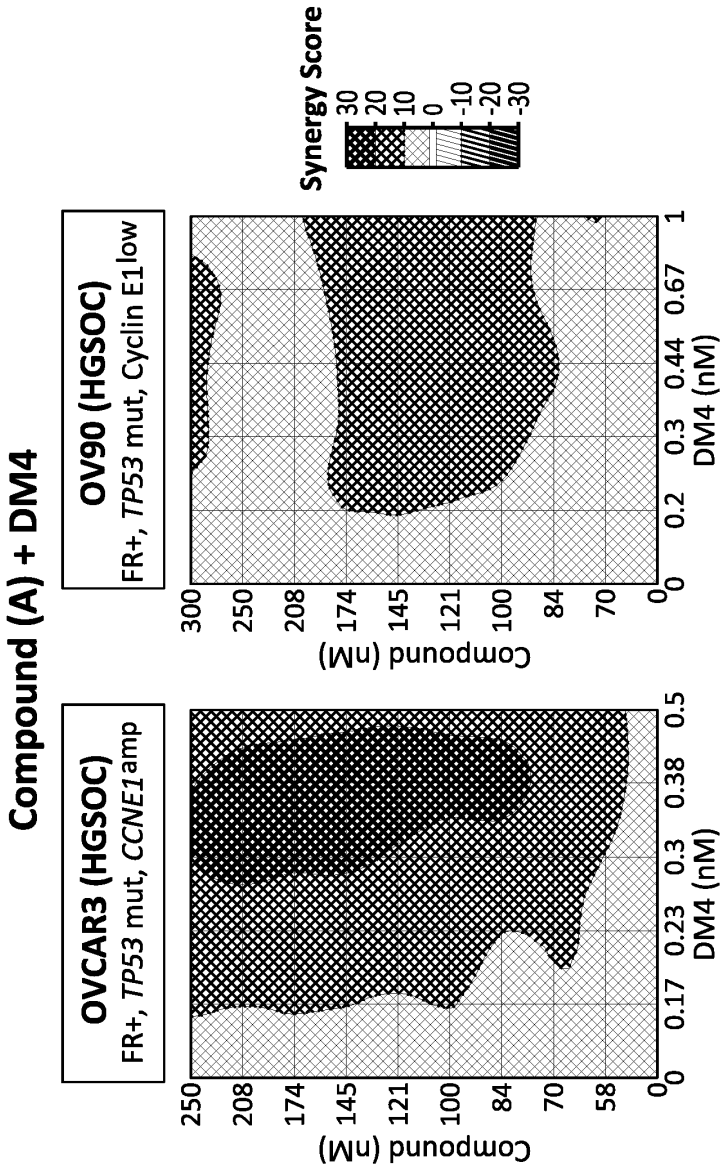

Compound (A) + DM4
OVCAR3 (HGSOC)
FR+, TP53 mut, CCNE1amp
OV90 (HGSOC)
FR+, TP53 mut, Cyclin E1low
Synergy Score
30
20
10
0
-10
-20
-30
Compound (nM)
DM4 (nM)
250
208
174
145
121
100
84
70
58
0
0.17
0.23
0.3
0.38
0.5
300
250
208
174
145
121
100
84
70
0
0.2
0.3
0.44
0.67
1

FIG. 1A

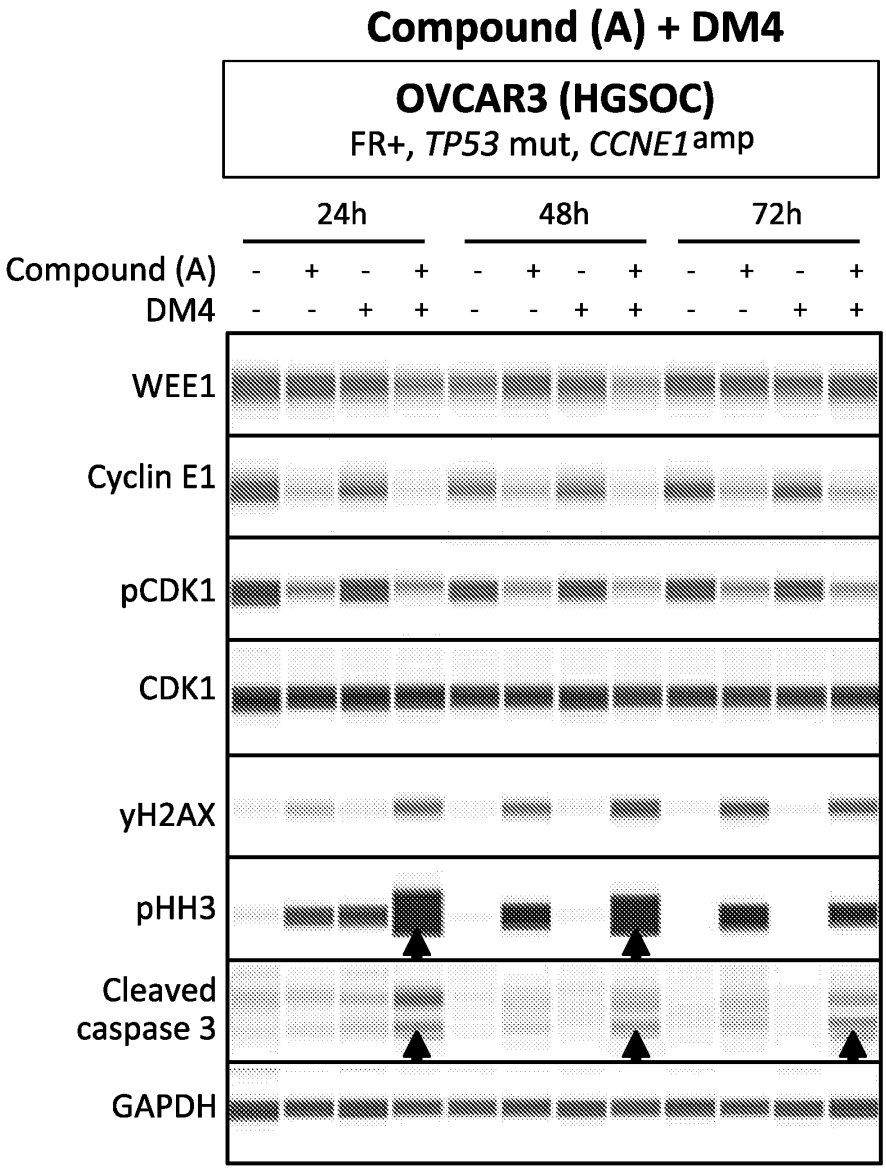

Compound (A) + DM4
OVCAR3 (HGSOC)
FR+, TP53 mut, CCNE1amp
24h
48h
72h
Compound (A) - + - + - + - + - + - +
DM4 - - + + - - + + - - + +
WEE1
Cyclin E1
pCDK1
CDK1
yH2AX
pHH3
Cleaved caspase 3
GAPDH

FIG. 1B

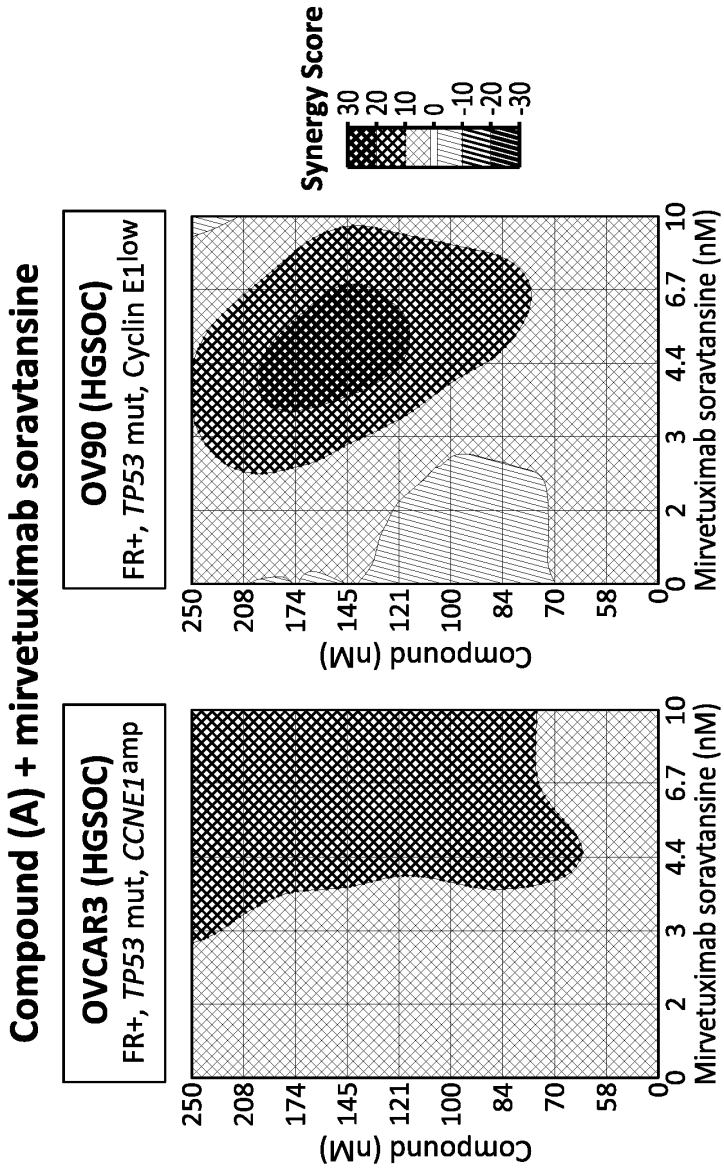

Compound (A) + mirvetuximab soravtansine
OVCAR3 (HGSOC)
FR+, TP53 mut, CCNE1amp
OV90 (HGSOC)
FR+, TP53 mut, Cyclin E1low
Synergy Score
30
20
10
0
-10
-20
-30
Compound (nM)
250
208
174
145
121
100
84
70
58
0
Mirvetuximab soravtansine (nM)
0
2
3
4.4
6.7
10

FIG. 1C

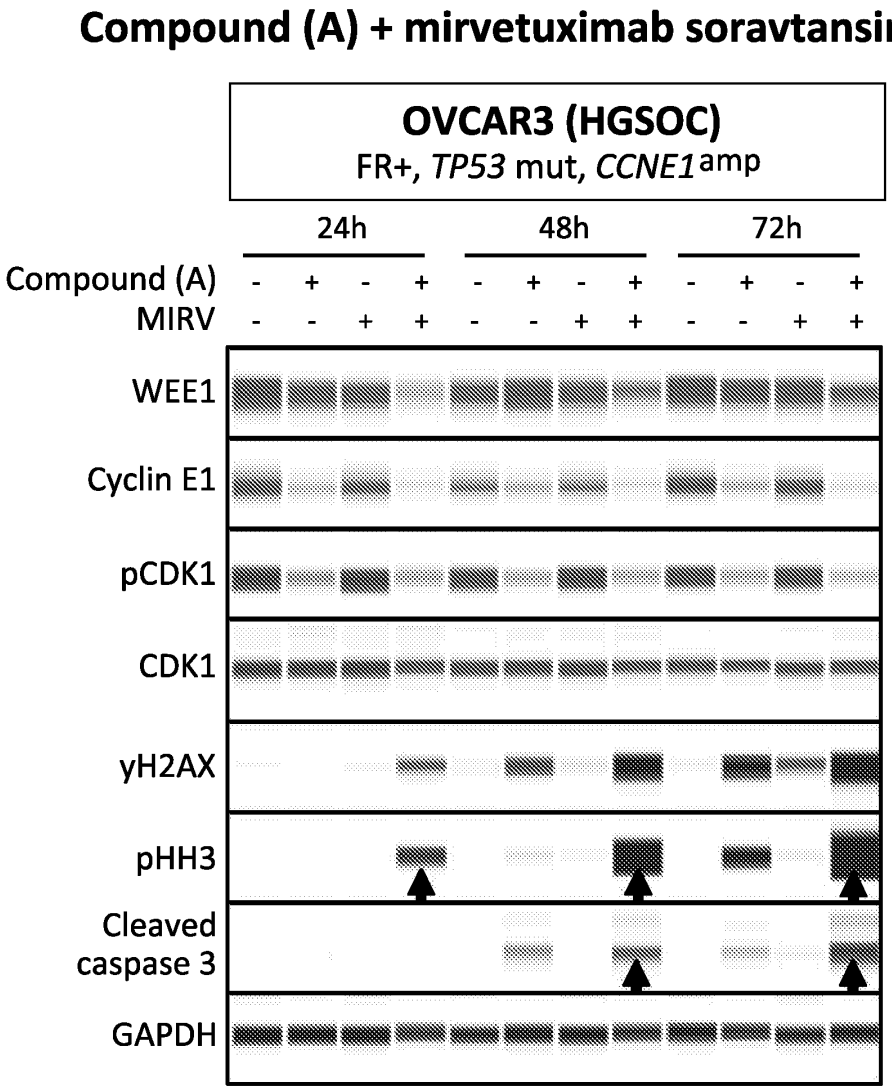

Compound (A) + mirvetuximab soravtansine
OVCAR3 (HGSOC)
FR+, TP53 mut, CCNE1 amp
24h
48h
72h
Compound (A)
MIRV
WEE1
Cyclin E1
pCDK1
CDK1
yH2AX
pHH3
Cleaved caspase 3
GAPDH

FIG. 1D

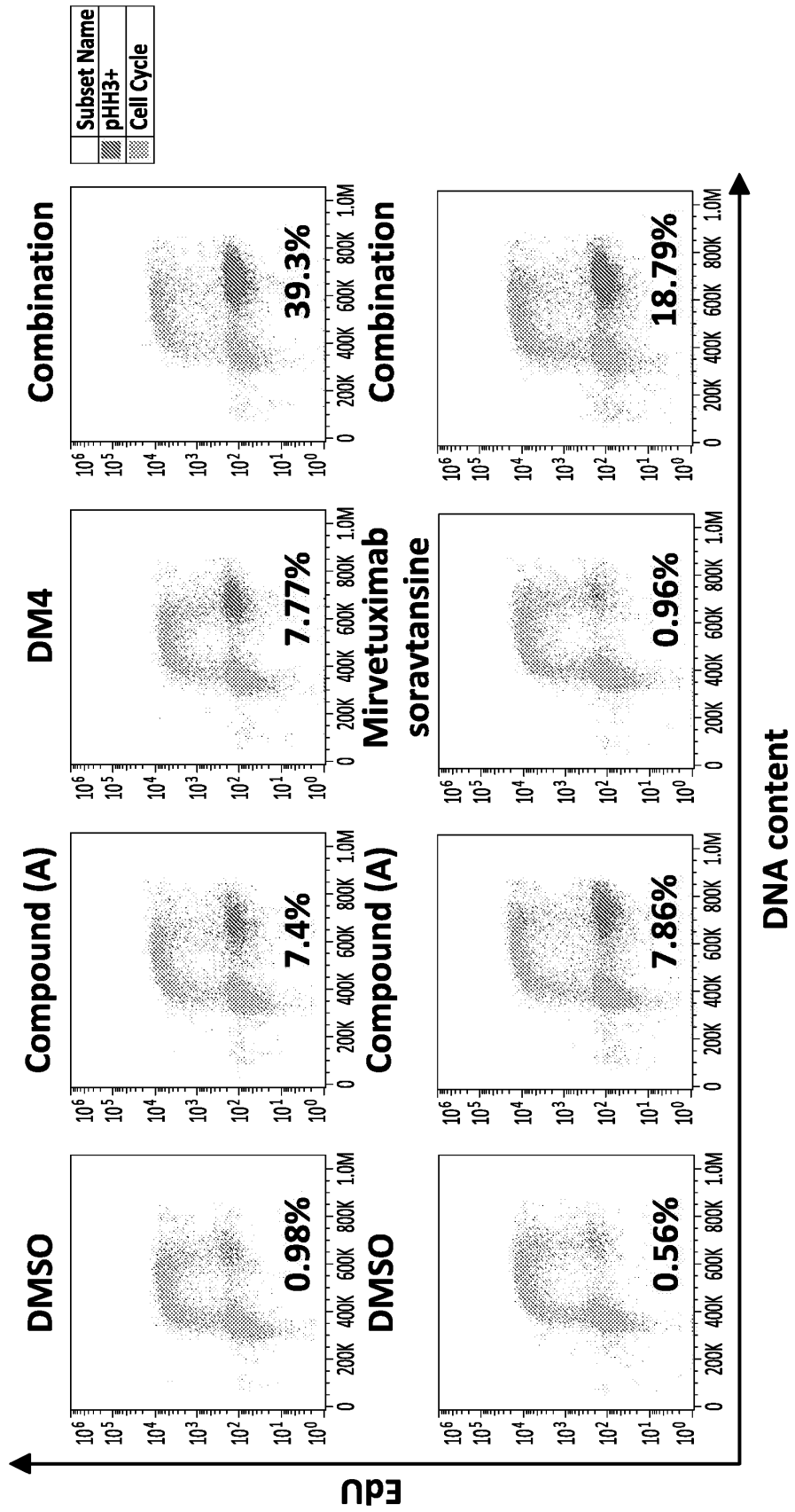

Subset Name
pHH3+
Cell Cycle
DMSO
Compound (A)
DM4
Combination
Mirvetuximab soravtansine
Combination
0.98%
7.4%
7.77%
39.3%
0.56%
7.86%
0.96%
18.79%
EdU
DNA content

FIG. 2A

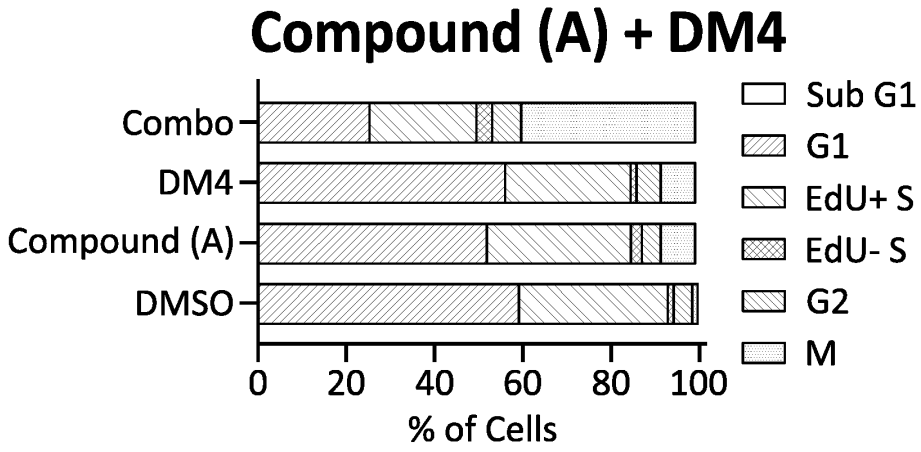

Compound (A) + DM4
Combo
DM4
Compound (A)
DMSO
0
20
40
60
80
100
% of Cells
Sub G1
G1
EdU+ S
EdU- S
G2
M

FIG. 2B

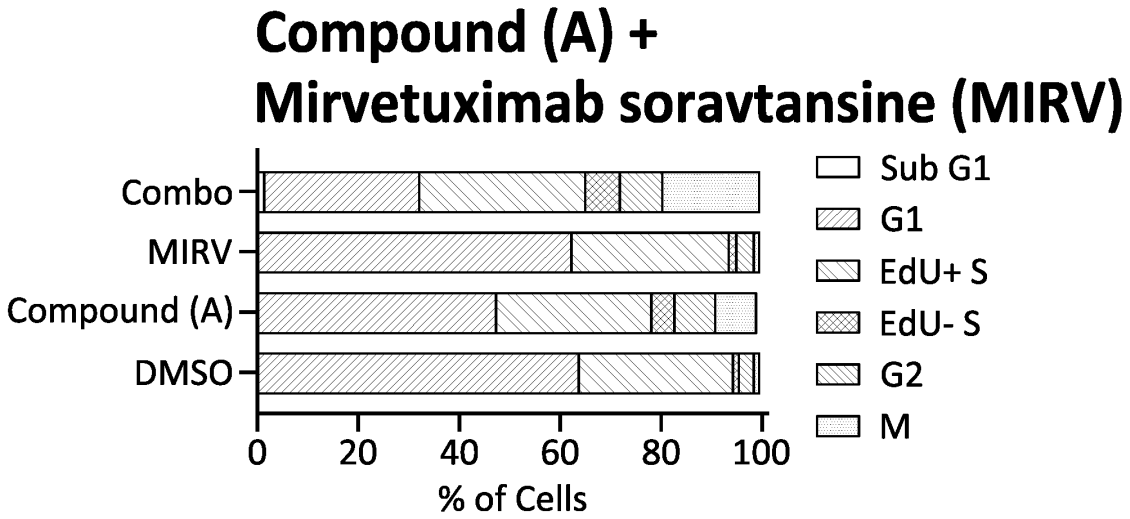

Compound (A) +
Mirvetuximab soravtansine (MIRV)
Combo
MIRV
Compound (A)
DMSO
0
20
40
60
80
100
% of Cells
Sub G1
G1
EdU+ S
EdU- S
G2
M

FIG. 2C

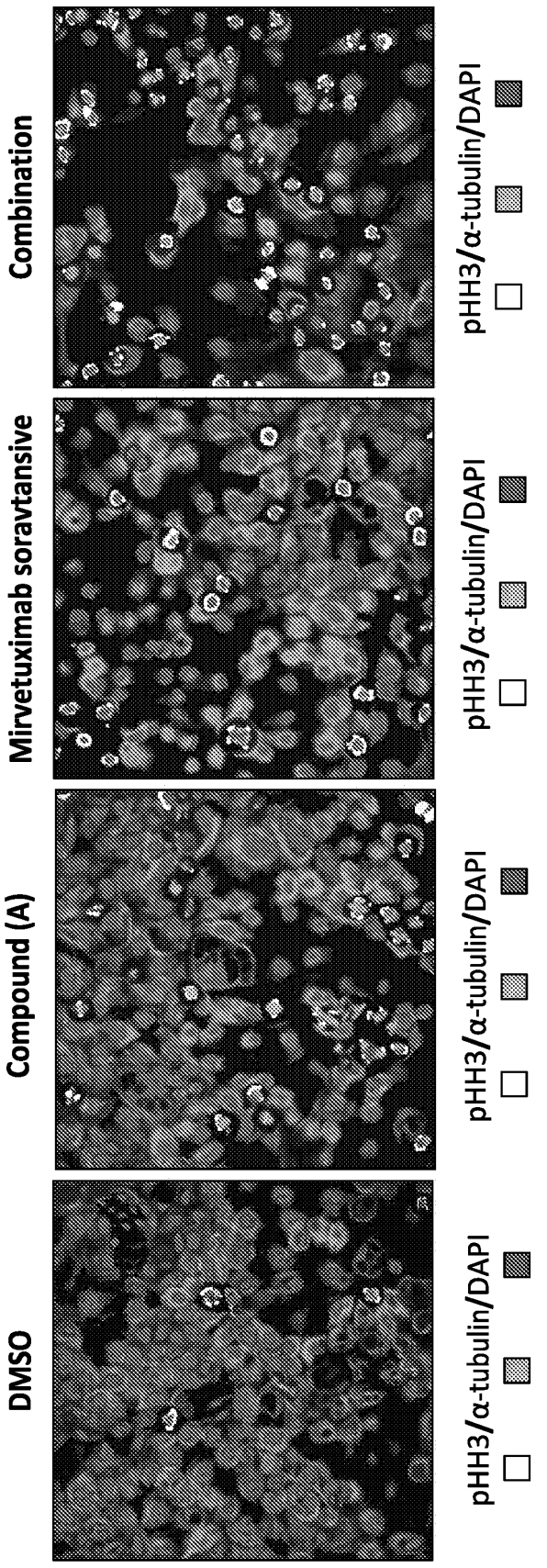

DMSO
Compound (A)
Mirvetuximab soravtansive
Combination
pHH3/α-tubulin/DAPI
pHH3/α-tubulin/DAPI
pHH3/α-tubulin/DAPI
pHH3/α-tubulin/DAPI

FIG. 3A

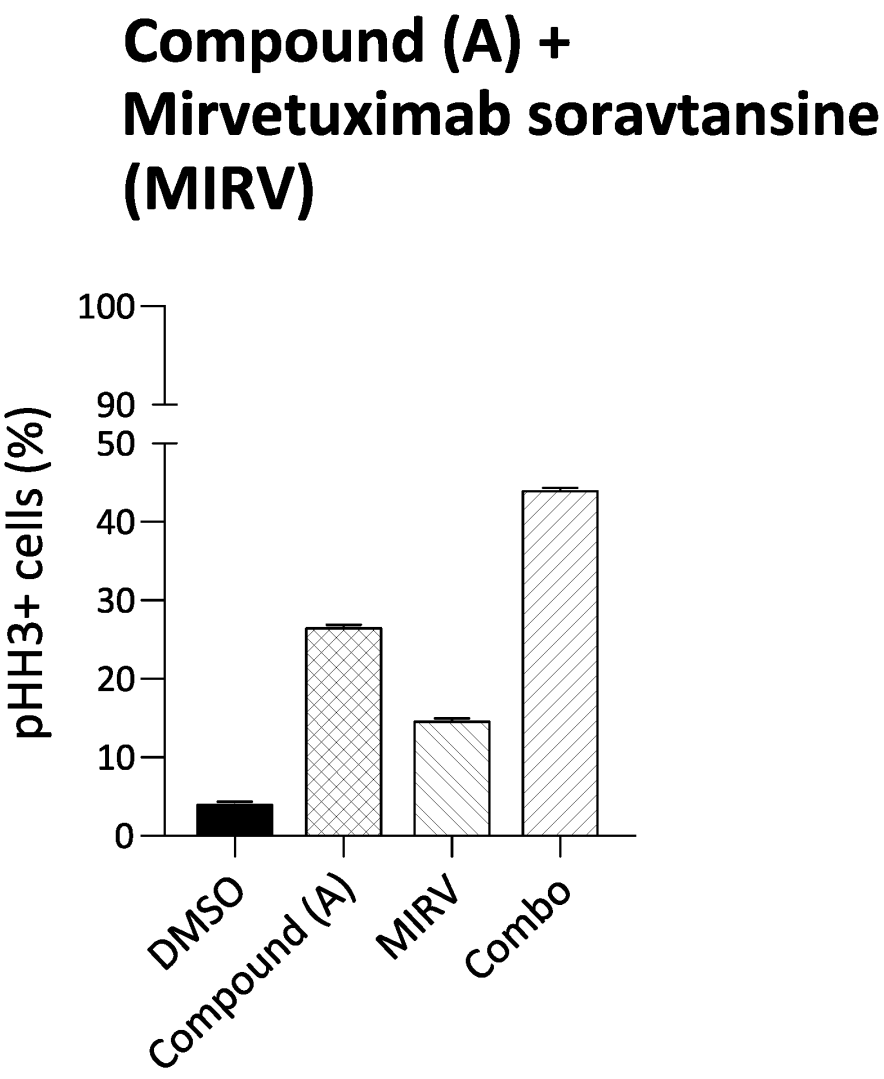
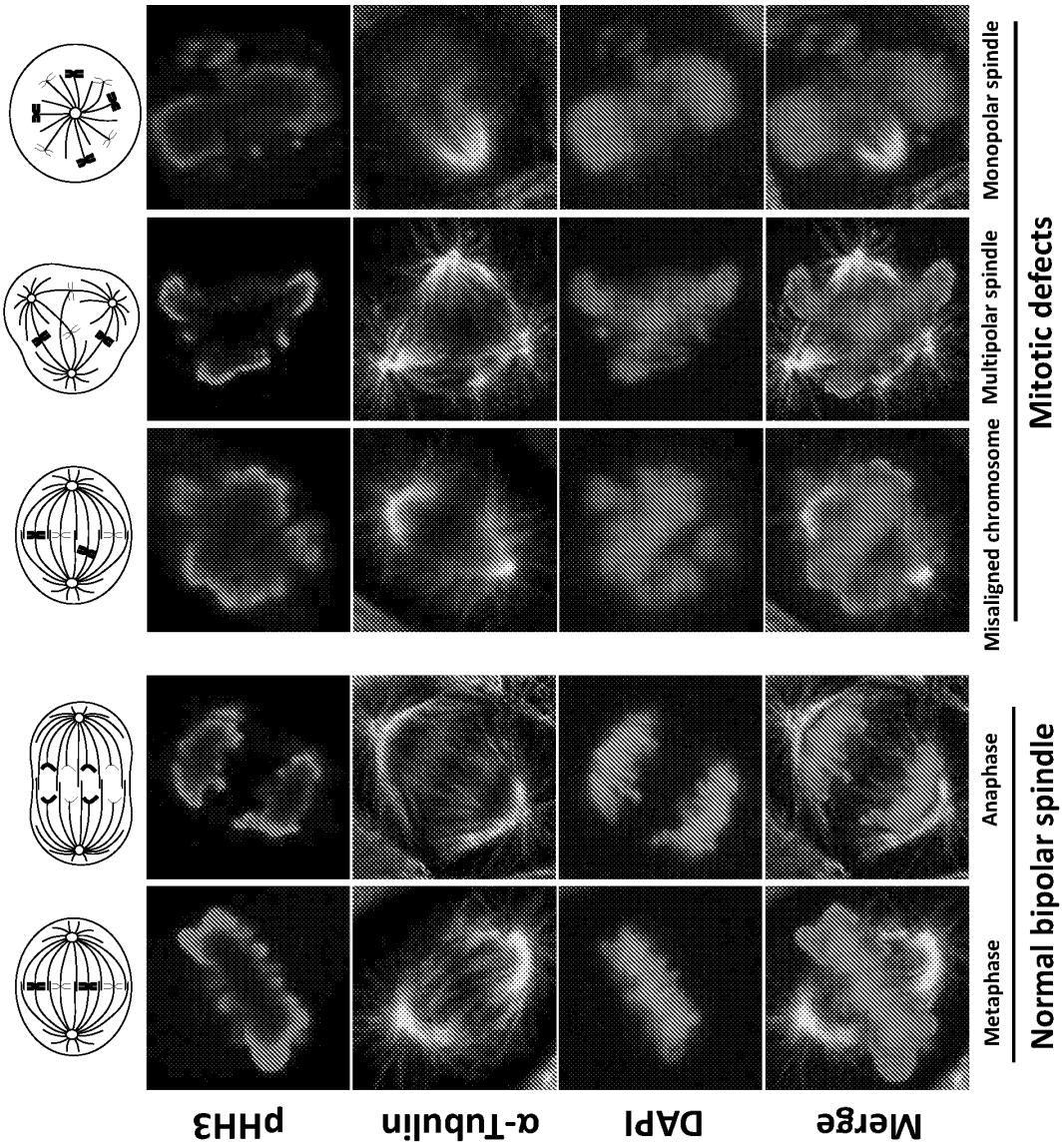

Compound (A) +
Mirvetuximab soravtansine
(MIRV)
pHH3+ cells (%)
100
90
50
40
30
20
10
0
DMSO
Compound (A)
MIRV
Combo

FIG. 3B

FIG. 3C


Merge
DAPI
α-Tubulin
pHH3
Metaphase
Anaphase
Normal bipolar spindle
Misaligned chromosome
Multipolar spindle
Monopolar spindle
Mitotic defects

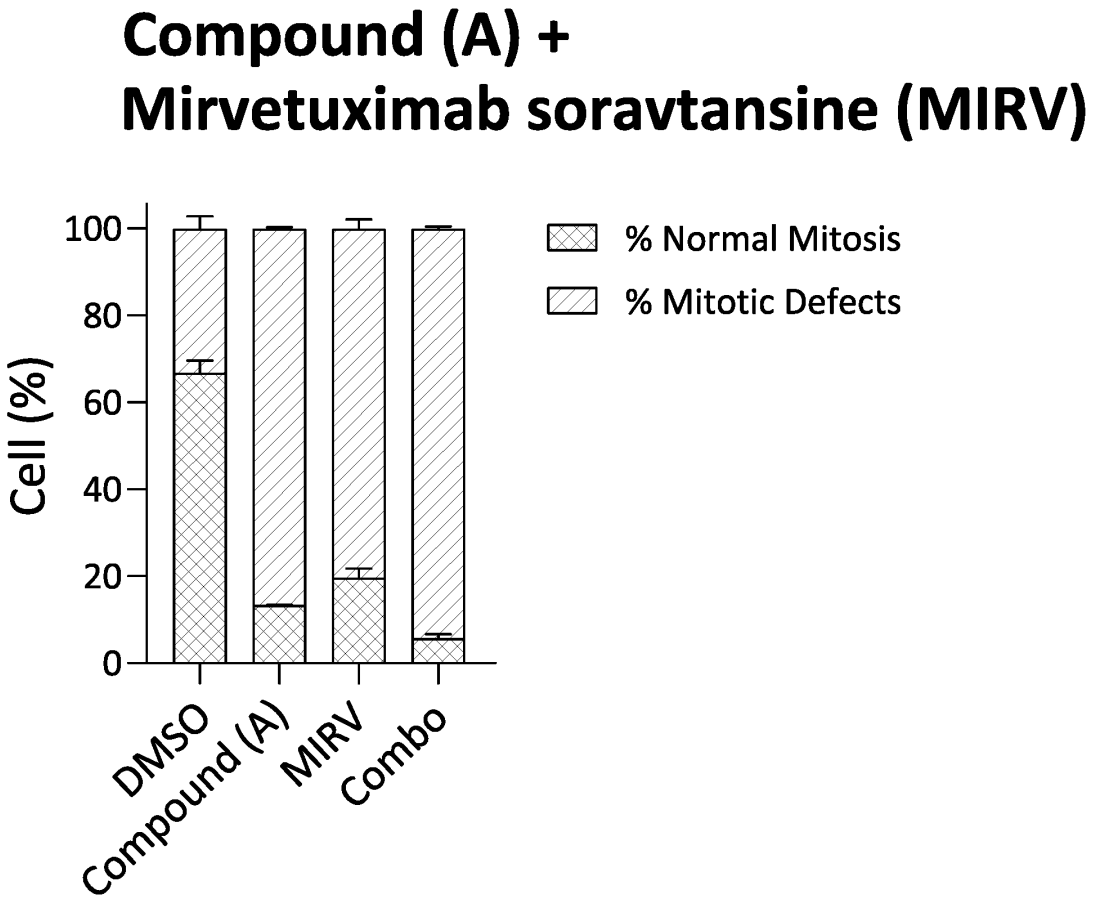

Compound (A) +
Mirvetuximab soravtansine (MIRV)
Cell (%)
100
80
60
40
20
0
% Normal Mitosis
% Mitotic Defects
DMSO
Compound (A)
MIRV
Combo

FIG. 3D

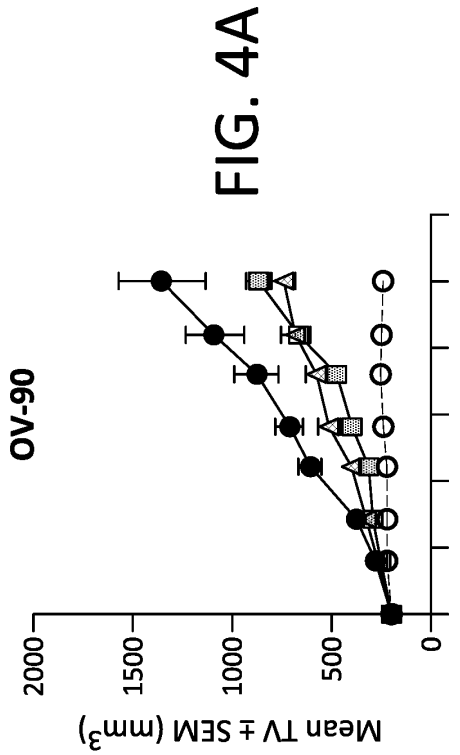


FIG. 4A

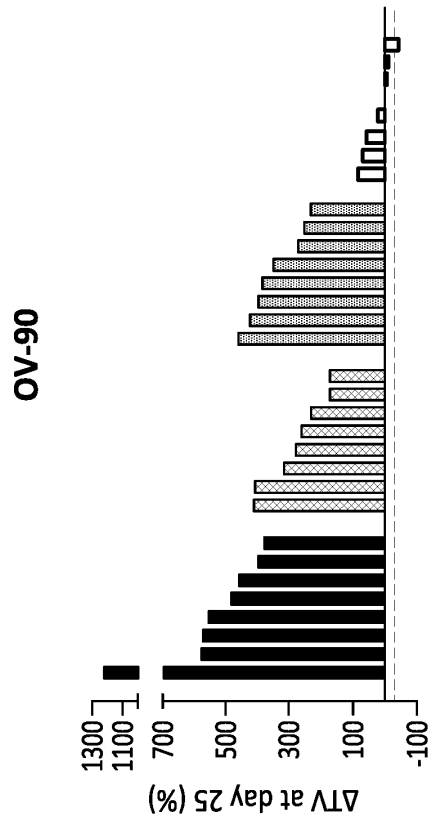


FIG. 4B

FIG. 4C