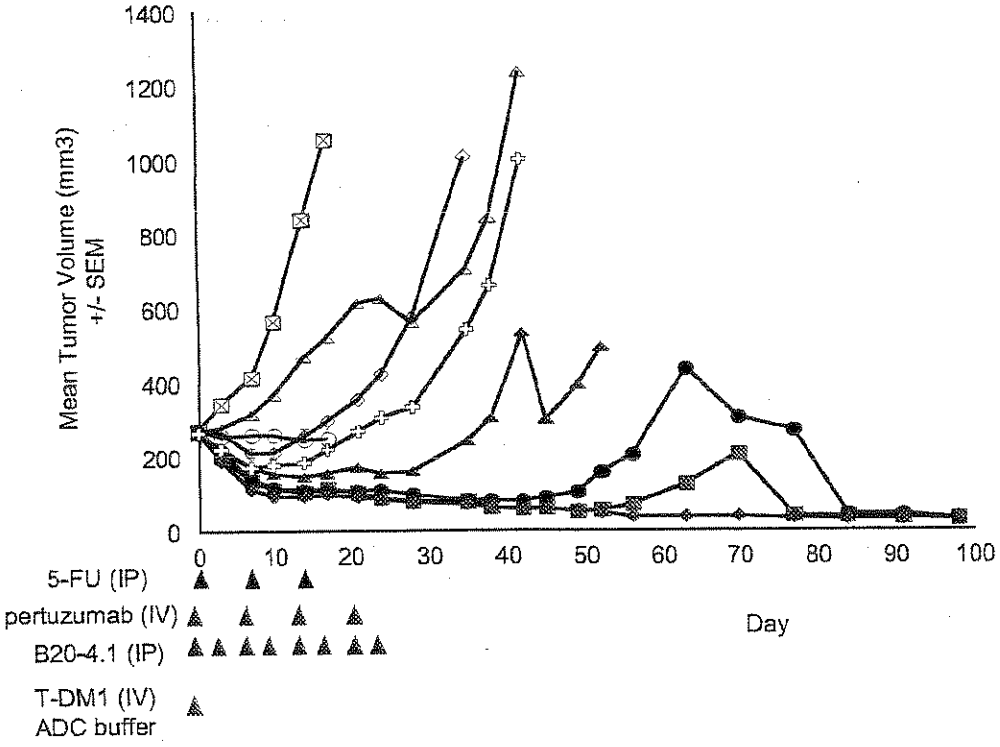



**Figure 11**

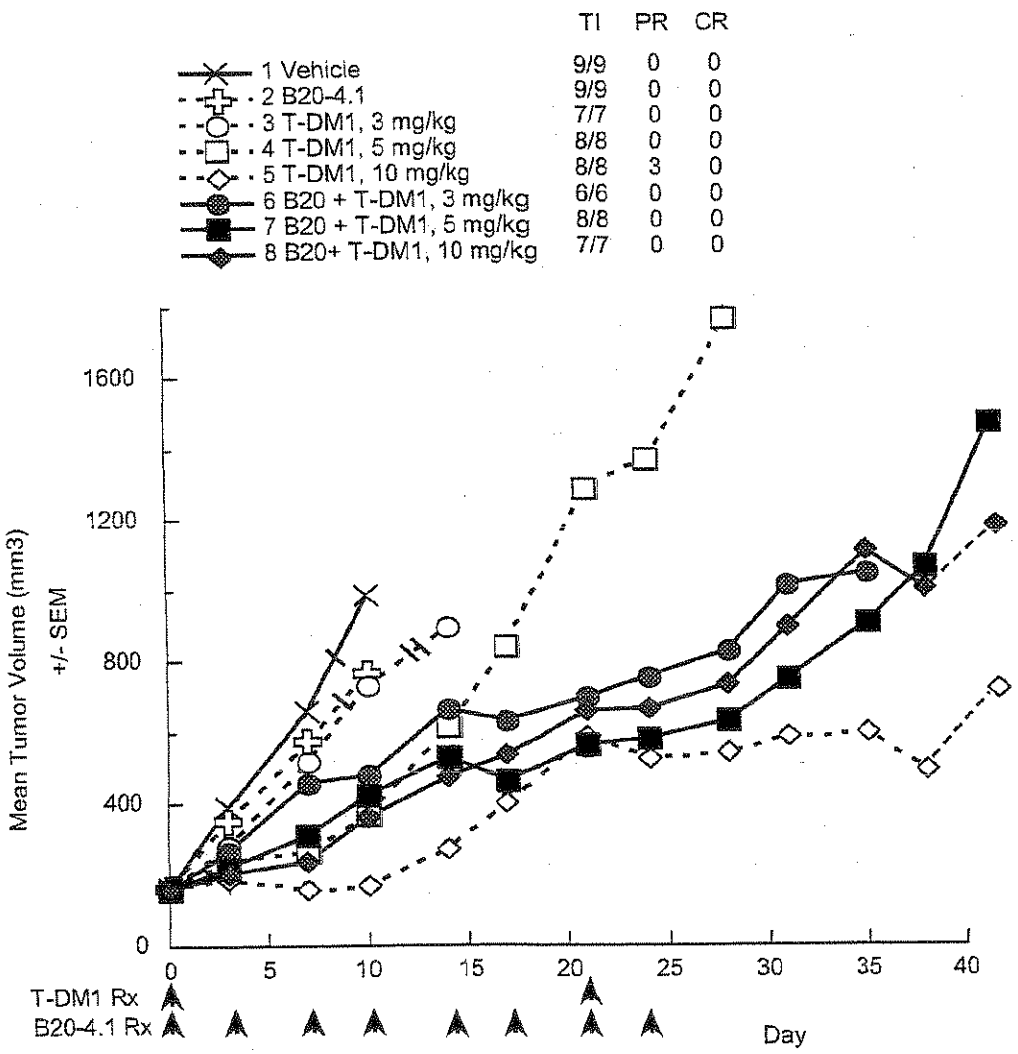

TI PR CR
1 Vehicle 9/9 0 0
2 B20-4.1 9/9 0 0
3 T-DM1, 3 mg/kg 7/7 0 0
4 T-DM1, 5 mg/kg 8/8 0 0
5 T-DM1, 10 mg/kg 8/8 3 0
6 B20 + T-DM1, 3 mg/kg 6/6 0 0
7 B20 + T-DM1, 5 mg/kg 8/8 0 0
8 B20+ T-DM1, 10 mg/kg 7/7 0 0
Mean Tumor Volume (mm3)
+/- SEM
1600
1200
800
400
0
0
5
10
15
20
25
30
35
40
T-DM1 Rx
B20-4.1 Rx
Day

**Figure 12**

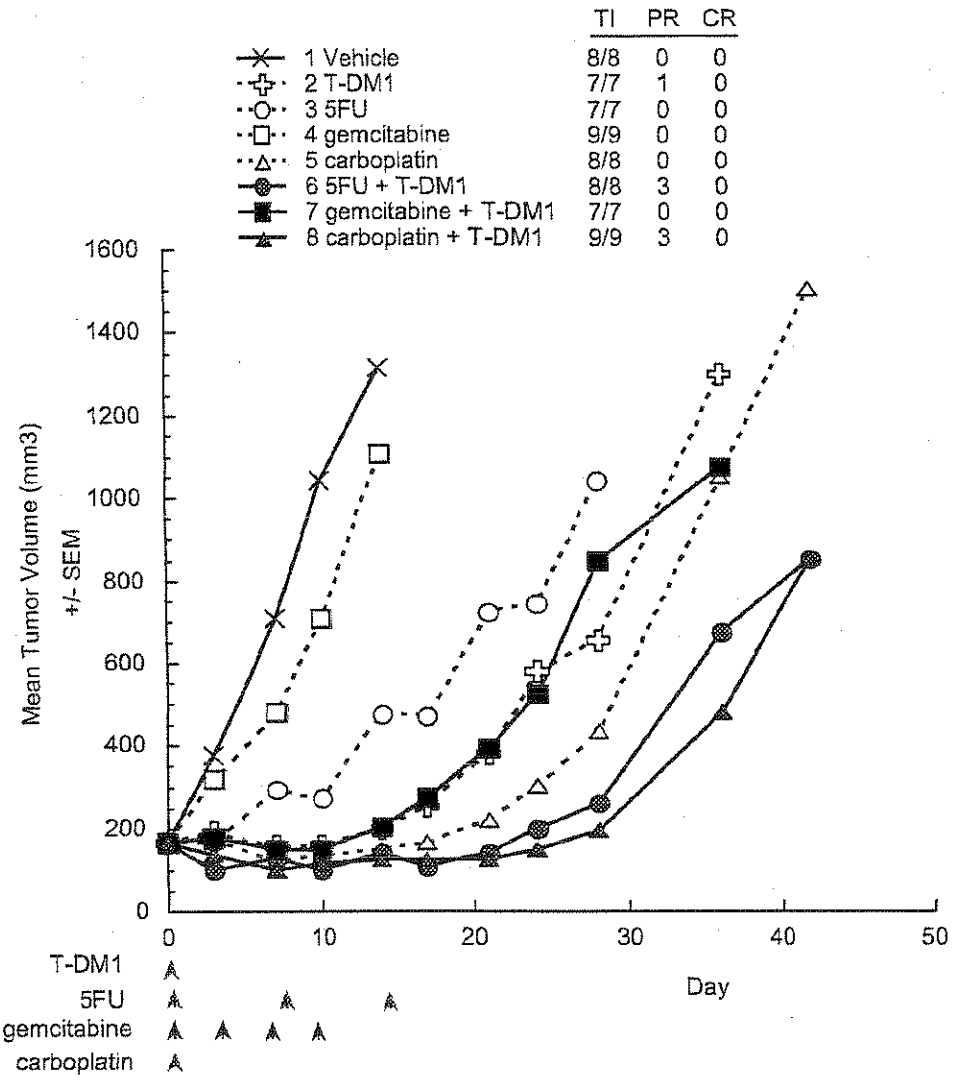

TI PR CR
1 Vehicle 8/8 0 0
2 T-DM1 7/7 1 0
3 5FU 7/7 0 0
4 gemcitabine 9/9 0 0
5 carboplatin 8/8 0 0
6 5FU + T-DM1 8/8 3 0
7 gemcitabine + T-DM1 7/7 0 0
8 carboplatin + T-DM1 9/9 3 0
Mean Tumor Volume (mm3)
+/- SEM
1600
1400
1200
1000
800
600
400
200
0
0
10
20
30
40
50
Day
T-DM1
5FU
gemcitabine
carboplatin

**Figure 13**

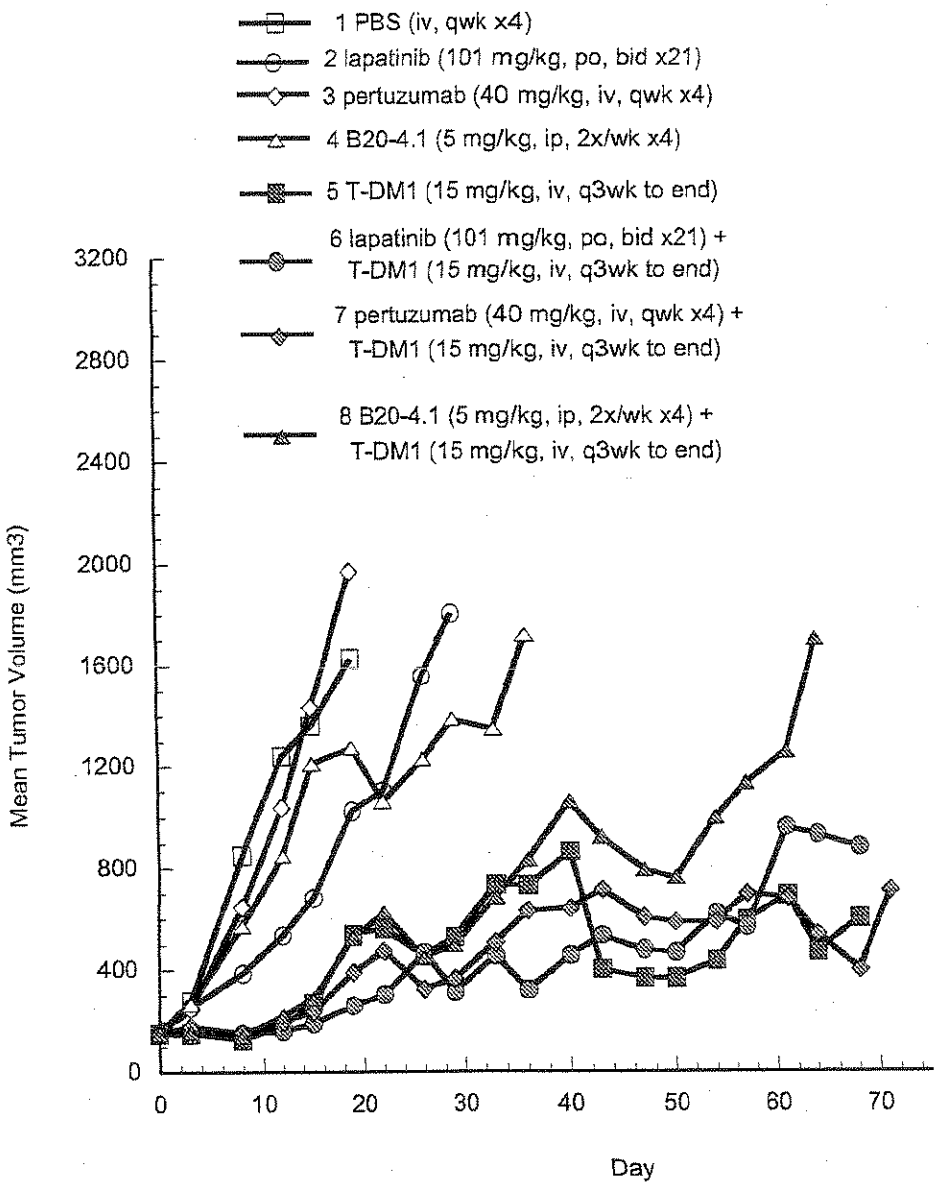

1 PBS (iv, qwk x4)
2 lapatinib (101 mg/kg, po, bid x21)
3 pertuzumab (40 mg/kg, iv, qwk x4)
4 B20-4.1 (5 mg/kg, ip, 2x/wk x4)
5 T-DM1 (15 mg/kg, iv, q3wk to end)
6 lapatinib (101 mg/kg, po, bid x21) + T-DM1 (15 mg/kg, iv, q3wk to end)
7 pertuzumab (40 mg/kg, iv, qwk x4) + T-DM1 (15 mg/kg, iv, q3wk to end)
8 B20-4.1 (5 mg/kg, ip, 2x/wk x4) + T-DM1 (15 mg/kg, iv, q3wk to end)
Mean Tumor Volume (mm3)
3200
2800
2400
2000
1600
1200
800
400
0
0
10
20
30
40
50
60
70
Day

**Figure 14**

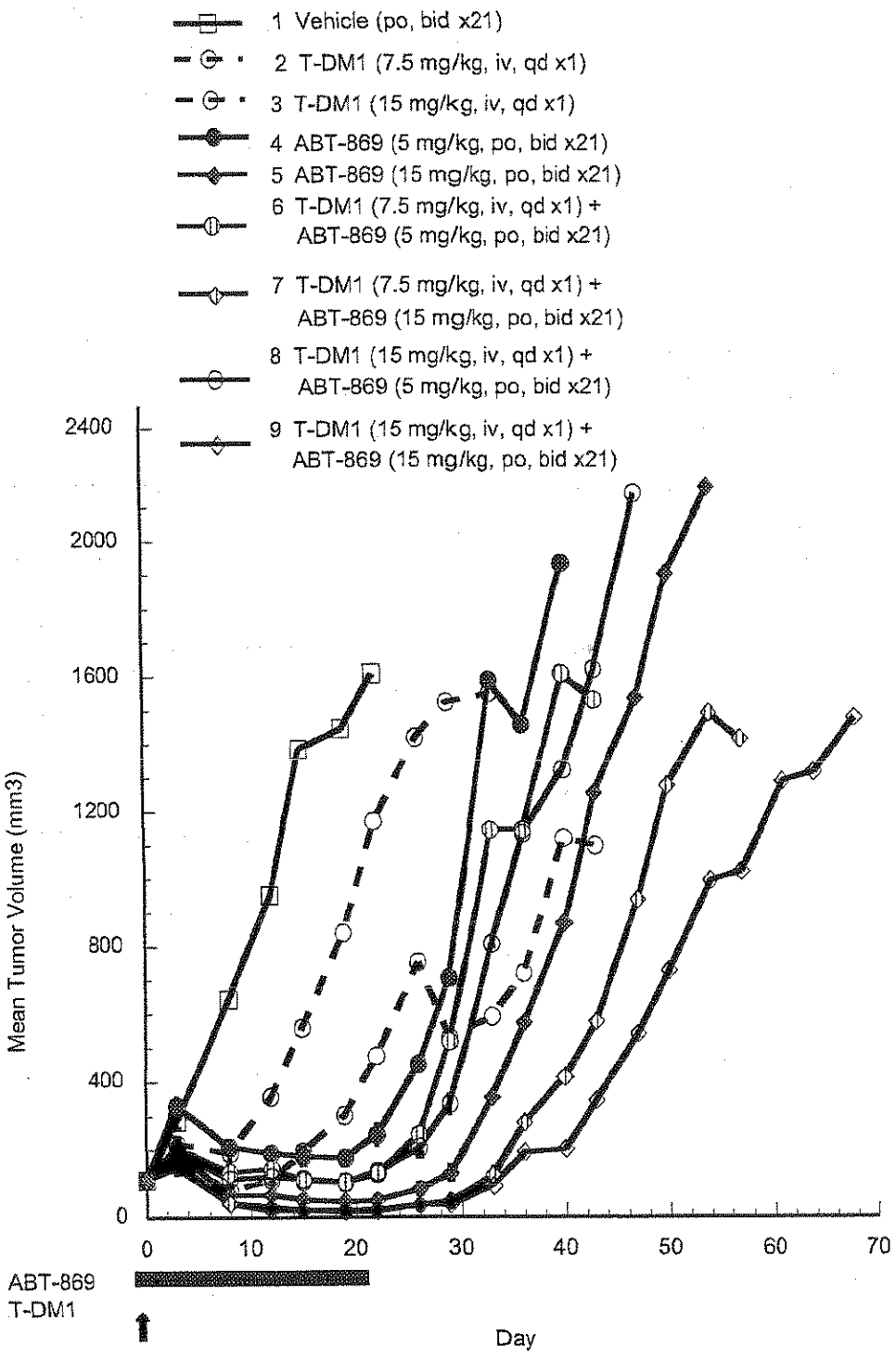

1 Vehicle (po, bid x21)
2 T-DM1 (7.5 mg/kg, iv, qd x1)
3 T-DM1 (15 mg/kg, iv, qd x1)
4 ABT-869 (5 mg/kg, po, bid x21)
5 ABT-869 (15 mg/kg, po, bid x21)
6 T-DM1 (7.5 mg/kg, iv, qd x1) + ABT-869 (5 mg/kg, po, bid x21)
7 T-DM1 (7.5 mg/kg, iv, qd x1) + ABT-869 (15 mg/kg, po, bid x21)
8 T-DM1 (15 mg/kg, iv, qd x1) + ABT-869 (5 mg/kg, po, bid x21)
9 T-DM1 (15 mg/kg, iv, qd x1) + ABT-869 (15 mg/kg, po, bid x21)
Mean Tumor Volume (mm3)
2400
2000
1600
1200
800
400
0
0
10
20
30
40
50
60
70
ABT-869
T-DM1
Day

Figure 15

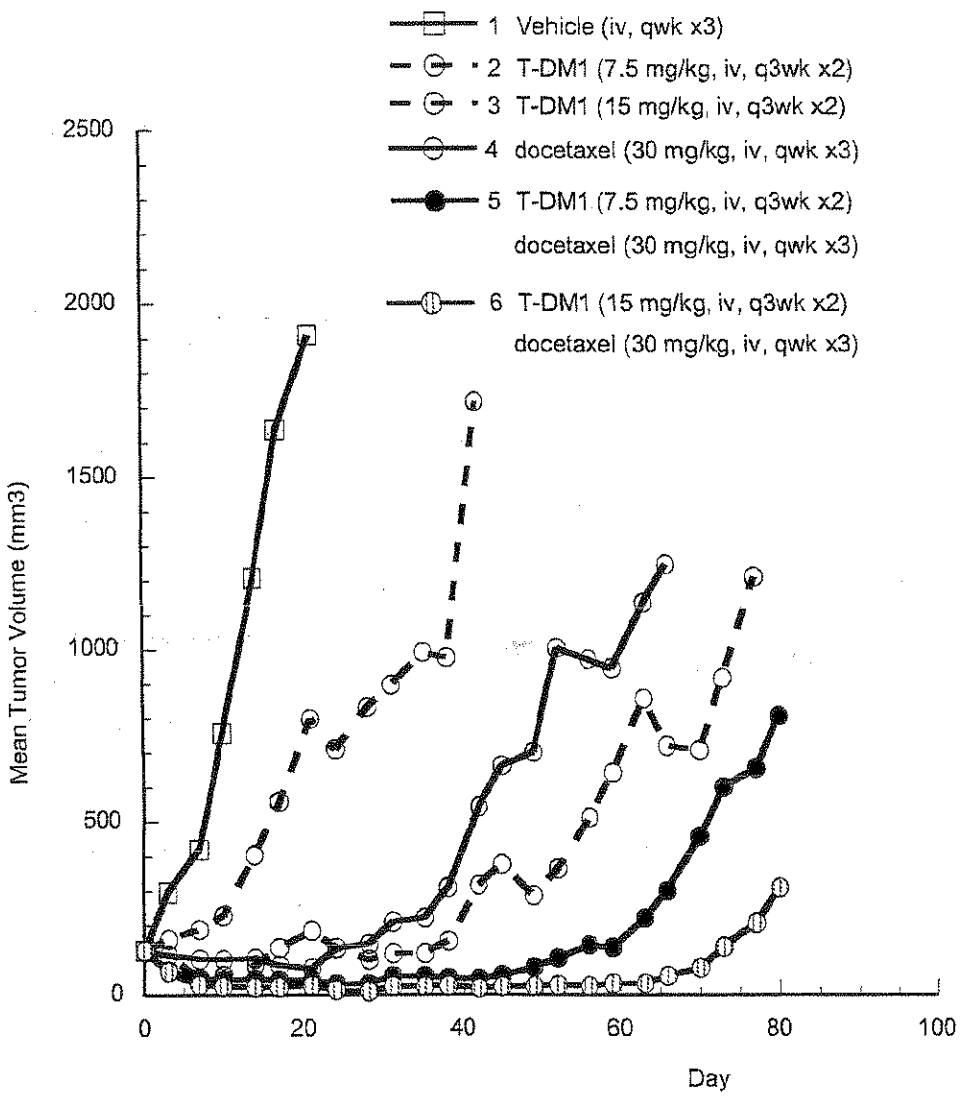

1 Vehicle (iv, qwk x3)
2 T-DM1 (7.5 mg/kg, iv, q3wk x2)
3 T-DM1 (15 mg/kg, iv, q3wk x2)
4 docetaxel (30 mg/kg, iv, qwk x3)
5 T-DM1 (7.5 mg/kg, iv, q3wk x2)
docetaxel (30 mg/kg, iv, qwk x3)
6 T-DM1 (15 mg/kg, iv, q3wk x2)
docetaxel (30 mg/kg, iv, qwk x3)
Mean Tumor Volume (mm3)
2500
2000
1500
1000
500
0
0
20
40
60
80
100
Day

**Figure 16**

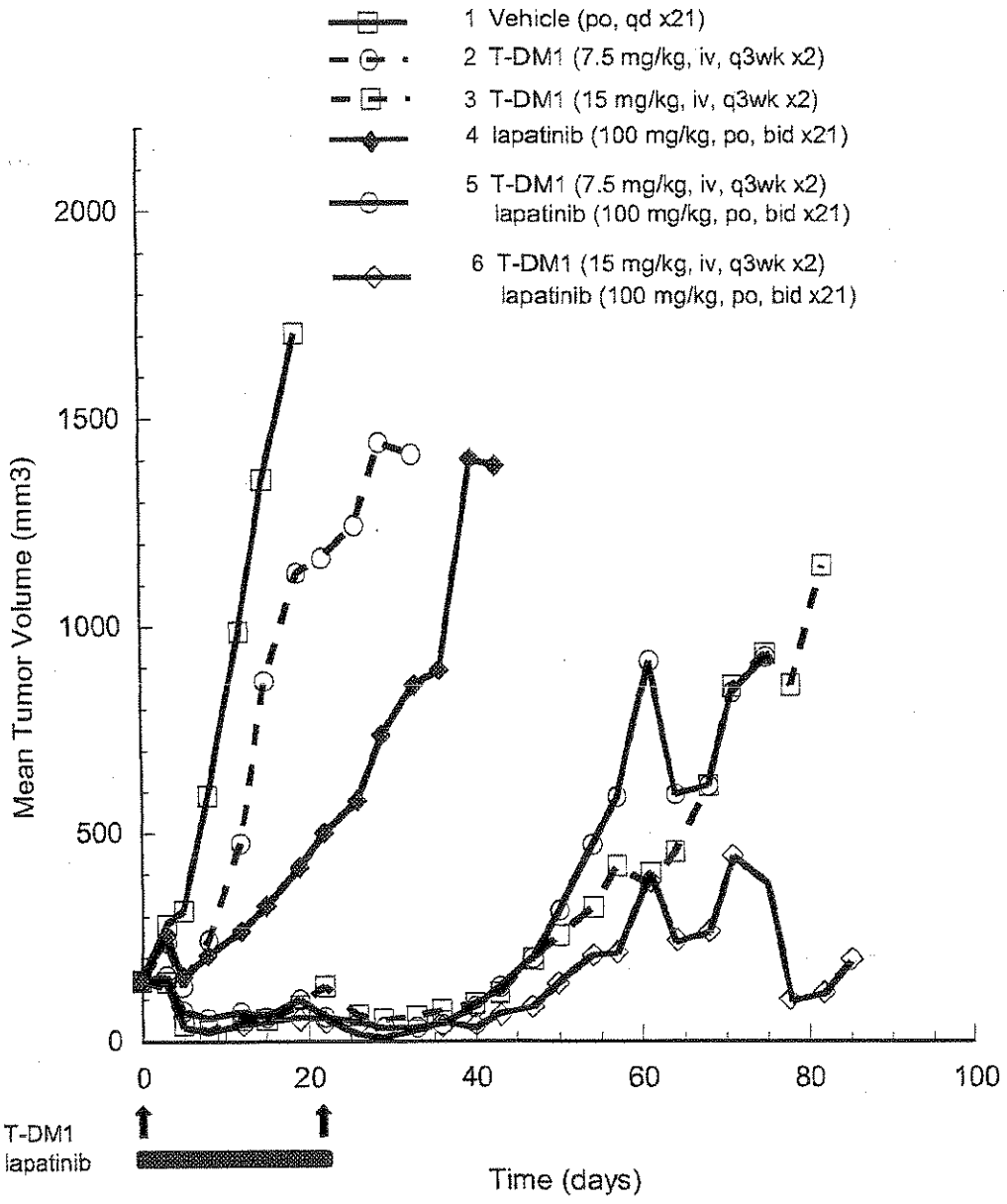

1 Vehicle (po, qd x21)
2 T-DM1 (7.5 mg/kg, iv, q3wk x2)
3 T-DM1 (15 mg/kg, iv, q3wk x2)
4 lapatinib (100 mg/kg, po, bid x21)
5 T-DM1 (7.5 mg/kg, iv, q3wk x2)
lapatinib (100 mg/kg, po, bid x21)
6 T-DM1 (15 mg/kg, iv, q3wk x2)
lapatinib (100 mg/kg, po, bid x21)
Mean Tumor Volume (mm3)
2000
1500
1000
500
0
0
20
40
60
80
100
T-DM1
lapatinib
Time (days)

**Figure 17**

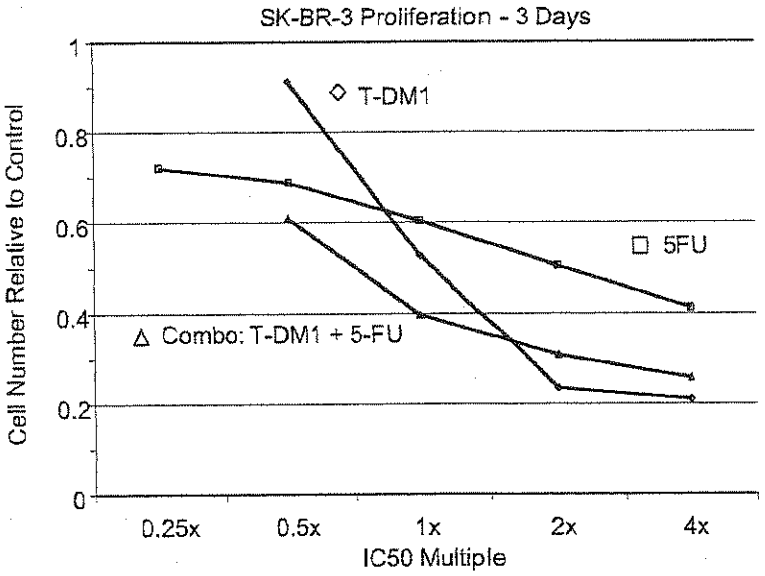



**Figure 18**

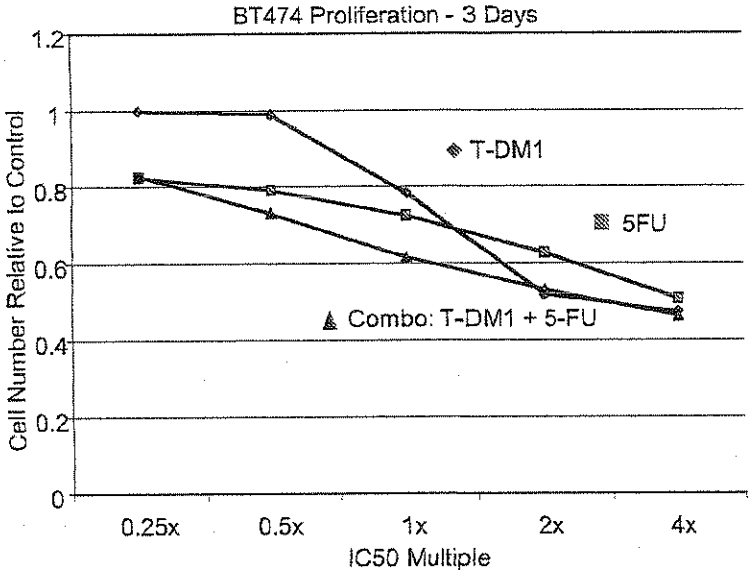



**Figure 19**

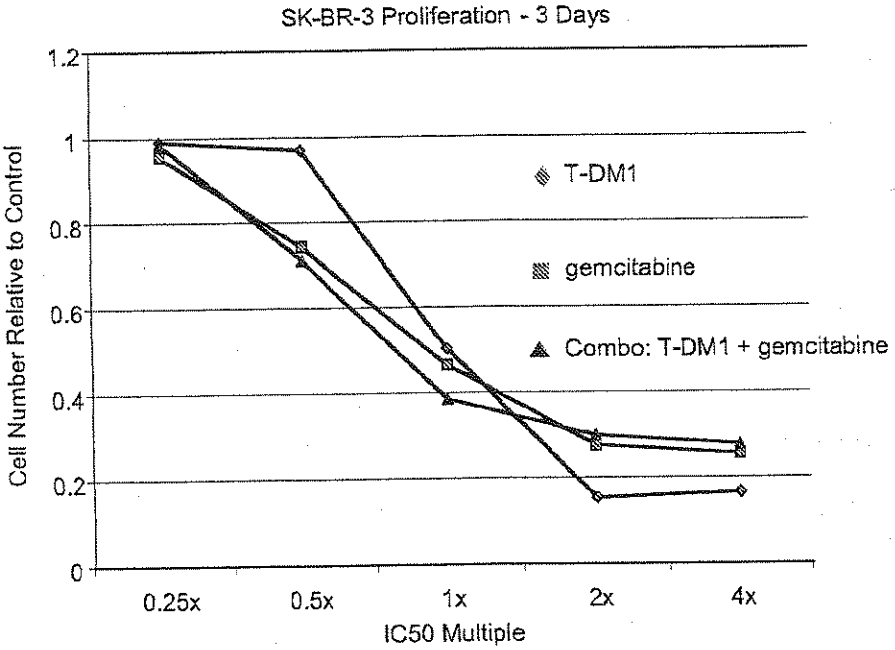



**Figure 20**

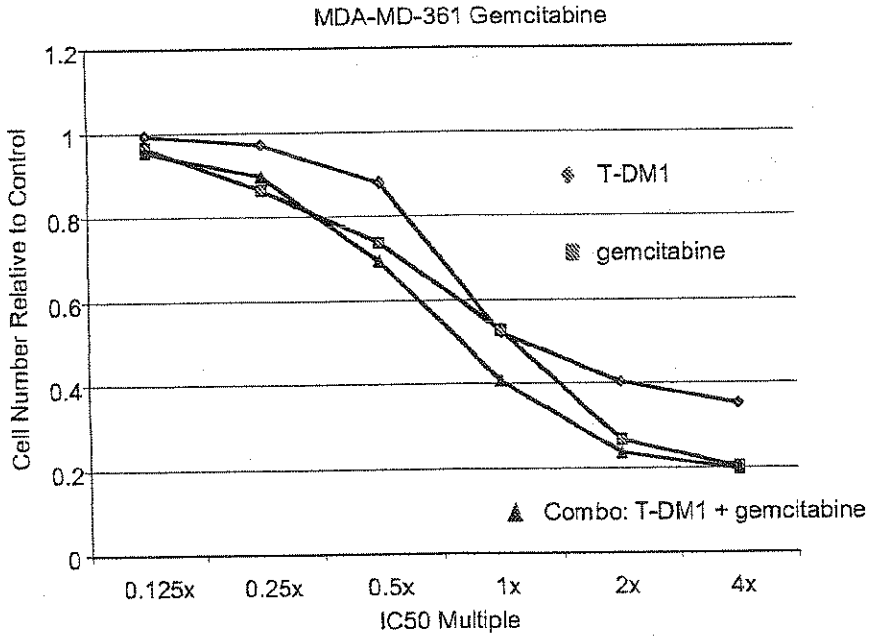



**Figure 21**

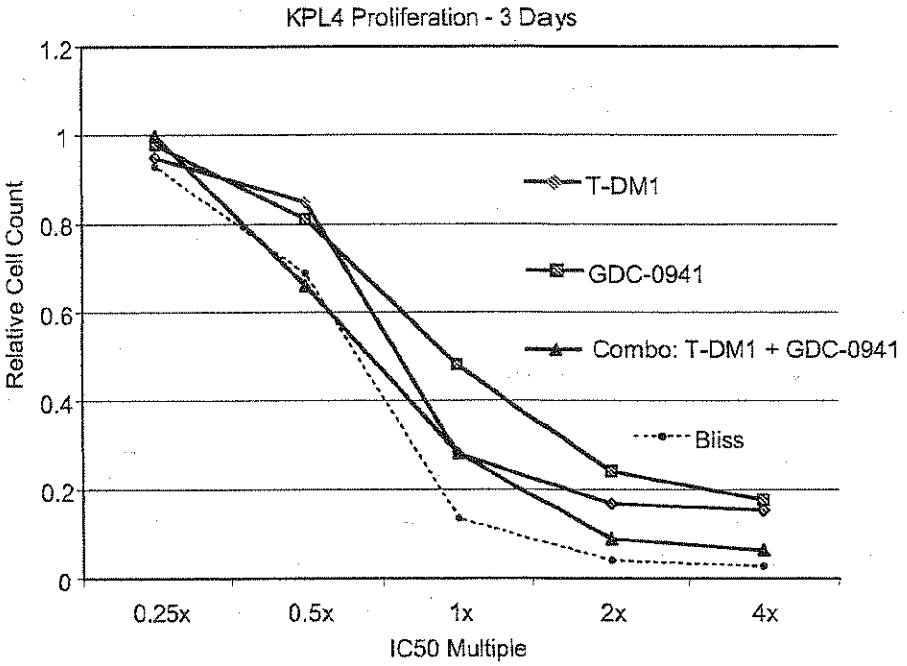



**Figure 22**

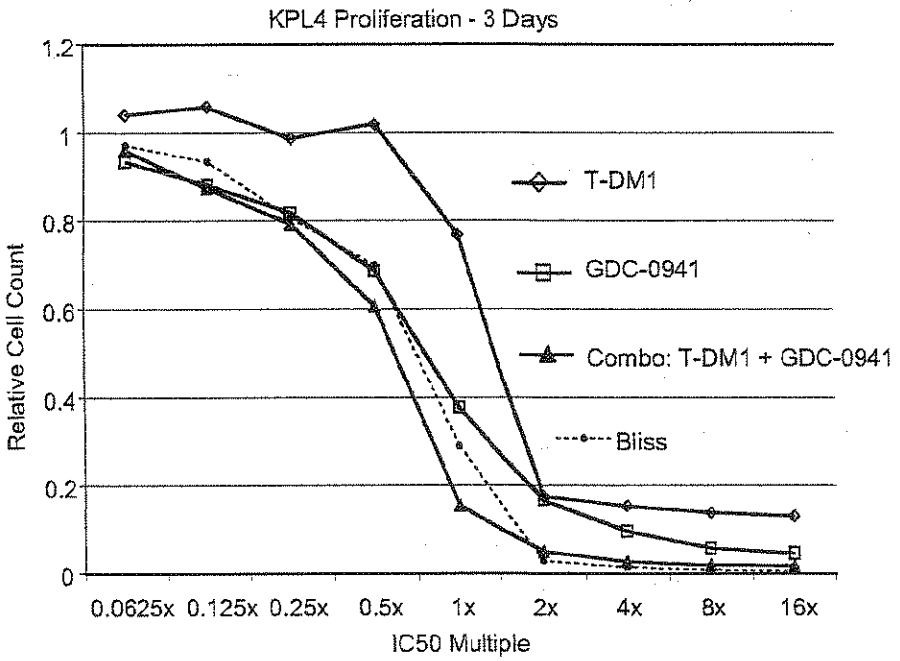



**Figure 23**

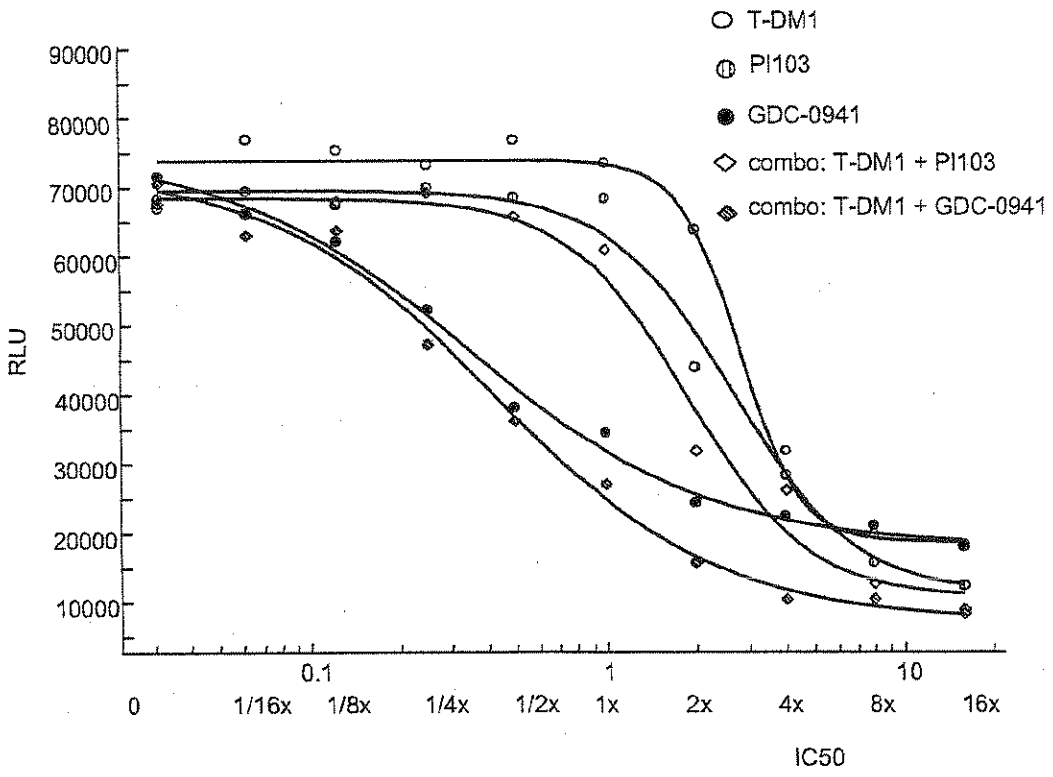

T-DM1
PI103
GDC-0941
combo: T-DM1 + PI103
combo: T-DM1 + GDC-0941
RLU
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
0.1
1
10
1/16x
1/8x
1/4x
1/2x
1x
2x
4x
8x
16x
IC50

**Figure 24**

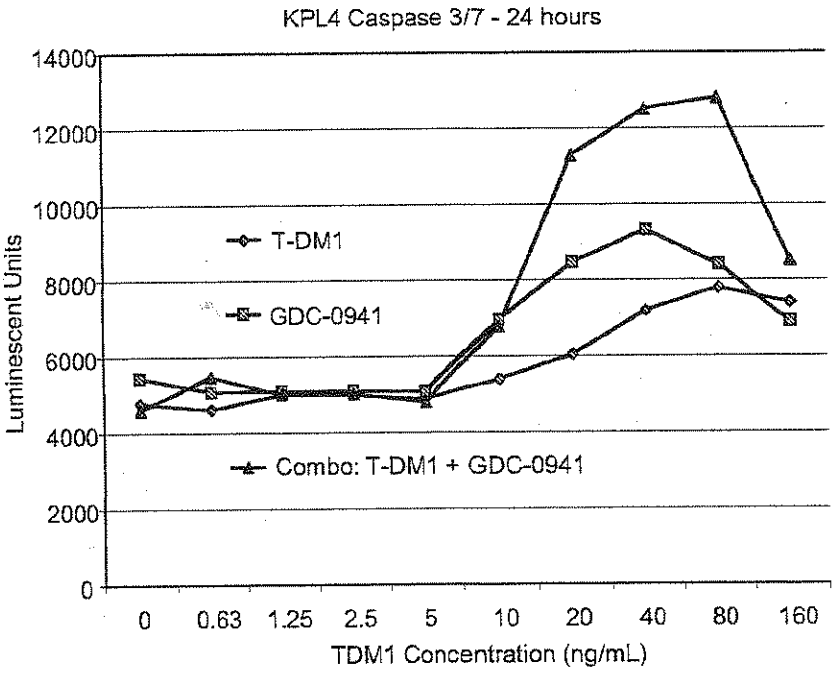



**Figure 25**

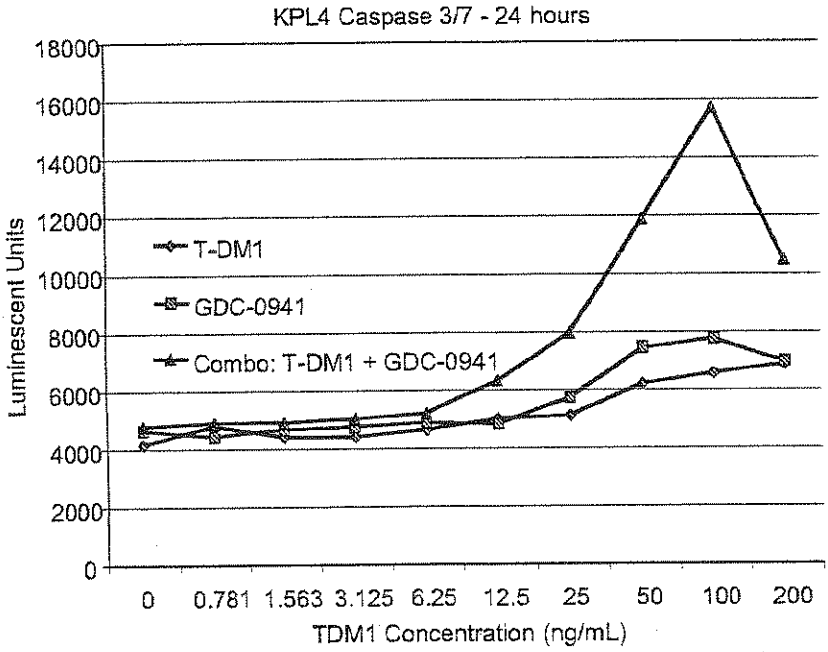



**Figure 26**

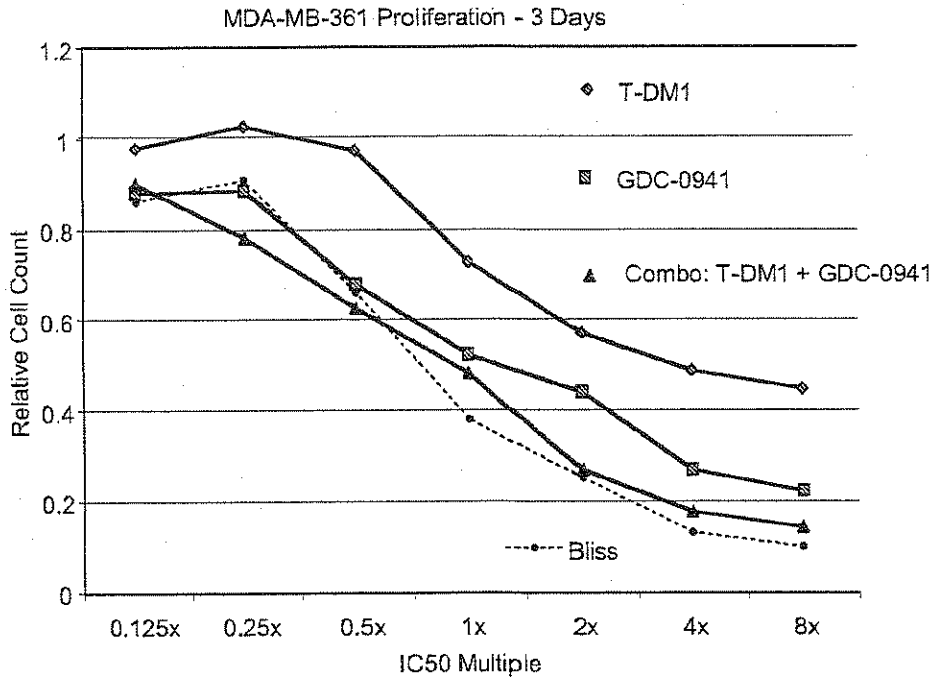



**Figure 27**

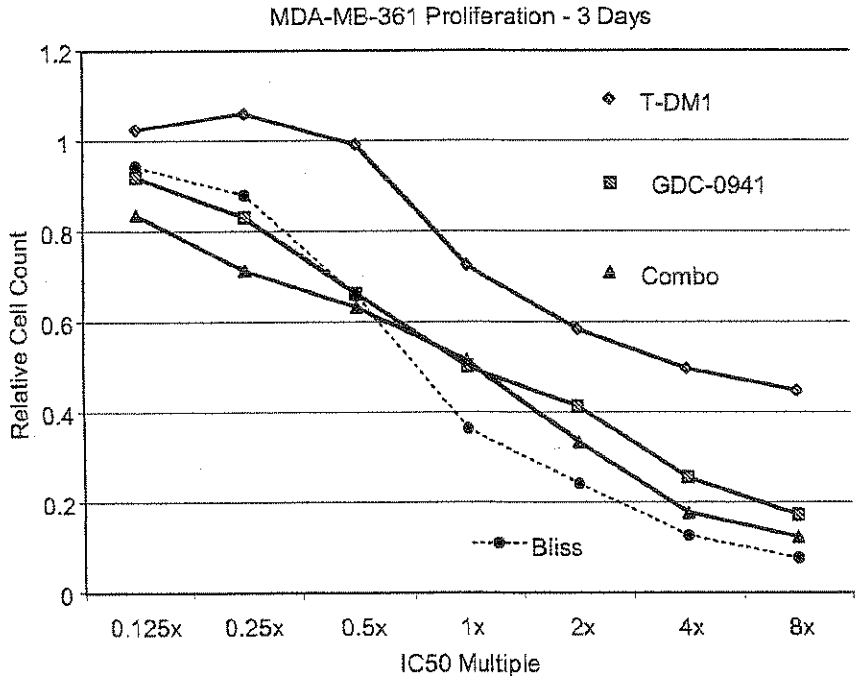



**Figure 28**

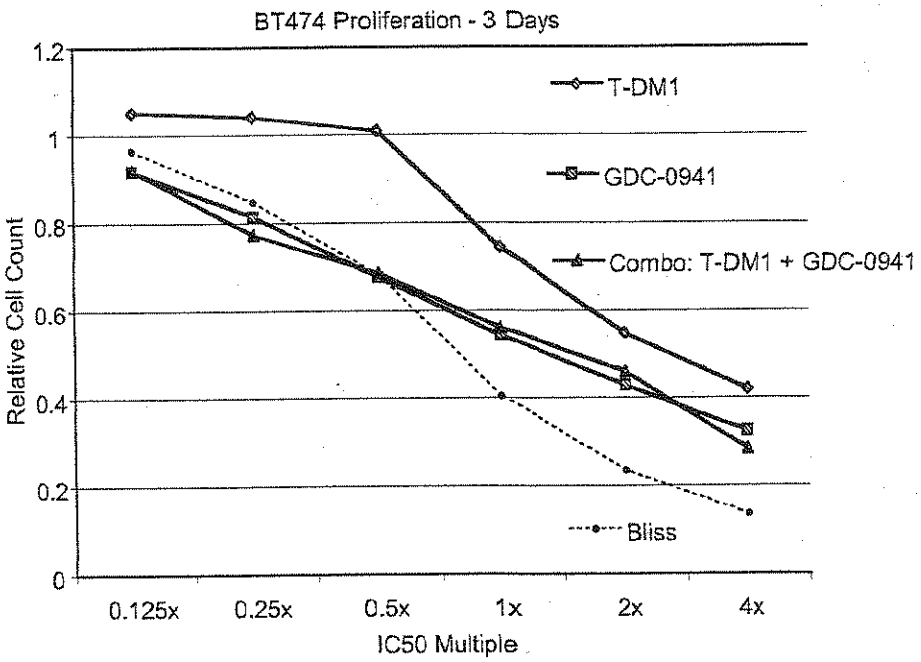



**Figure 29**

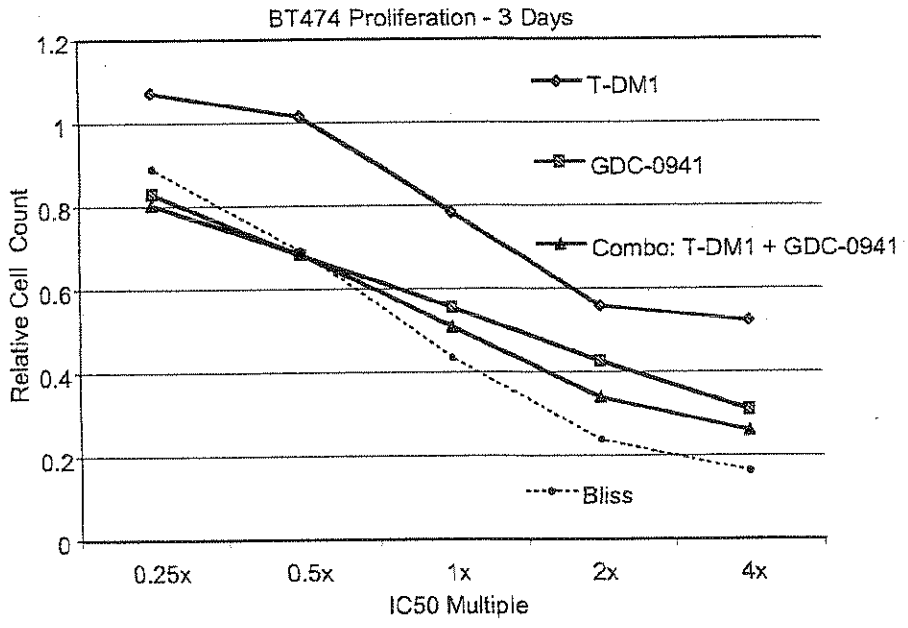



**Figure 30**

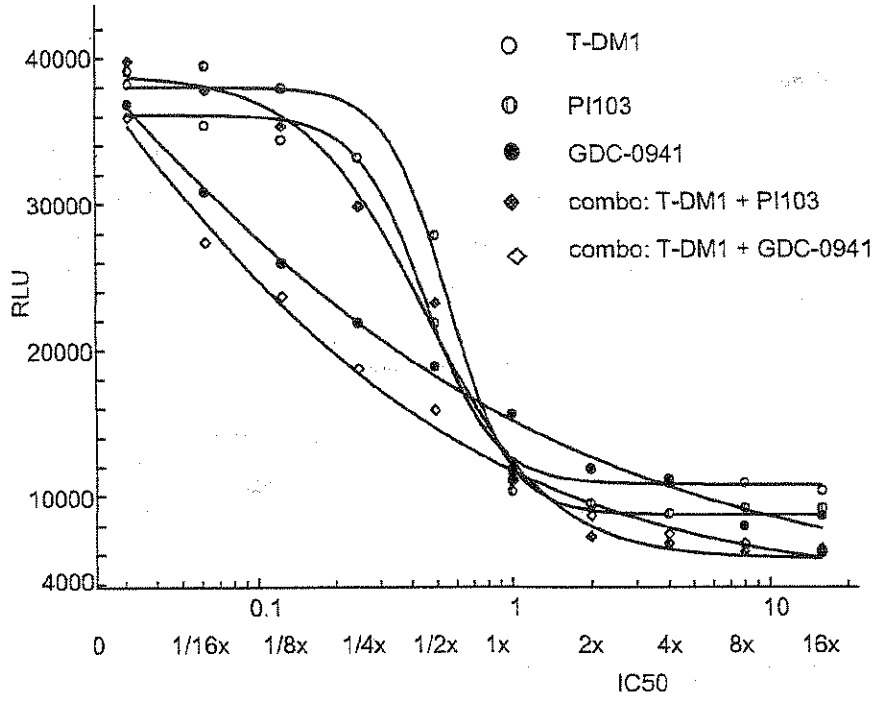



**Figure 31**

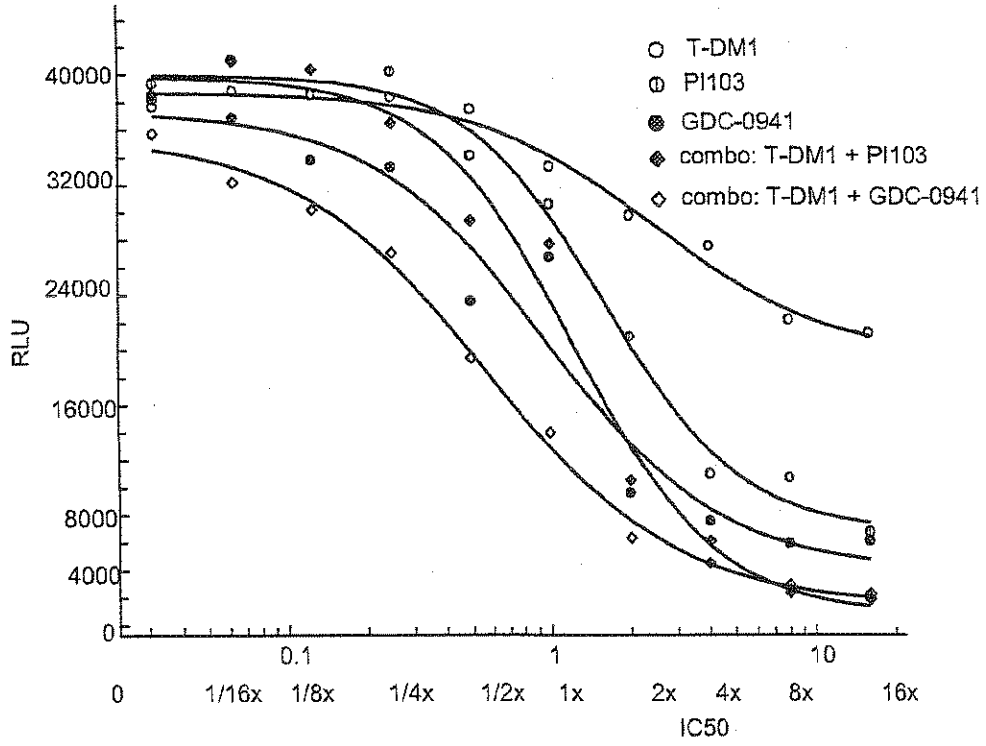



**Figure 32**

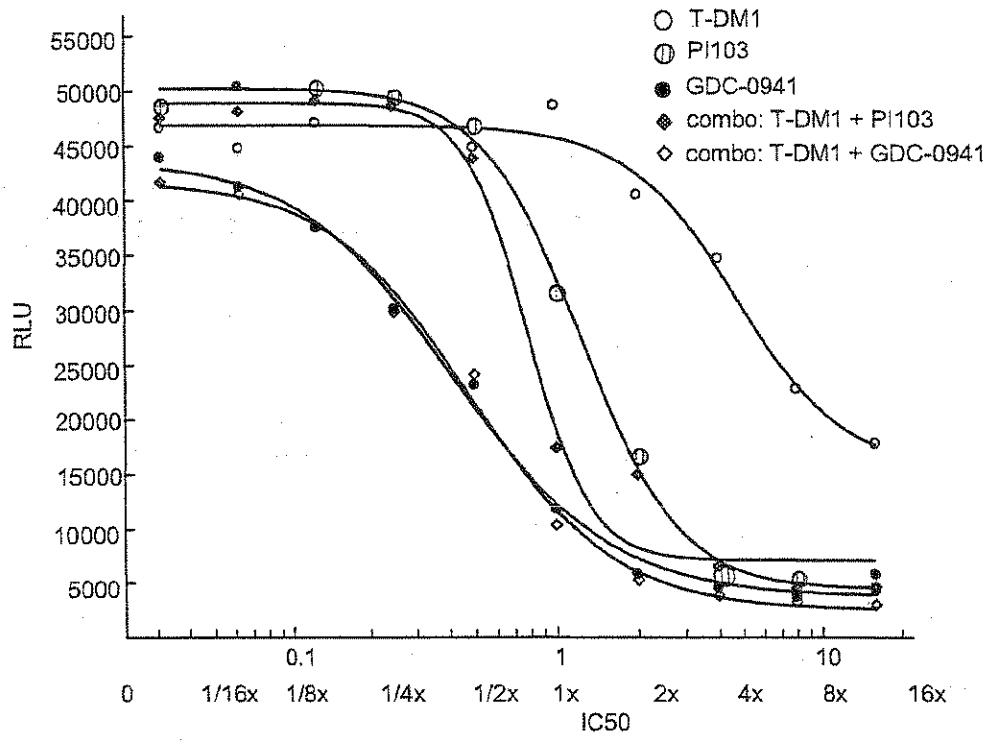

T-DM1
PI103
GDC-0941
combo: T-DM1 + PI103
combo: T-DM1 + GDC-0941
RLU
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0.1
1
10
0
1/16x
1/8x
1/4x
1/2x
1x
2x
4x
8x
16x
IC50

**Figure 33**

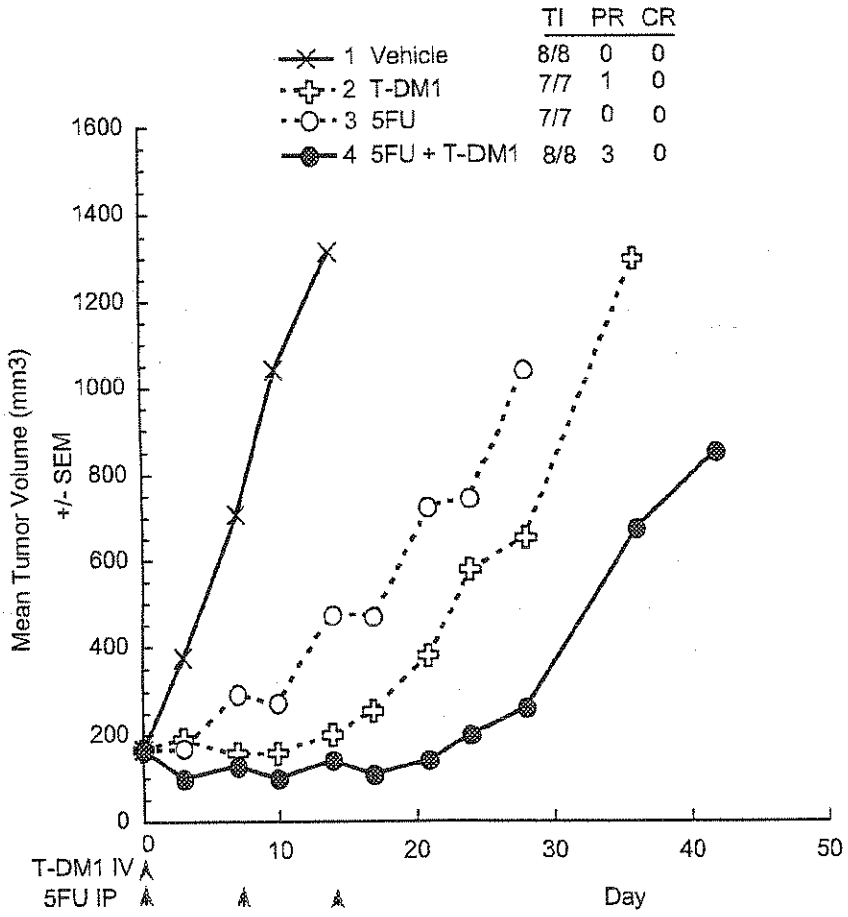

TI PR CR
1 Vehicle 8/8 0 0
2 T-DM1 7/7 1 0
3 5FU 7/7 0 0
4 5FU + T-DM1 8/8 3 0
Mean Tumor Volume (mm3)
+/- SEM
1600
1400
1200
1000
800
600
400
200
0
0
10
20
30
40
50
Day
T-DM1 IV
5FU IP

**Figure 34**

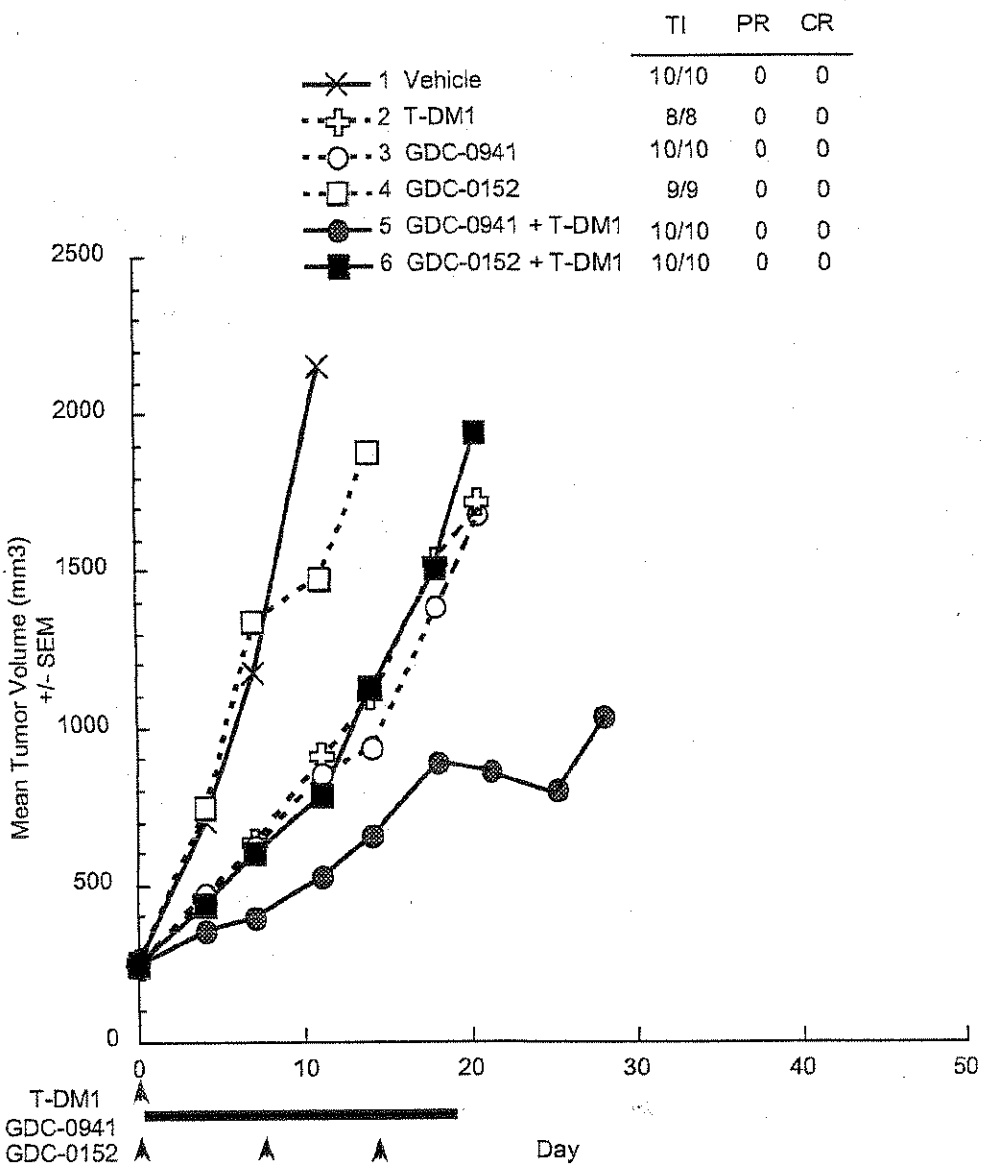

TI PR CR
1 Vehicle 10/10 0 0
2 T-DM1 8/8 0 0
3 GDC-0941 10/10 0 0
4 GDC-0152 9/9 0 0
5 GDC-0941 + T-DM1 10/10 0 0
6 GDC-0152 + T-DM1 10/10 0 0
Mean Tumor Volume (mm3) +/- SEM
2500
2000
1500
1000
500
0
0
10
20
30
40
50
Day
T-DM1
GDC-0941
GDC-0152

**Figure 35**

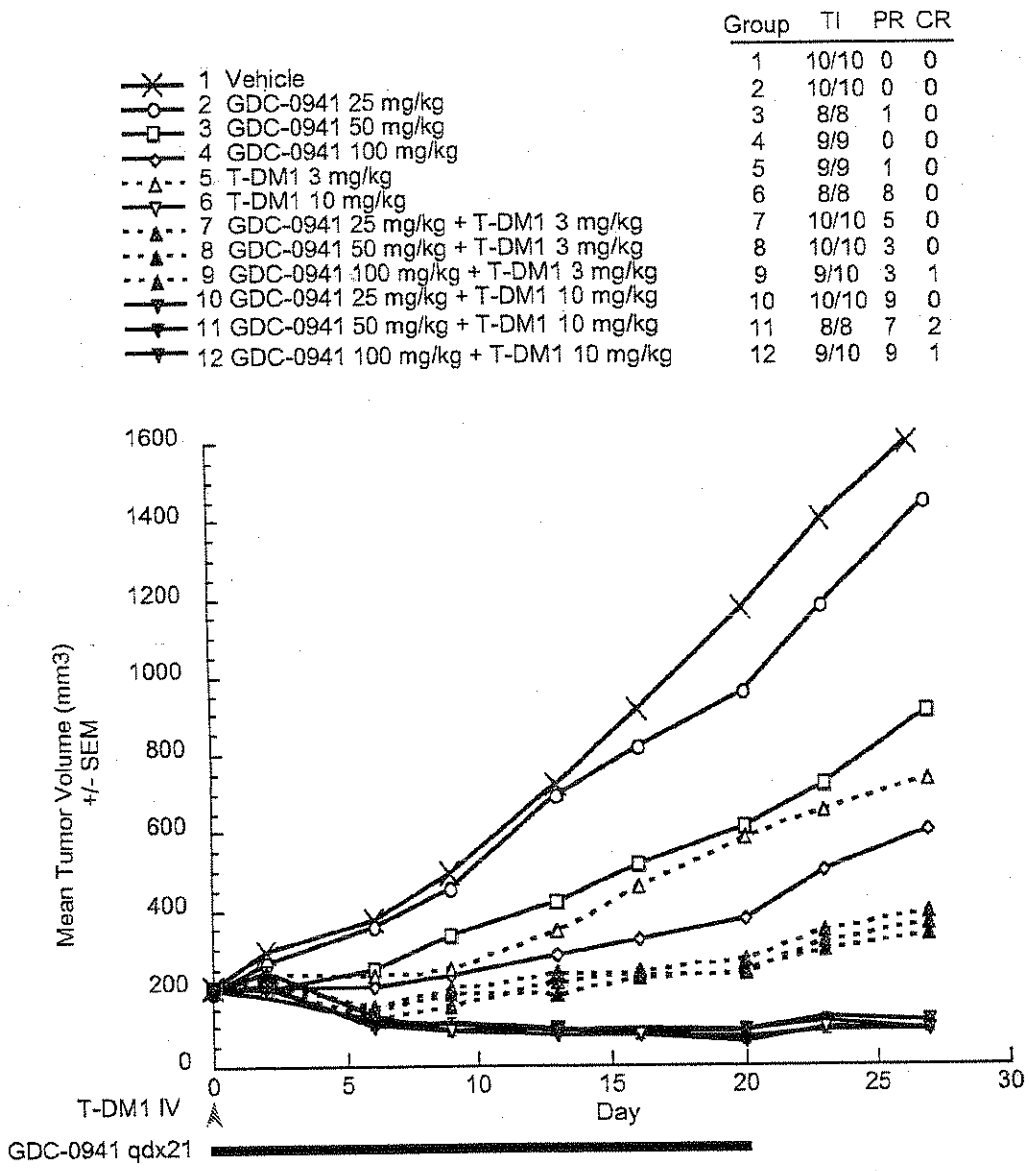

1 Vehicle
2 GDC-0941 25 mg/kg
3 GDC-0941 50 mg/kg
4 GDC-0941 100 mg/kg
5 T-DM1 3 mg/kg
6 T-DM1 10 mg/kg
7 GDC-0941 25 mg/kg + T-DM1 3 mg/kg
8 GDC-0941 50 mg/kg + T-DM1 3 mg/kg
9 GDC-0941 100 mg/kg + T-DM1 3 mg/kg
10 GDC-0941 25 mg/kg + T-DM1 10 mg/kg
11 GDC-0941 50 mg/kg + T-DM1 10 mg/kg
12 GDC-0941 100 mg/kg + T-DM1 10 mg/kg
Group TI PR CR
1 10/10 0 0
2 10/10 0 0
3 8/8 1 0
4 9/9 0 0
5 9/9 1 0
6 8/8 8 0
7 10/10 5 0
8 10/10 3 0
9 9/10 3 1
10 10/10 9 0
11 8/8 7 2
12 9/10 9 1
Mean Tumor Volume (mm3) +/- SEM
1600
1400
1200
1000
800
600
400
200
0
0
5
10
15
20
25
30
Day
T-DM1 IV
GDC-0941 qdx21

**Figure 36**

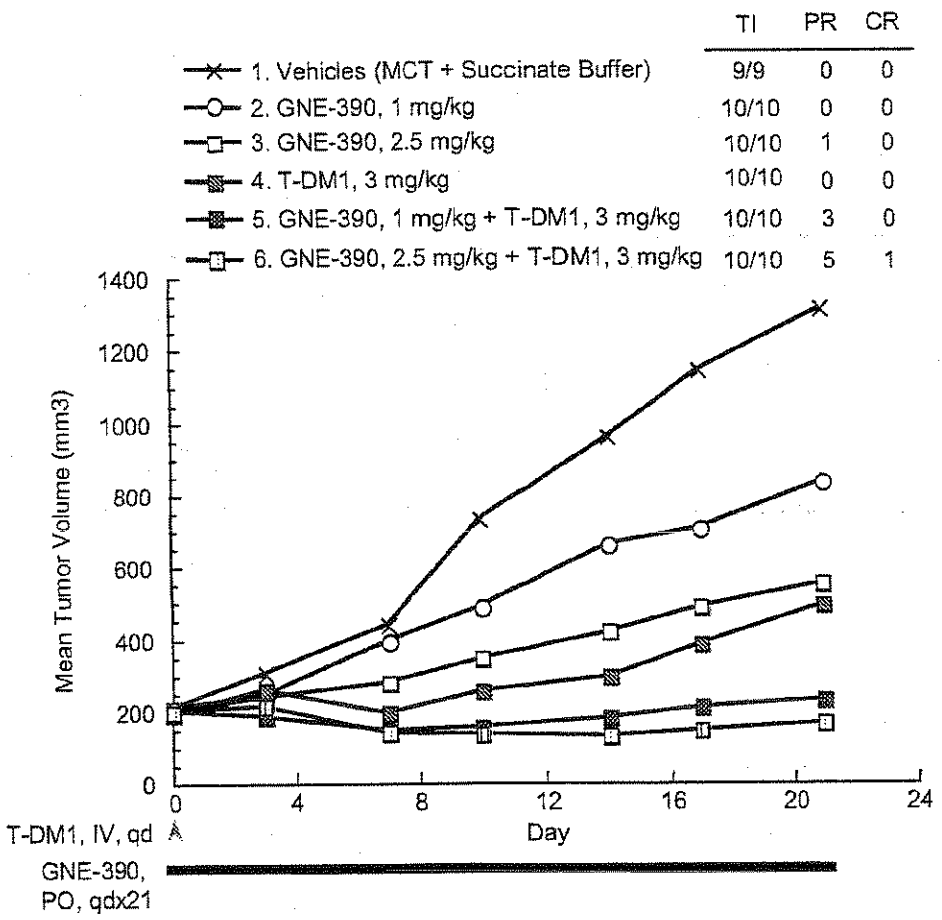

TI PR CR
1. Vehicles (MCT + Succinate Buffer) 9/9 0 0
2. GNE-390, 1 mg/kg 10/10 0 0
3. GNE-390, 2.5 mg/kg 10/10 1 0
4. T-DM1, 3 mg/kg 10/10 0 0
5. GNE-390, 1 mg/kg + T-DM1, 3 mg/kg 10/10 3 0
6. GNE-390, 2.5 mg/kg + T-DM1, 3 mg/kg 10/10 5 1
Mean Tumor Volume (mm3)
1400
1200
1000
800
600
400
200
0
0
4
8
12
16
20
24
Day
T-DM1, IV, qd
GNE-390, PO, qdx21

**Figure 37**