Figure 1

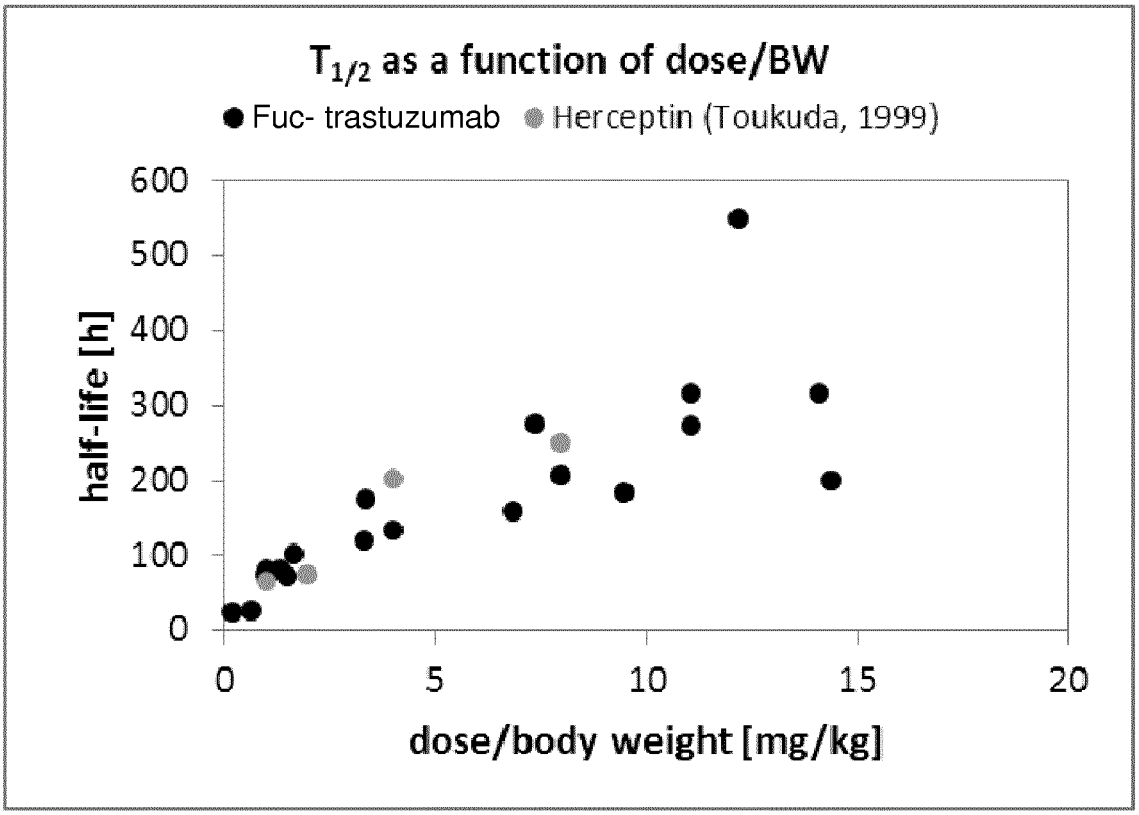
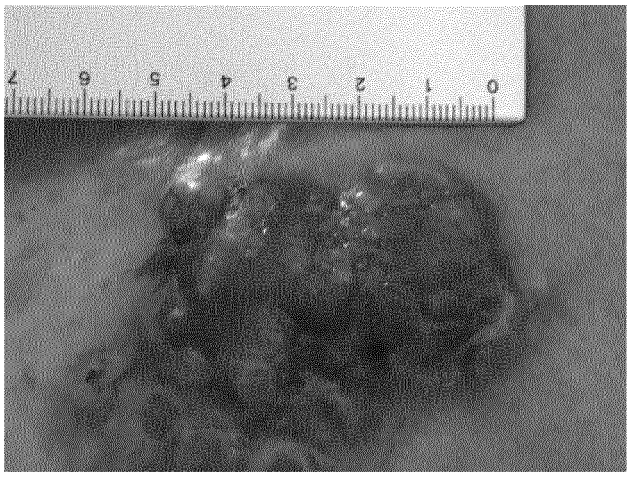
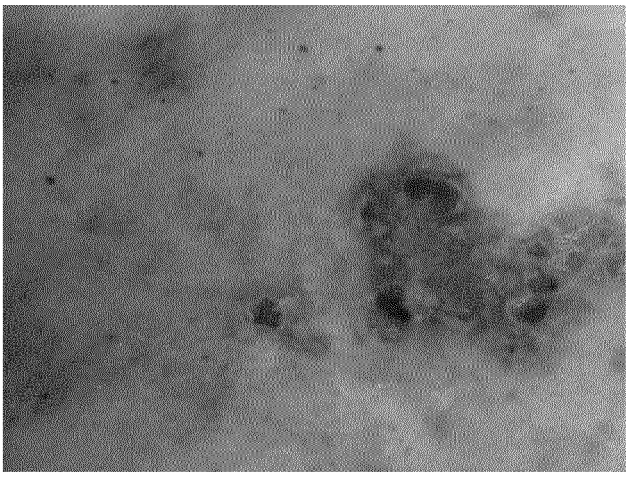

$T_{1/2}$ as a function of dose/BW
Fuc- trastuzumab
Herceptin (Toukuda, 1999)
half-life [h]
600
500
400
300
200
100
0
0
5
10
15
20
dose/body weight [mg/kg]

Figure 2

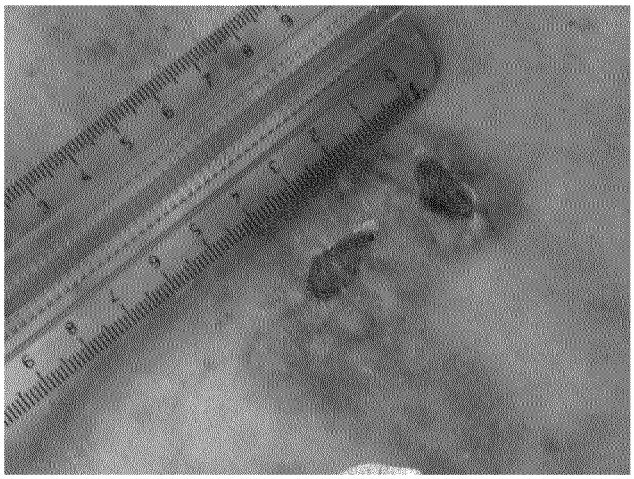
A



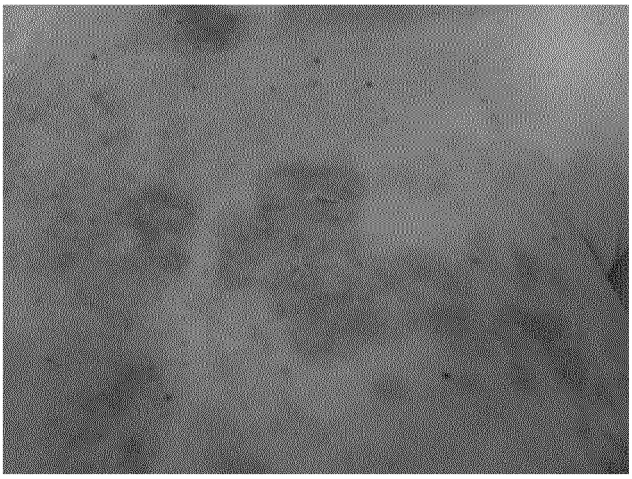
B



C



D



E

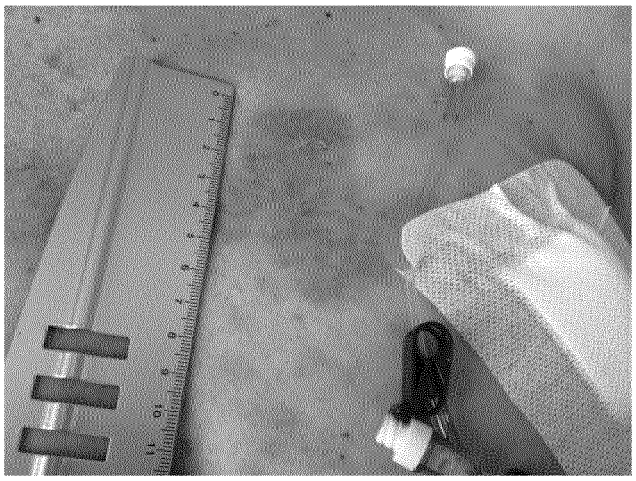


Figure 3

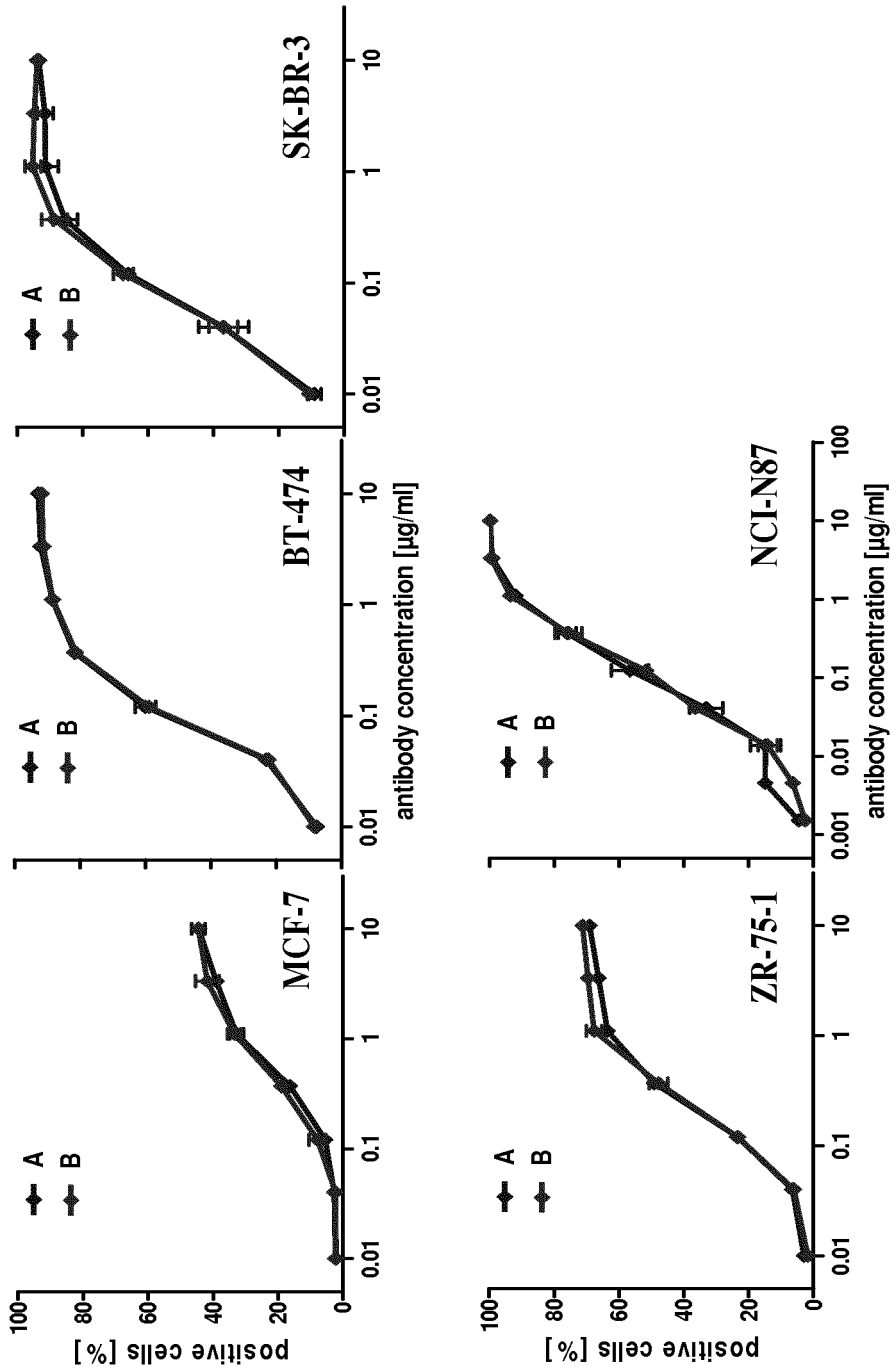

positive cells [%]
antibody concentration [µg/ml]
A
B
MCF-7
BT-474
SK-BR-3
ZR-75-1
NCI-N87

Figure 4

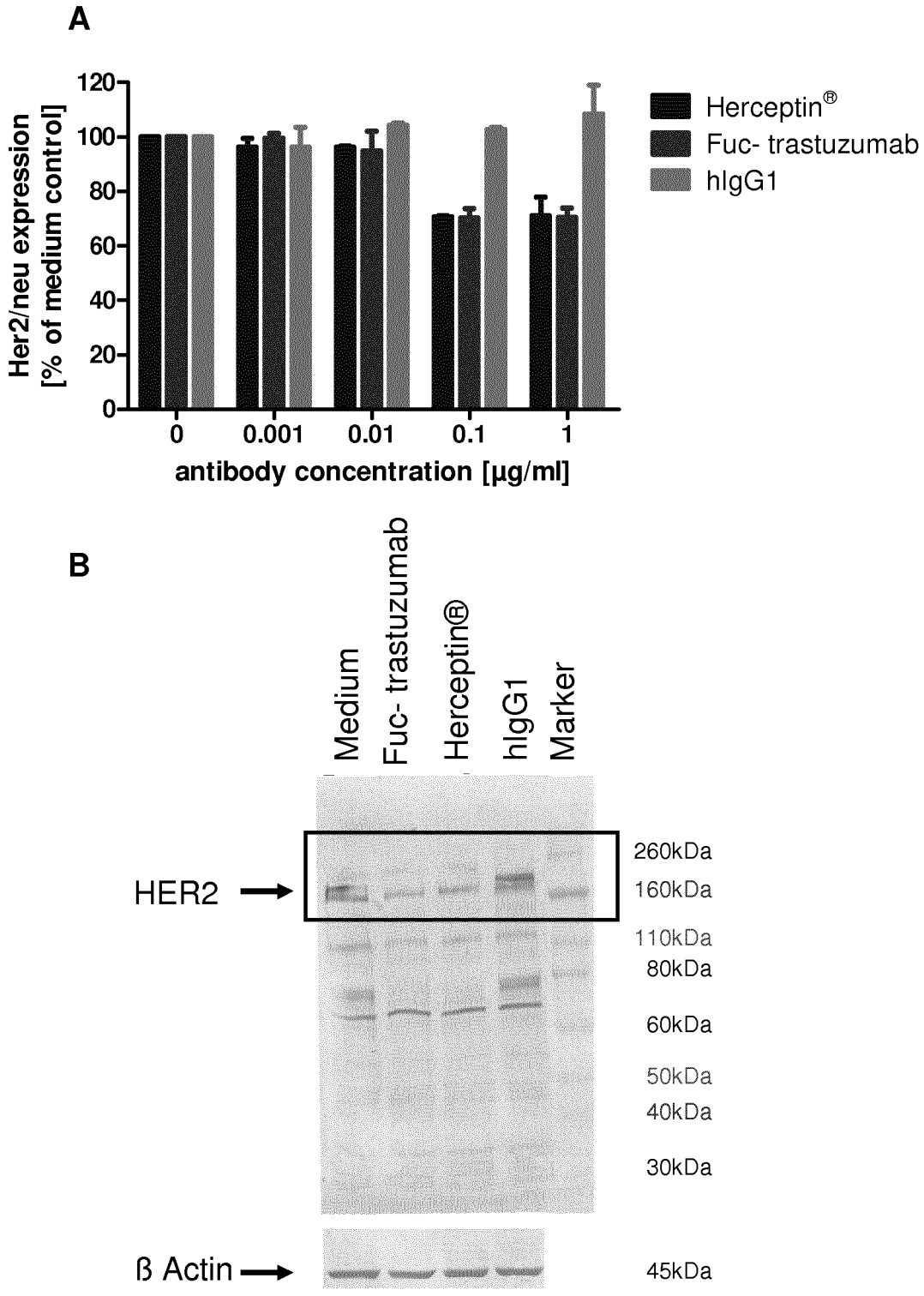

A
Her2/neu expression [% of medium control]
120
100
80
60
40
20
0
0
0.001
0.01
0.1
1
antibody concentration [µg/ml]
Herceptin®
Fuc- trastuzumab
hIgG1
B
Medium
Fuc- trastuzumab
Herceptin®
hIgG1
Marker
HER2
ß Actin
260kDa
160kDa
110kDa
80kDa
60kDa
50kDa
40kDa
30kDa
45kDa

Figure 5

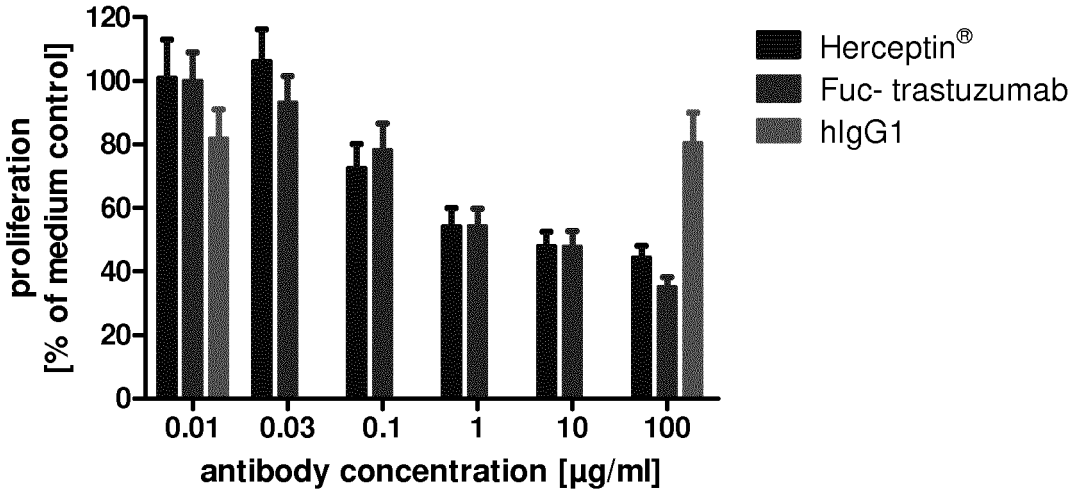

proliferation
[% of medium control]
120
100
80
60
40
20
0
0.01
0.03
0.1
1
10
100
antibody concentration [µg/ml]
Herceptin®
Fuc- trastuzumab
hIgG1

Figure 6

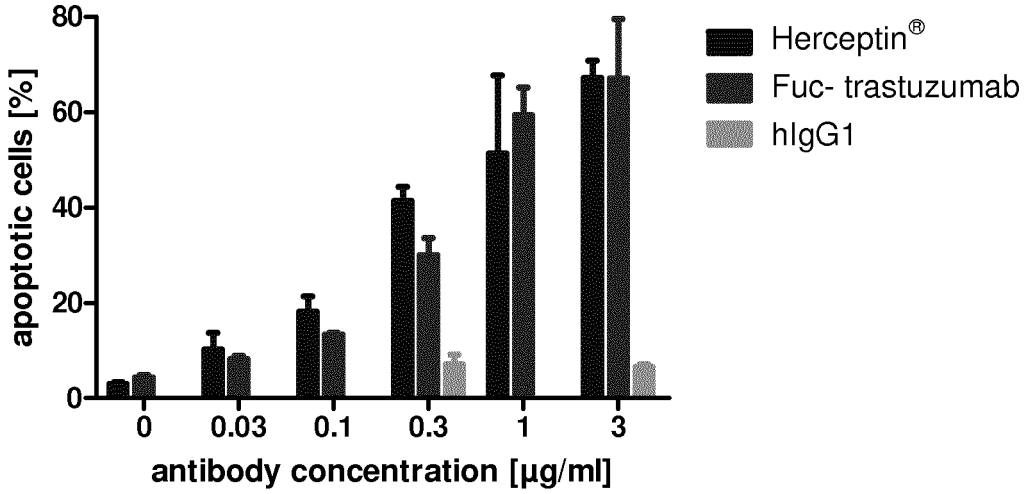

80
60
40
20
0
apoptotic cells [%]
0
0.03
0.1
0.3
1
3
antibody concentration [µg/ml]
Herceptin®
Fuc- trastuzumab
hIgG1

Figure 7

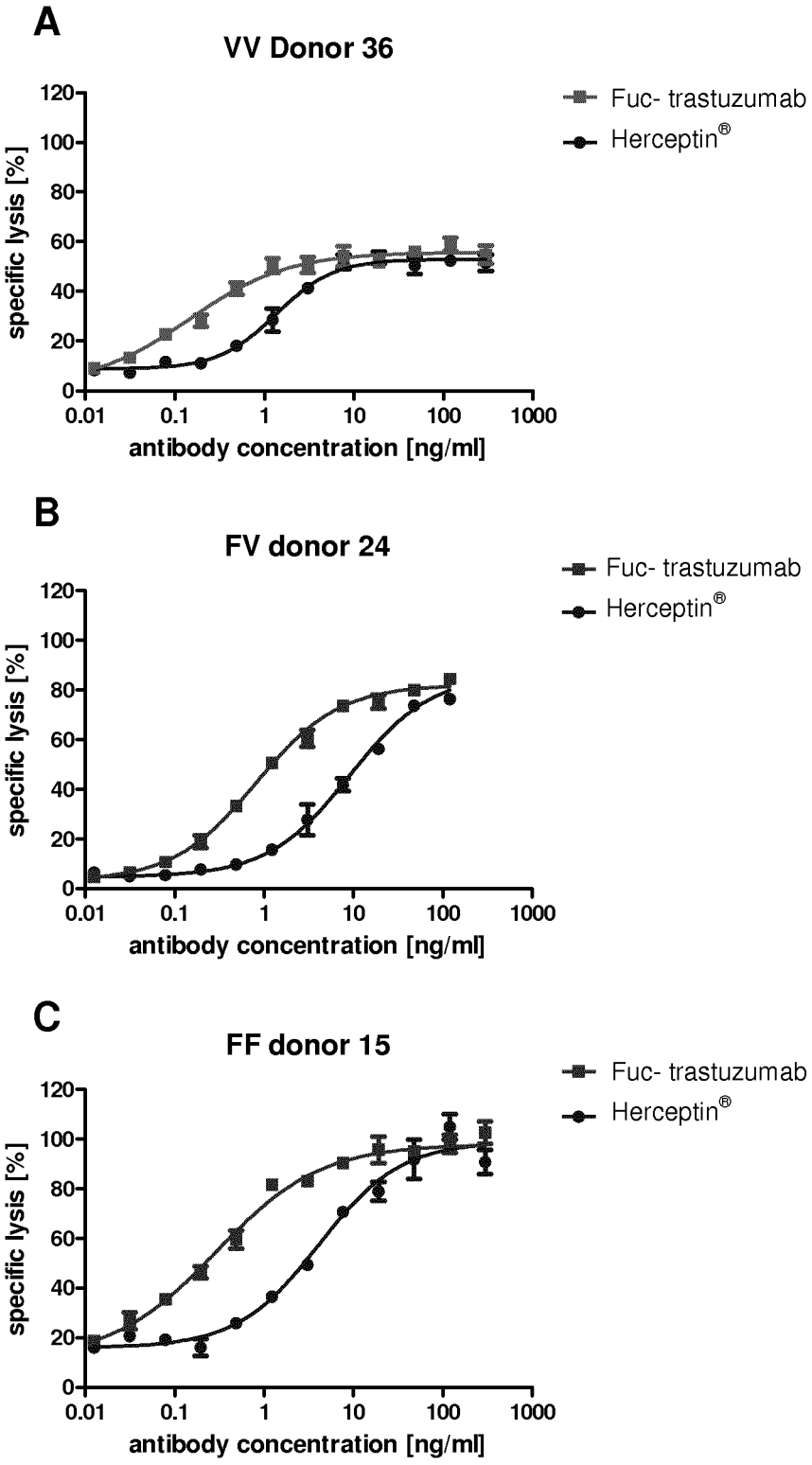

A
VV Donor 36
Fuc- trastuzumab
Herceptin®
specific lysis [%]
antibody concentration [ng/ml]
B
FV donor 24
Fuc- trastuzumab
Herceptin®
specific lysis [%]
antibody concentration [ng/ml]
C
FF donor 15
Fuc- trastuzumab
Herceptin®
specific lysis [%]
antibody concentration [ng/ml]

Figure 8

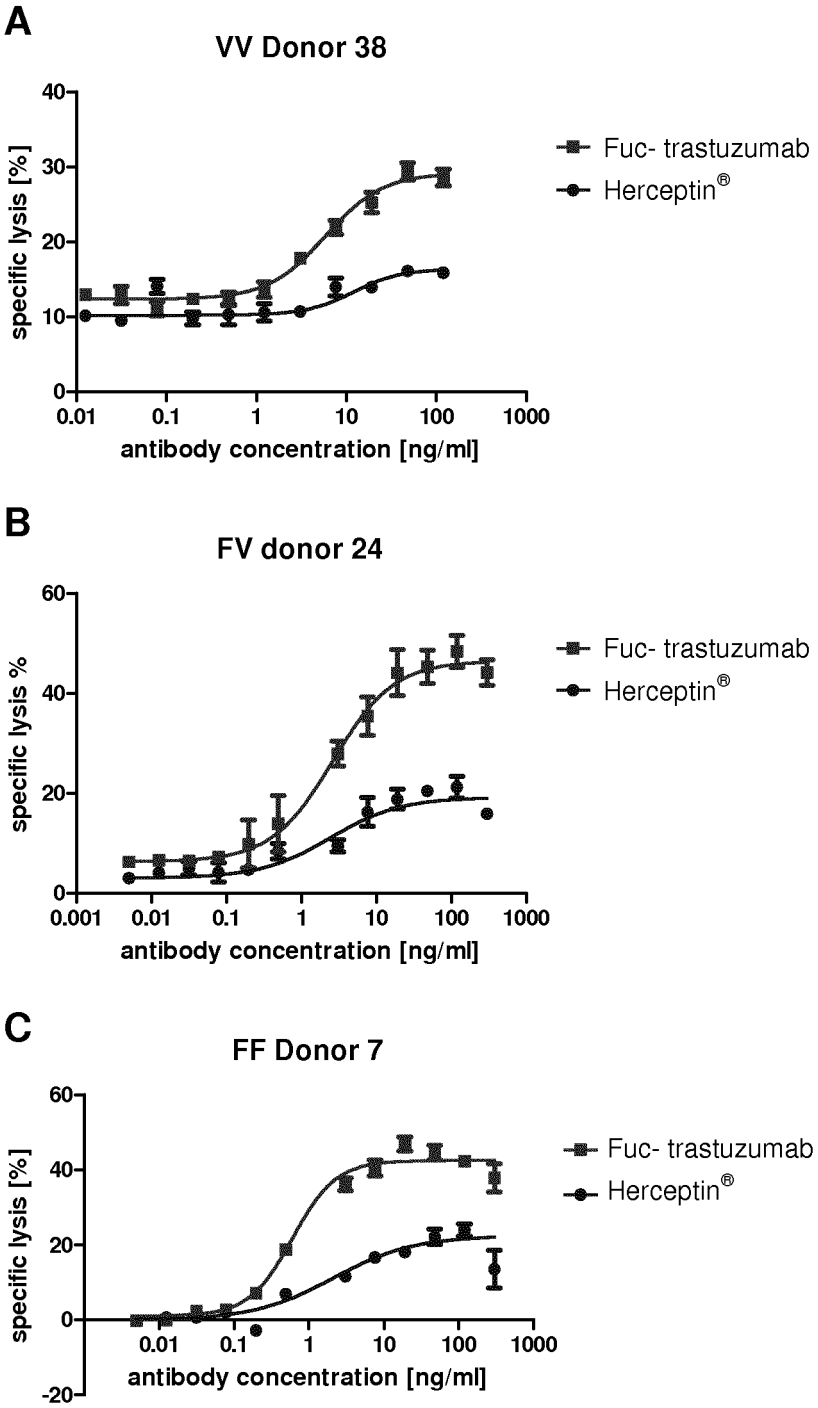

A
VV Donor 38
specific lysis [%]
40
30
20
10
0
0.01
0.1
1
10
100
1000
antibody concentration [ng/ml]
Fuc- trastuzumab
Herceptin®
B
FV donor 24
specific lysis %
60
40
20
0
0.001
0.01
0.1
1
10
100
1000
antibody concentration [ng/ml]
Fuc- trastuzumab
Herceptin®
C
FF Donor 7
specific lysis [%]
60
40
20
0
-20
0.01
0.1
1
10
100
1000
antibody concentration [ng/ml]
Fuc- trastuzumab
Herceptin®

Figure 9

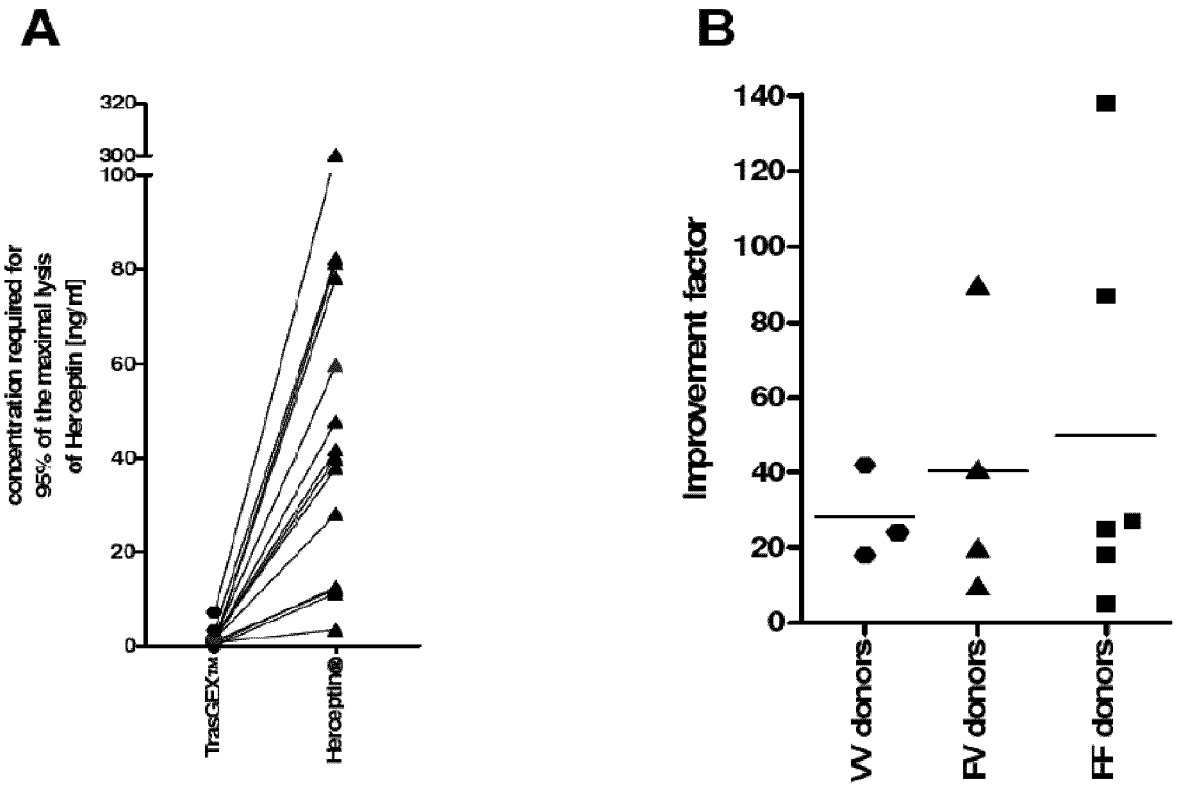

A
320
300
100
80
60
40
20
0
concentration required for 95% of the maximal lysis of Herceptin [ng/ml]
TrasGEX™
Herceptin®
B
140
120
100
80
60
40
20
0
Improvement factor
VV donors
FV donors
FF donors

Figure 10

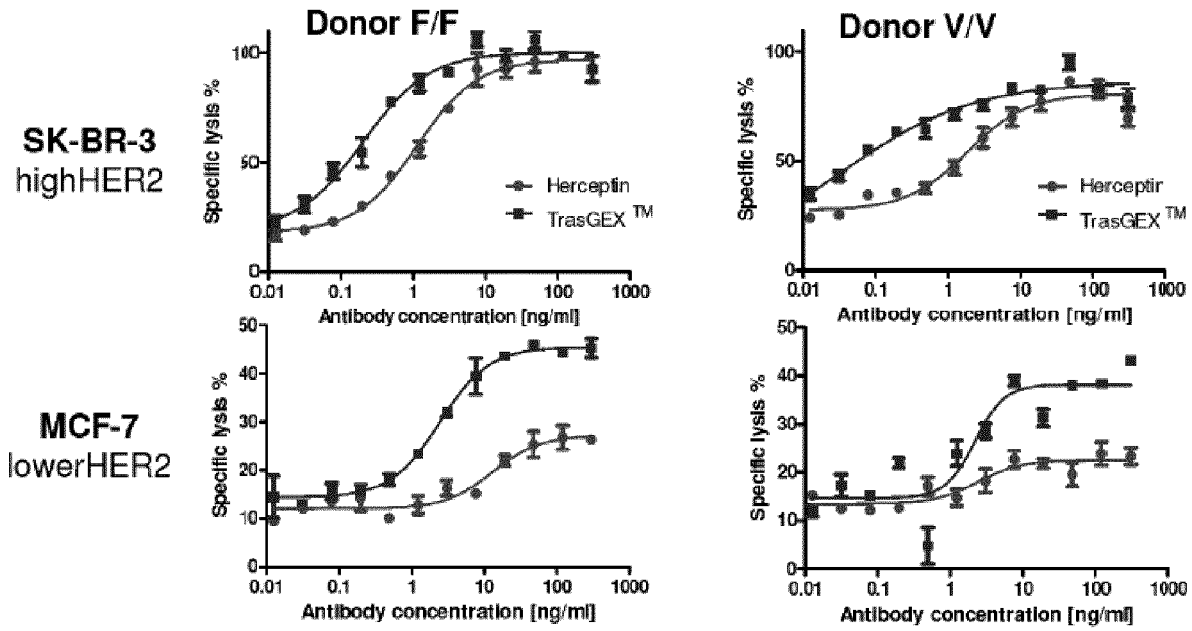


Figure 11

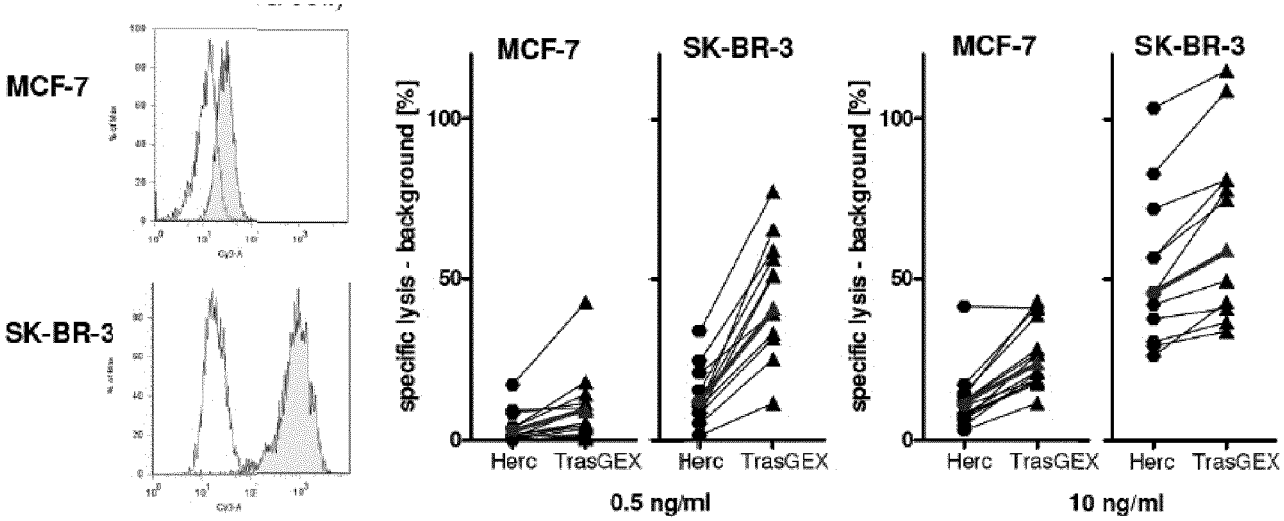


Figure 12

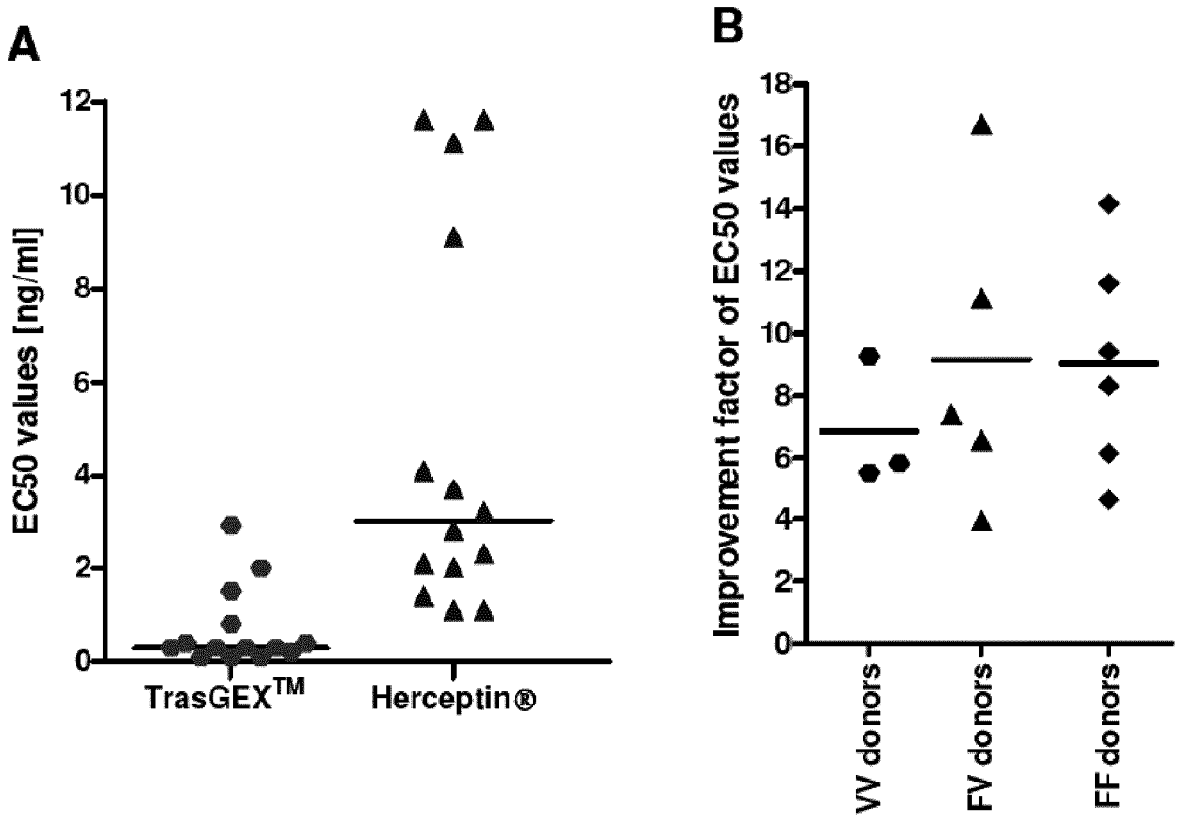
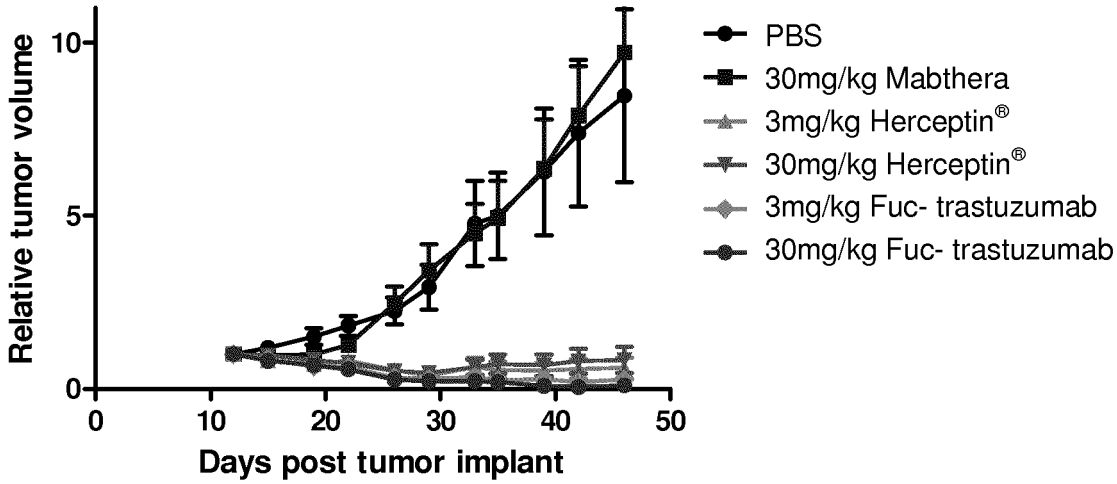

A
EC50 values [ng/ml]
12
10
8
6
4
2
0
TrasGEX™
Herceptin®
B
Improvement factor of EC50 values
18
16
14
12
10
8
6
4
2
0
VV donors
FV donors
FF donors

Figure 13

A


Relative tumor volume
10
5
0
0
10
20
30
40
50
Days post tumor implant
PBS
30mg/kg Mabthera
3mg/kg Herceptin®
30mg/kg Herceptin®
3mg/kg Fuc- trastuzumab
30mg/kg Fuc- trastuzumab

B

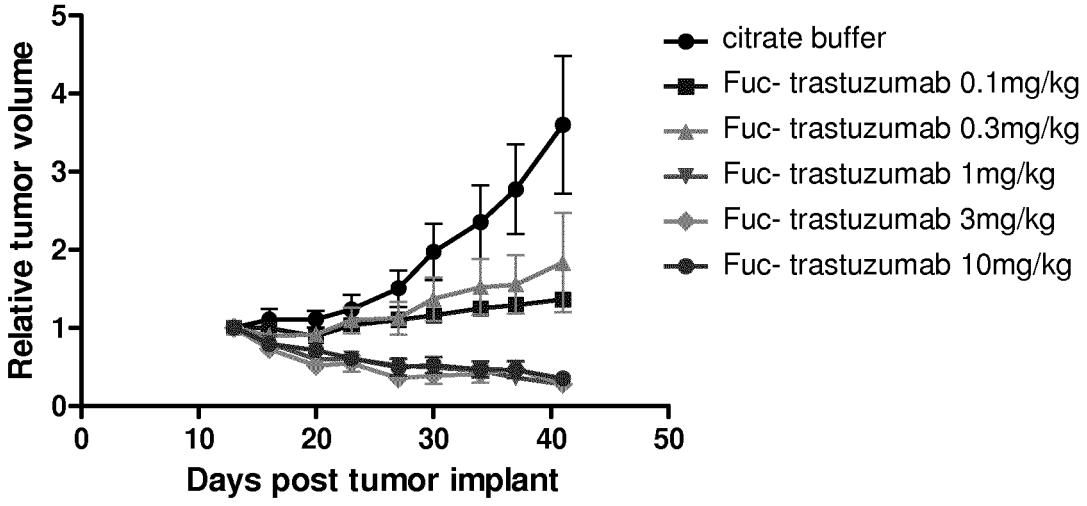

Relative tumor volume
5
4
3
2
1
0
0
10
20
30
40
50
Days post tumor implant
citrate buffer
Fuc- trastuzumab 0.1mg/kg
Fuc- trastuzumab 0.3mg/kg
Fuc- trastuzumab 1mg/kg
Fuc- trastuzumab 3mg/kg
Fuc- trastuzumab 10mg/kg

Figure 14

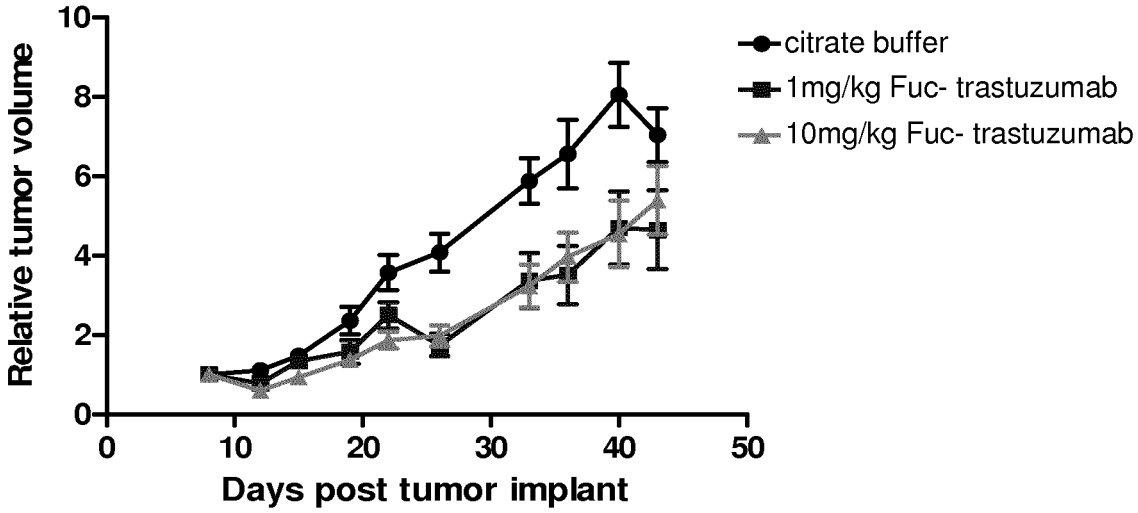
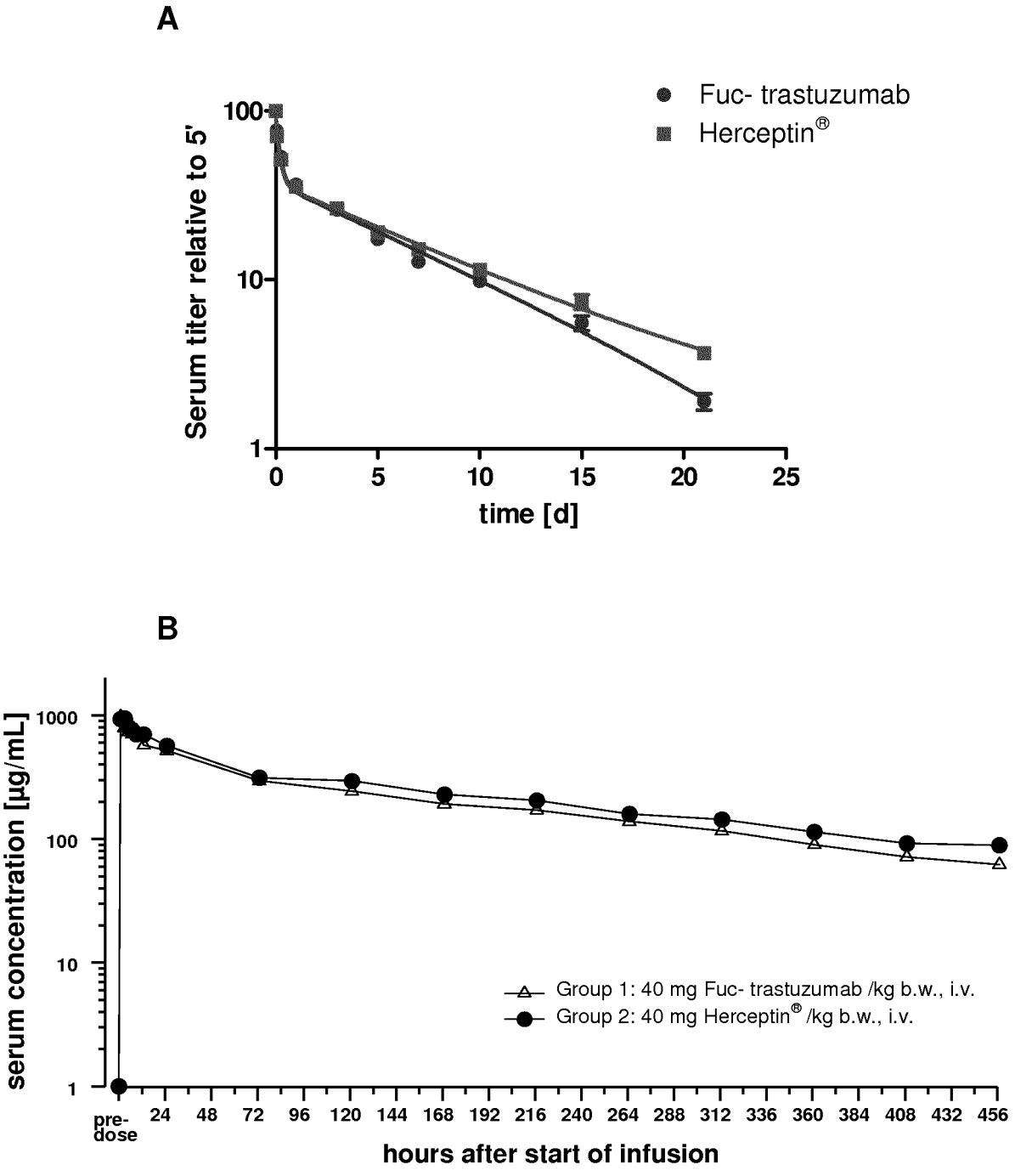

Relative tumor volume
10
8
6
4
2
0
0
10
20
30
40
50
Days post tumor implant
citrate buffer
1mg/kg Fuc- trastuzumab
10mg/kg Fuc- trastuzumab

Figure 15


A
Fuc- trastuzumab
Herceptin®
Serum titer relative to 5'
100
10
1
0
5
10
15
20
25
time [d]
B
serum concentration [µg/mL]
1000
100
10
1
Group 1: 40 mg Fuc- trastuzumab /kg b.w., i.v.
Group 2: 40 mg Herceptin® /kg b.w., i.v.
pre-dose
24
48
72
96
120
144
168
192
216
240
264
288
312
336
360
384
408
432
456
hours after start of infusion