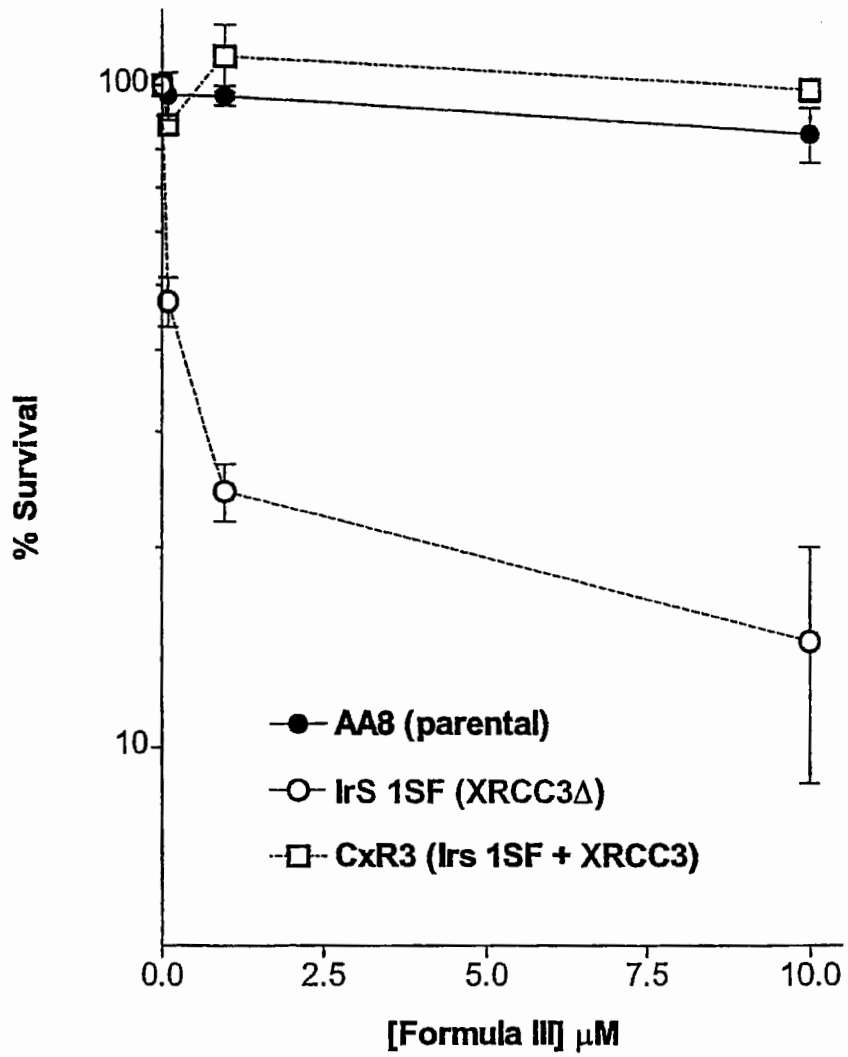

100
10
% Survival
AA8 (parental)
IrS 1SF (XRCC3Δ)
CxR3 (Irs 1SF + XRCC3)
0.0
2.5
5.0
7.5
10.0
[Formula III] μM

Fig. 1

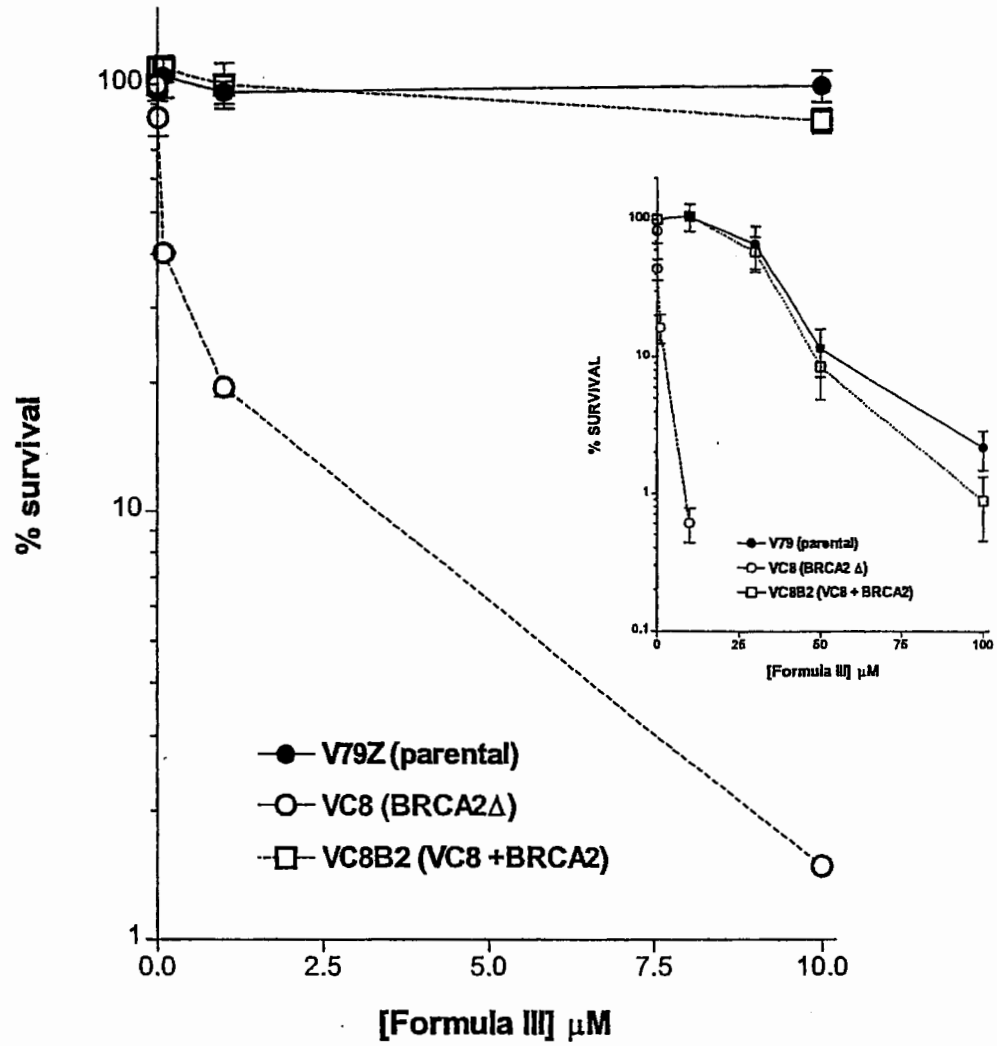

100
10
1
% survival
0.0
2.5
5.0
7.5
10.0
[Formula III] μM
V79Z (parental)
VC8 (BRCA2Δ)
VC8B2 (VC8 +BRCA2)
% SURVIVAL
100
10
1
0.1
0
25
50
75
100
[Formula III] μM
V79 (parental)
VC8 (BRCA2 Δ)
VC8B2 (VC8 + BRCA2)

Fig. 2

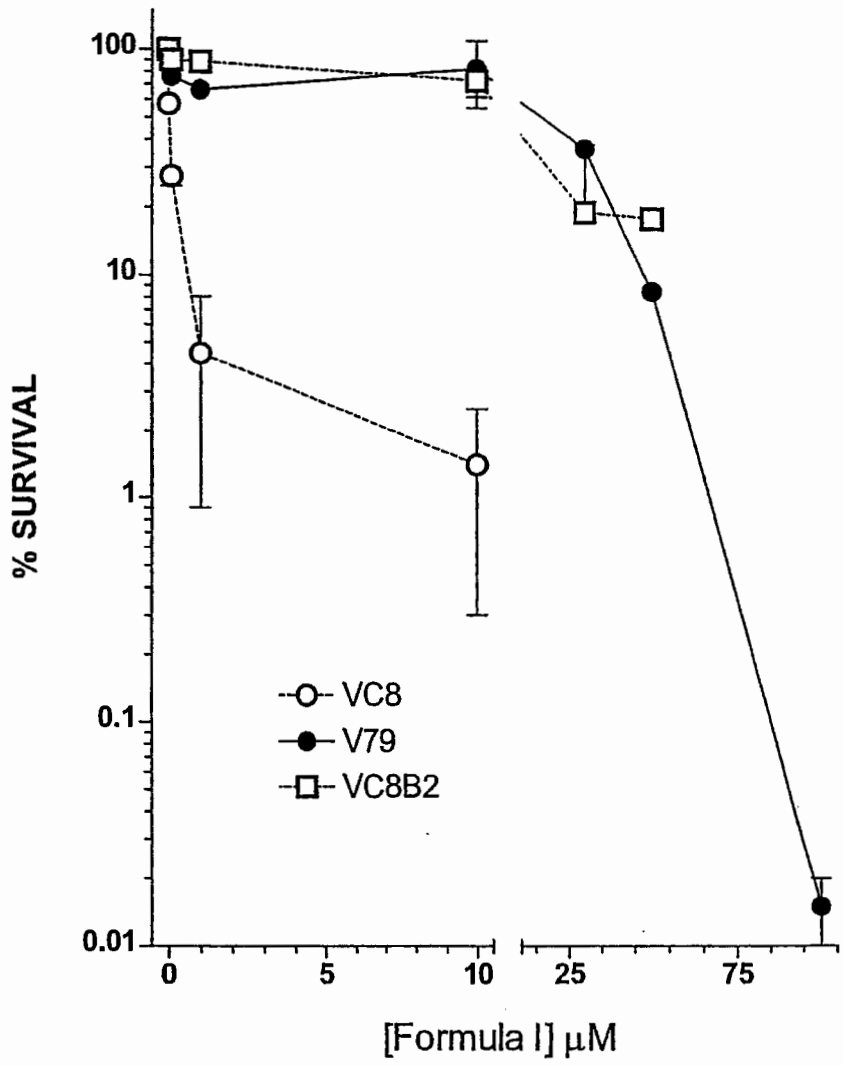


Fig. 3

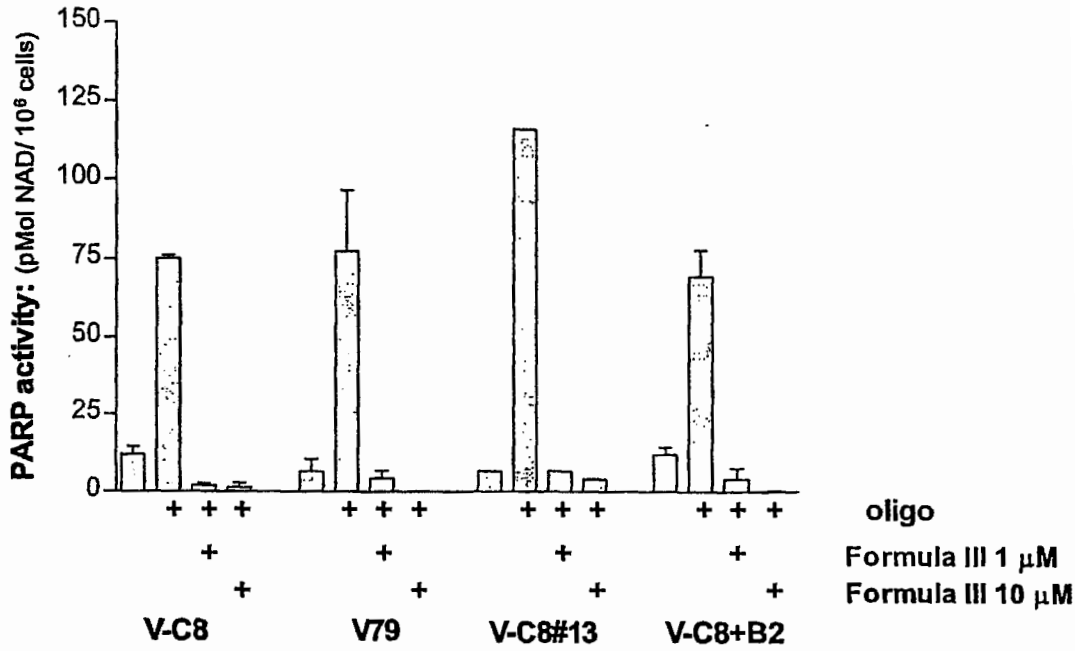

PARP activity: (pMol NAD/ 10⁶ cells)
150
125
100
75
50
25
0
oligo
Formula III 1 μM
Formula III 10 μM
V-C8
V79
V-C8#13
V-C8+B2

Fig. 4

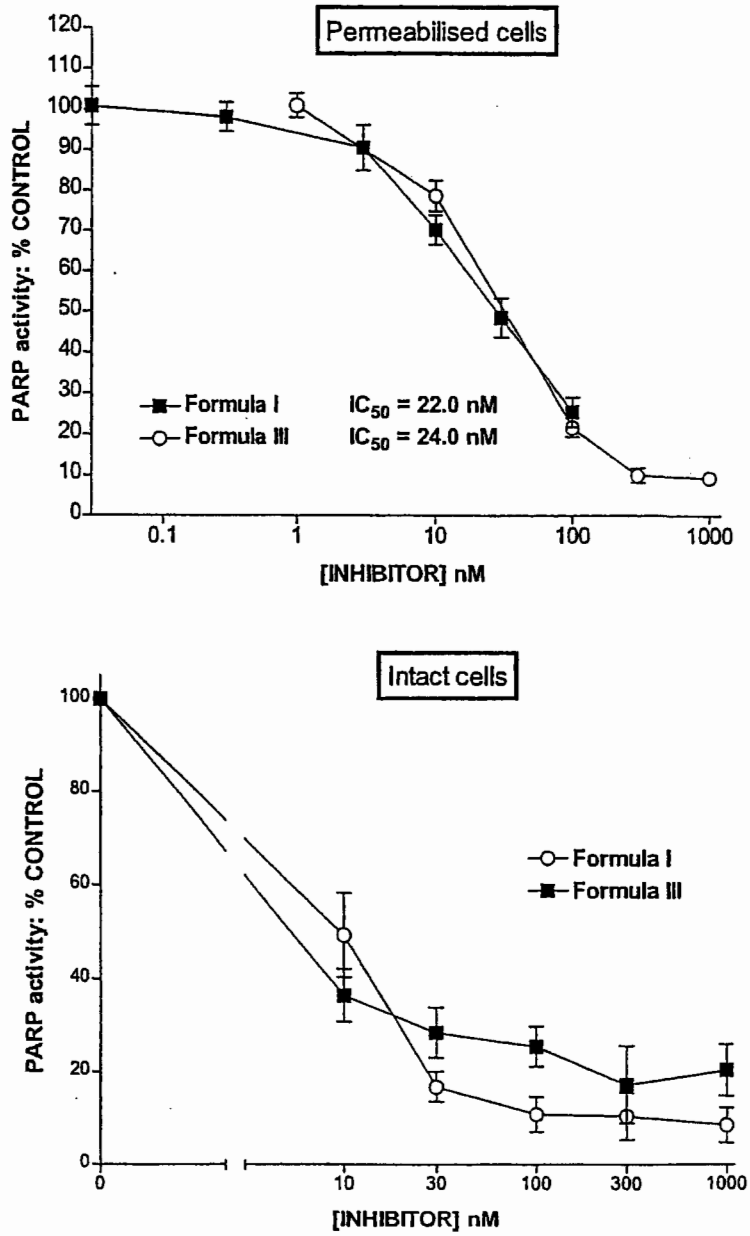
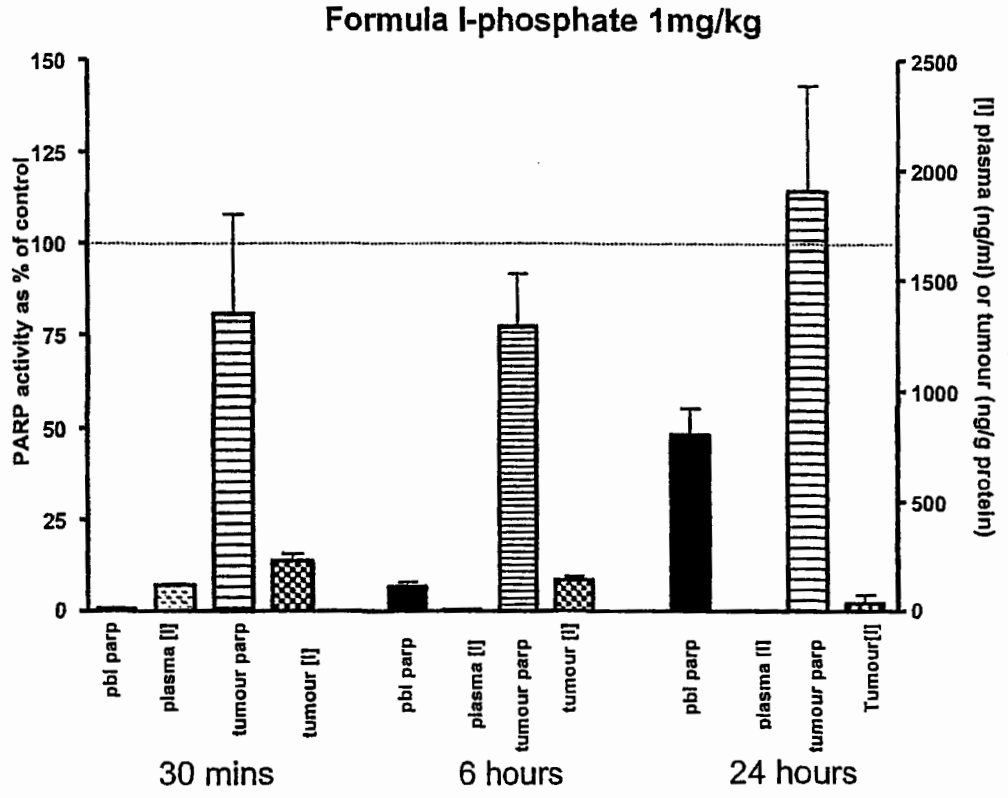

Permeabilised cells
PARP activity: % CONTROL
120
110
100
90
80
70
60
50
40
30
20
10
0
0.1
1
10
100
1000
[INHIBITOR] nM
Formula I
Formula III
IC50 = 22.0 nM
IC50 = 24.0 nM
Intact cells
PARP activity: % CONTROL
100
80
60
40
20
0
0
10
30
100
300
1000
[INHIBITOR] nM
Formula I
Formula III

Fig 5


Formula I-phosphate 1mg/kg
PARP activity as % of control
[I] plasma (ng/ml) or tumour (ng/g protein)
150
125
100
75
50
25
0
2500
2000
1500
1000
500
0
pbl parp
plasma [I]
tumour parp
tumour [I]
pbl parp
plasma [I]
tumour parp
tumour [I]
pbl parp
plasma [I]
tumour parp
Tumour[I]
30 mins
6 hours
24 hours

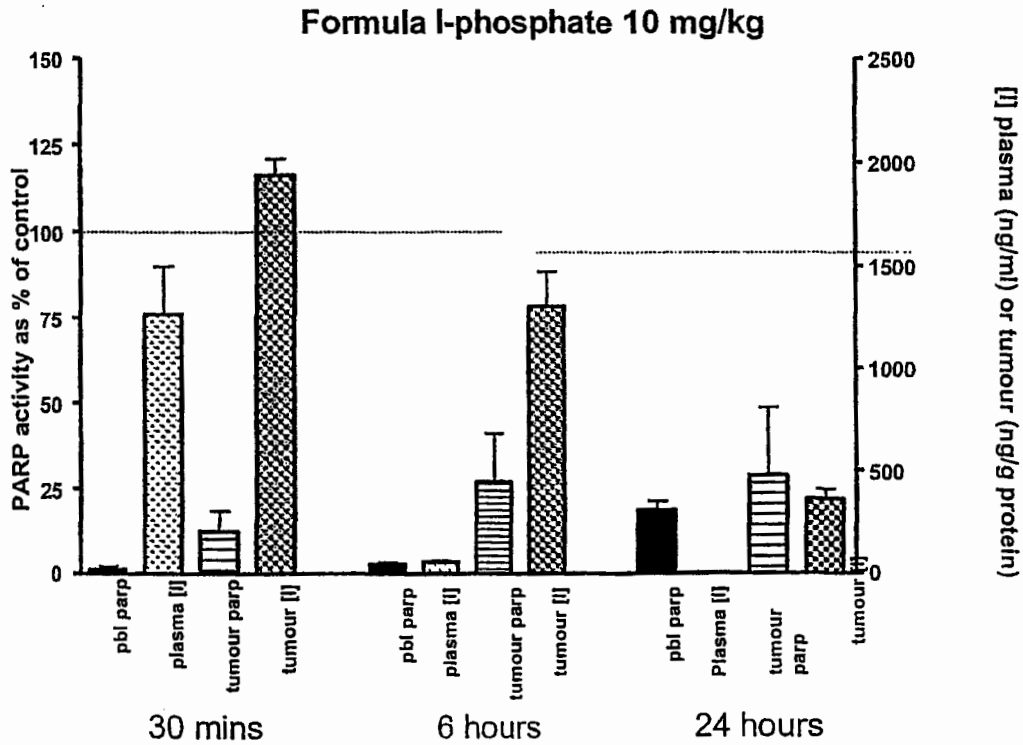

Formula I-phosphate 10 mg/kg
PARP activity as % of control
[I] plasma (ng/ml) or tumour (ng/g protein)
150
125
100
75
50
25
0
2500
2000
1500
1000
500
0
pbl parp
plasma [I]
tumour parp
tumour [I]
pbl parp
plasma [I]
tumour parp
tumour [I]
pbl parp
Plasma [I]
tumour parp
tumour
30 mins
6 hours
24 hours

Fig. 6

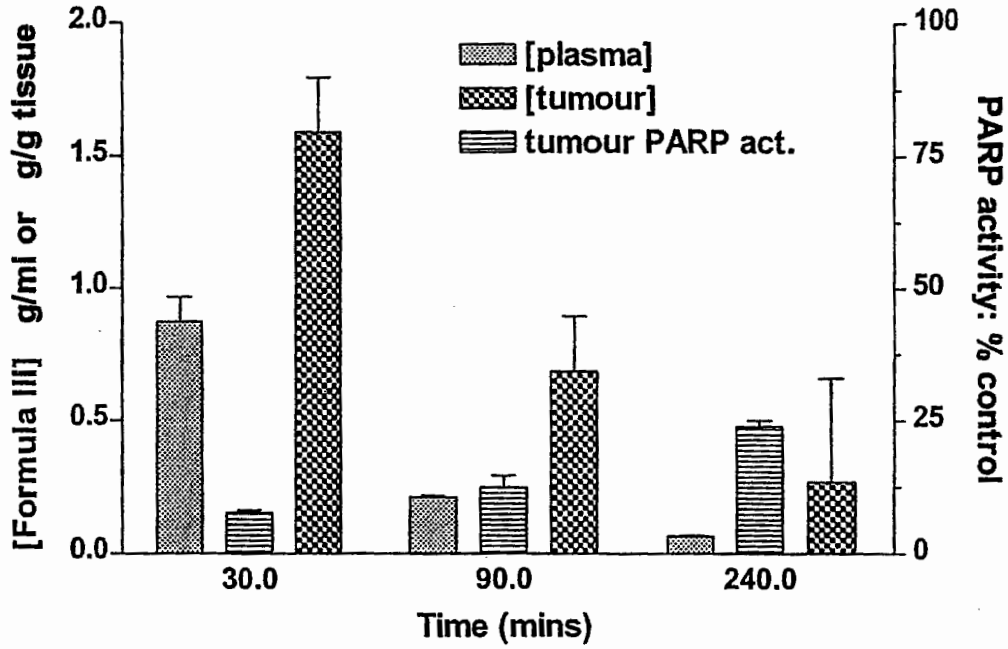

[Formula III] g/ml or g/g tissue
2.0
1.5
1.0
0.5
0.0
[plasma]
[tumour]
tumour PARP act.
100
75
50
25
0
PARP activity: % control
30.0
90.0
240.0
Time (mins)

Fig 7

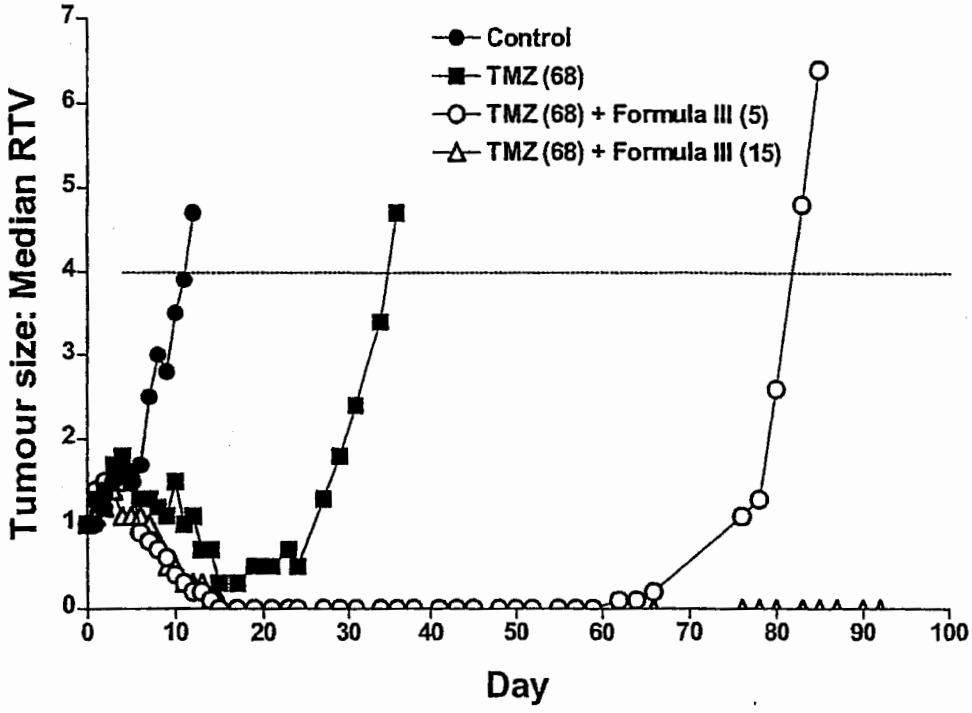

Control
TMZ (68)
TMZ (68) + Formula III (5)
TMZ (68) + Formula III (15)
Tumour size: Median RTV
Day
0
1
2
3
4
5
6
7
0
10
20
30
40
50
60
70
80
90
100

Fig. 8

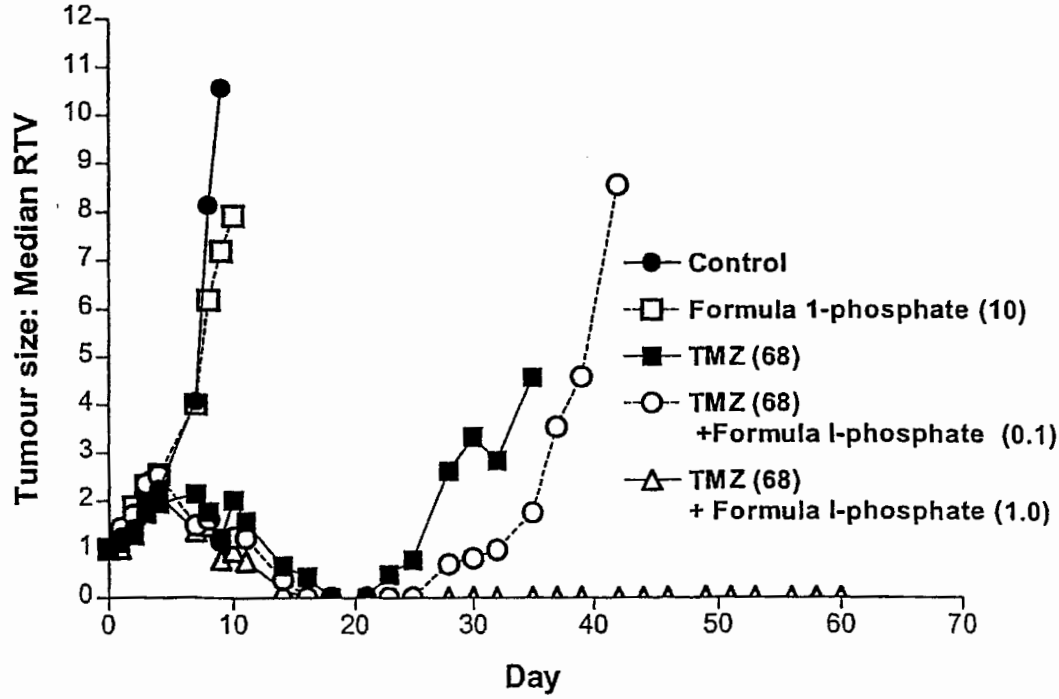

Control
Formula 1-phosphate (10)
TMZ (68)
TMZ (68)
+Formula I-phosphate (0.1)
TMZ (68)
+ Formula I-phosphate (1.0)
Tumour size: Median RTV
Day
0
1
2
3
4
5
6
7
8
9
10
11
12
0
10
20
30
40
50
60
70

Fig 9