FIGURE 1

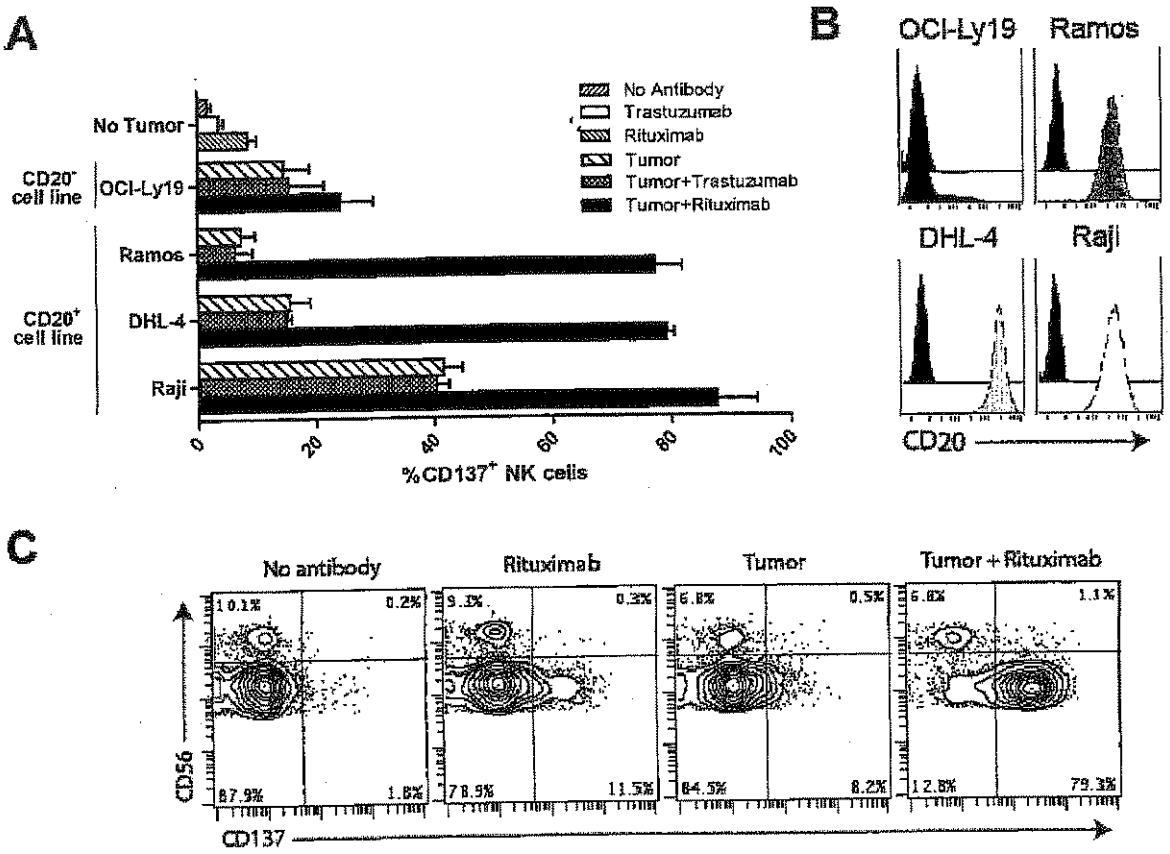

A
No Antibody
Trastuzumab
Rituximab
Tumor
Tumor+Trastuzumab
Tumor+Rituximab
No Tumor
CD20⁻ cell line
OCI-Ly19
Ramos
CD20⁺ cell line
DHL-4
Raji
0
20
40
60
80
100
%CD137⁺ NK cells
B
OCI-Ly19
Ramos
DHL-4
Raji
CD20
C
No antibody
Rituximab
Tumor
Tumor + Rituximab
10.1%
0.2%
87.9%
1.8%
9.3%
0.3%
78.9%
11.5%
6.8%
0.5%
84.5%
8.2%
6.8%
1.1%
12.8%
79.3%
CD56
CD137

FIGURE 2

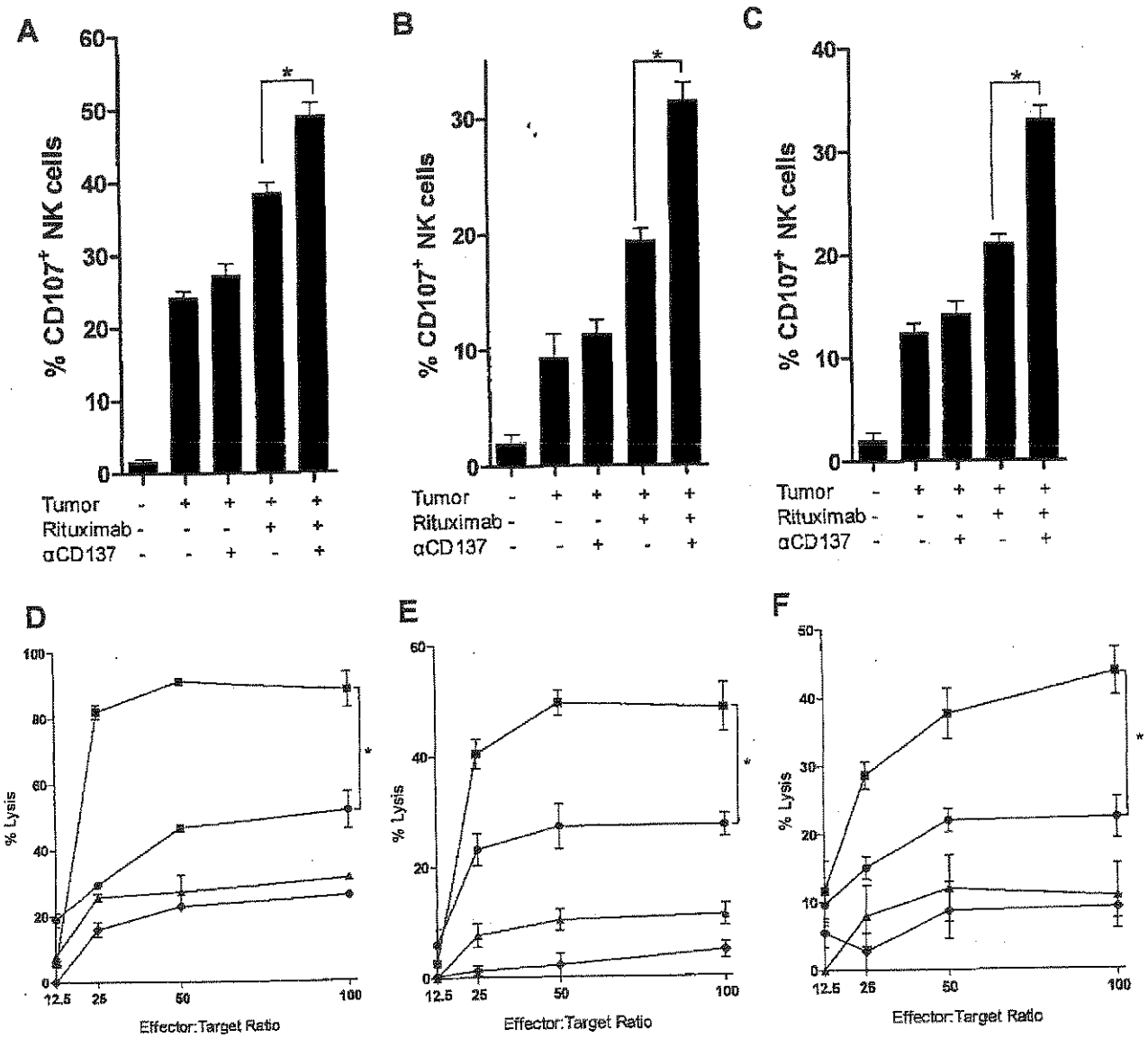

A
B
C
% CD107+ NK cells
Tumor
Rituximab
αCD137
D
E
F
% Lysis
Effector:Target Ratio
12.5
25
50
100

FIGURE 3

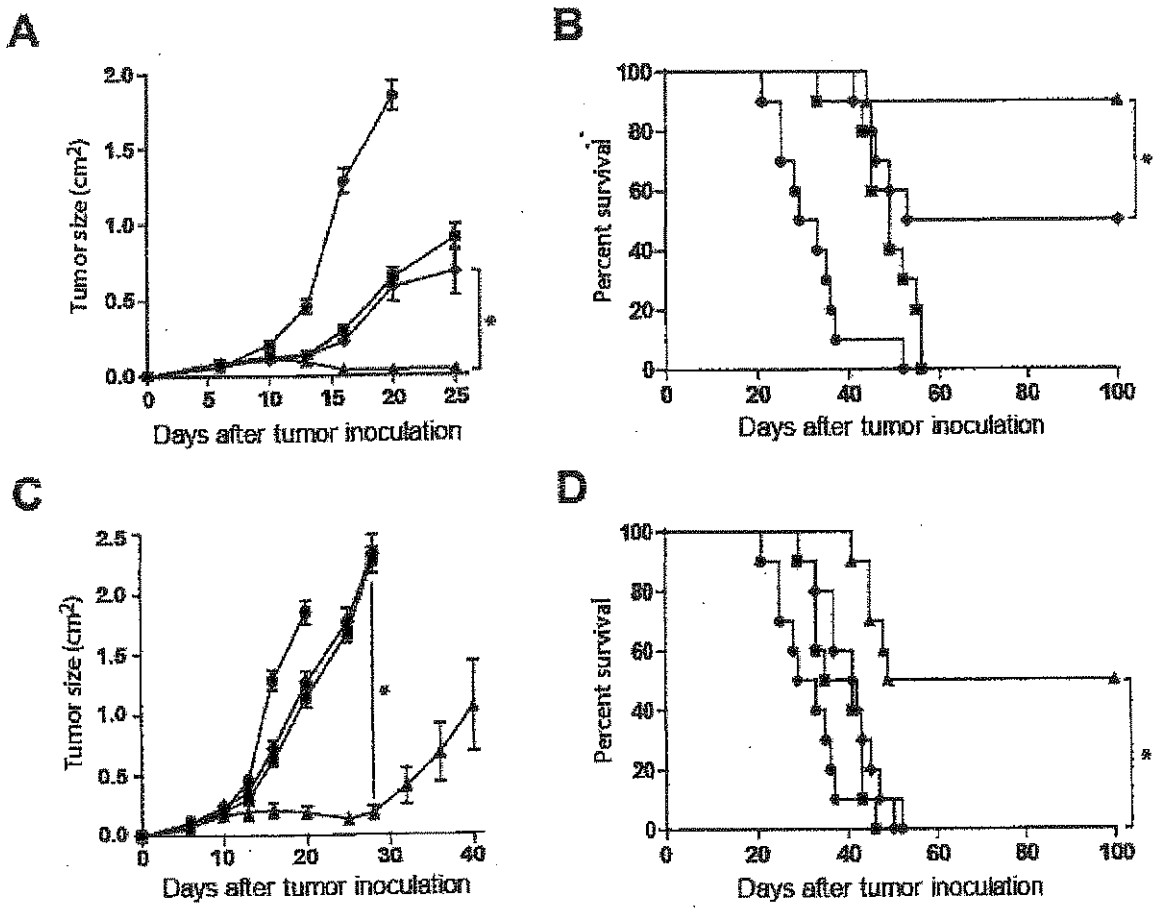

A
Tumor size (cm²)
Days after tumor inoculation
B
Percent survival
Days after tumor inoculation
C
Tumor size (cm²)
Days after tumor inoculation
D
Percent survival
Days after tumor inoculation

FIGURE 4

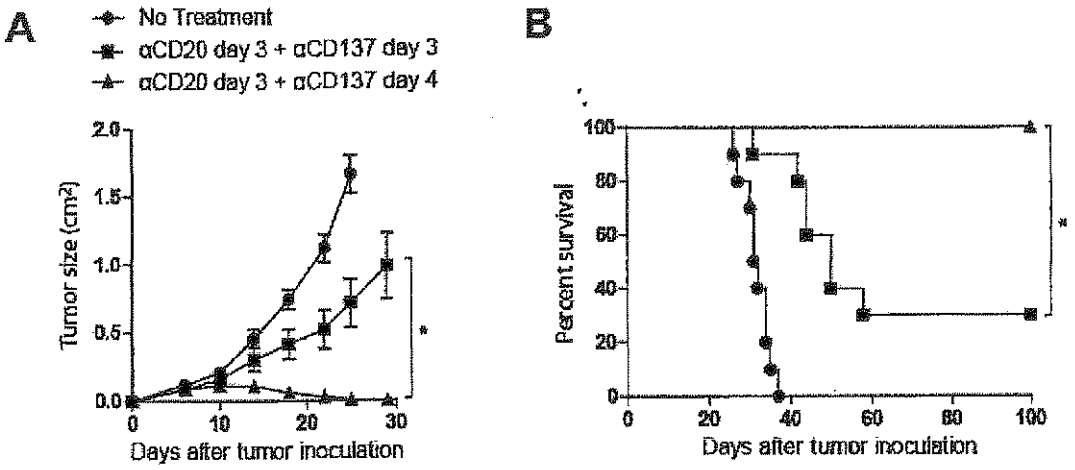

A
No Treatment
αCD20 day 3 + αCD137 day 3
αCD20 day 3 + αCD137 day 4
Tumor size (cm²)
2.0
1.5
1.0
0.5
0.0
0
10
20
30
Days after tumor inoculation
*
B
Percent survival
100
80
60
40
20
0
0
20
40
60
80
100
Days after tumor inoculation
*

FIGURE 5

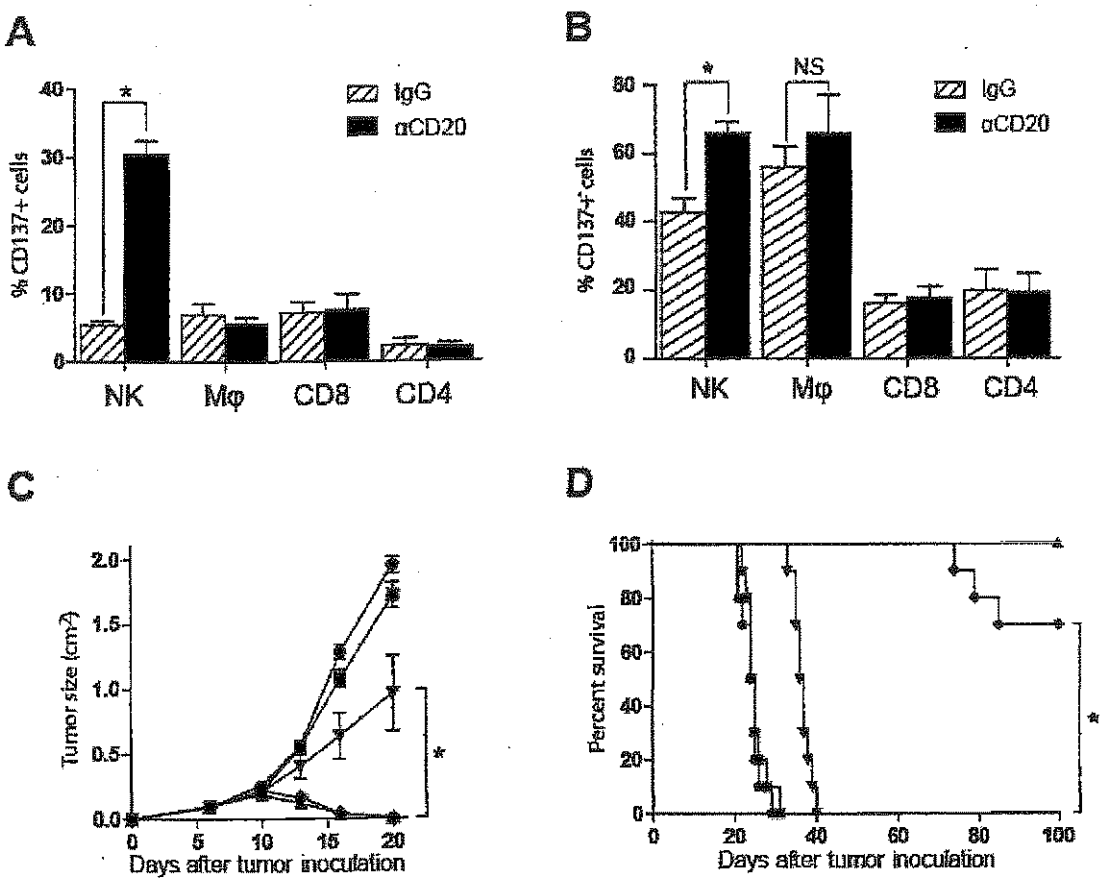

A
B
C
D
% CD137+ cells
% CD137+ cells
IgG
αCD20
NS
NK
Mφ
CD8
CD4
Tumor size (cm2)
Days after tumor inoculation
Percent survival
Days after tumor inoculation

FIGURE 6

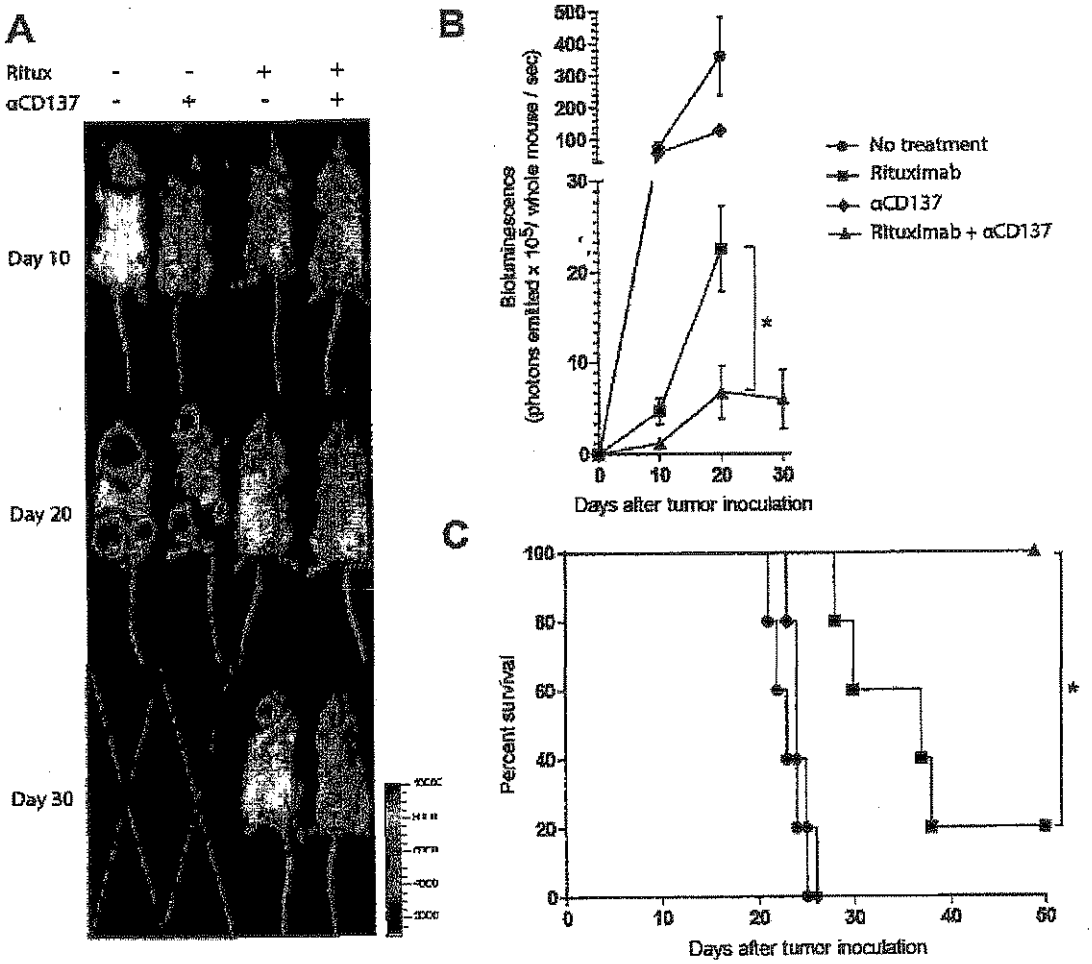

A
Ritux - - + +
αCD137 - + - +
Day 10
Day 20
Day 30
B
Bioluminescence (photons emitted x 10^5) whole mouse / sec
500
400
300
200
100
30
20
10
0
0 10 20 30
Days after tumor inoculation
No treatment
Rituximab
αCD137
Rituximab + αCD137
*
C
Percent survival
100
80
60
40
20
0
0 10 20 30 40 50
Days after tumor inoculation
*

FIGURE 7

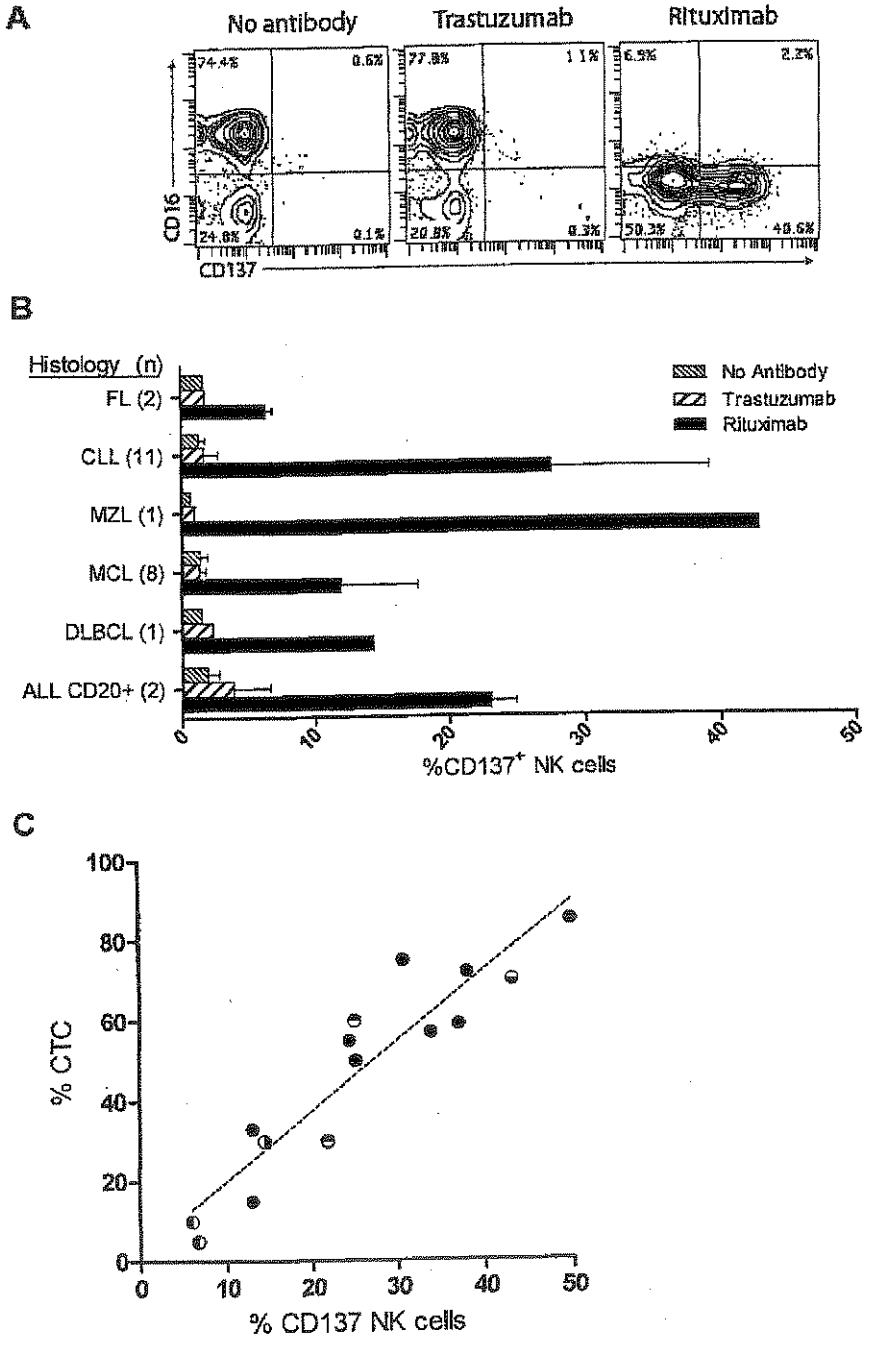

A
No antibody
Trastuzumab
Rituximab
74.4%
0.6%
24.8%
0.1%
77.8%
1.1%
20.8%
0.3%
6.5%
2.2%
50.3%
40.6%
CD16
CD137
B
Histology (n)
FL (2)
CLL (11)
MZL (1)
MCL (8)
DLBCL (1)
ALL CD20+ (2)
No Antibody
Trastuzumab
Rituximab
0
10
20
30
40
50
%CD137+ NK cells
C
100
80
60
40
20
0
% CTC
0
10
20
30
40
50
% CD137 NK cells

FIGURE 8

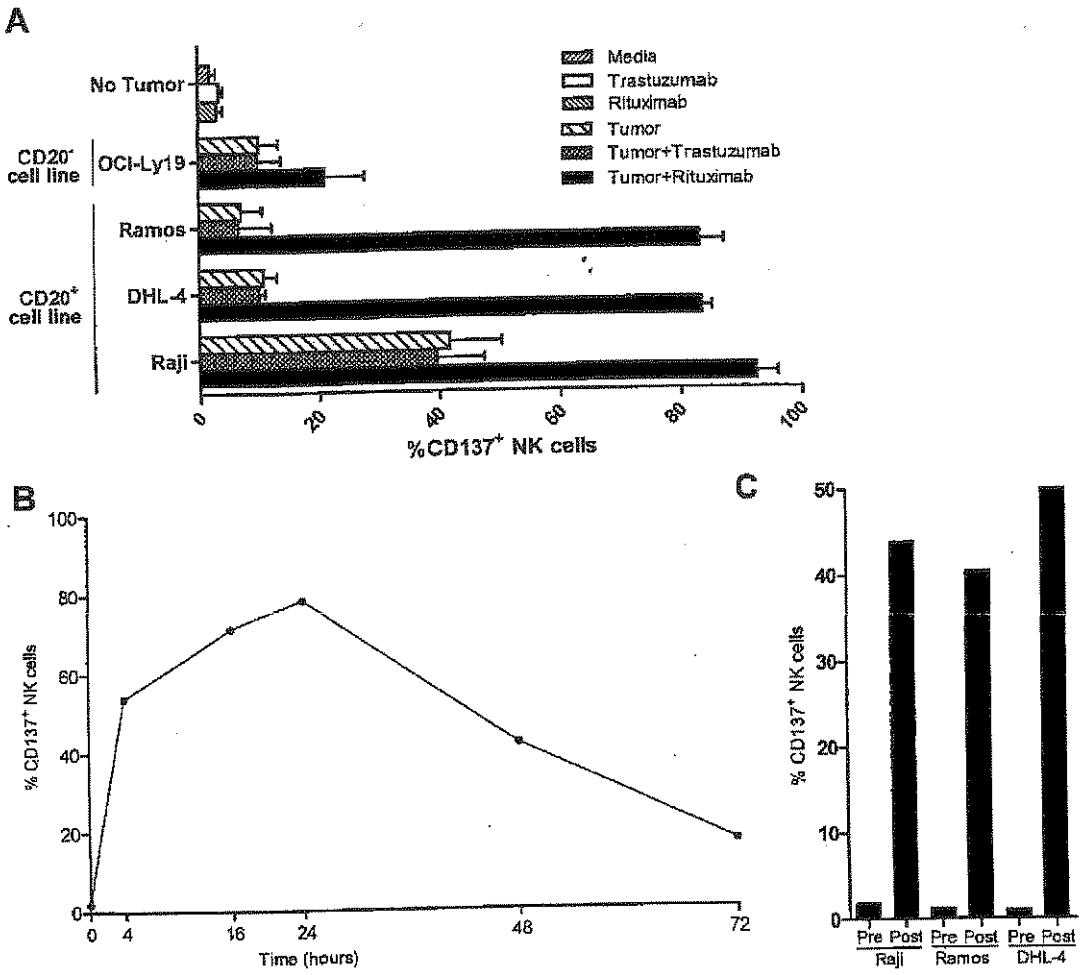

A
Media
Trastuzumab
Rituximab
Tumor
Tumor+Trastuzumab
Tumor+Rituximab
No Tumor
CD20⁻ cell line
OCI-Ly19
CD20⁺ cell line
Ramos
DHL-4
Raji
0
20
40
60
80
100
%CD137⁺ NK cells
B
% CD137⁺ NK cells
0
20
40
60
80
100
0
4
16
24
48
72
Time (hours)
C
% CD137⁺ NK cells
0
10
20
30
40
50
Pre Post
Raji
Pre Post
Ramos
Pre Post
DHL-4

FIGURE 9

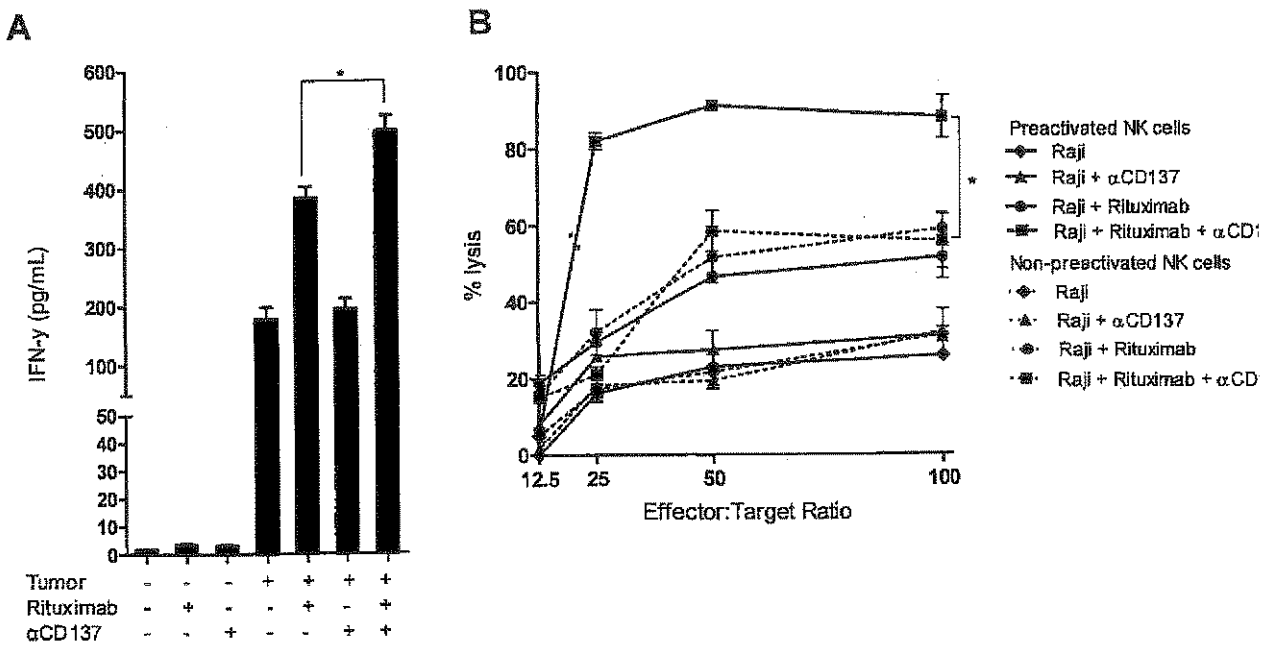

A
IFN-γ (pg/mL)
600
500
400
300
200
100
50
40
30
20
10
0
*
Tumor - - - + + + +
Rituximab - + - - + - +
αCD137 - - + - - + +
B
% lysis
100
80
60
40
20
0
12.5
25
50
100
Effector:Target Ratio
*
Preactivated NK cells
Raji
Raji + αCD137
Raji + Rituximab
Raji + Rituximab + αCD1
Non-prestivated NK cells
Raji
Raji + αCD137
Raji + Rituximab
Raji + Rituximab + αCD

Figure 10

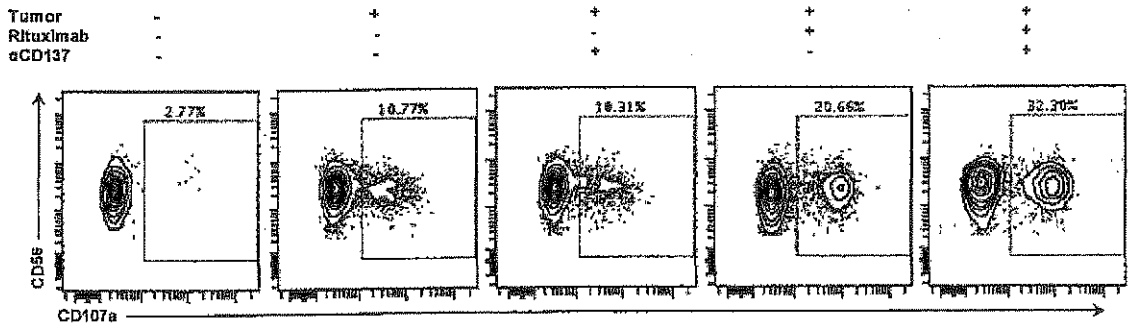


FIGURE 11

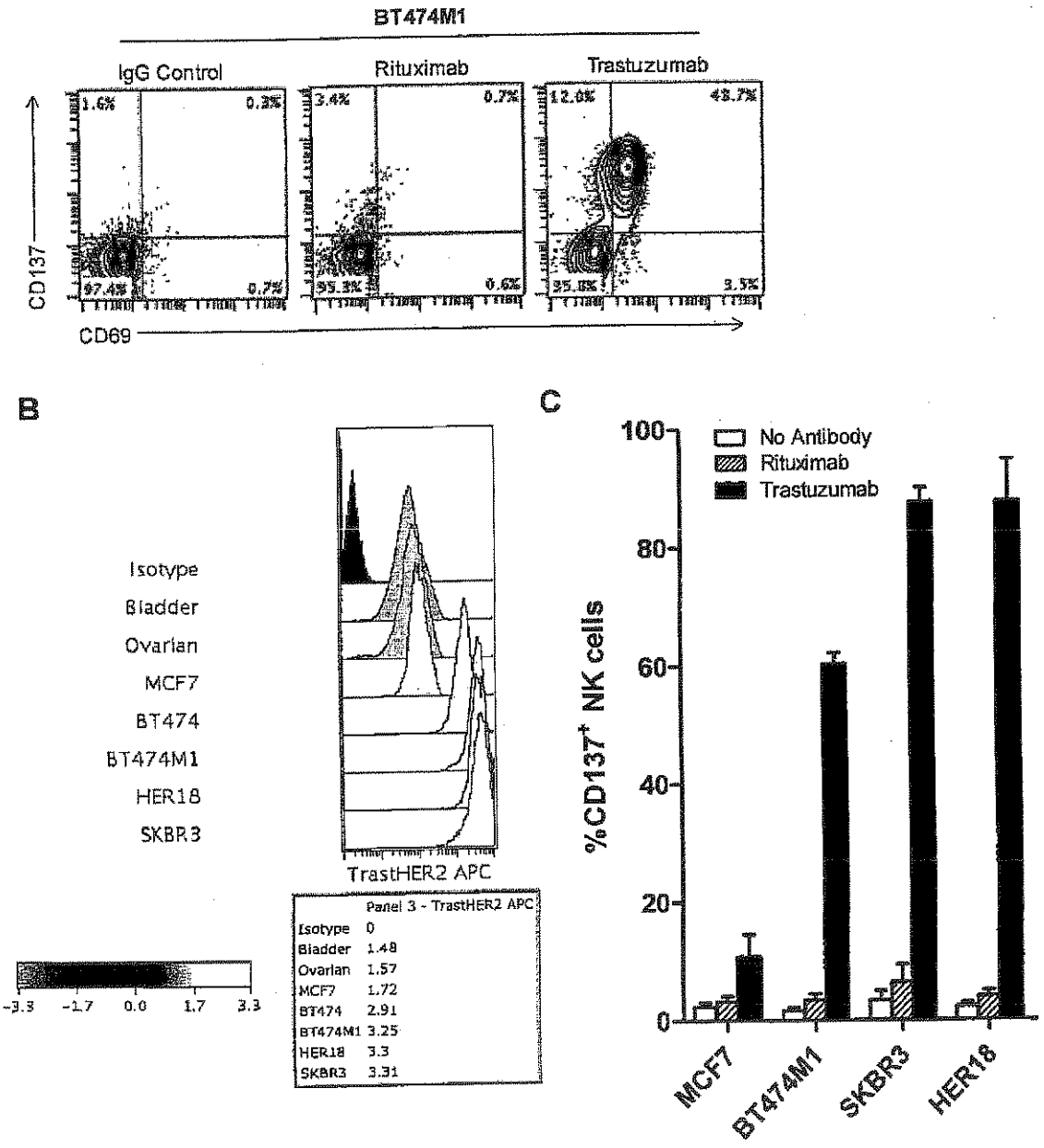

A
BT474M1
IgG Control
Rituximab
Trastuzumab
CD137
CD69
1.6%
0.2%
97.4%
0.7%
3.4%
0.7%
95.3%
0.6%
12.0%
45.7%
35.8%
3.5%
B
Isotype
Bladder
Ovarian
MCF7
BT474
BT474M1
HER18
SKBR3
TrastHER2 APC
-3.3
-1.7
0.0
1.7
3.3
Panel 3 - TrastHER2 APC
Isotype 0
Bladder 1.48
Ovarian 1.57
MCF7 1.72
BT474 2.91
BT474M1 3.25
HER18 3.3
SKBR3 3.31
C
No Antibody
Rituximab
Trastuzumab
%CD137+ NK cells
100
80
60
40
20
0
MCF7
BT474M1
SKBR3
HER18

FIGURE 12

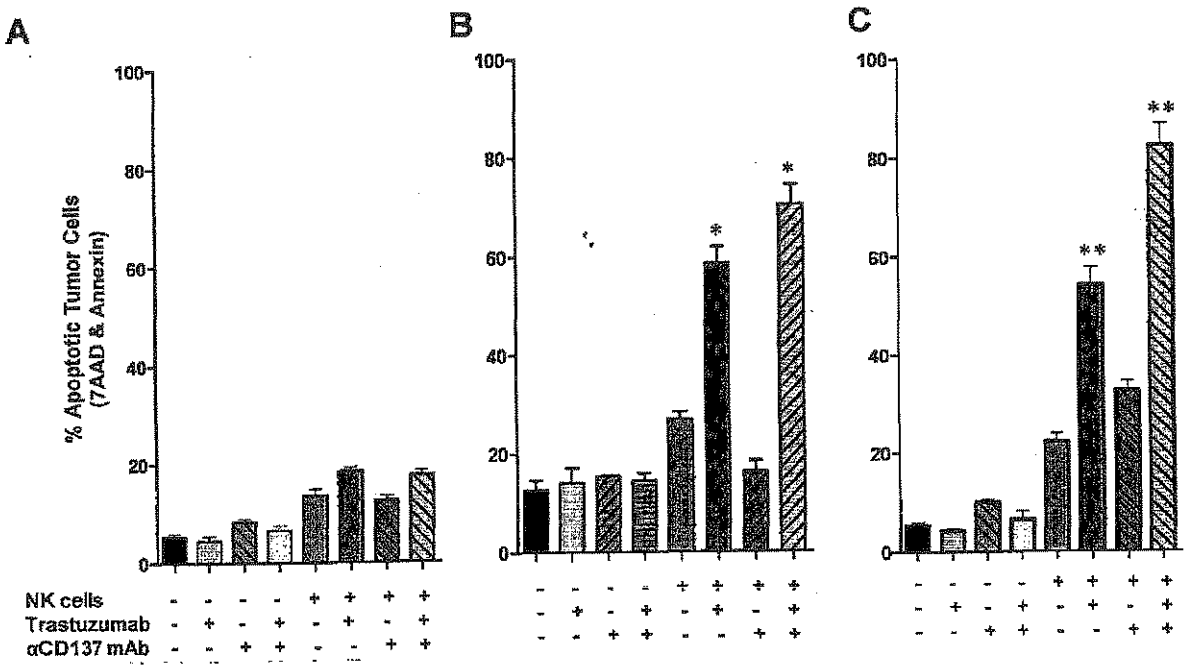

A
B
C
% Apoptotic Tumor Cells (7AAD & Annexin)
100
80
60
40
20
0
NK cells
Trastuzumab
αCD137 mAb
*
**

FIGURE 13

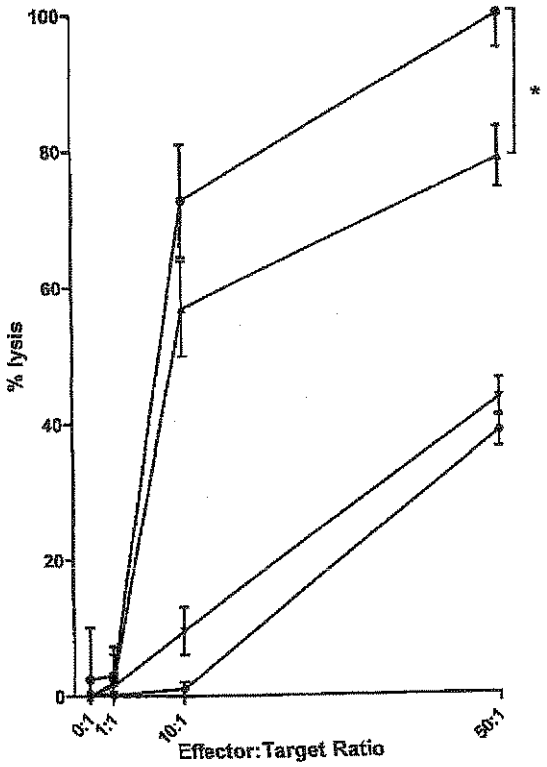


FIGURE 14

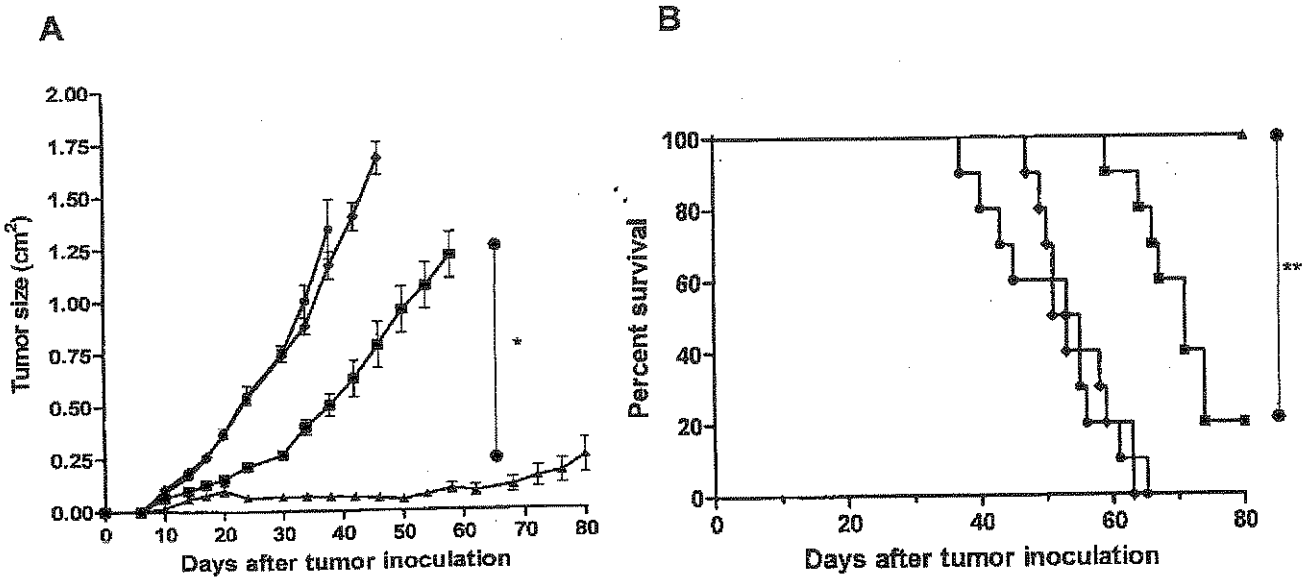

A
Tumor size (cm²)
2.00
1.75
1.50
1.25
1.00
0.75
0.50
0.25
0.00
0
10
20
30
40
50
60
70
80
Days after tumor inoculation
*
B
Percent survival
100
80
60
40
20
0
0
20
40
60
80
Days after tumor inoculation
**

FIGURE 15

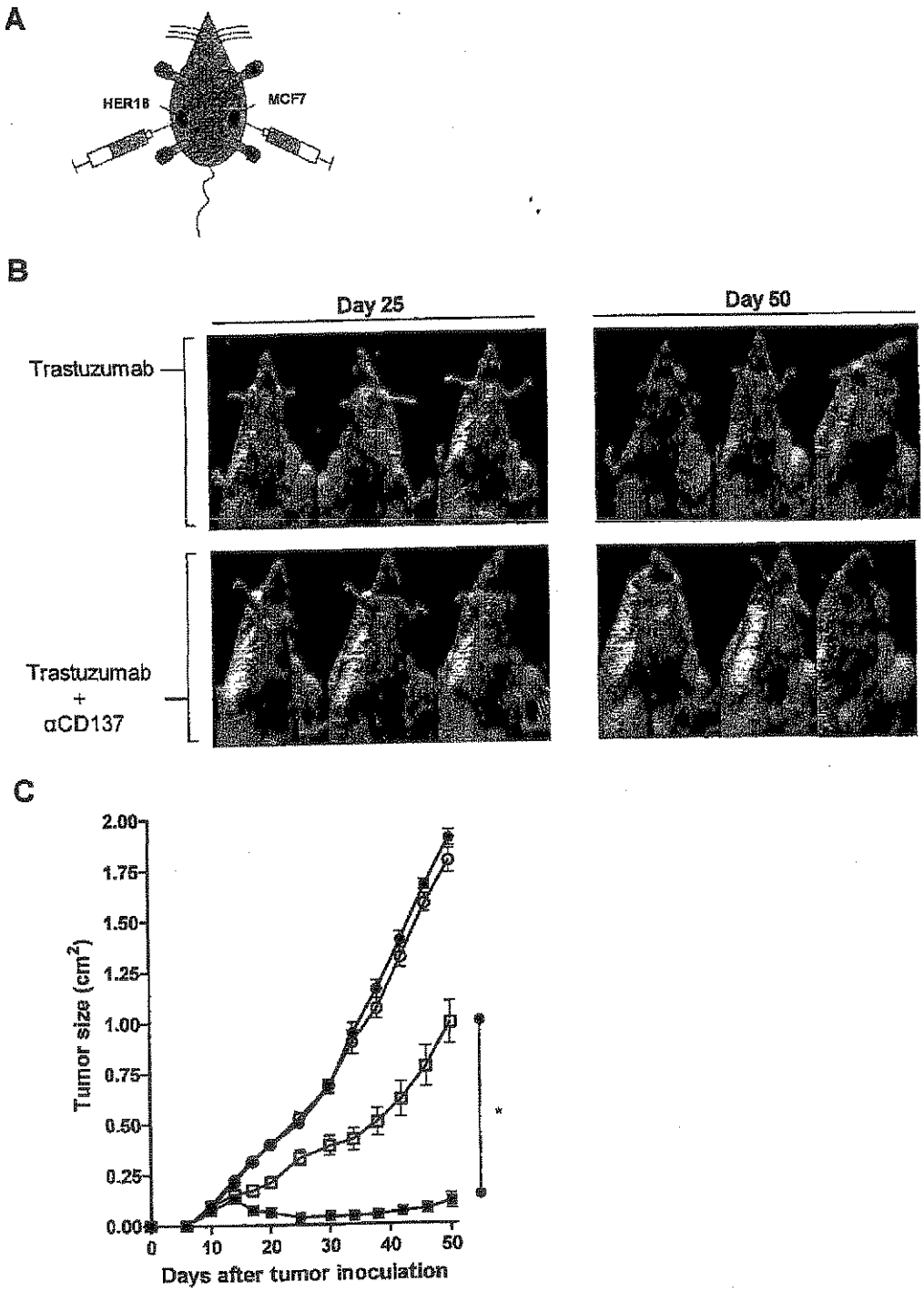

A
HER18
MCF7
B
Day 25
Day 50
Trastuzumab
Trastuzumab
+
αCD137
C
Tumor size (cm²)
2.00
1.75
1.50
1.25
1.00
0.75
0.50
0.25
0.00
0
10
20
30
40
50
Days after tumor inoculation
*

FIGURE 16

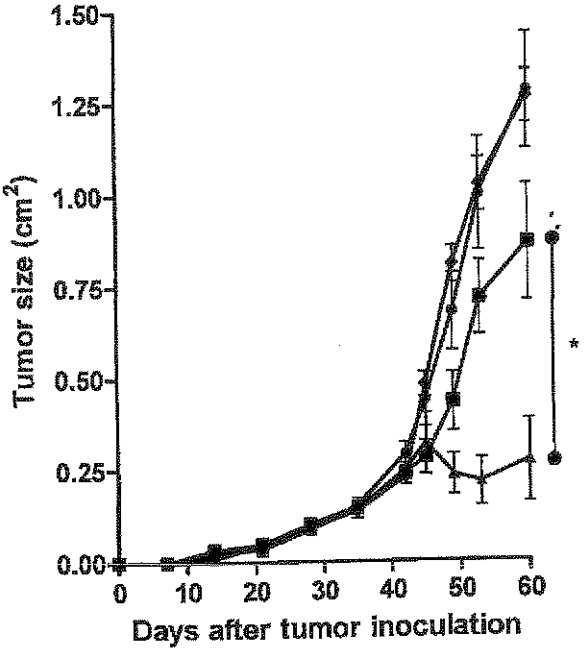

1.50
1.25
1.00
0.75
0.50
0.25
0.00
Tumor size (cm2)
0
10
20
30
40
50
60
Days after tumor inoculation
*

FIGURE 17

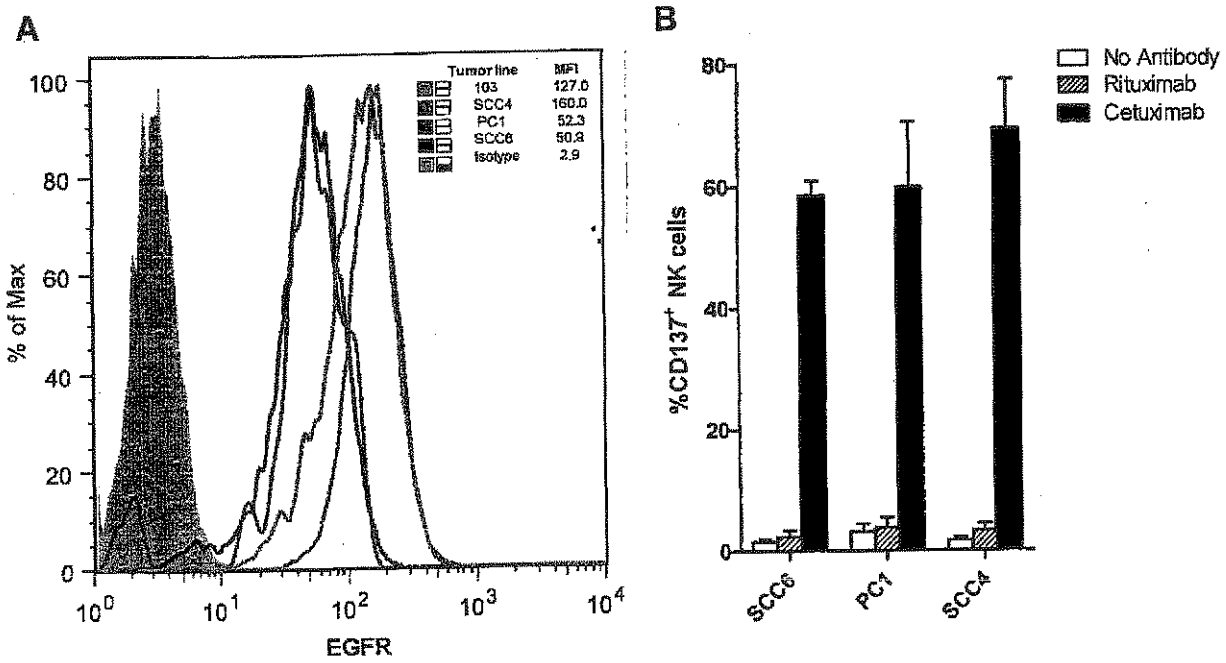

A
% of Max
EGFR
Tumor line
MFI
103
127.0
SCC4
160.0
PC1
52.3
SCC6
50.8
Isotype
2.9
B
%CD137+ NK cells
No Antibody
Rituximab
Cetuximab
SCC6
PC1
SCC4

FIGURE 18

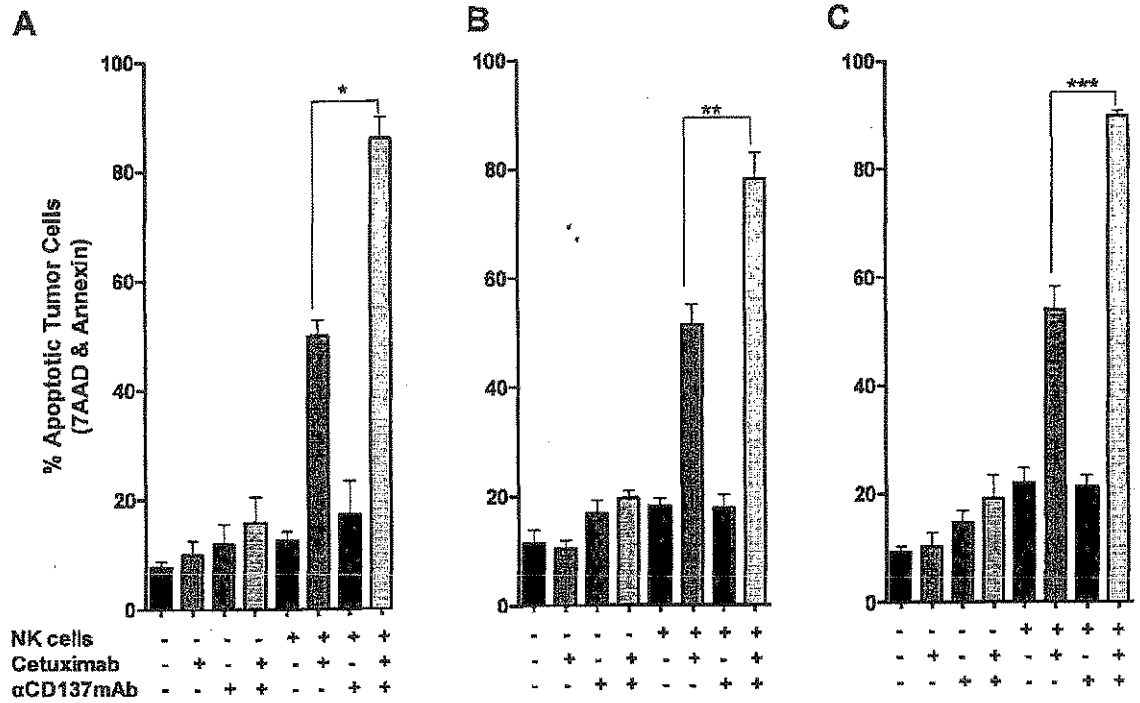

A
B
C
% Apoptotic Tumor Cells (7AAD & Annexin)
100
80
60
40
20
0
*
**
***
NK cells
Cetuximab
αCD137mAb

FIGURE 19

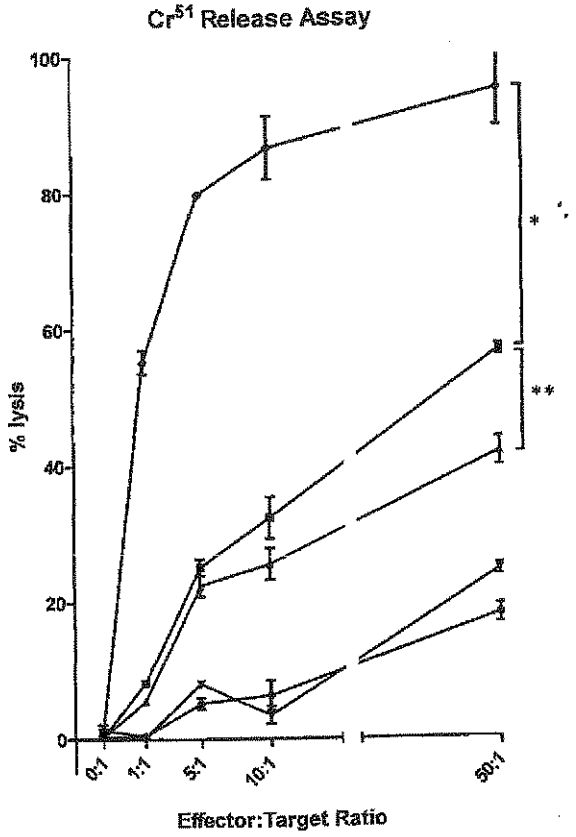

Cr51 Release Assay
100
80
60
40
20
0
% lysis
0:1
1:1
5:1
10:1
50:1
Effector:Target Ratio
*
**

FIGURE 20

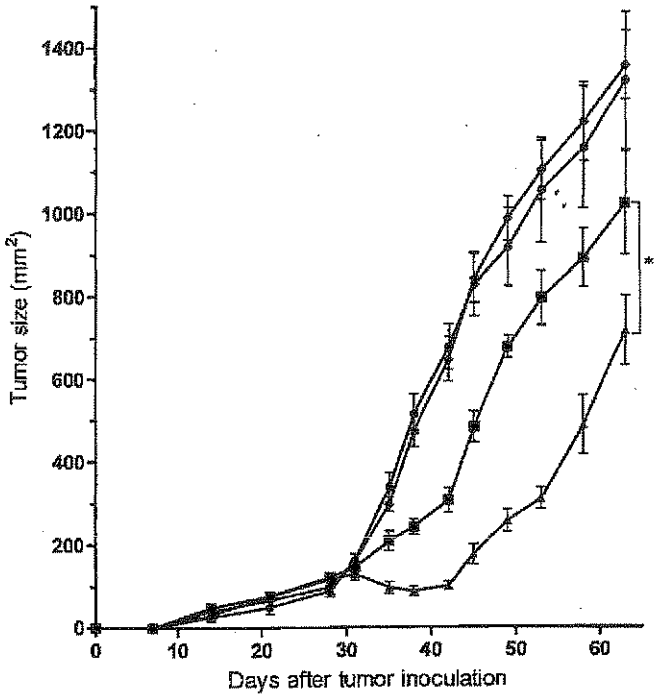
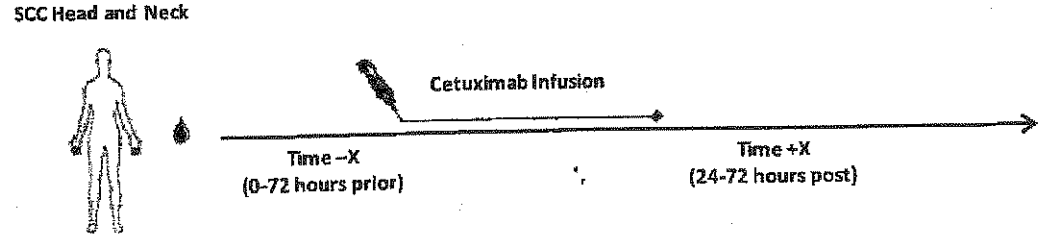
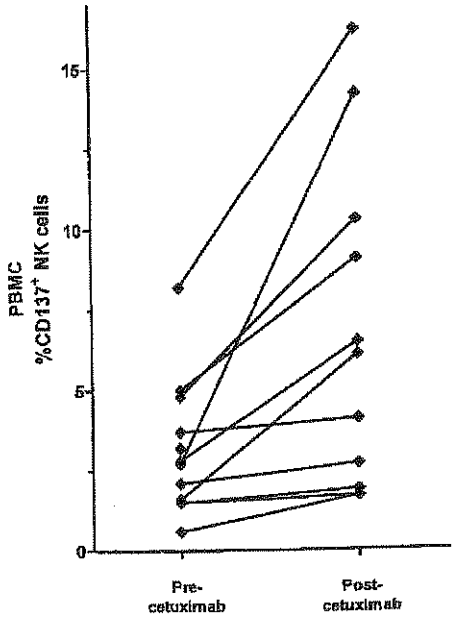

Tumor size (mm²)
1400
1200
1000
800
600
400
200
0
0
10
20
30
40
50
60
Days after tumor inoculation
*
*

FIGURE 21

A


SCC Head and Neck
Cetuximab Infusion
Time –X
(0-72 hours prior)
Time +X
(24-72 hours post)

B


PBMC
%CD137+ NK cells
15
10
5
0
Pre-
cetuximab
Post-
cetuximab