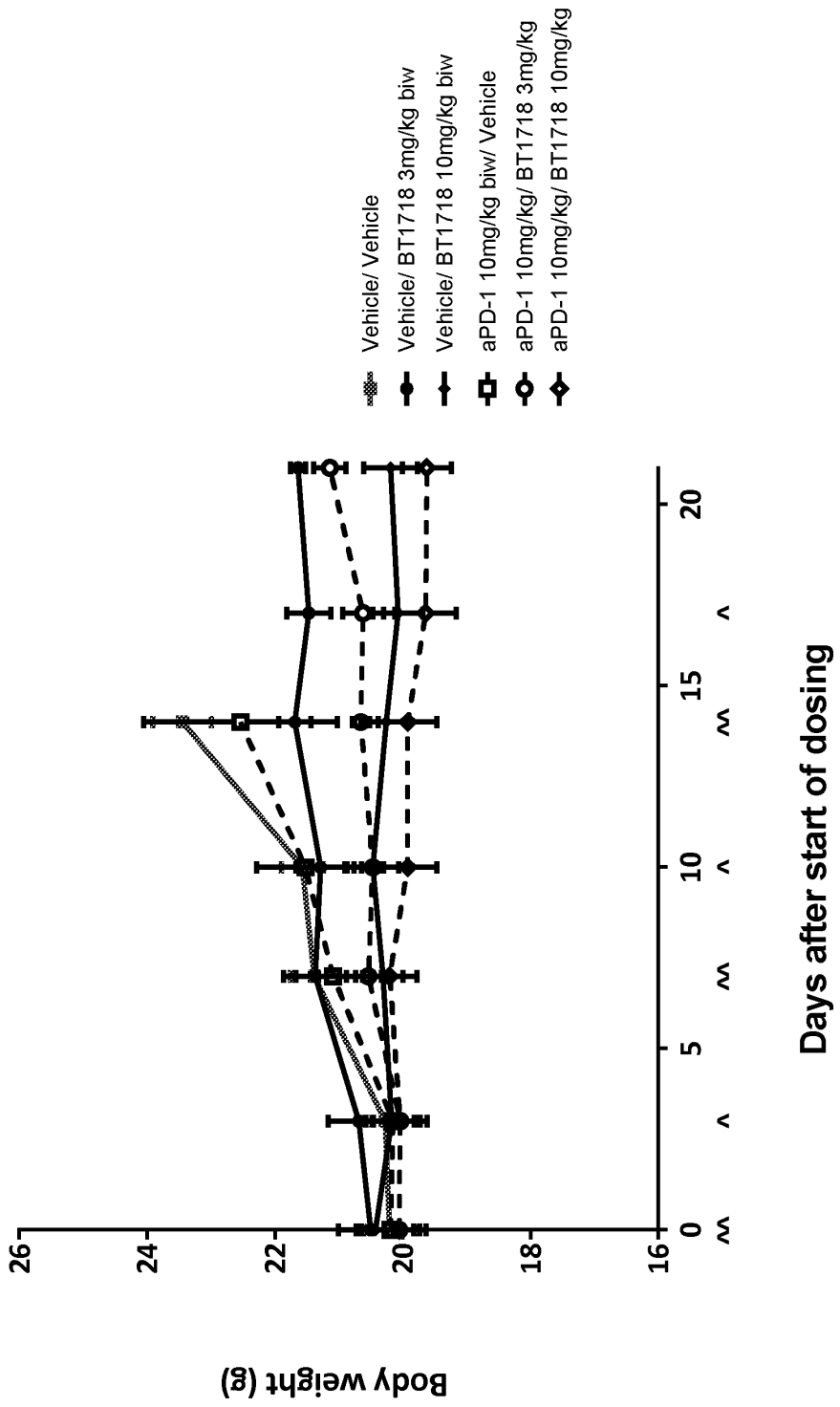

Vehicle/ Vehicle
Vehicle/ BT1718 3mg/kg biw
Vehicle/ BT1718 10mg/kg biw
aPD-1 10mg/kg biw/ Vehicle
aPD-1 10mg/kg/ BT1718 3mg/kg
aPD-1 10mg/kg/ BT1718 10mg/kg
Body weight (g)
26
24
22
20
18
16
0
5
10
15
20
Days after start of dosing

FIG. 1

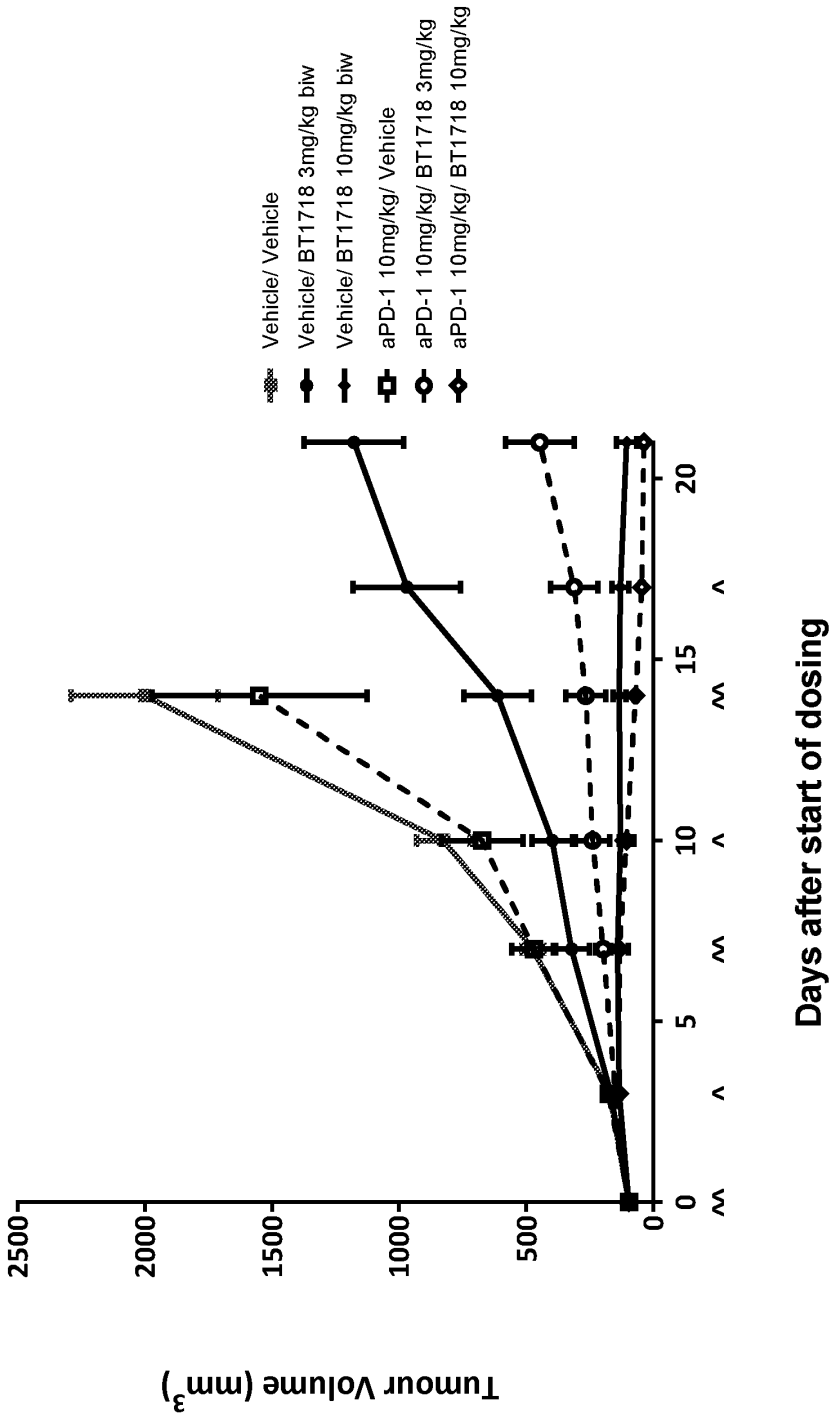
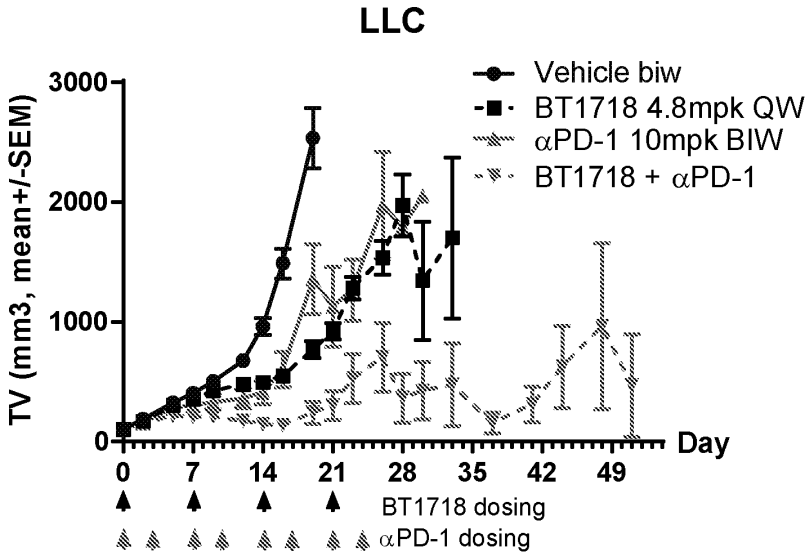
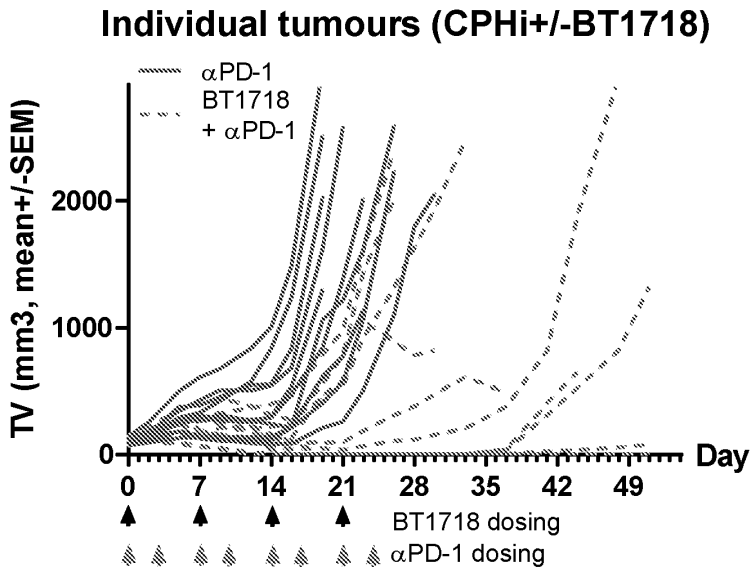

Vehicle/ Vehicle
Vehicle/ BT1718 3mg/kg biw
Vehicle/ BT1718 10mg/kg biw
aPD-1 10mg/kg/ Vehicle
aPD-1 10mg/kg/ BT1718 3mg/kg
aPD-1 10mg/kg/ BT1718 10mg/kg
Tumour Volume (mm3)
2500
2000
1500
1000
500
0
0
5
10
15
20
Days after start of dosing

FIG. 2

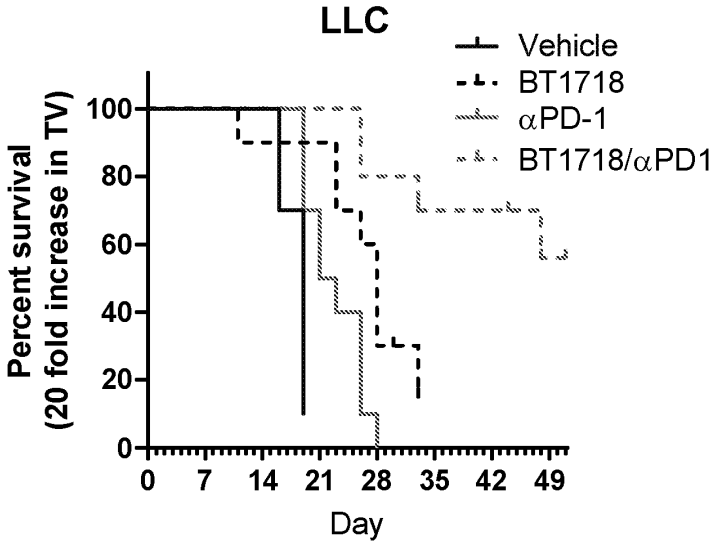

LLC
Vehicle biw
BT1718 4.8mpk QW
αPD-1 10mpk BIW
BT1718 + αPD-1
TV (mm3, mean+/-SEM)
3000
2000
1000
0
Day
0 7 14 21 28 35 42 49
BT1718 dosing
αPD-1 dosing

(A)


Individual tumours (CPHi+/-BT1718)
αPD-1
BT1718
+ αPD-1
TV (mm3, mean+/-SEM)
2000
1000
0
Day
0 7 14 21 28 35 42 49
BT1718 dosing
αPD-1 dosing

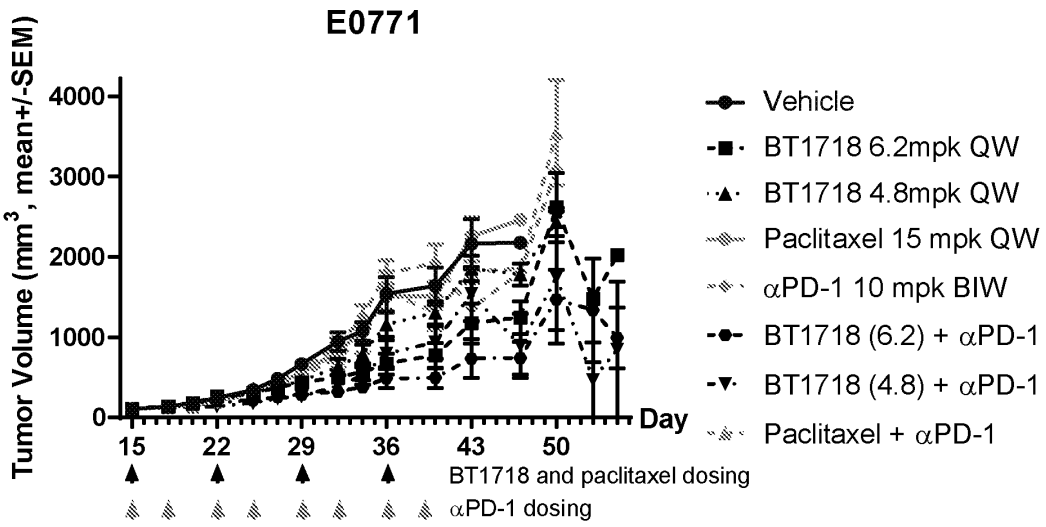
(B)

FIG. 3



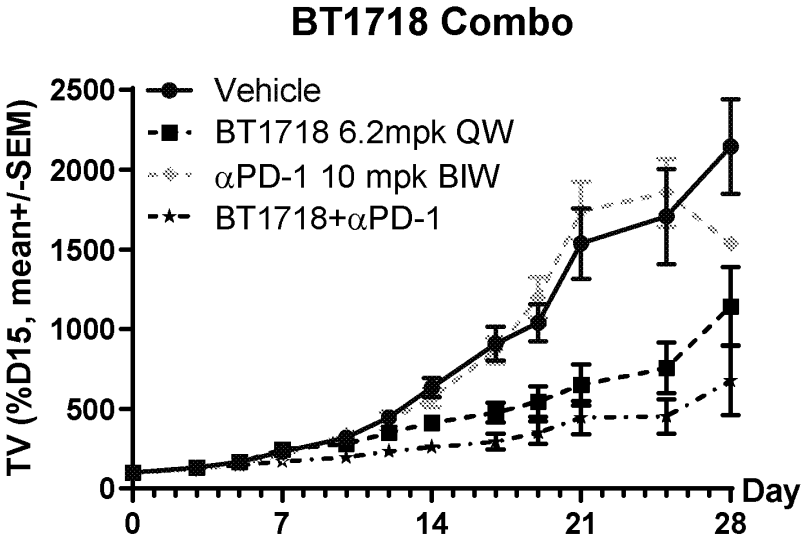
(C)

FIG. 3 (ctd)

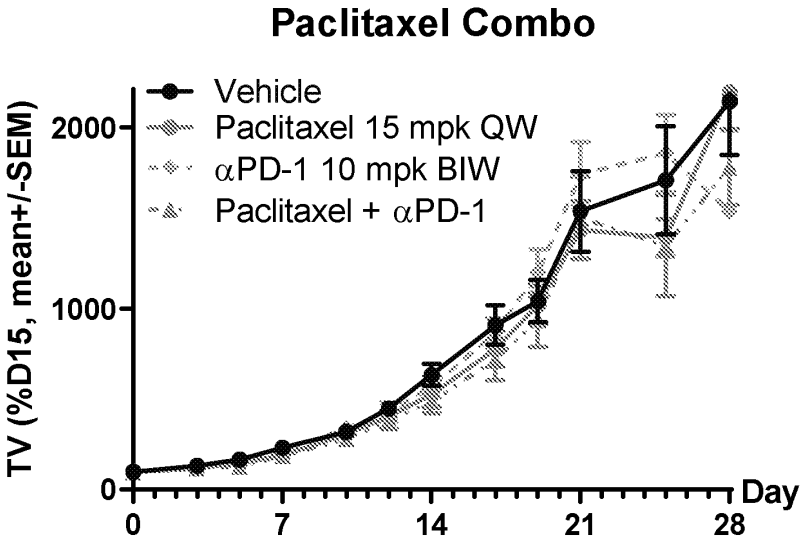


(A)

FIG. 4

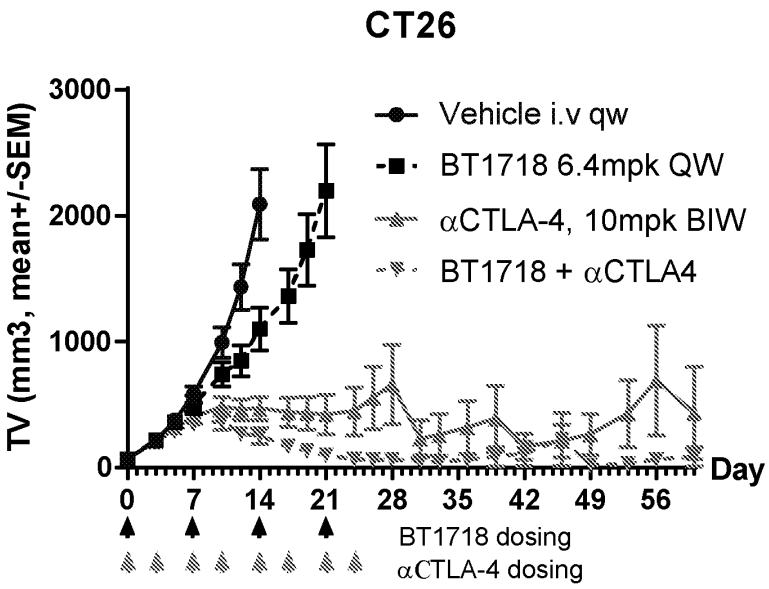

BT1718 Combo
Vehicle
BT1718 6.2mpk QW
αPD-1 10 mpk BIW
BT1718+αPD-1
TV (%D15, mean+/-SEM)
2500
2000
1500
1000
500
0
0
7
14
21
28
Day

(B)

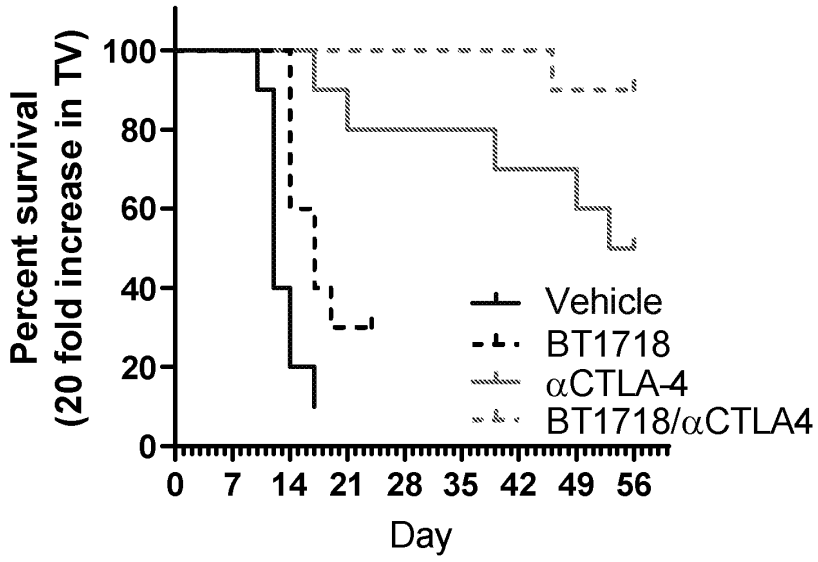

Paclitaxel Combo
Vehicle
Paclitaxel 15 mpk QW
αPD-1 10 mpk BIW
Paclitaxel + αPD-1
TV (%D15, mean+/-SEM)
2000
1000
0
0
7
14
21
28
Day

(C)

FIG. 4 (ctd)

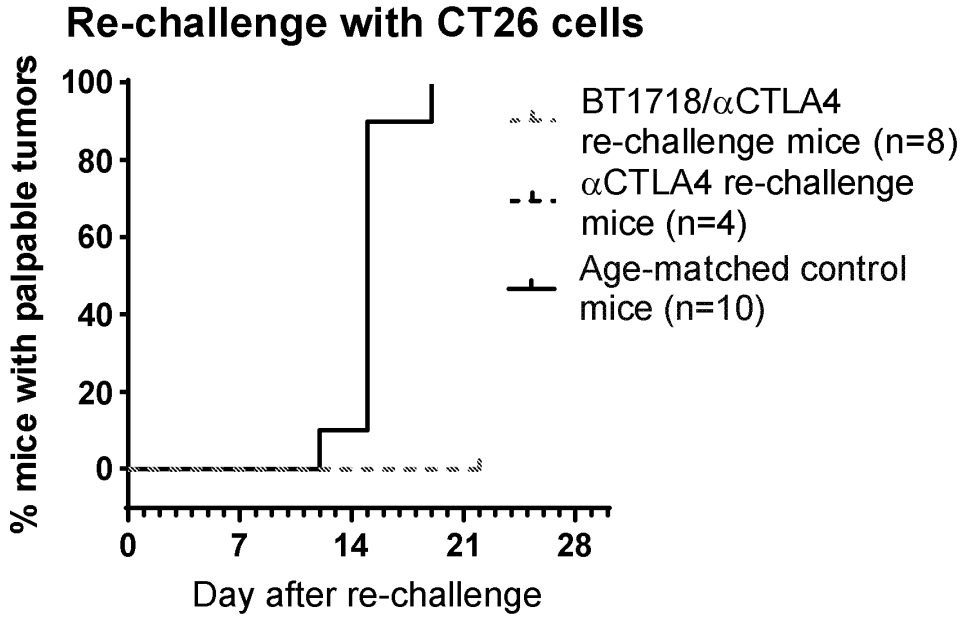

CT26
TV (mm3, mean+/-SEM)
3000
2000
1000
0
Vehicle i.v qw
BT1718 6.4mpk QW
αCTLA-4, 10mpk BIW
BT1718 + αCTLA4
Day
0 7 14 21 28 35 42 49 56
BT1718 dosing
αCTLA-4 dosing

(A)


Percent survival
(20 fold increase in TV)
100
80
60
40
20
0
Vehicle
BT1718
αCTLA-4
BT1718/αCTLA4
0 7 14 21 28 35 42 49 56
Day

(B)

FIG. 5


Re-challenge with CT26 cells
% mice with palpable tumors
100
80
60
40
20
0
0
7
14
21
28
Day after re-challenge
BT1718/αCTLA4 re-challenge mice (n=8)
αCTLA4 re-challenge mice (n=4)
Age-matched control mice (n=10)

(C)

FIG. 5 (ctd)

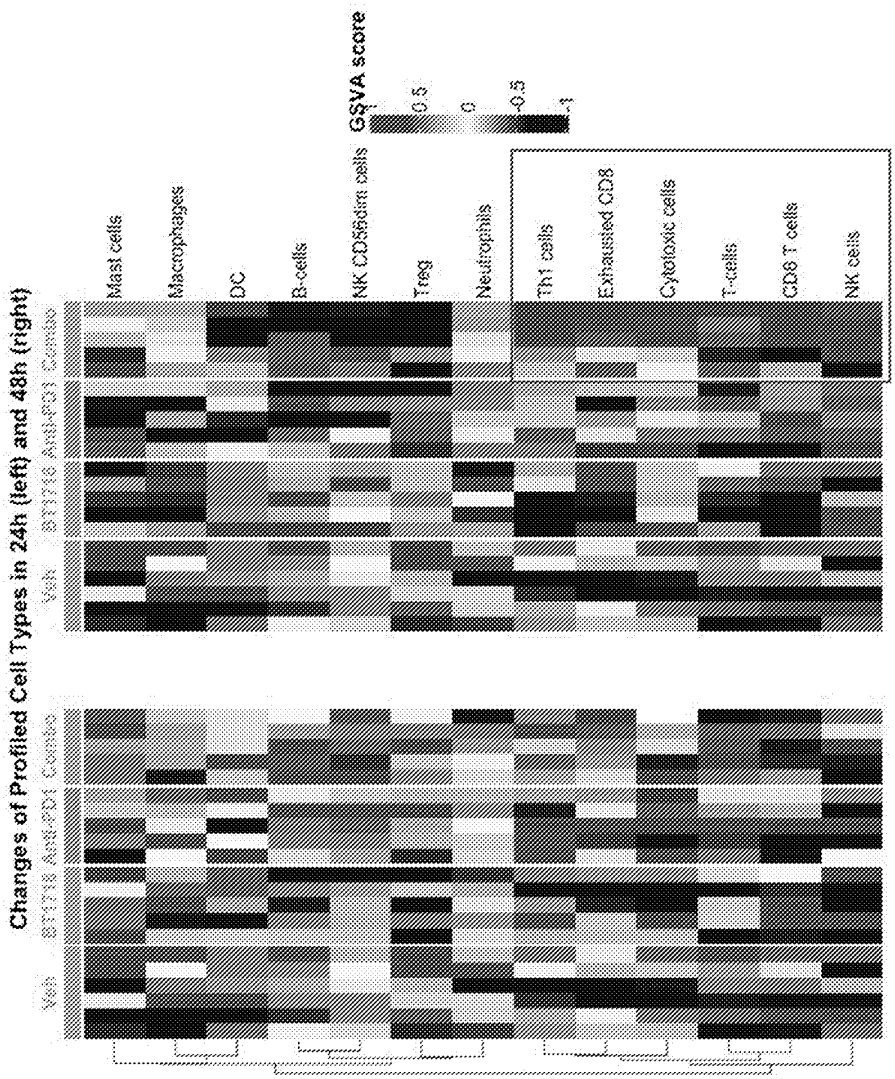

Changes of Profiled Cell Types in 24h (left) and 48h (right)
Veh
BT1718
Anti-PD1
Combo
Mast cells
Macrophages
DC
B-cells
NK CD56dim cells
Treg
Neutrophils
Th1 cells
Exhausted CD8
Cytotoxic cells
T-cells
CD8 T cells
NK cells
GSVA score
1
0.5
0
-0.5
-1

FIG. 6

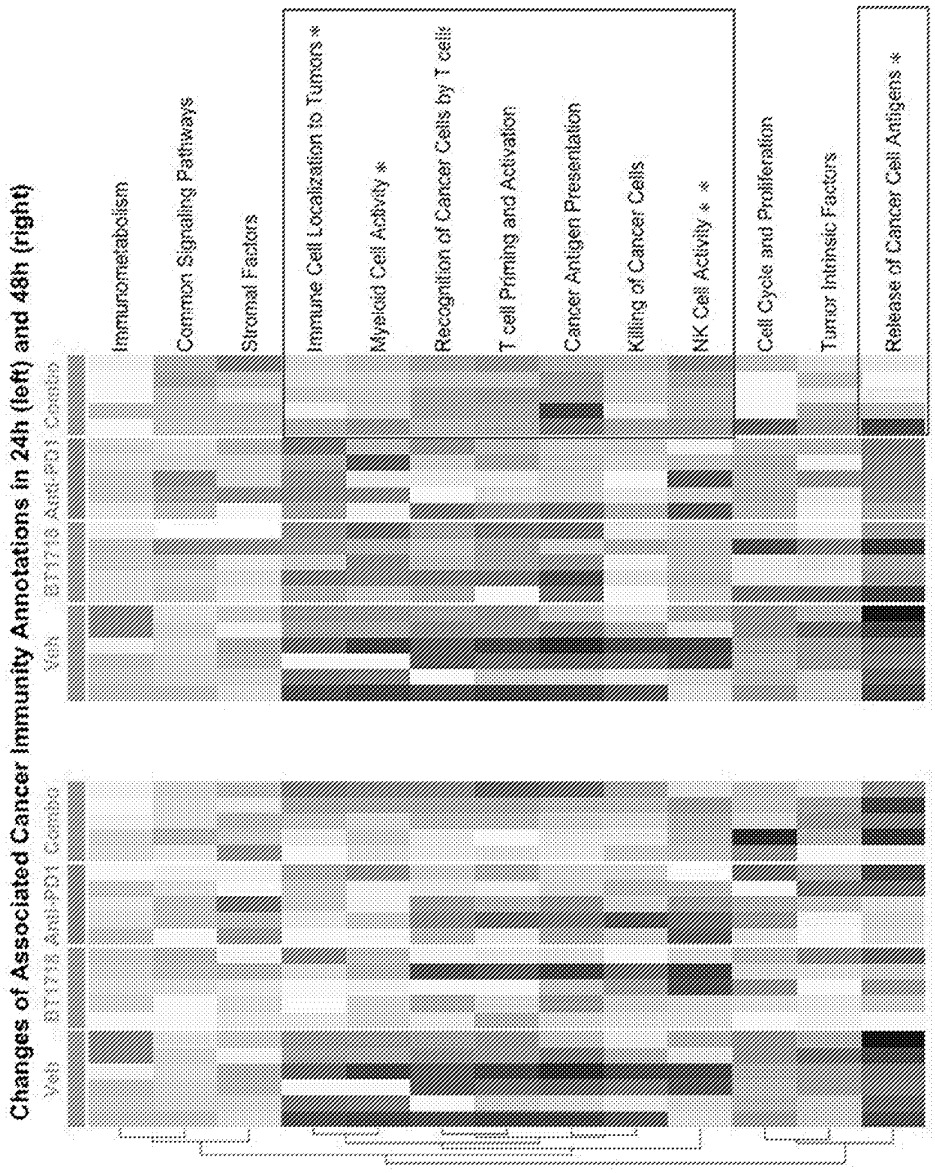

Changes of Associated Cancer Immunity Annotations in 24h (left) and 48h (right)
Veh
BT1718 Anti-PD1 Combo
Immunometabolism
Common Signaling Pathways
Stromal Factors
Immune Cell Localization to Tumors *
Myeloid Cell Activity *
Recognition of Cancer Cells by T cells
T cell Priming and Activation
Cancer Antigen Presentation
Killing of Cancer Cells
NK Cell Activity * *
Cell Cycle and Proliferation
Tumor Intrinsic Factors
Release of Cancer Cell Antigens *

FIG. 7

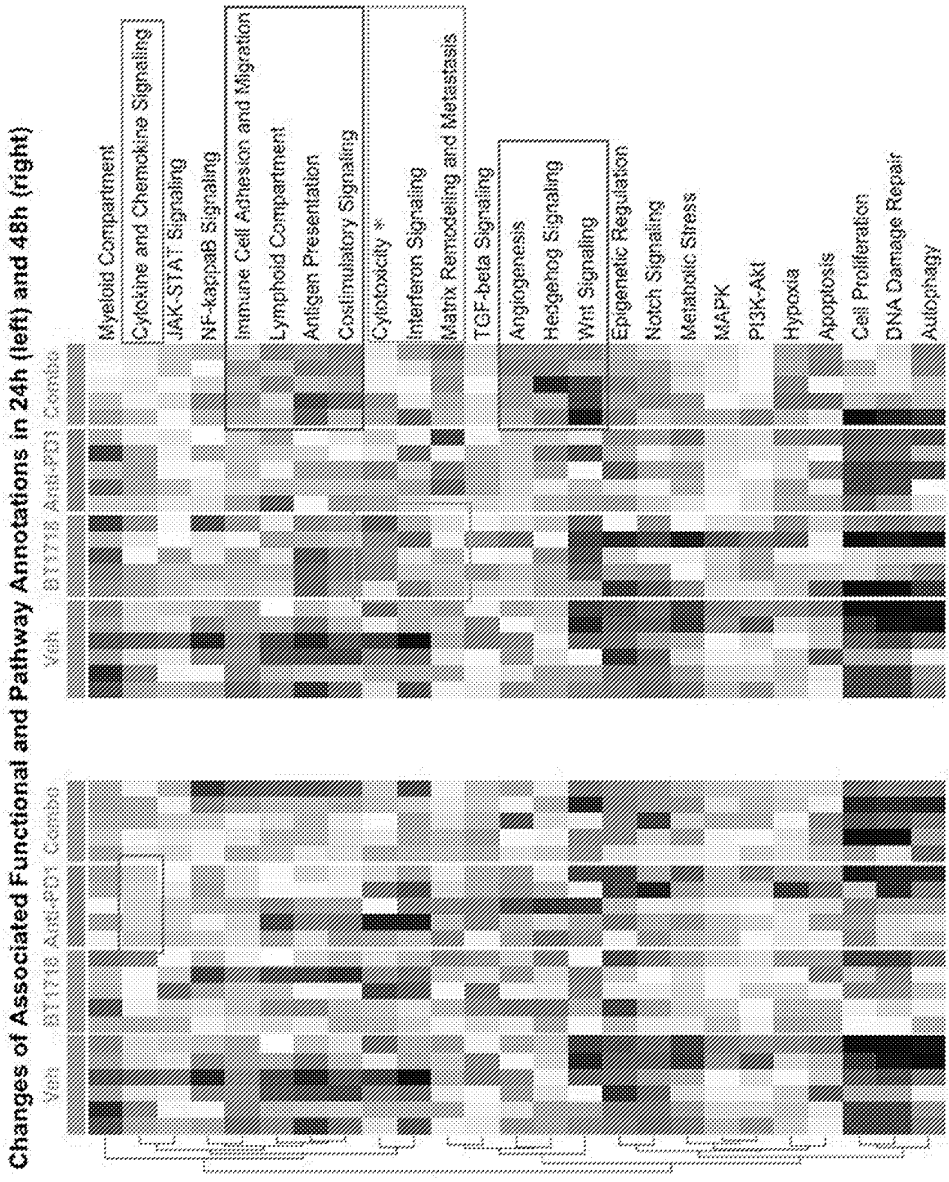

Changes of Associated Functional and Pathway Annotations in 24h (left) and 48h (right)
Veh
BT1718
Anti-PD1
Combo
Myeloid Compartment
Cytokine and Chemokine Signaling
JAK-STAT Signaling
NF-kappaB Signaling
Immune Cell Adhesion and Migration
Lymphoid Compartment
Antigen Presentation
Costimulatory Signaling
Cytotoxicity *
Interferon Signaling
Matrix Remodeling and Metastasis
TGF-beta Signaling
Angiogenesis
Hedgehog Signaling
Wnt Signaling
Epigenetic Regulation
Notch Signaling
Metabolic Stress
MAPK
PI3K-Akt
Hypoxia
Apoptosis
Cell Proliferation
DNA Damage Repair
Autophagy

FIG. 8