[Figure 1]

SEQ ID No: 1 - Amino acid sequence of a heavy chain of the anti-TROP2 antibody

MKHLWFFLLLVAAPRWVLSQVQLVQSGAEVKKPGASVK
VSCKASGYTFTTAGMQWVRQAPGQGLEWMGWINTHSGV
PKYAEDFKGRVTISADTSTSTAYLQLSSLKSEDTAVYY
CARSGFGSSYWYFDVWGQGTLVTVSSASTKGPSVFPLA
PSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV
HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHK
PSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLF
PPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDG
VEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY
KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREE
MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTP
PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALH
NHYTQKSLSLSPGK

Signal sequence (1-19), Variable region (20-140), Constant region (141-470)

[Figure 2]

SEQ ID NO: 2 - Amino acid sequence of a light chain of the anti-TROP2 antibody

MVLQTQVFISLLLWISGAYGDIQMTQSPSSLSASVGDR
VTITCKASQDVSTAVAWYQQKPGKAPKLLIYSASYRYT
GVPSRFSGSGSGTDFTLTISSLQPEDFAVYYCQQHYIT
PLTFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASV
VCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKD
STYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKS
FNRGEC

Signal sequence (1-20), Variable region (21-129), Constant region (130-234)

[Figure 3]
SEQ ID NO: 3 - Amino acid sequence of heavy chain CDRH1
TAGMQ

[Figure 4]
SEQ ID NO: 4 - Amino acid sequence of heavy chain CDRH2
WINTHSGVPKYAEDFKG

[Figure 5]
SEQ ID NO: 5 - Amino acid sequence of heavy chain CDRH3
SGFGSSYWYFDV

[Figure 6]
SEQ ID NO: 6 - Amino acid sequence of light chain CDRL1
KASQDVSTAVA

[Figure 7]
SEQ ID NO: 7 - Amino acid sequence of light chain CDRL2
SASYRYT

[Figure 8]
SEQ ID NO: 8 - Amino acid sequence of light chain CDRL3
QQHYITPLT

[Figure 9]

SEQ ID NO: 9 - Amino acid sequence of heavy chain variable region

QVQLVQSGAEVKKPGASVKVSCKASGYTFTTAGMQWVR
QAPGQGLEWMGWINTHSGVPKYAEDFKGRVTISADTST
STAYLQLSSLKSEDTAVYYCARSGFGSSYWYFDVWGQG
TLVTVSS

[Figure 10]

SEQ ID NO: 10 - Amino acid sequence of light chain variable region

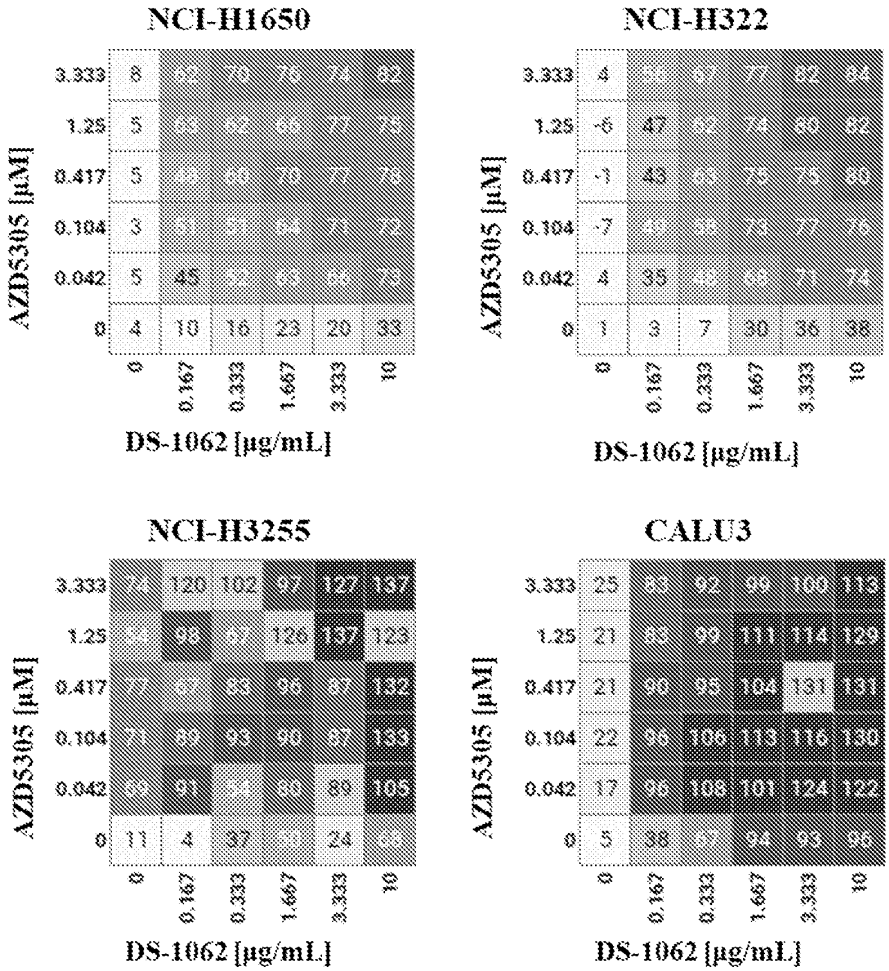
DIQMTQSPSSLSASVGDRVTITCKASQDVSTAVAWYQQ
KPGKAPKLLIYSASYRYTGVPSRFSGSGSGTDFTLTIS
SLQPEDFAVYYCQQHYITPLTFGQGTKLEIKRT

[Figure 11]

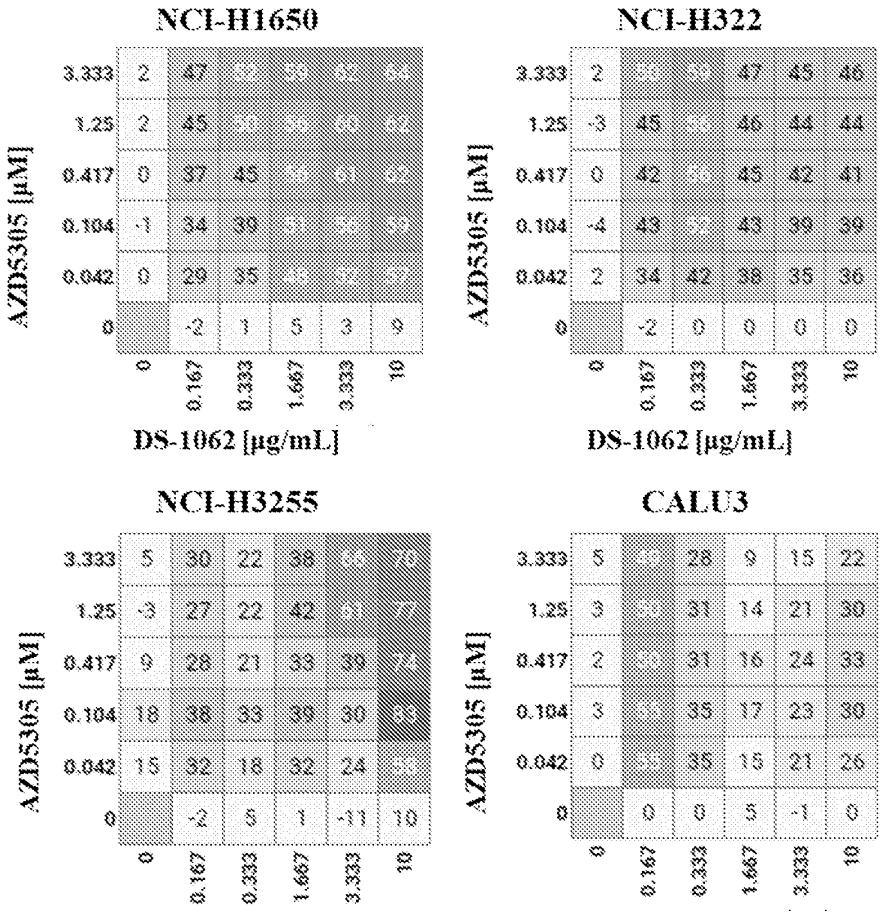
SEQ ID NO: 11 - Amino acid sequence of heavy chain

QVQLVQSGAEVKKPGASVKVSCKASGYTFTTAGMQWVR
QAPGQGLEWMGWINTHSGVPKYAEDFKGRVTISADTST
STAYLQLSSLKSEDTAVYYCARSGFGSSYWYFDVWGQG
TLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKD
YFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVV
TVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTH
TCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCV
VVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISK
AKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSD
IAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG

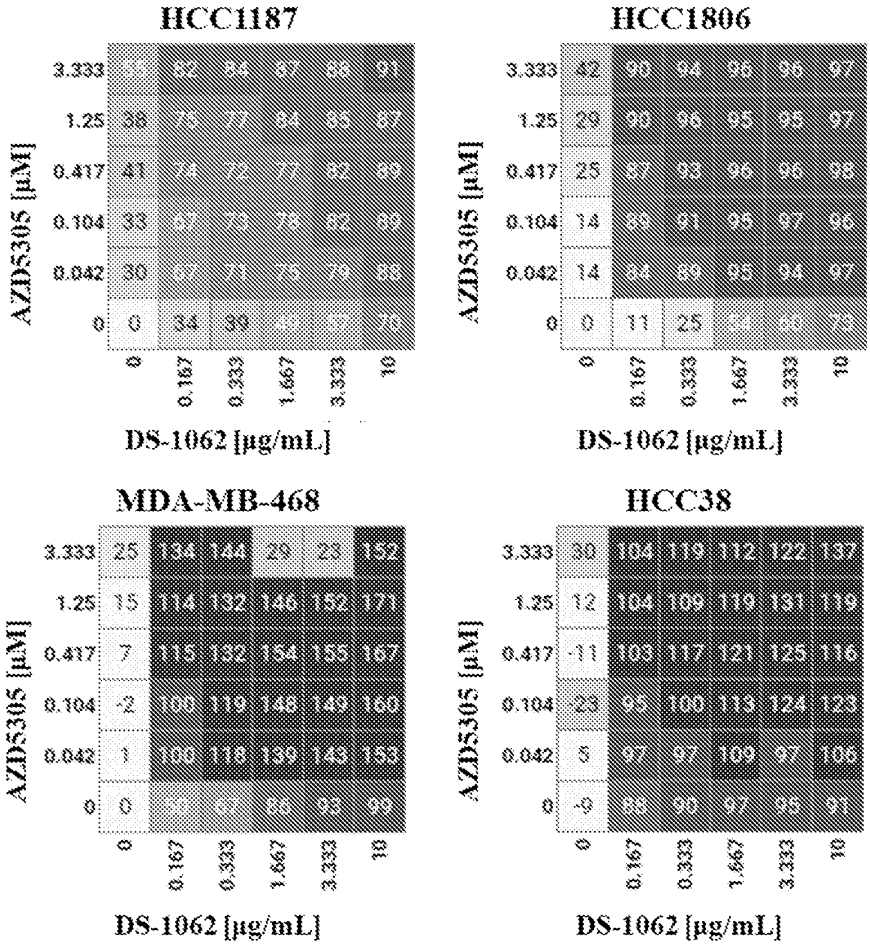
[Figure 12A]


NCI-H1650
AZD5305 [μM]
3.333
1.25
0.417
0.104
0.042
0
0
0.167
0.333
1.667
3.333
10
DS-1062 [μg/mL]
NCI-H322
AZD5305 [μM]
DS-1062 [μg/mL]
NCI-H3255
AZD5305 [μM]
DS-1062 [μg/mL]
CALU3
AZD5305 [μM]
DS-1062 [μg/mL]

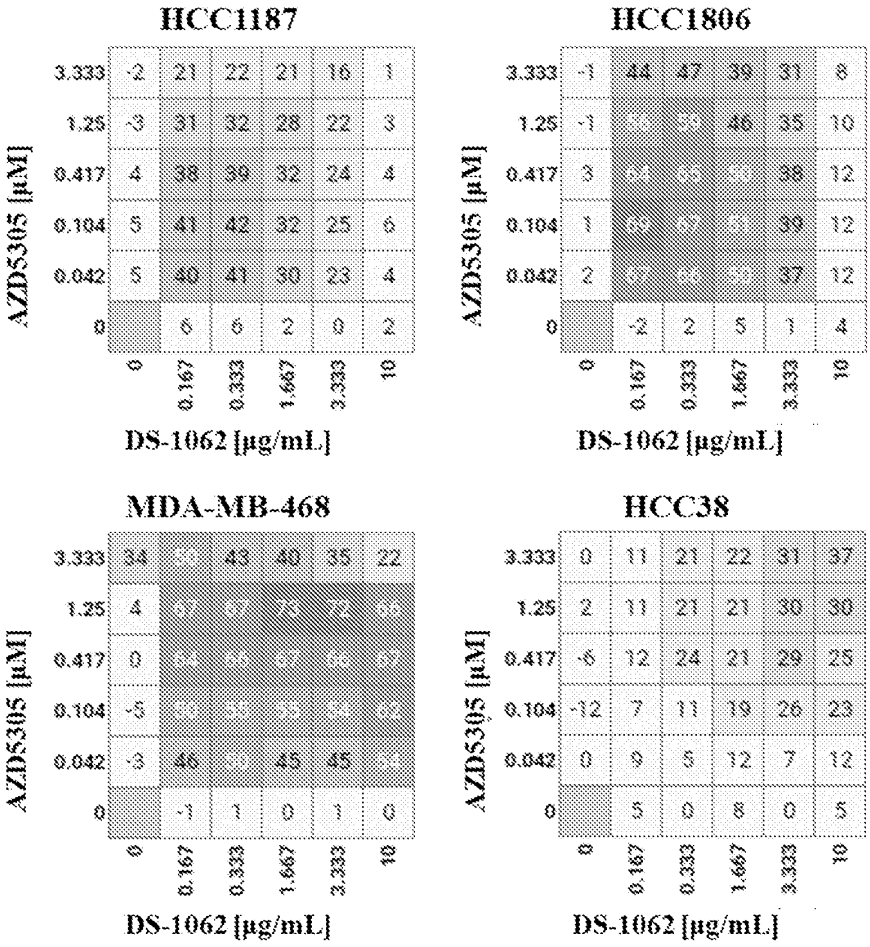
[Figure 12B]


NCI-H1650
AZD5305 [µM]
3.333 2 47 52 59 65 64
1.25 2 45 50 56 66 62
0.417 0 37 45 52 61 62
0.104 -1 34 39 47 52 59
0.042 0 29 35 40 46 52
0 -2 1 5 3 9
0 0.167 0.333 1.667 3.333 10
DS-1062 [µg/mL]
NCI-H322
AZD5305 [µM]
3.333 2 47 45 46
1.25 -3 45 46 44 44
0.417 0 42 45 42 41
0.104 -4 43 43 39 39
0.042 2 34 42 38 35 36
0 -2 0 0 0 0
0 0.167 0.333 1.667 3.333 10
DS-1062 [µg/mL]
NCI-H3255
AZD5305 [µM]
3.333 5 30 22 38 46 76
1.25 -3 27 22 42 57 77
0.417 9 28 21 33 39 74
0.104 18 38 33 39 50 80
0.042 15 32 18 32 24 54
0 -2 5 1 -11 10
0 0.167 0.333 1.667 3.333 10
CALU3
AZD5305 [µM]
3.333 5 28 9 15 22
1.25 3 31 14 21 30
0.417 2 31 16 24 33
0.104 3 35 17 23 30
0.042 0 35 15 21 26
0 0 0 5 -1 0
0 0.167 0.333 1.667 3.333 10

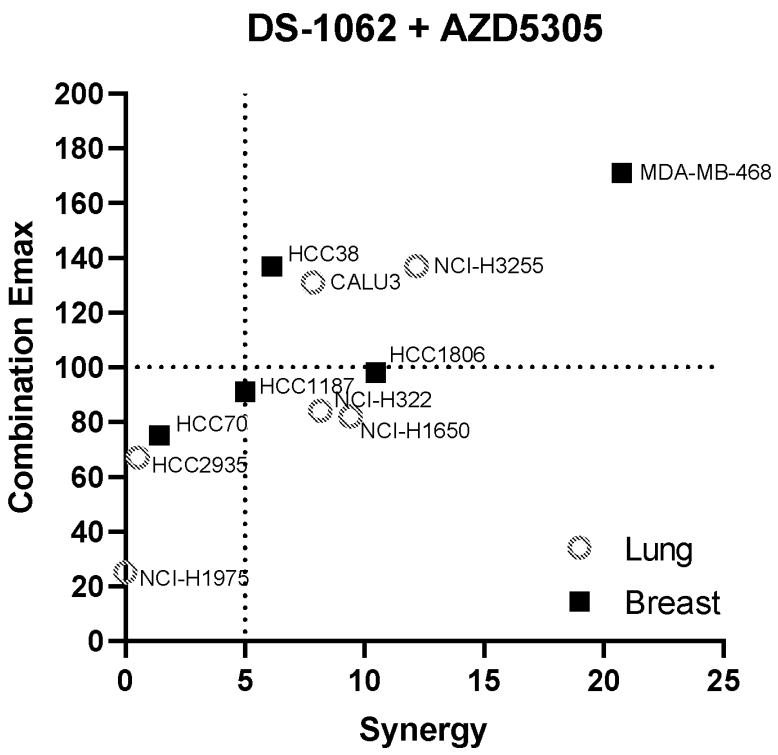
[Figure 13A]


HCC1187
AZD5305 [μM]
3.333 42 82 84 87 88 91
1.25 38 75 77 84 85 87
0.417 41 74 72 77 82 89
0.104 33 67 73 78 82 89
0.042 30 67 71 78 79 88
0 0 34 39 49 57 76
0 0.167 0.333 1.667 3.333 10
DS-1062 [μg/mL]
HCC1806
AZD5305 [μM]
3.333 42 99 94 96 96 97
1.25 29 99 96 95 95 97
0.417 25 97 93 96 96 98
0.104 14 88 91 95 97 96
0.042 14 94 89 95 94 97
0 0 11 25 54 69 78
0 0.167 0.333 1.667 3.333 10
DS-1062 [μg/mL]
MDA-MB-468
AZD5305 [μM]
3.333 25 134 144 29 23 152
1.25 15 114 132 146 152 171
0.417 7 115 132 154 155 167
0.104 -2 100 119 148 149 160
0.042 1 100 118 139 143 153
0 0 58 67 86 93 99
0 0.167 0.333 1.667 3.333 10
DS-1062 [μg/mL]
HCC38
AZD5305 [μM]
3.333 30 104 110 112 122 137
1.25 12 104 109 119 131 119
0.417 -11 103 117 121 125 116
0.104 -23 95 100 113 124 123
0.042 -5 97 97 109 97 106
0 -9 88 90 97 95 91
0 0.167 0.333 1.667 3.333 10
DS-1062 [μg/mL]

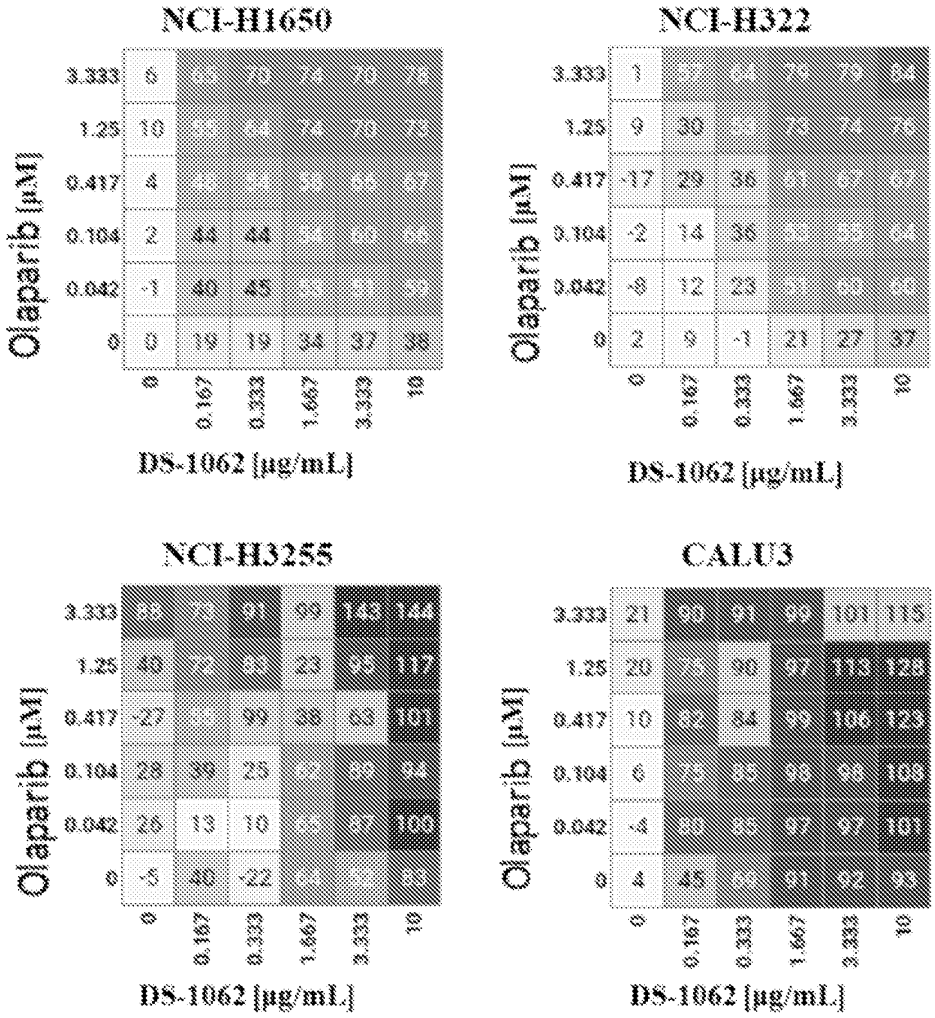
[Figure 13B]


HCC1187
AZD5305 [μM]
3.333 -2 21 22 21 16 1
1.25 -3 31 32 28 22 3
0.417 4 38 39 32 24 4
0.104 5 41 42 32 25 6
0.042 5 40 41 30 23 4
0 6 6 2 0 2
0 0.167 0.333 1.667 3.333 10
DS-1062 [μg/mL]
HCC1806
AZD5305 [μM]
3.333 -1 44 47 39 31 8
1.25 -1 50 50 46 35 10
0.417 3 52 54 45 38 12
0.104 1 52 57 47 39 12
0.042 2 47 50 42 37 12
0 -2 2 5 1 4
0 0.167 0.333 1.667 3.333 10
DS-1062 [μg/mL]
MDA-MB-468
AZD5305 [μM]
3.333 34 50 43 40 35 22
1.25 4 47 57 49 42 30
0.417 0 44 55 47 40 27
0.104 -5 39 50 43 36 23
0.042 -3 46 57 45 45 32
0 -1 1 0 1 0
0 0.167 0.333 1.667 3.333 10
DS-1062 [μg/mL]
HCC38
AZD5305 [μM]
3.333 0 11 21 22 31 37
1.25 2 11 21 21 30 30
0.417 -6 12 24 21 29 25
0.104 -12 7 11 19 26 23
0.042 0 9 5 12 7 12
0 5 0 8 0 5
0 0.167 0.333 1.667 3.333 10
DS-1062 [μg/mL]

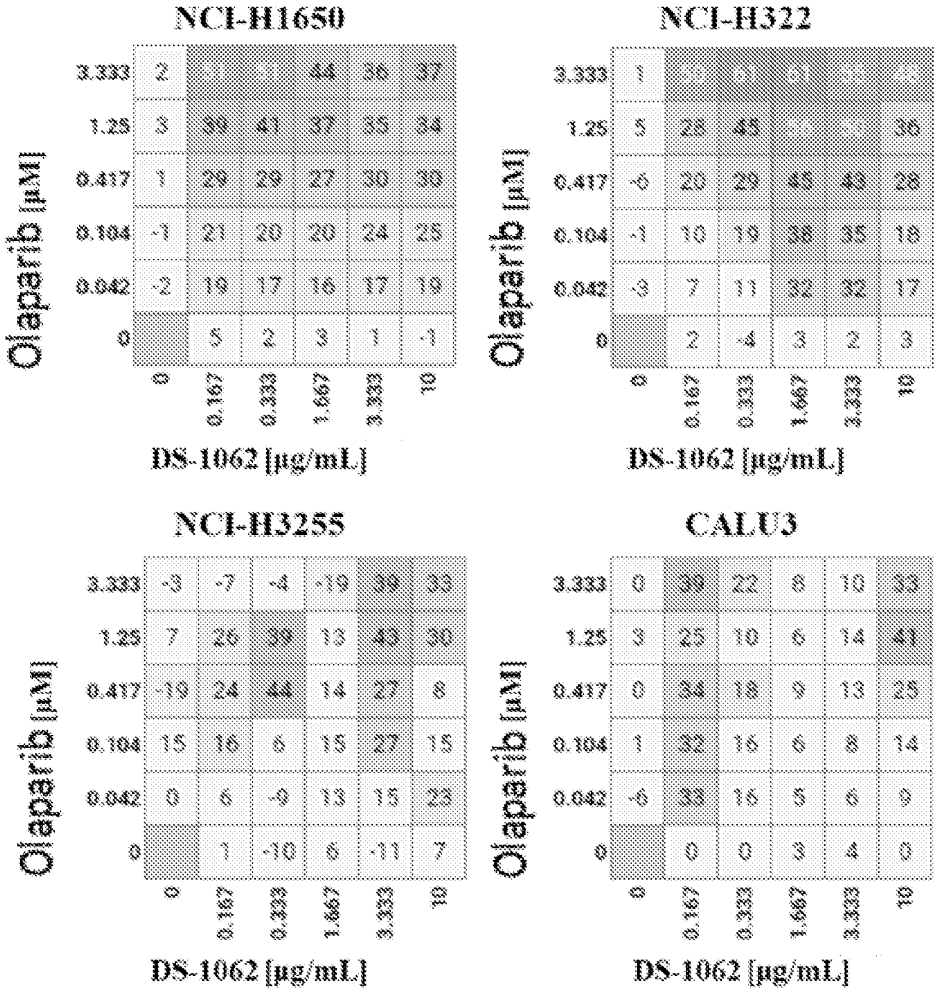
[Figure 14]


DS-1062 + AZD5305
Combination Emax
Synergy
200
180
160
140
120
100
80
60
40
20
0
0
5
10
15
20
25
MDA-MB-468
HCC38
CALU3
NCI-H3255
HCC1806
HCC1187
NCI-H322
NCI-H1650
HCC70
HCC2935
NCI-H1975
Lung
Breast

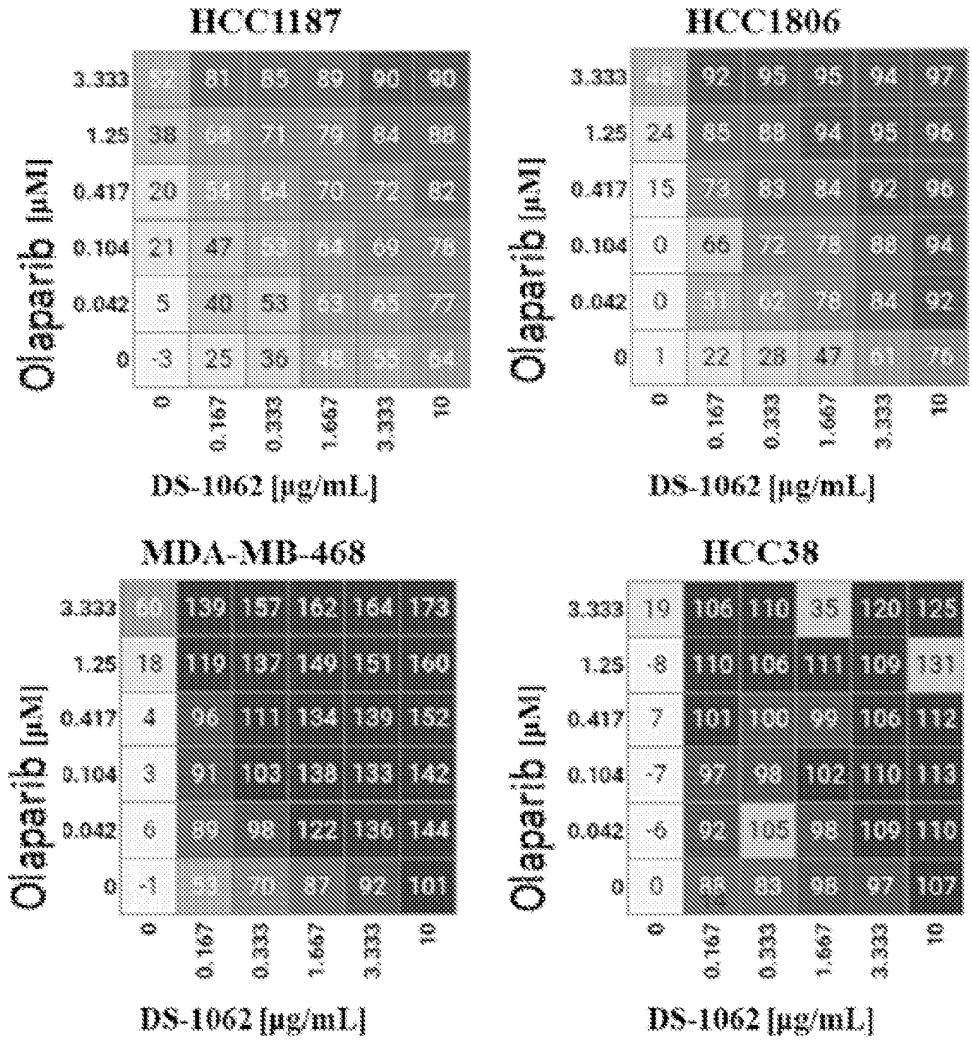
[Figure 15A]


NCI-H1650
Olaparib [μM]
3.333
1.25
0.417
0.104
0.042
0
6
10
4
2
-1
0
19
19
34
37
38
0
0.167
0.333
1.667
3.333
10
DS-1062 [μg/mL]
NCI-H322
Olaparib [μM]
3.333
1.25
0.417
0.104
0.042
0
1
9
-17
-2
-8
2
9
-1
21
27
37
0
0.167
0.333
1.667
3.333
10
DS-1062 [μg/mL]
NCI-H3255
Olaparib [μM]
3.333
1.25
0.417
0.104
0.042
0
-5
40
-22
0
0.167
0.333
1.667
3.333
10
DS-1062 [μg/mL]
CALU3
Olaparib [μM]
3.333
1.25
0.417
0.104
0.042
0
21
20
10
6
-4
4
45
0
0.167
0.333
1.667
3.333
10
DS-1062 [μg/mL]

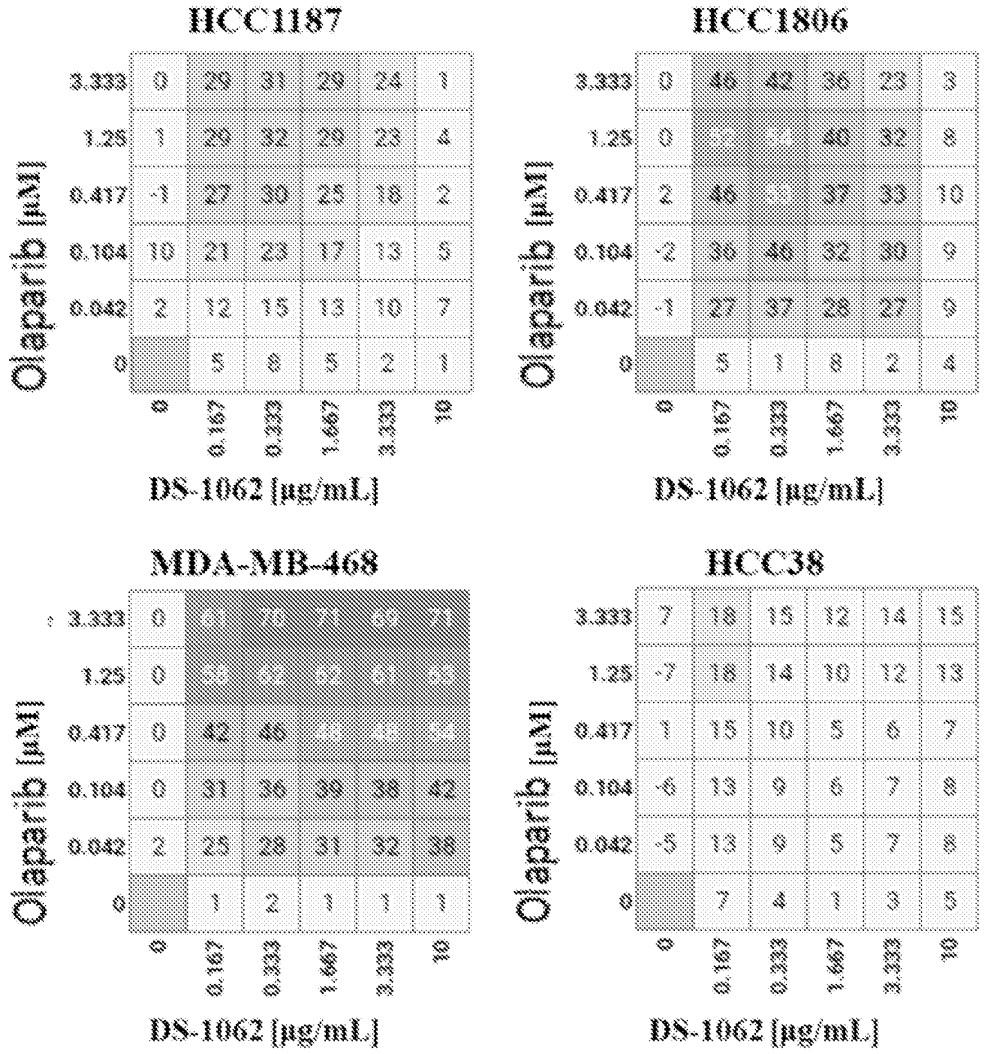
[Figure 15B]


NCI-H1650
Olaparib [μM]
3.333 2 44 36 37
1.25 3 39 41 37 35 34
0.417 1 29 29 27 30 30
0.104 -1 21 20 20 24 25
0.042 -2 19 17 16 17 19
0 5 2 3 1 -1
0 0.167 0.333 1.667 3.333 10
DS-1062 [μg/mL]
NCI-H322
Olaparib [μM]
3.333 1 5 28 45 36
1.25 5 28 45 36
0.417 -6 20 29 45 43 28
0.104 -1 10 19 38 35 18
0.042 -3 7 11 32 32 17
0 2 -4 3 2 3
0 0.167 0.333 1.667 3.333 10
DS-1062 [μg/mL]
NCI-H3255
Olaparib [μM]
3.333 -3 -7 -4 -19 39 33
1.25 7 26 39 13 43 30
0.417 -19 24 44 14 27 8
0.104 15 16 6 15 27 15
0.042 0 6 -9 13 15 23
0 1 -10 6 -11 7
0 0.167 0.333 1.667 3.333 10
DS-1062 [μg/mL]
CALU3
Olaparib [μM]
3.333 0 39 22 8 10 33
1.25 3 25 10 6 14 41
0.417 0 34 18 9 13 25
0.104 1 32 16 6 8 14
0.042 -6 33 16 5 6 9
0 0 0 3 4 0
0 0.167 0.333 1.667 3.333 10
DS-1062 [μg/mL]

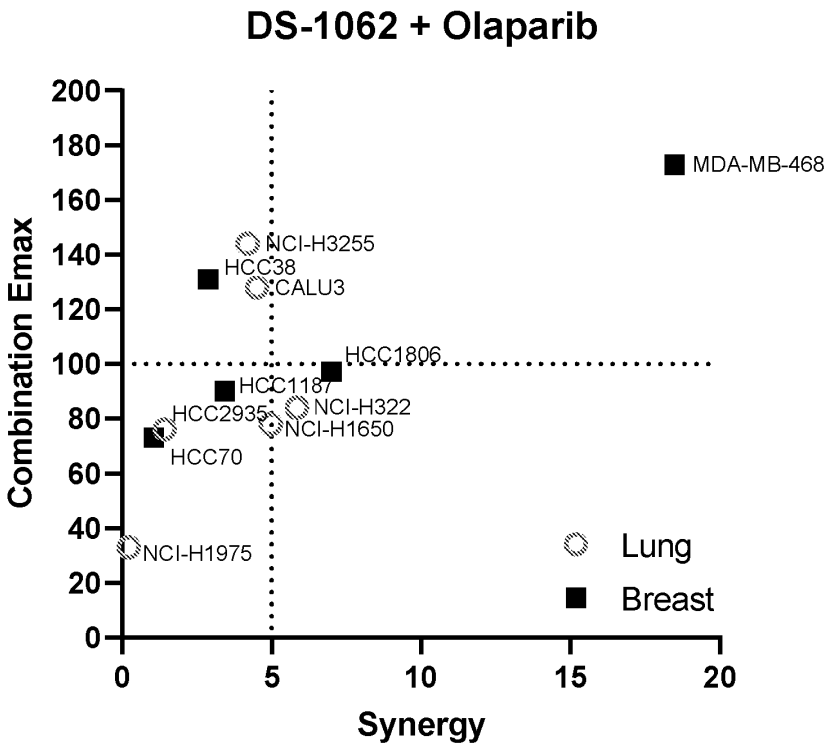
[Figure 16A]


HCC1187
Olaparib [μM]
3.333
1.25
0.417
0.104
0.042
0
0 0.167 0.333 1.667 3.333 10
DS-1062 [μg/mL]
HCC1806
Olaparib [μM]
3.333
1.25
0.417
0.104
0.042
0
0 0.167 0.333 1.667 3.333 10
DS-1062 [μg/mL]
MDA-MB-468
Olaparib [μM]
3.333
1.25
0.417
0.104
0.042
0
0 0.167 0.333 1.667 3.333 10
DS-1062 [μg/mL]
HCC38
Olaparib [μM]
3.333
1.25
0.417
0.104
0.042
0
0 0.167 0.333 1.667 3.333 10
DS-1062 [μg/mL]

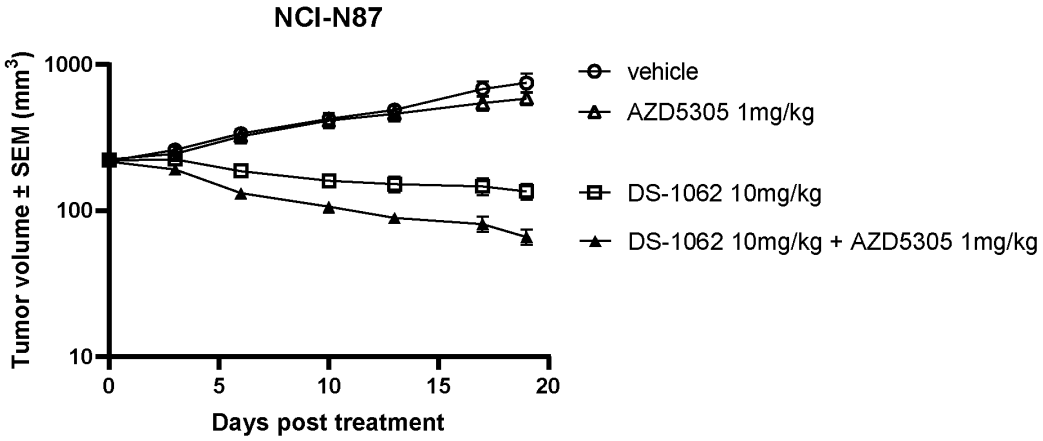
[Figure 16B]


HCC1187
Olaparib [μM]
3.333 0 29 31 29 24 1
1.25 1 29 32 29 23 4
0.417 -1 27 30 25 18 2
0.104 10 21 23 17 13 5
0.042 2 12 15 13 10 7
0 5 8 5 2 1
0 0.167 0.333 1.667 3.333 10
DS-1062 [μg/mL]
HCC1806
Olaparib [μM]
3.333 0 46 42 36 23 3
1.25 0 40 32 8
0.417 2 46 37 33 10
0.104 -2 36 46 32 30 9
0.042 -1 27 37 28 27 9
0 5 1 8 2 4
0 0.167 0.333 1.667 3.333 10
DS-1062 [μg/mL]
MDA-MB-468
Olaparib [μM]
3.333 0
1.25 0
0.417 0 42 46
0.104 0 31 36 38 42
0.042 2 25 28 31 32 38
0 1 2 1 1 1
0 0.167 0.333 1.667 3.333 10
DS-1062 [μg/mL]
HCC38
Olaparib [μM]
3.333 7 18 15 12 14 15
1.25 -7 18 14 10 12 13
0.417 1 15 10 5 6 7
0.104 -6 13 9 6 7 8
0.042 -5 13 9 5 7 8
0 7 4 1 3 5
0 0.167 0.333 1.667 3.333 10
DS-1062 [μg/mL]

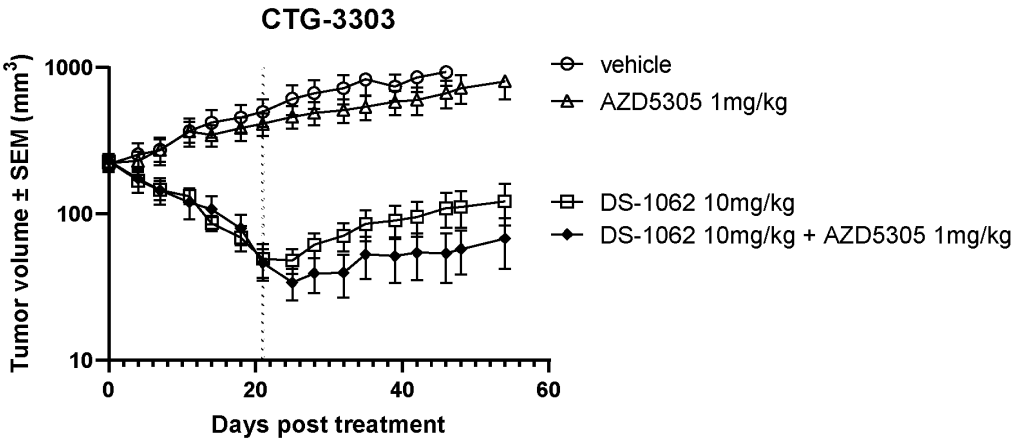
[Figure 17]



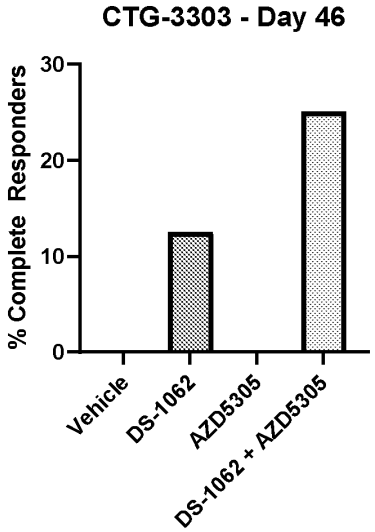
[Figure 18]



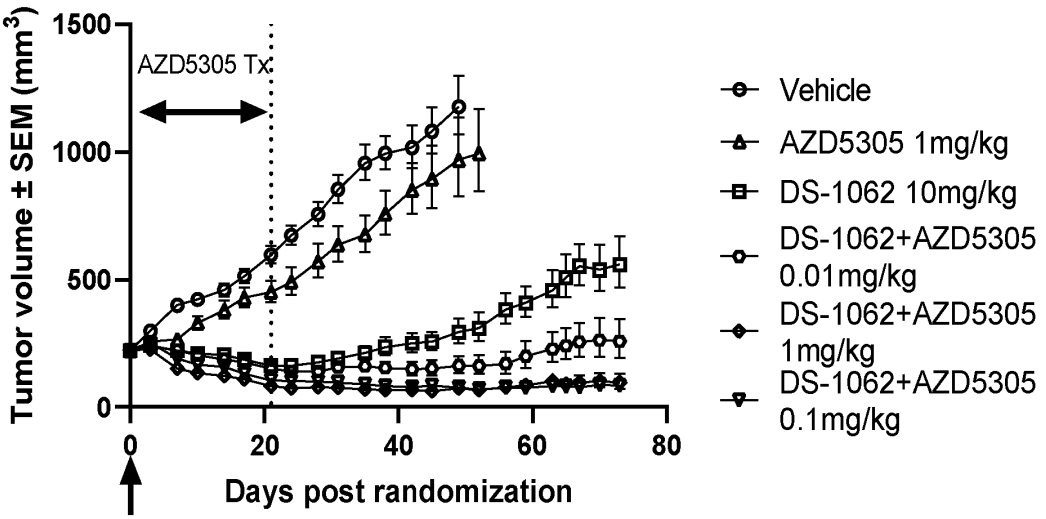
[Figure 19A]



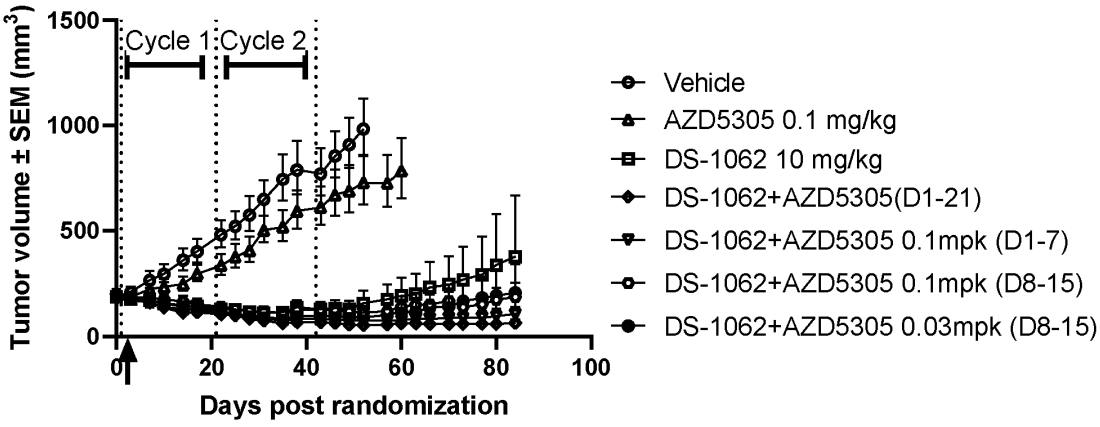
[Figure 19B]



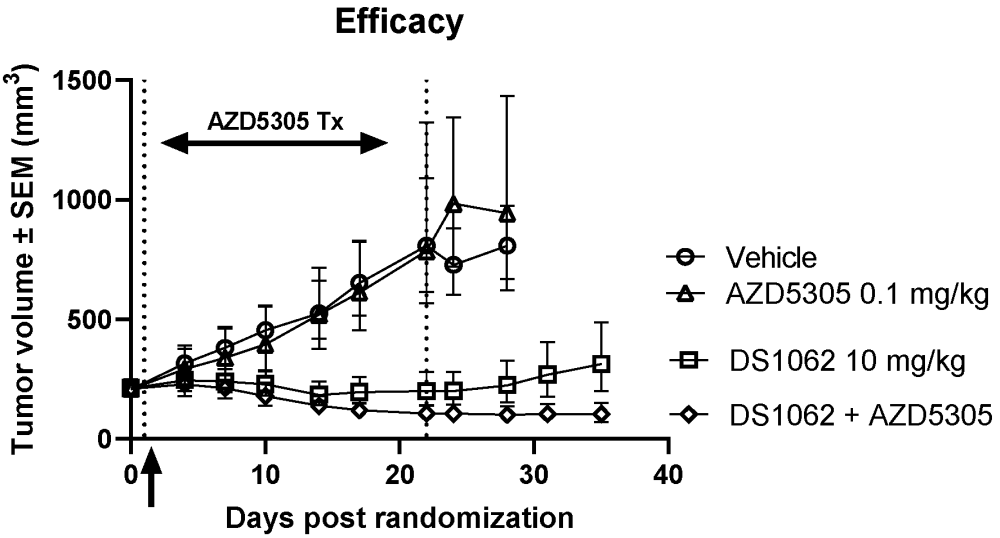
[Figure 20]



[Figure 21]



[Figure 22]


Efficacy
Tumor volume ± SEM (mm3)
1500
1000
500
0
AZD5305 Tx
0
10
20
30
40
Days post randomization
Vehicle
AZD5305 0.1 mg/kg
DS1062 10 mg/kg
DS1062 + AZD5305