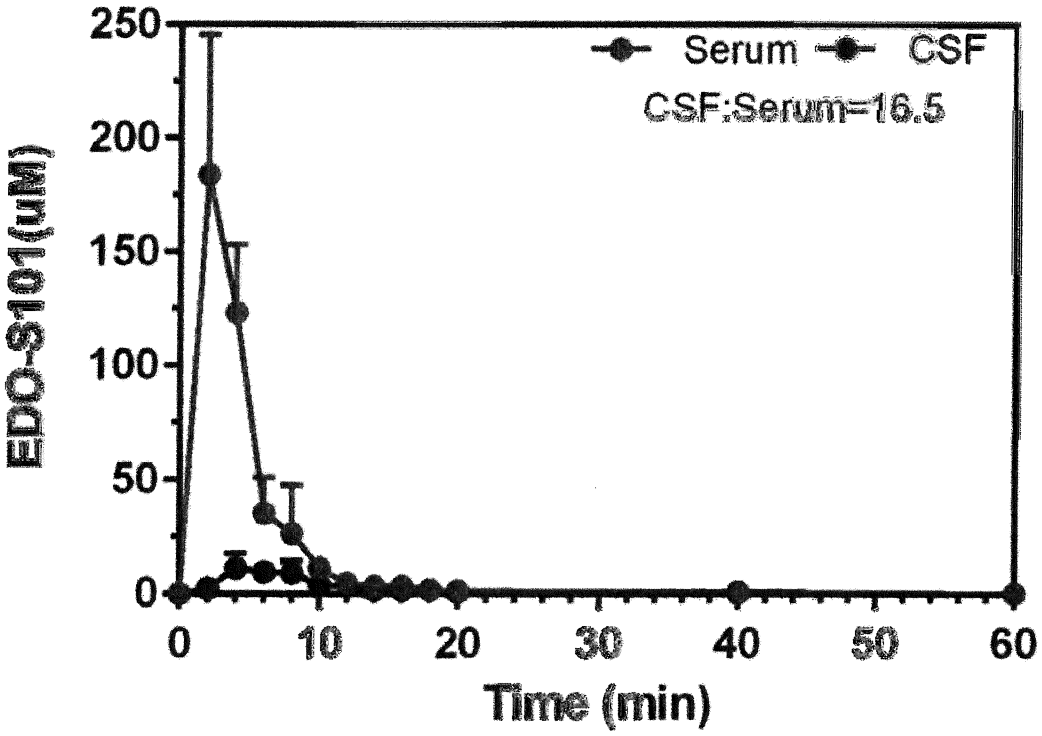

250
200
150
100
50
0
EDO-S101(uM)
Serum
CSF
CSF:Serum=16.5
0
10
20
30
40
50
60
Time (min)

Figure 1

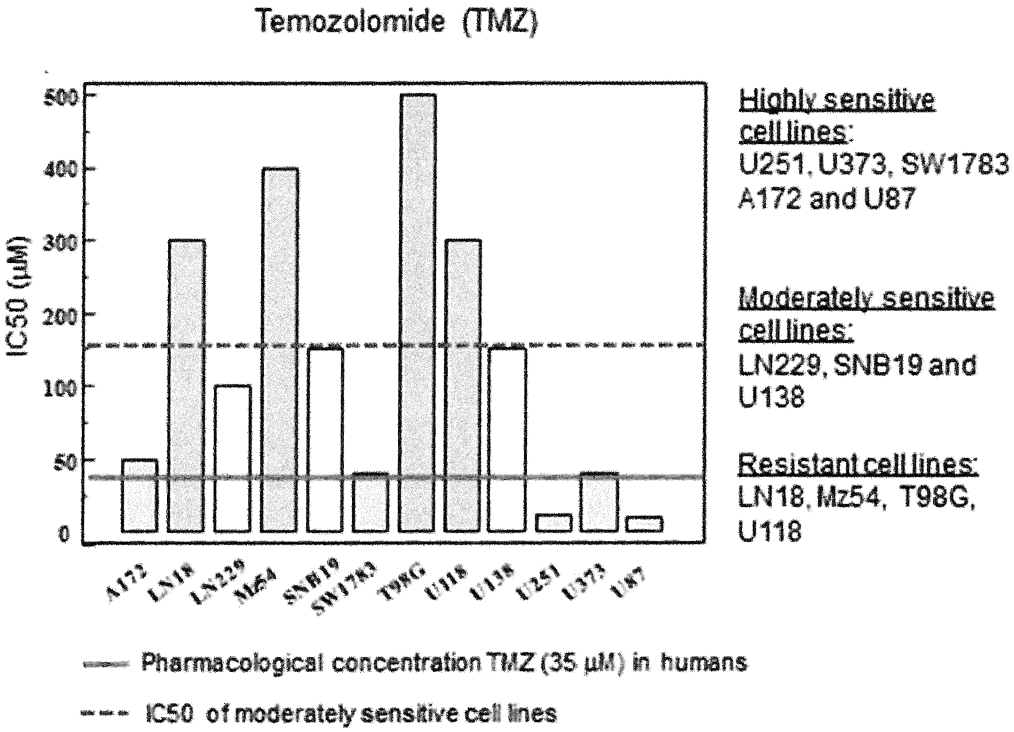

Temozolomide (TMZ)
IC50 (µM)
500
400
300
200
100
50
0
A172
LN18
LN229
Mz54
SNB19
SW1783
T98G
U118
U138
U251
U373
U87
Highly sensitive cell lines:
U251, U373, SW1783
A172 and U87
Moderately sensitive cell lines:
LN229, SNB19 and U138
Resistant cell lines:
LN18, Mz54, T98G, U118
Pharmacological concentration TMZ (35 µM) in humans
IC50 of moderately sensitive cell lines

Figure 2

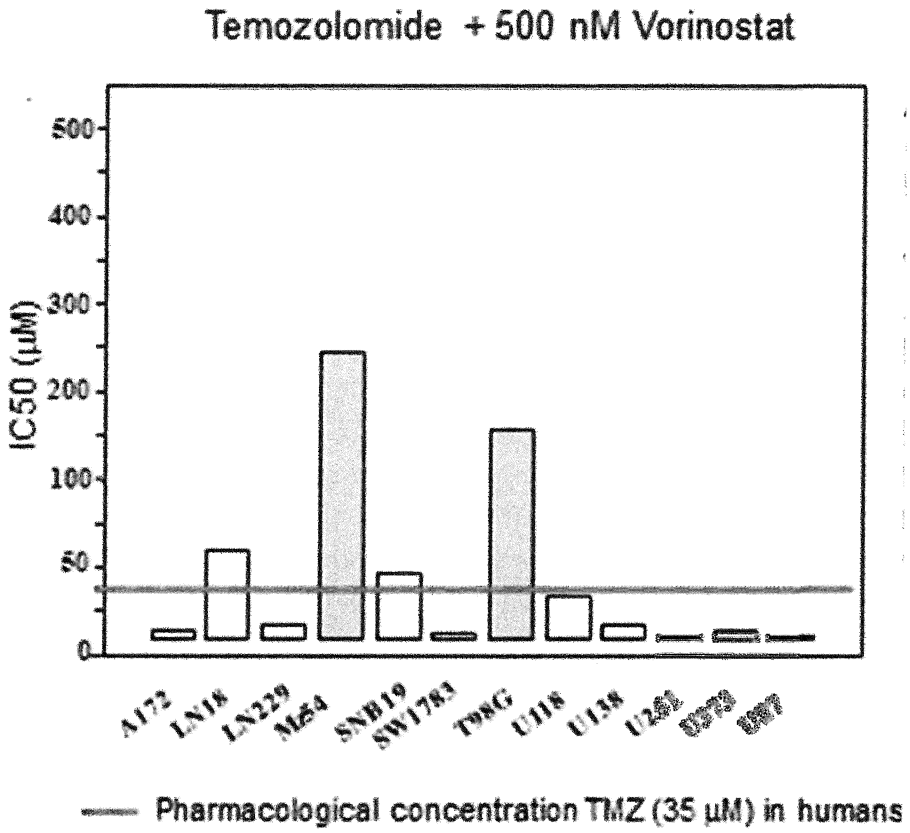

Temozolomide + 500 nM Vorinostat
IC50 (µM)
500
400
300
200
100
50
0
A172
LN18
LN229
M64
SNB19
SW1783
T98G
U118
U138
U251
Pharmacological concentration TMZ (35 µM) in humans

Figure 3

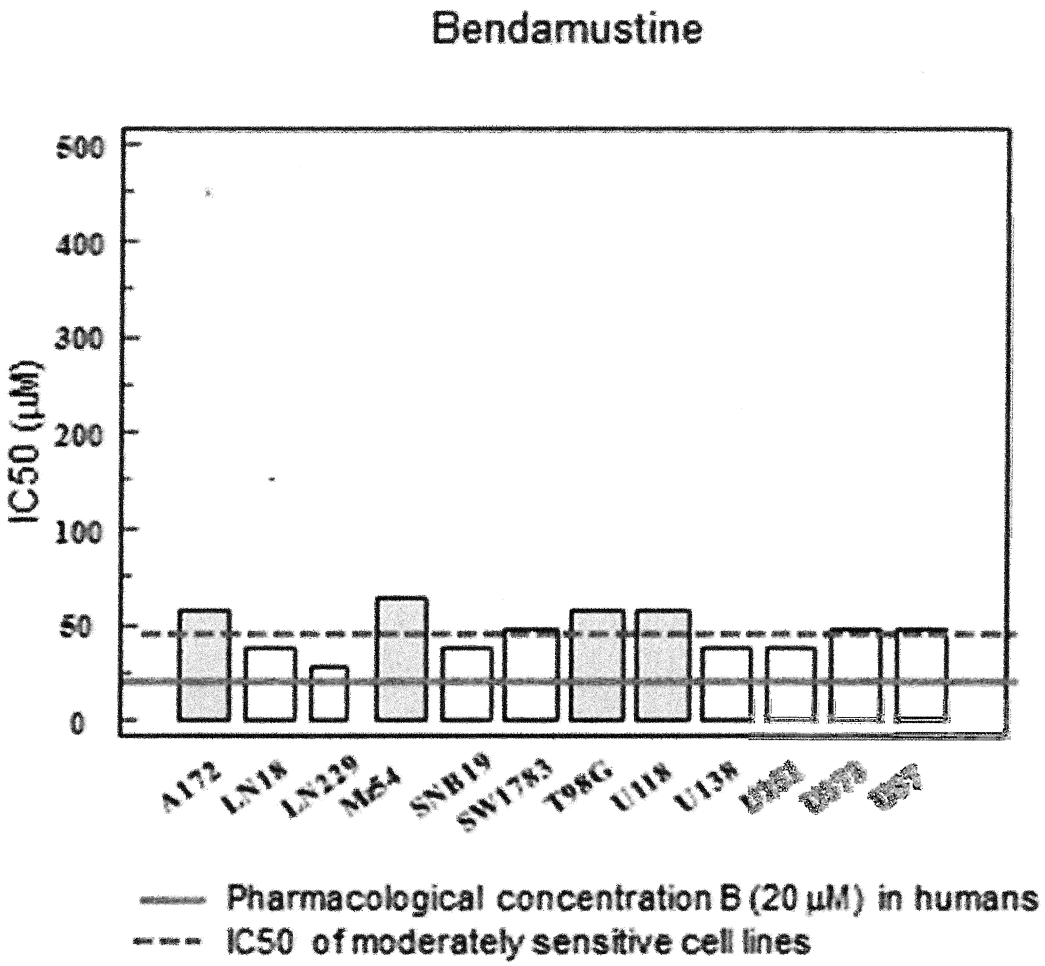

Bendamustine
500
400
300
200
100
50
0
IC50 (μM)
A172
LN18
LN229
M64
SNB19
SW1783
T98G
U118
U138
Pharmacological concentration B (20 μM) in humans
IC50 of moderately sensitive cell lines

Figure 4

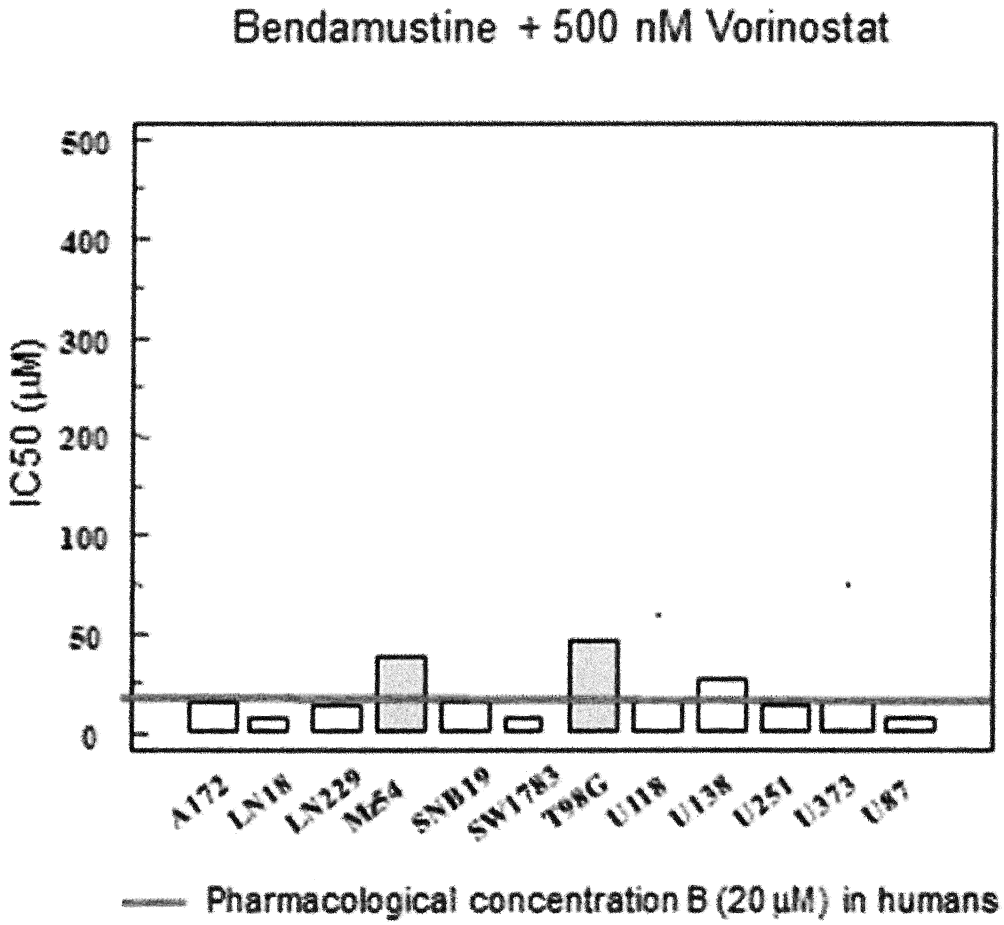

Bendamustine + 500 nM Vorinostat
IC50 (µM)
500
400
300
200
100
50
0
A172
LN18
LN229
M64
SNB19
SW1783
T98G
U118
U138
U251
U373
U87
Pharmacological concentration B (20 µM) in humans

Figure 5

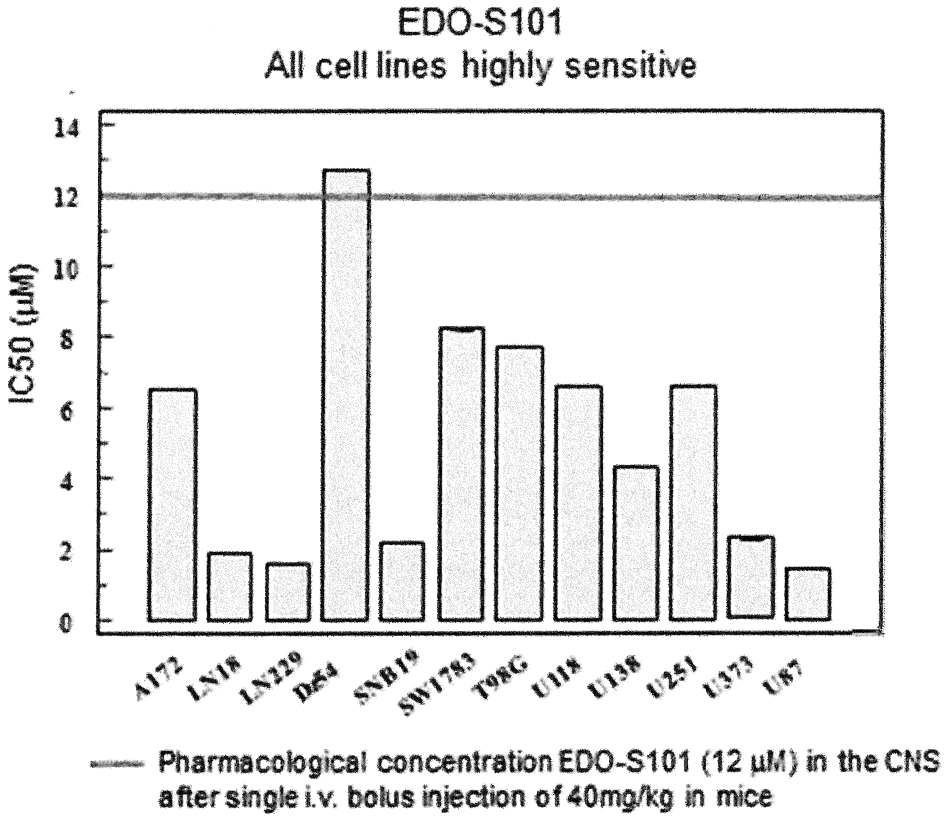

EDO-S101
All cell lines highly sensitive
IC50 (µM)
14
12
10
8
6
4
2
0
A172
LN18
LN229
D54
SNB19
SW1783
T98G
U118
U138
U251
U373
U87
Pharmacological concentration EDO-S101 (12 µM) in the CNS
after single i.v. bolus injection of 40mg/kg in mice

Figure 6

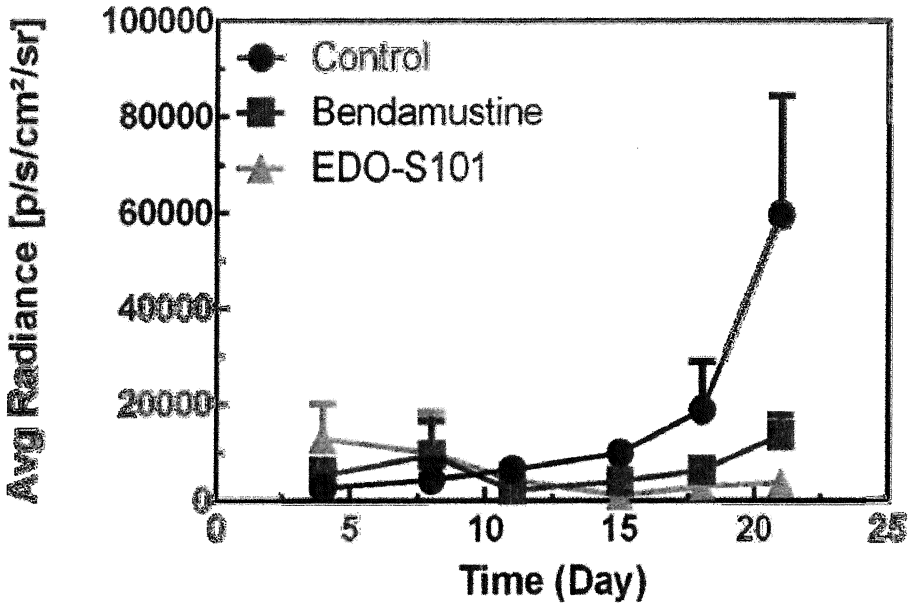


Figure 7a

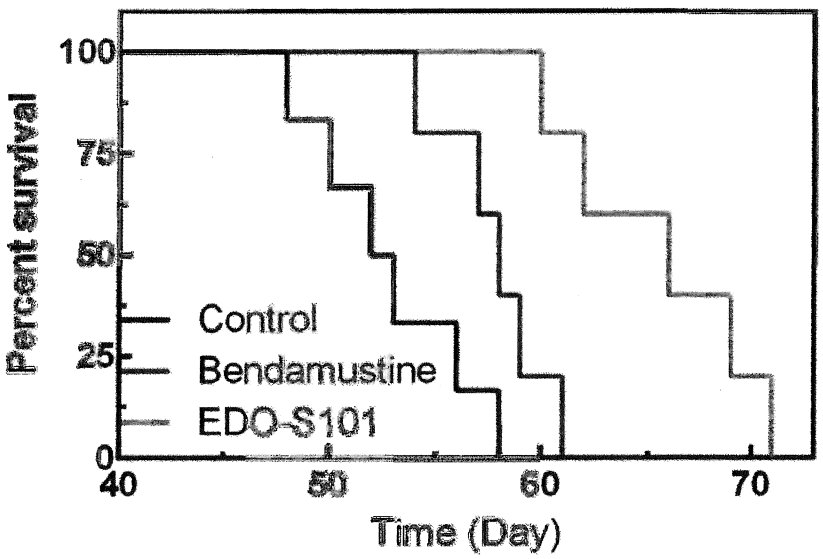


Figure 7b

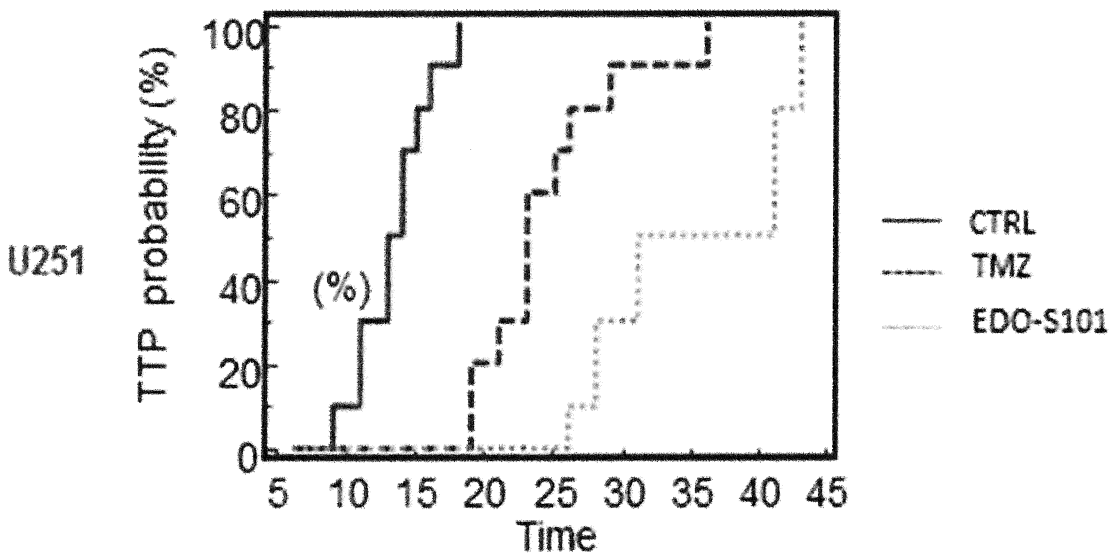

U251
TTP probability (%)
100
80
60
40
20
0
(%)
5
10
15
20
25
30
35
40
45
Time
CTRL
TMZ
EDO-S101

Figure 8

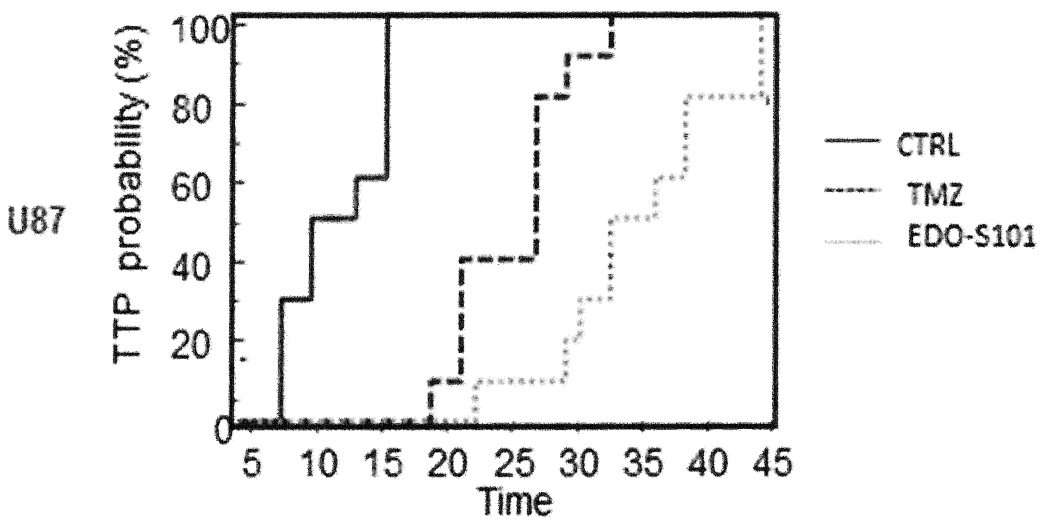

U87
TTP probability (%)
100
80
60
40
20
0
5
10
15
20
25
30
35
40
45
Time
CTRL
TMZ
EDO-S101

Figure 9

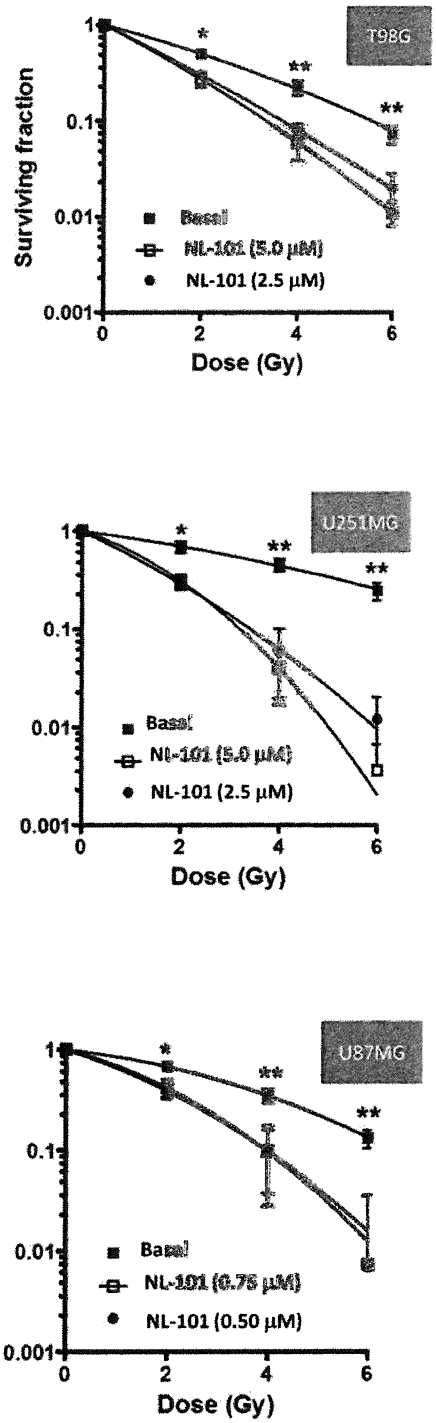

T98G
U251MG
U87MG
Surviving fraction
Dose (Gy)
Basal
NL-101 (5.0 µM)
NL-101 (2.5 µM)
NL-101 (0.75 µM)
NL-101 (0.50 µM)
*
**
1
0.1
0.01
0.001
0
2
4
6

Figure 10

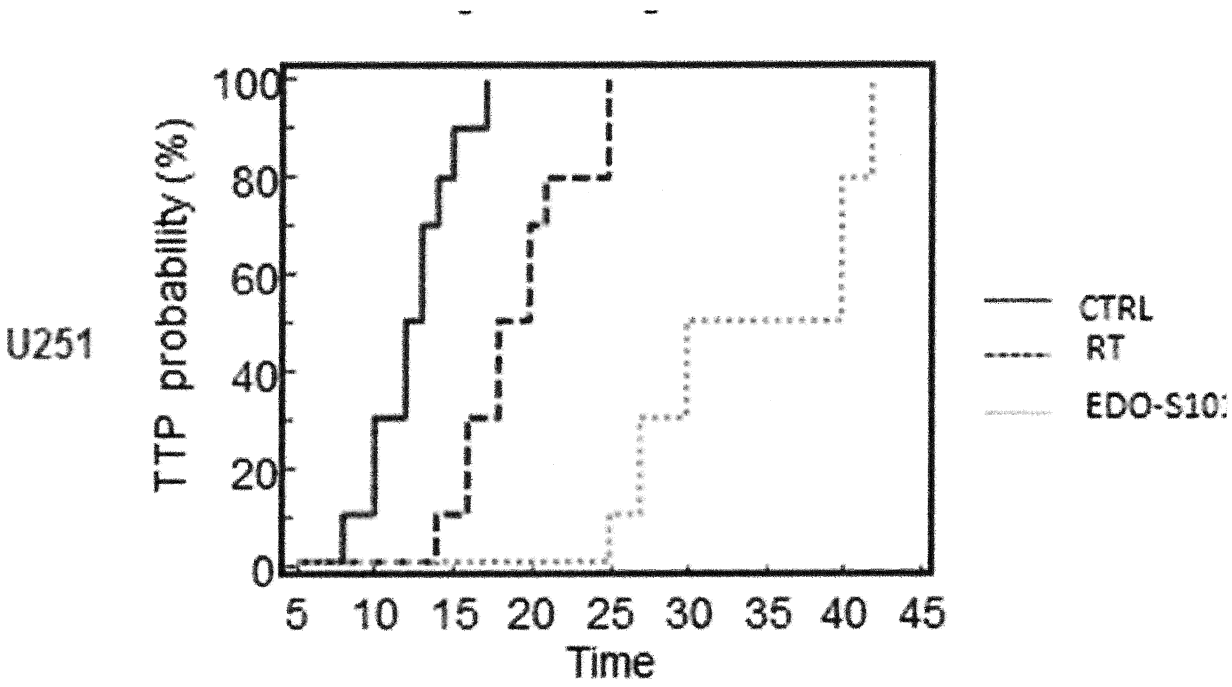

U251
TTP probability (%)
100
80
60
40
20
0
5
10
15
20
25
30
35
40
45
Time
CTRL
RT
EDO-S10

Figure 11

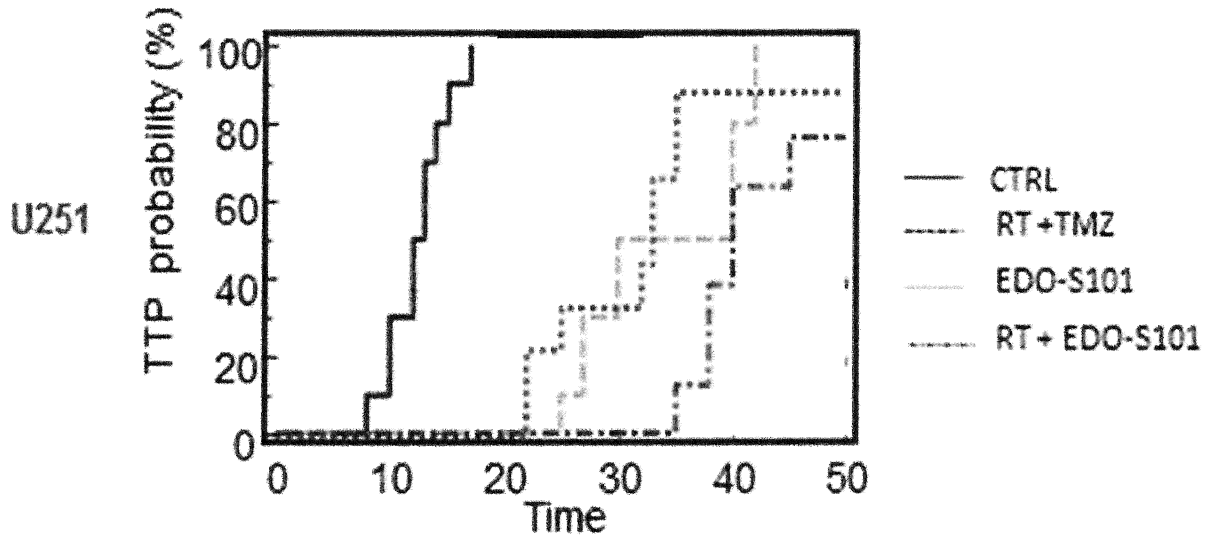

U251
TTP probability (%)
100
80
60
40
20
0
0
10
20
30
40
50
Time
CTRL
RT+TMZ
EDO-S101
RT + EDO-S101

Figure 12

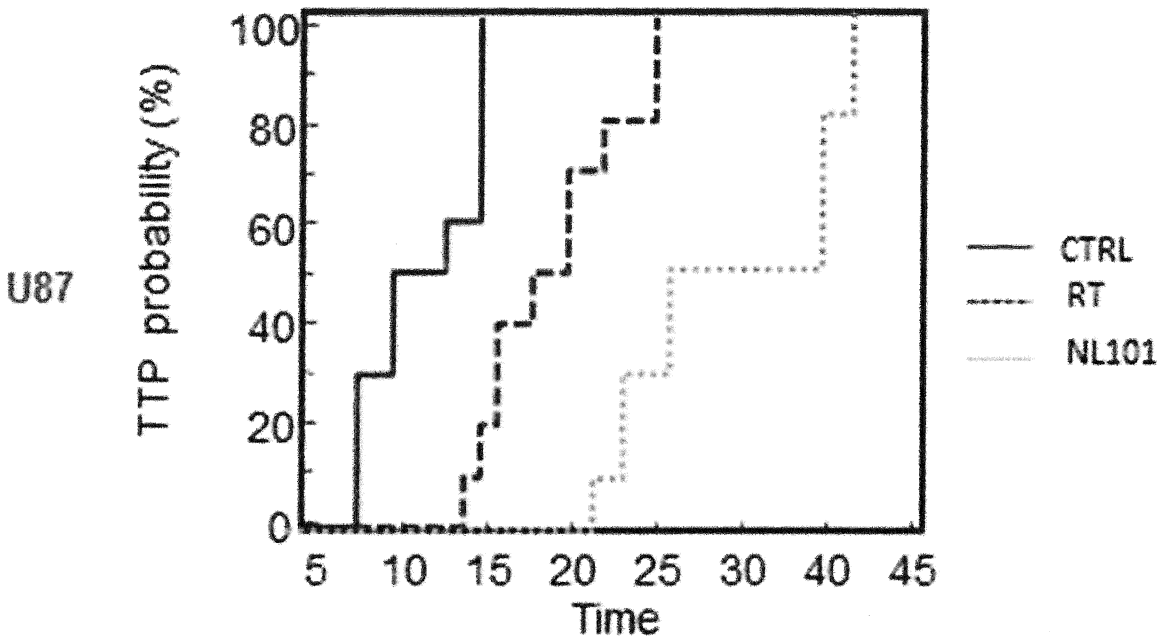

U87
TTP probability (%)
100
80
60
40
20
0
5
10
15
20
25
30
40
45
Time
CTRL
RT
NL101

Figure 13

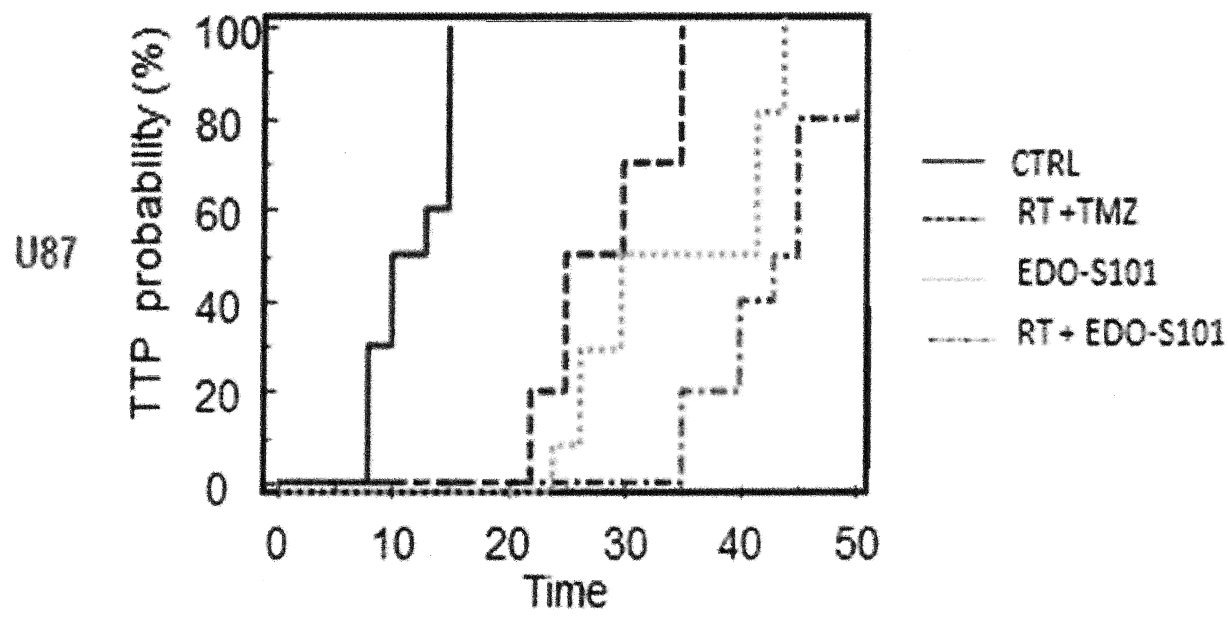

U87
TTP probability (%)
100
80
60
40
20
0
0
10
20
30
40
50
Time
CTRL
RT +TMZ
EDO-S101
RT + EDO-S101

Figure 14

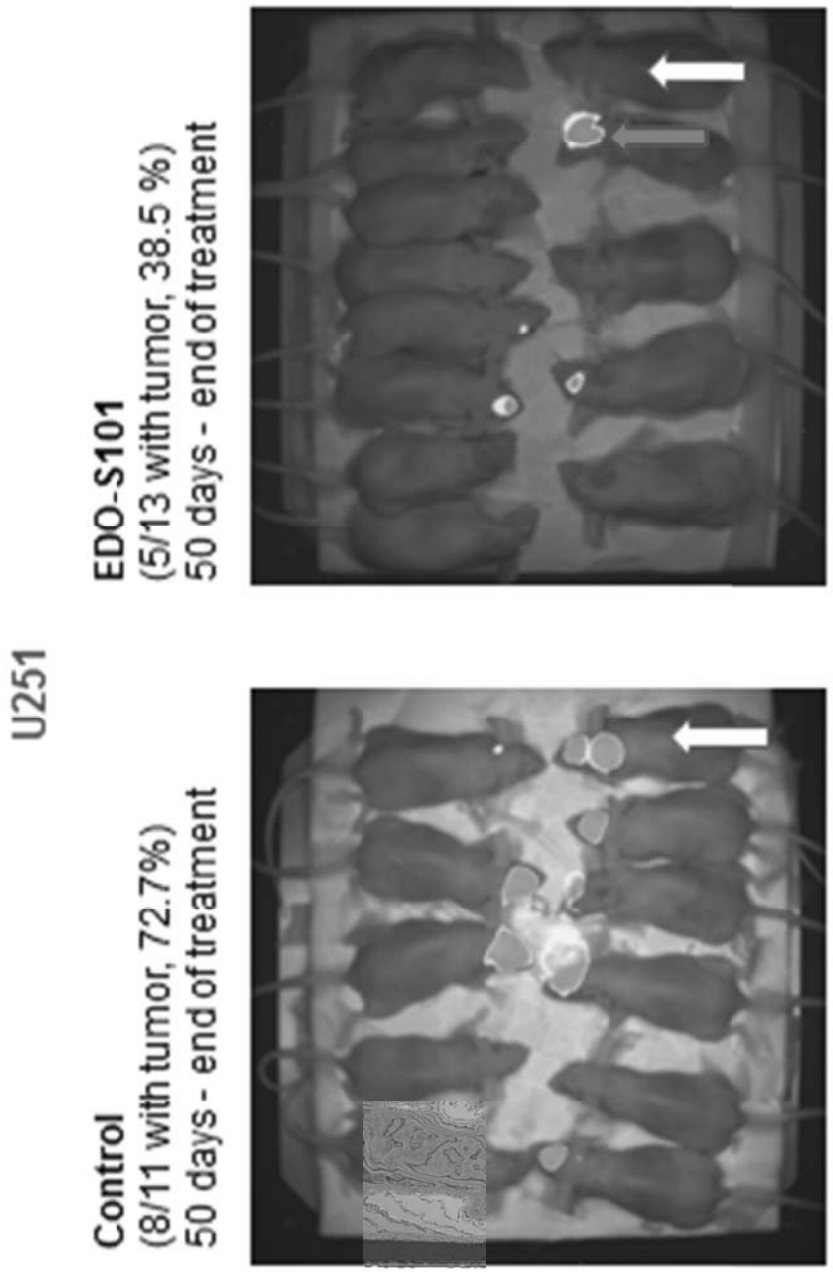

U251
Control
(8/11 with tumor, 72.7%)
50 days - end of treatment
EDO-S101
(5/13 with tumor, 38.5 %)
50 days - end of treatment

Figure 15

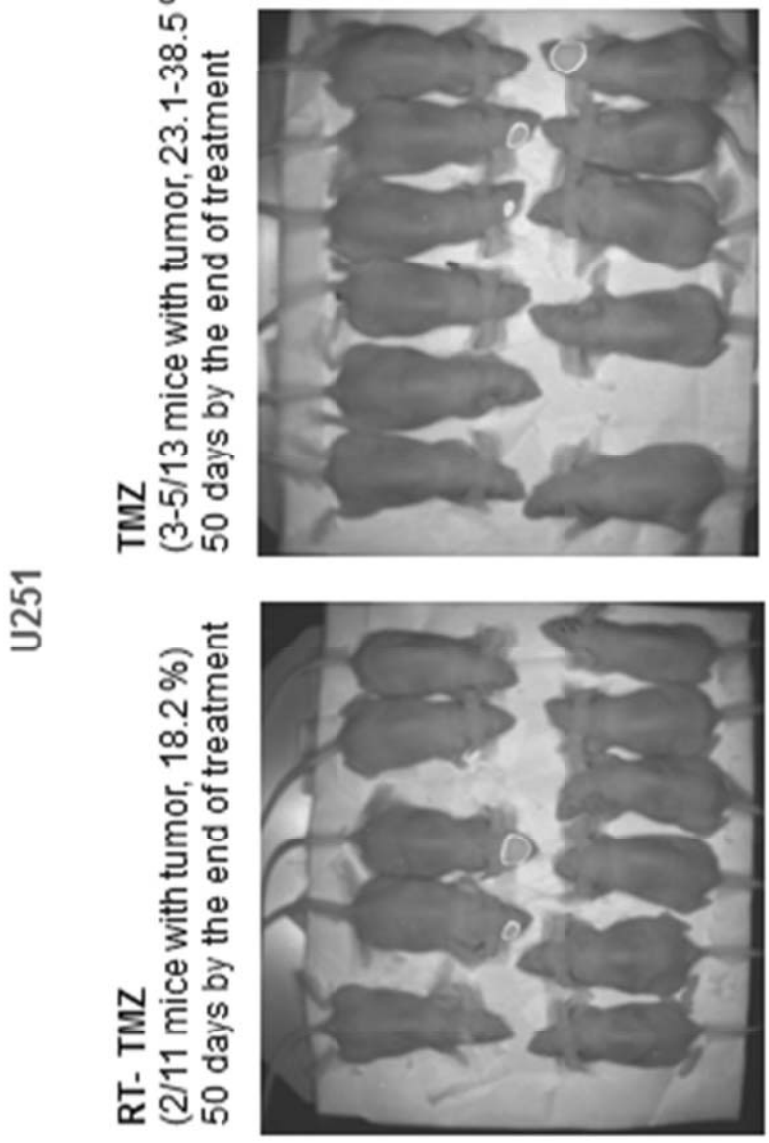

U251
RT- TMZ
(2/11 mice with tumor, 18.2 %)
50 days by the end of treatment
TMZ
(3-5/13 mice with tumor, 23.1-38.5 %)
50 days by the end of treatment

Figure 16

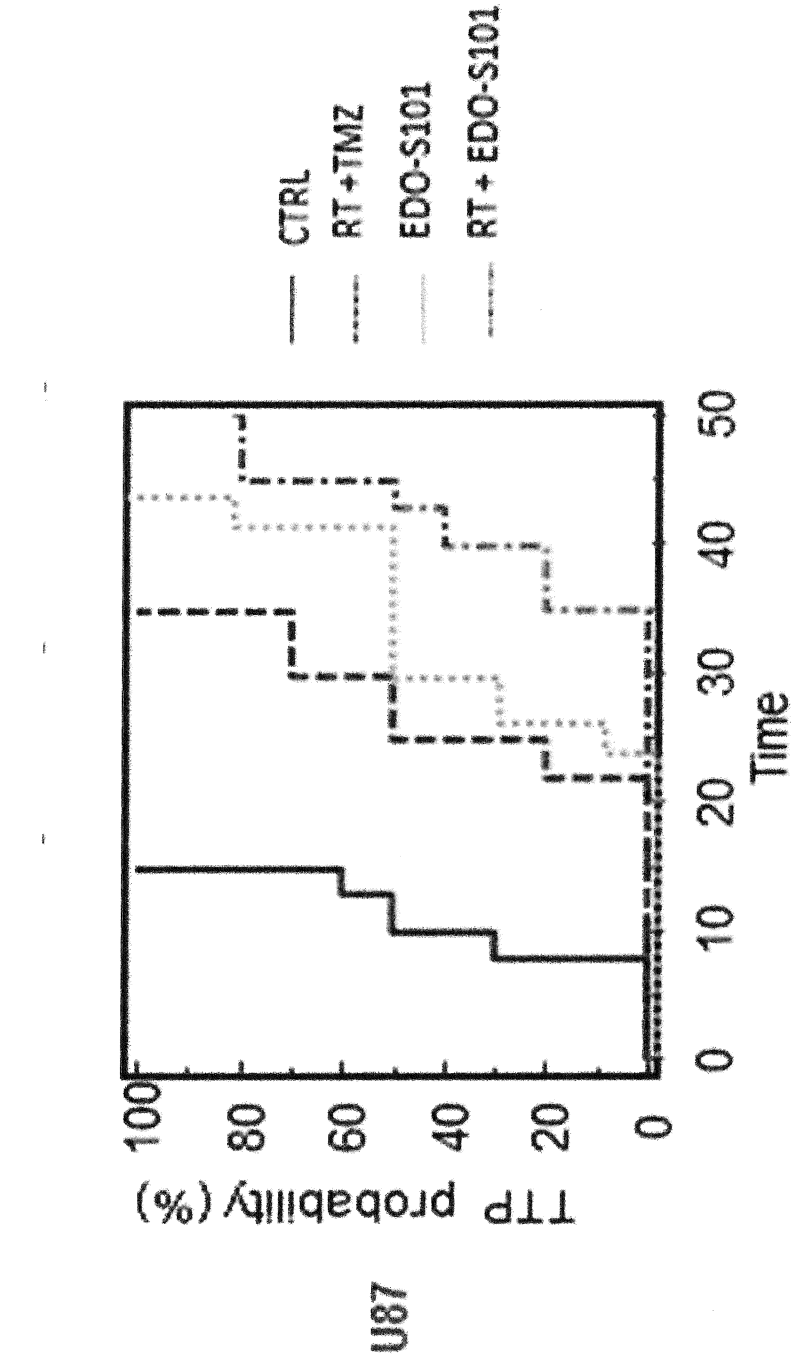

U87
TTP probability (%)
100
80
60
40
20
0
0
10
20
30
40
50
Time
CTRL
RT + TMZ
EDO-S101
RT + EDO-S101

Figure 17

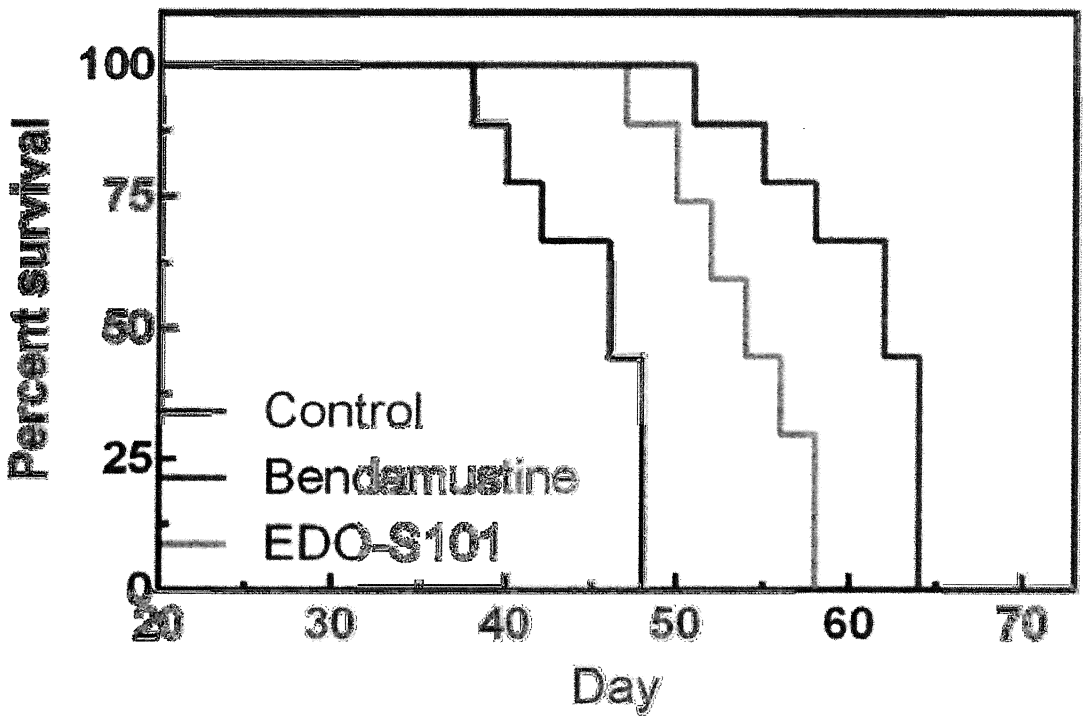

Percent survival
100
75
50
25
0
Control
Bendamustine
EDO-S101
20
30
40
50
60
70
Day

Figure 18

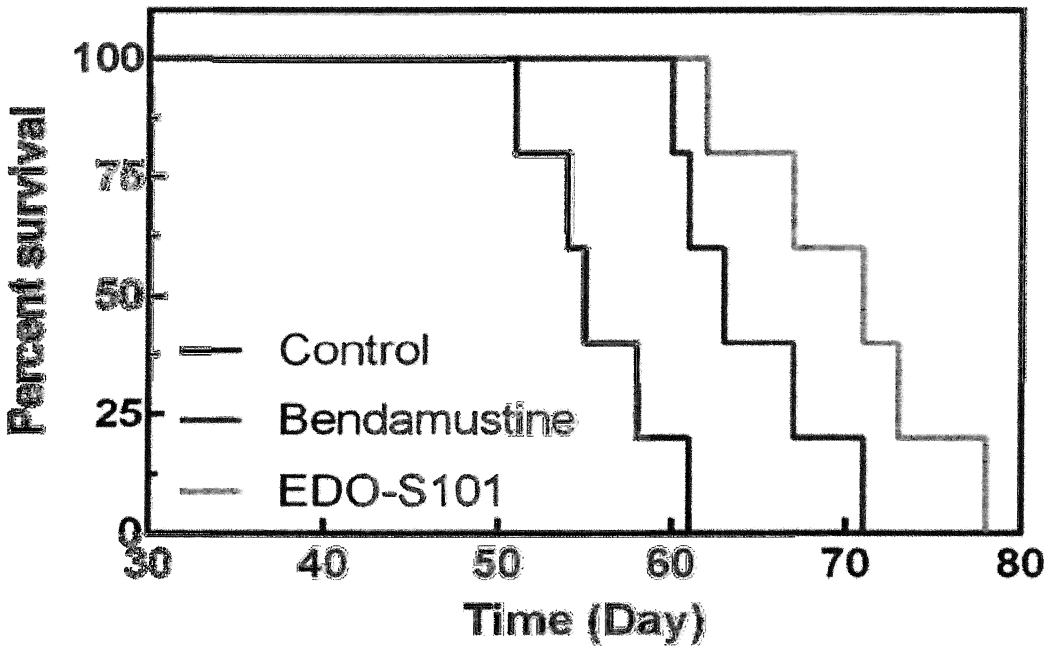

Percent survival
100
75
50
25
0
30
40
50
60
70
80
Time (Day)
Control
Bendamustine
EDO-S101

Figure 19