Figure 1

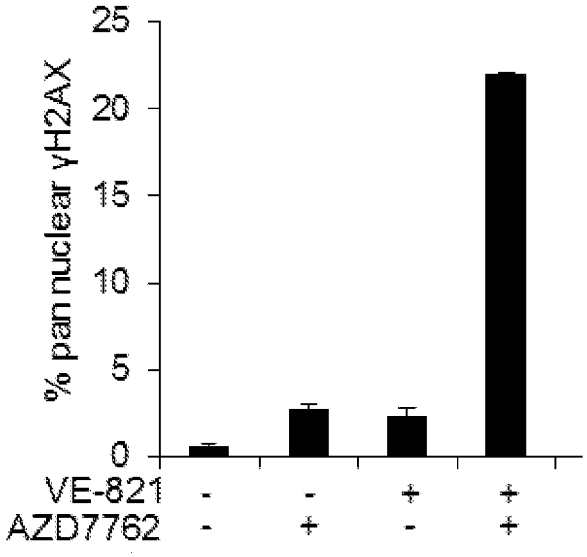


Figure 2a

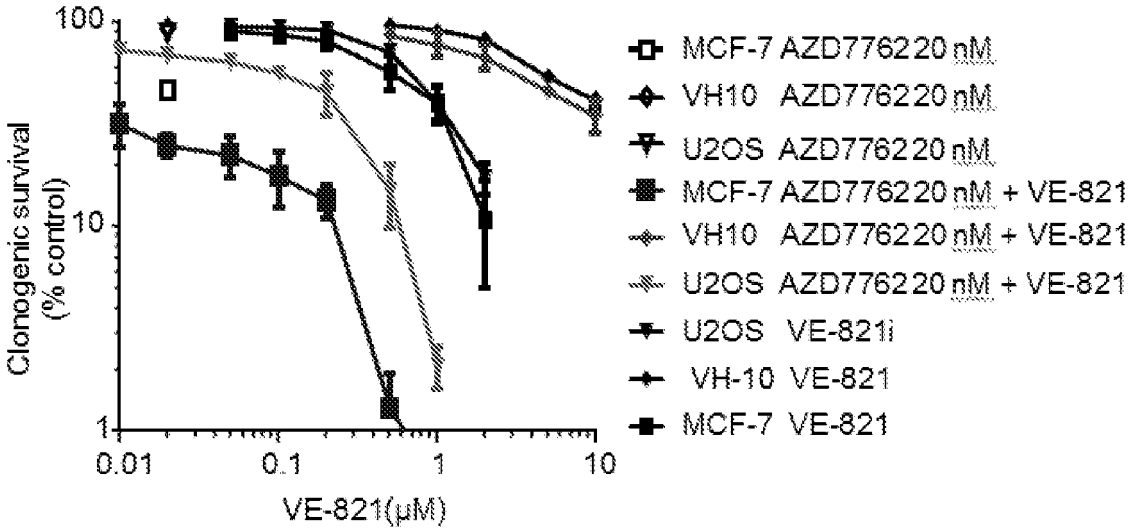


Figure 2b

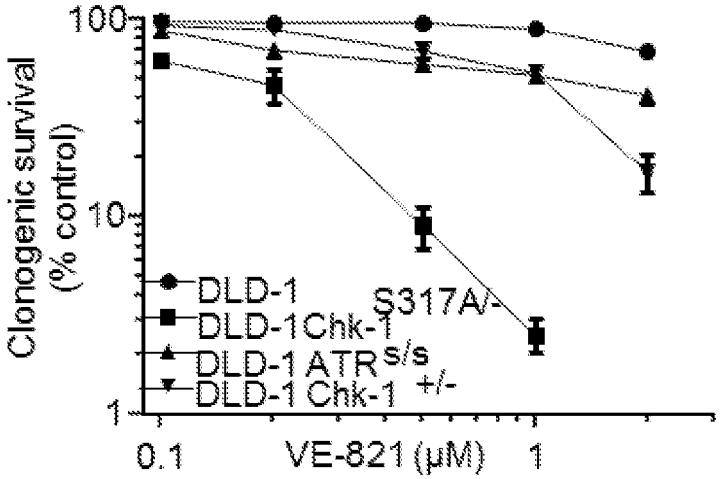


Figure 2c

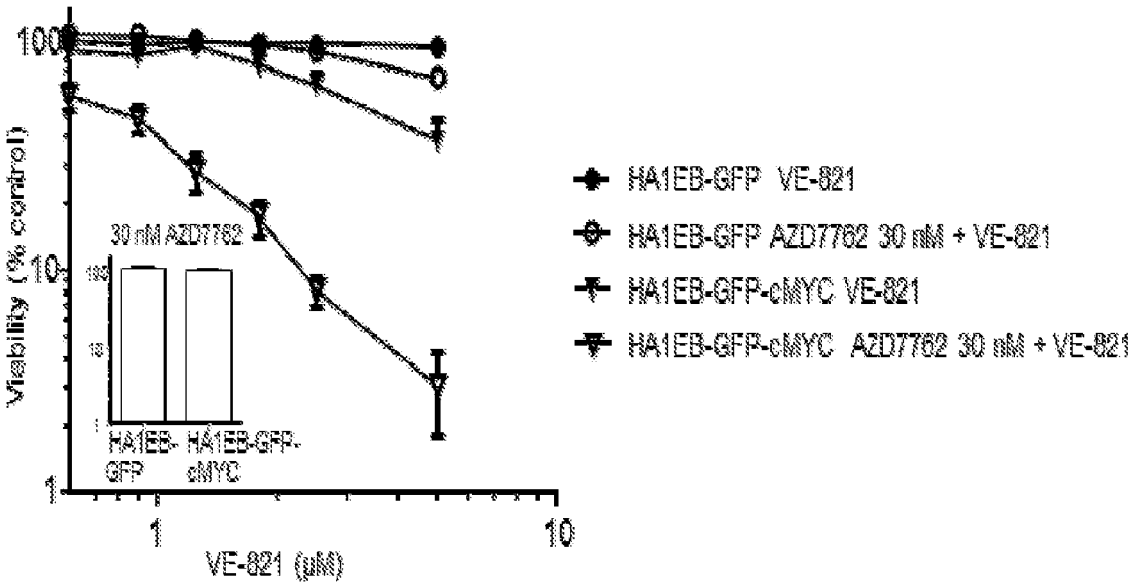


Figure 2d

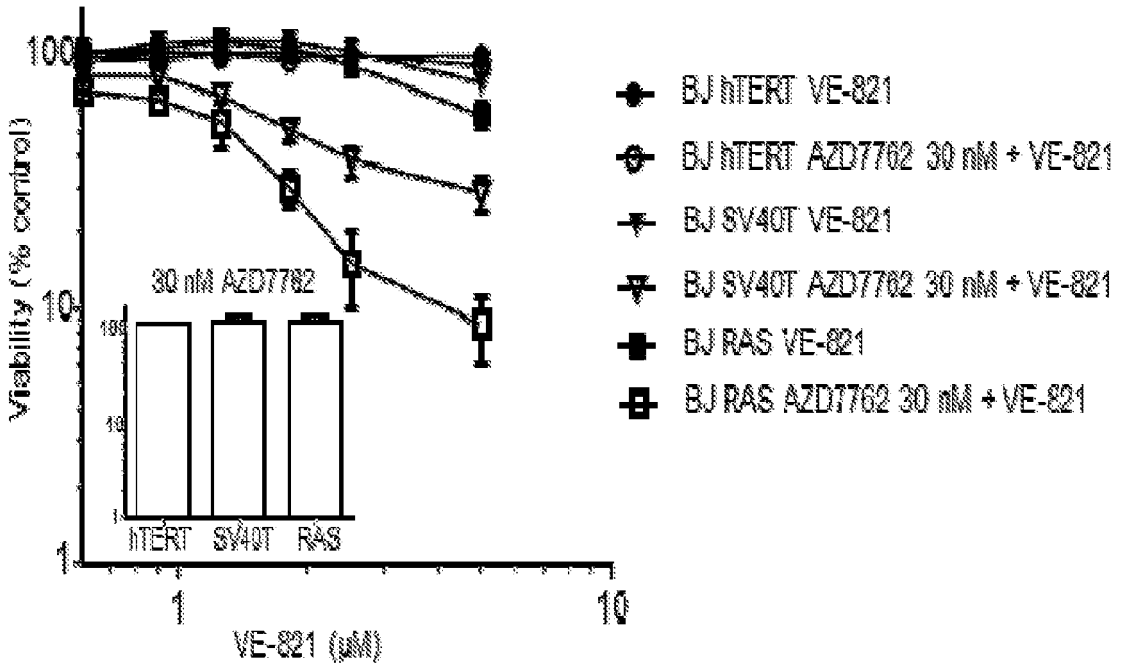


Figure 3a

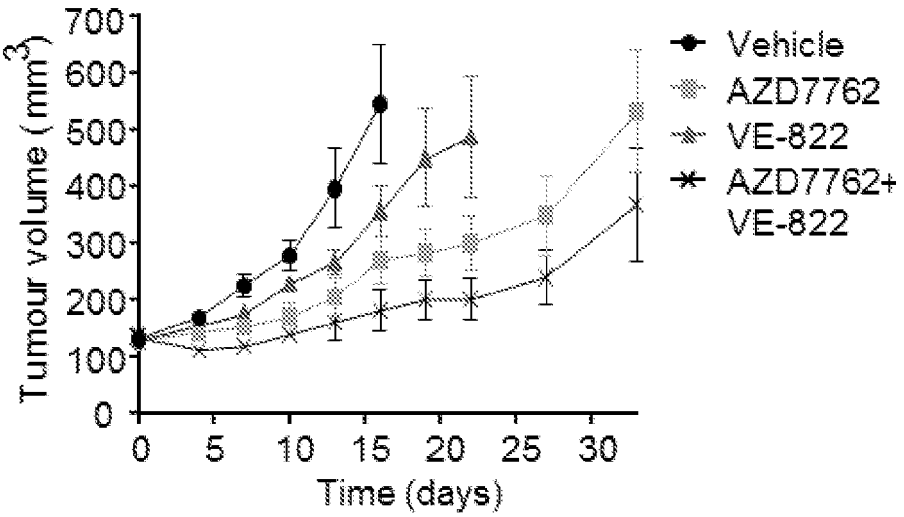

Tumour volume (mm3)
700
600
500
400
300
200
100
0
0
5
10
15
20
25
30
Time (days)
Vehicle
AZD7762
VE-822
AZD7762+
VE-822

Figure 3b

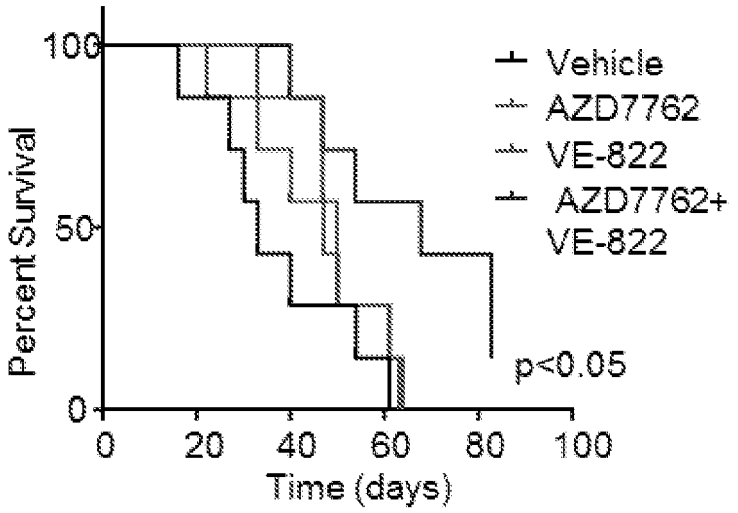


Figure 4a

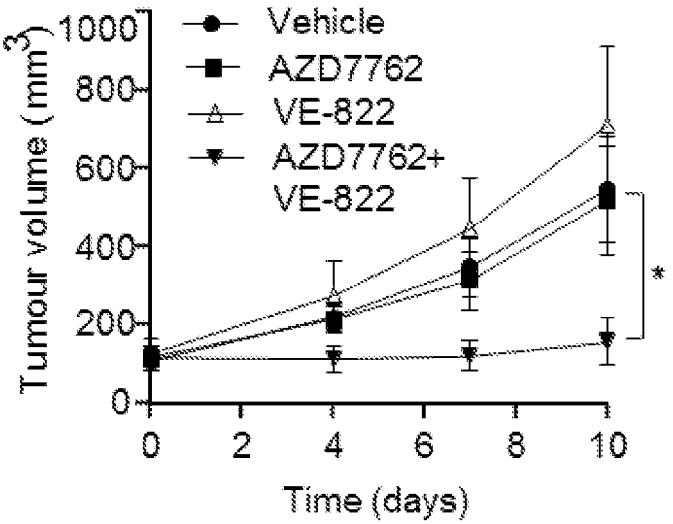


Figure 4b

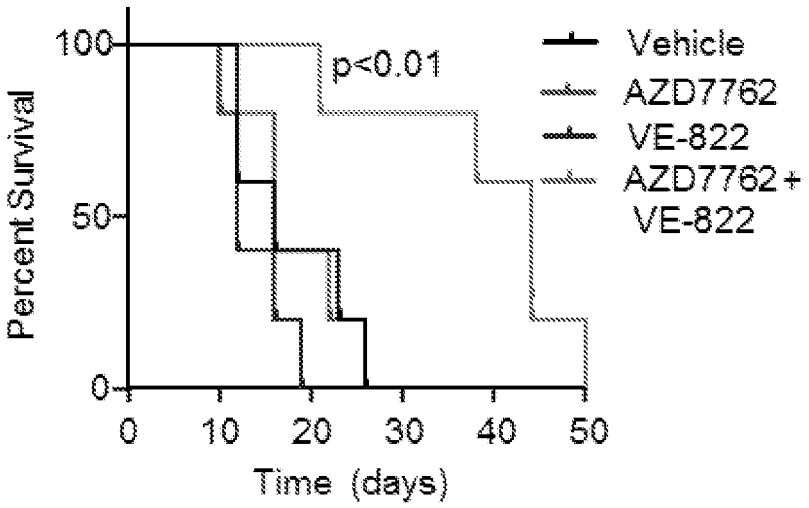


Figure 5

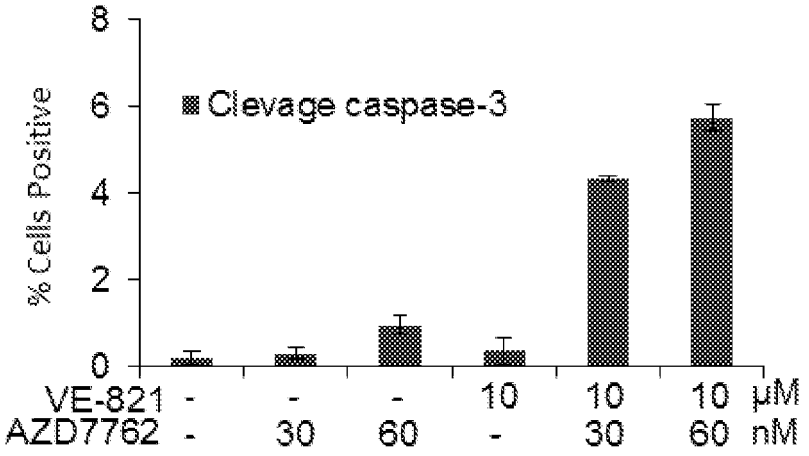


Figure 6a

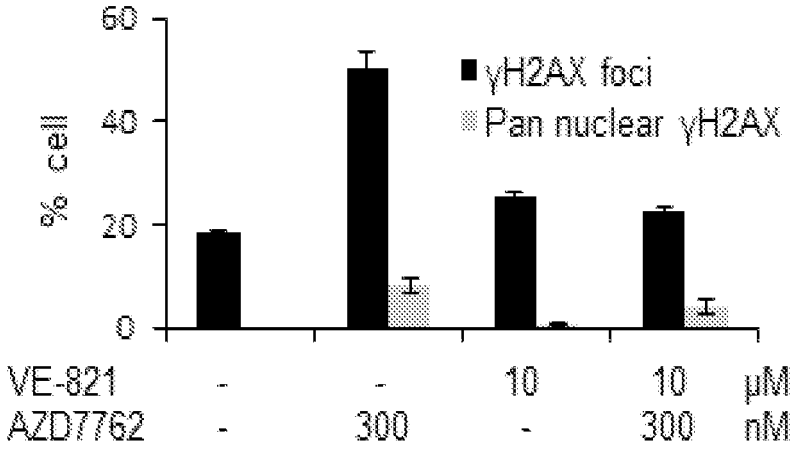


Figure 6b

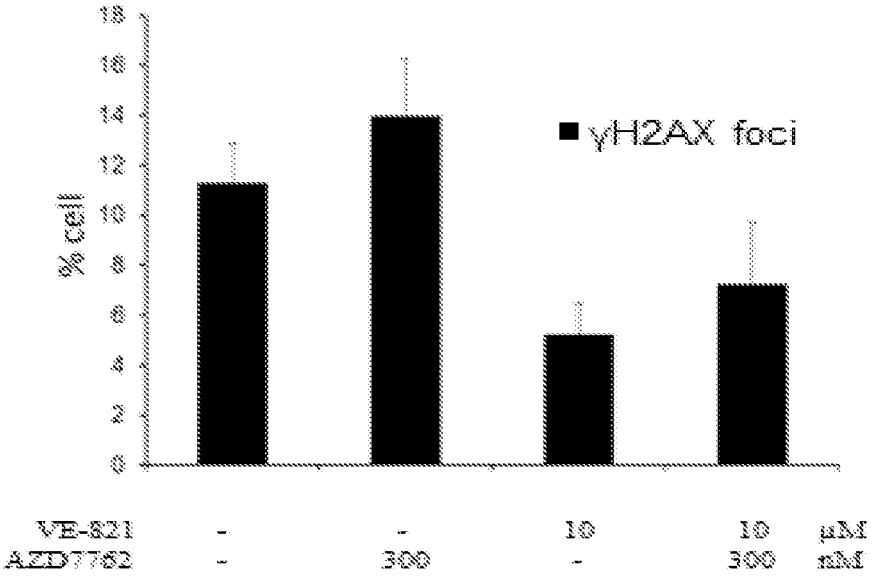


Figure 6c

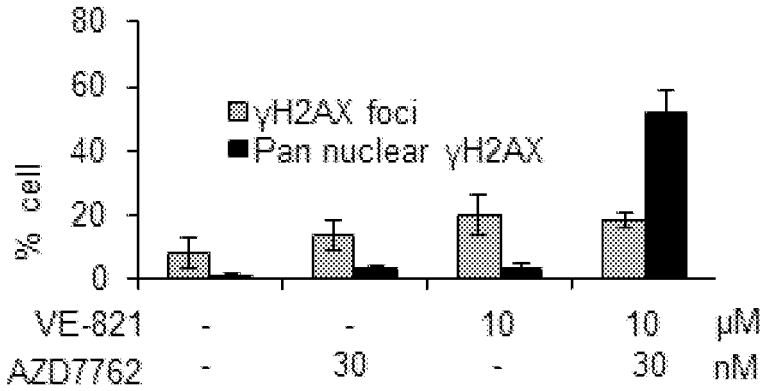


Figure 6d

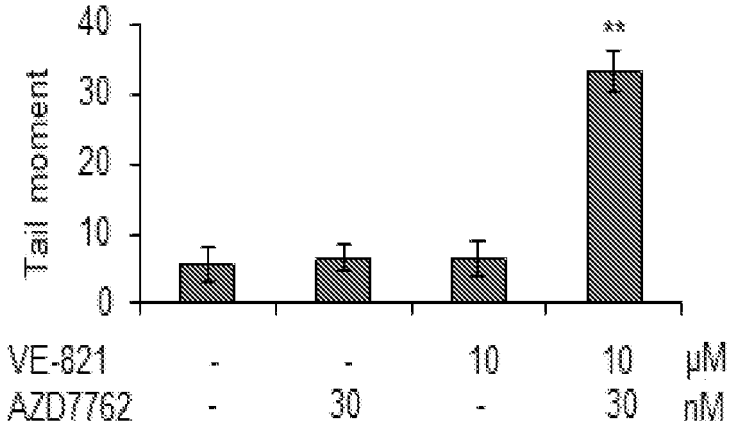


Figure 7a

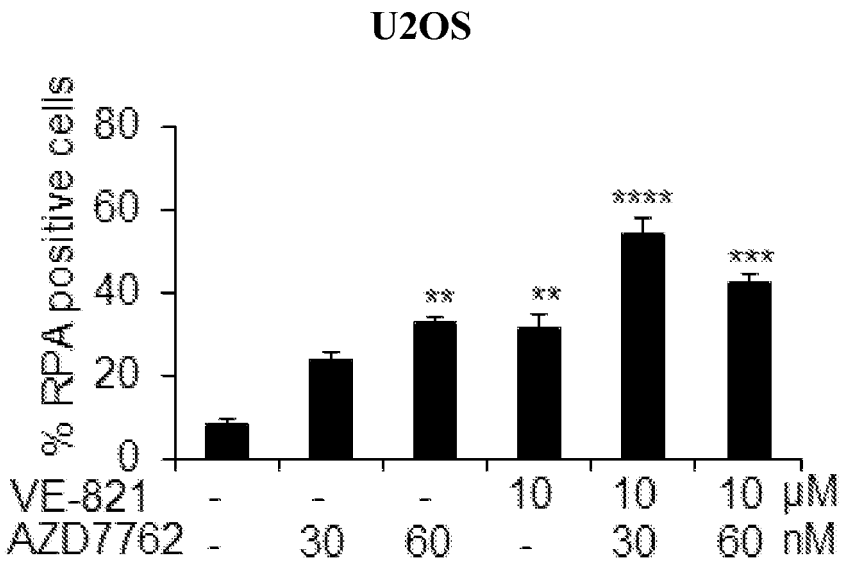


Figure 7b

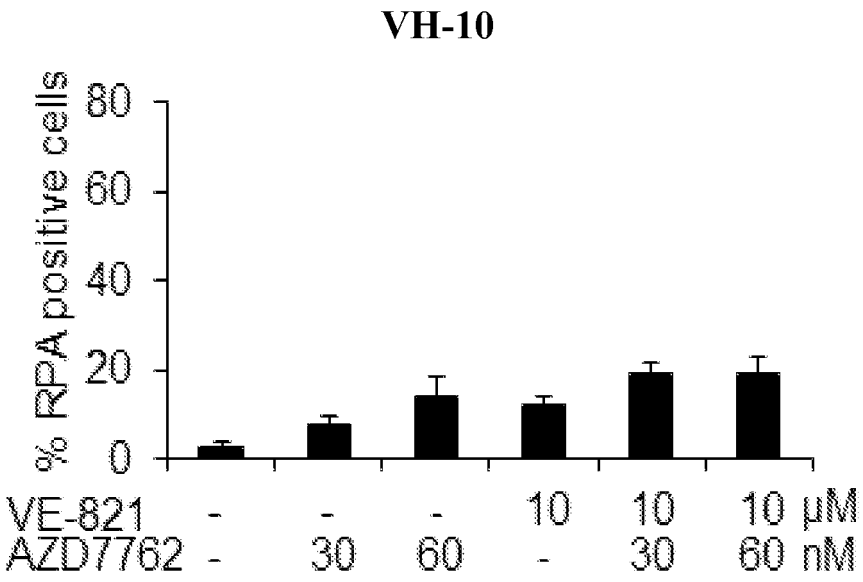
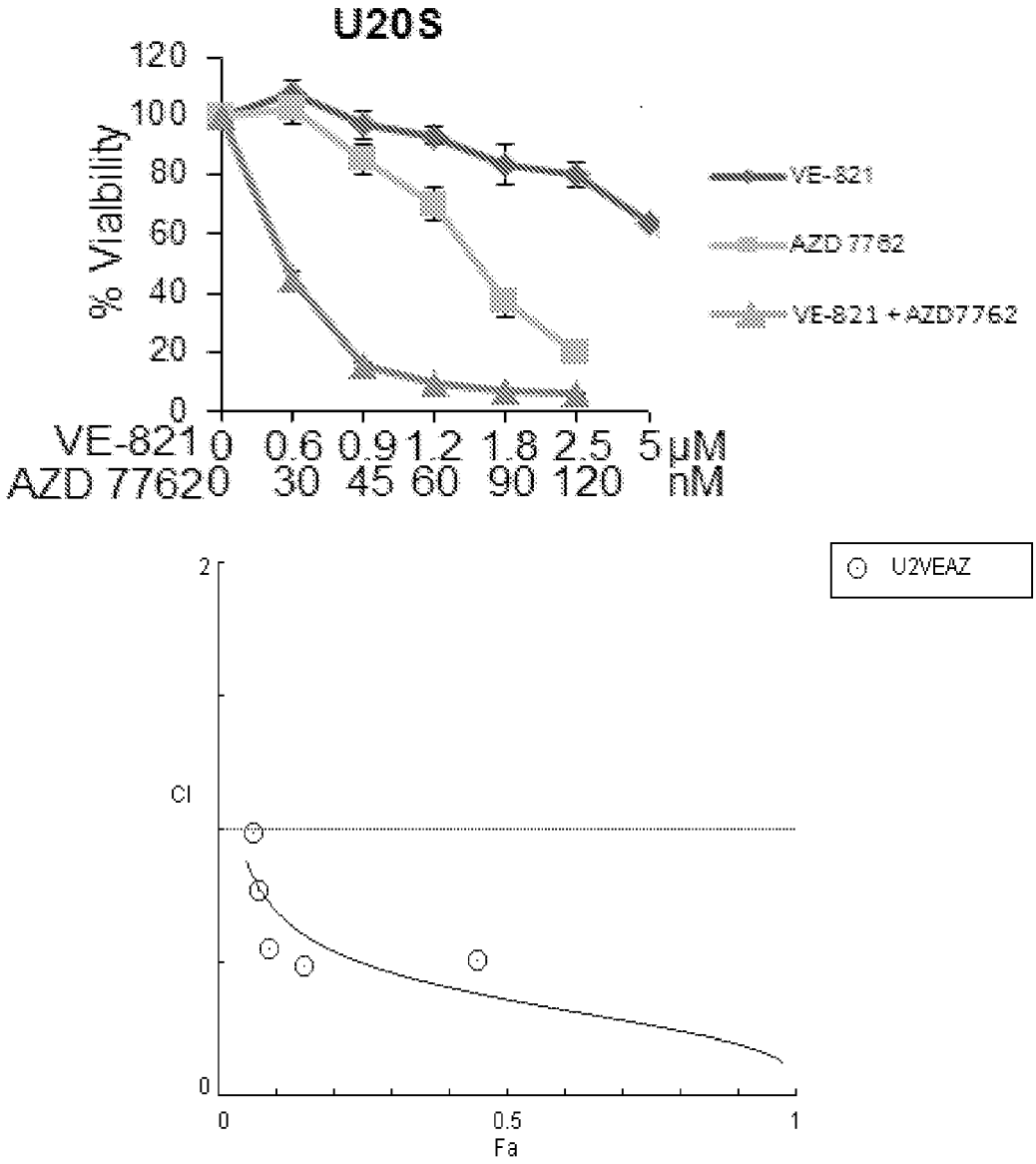
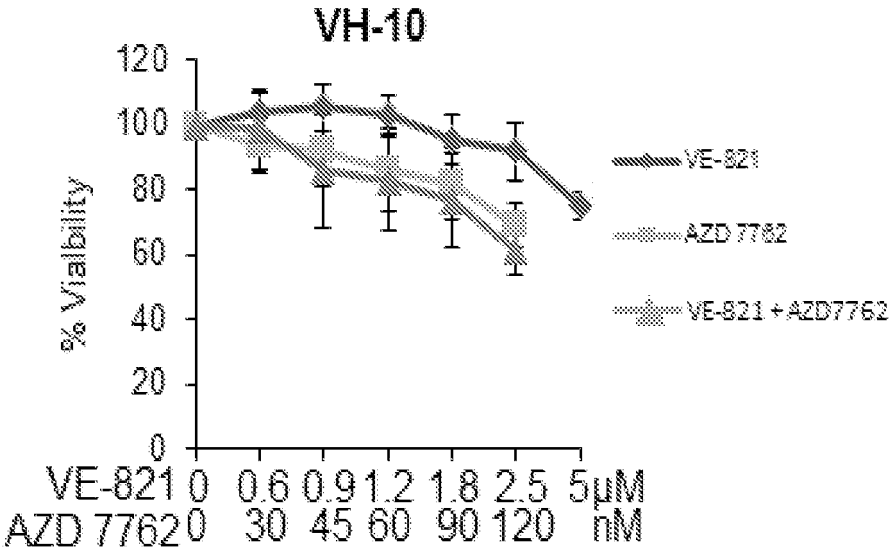


Figure 8a


U20S
% Viability
120
100
80
60
40
20
0
VE-821
AZD 7762
VE-821 + AZD7762
VE-821 0 0.6 0.9 1.2 1.8 2.5 5 μM
AZD 77620 30 45 60 90 120 nM
U2VEAZ
CI
2
0
0
0.5
1
Fa

4

Figure 8b


VH-10
120
100
80
60
40
20
0
% Vialbility
VE-821
AZD 7762
VE-821 +AZD7762
VE-821 0 0.6 0.9 1.2 1.8 2.5 5μM
AZD 7762 0 30 45 60 90 120 nM

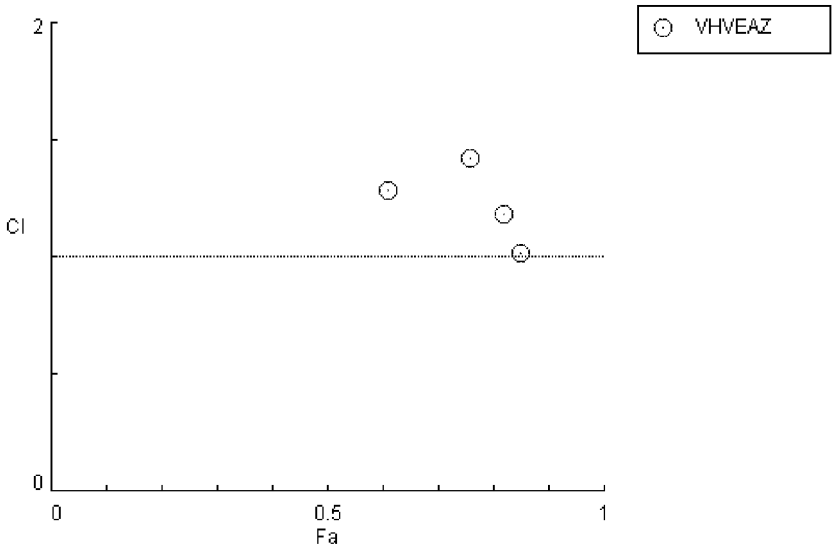
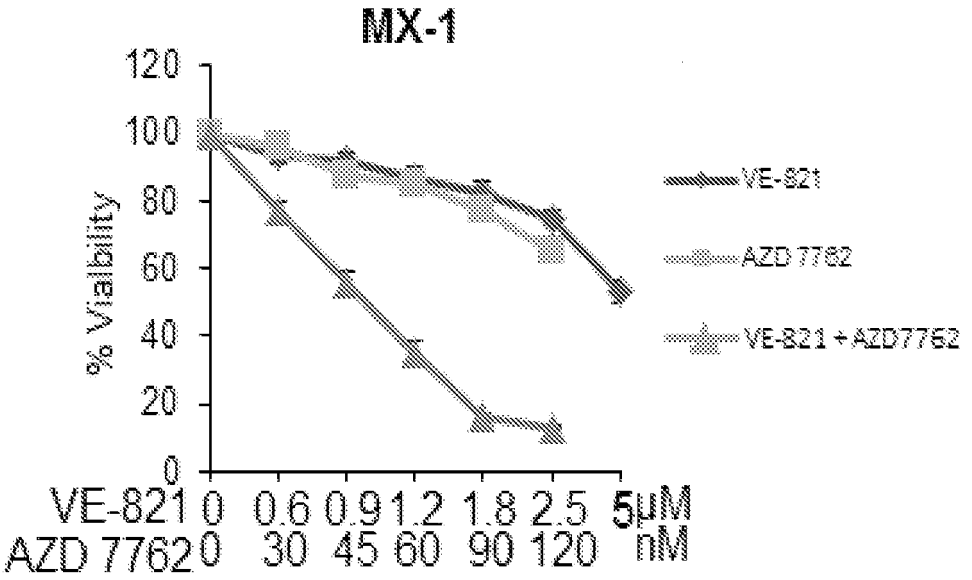

VHVEAZ
2
CI
0
0
0.5
1
Fa

Figure 8c


MX-1
120
100
80
60
40
20
0
% Vialbility
VE-821
AZD 7762
VE-821 + AZD7762
VE-821 0 0.6 0.9 1.2 1.8 2.5 5μM
AZD 7762 0 30 45 60 90 120 nM

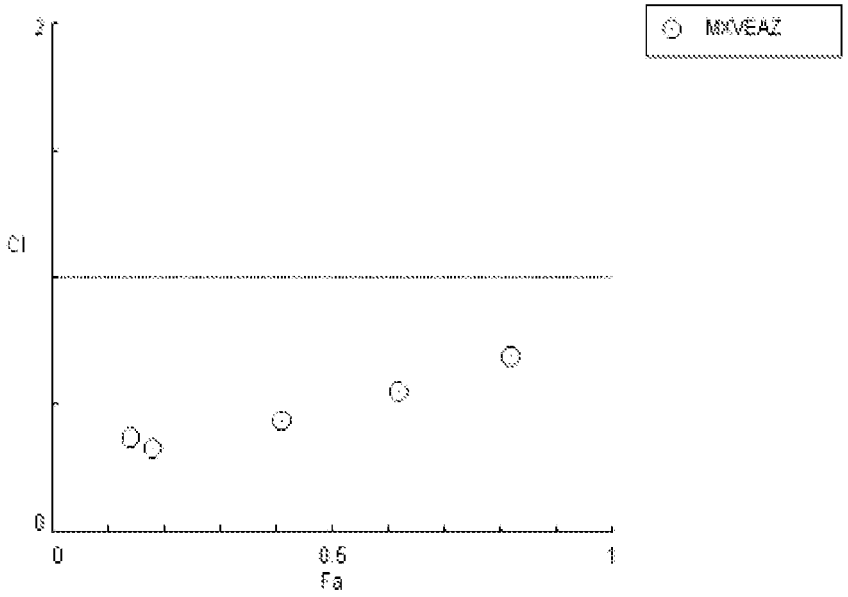
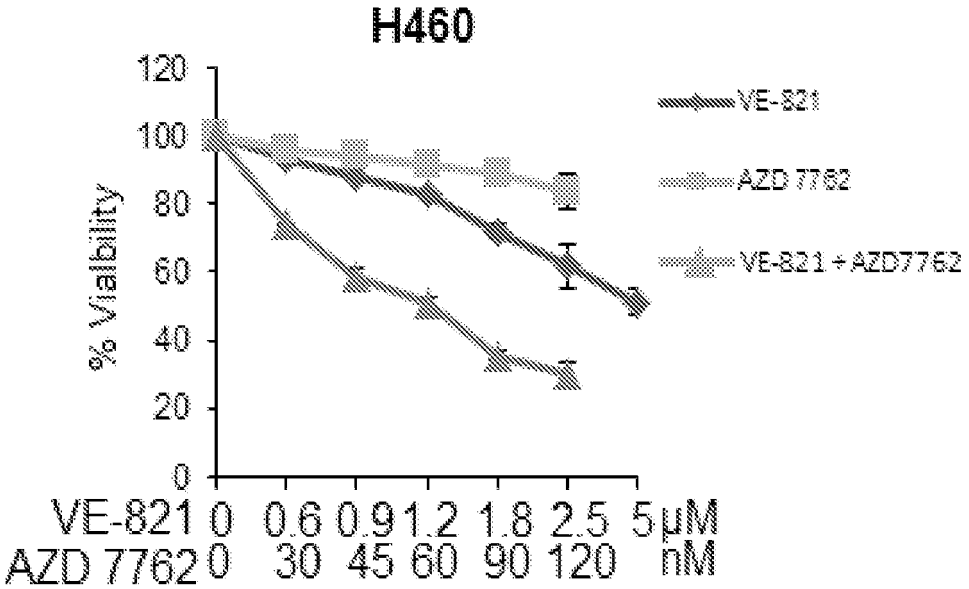

MXVEAZ
CI
1
0
0
0.5
1
Fa

Figure 8d


H460
% Viability
120
100
80
60
40
20
0
VE-821
AZD 7762
VE-821 + AZD7762
VE-821 0 0.6 0.9 1.2 1.8 2.5 5 μM
AZD 7762 0 30 45 60 90 120 nM

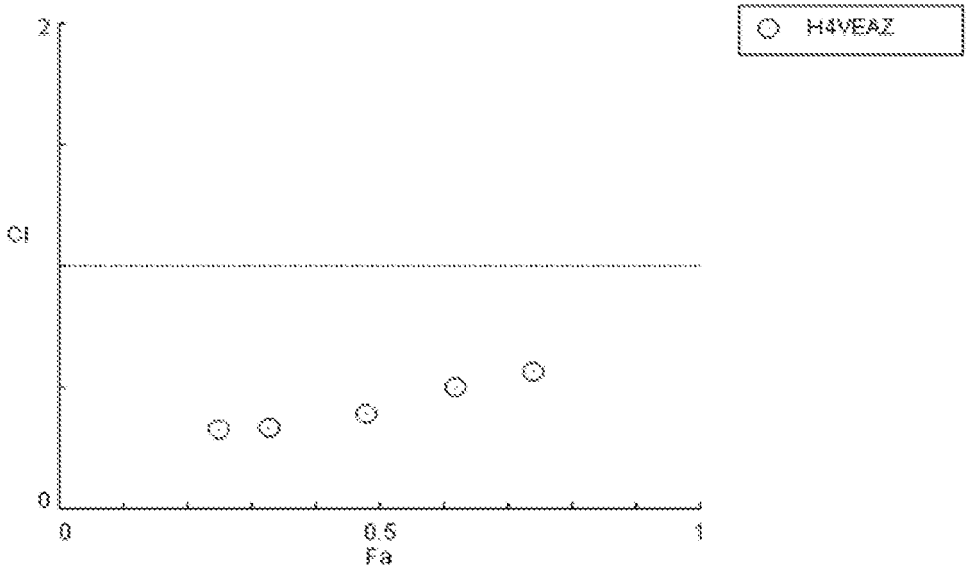

H4VEAZ
CI
2
0
0
0.5
1
Fa

Figure 8e

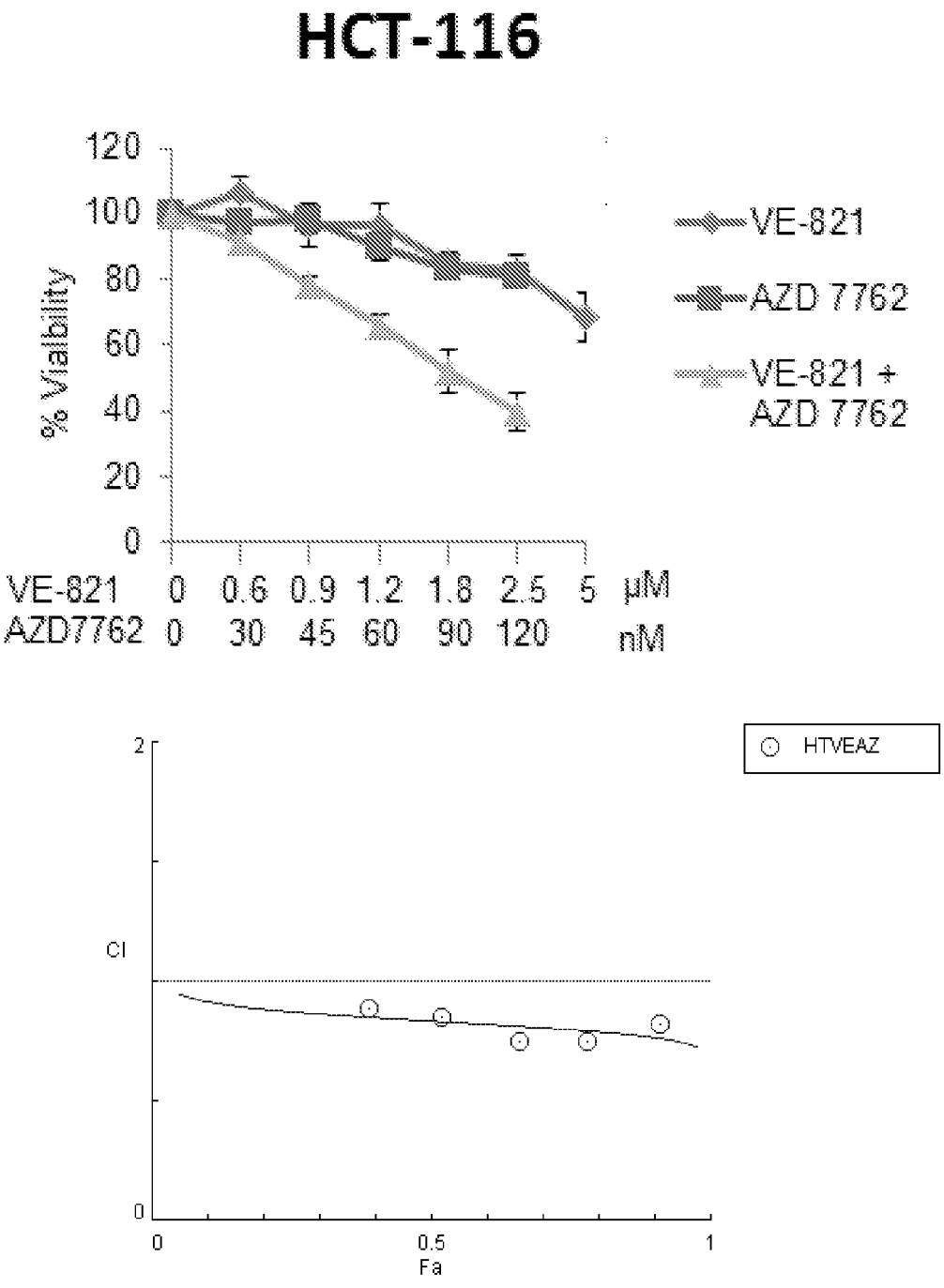

HCT-116
120
100
80
60
40
20
0
% Viability
VE-821
AZD 7762
VE-821 +
AZD 7762
VE-821 0 0.6 0.9 1.2 1.8 2.5 5 μM
AZD7762 0 30 45 60 90 120 nM
HTVEAZ
CI
2
0
0
0.5
1
Fa

Figure 8f

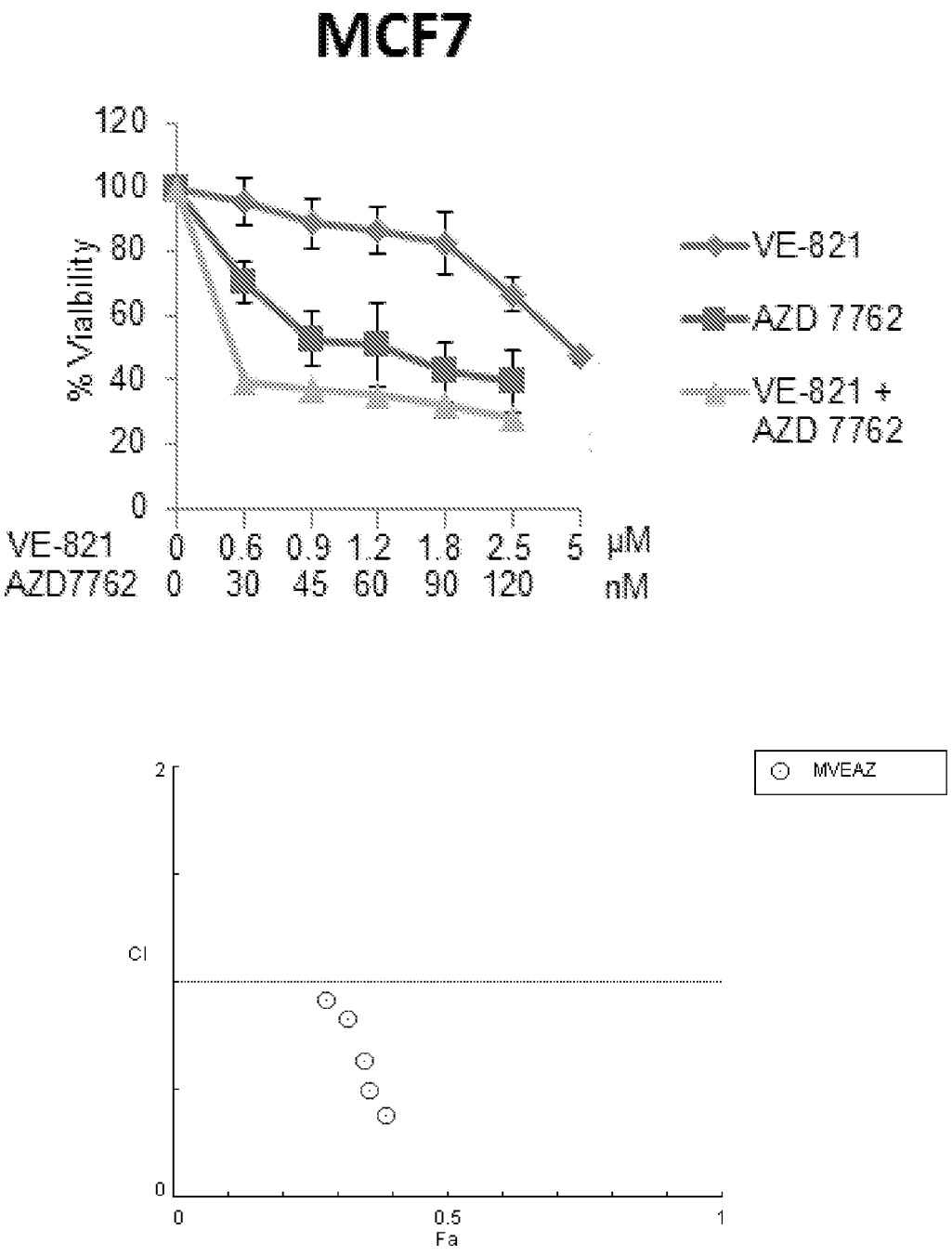

MCF7
120
100
80
60
40
20
0
% Viability
VE-821
AZD 7762
VE-821 + AZD 7762
VE-821 0 0.6 0.9 1.2 1.8 2.5 5 μM
AZD7762 0 30 45 60 90 120 nM
MVEAZ
2
CI
0
0
0.5
1
Fa

Figure 8g

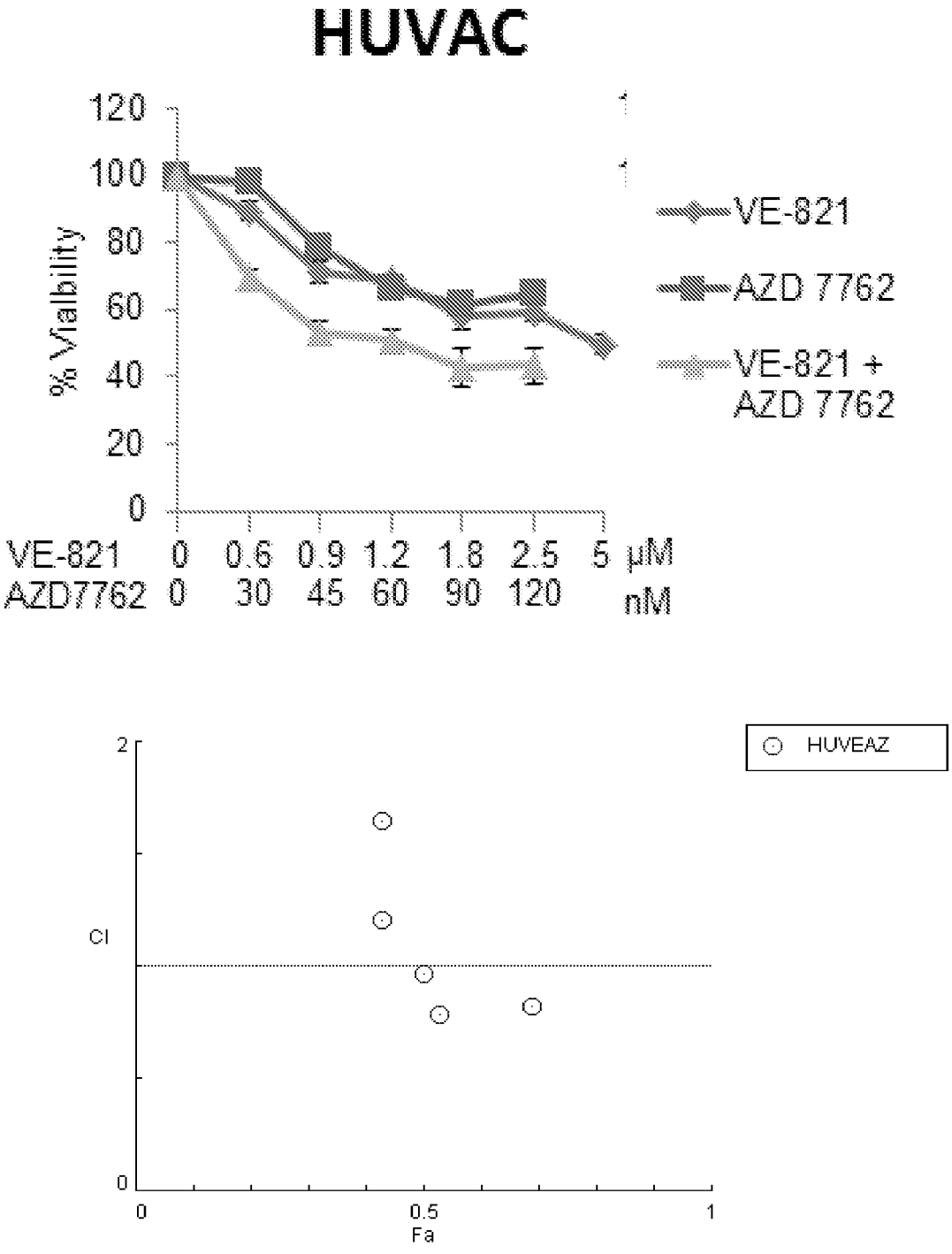

HUVAC
120
100
80
60
40
20
0
% Viability
VE-821
AZD 7762
VE-821 +
AZD 7762
VE-821 0 0.6 0.9 1.2 1.8 2.5 5 μM
AZD7762 0 30 45 60 90 120 nM
HUVEAZ
2
CI
0
0
0.5
1
Fa

Figure 8h

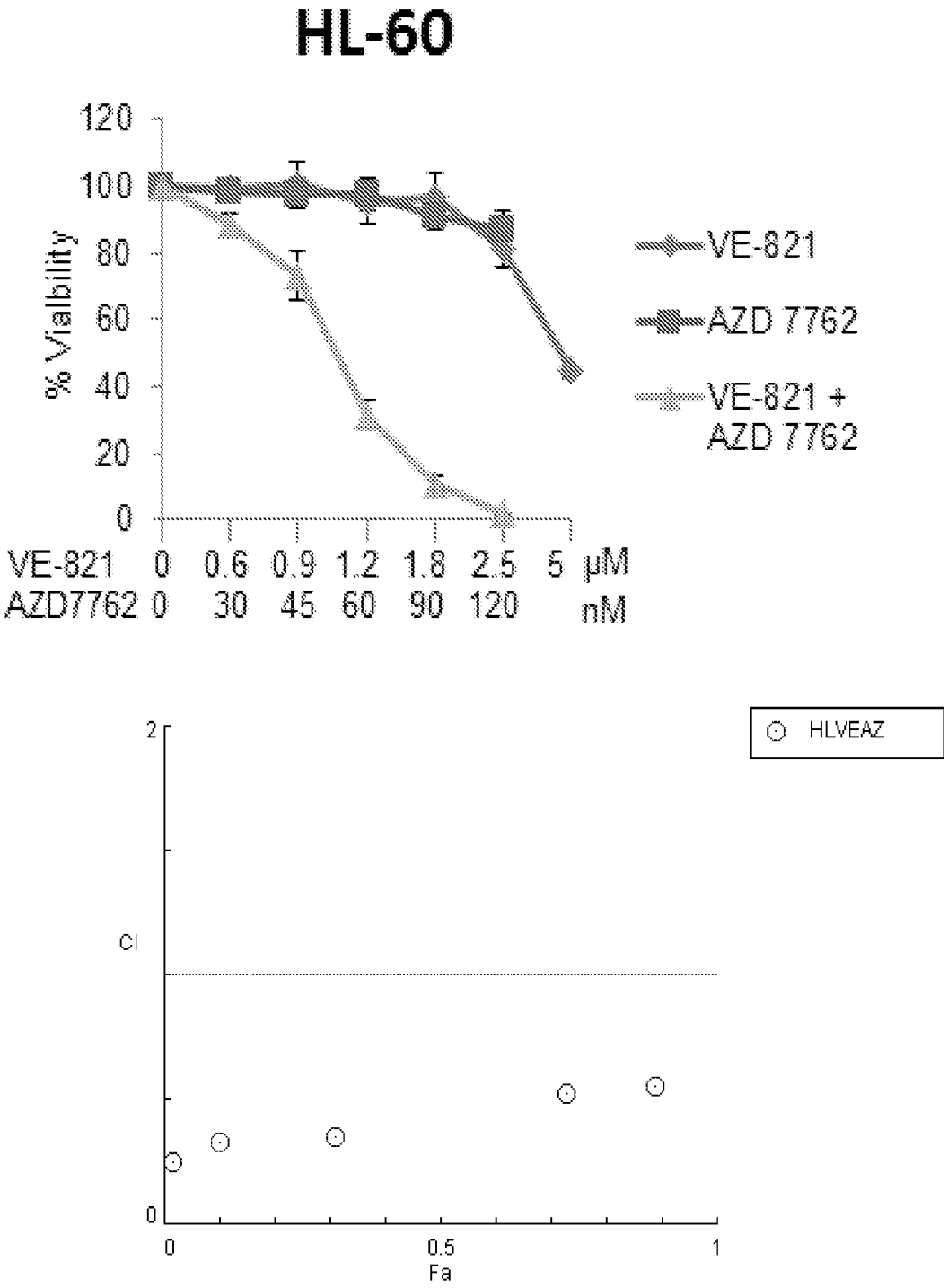
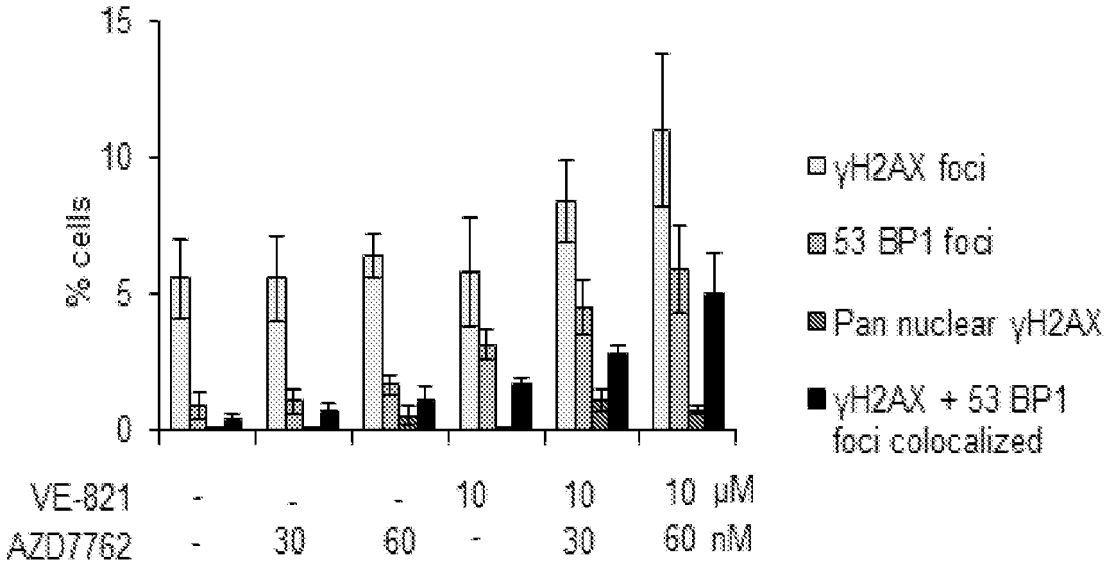
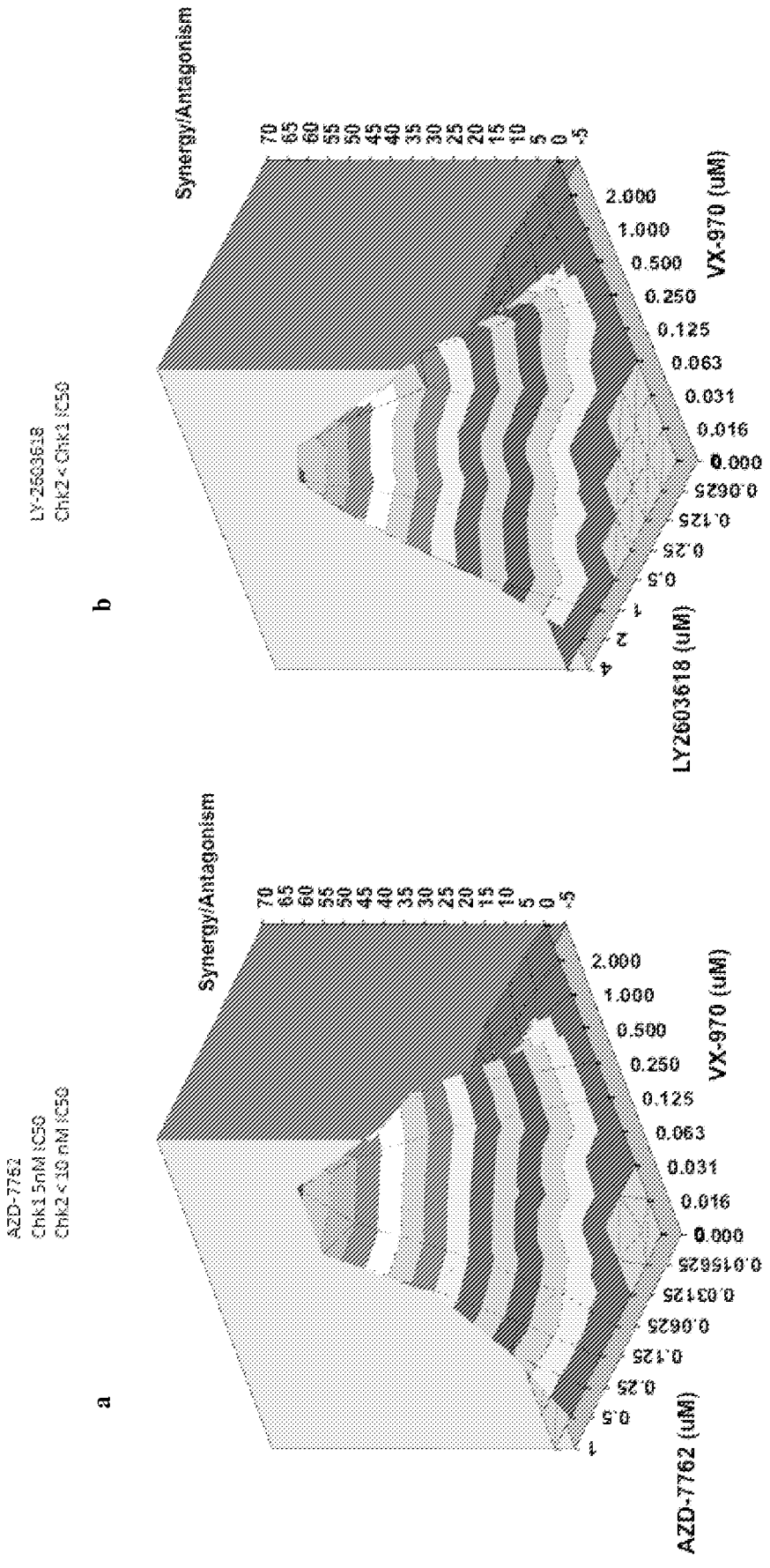
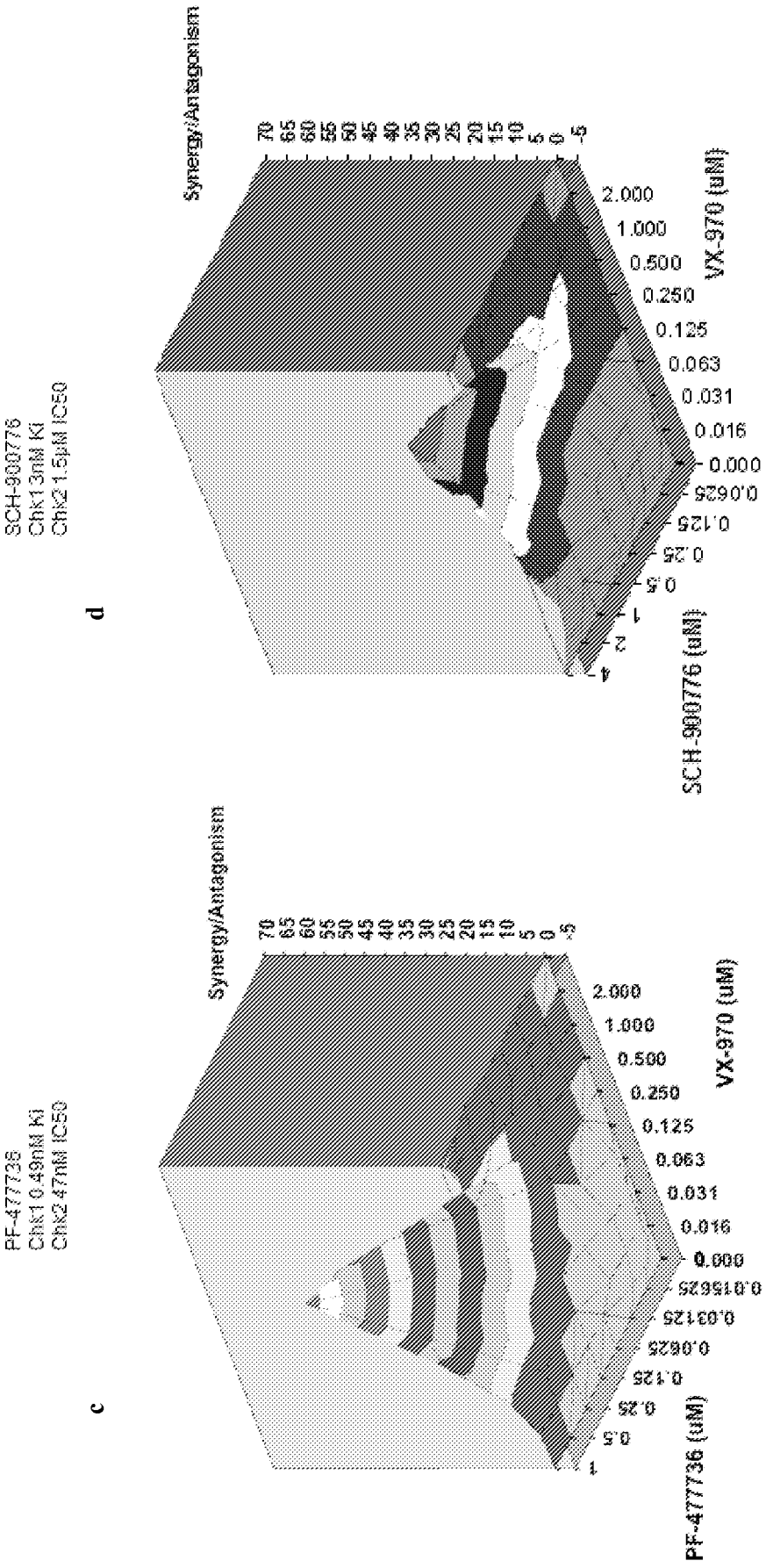

HL-60
% Viability
120
100
80
60
40
20
0
VE-821
AZD 7762
VE-821 + AZD 7762
VE-821 0 0.6 0.9 1.2 1.8 2.5 5 μM
AZD7762 0 30 45 60 90 120 nM
HLVEAZ
CI
2
0
0
0.5
1
Fa

Figure 9


15
10
5
0
% cells
γH2AX foci
53 BP1 foci
Pan nuclear γH2AX
γH2AX + 53 BP1 foci colocalized
VE-821 - - - 10 10 10 μM
AZD7762 - 30 60 - 30 60 nM

Figures 10a-d




c
PF-477736
Chk1 0.49nM Ki
Chk2 47nM IC50
Synergy/Antagonism
70 65 60 55 50 45 40 35 30 25 20 15 10 5 0 -5
VX-970 (uM)
2.000 1.000 0.500 0.250 0.125 0.063 0.031 0.016 0.000
PF-477736 (uM)
0.015625 0.03125 0.0625 0.125 0.25 0.5 1
d
SCH-900776
Chk1 3nM Ki
Chk2 1.5μM IC50
Synergy/Antagonism
70 65 60 55 50 45 40 35 30 25 20 15 10 5 0 -5
VX-970 (uM)
2.000 1.000 0.500 0.250 0.125 0.063 0.031 0.016 0.000
SCH-900776 (uM)
0.0625 0.125 0.25 0.5 1 2 4