Drawings

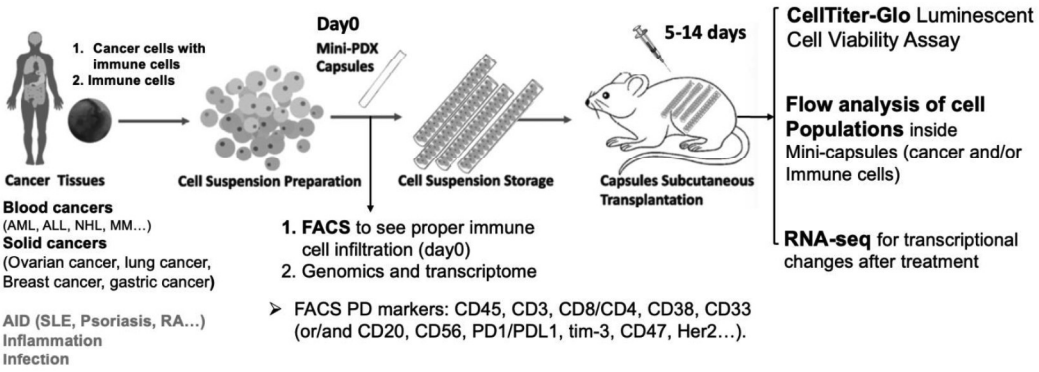


FIG. 1

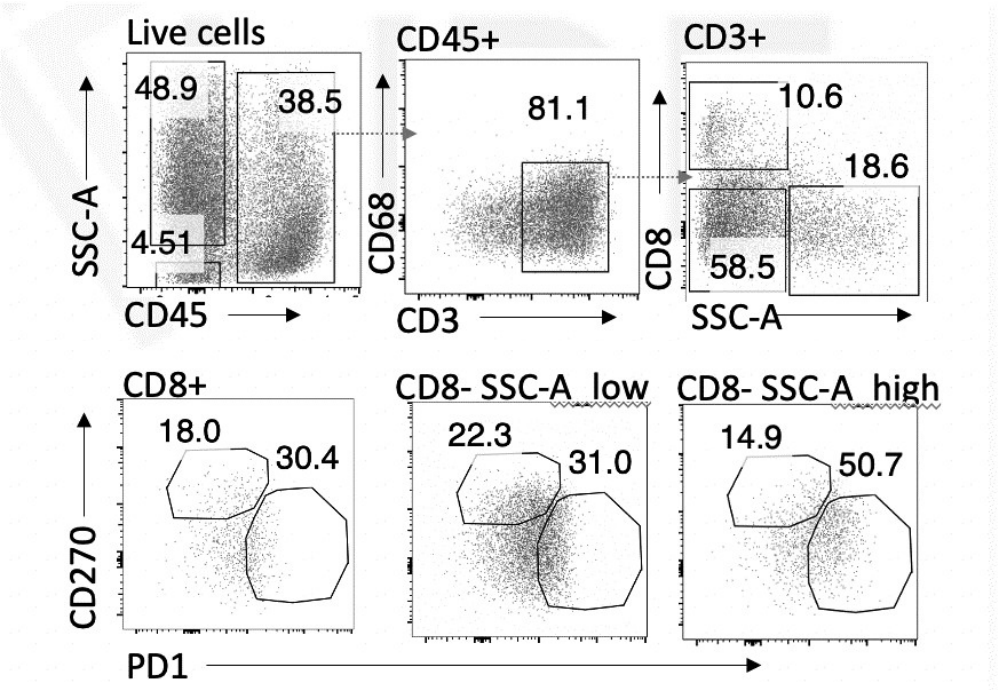


FIG. 2

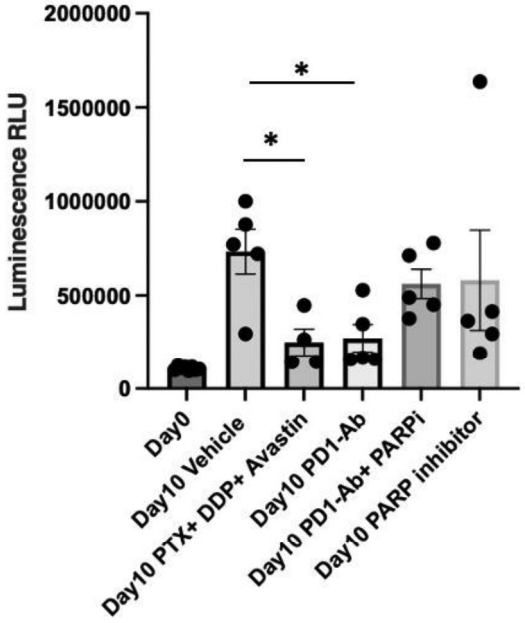

Luminescence RLU
2000000
1500000
1000000
500000
0
*
*
Day0
Day10 Vehicle
Day10 PTX+ DDP+ Avastin
Day10 PD1-Ab
Day10 PD1-Ab+ PARPi
Day10 PARP inhibitor

FIG. 3

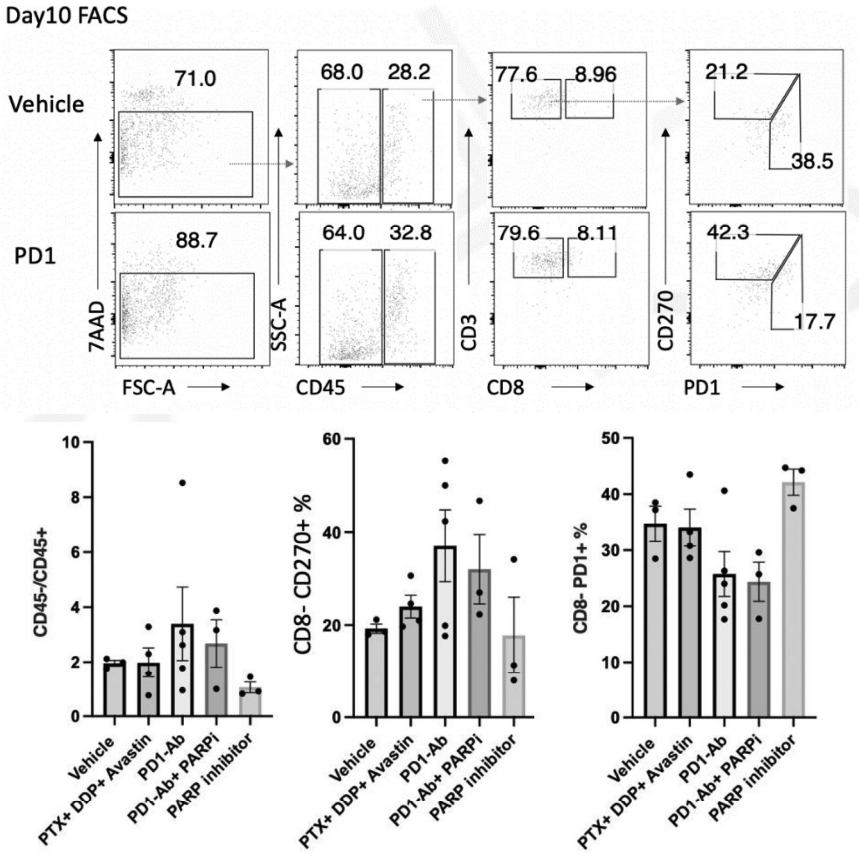

Day10 FACS
Vehicle
PD1
71.0
88.7
68.0
28.2
64.0
32.8
77.6
8.96
79.6
8.11
21.2
38.5
42.3
17.7
7AAD
FSC-A
SSC-A
CD45
CD3
CD8
CD270
PD1
CD45-/CD45+
CD8- CD270+ %
CD8- PD1+ %
Vehicle
PTX+ DDP+ Avastin
PD1-Ab
PD1-Ab+ PARPi
PARP inhibitor

FIG. 4

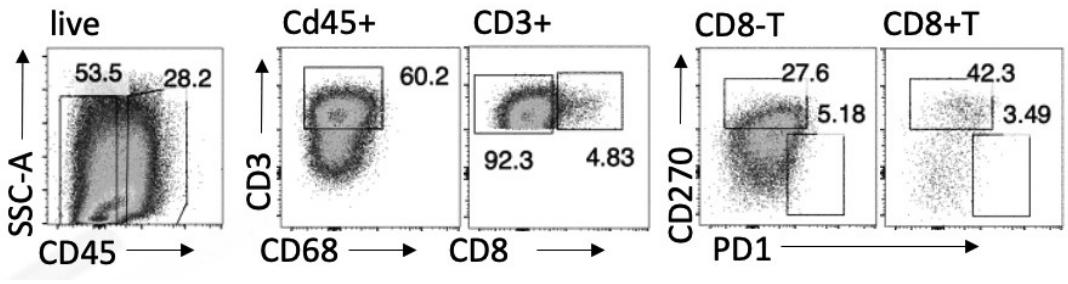

live
53.5
28.2
SSC-A
CD45
Cd45+
60.2
CD3
CD68
CD3+
92.3
4.83
CD8
CD8-T
27.6
5.18
CD270
PD1
CD8+T
42.3
3.49

FIG. 5

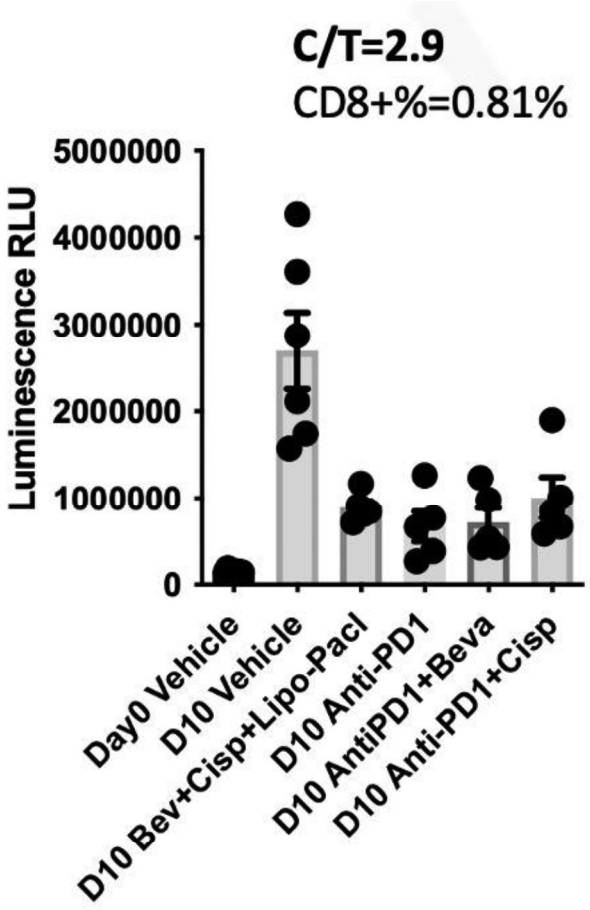

C/T=2.9
CD8+%=0.81%
Luminescence RLU
5000000
4000000
3000000
2000000
1000000
0
Day0 Vehicle
D10 Vehicle
D10 Bev+Cisp+Lipo-Pacl
D10 Anti-PD1
D10 AntiPD1+Beva
D10 Anti-PD1+Cisp

FIG. 6

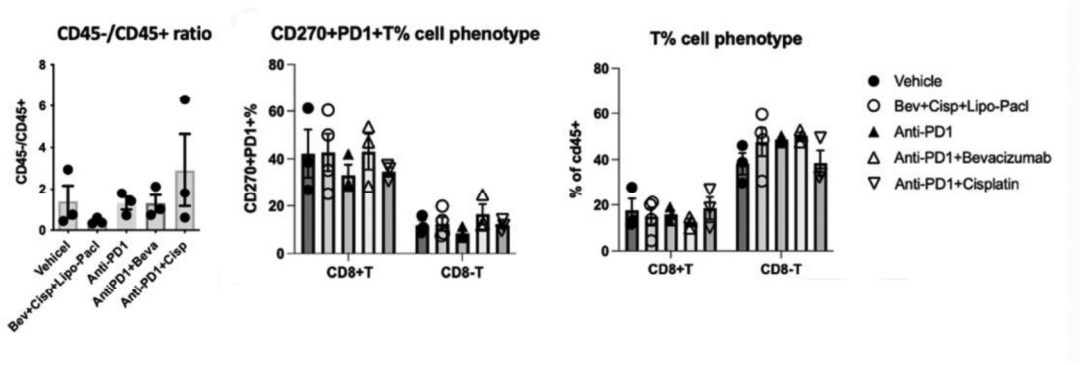

CD45-/CD45+ ratio
CD45-/CD45+
Vehicel
Bev+Cisp+Lipo-Pacl
Anti-PD1
AntiPD1+Beva
Anti-PD1+Cisp
CD270+PD1+T% cell phenotype
CD270+PD1+%
CD8+T
CD8-T
T% cell phenotype
% of cd45+
CD8+T
CD8-T
Vehicle
Bev+Cisp+Lipo-Pacl
Anti-PD1
Anti-PD1+Bevacizumab
Anti-PD1+Cisplatin

FIG. 7

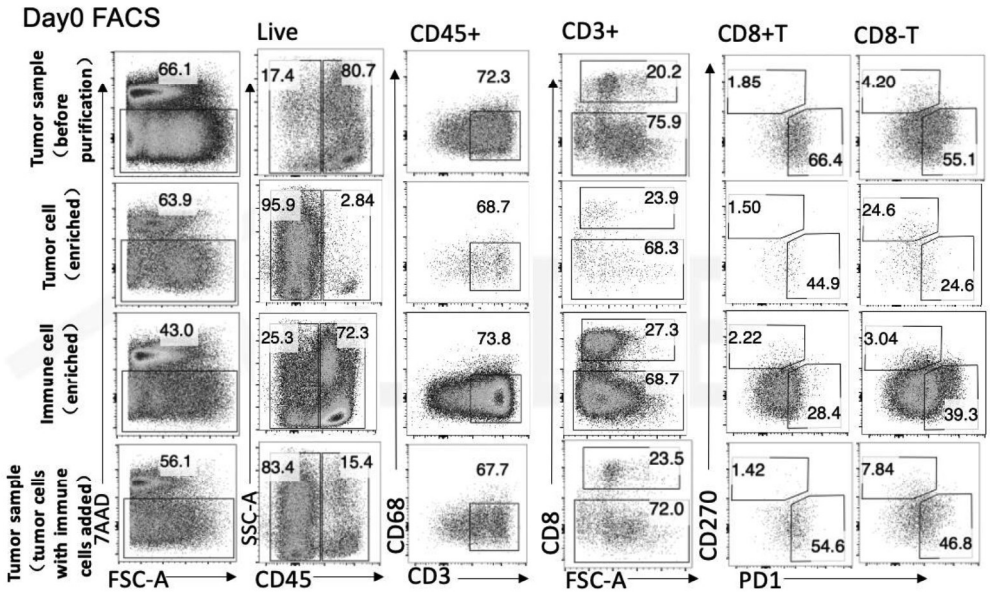

Day0 FACS
Live
CD45+
CD3+
CD8+T
CD8-T
Tumor sample (before purification)
Tumor cell (enriched)
Immune cell (enriched)
Tumor sample (tumor cells with immune cells added)
66.1
17.4
80.7
72.3
20.2
75.9
1.85
66.4
4.20
55.1
63.9
95.9
2.84
68.7
23.9
68.3
1.50
44.9
24.6
24.6
43.0
25.3
72.3
73.8
27.3
68.7
2.22
28.4
3.04
39.3
56.1
83.4
15.4
67.7
23.5
72.0
1.42
54.6
7.84
46.8
7AAD
FSC-A
SSC-A
CD45
CD68
CD3
CD8
FSC-A
CD270
PD1

FIG. 8

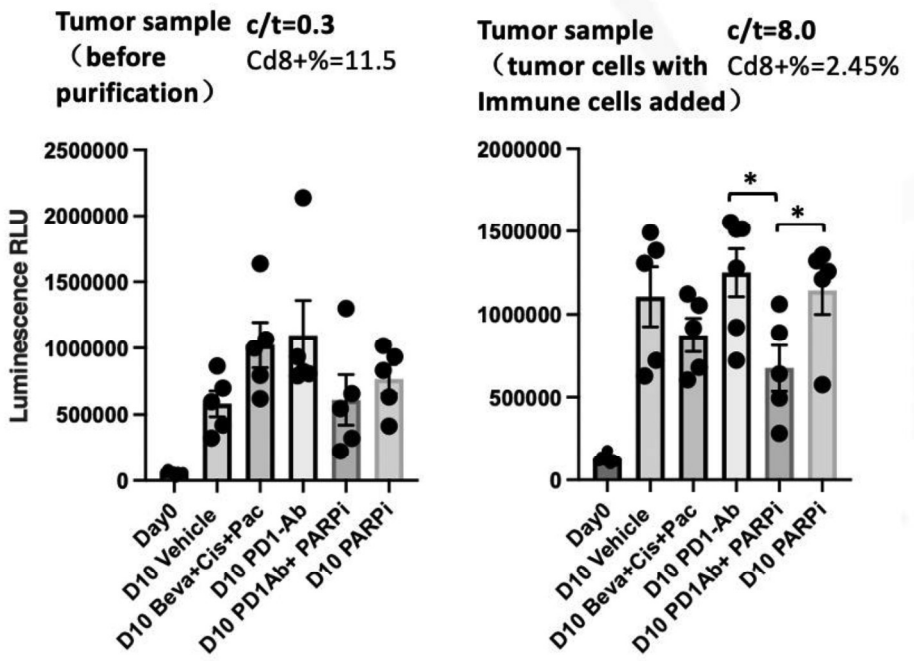

Tumor sample （before purification） c/t=0.3 Cd8+%=11.5
Tumor sample （tumor cells with Immune cells added） c/t=8.0 Cd8+%=2.45%
Luminescence RLU
2500000
2000000
1500000
1000000
500000
0
Day0
D10 Vehicle
D10 Beva+Cis+Pac
D10 PD1-Ab
D10 PD1Ab+ PARPi
D10 PARPi
*
*

FIG. 9

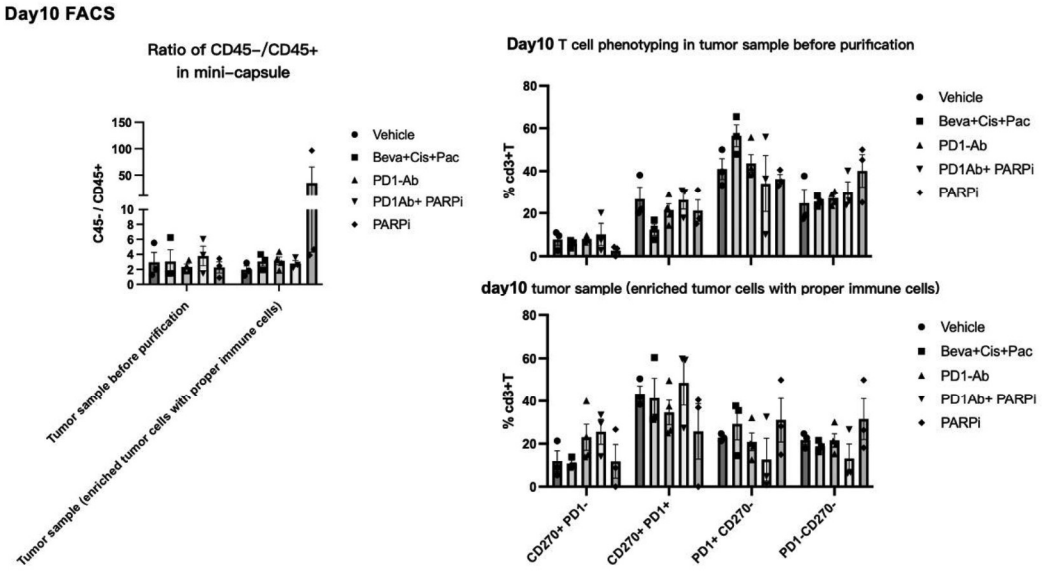

Day10 FACS
Ratio of CD45−/CD45+ in mini−capsule
C45-/ CD45+
Vehicle
Beva+Cis+Pac
PD1-Ab
PD1Ab+ PARPi
PARPi
Tumor sample before purification
Tumor sample (enriched tumor cells with proper immune cells)
Day10 T cell phenotyping in tumor sample before purification
% cd3+T
day10 tumor sample (enriched tumor cells with proper immune cells)
CD270+ PD1-
CD270+ PD1+
PD1+ CD270-
PD1-CD270-

FIG. 10

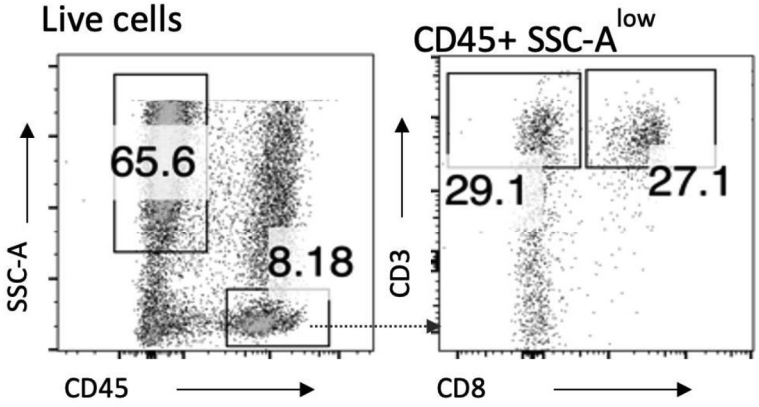

Live cells
CD45+ SSC-A low
65.6
8.18
29.1
27.1
SSC-A
CD3
CD45
CD8

FIG. 11

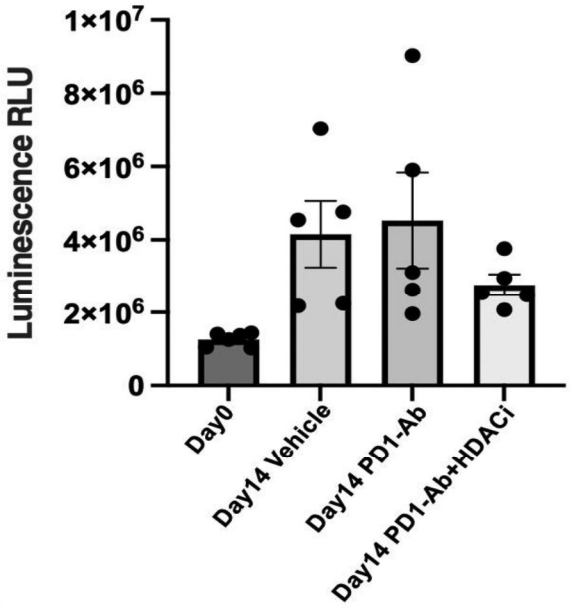

Luminescence RLU
1×10^7
8×10^6
6×10^6
4×10^6
2×10^6
0
Day0
Day14 Vehicle
Day14 PD1-Ab
Day14 PD1-Ab+HDACi

FIG. 12

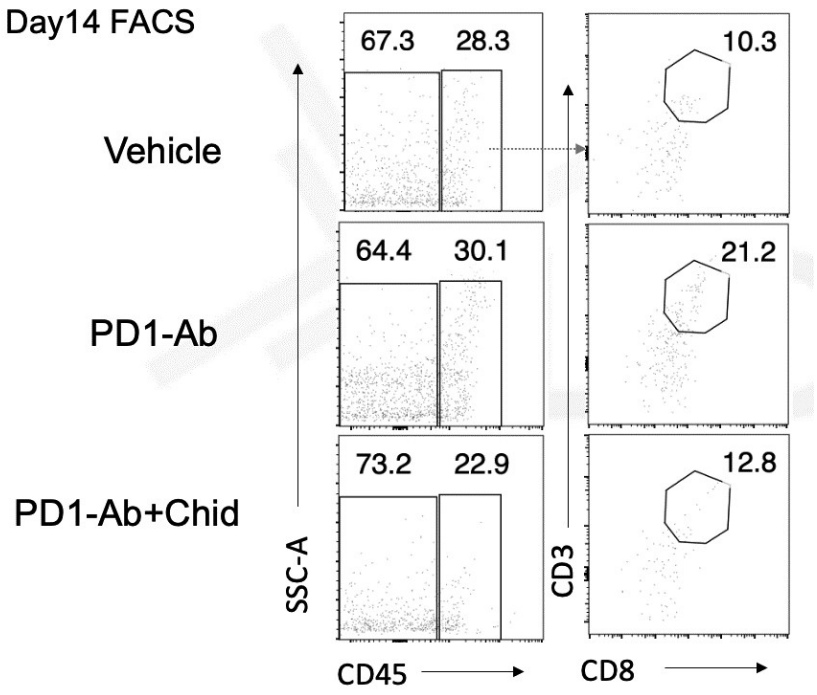

Day14 FACS
Vehicle
PD1-Ab
PD1-Ab+Chid
67.3
28.3
10.3
64.4
30.1
21.2
73.2
22.9
12.8
SSC-A
CD3
CD45
CD8

FIG. 13

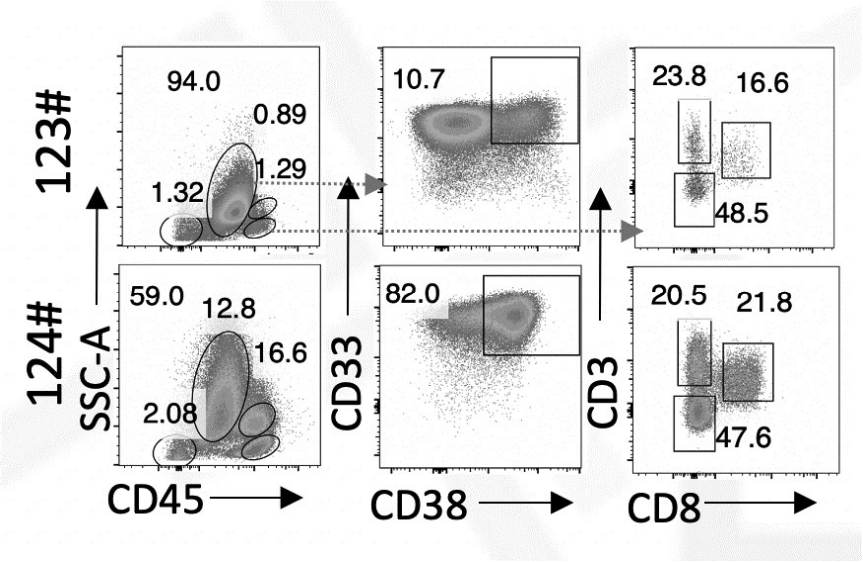

123#
124#
SSC-A
94.0
0.89
1.29
1.32
10.7
23.8
16.6
48.5
59.0
12.8
16.6
2.08
82.0
20.5
21.8
47.6
CD33
CD3
CD45
CD38
CD8

FIG. 14

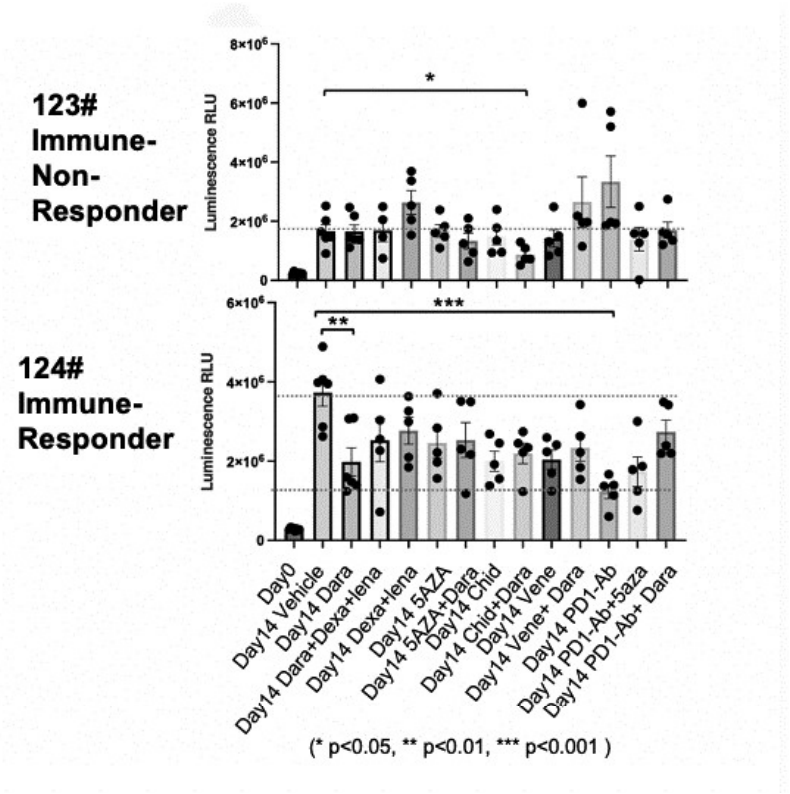

123#
Immune-
Non-
Responder
124#
Immune-
Responder
Luminescence RLU
8×10⁶
6×10⁶
4×10⁶
2×10⁶
0
6×10⁶
4×10⁵
2×10⁶
0
*
**
***
Day0
Day14 Vehicle
Day14 Dara
Day14 Dara+Dexa+Iena
Day14 Dexa+Iena
Day14 5AZA
Day14 5AZA+Dara
Day14 Chid
Day14 Chid+Dara
Day14 Vene
Day14 Vene+ Dara
Day14 PD1-Ab
Day14 PD1-Ab+5aza
Day14 PD1-Ab+ Dara
(* p<0.05, ** p<0.01, *** p<0.001)

FIG. 15

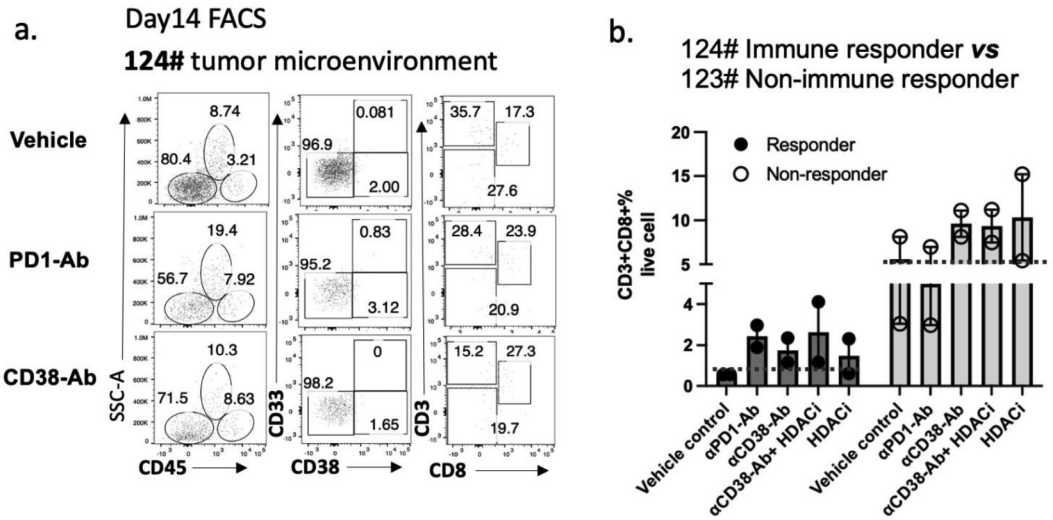

a.
Day14 FACS
124# tumor microenvironment
Vehicle
PD1-Ab
CD38-Ab
SSC-A
CD45
CD38
CD33
CD3
CD8
8.74
80.4
3.21
0.081
96.9
2.00
35.7
17.3
27.6
19.4
56.7
7.92
0.83
95.2
3.12
28.4
23.9
20.9
10.3
71.5
8.63
0
98.2
1.65
15.2
27.3
19.7
b.
124# Immune responder vs
123# Non-immune responder
Responder
Non-responder
CD3+CD8+%
live cell
20
15
10
5
4
2
0
Vehicle control
αPD1-Ab
αCD38-Ab
αCD38-Ab+ HDACi
HDACi
Vehicle control
αPD1-Ab
αCD38-Ab
αCD38-Ab+ HDACi
HDACi

FIG. 16

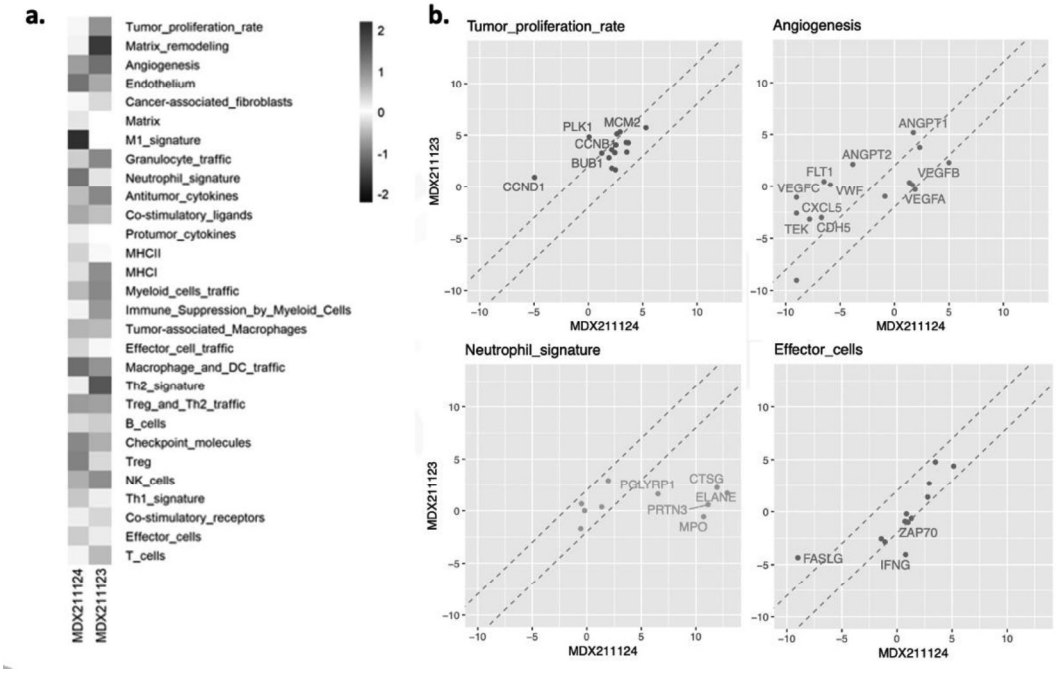

a.
Tumor_proliferation_rate
Matrix_remodeling
Angiogenesis
Endothelium
Cancer-associated_fibroblasts
Matrix
M1_signature
Granulocyte_traffic
Neutrophil_signature
Antitumor_cytokines
Co-stimulatory_ligands
Protumor_cytokines
MHCII
MHCI
Myeloid_cells_traffic
Immune_Suppression_by_Myeloid_Cells
Tumor-associated_Macrophages
Effector_cell_traffic
Macrophage_and_DC_traffic
Th2_signature
Treg_and_Th2_traffic
B_cells
Checkpoint_molecules
Treg
NK_cells
Th1_signature
Co-stimulatory_receptors
Effector_cells
T_cells
MDX211124
MDX211123
2
1
0
-1
-2
b.
Tumor_proliferation_rate
PLK1
MCM2
CCNB1
BUB1
CCND1
Angiogenesis
ANGPT1
ANGPT2
FLT1
VEGFB
VEGFC
VWF
VEGFA
CXCL5
TEK
CDH5
Neutrophil_signature
PGLYRP1
CTSG
ELANE
PRTN3
MPO
Effector_cells
ZAP70
FASLG
IFNG
MDX211123
MDX211124

FIG. 17

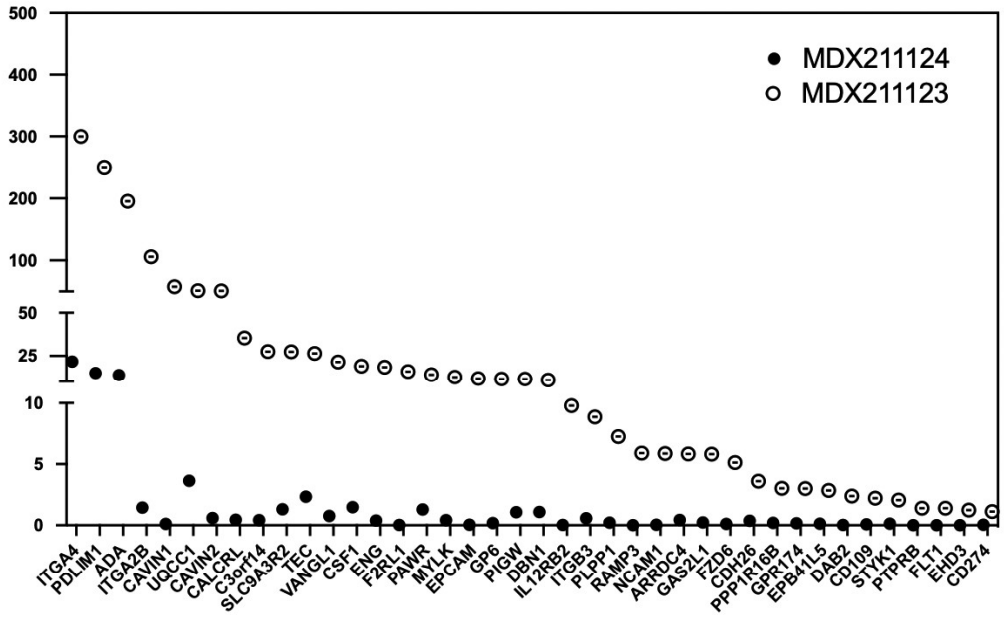

MDX211124
MDX211123
500
400
300
200
100
50
25
10
5
0
ITGA4
PDLIM1
ADA
ITGA2B
CAVIN1
UQCC1
CAVIN2
CALCRL
C3orf14
SLC9A3R2
TEC
VANGL1
CSF1
EING
F2RL1
PAWR
MYLK
EPCAM
GP6
PIGW
DBN1
IL12RB2
ITGB3
PLPP1
RAMP3
NCAM1
ARRDC4
GAS2L1
FZD6
CDH26
PPP1R16B
GPR174
EPB41L5
DAB2
CD109
STYK1
PTPRB
FLT1
EHD3
CD274

FIG. 18

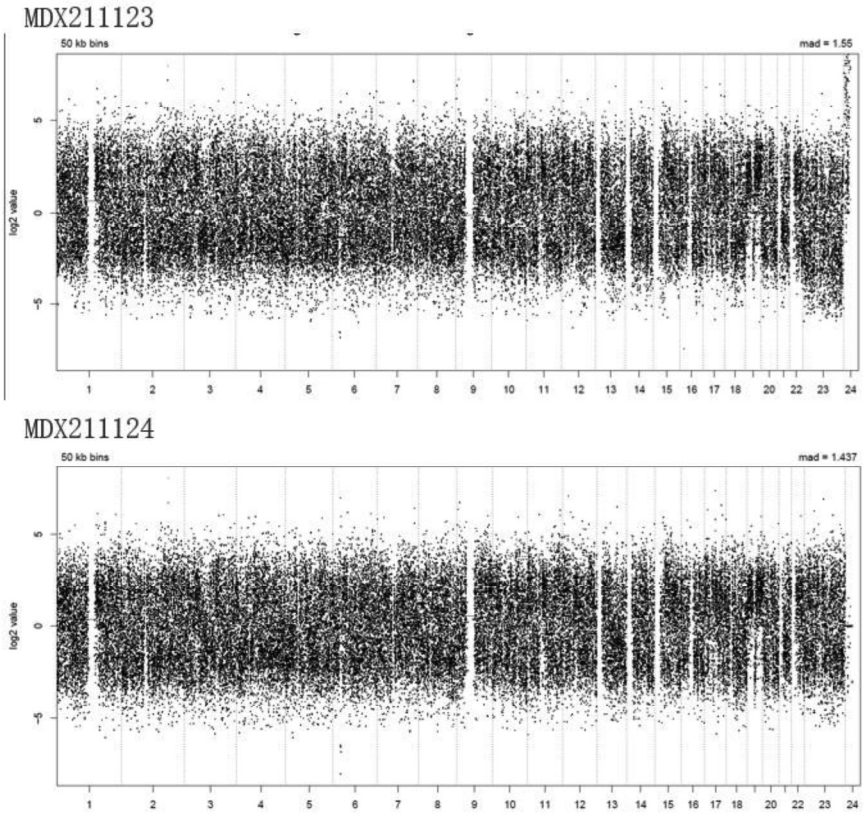

MDX211123
50 kb bins
mad = 1.55
log2 value
MDX211124
50 kb bins
mad = 1.437
log2 value

FIG. 19

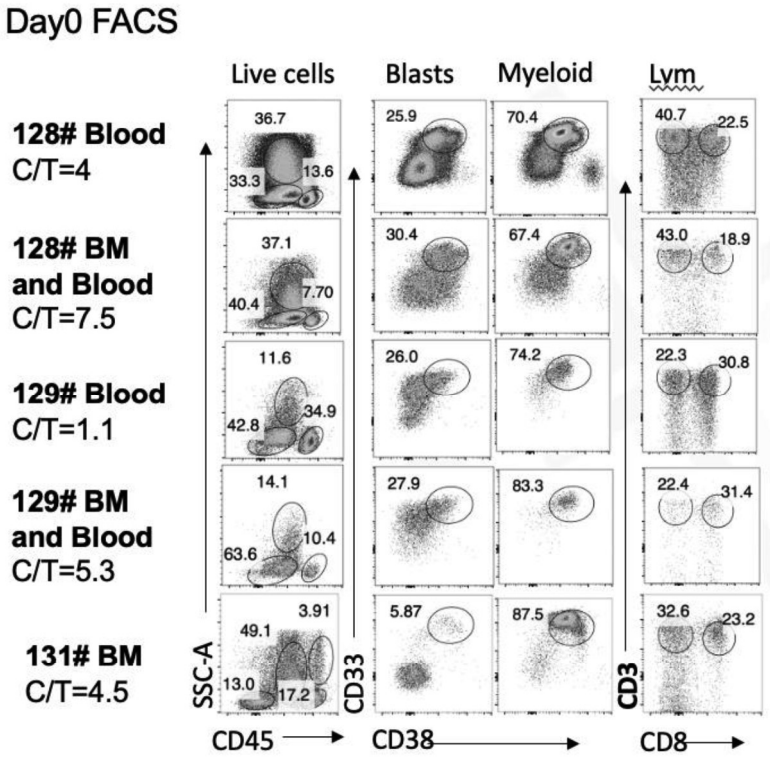

Day0 FACS
Live cells
Blasts
Myeloid
Lym
128# Blood
C/T=4
128# BM
and Blood
C/T=7.5
129# Blood
C/T=1.1
129# BM
and Blood
C/T=5.3
131# BM
C/T=4.5
SSC-A
CD45
CD33
CD38
CD3
CD8

FIG. 20

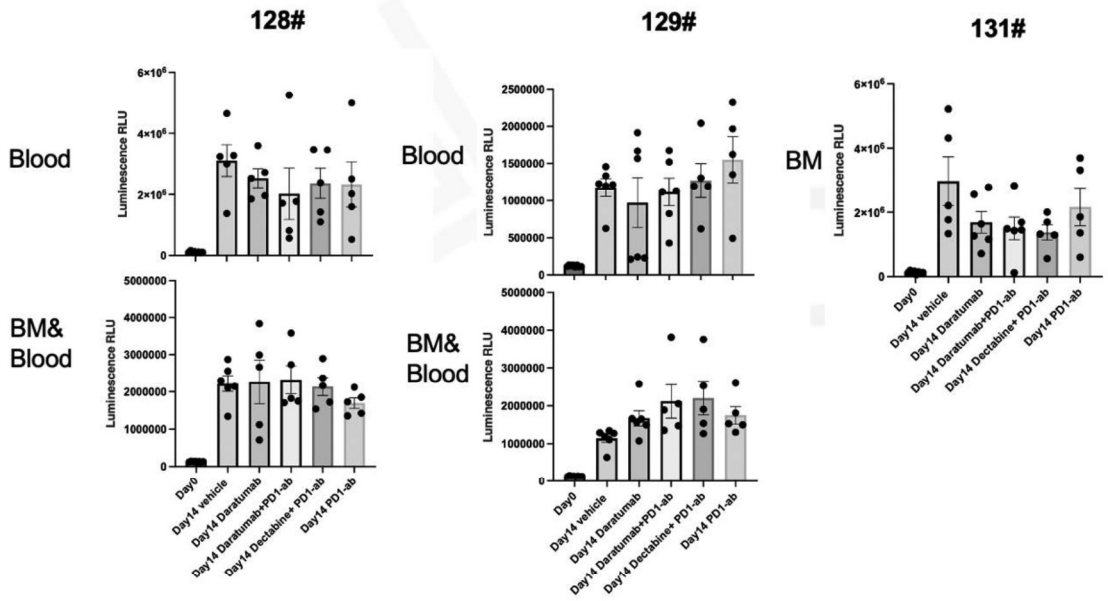

128#
129#
131#
Blood
BM&
Blood
BM
Luminescence RLU
Day0
Day14 vehicle
Day14 Daratumab
Day14 Daratumab+PD1-ab
Day14 Dectabine+ PD1-ab
Day14 PD1-ab

FIG. 21

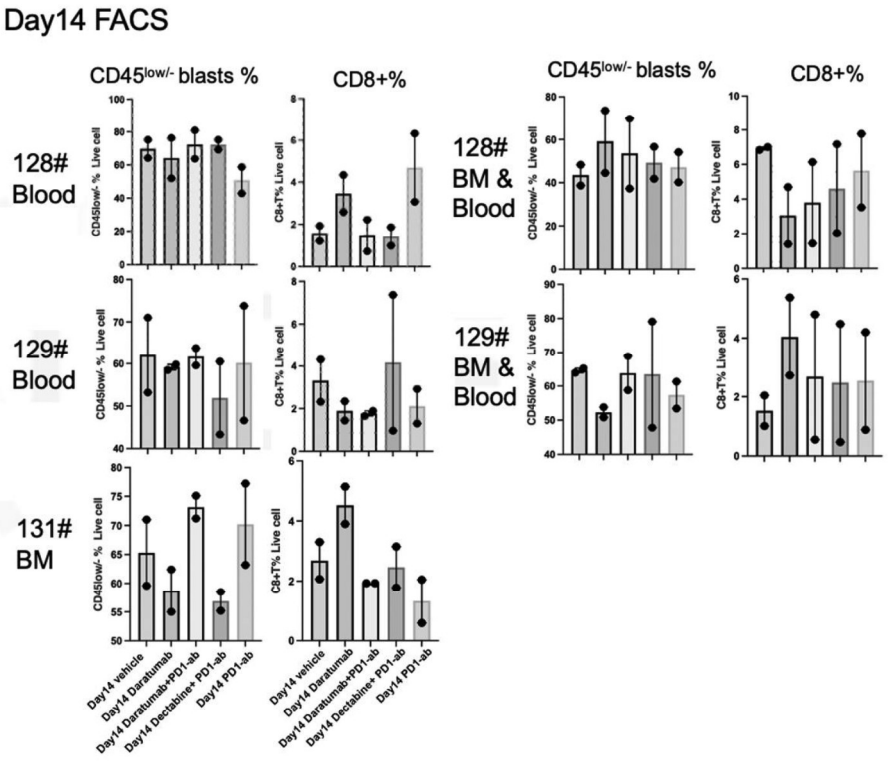

Day14 FACS
CD45low/- blasts %
CD8+%
128#
Blood
129#
Blood
131#
BM
128#
BM &
Blood
129#
BM &
Blood
CD45low/- % Live cell
C8+T% Live cell
Day14 vehicle
Day14 Daratumab
Day14 Daratumab+PD1-ab
Day14 Dectabine+ PD1-ab
Day14 PD1-ab

FIG. 22

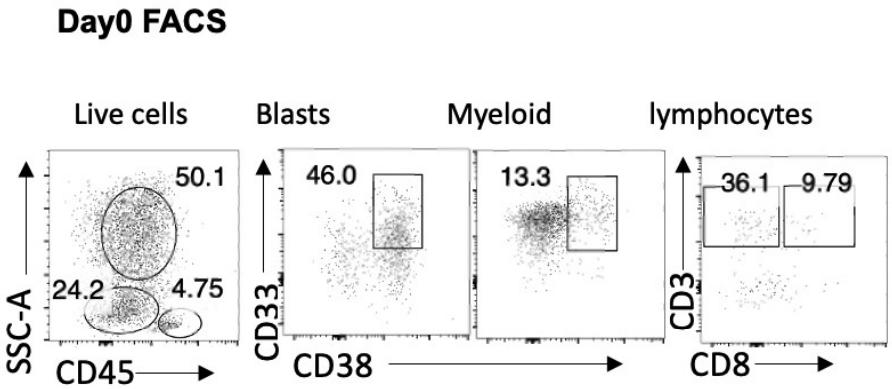

Day0 FACS
Live cells
Blasts
Myeloid
lymphocytes
50.1
24.2
4.75
SSC-A
CD45
46.0
13.3
CD33
CD38
36.1
9.79
CD3
CD8

FIG. 23

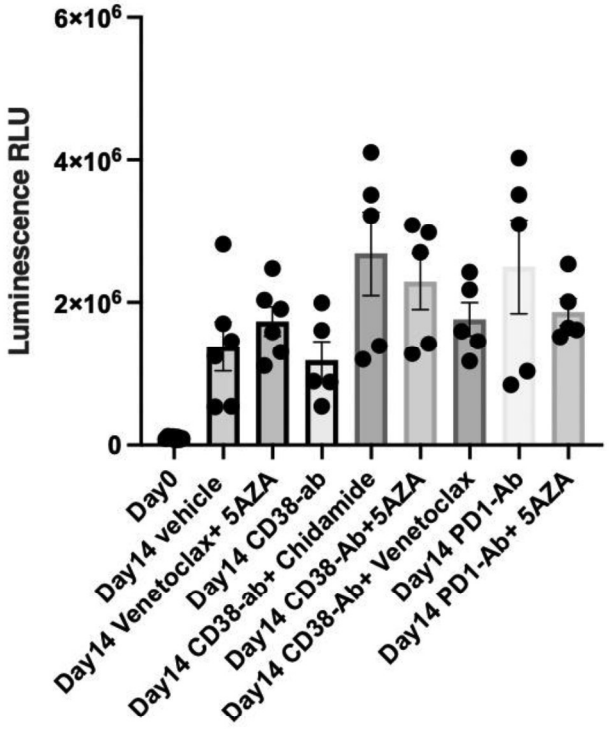

6×10^6
4×10^6
2×10^6
0
Luminescence RLU
Day0
Day14 vehicle
Day14 Venetoclax+ 5AZA
Day14 CD38-ab
Day14 CD38-ab+ Chidamide
Day14 CD38-Ab+5AZA
Day14 CD38-Ab+ Venetoclax
Day14 PD1-Ab
Day14 PD1-Ab+ 5AZA

FIG. 24

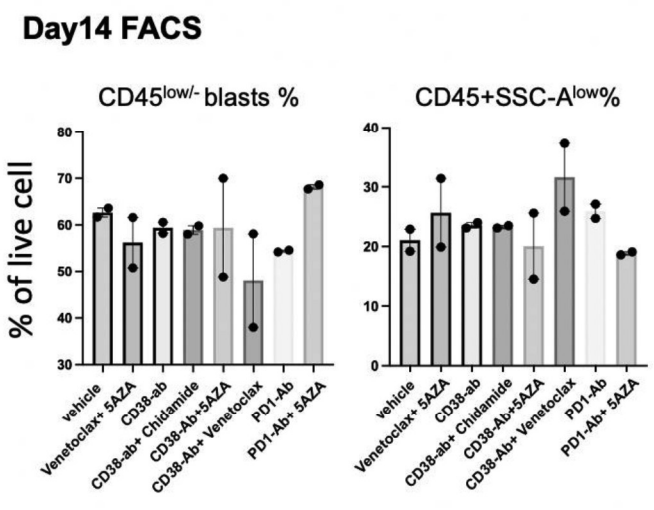

Day14 FACS
CD45low/- blasts %
CD45+SSC-Alow%
% of live cell
vehicle
Venetoclax+ 5AZA
CD38-ab
CD38-ab+ Chidamide
CD38-Ab+5AZA
CD38-Ab+ Venetoclax
PD1-Ab
PD1-Ab+ 5AZA

FIG. 25

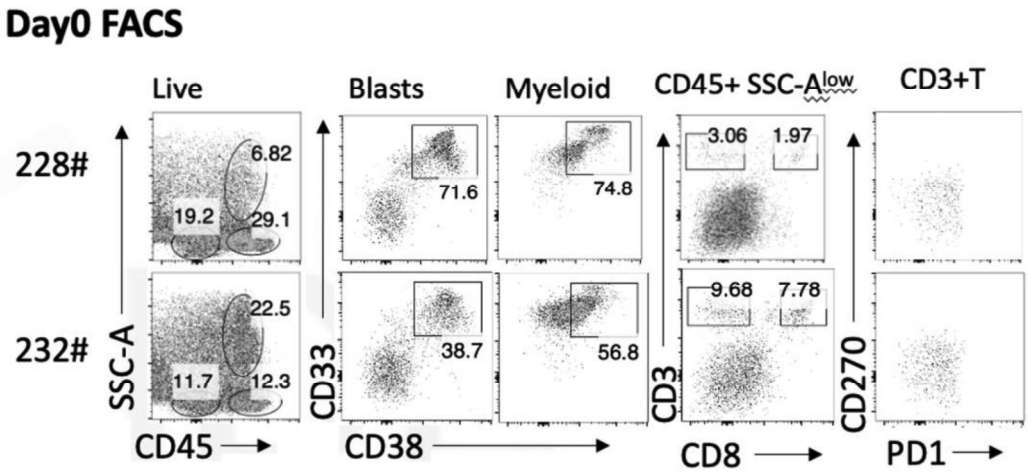

Day0 FACS
Live
Blasts
Myeloid
CD45+ SSC-Alow
CD3+T
228#
232#
6.82
19.2
29.1
22.5
11.7
12.3
71.6
74.8
38.7
56.8
3.06
1.97
9.68
7.78
SSC-A
CD45
CD33
CD38
CD3
CD8
CD270
PD1

FIG. 26

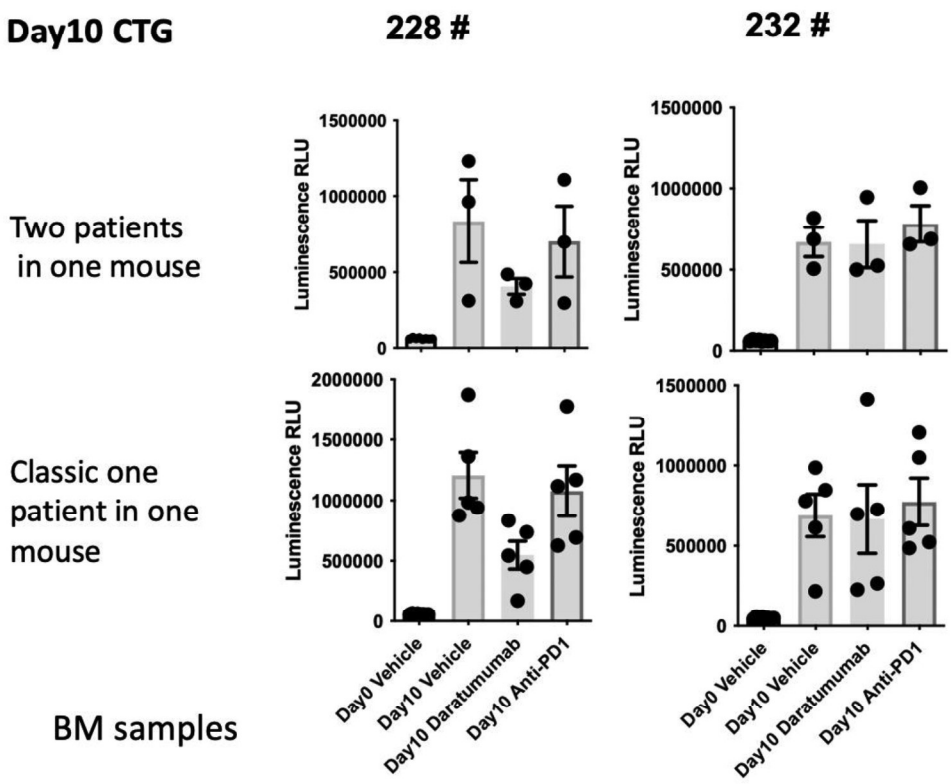

Day10 CTG
228 #
232 #
Two patients in one mouse
Classic one patient in one mouse
BM samples
Luminescence RLU
1500000
1000000
500000
0
2000000
Day0 Vehicle
Day10 Vehicle
Day10 Daratumumab
Day10 Anti-PD1

FIG. 27

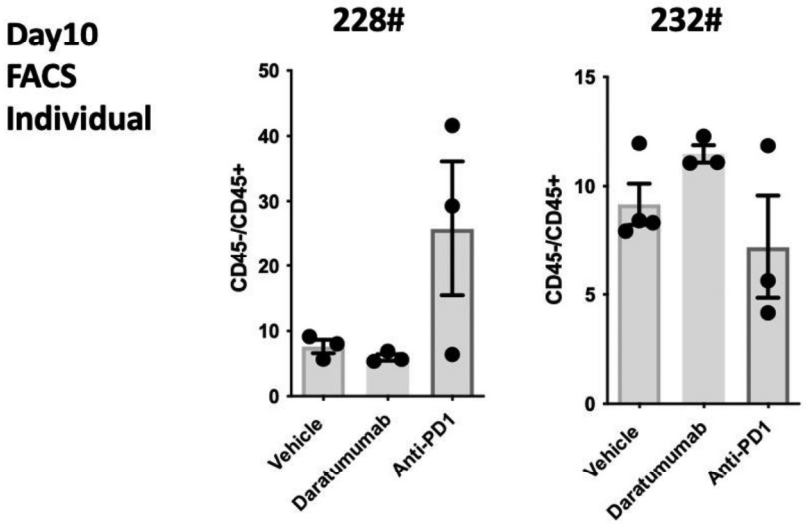

Day10
FACS
Individual
228#
232#
CD45-/CD45+
50
40
30
20
10
0
15
5
Vehicle
Daratumumab
Anti-PD1

FIG. 28