FIG. 1

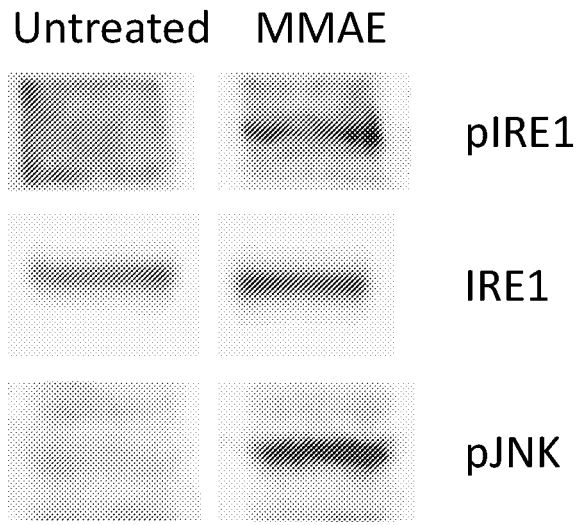


FIG. 2A

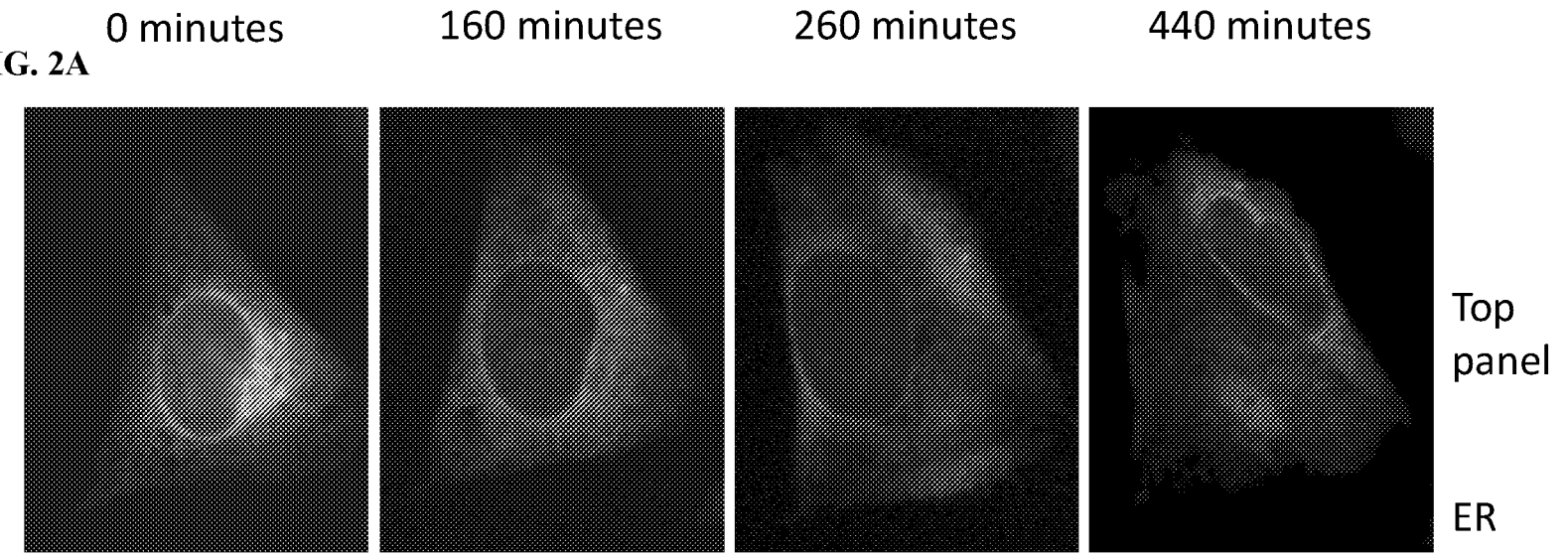

0 minutes
160 minutes
260 minutes
440 minutes
Top panel
ER

FIG. 2B

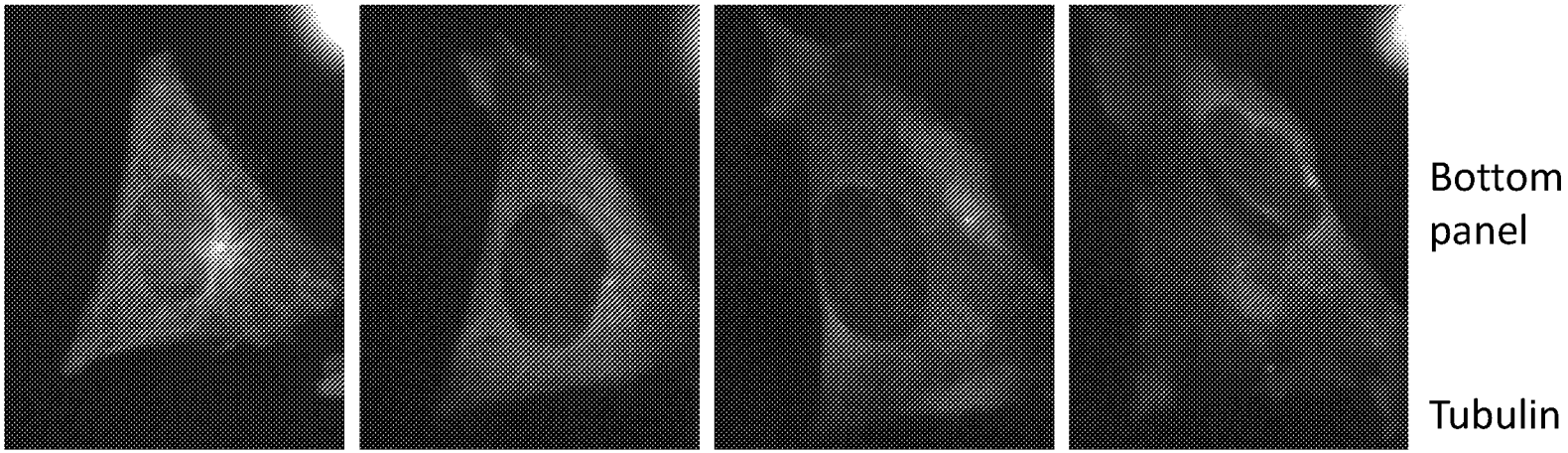

Bottom panel
Tubulin

FIG. 3A

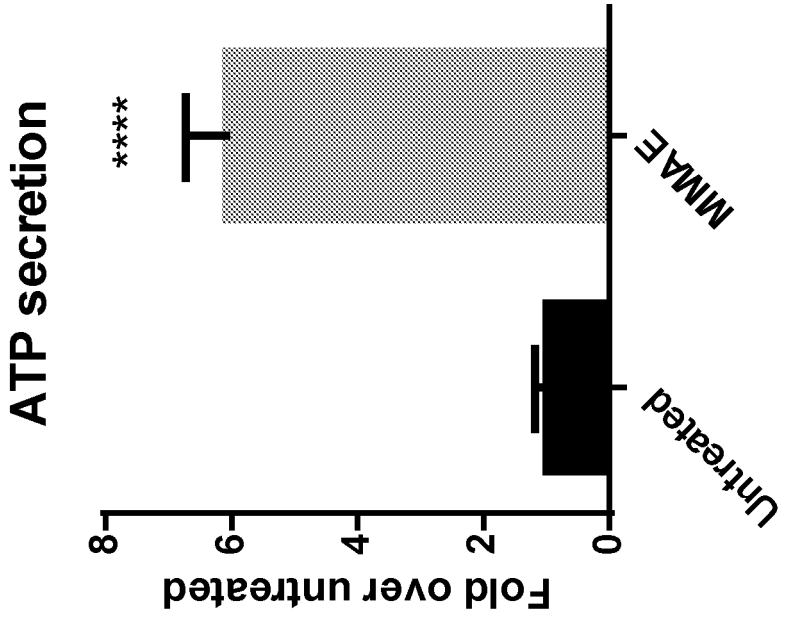

ATP secretion
****
Fold over untreated
0
2
4
6
8
Untreated
MMAE

FIG. 3B

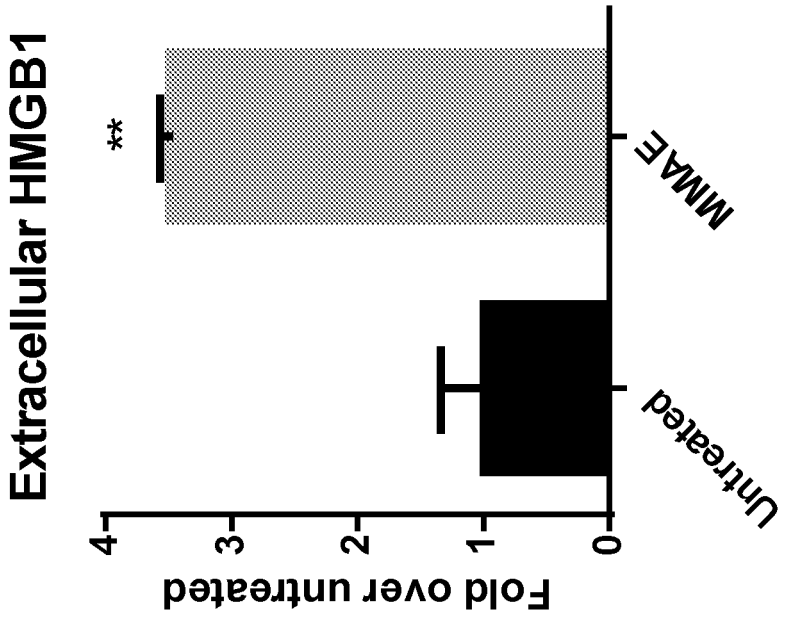

Extracellular HMGB1
**
Fold over untreated
0
1
2
3
4
Untreated
MMAE

FIG. 4A

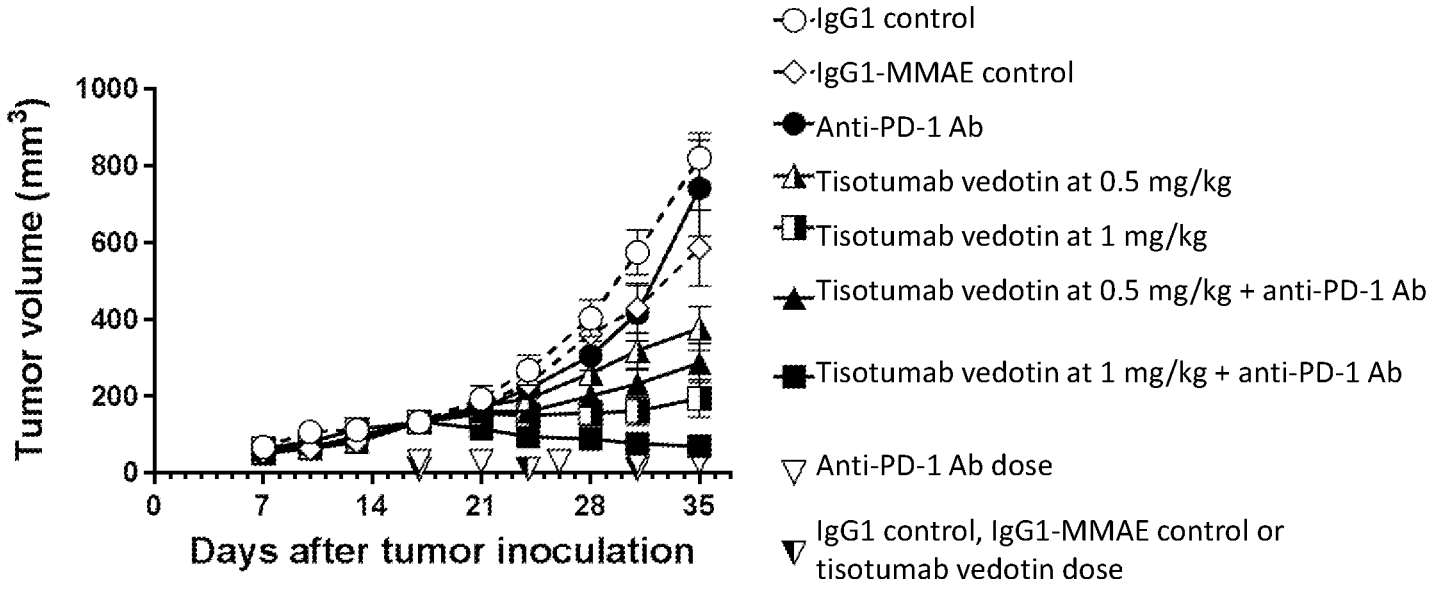

Tumor volume (mm3)
1000
800
600
400
200
0
0
7
14
21
28
35
Days after tumor inoculation
IgG1 control
IgG1-MMAE control
Anti-PD-1 Ab
Tisotumab vedotin at 0.5 mg/kg
Tisotumab vedotin at 1 mg/kg
Tisotumab vedotin at 0.5 mg/kg + anti-PD-1 Ab
Tisotumab vedotin at 1 mg/kg + anti-PD-1 Ab
Anti-PD-1 Ab dose
IgG1 control, IgG1-MMAE control or tisotumab vedotin dose

FIG. 4B

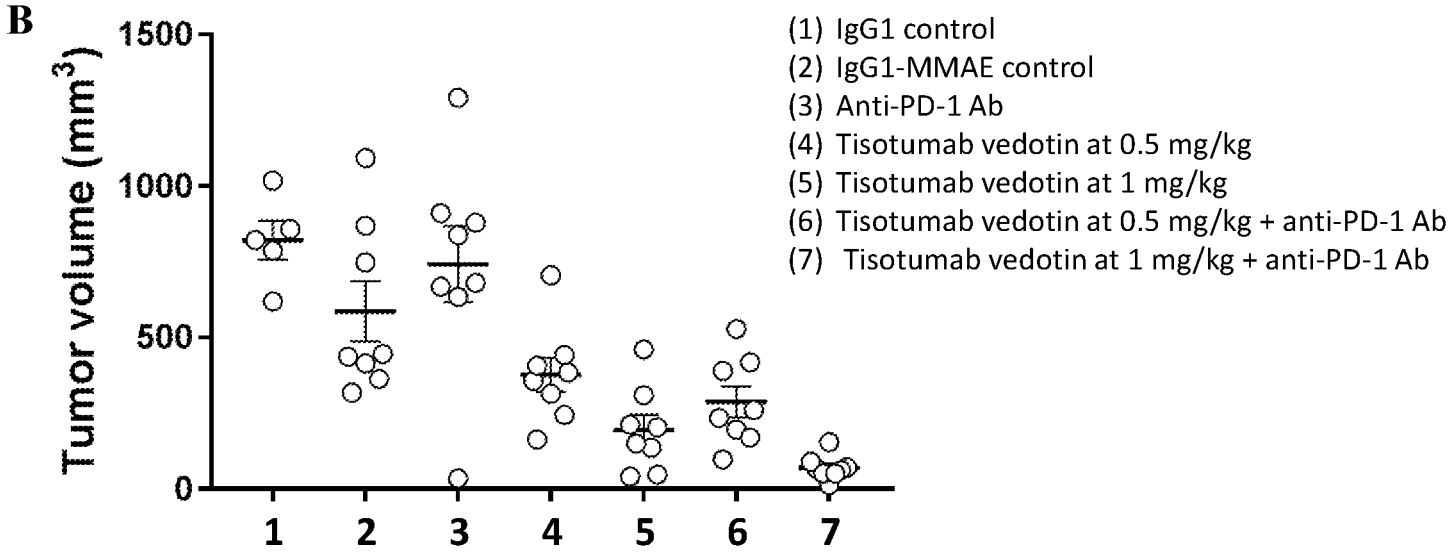

B
Tumor volume (mm3)
1500
1000
500
0
1
2
3
4
5
6
7
(1) IgG1 control
(2) IgG1-MMAE control
(3) Anti-PD-1 Ab
(4) Tisotumab vedotin at 0.5 mg/kg
(5) Tisotumab vedotin at 1 mg/kg
(6) Tisotumab vedotin at 0.5 mg/kg + anti-PD-1 Ab
(7) Tisotumab vedotin at 1 mg/kg + anti-PD-1 Ab

FIG. 5A

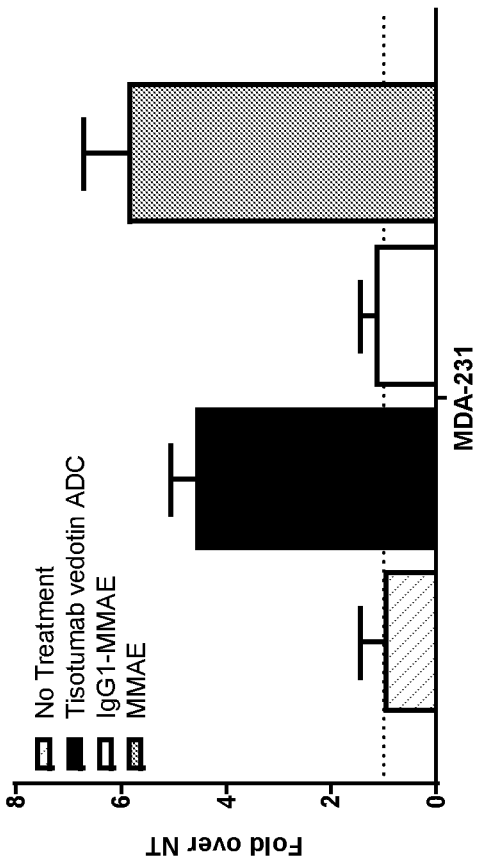

ATP Secretion
No Treatment
Tisotumab vedotin ADC
IgG1-MMAE
MMAE
Fold over NT
0
2
4
6
8
MDA-231

FIG. 5B

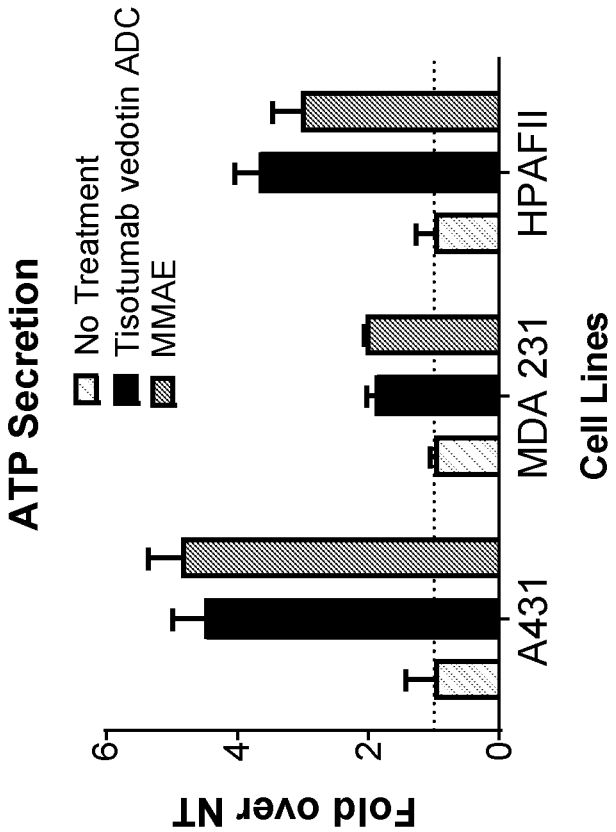

ATP Secretion
No Treatment
Tisotumab vedotin ADC
MMAE
Fold over NT
0
2
4
6
A431
MDA 231
HPAFII
Cell Lines

FIG. 5C

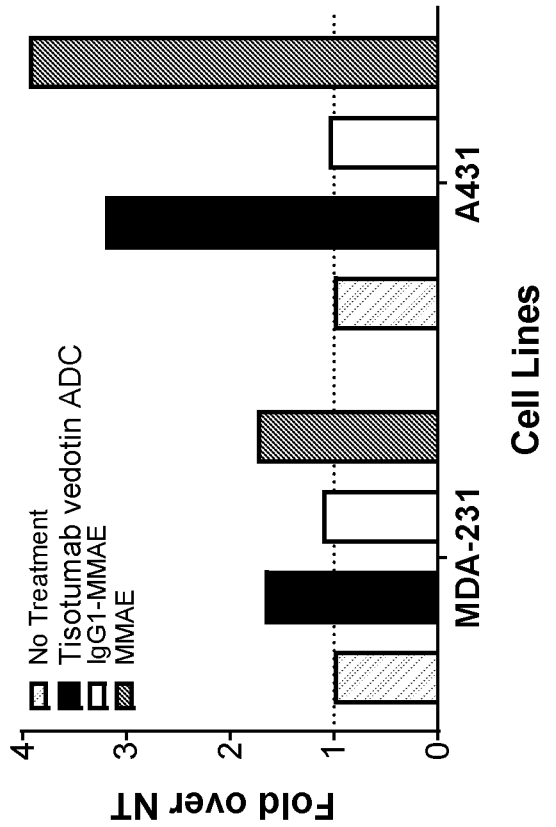

HMGB1 Release
No Treatment
Tisotumab vedotin ADC
IgG1-MMAE
MMAE
Fold over NT
0
1
2
3
4
MDA-231
A431
Cell Lines

FIG. 6

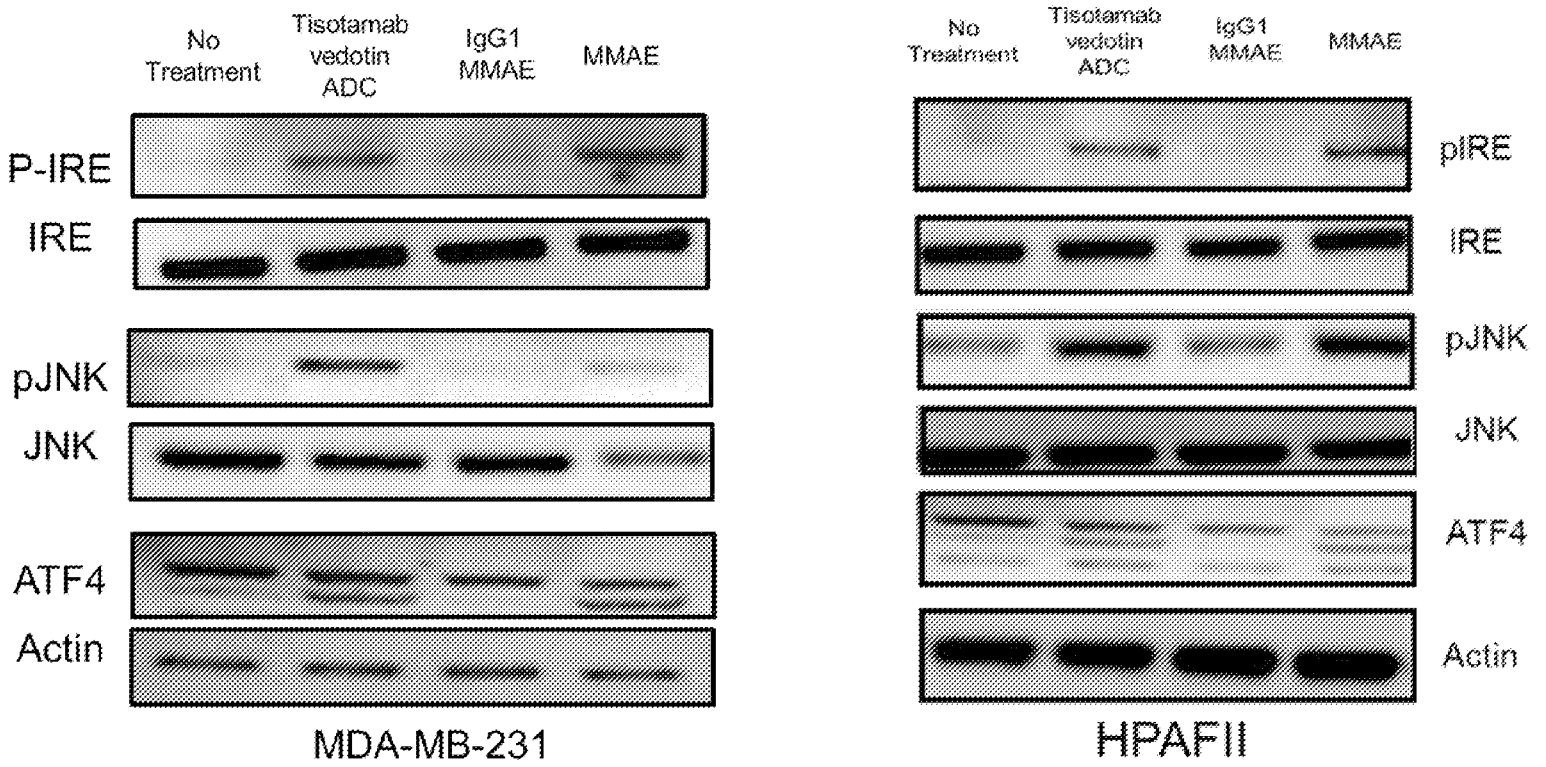

No Treatment
Tisotamab vedotin ADC
IgG1 MMAE
MMAE
P-IRE
IRE
pJNK
JNK
ATF4
Actin
MDA-MB-231
No Treatment
Tisotamab vedotin ADC
IgG1 MMAE
MMAE
pIRE
IRE
pJNK
JNK
ATF4
Actin
HPAFII

FIG. 7A

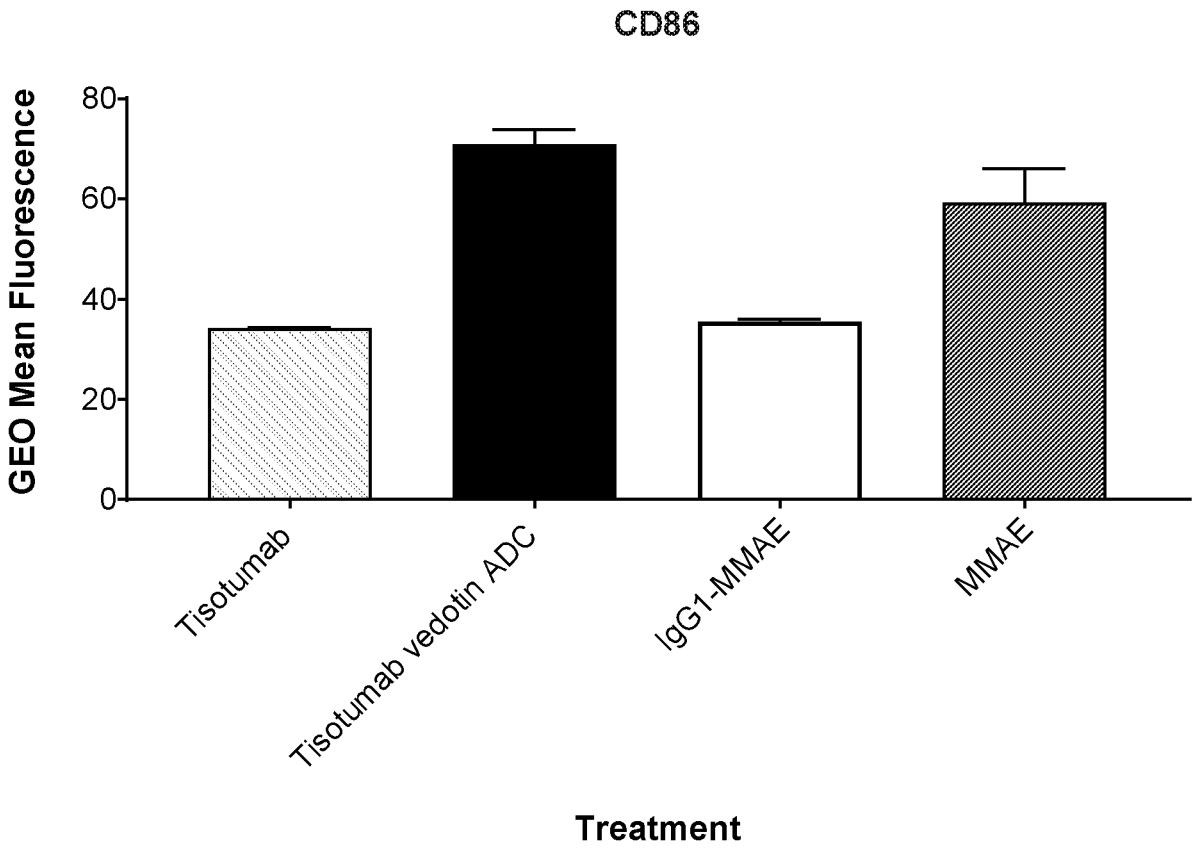

CD86
GEO Mean Fluorescence
80
60
40
20
0
Tisotumab
Tisotumab vedotin ADC
IgG1-MMAE
MMAE
Treatment

FIG. 7B

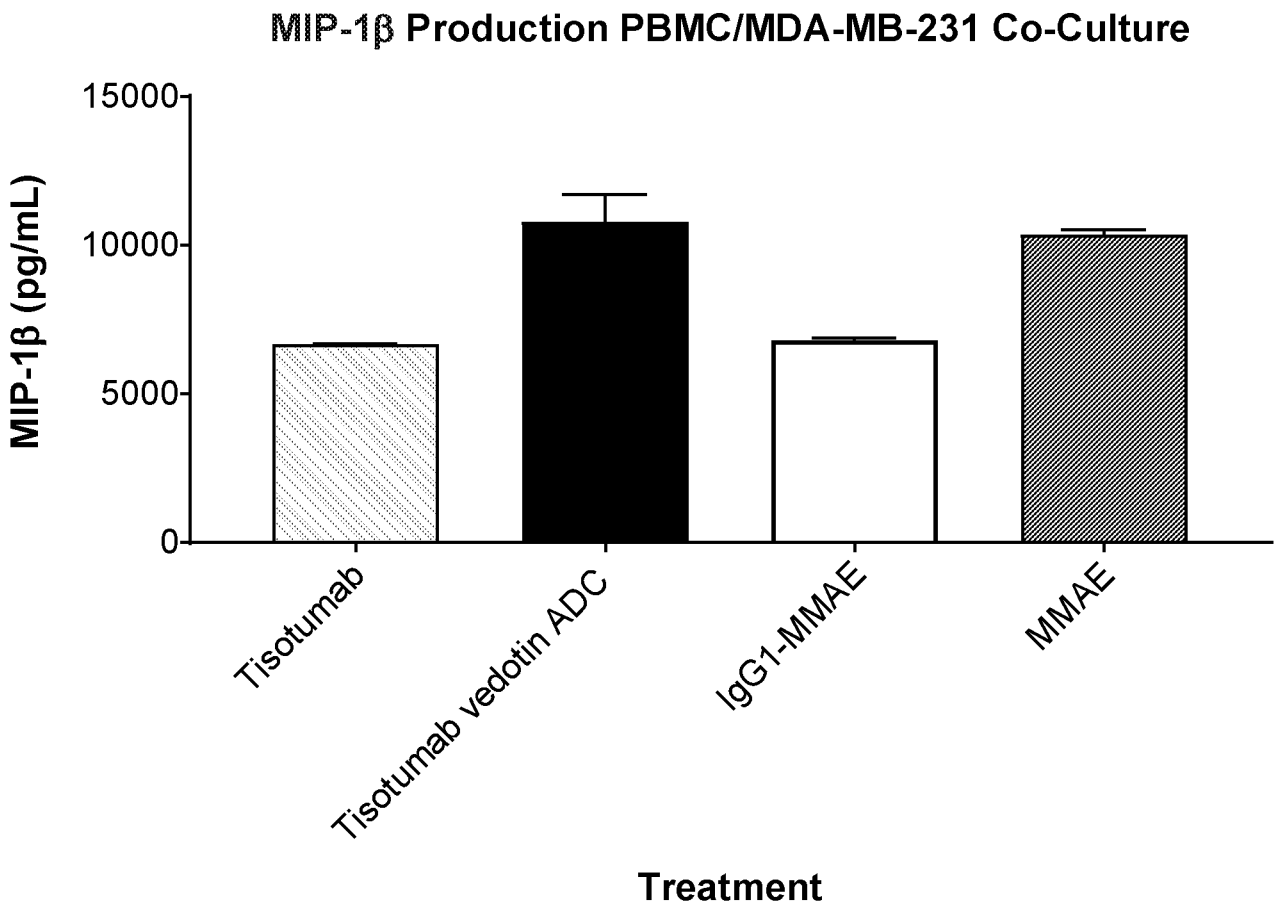

MIP-1β Production PBMC/MDA-MB-231 Co-Culture
MIP-1β (pg/mL)
15000
10000
5000
0
Tisotumab
Tisotumab vedotin ADC
IgG1-MMAE
MMAE
Treatment

FIG. 8A

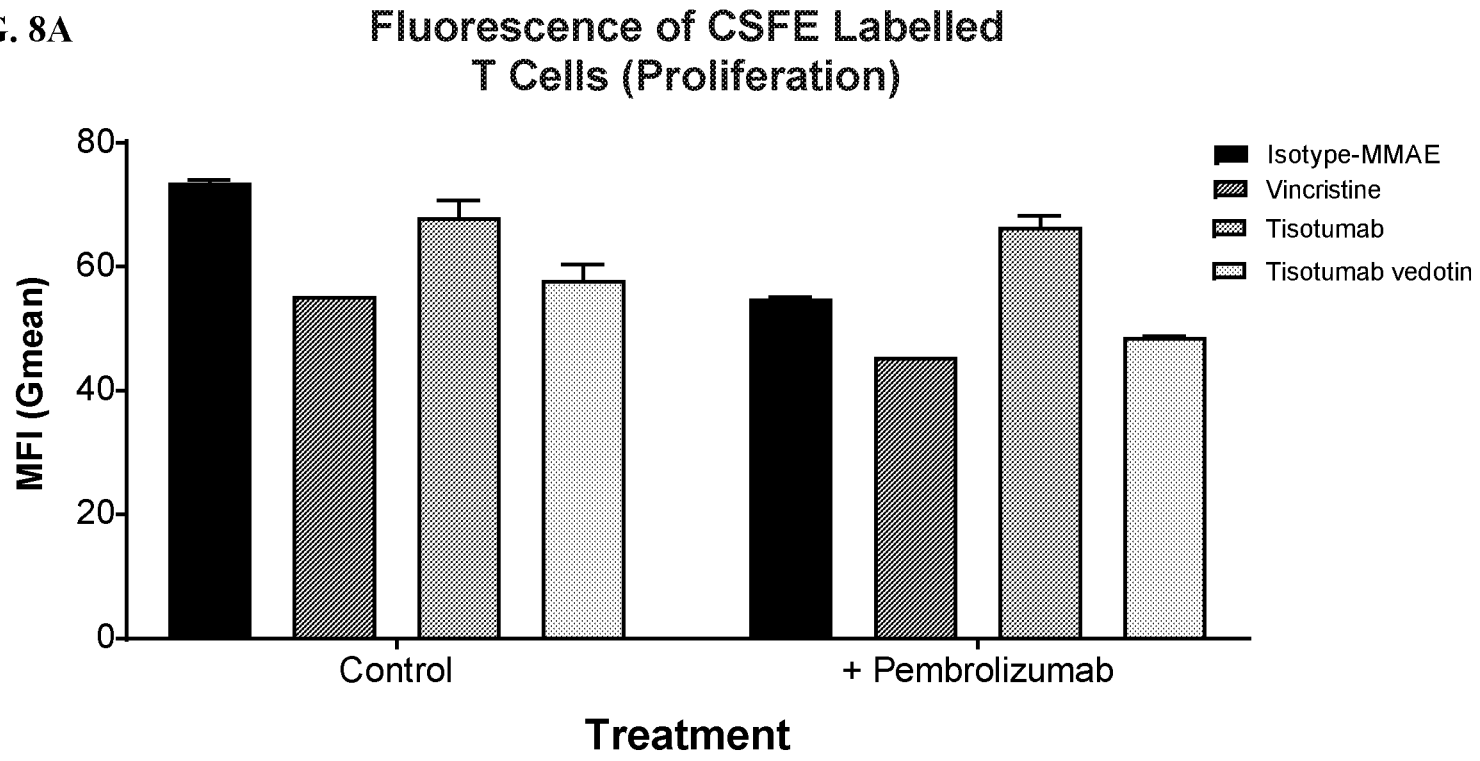

Fluorescence of CSFE Labelled
T Cells (Proliferation)
MFI (Gmean)
80
60
40
20
0
Control
+ Pembrolizumab
Treatment
Isotype-MMAE
Vincristine
Tisotumab
Tisotumab vedotin

FIG. 8B

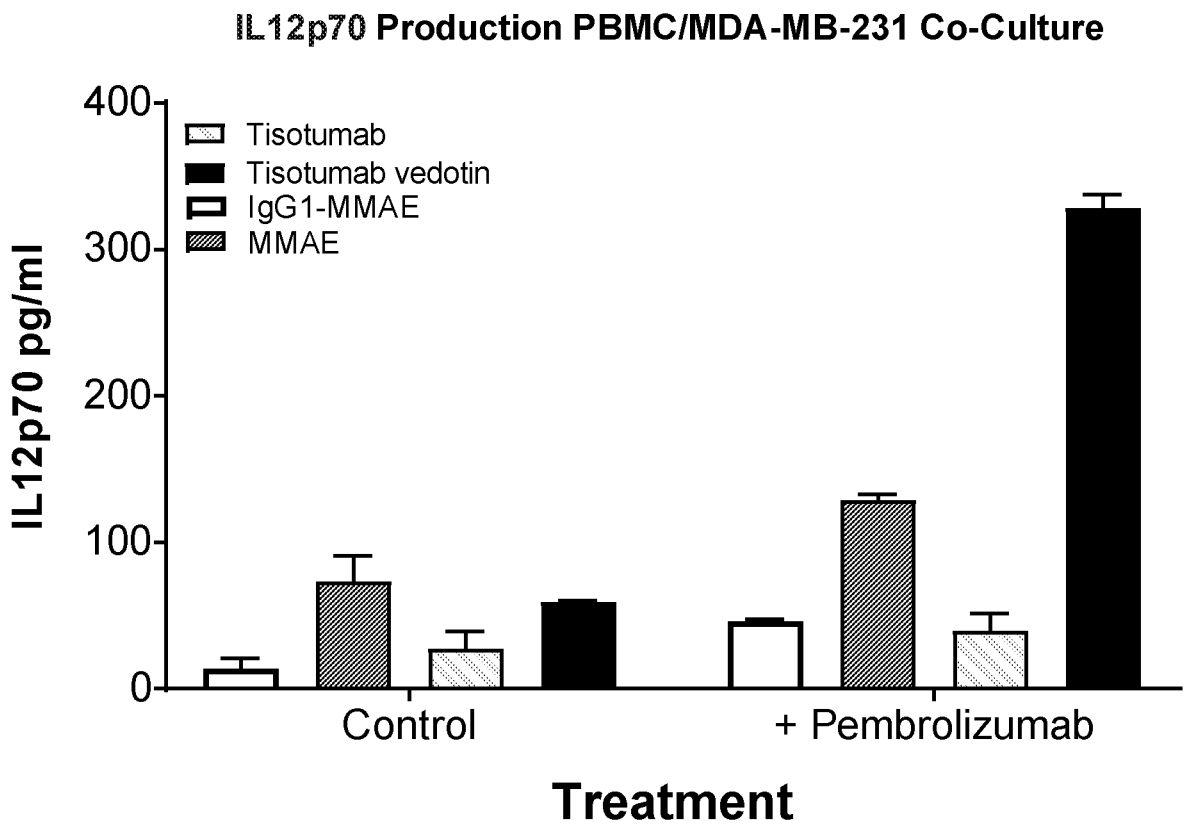
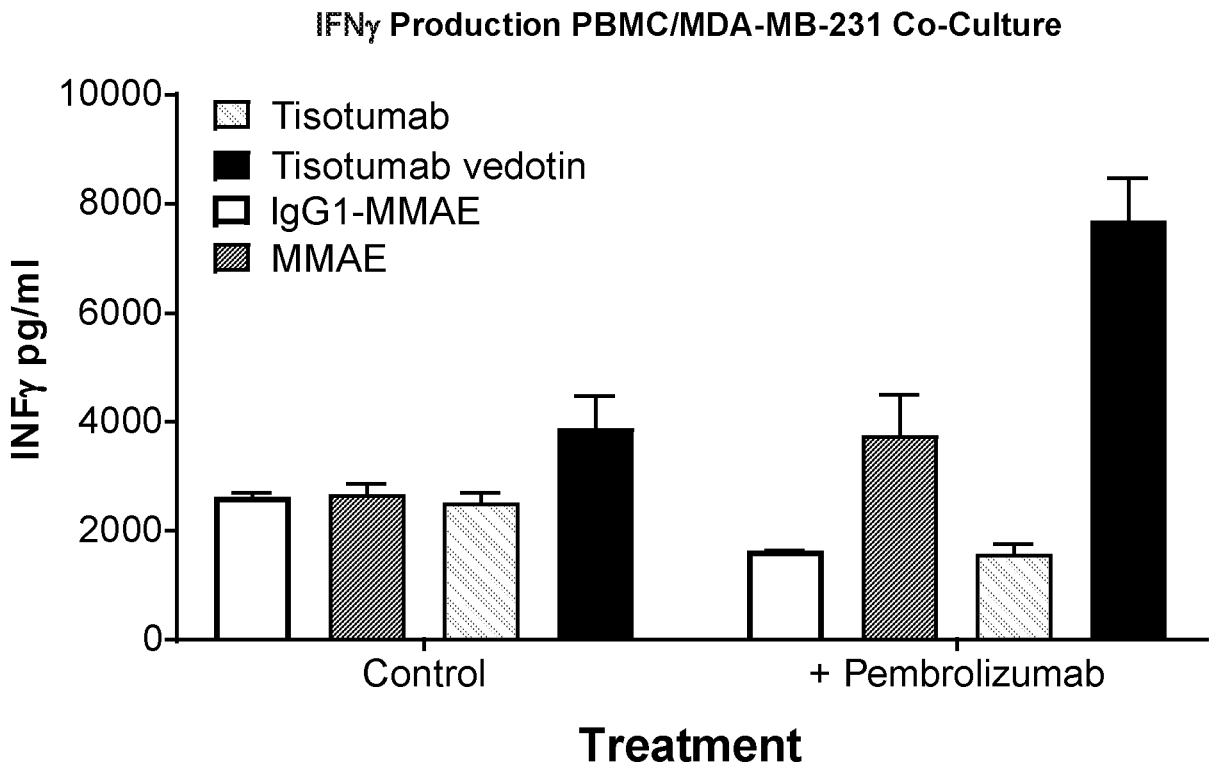

IL12p70 Production PBMC/MDA-MB-231 Co-Culture
IL12p70 pg/ml
400
300
200
100
0
Tisotumab
Tisotumab vedotin
IgG1-MMAE
MMAE
Control
+ Pembrolizumab
Treatment

FIG. 8C


IFNγ Production PBMC/MDA-MB-231 Co-Culture
10000
8000
6000
4000
2000
0
INFγ pg/ml
Tisotumab
Tisotumab vedotin
IgG1-MMAE
MMAE
Control
+ Pembrolizumab
Treatment