FIG. 1

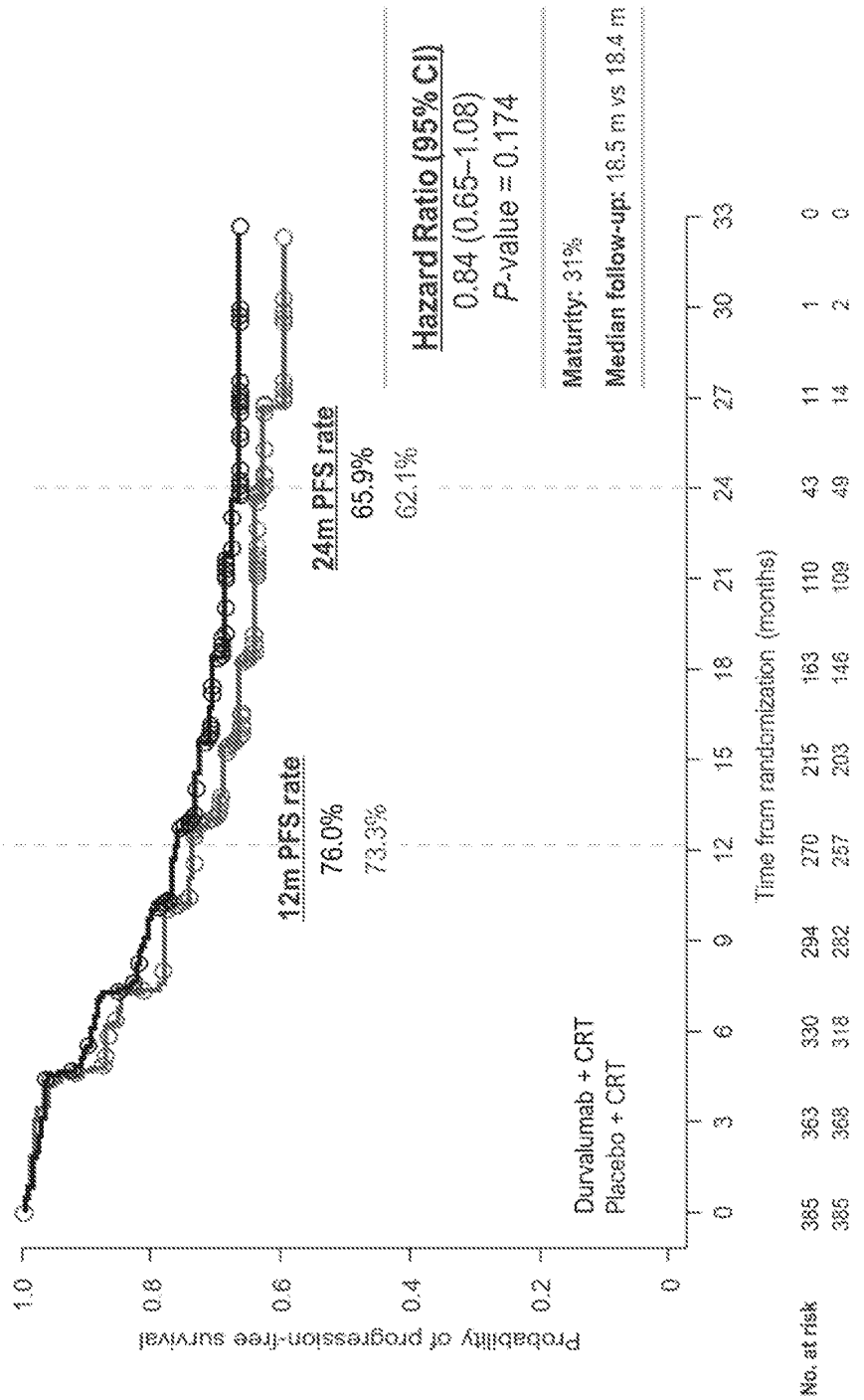

Probability of progression-free survival
1.0
0.8
0.6
0.4
0.2
0
Durvalumab + CRT
Placebo + CRT
12m PFS rate
76.0%
73.3%
24m PFS rate
65.9%
62.1%
Hazard Ratio (95% CI)
0.84 (0.65–1.08)
P-value = 0.174
Maturity: 31%
Median follow-up: 18.5 m vs 18.4 m
0 3 6 9 12 15 18 21 24 27 30 33
Time from randomization (months)
No. at risk
Durvalumab + CRT 385 363 330 294 270 215 163 110 43 11 1 0
Placebo + CRT 385 368 318 282 257 203 146 109 49 14 2 0

FIG. 2

Cut-point	N (prevalence)	HR (95% CI)
ITT	770 (100%)	0.84 (0.65, 1.08)
TAP>=1%	708 (96%)	0.83 (0.64, 1.09)
TAP>=5%	611 (83%)	0.84 (0.63, 1.13)
TAP>=10%	481 (66%)	0.79 (0.57, 1.10)
TAP>=20%	369 (50%)	0.62 (0.42, 0.91)
TAP>=30%	298 (40%)	0.62 (0.40, 0.95)
TAP>=40%	233 (32%)	0.65 (0.40, 1.02)
TAP>=50%	189 (26%)	0.54 (0.31, 0.90)
TAP>=60%	162 (22%)	0.44 (0.24, 0.77)

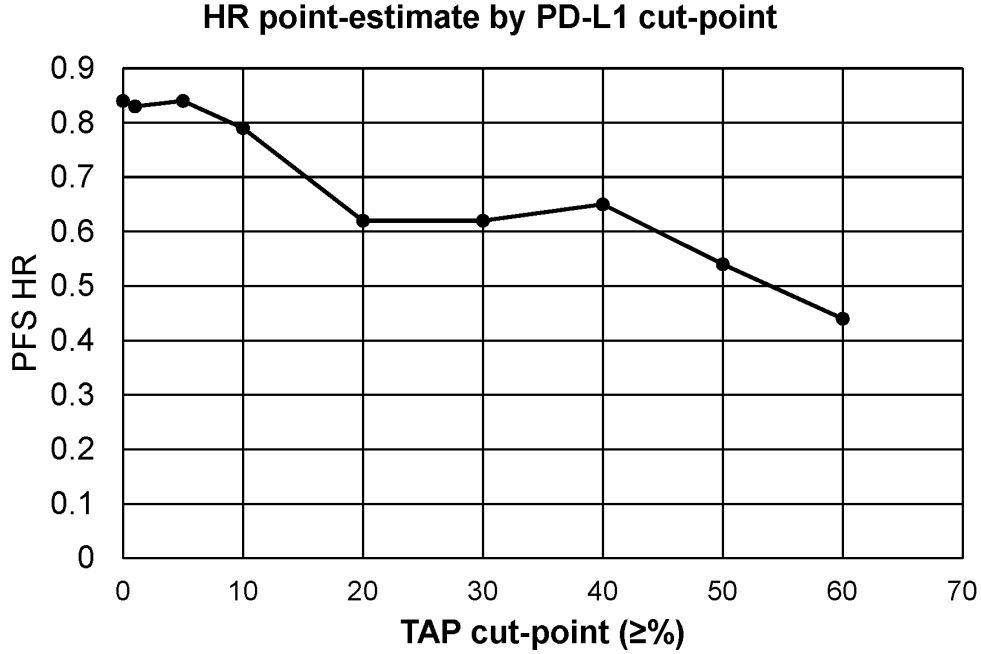


FIG. 3

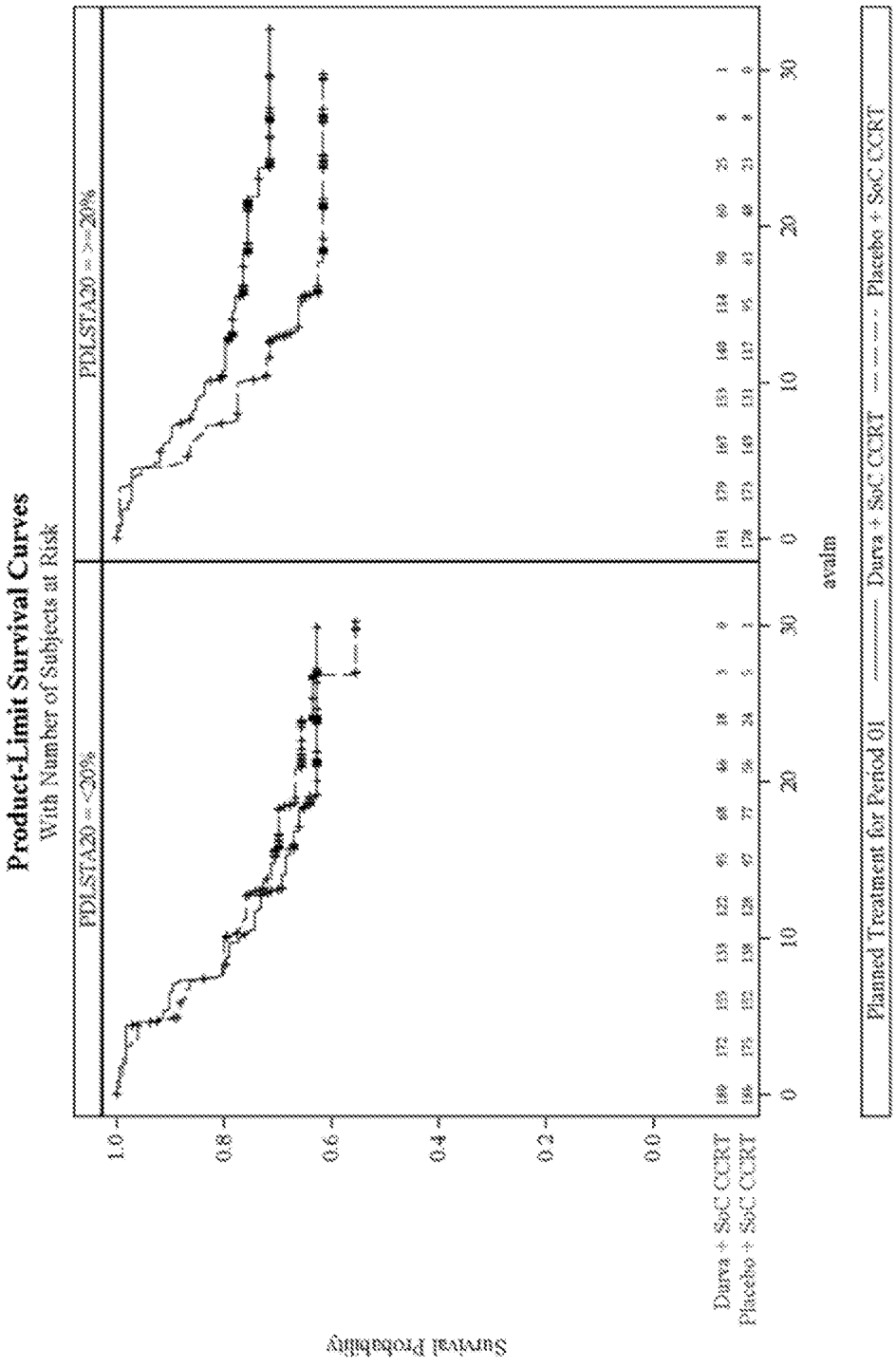

Product-Limit Survival Curves
With Number of Subjects at Risk
PDLSTA20 = <20%
PDLSTA20 = >=20%
Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
Durva + SoC CCRT
Placebo + SoC CCRT
0
10
20
30
avalm
Planned Treatment for Period 01
Durva + SoC CCRT
Placebo + SoC CCRT

FIG. 4

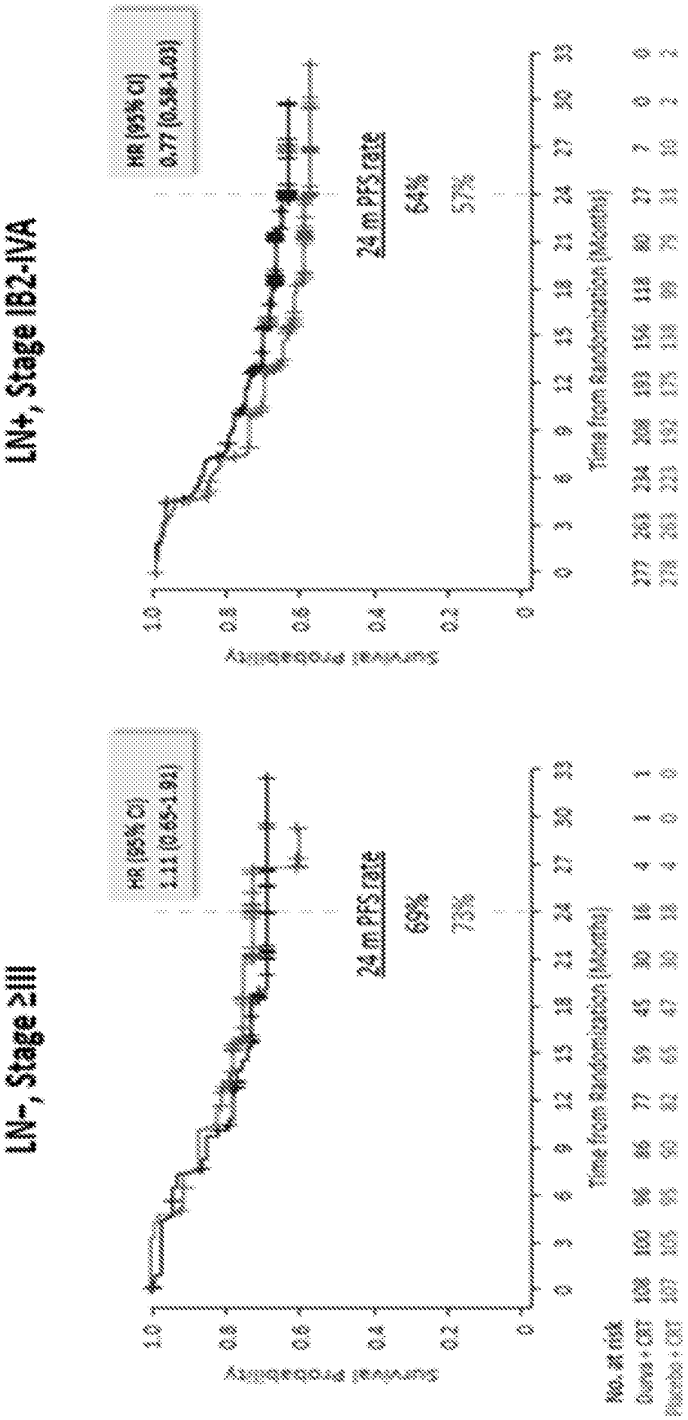

LN+, Stage IB2-IVA
HR (95% CI)
0.77 (0.58-1.03)
24 m PFS rate
64%
57%
Survival Probability
Time from Randomization (Months)
LN-, Stage ≥IIII
HR (95% CI)
1.11 (0.65-1.91)
24 m PFS rate
69%
73%
Survival Probability
Time from Randomization (Months)
No. at risk

FIG. 5

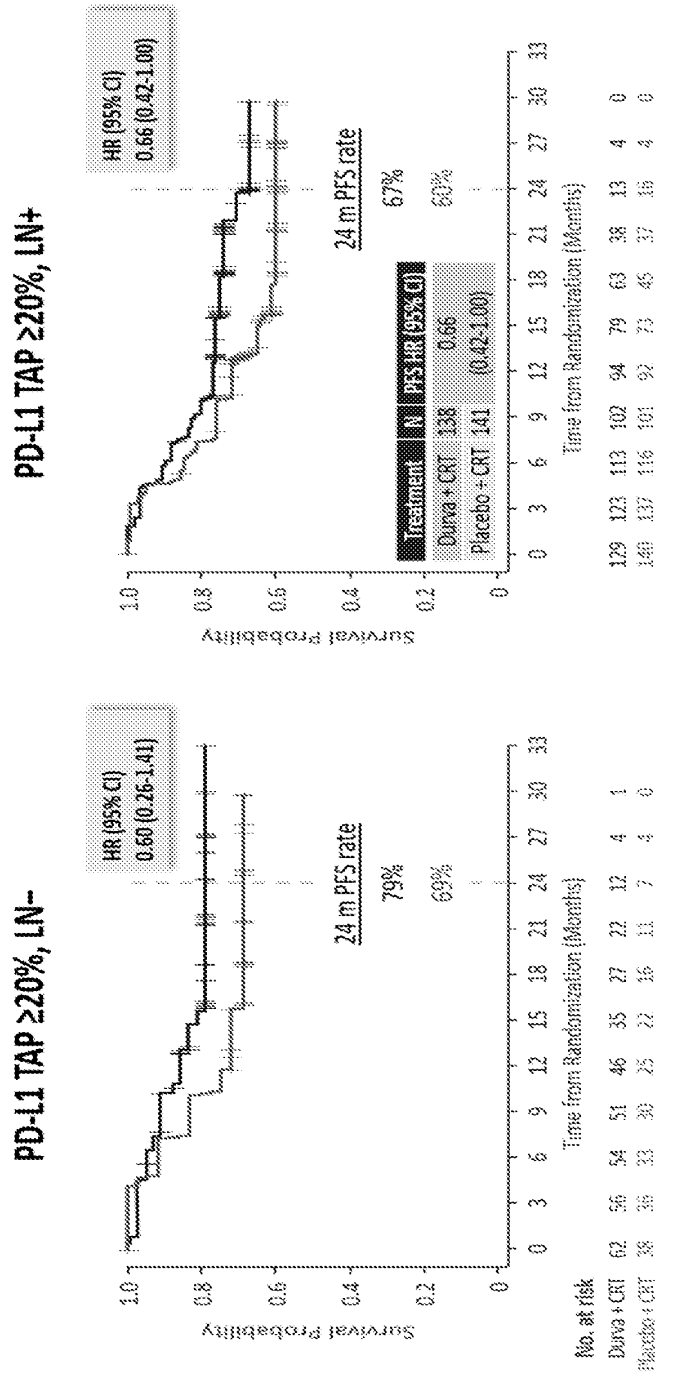
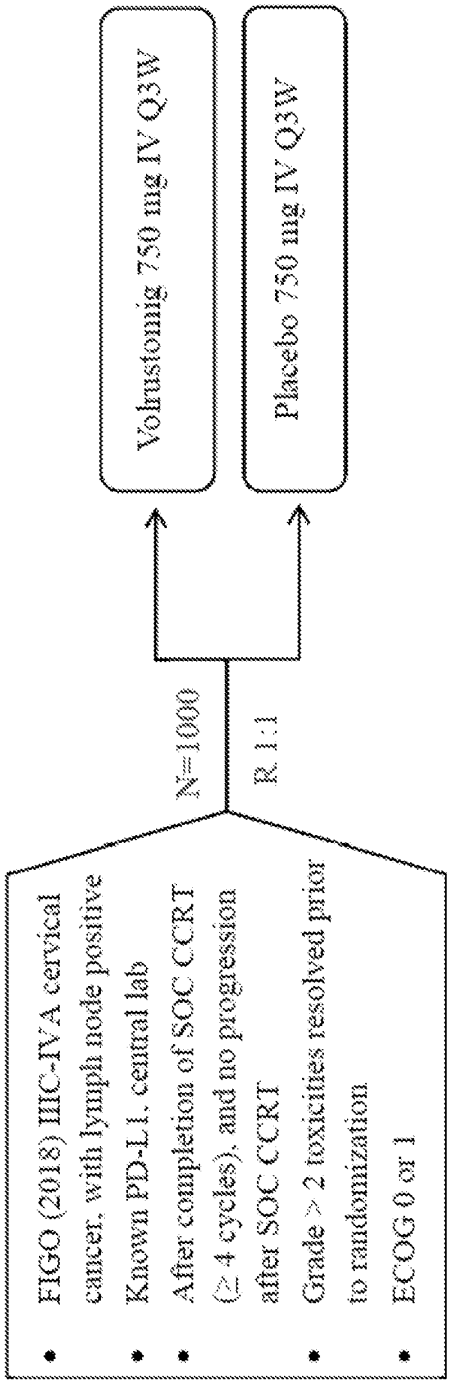

PD-L1 TAP ≥20%, LN+
HR (95% CI)
0.66 (0.42-1.00)
24 m PFS rate
67%
69%
Treatment N PFS HR (95% CI)
Durva + CRT 138 0.66
Placebo + CRT 141 (0.42-1.00)
Survival Probability
Time from Randomization (Months)
PD-L1 TAP ≥20%, LN-
HR (95% CI)
0.60 (0.26-1.41)
24 m PFS rate
79%
69%
Survival Probability
Time from Randomization (Months)
No. at risk
Durva + CRT 62 56 54 51 46 35 27 22 12 4 1
Placebo + CRT 38 36 33 30 25 22 16 11 7 4 0
129 123 113 102 94 79 63 38 13 4 0
141 137 116 101 92 73 45 37 16 4 0

FIG. 6


FIGO (2018) IIIC-IVA cervical cancer, with lymph node positive
Known PD-L1, central lab
After completion of SOC CCRT (≥ 4 cycles), and no progression after SOC CCRT
Grade > 2 toxicities resolved prior to randomization
ECOG 0 or 1
N=1000
R 1:1
Volrustomig 750 mg IV Q3W
Placebo 750 mg IV Q3W

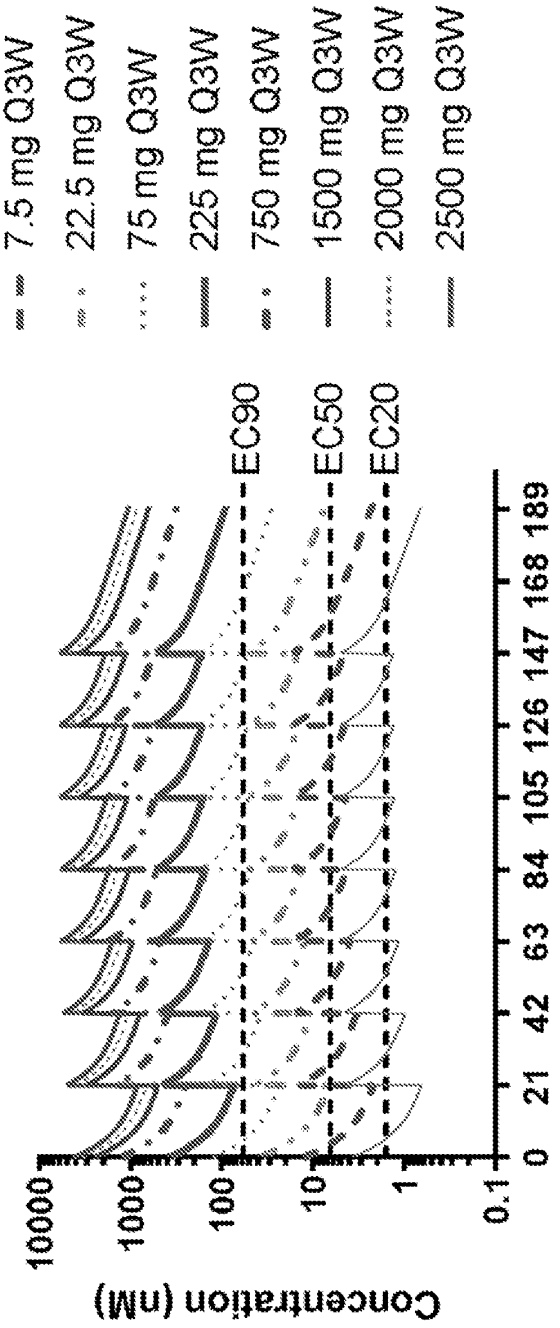

2.25 mg Q3W
7.5 mg Q3W
22.5 mg Q3W
75 mg Q3W
225 mg Q3W
750 mg Q3W
1500 mg Q3W
2000 mg Q3W
2500 mg Q3W
EC90
EC50
EC20
Concentration (nM)
10000
1000
100
10
1
0.1
0
21
42
63
84
105
126
147
168
189
Time (day)

FIG. 7

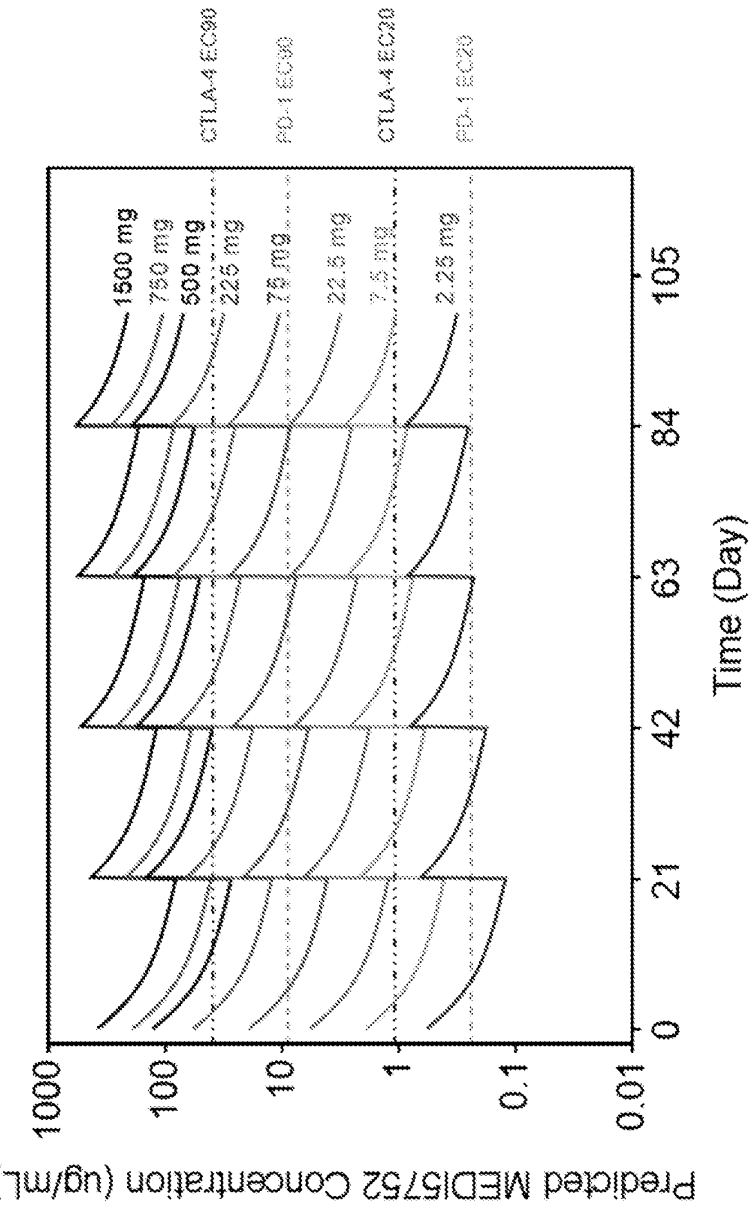

CTLA-4 EC90
PD-1 EC90
CTLA-4 EC20
PD-1 EC20
1500 mg
750 mg
500 mg
225 mg
75 mg
22.5 mg
7.5 mg
2.25 mg
1000
100
10
1
0.1
0.01
0
21
42
63
84
105
Time (Day)
Predicted MEDI5752 Concentration (ug/mL)

FIG. 8

FIG. 9A

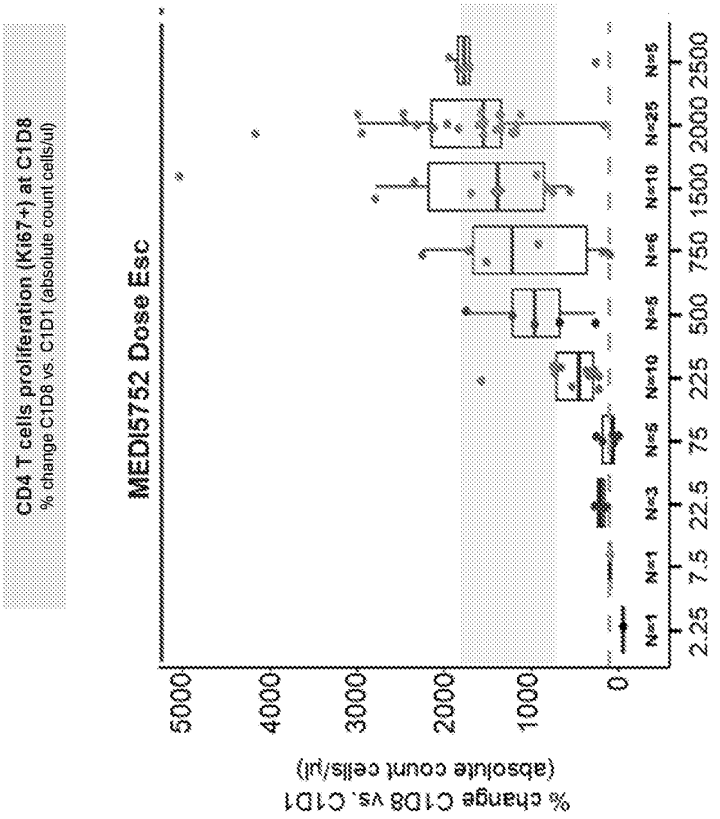
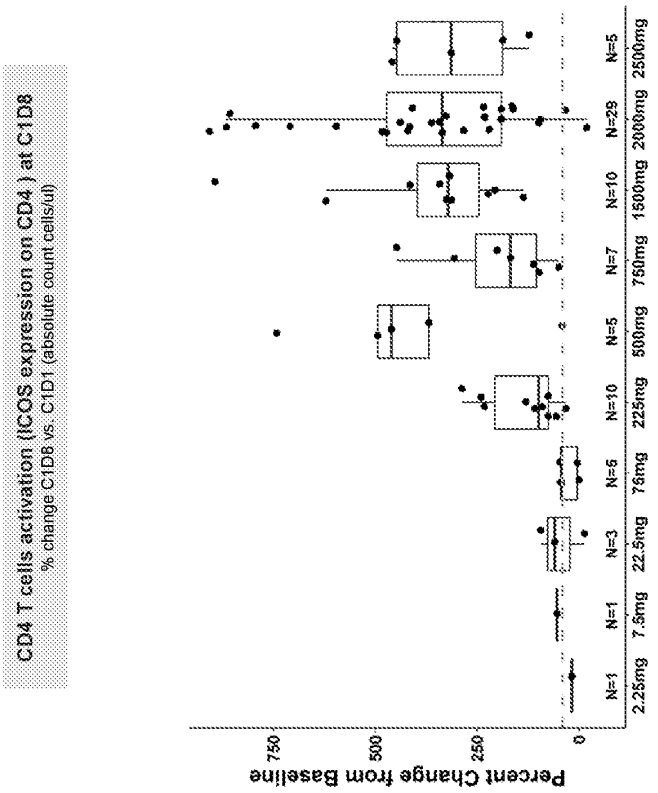
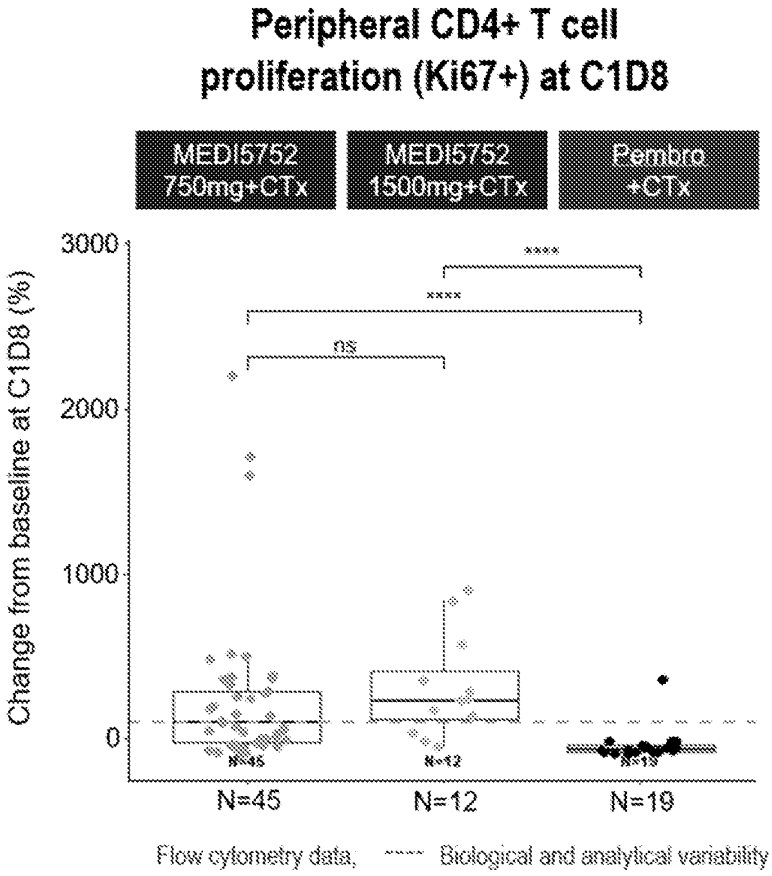

CD4 T cells proliferation (Ki67+) at C1D8
% change C1D8 vs. C1D1 (absolute count cells/ul)
MEDI5752 Dose Esc
% change C1D8 vs. C1D1 (absolute count cells/ul)
5000
4000
3000
2000
1000
0
N=1 N=1 N=3 N=6 N=10 N=5 N=6 N=10 N=25 N=5
2.25 7.5 22.5 75 225 500 750 1500 2000 2500
MEDI5752
---100% reference of technical and biological variability

FIG. 9B


CD4 T cells activation (ICOS expression on CD4) at C1D8
% change C1D8 vs. C1D1 (absolute count cells/ul)
Percent Change from Baseline
750
500
250
0
N=1 N=1 N=3 N=6 N=10 N=5 N=7 N=10 N=29 N=5
2.25mg 7.5mg 22.5mg 75mg 225mg 500mg 750mg 1500mg 2000mg 2500mg
MEDI5752
--- 40% reference of technical and biological variability


Peripheral CD4+ T cell proliferation (Ki67+) at C1D8
MEDI5752 750mg+CTx
MEDI5752 1500mg+CTx
Pembro +CTx
Change from baseline at C1D8 (%)
3000
2000
1000
0
****
****
ns
N=45
N=12
N=19
Flow cytometry data,
Biological and analytical variability

T cell expansion

FIG. 10A

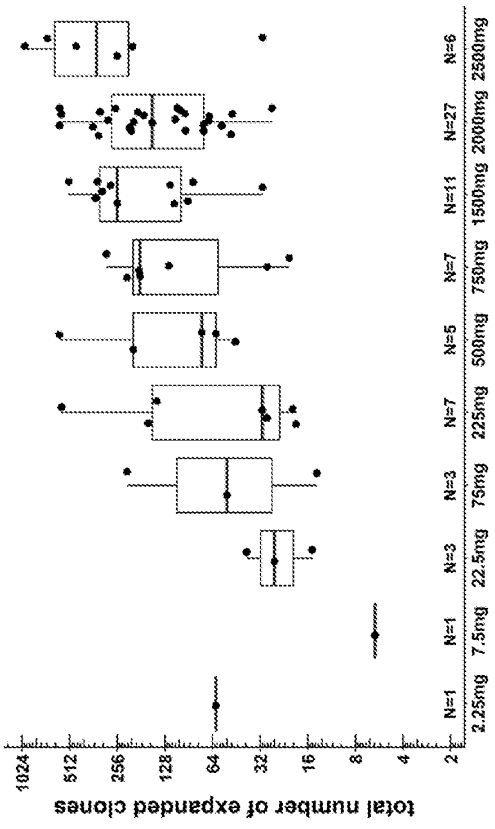


FIG. 10B

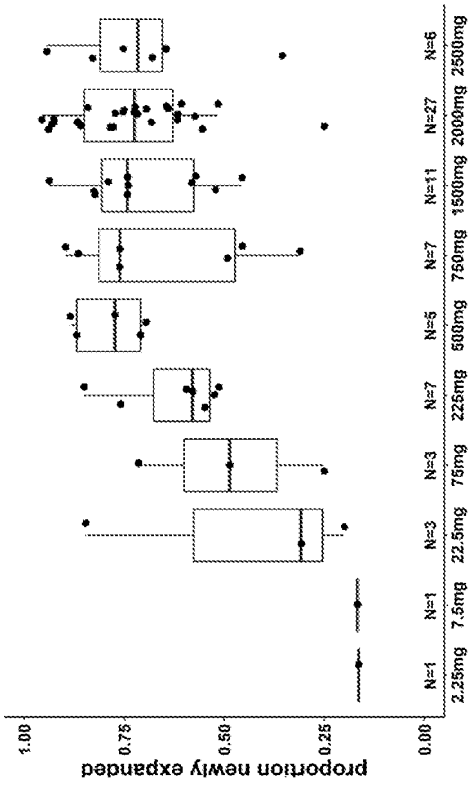
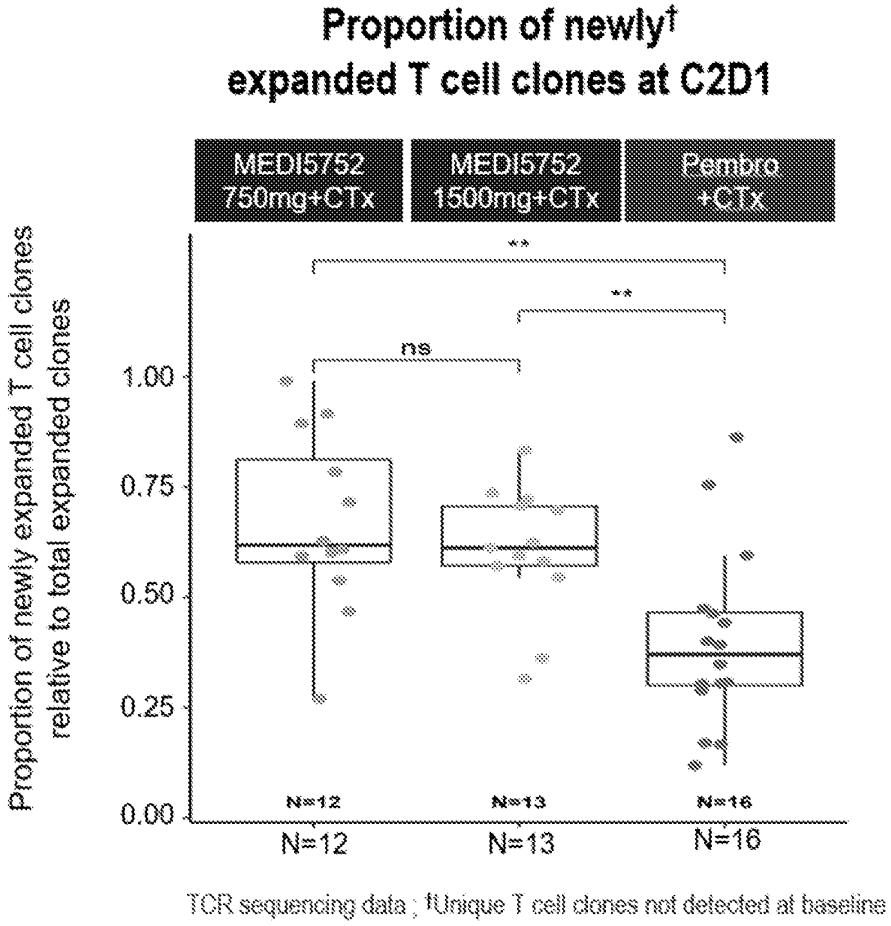


FIG. 10C



TCR sequencing data ; †Unique T cell clones not detected at baseline

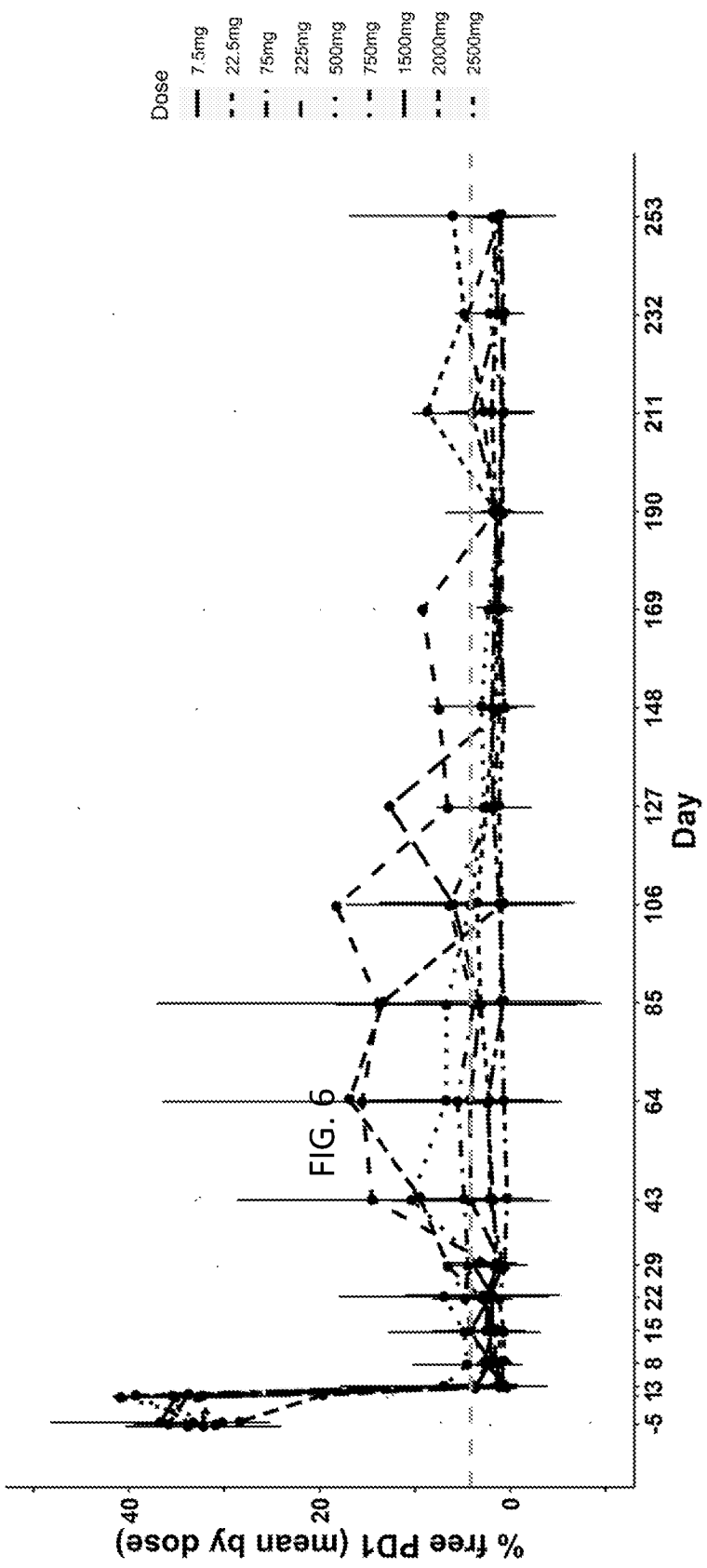

Dose
7.5mg
22.5mg
75mg
225mg
500mg
750mg
1500mg
2000mg
2500mg
% free PD1 (mean by dose)
40
20
0
-5 13 8 15 22 29 43 64 85 106 127 148 169 190 211 232 253
Day

FIG. 6

FIG. 11

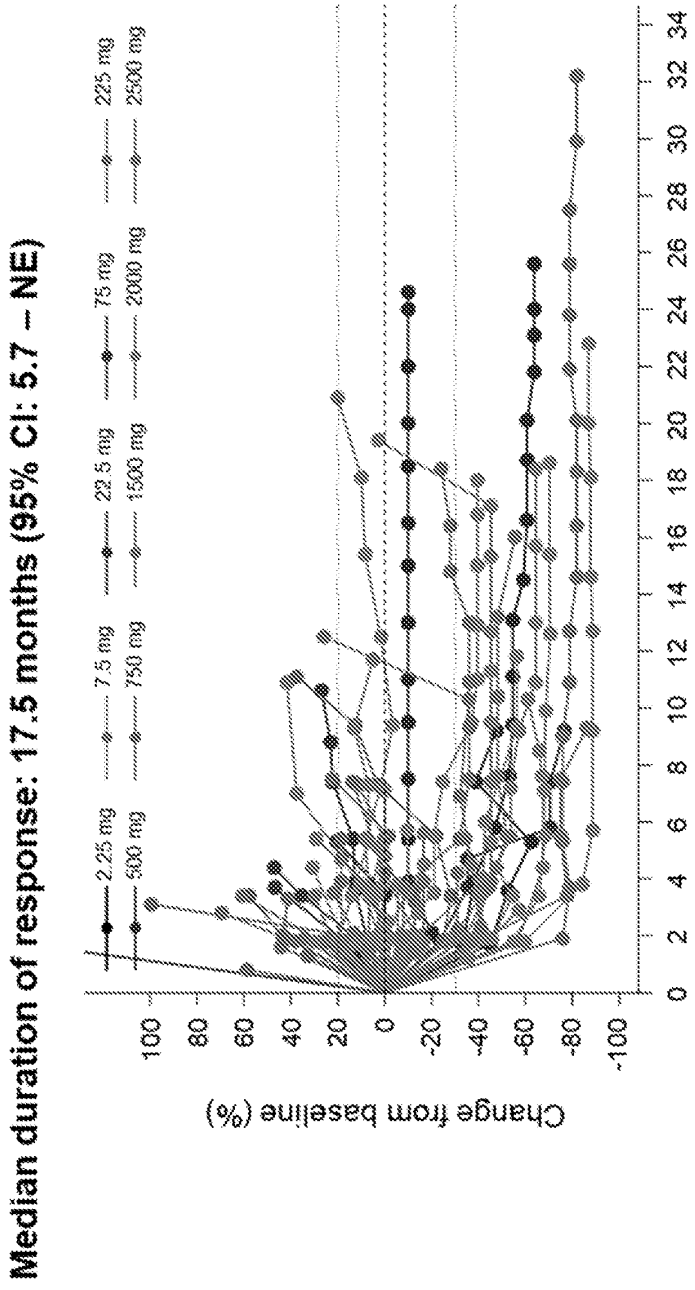

Median duration of response: 17.5 months (95% CI: 5.7 – NE)
2.25 mg
7.5 mg
22.5 mg
75 mg
225 mg
600 mg
750 mg
1500 mg
2000 mg
2500 mg
Change from baseline (%)
100
80
60
40
20
0
-20
-40
-60
-80
-100
0
2
4
6
8
10
12
14
16
18
20
22
24
26
28
30
32
34
Time (months)

FIG. 12

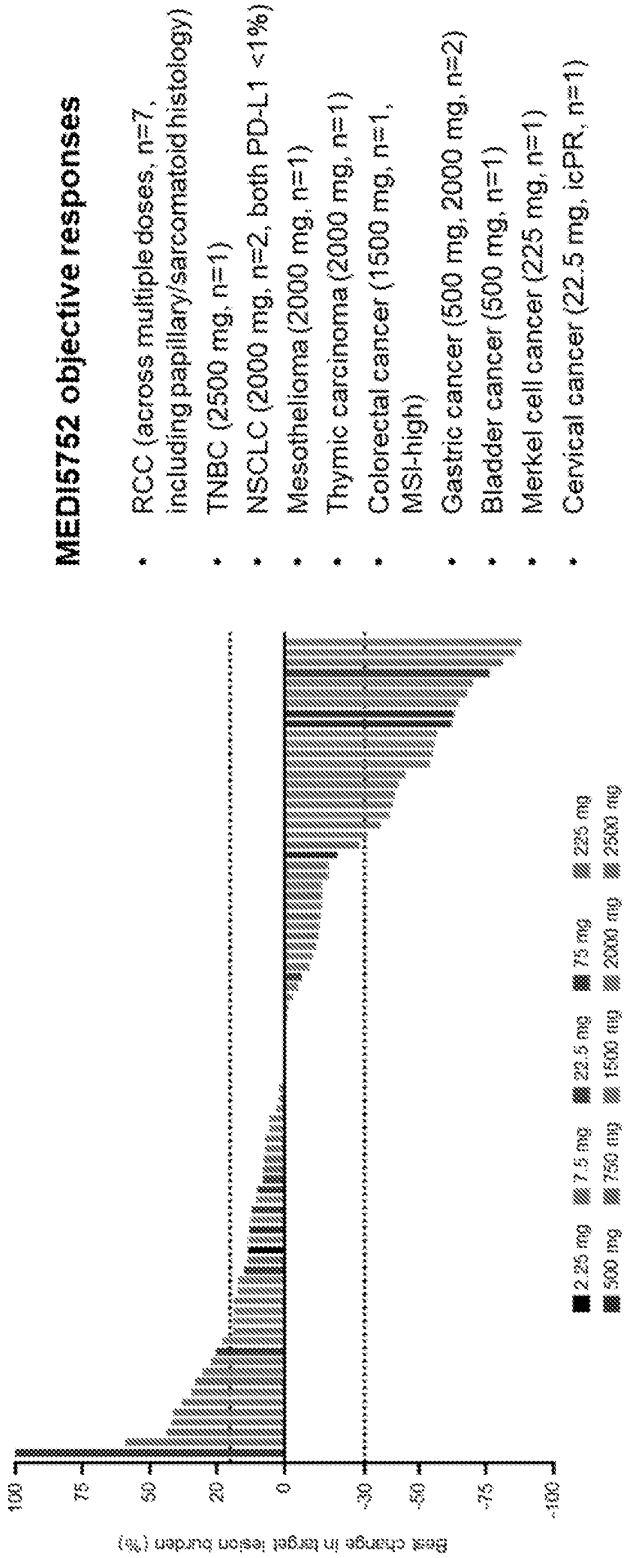

MEDI5752 objective responses
RCC (across multiple doses, n=7, including papillary/sarcomatoid histology)
TNBC (2500 mg, n=1)
NSCLC (2000 mg, n=2, both PD-L1 <1%)
Mesothelioma (2000 mg, n=1)
Thymic carcinoma (2000 mg, n=1)
Colorectal cancer (1500 mg, n=1, MSI-high)
Gastric cancer (500 mg, 2000 mg, n=2)
Bladder cancer (500 mg, n=1)
Merkel cell cancer (225 mg, n=1)
Cervical cancer (22.5 mg, icPR, n=1)
Best change in target lesion burden (%)
100
75
50
20
0
-30
-50
-75
-100
2.25 mg
7.5 mg
22.5 mg
75 mg
225 mg
500 mg
750 mg
1500 mg
2000 mg
2500 mg

FIG. 13

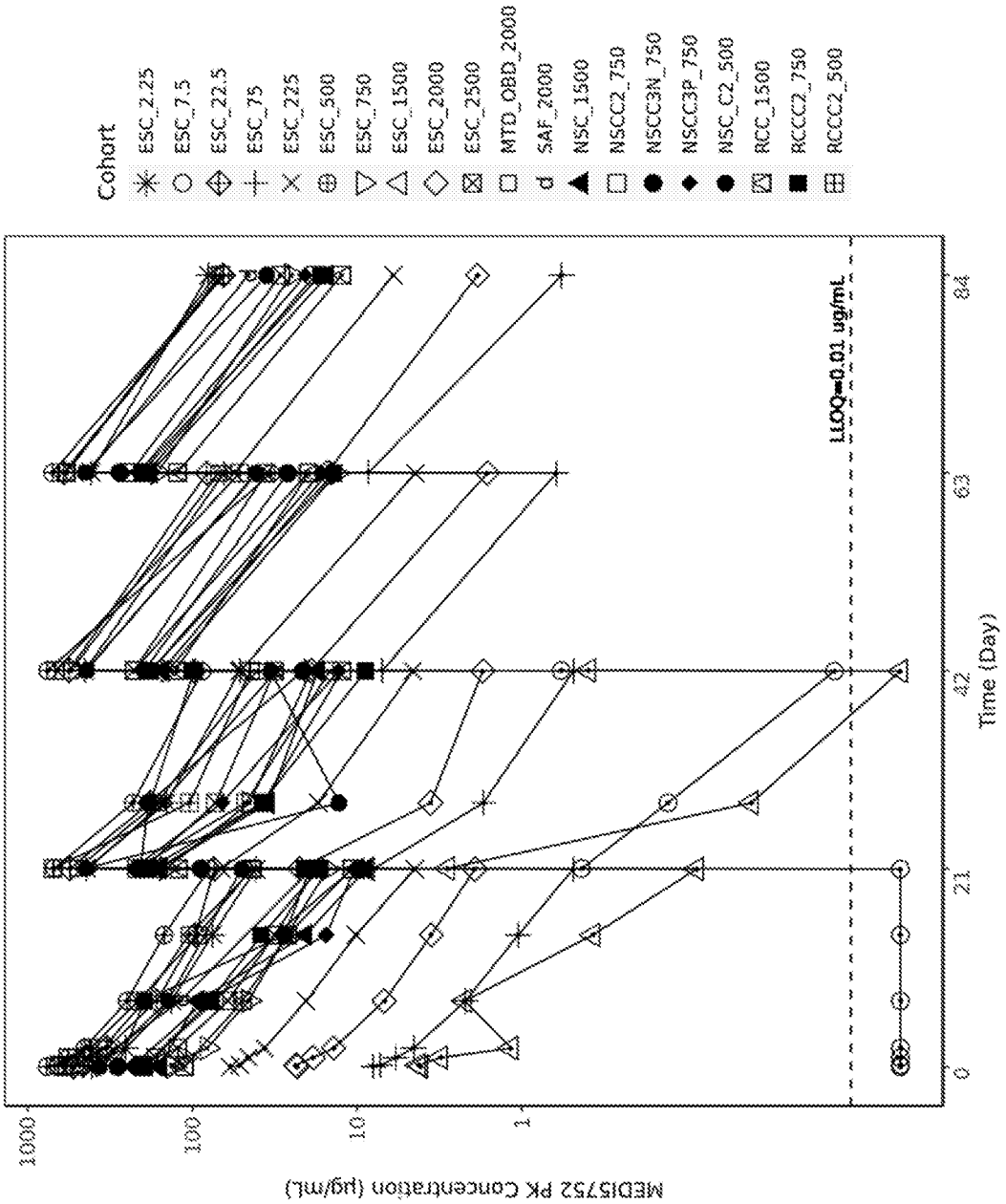
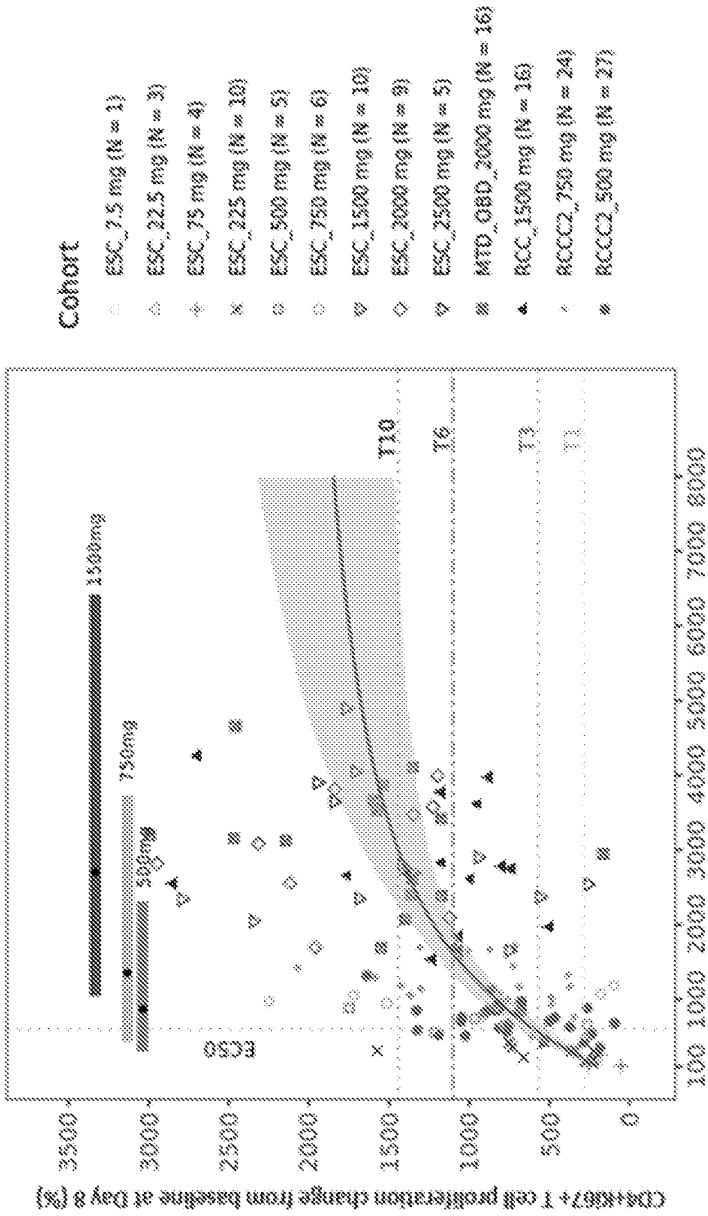

Cohort
ESC_2.25
ESC_7.5
ESC_22.5
ESC_75
ESC_225
ESC_500
ESC_750
ESC_1500
ESC_2000
ESC_2500
MTD_OBD_2000
SAF_2000
NSC_1500
NSCC2_750
NSCC3N_750
NSCC3P_750
NSC_C2_500
RCC_1500
RCCC2_750
RCCC2_500
LLOQ=0.01 ug/mL
MEDI5752 PK Concentration (µg/mL)
1000
100
10
1
0
21
42
63
84
Time (Day)

FIG. 14

FIG. 15


Exposure (Ctrough) vs Peripheral PD Effect (CD4 T cell proliferation)
Cohort
ESC_7.5 mg (N = 1)
ESC_22.5 mg (N = 3)
ESC_75 mg (N = 4)
ESC_225 mg (N = 10)
ESC_500 mg (N = 5)
ESC_750 mg (N = 6)
ESC_1500 mg (N = 10)
ESC_2000 mg (N = 8)
ESC_2500 mg (N = 5)
MTD_QBD_2000 mg (N = 16)
RCC_1500 mg (N = 16)
RCCC2_750 mg (N = 24)
RCCC2_500 mg (N = 27)
1500mg
750mg
500mg
EC50
T10
T6
T3
T1
CD4+Ki67+ T cell proliferation change from baseline at Day 8 (%)
AUC first cycle (µg · day/mL)
3500
3000
2500
2000
1500
1000
500
0
100
1000
2000
3000
4000
5000
6000
7000
8000