FIGURE I

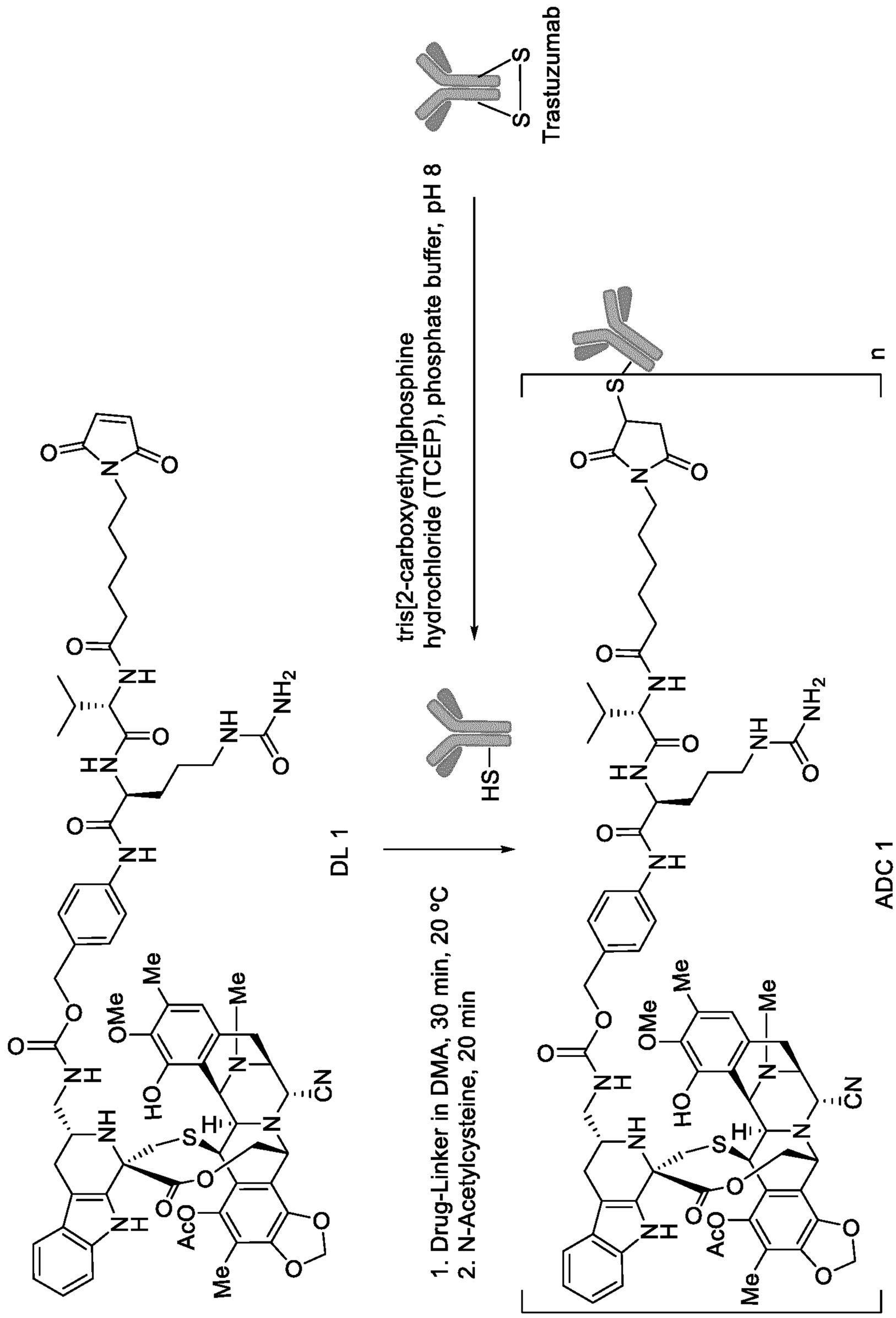

Trastuzumab
S
S
tris[2-carboxyethyl]phosphine
hydrochloride (TCEP), phosphate buffer, pH 8
n
DL 1
HS
1. Drug-Linker in DMA, 30 min, 20 °C
2. N-Acetylcysteine, 20 min
ADC 1

FIGURE 2

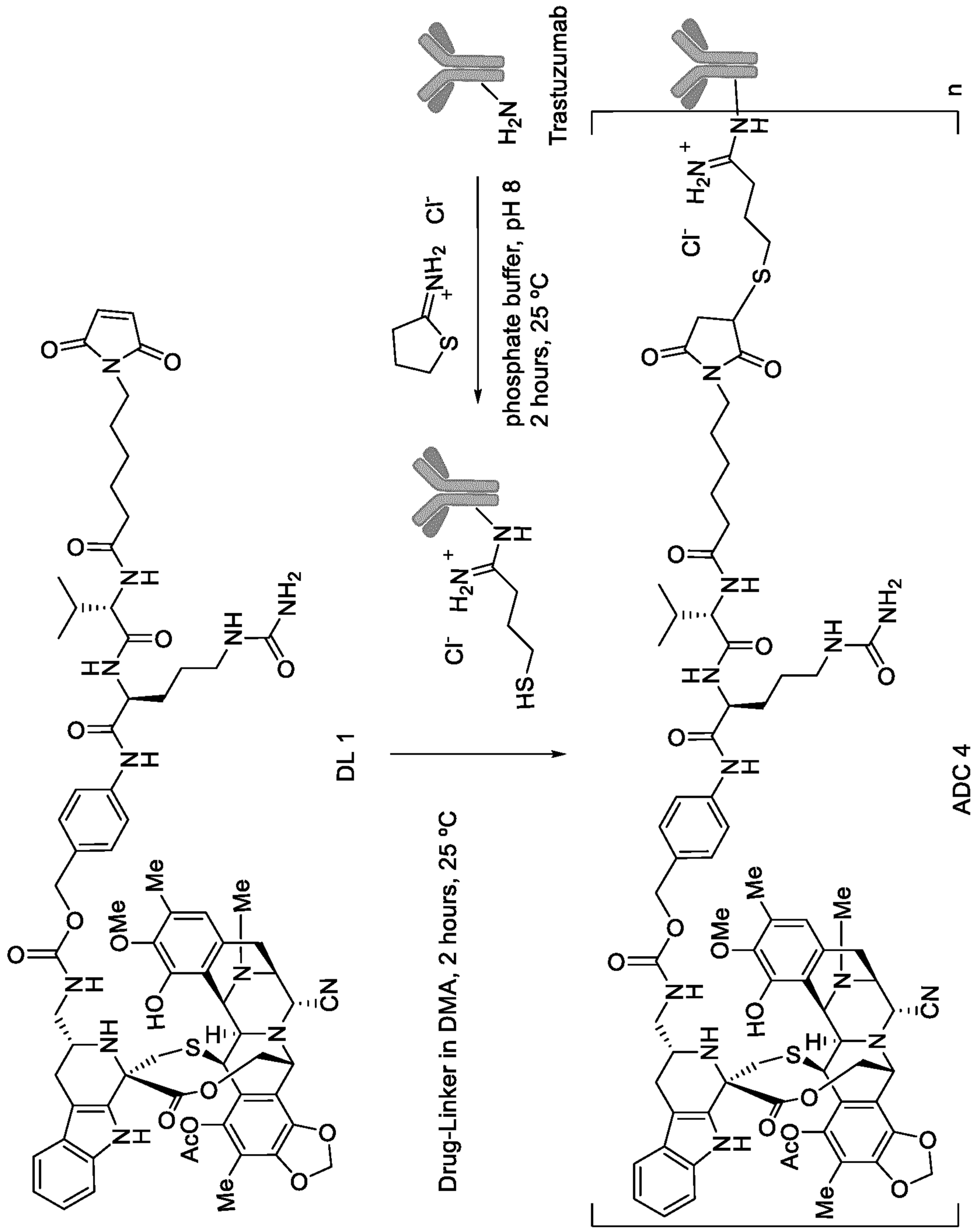

Trastuzumab
H_2N
n
DL 1
phosphate buffer, pH 8
2 hours, 25 °C
Drug-Linker in DMA, 2 hours, 25 °C
ADC 4

FIGURE 3

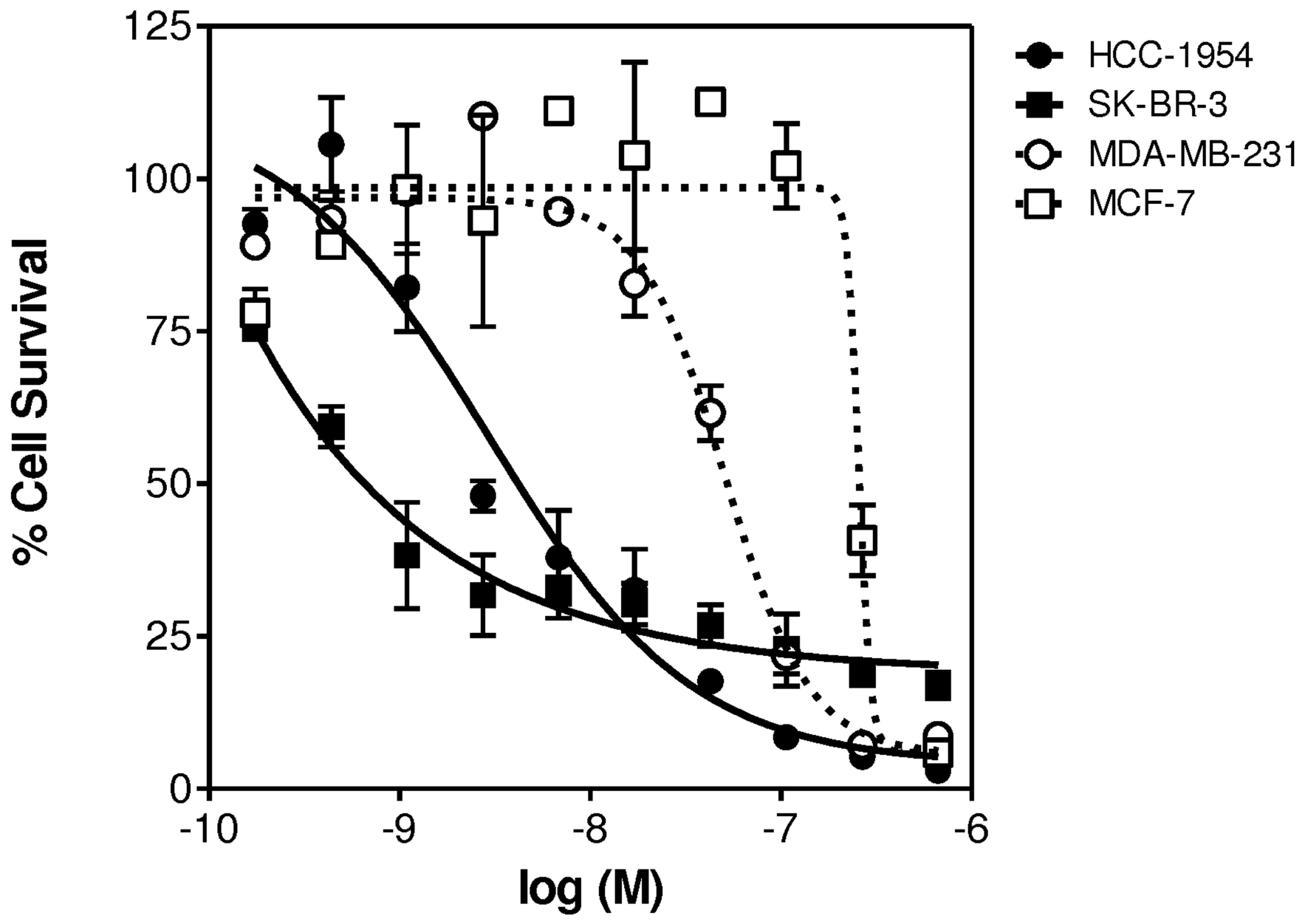
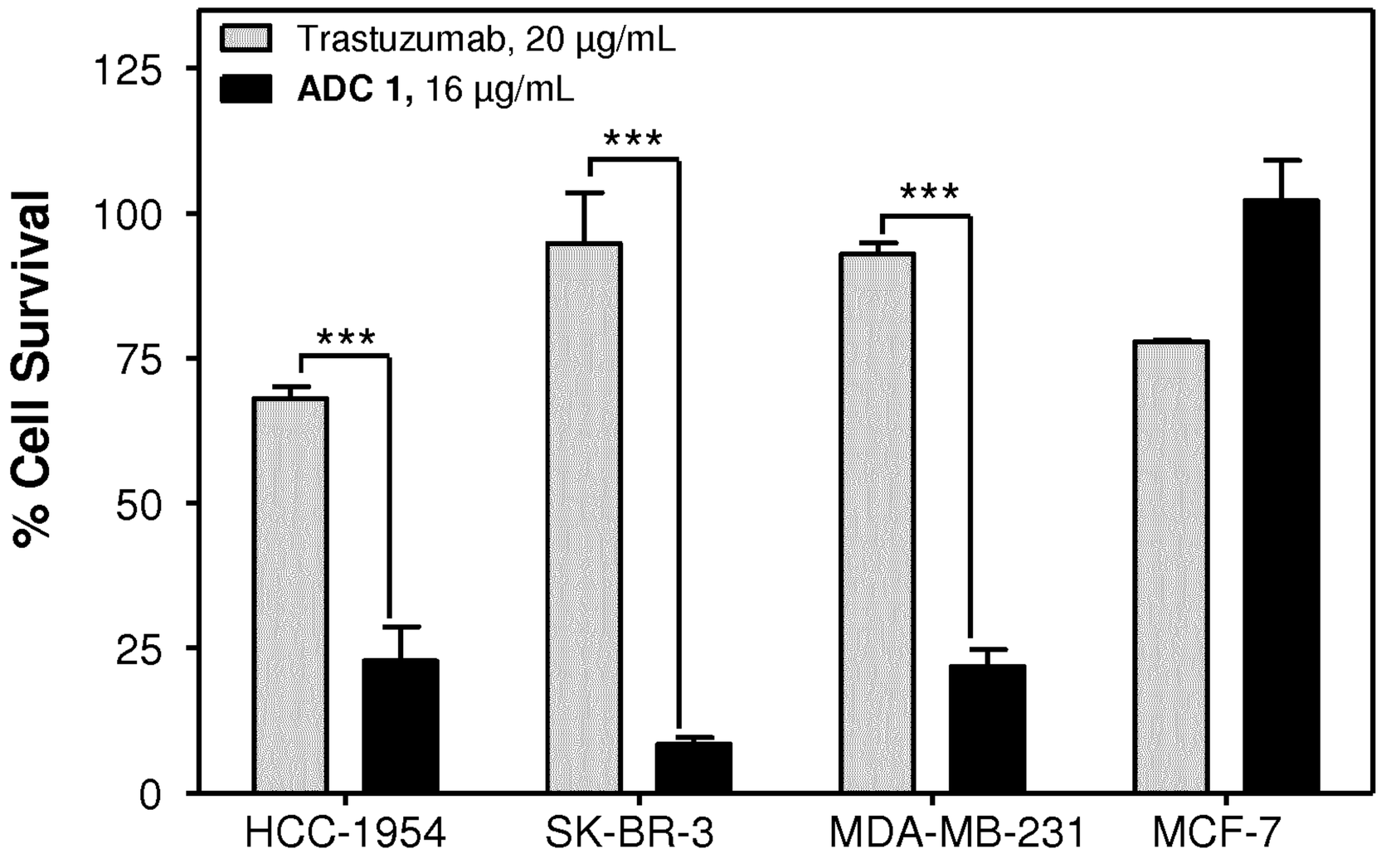

125
100
75
50
25
0
% Cell Survival
-10
-9
-8
-7
-6
log (M)
HCC-1954
SK-BR-3
MDA-MB-231
MCF-7

FIGURE 4


Trastuzumab, 20 µg/mL
ADC 1, 16 µg/mL
% Cell Survival
125
100
75
50
25
0
***
***
***
HCC-1954
SK-BR-3
MDA-MB-231
MCF-7

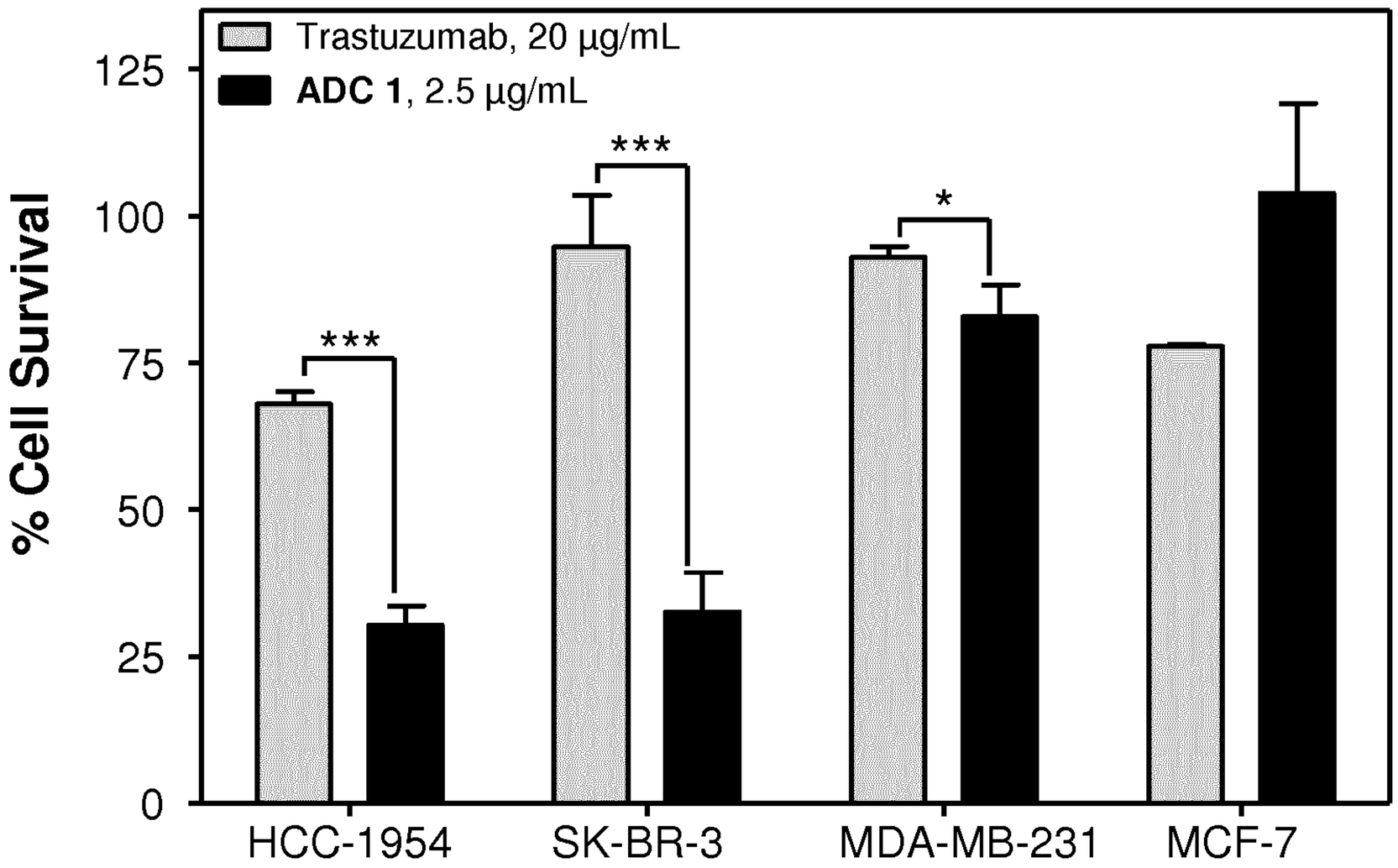

Trastuzumab, 20 µg/mL
ADC 1, 2.5 µg/mL
% Cell Survival
125
100
75
50
25
0
***
***
*
HCC-1954
SK-BR-3
MDA-MB-231
MCF-7

FIGURE 5

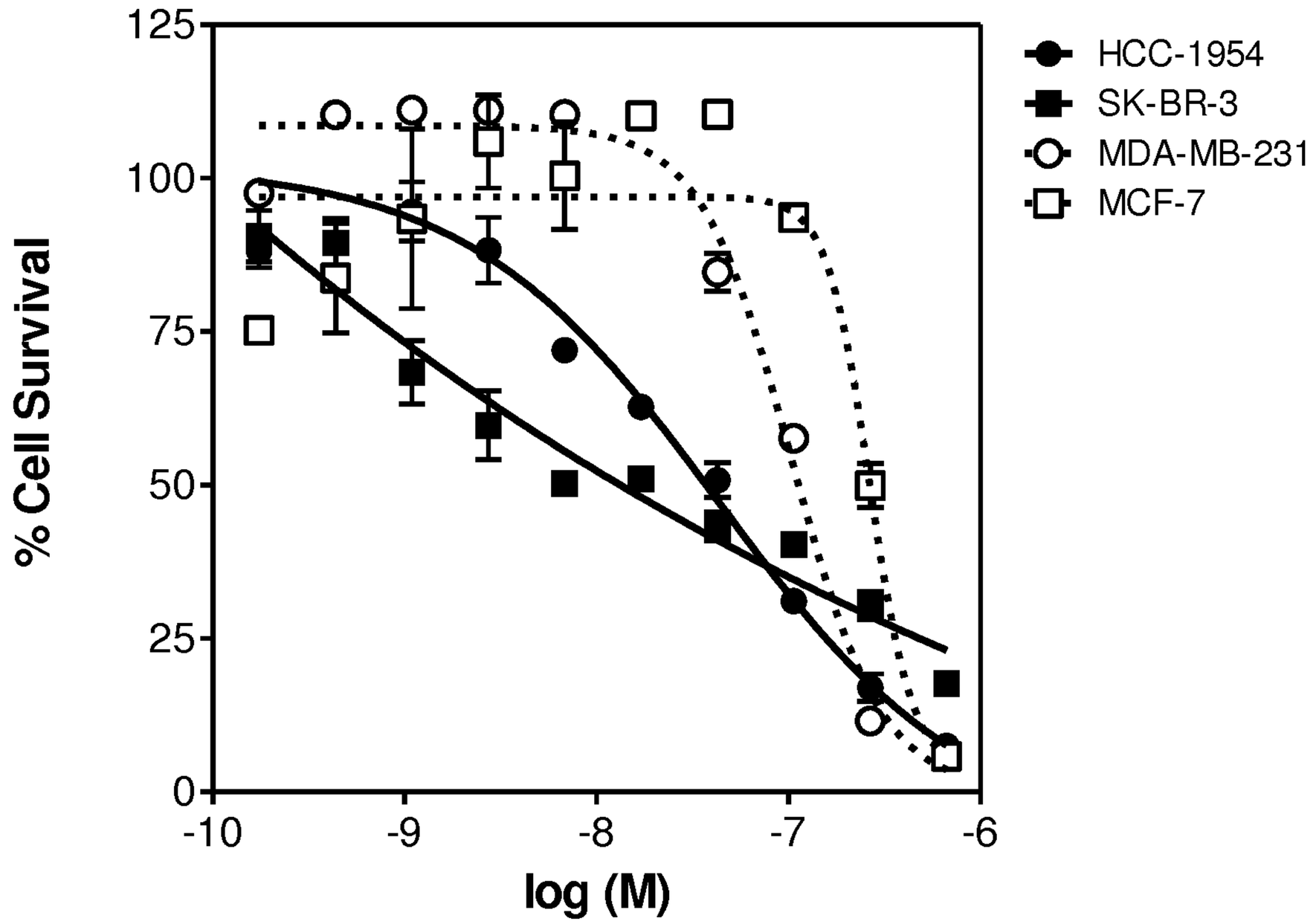

125
100
75
50
25
0
% Cell Survival
-10
-9
-8
-7
-6
log (M)
HCC-1954
SK-BR-3
MDA-MB-231
MCF-7

FIGURE 6

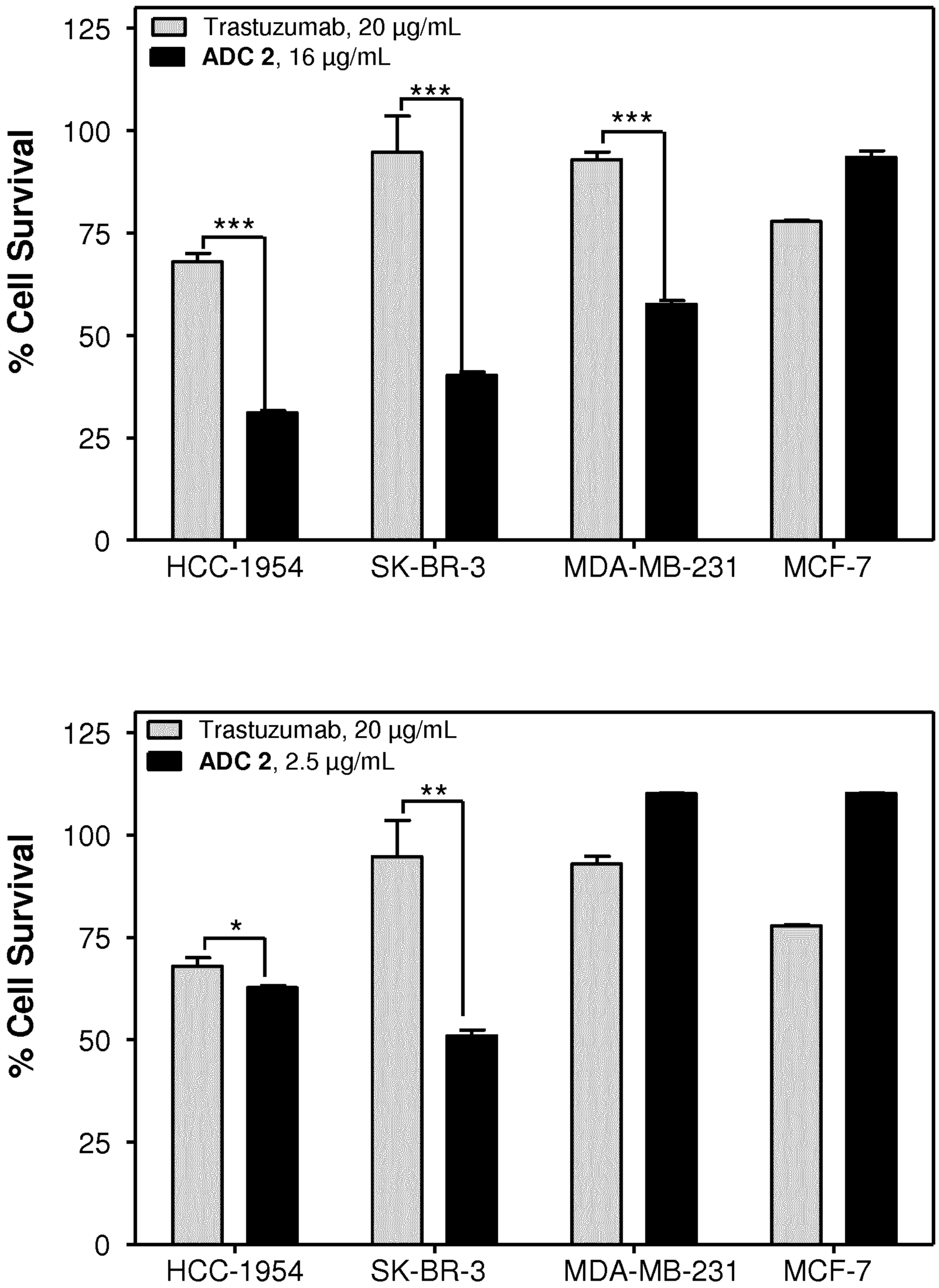

Trastuzumab, 20 µg/mL
ADC 2, 16 µg/mL
% Cell Survival
125
100
75
50
25
0
***
***
***
HCC-1954
SK-BR-3
MDA-MB-231
MCF-7
Trastuzumab, 20 µg/mL
ADC 2, 2.5 µg/mL
*
**
HCC-1954
SK-BR-3
MDA-MB-231
MCF-7

FIGURE 7

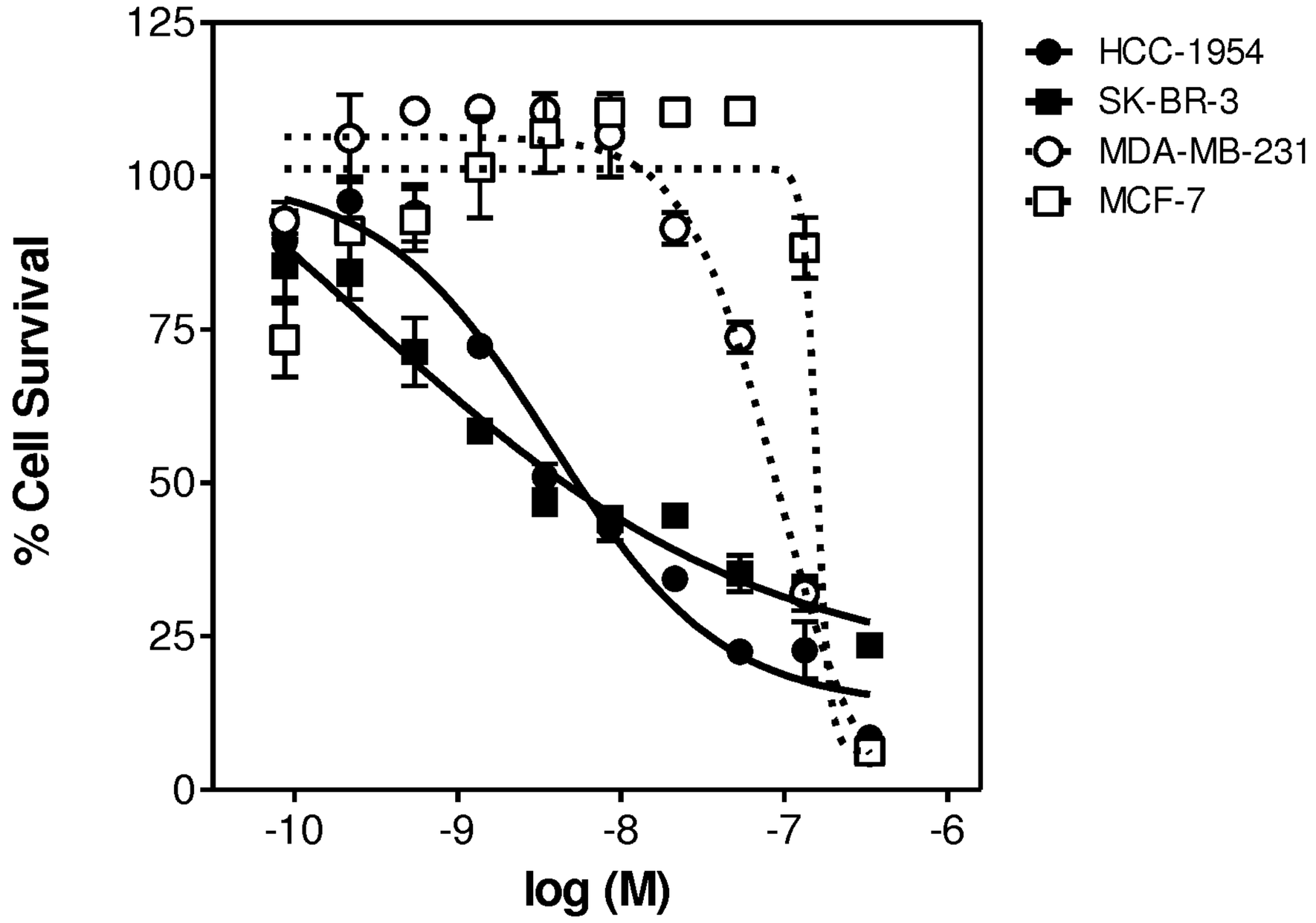
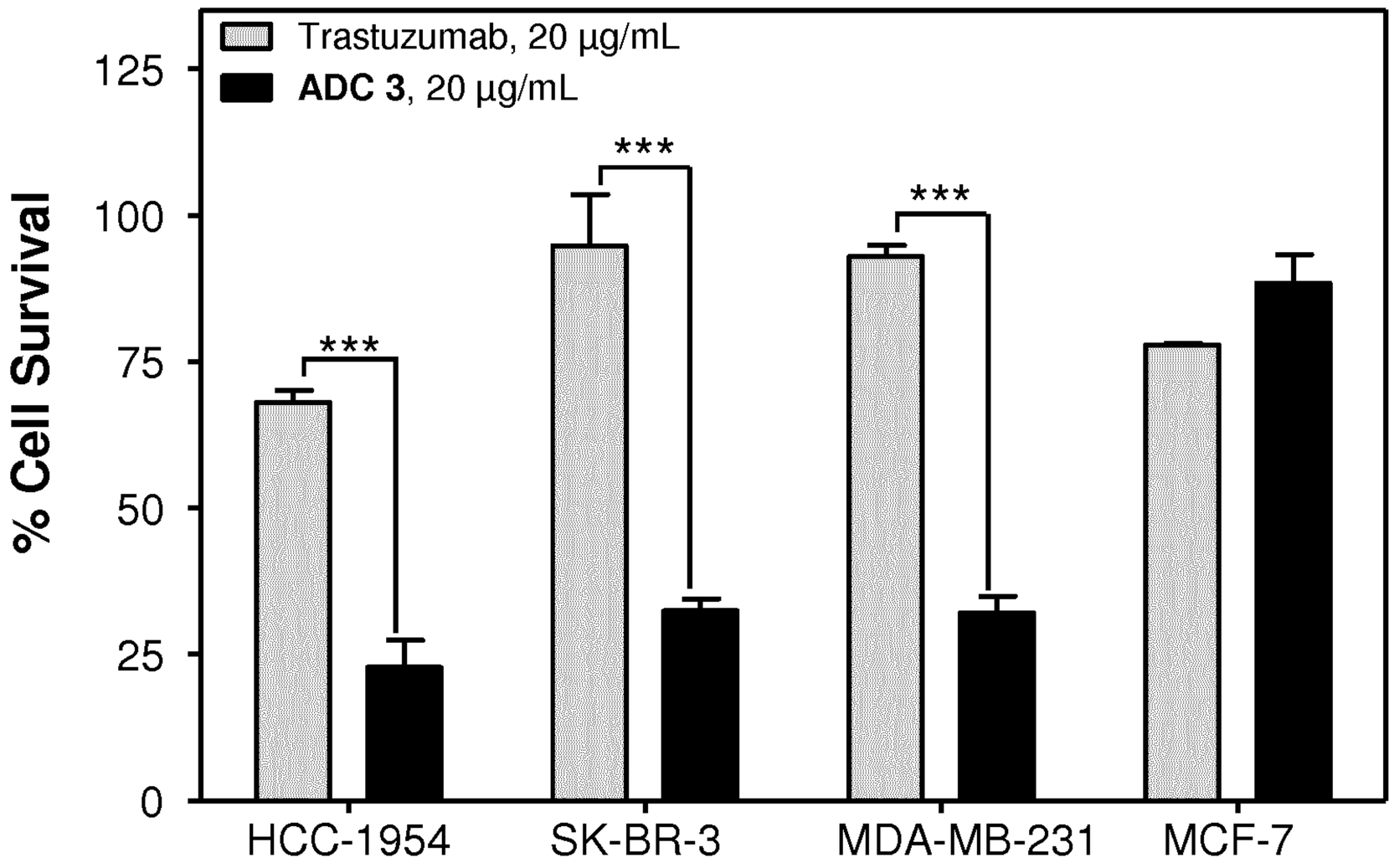

125
100
75
50
25
0
% Cell Survival
-10
-9
-8
-7
-6
log (M)
HCC-1954
SK-BR-3
MDA-MB-231
MCF-7

FIGURE 8


Trastuzumab, 20 µg/mL
ADC 3, 20 µg/mL
% Cell Survival
125
100
75
50
25
0
***
***
***
HCC-1954
SK-BR-3
MDA-MB-231
MCF-7

Trastuzumab, 20 µg/mL
ADC 3, 3 µg/mL
% Cell Survival
125
100
75
50
25
0
***
***
HCC-1954
SK-BR-3
MDA-MB-231
MCF-7

FIGURE 9

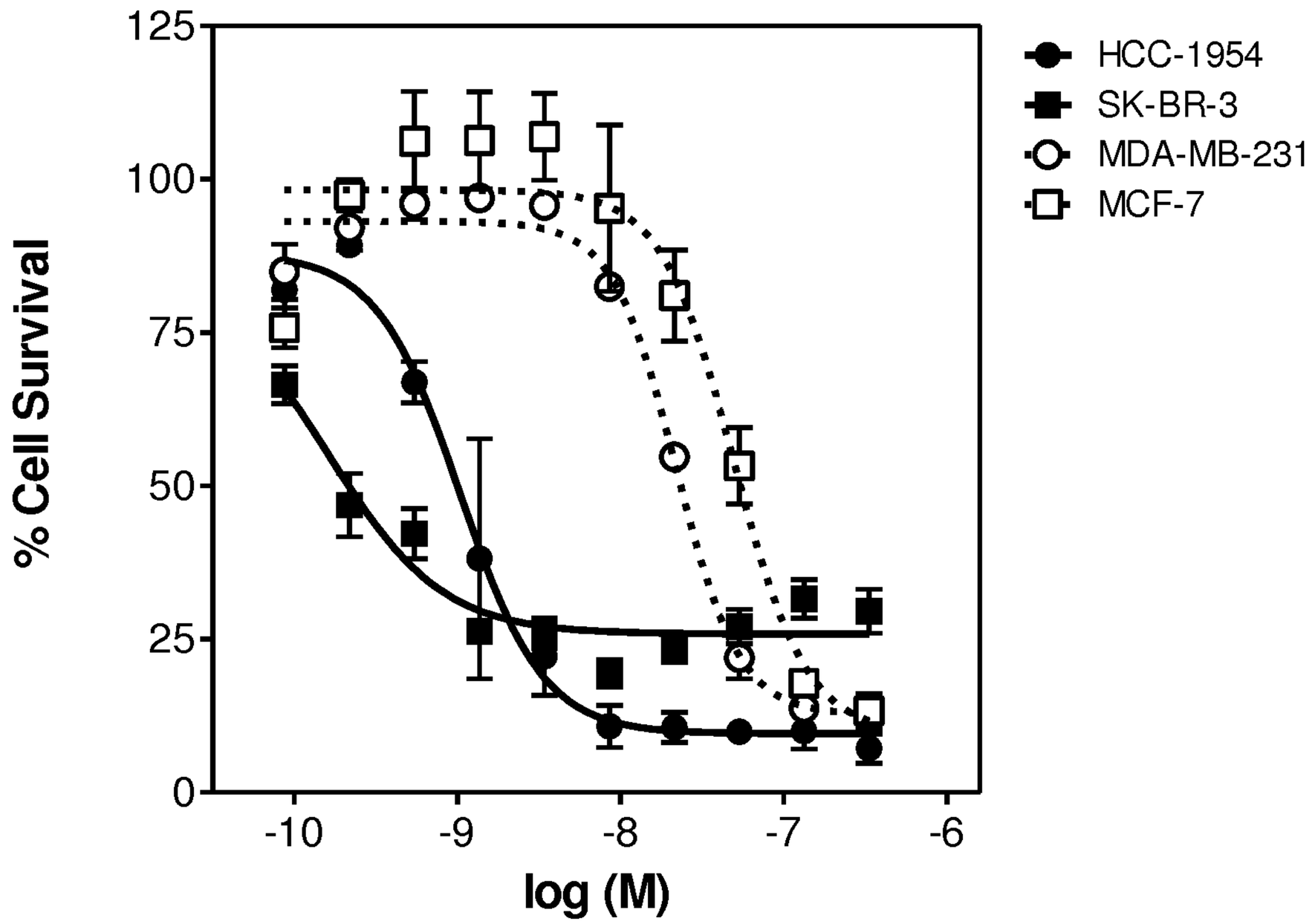
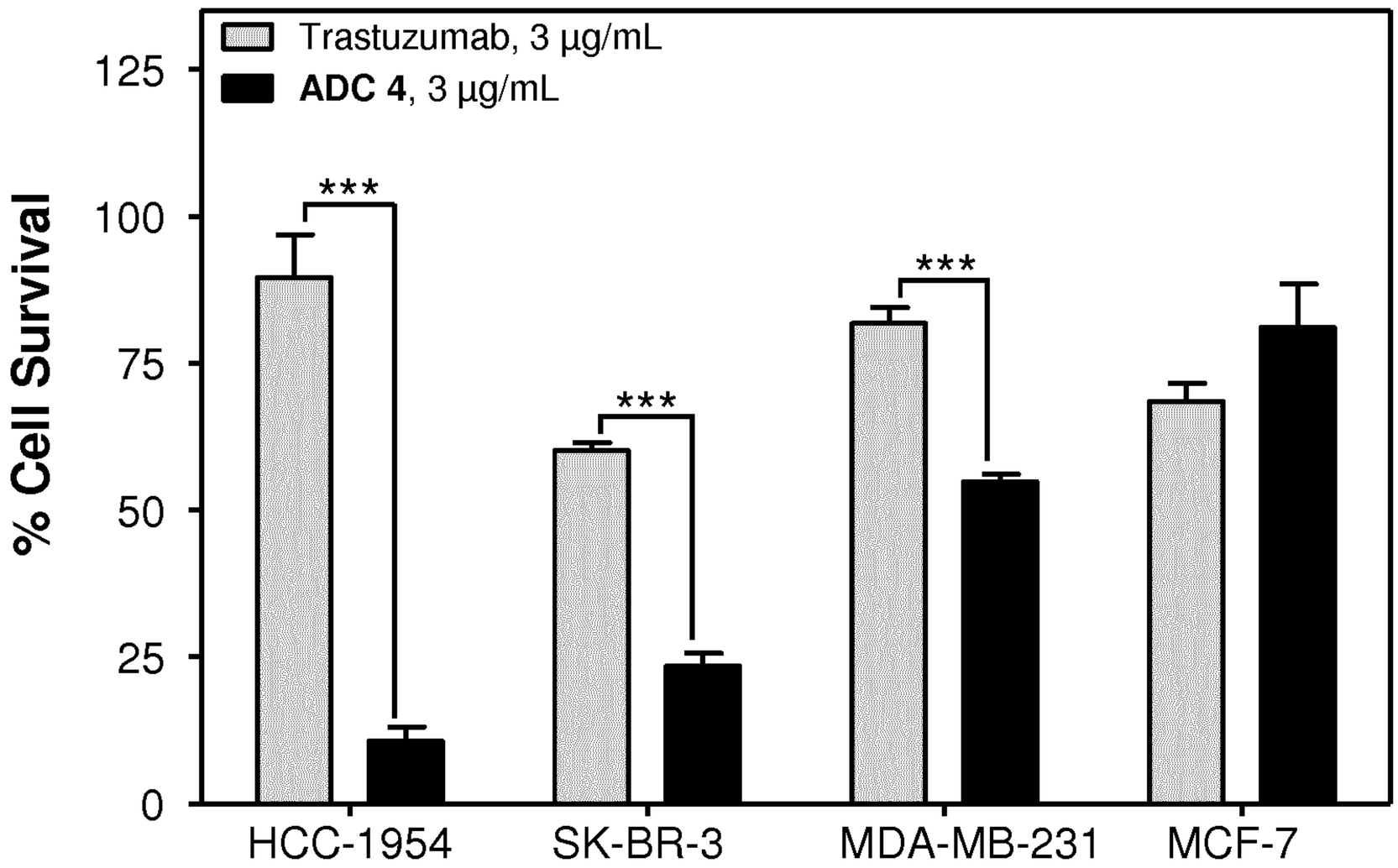

125
100
75
50
25
0
% Cell Survival
-10
-9
-8
-7
-6
log (M)
HCC-1954
SK-BR-3
MDA-MB-231
MCF-7

FIGURE 10


Trastuzumab, 3 µg/mL
ADC 4, 3 µg/mL
% Cell Survival
125
100
75
50
25
0
***
***
***
HCC-1954
SK-BR-3
MDA-MB-231
MCF-7

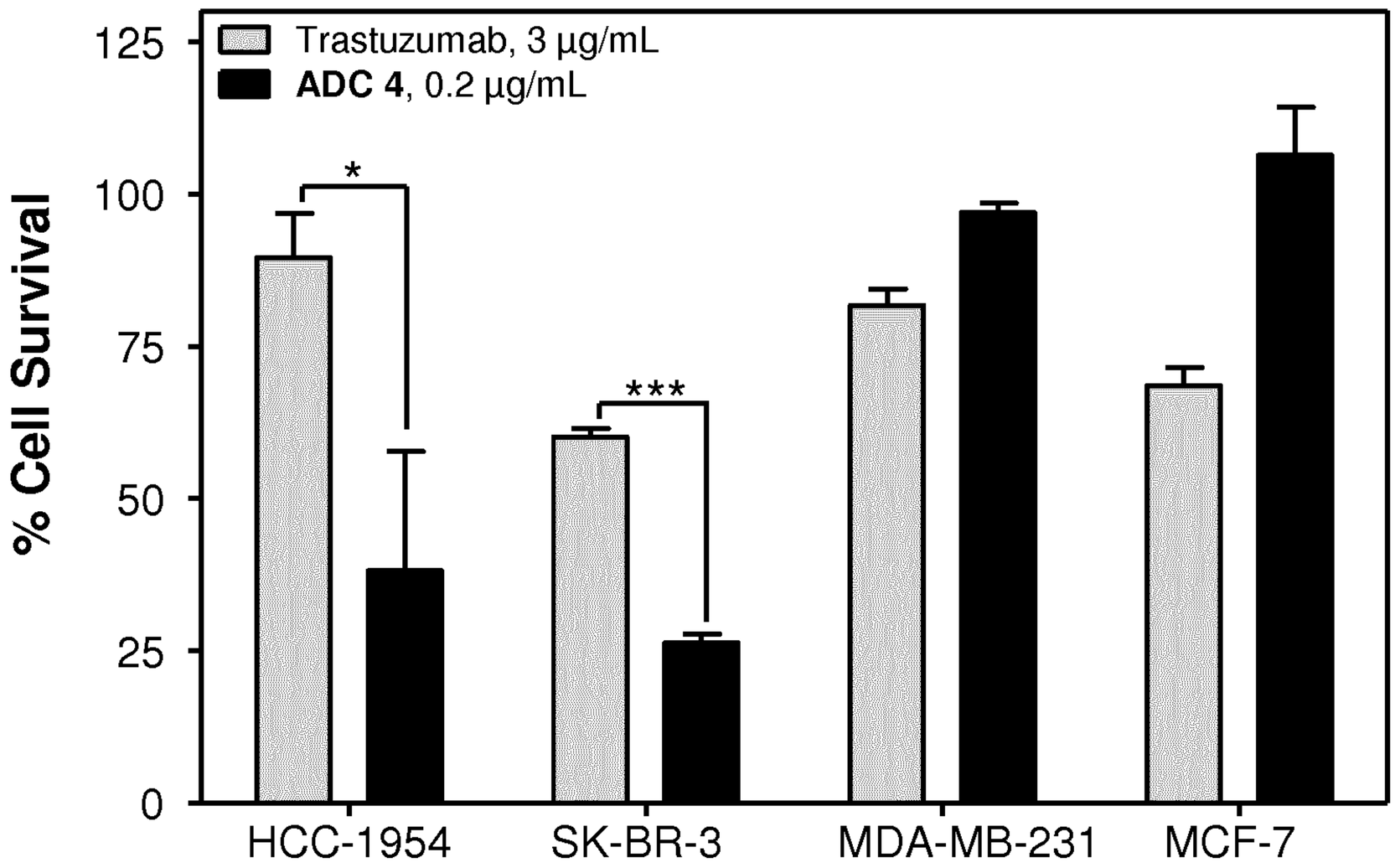

Trastuzumab, 3 µg/mL
ADC 4, 0.2 µg/mL
% Cell Survival
125
100
75
50
25
0
*
***
HCC-1954
SK-BR-3
MDA-MB-231
MCF-7

FIGURE 11

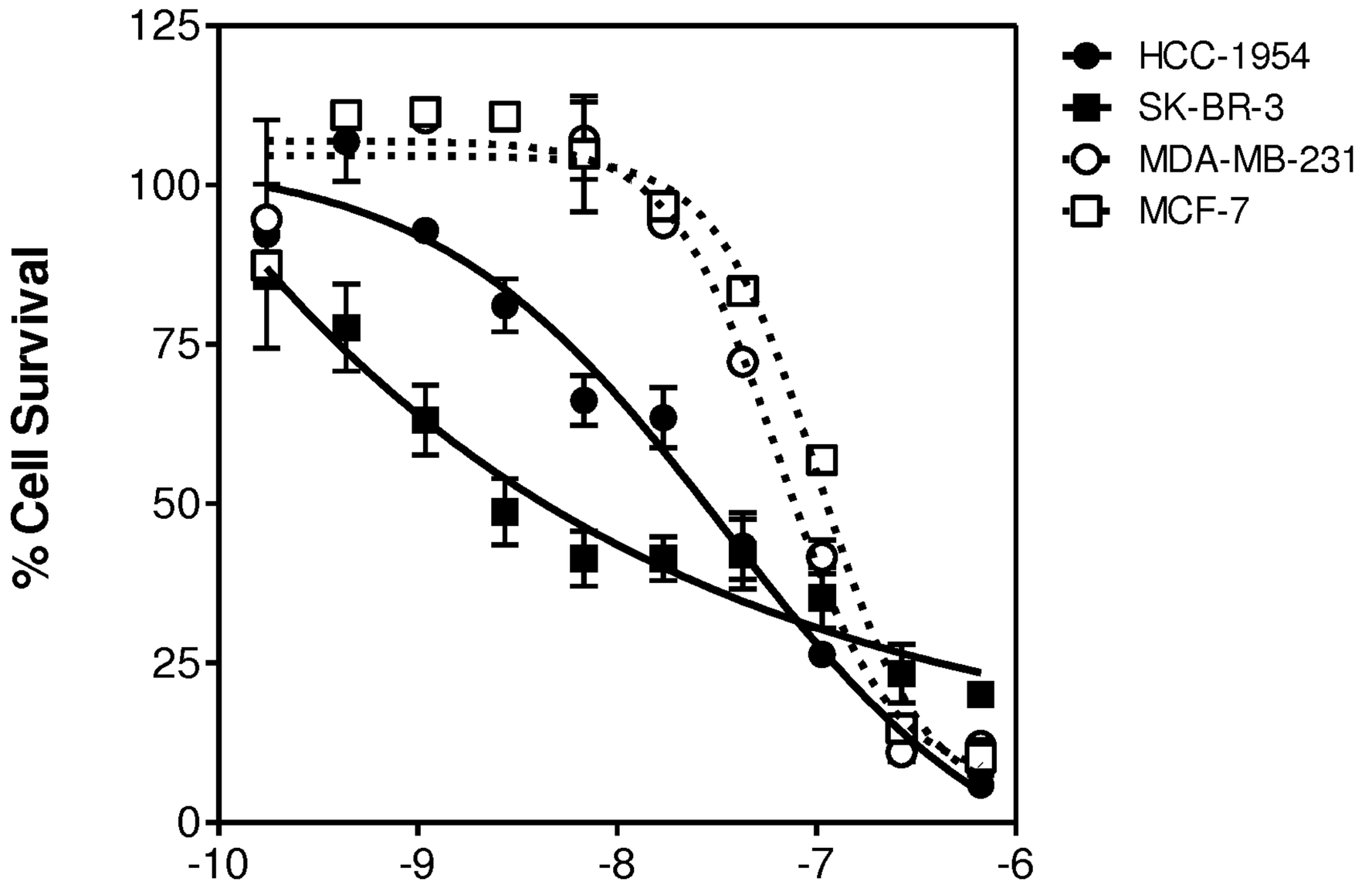


FIGURE 12

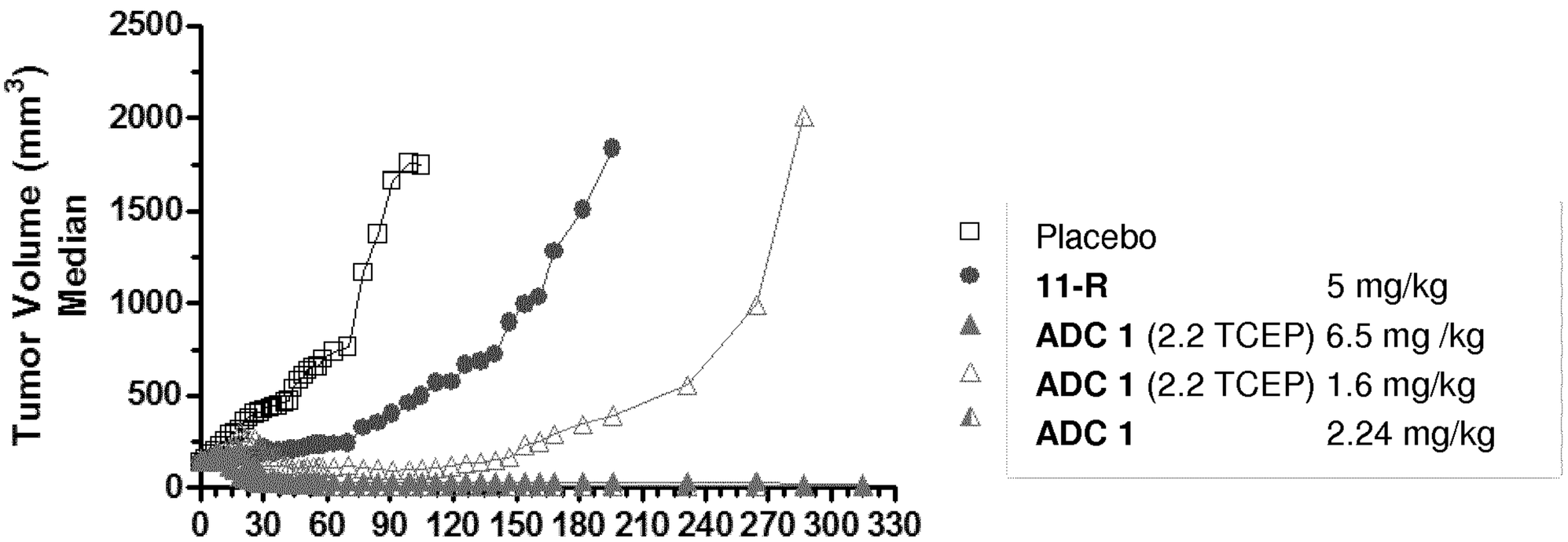


FIGURE 13

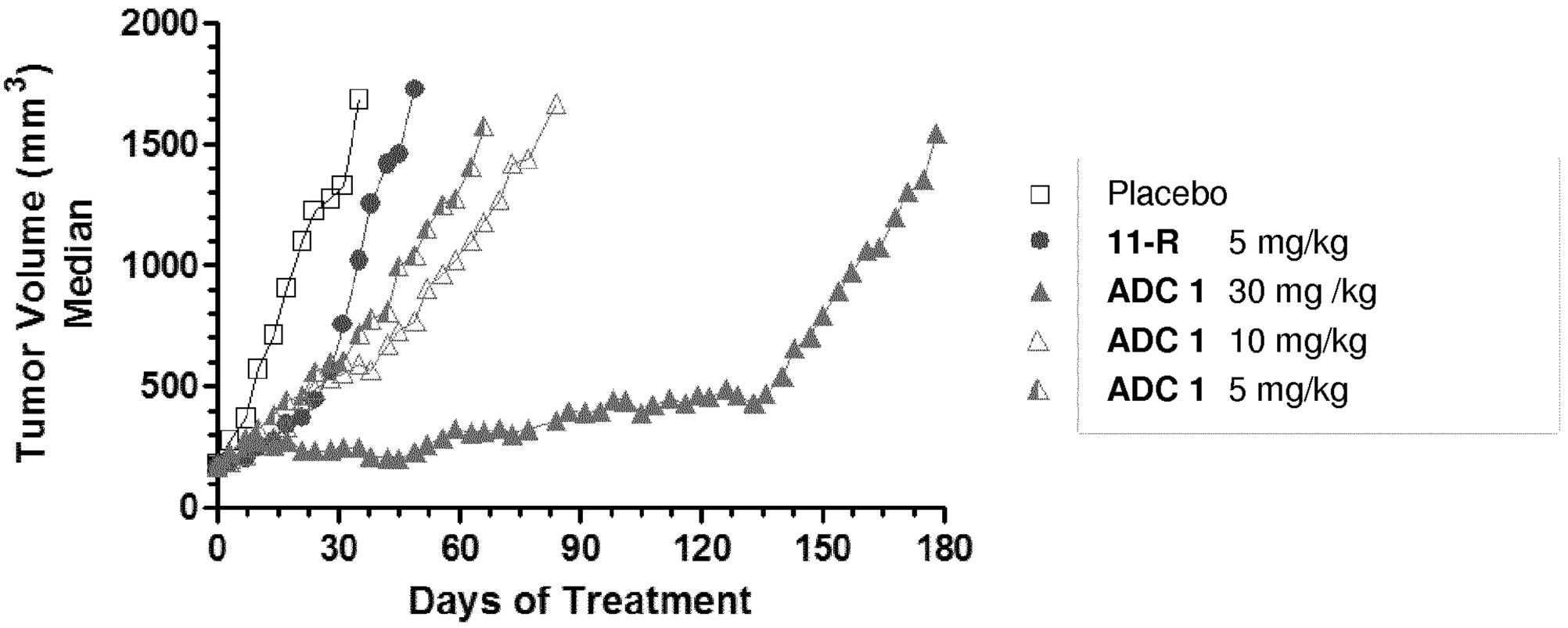


FIGURE 14

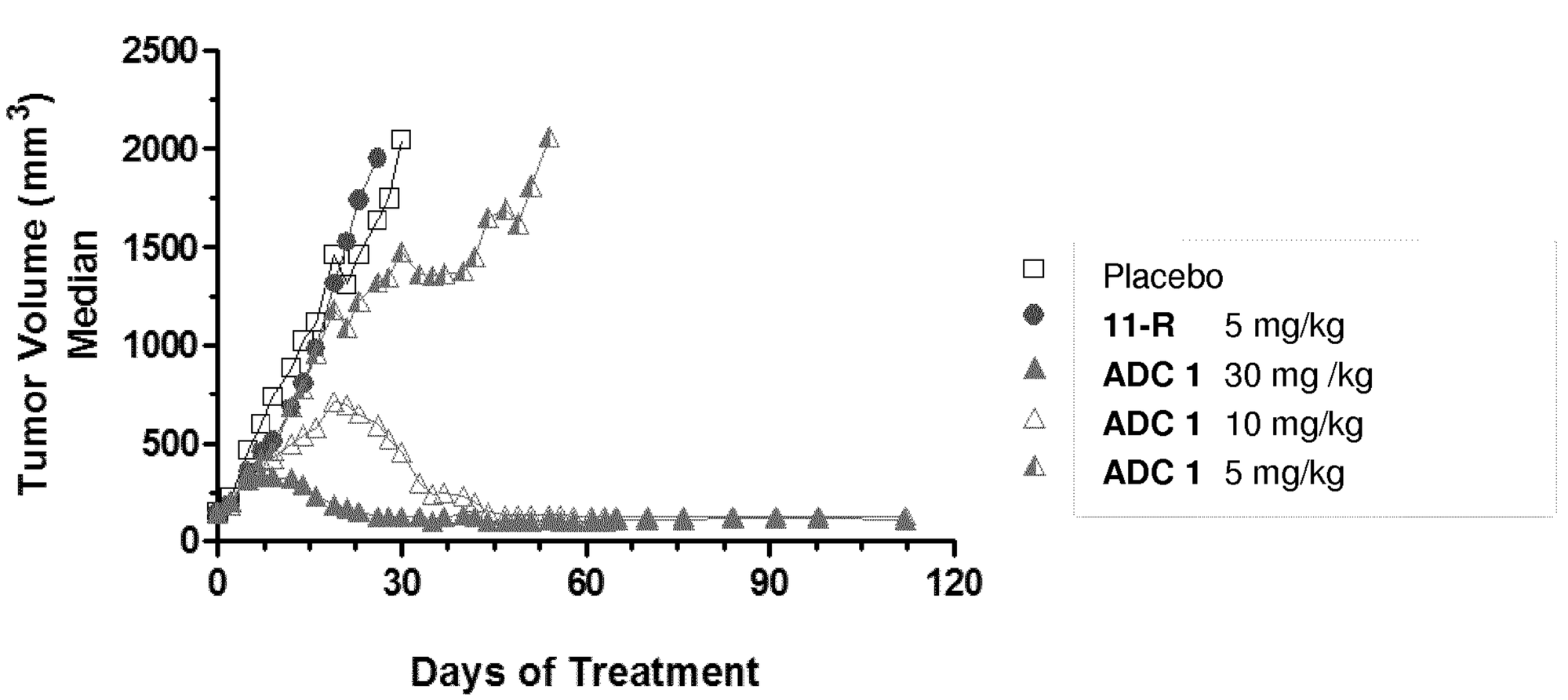


FIGURE 15

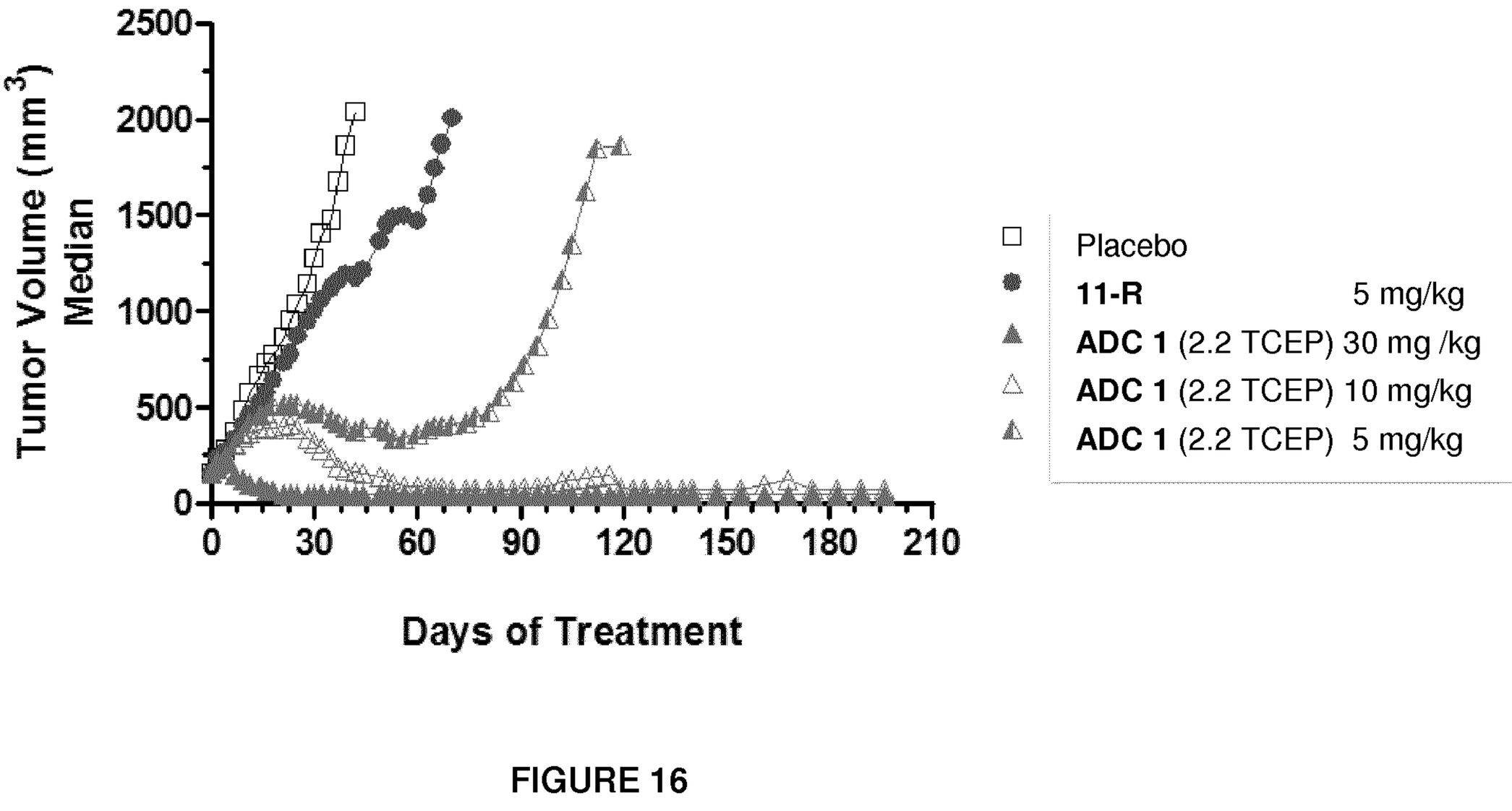


FIGURE 16

