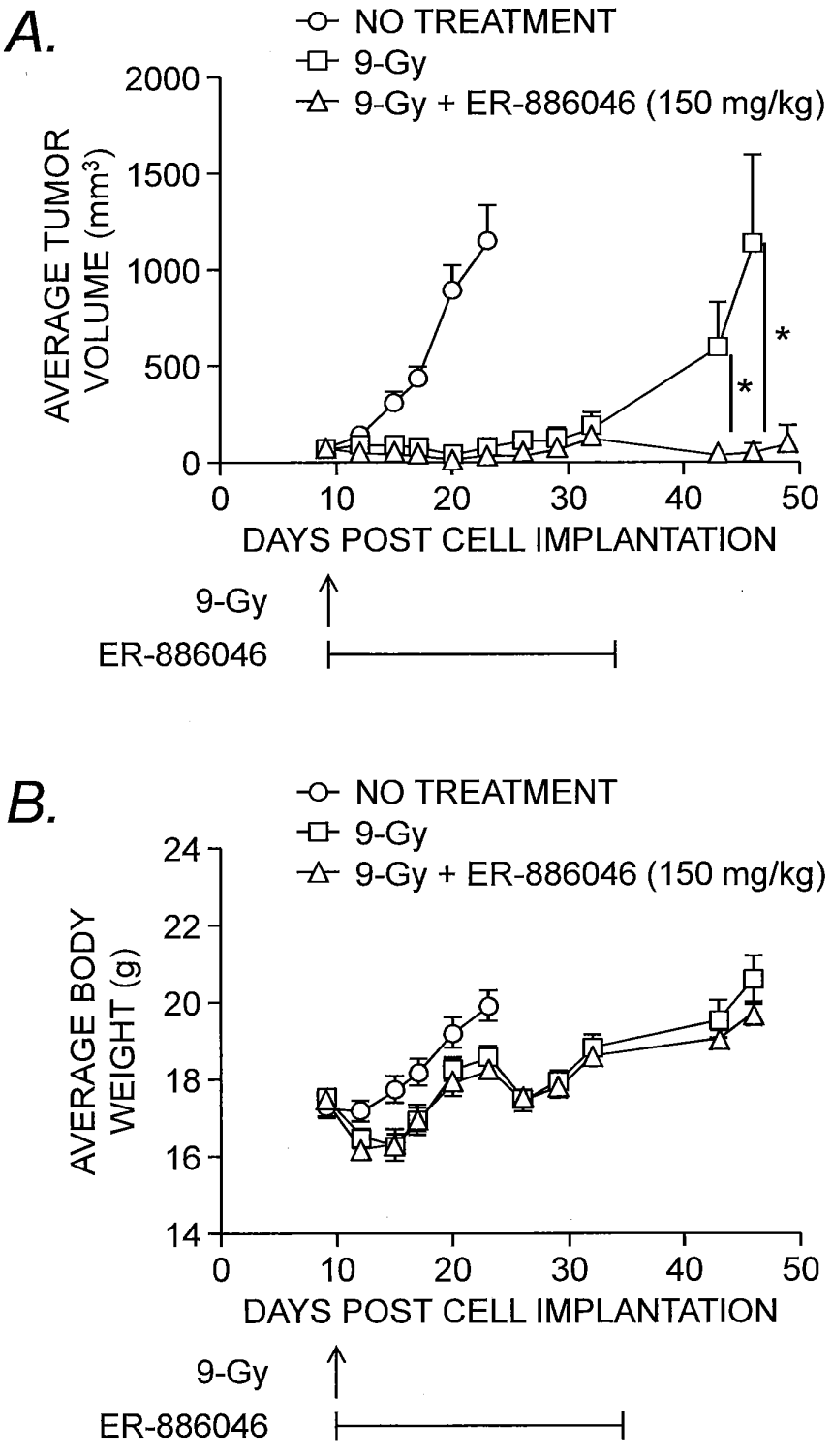

A.
NO TREATMENT
9-Gy
9-Gy + ER-886046 (150 mg/kg)
AVERAGE TUMOR VOLUME (mm3)
2000
1500
1000
500
0
0
10
20
30
40
50
DAYS POST CELL IMPLANTATION
*
*
9-Gy
ER-886046
B.
NO TREATMENT
9-Gy
9-Gy + ER-886046 (150 mg/kg)
AVERAGE BODY WEIGHT (g)
24
22
20
18
16
14
0
10
20
30
40
50
DAYS POST CELL IMPLANTATION
9-Gy
ER-886046

FIG. 1

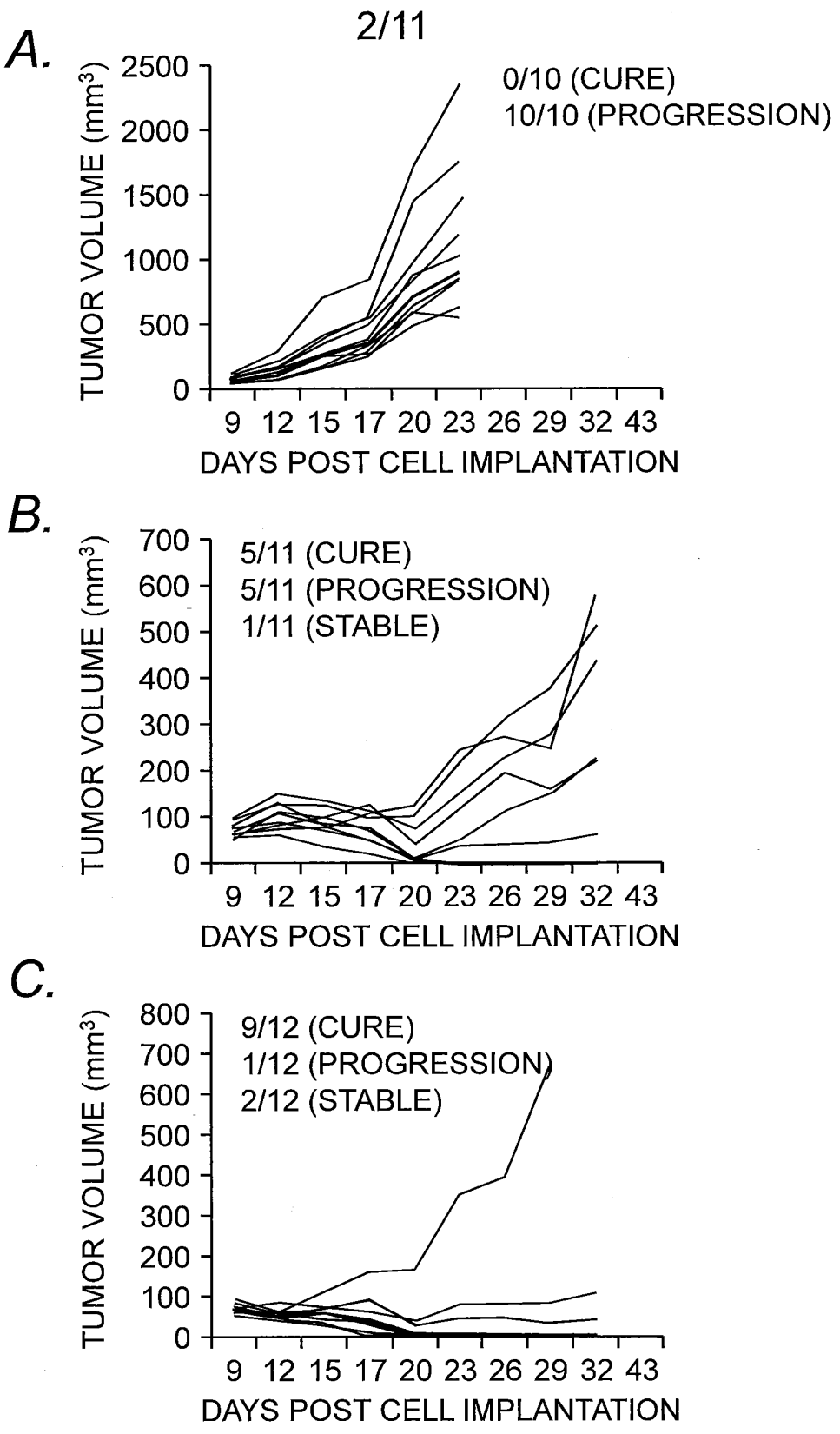

2/11
A.
TUMOR VOLUME (mm3)
2500
2000
1500
1000
500
0
0/10 (CURE)
10/10 (PROGRESSION)
9 12 15 17 20 23 26 29 32 43
DAYS POST CELL IMPLANTATION
B.
TUMOR VOLUME (mm3)
700
600
500
400
300
200
100
0
5/11 (CURE)
5/11 (PROGRESSION)
1/11 (STABLE)
9 12 15 17 20 23 26 29 32 43
DAYS POST CELL IMPLANTATION
C.
TUMOR VOLUME (mm3)
800
700
600
500
400
300
200
100
0
9/12 (CURE)
1/12 (PROGRESSION)
2/12 (STABLE)
9 12 15 17 20 23 26 29 32 43
DAYS POST CELL IMPLANTATION

FIG. 2

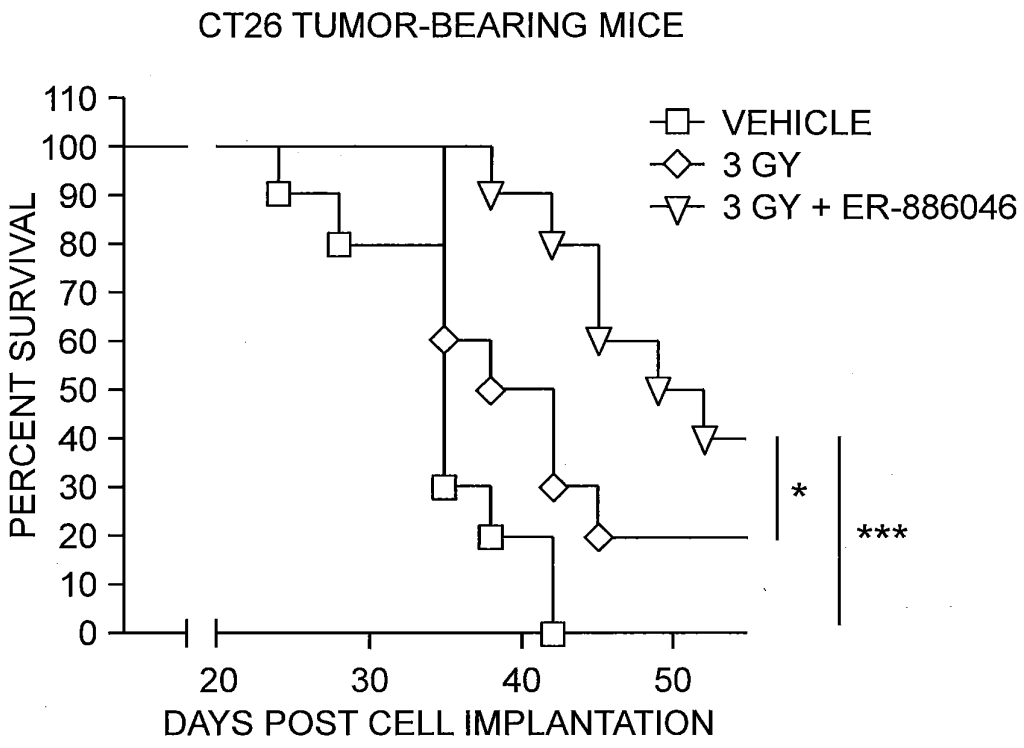

CT26 TUMOR-BEARING MICE
PERCENT SURVIVAL
110
100
90
80
70
60
50
40
30
20
10
0
20
30
40
50
DAYS POST CELL IMPLANTATION
VEHICLE
3 GY
3 GY + ER-886046
*
***

FIG. 3

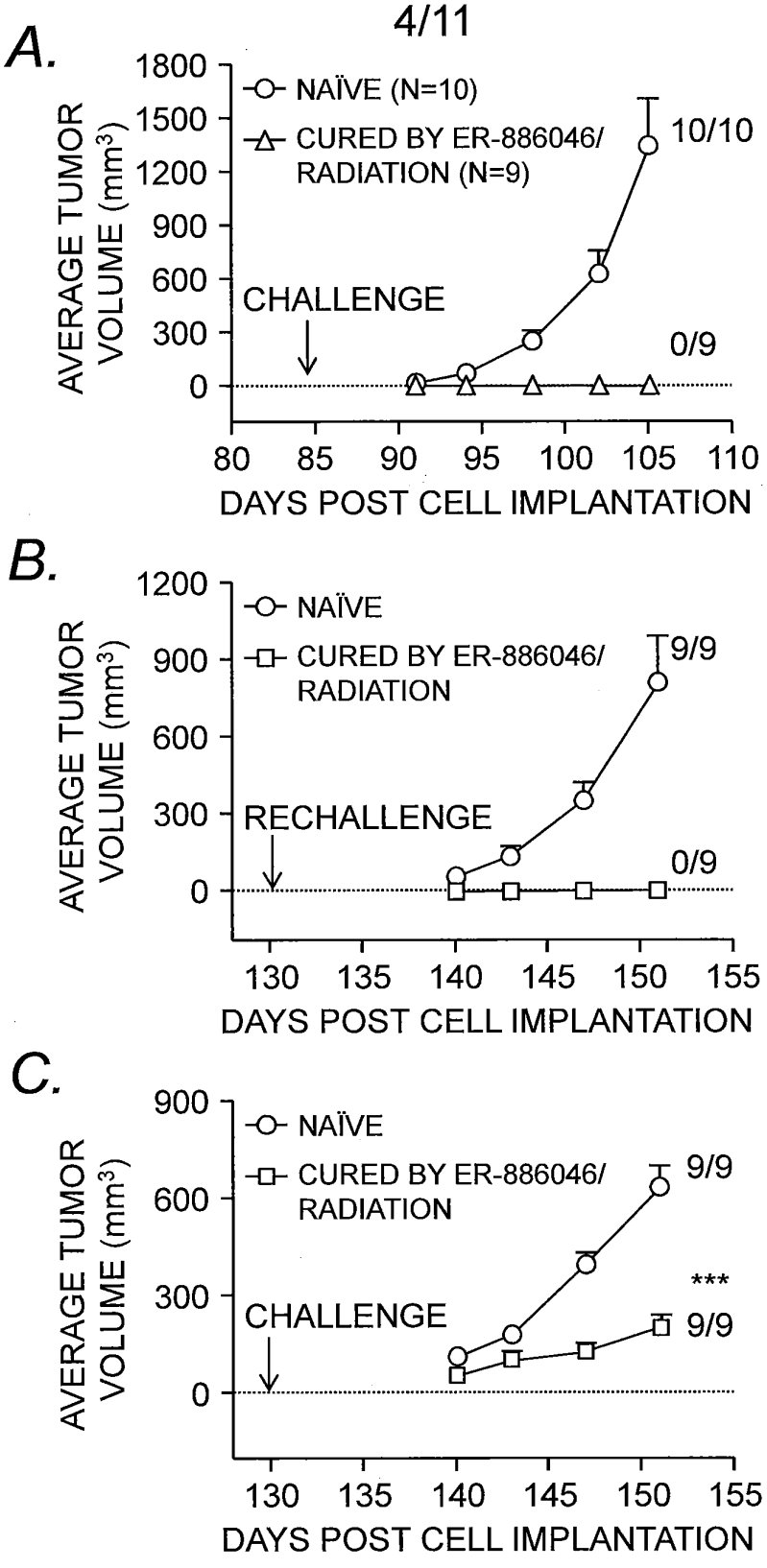
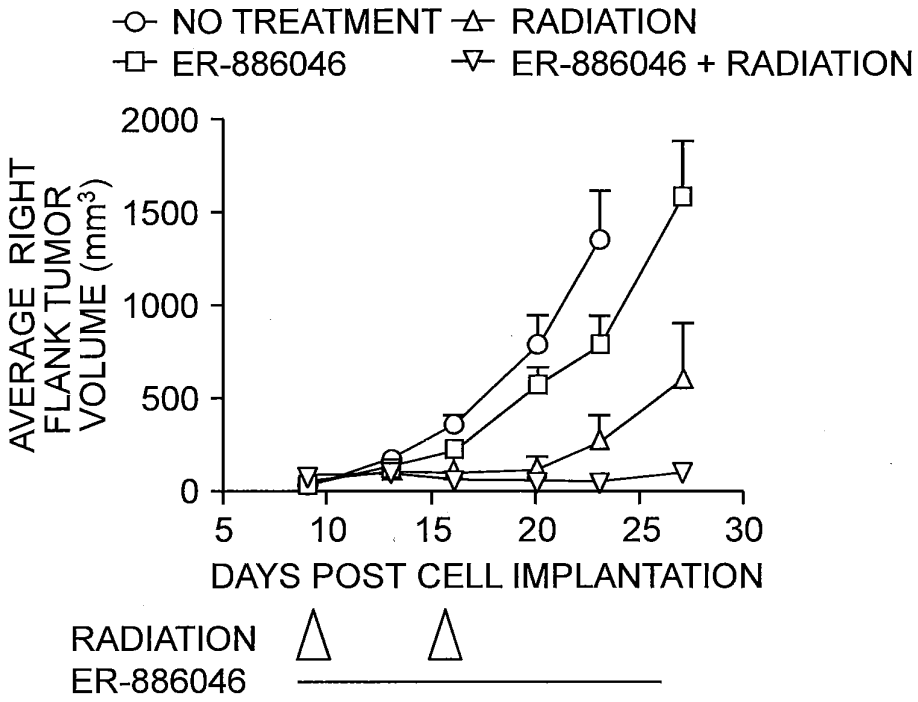

A.
AVERAGE TUMOR VOLUME (mm³)
1800
1500
1200
900
600
300
0
NAÏVE (N=10)
CURED BY ER-886046/ RADIATION (N=9)
10/10
0/9
CHALLENGE
80 85 90 95 100 105 110
DAYS POST CELL IMPLANTATION
B.
AVERAGE TUMOR VOLUME (mm³)
1200
900
600
300
0
NAÏVE
CURED BY ER-886046/ RADIATION
9/9
0/9
RECHALLENGE
130 135 140 145 150 155
DAYS POST CELL IMPLANTATION
C.
AVERAGE TUMOR VOLUME (mm³)
900
600
300
0
NAÏVE
CURED BY ER-886046/ RADIATION
9/9
***
9/9
CHALLENGE
130 135 140 145 150 155
DAYS POST CELL IMPLANTATION

FIG. 4

A.


NO TREATMENT
RADIATION
ER-886046
ER-886046 + RADIATION
AVERAGE RIGHT FLANK TUMOR VOLUME (mm³)
2000
1500
1000
500
0
5
10
15
20
25
30
DAYS POST CELL IMPLANTATION
RADIATION
ER-886046

B.

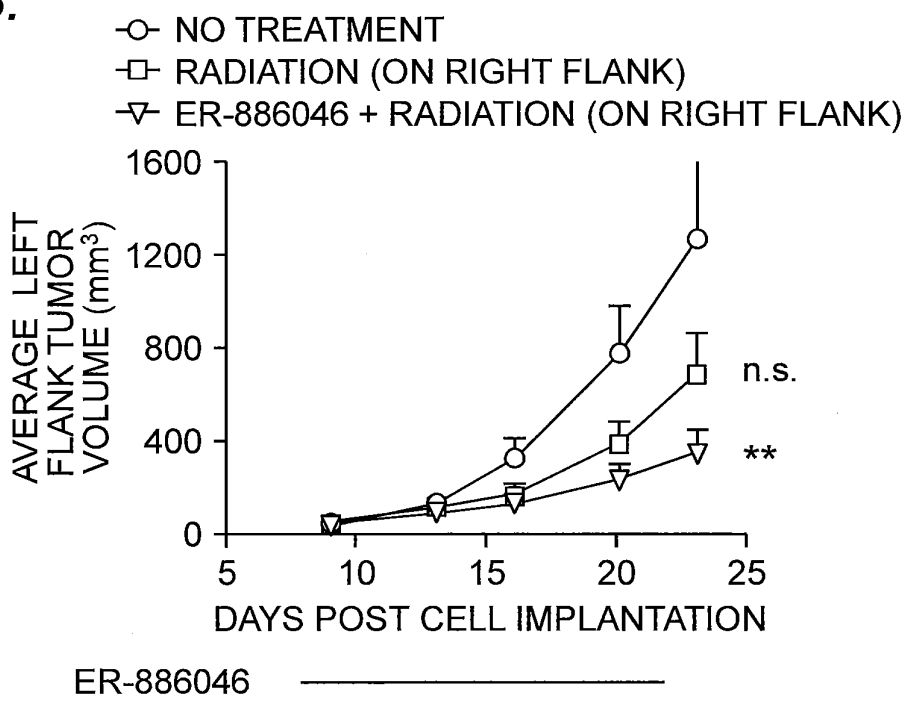
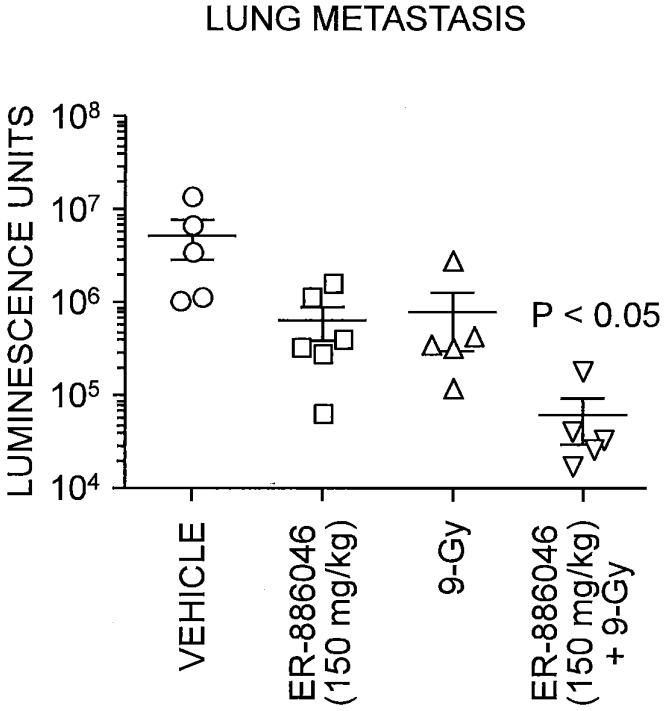

NO TREATMENT
RADIATION (ON RIGHT FLANK)
ER-886046 + RADIATION (ON RIGHT FLANK)
AVERAGE LEFT FLANK TUMOR VOLUME (mm³)
1600
1200
800
400
0
5
10
15
20
25
DAYS POST CELL IMPLANTATION
n.s.
**
ER-886046

FIG. 5

A.


LUNG METASTASIS
LUMINESCENCE UNITS
10^8
10^7
10^6
10^5
10^4
P < 0.05
VEHICLE
ER-886046 (150 mg/kg)
9-Gy
ER-886046 (150 mg/kg) + 9-Gy

B.

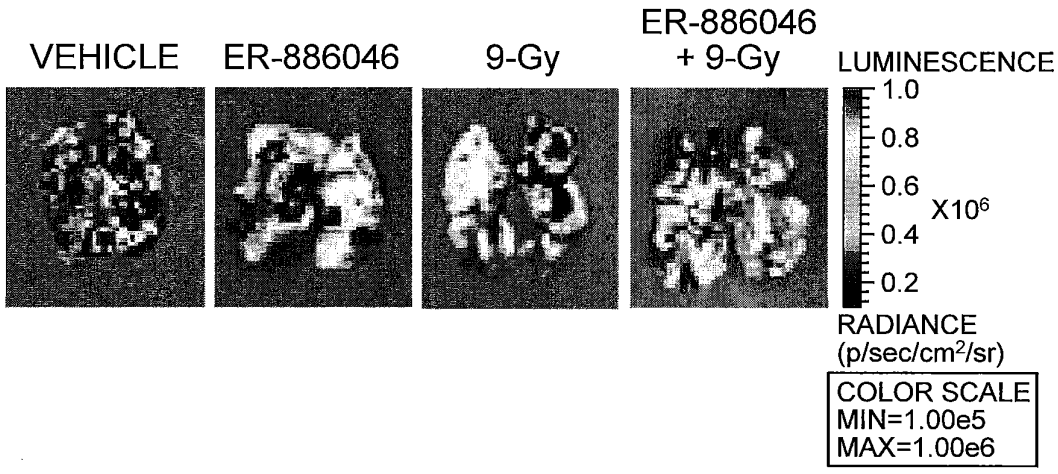
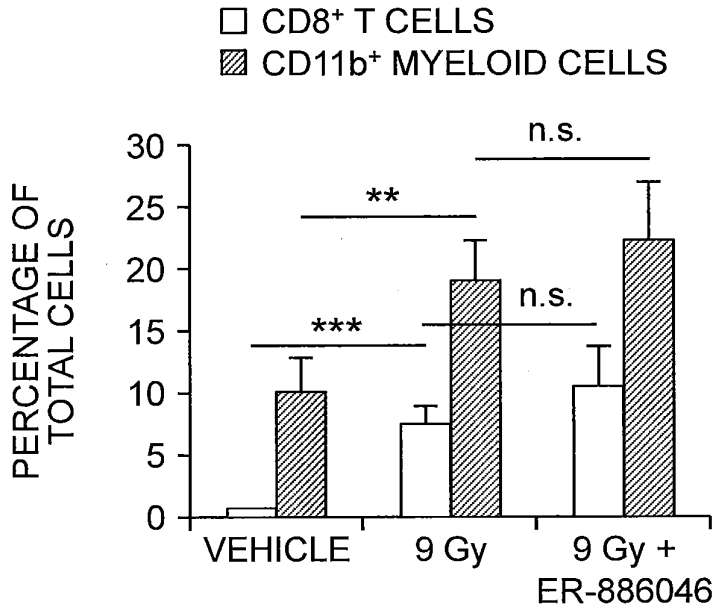

VEHICLE
ER-886046
9-Gy
ER-886046 + 9-Gy
LUMINESCENCE
1.0
0.8
0.6
0.4
0.2
X10^6
RADIANCE (p/sec/cm^2/sr)
COLOR SCALE
MIN=1.00e5
MAX=1.00e6

FIG. 6

A.


CD8+ T CELLS
CD11b+ MYELOID CELLS
PERCENTAGE OF TOTAL CELLS
30
25
20
15
10
5
0
**
***
n.s.
n.s.
VEHICLE
9 Gy
9 Gy + ER-886046

B.

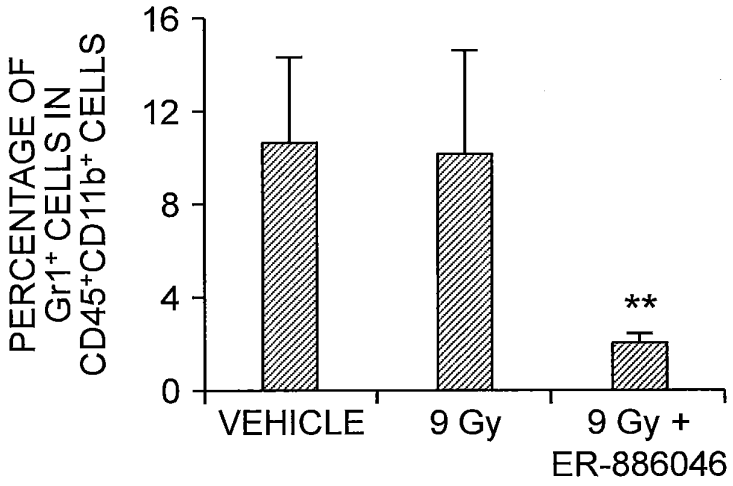
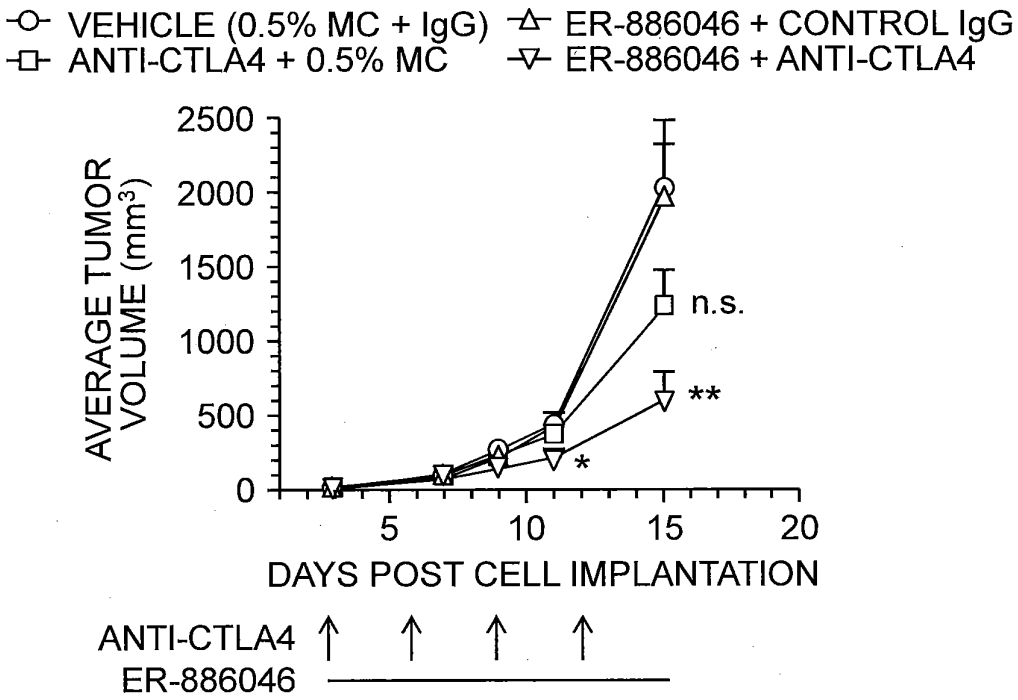

PERCENTAGE OF Gr1+ CELLS IN CD45+CD11b+ CELLS
16
12
8
4
0
**
VEHICLE
9 Gy
9 Gy + ER-886046

FIG. 7

A.


VEHICLE (0.5% MC + IgG)
ANTI-CTLA4 + 0.5% MC
ER-886046 + CONTROL IgG
ER-886046 + ANTI-CTLA4
AVERAGE TUMOR VOLUME (mm3)
2500
2000
1500
1000
500
0
5
10
15
20
DAYS POST CELL IMPLANTATION
n.s.
**
*
ANTI-CTLA4
ER-886046

B.

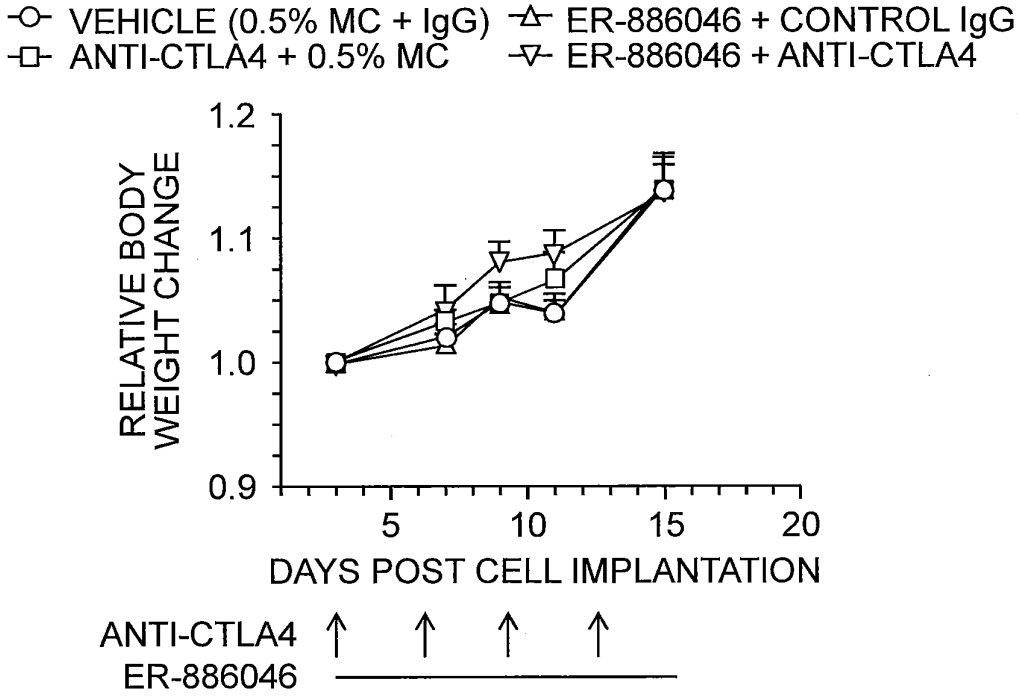
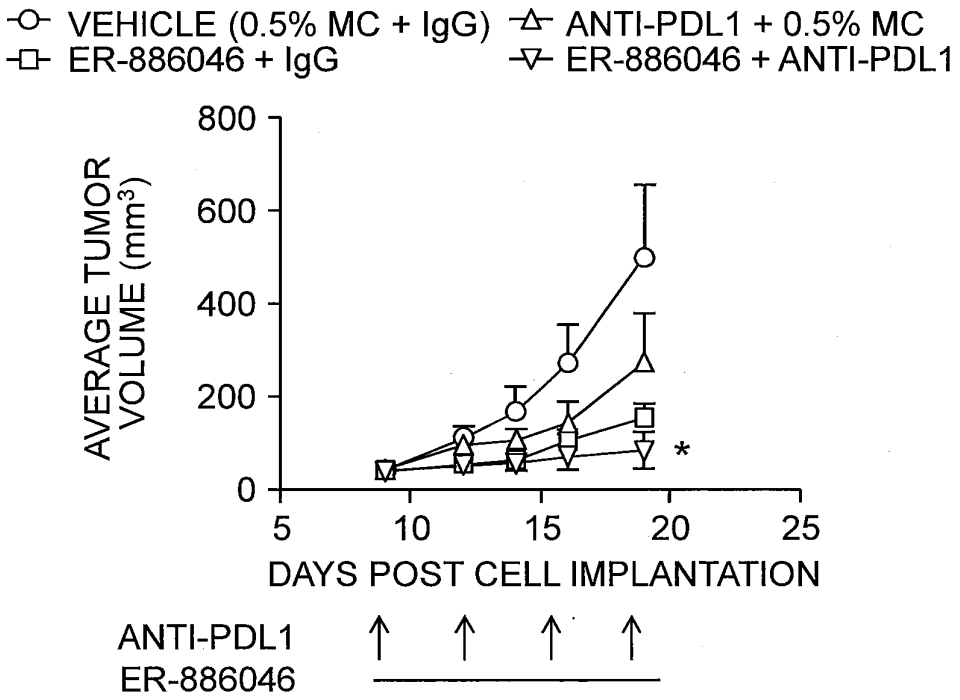

VEHICLE (0.5% MC + IgG)
ANTI-CTLA4 + 0.5% MC
ER-886046 + CONTROL IgG
ER-886046 + ANTI-CTLA4
RELATIVE BODY WEIGHT CHANGE
1.2
1.1
1.0
0.9
5
10
15
20
DAYS POST CELL IMPLANTATION
ANTI-CTLA4
ER-886046

FIG. 8

A.


VEHICLE (0.5% MC + IgG)
ANTI-PDL1 + 0.5% MC
ER-886046 + IgG
ER-886046 + ANTI-PDL1
AVERAGE TUMOR VOLUME (mm3)
800
600
400
200
0
5
10
15
20
25
*
DAYS POST CELL IMPLANTATION
ANTI-PDL1
ER-886046

B.

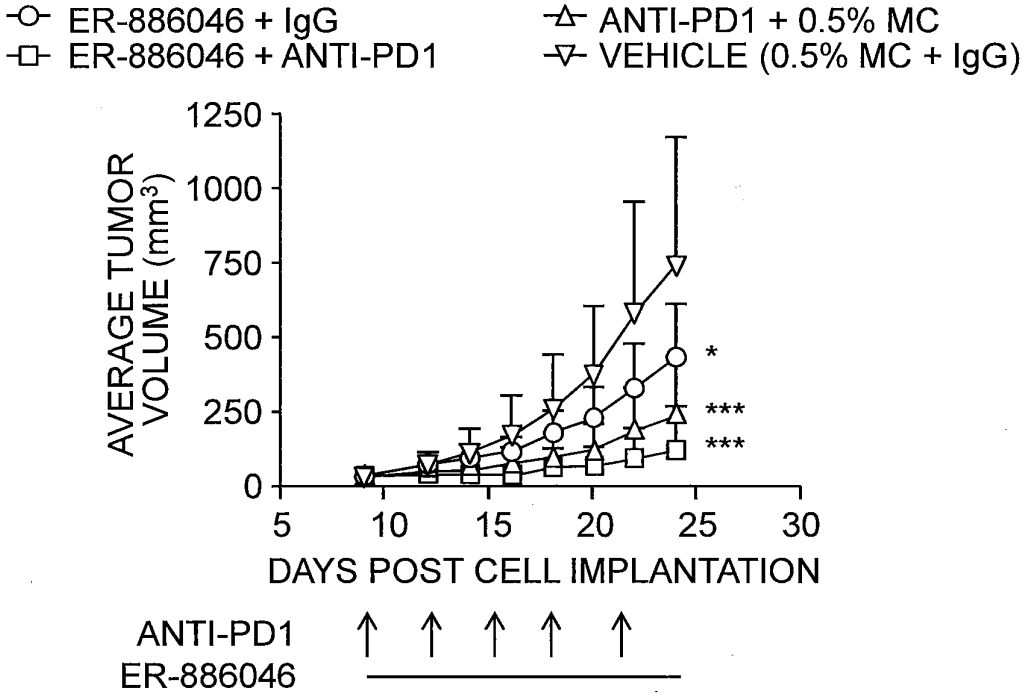

ER-886046 + IgG
ANTI-PD1 + 0.5% MC
ER-886046 + ANTI-PD1
VEHICLE (0.5% MC + IgG)
AVERAGE TUMOR VOLUME (mm3)
1250
1000
750
500
250
0
5
10
15
20
25
30
*
***
***
DAYS POST CELL IMPLANTATION
ANTI-PD1
ER-886046

FIG. 9

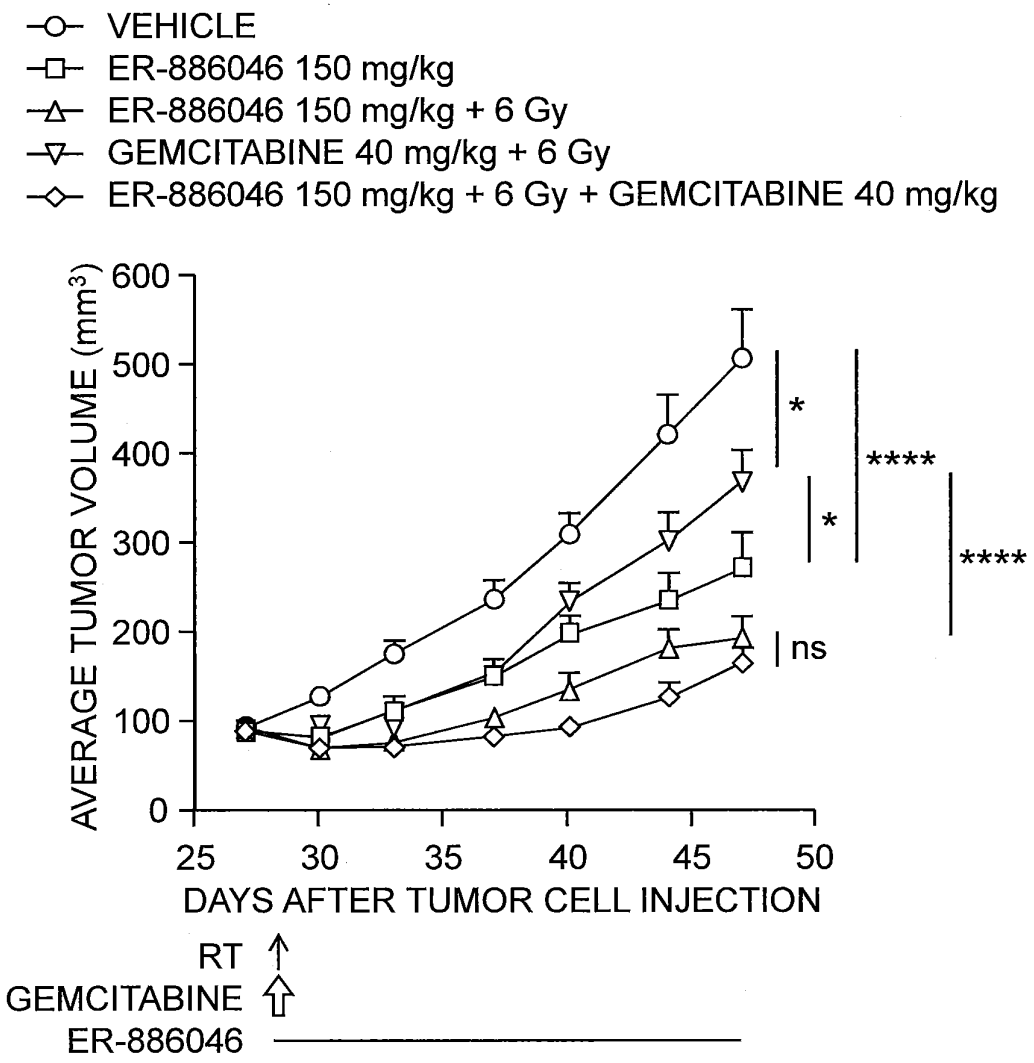
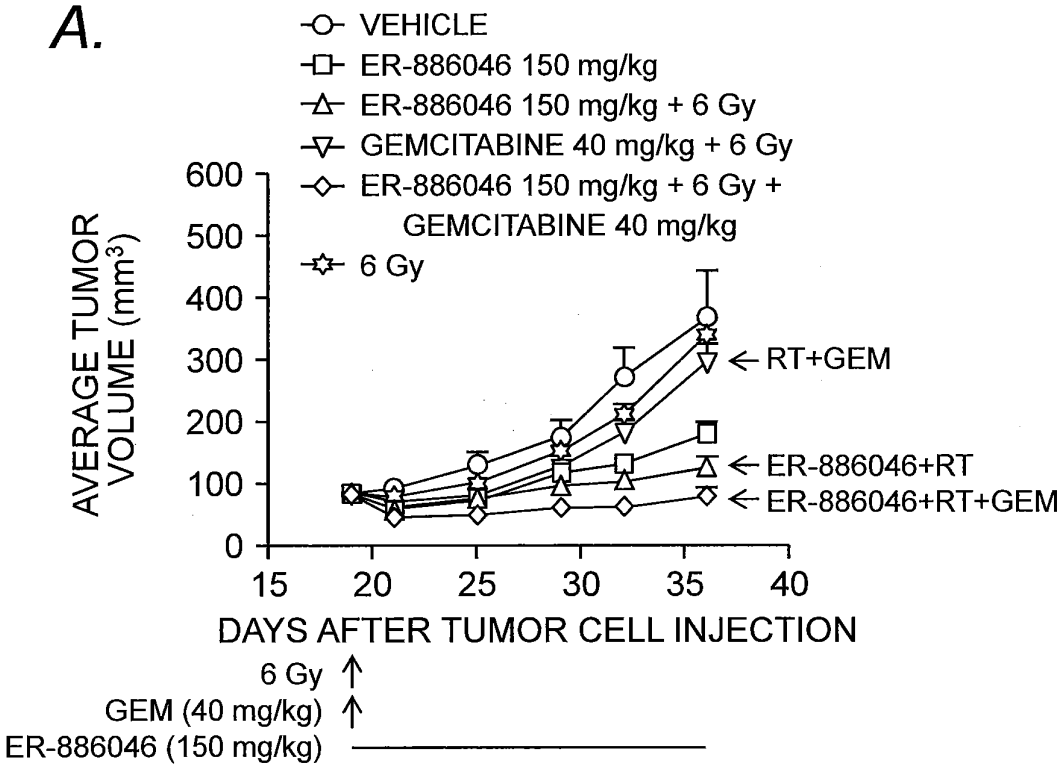

VEHICLE
ER-886046 150 mg/kg
ER-886046 150 mg/kg + 6 Gy
GEMCITABINE 40 mg/kg + 6 Gy
ER-886046 150 mg/kg + 6 Gy + GEMCITABINE 40 mg/kg
AVERAGE TUMOR VOLUME (mm3)
600
500
400
300
200
100
0
25
30
35
40
45
50
DAYS AFTER TUMOR CELL INJECTION
*
*
****
****
ns
RT
GEMCITABINE
ER-886046

FIG. 10


A.
VEHICLE
ER-886046 150 mg/kg
ER-886046 150 mg/kg + 6 Gy
GEMCITABINE 40 mg/kg + 6 Gy
ER-886046 150 mg/kg + 6 Gy + GEMCITABINE 40 mg/kg
6 Gy
AVERAGE TUMOR VOLUME (mm3)
600
500
400
300
200
100
0
15
20
25
30
35
40
DAYS AFTER TUMOR CELL INJECTION
← RT+GEM
← ER-886046+RT
← ER-886046+RT+GEM
6 Gy
GEM (40 mg/kg)
ER-886046 (150 mg/kg)

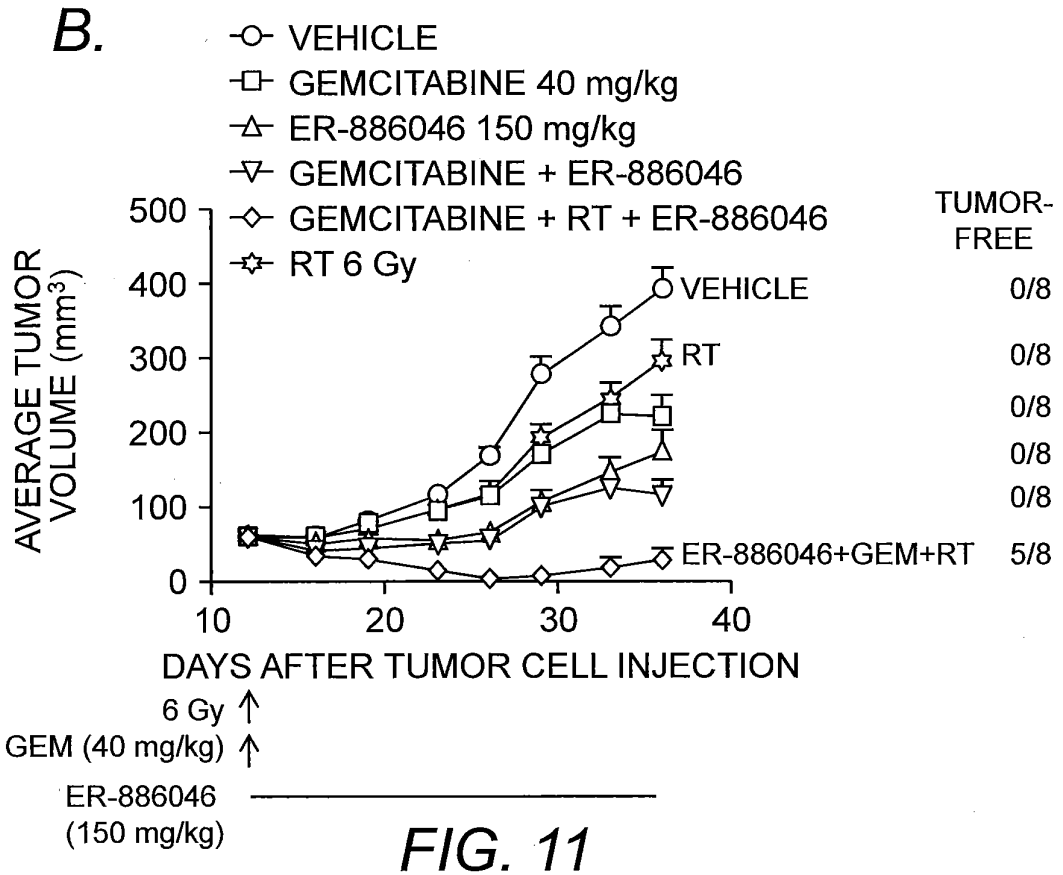

B.
VEHICLE
GEMCITABINE 40 mg/kg
ER-886046 150 mg/kg
GEMCITABINE + ER-886046
GEMCITABINE + RT + ER-886046
RT 6 Gy
AVERAGE TUMOR VOLUME (mm3)
500
400
300
200
100
0
10
20
30
40
DAYS AFTER TUMOR CELL INJECTION
TUMOR-FREE
VEHICLE 0/8
RT 0/8
0/8
0/8
0/8
ER-886046+GEM+RT 5/8
6 Gy
GEM (40 mg/kg)
ER-886046 (150 mg/kg)

FIG. 11