

## Supplementary Materials

**Supplementary Table 1.**

<b>CD8 effector vs exhausted</b>	<b>PD1 High</b>	<b>MYC Targets</b>	<b>TP53 Targets (cell cycle)</b>
ACOT8	CKS1B	ANLN	CDKN1A
ADAMTS6	MCM5	ASPM	GAS2L1
ADGRL2	CENPM	AURKA	HRAS
ADIPOQ	MCM3	BIRC5	JAG2
ADORA2A	MCM7	BRCA2	LTBP2
ADPRM	TK1	BUB1	NEDD9
AGR2	FEN1	CCNB1	SEPTIN9
AIF1L	UBE2T	CCNB2	SFN
ALOX5AP	TUBB	CDK1	TP53
ALS2	STMN1	CDKN3	
AOPEP	NUSAP1	CKS1B	
ARHGAP30	TROAP	CKS2	
ARHGAP8	CHAF1A	CLIC4	
ARL4C	TRAIP	DCTPP1	
ATOX1	CDKN3	DTL	
ATP8A1	NDC80	E2F8	
B4GALT1	RNASEH2A	ECT2	
BAK1	CENPA	FAM136A	
BATF2	SMC2	FDPS	
BBS4	SPAG5	GMNN	
BCL2L14	CENPE	GSDME	
BCL9L	CENPF	HMGB2	
BEND6	RAD51AP1PLK4	HMGN2	
C19orf12	KIF2C	HNRNPLL	
C19orf53	UBE2C	IDI1	
C1orf54	CHEK1	KIF20A	
C3orf80	ZWINT	KPNA2	
C9orf64	MTRF2	MKI67	
CA2	CDCA5	NUDCD2	
CASP7	RMI2	NUP54	
CASS4	SPC24	PCLAF	
CCDC12	CKAP2L	PCNA	
CCND3	CDCA2	PLK1	
CCRL2	ESCO2	RACGAP1	
CD40	ECT2	RRM1	

CD86	SKA1	STRAP	
CDC42EP2	SKA3	TFDP1	
CESSA	TPX2	TOP2A	
CFAP126	FOXM1	TSPAN4	
CFAP36	ORC6	TXN	
CFAP410	POLA2	UBE2S	
CLCN1	POC1A	UCHL5	
CLEC6A	ASPM	YBX3	
COA5	RACGAP1		
CSF1	UHRF1		
CSF2	HIST1H1B		
CTSK	HELLS		
CUEDC1	HMMR		
D2HGDH	BIRC5		
DAAM1	INCENP		
DAPP1	FAM111B		
DDX58	KIF11		
DENND2B	KIFC1		
DENR	CENPW		
DHRS7	MAD2L1		
DNAL1	MCM2		
DOCK8	MCM4		
DOK1	MKI67		
DTX3L	MTHFD1		
ENG	MYBL2		
ENPP4	NEK2		
EPSTI1	GTSE1		
F11R	DTL		
FAM209A	GINS2		
FAM221A	PLK1		
FCER1G	POLE2		
FECH	ANLN		
FRMD4A	NCAPG2		
FXN	SPDL1		
GBP2	PARPBP		
GBP4	FANCL		
GCH1	CDCA8		
GCHFR	CEP55		
GDI1	CENPQ		
GMPPB	FANCI		
GPR18	HJURP		

GSAP	MCM10		
GSDMD	ASF1B		
GSN	C1orf112		
GZMB	PRR11		
HK1	DEPDC1B		
HLA-B	KIF15		
HLA-C	SPC25		
HSPB11	BARD1		
IDNK	RAD51		
IFIT1	RFC4		
IFITM3	RRM2		
IFNG	CLSPN		
IFT80	NCAPG		
IKZF2	STIL		
IL12A	BRCA1		
IL12RB1	BRCA2		
IL2RB	AURKA		
IP6K1	BUB1		
IRF1	BUB1B		
IRF7	TOP2A		
IRGM	TTK		
ISG20	TYMS		
ITM2B	DSCC1		
ITPR1	CENPU		
KIF13B	SUV39H2		
LAMTOR4	SHCBP1		
LGALS3BP	ATAD5		
LGALS9B	DSN1		
LLGL1	DIAPH3		
LYN	CDC45		
LYST	CDCA3		
MAF	NUF2		
MCEMP1	RAD54L		
MED15	GGH		
MIDN	CCNA2		
MPEG1	TIMELESS		
MYCBP2	CCNF		
MZT2B	PRC1		
NACC2	PKMYT1		
NAGA	CCNB2		
NBAS	AURKB		

NDUFA7	KIF23		
NIT1	DLGAP5		
NKG7	ARHGAP11A		
NOD1	CDK1		
NQO2	MELK		
NSG2	CDC6		
NT5C3A	CDC20		
OAS1	DEPDC1		
OAS2	KIF4A		
OAS3	KIF14		
OCEL1	POLQ		
P3H1	E2F2		
PAGR1	MND1		
PARP11			
PARP12			
PARP14			
PARP8			
PCBD1			
PDE1B			
PDE8A			
PDLIM4			
PLAC8			
PLSCR3			
PLXNA3			
PSMB8			
PSMB9			
PTK2			
RAB19			
RBM43			
RERE			
RGS12			
RIN1			
RSAD2			
SCLY			
SERPINB6			
SERPINB9			
SESTD1			
SGCB			
SH3BP2			
SIAE			
SIN3B			

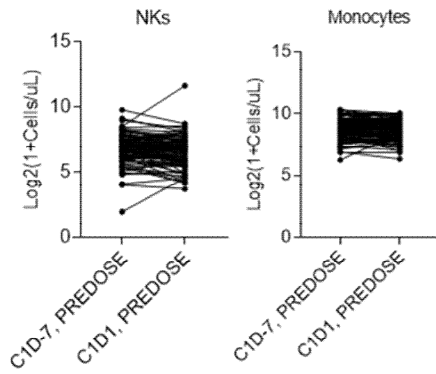
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SOCS1			
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SPATA13			
SQOR			
STAT1			
STMP1			
SUCO			
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TAPBP			
TAPBPL			
TBX21			
TFEC			
TLR4			
TMBIM6			
TMEM106A			
TMEM140			
TMEM219			
TMEM87A			
TOR3A			
TP53BP1			
TRAF5			
TRAFD1			
TRIM5			
TSGA10			
TTYH3			
UBALD2			
UHRF1			
UMODL1			
UNC93B1			
VGLL4			
WLS			
XDH			
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ZNF513			
ZNF691			

ZNFX1			
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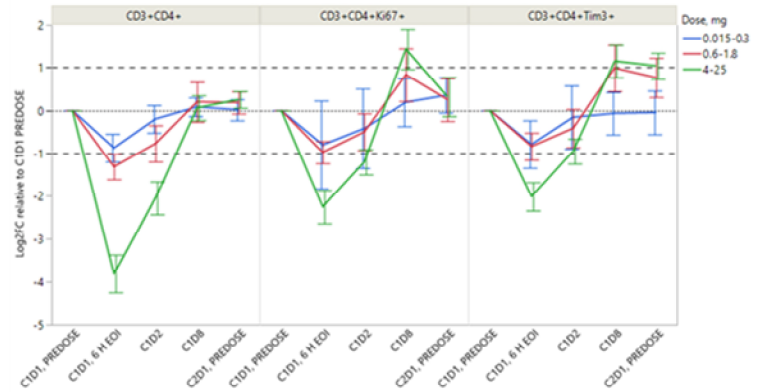
## Supplemental figures

**Supplementary Figure 1.** (A) Flow cytometric analysis of peripheral natural killer (NK) cells (CD16+/CD56+) and monocytes (CD14+) before obinutuzumab pretreatment (Gpt; C1D-7, predose) and before the first glofitamab infusion (C1D1, predose). (B) Graphs represent Log<sub>2</sub> fold change from baseline (C1D1 predose) of peripheral CD4+ T-cell subsets at indicated timepoints during cycle 1, as measured by flow cytometry. Error bars indicate confidence intervals. (C) Box plots (left) represent Log<sub>2</sub> fold change from baseline (C1D1 predose) of peripheral CD3+ T cells at 6 hours post-end of infusion (6H post-EOI) of cycle 2 day 1 (top) and cycle 5 day 1 (bottom) in relation to the best overall response (BOR), as measured by flow cytometry. Scatter plots (right) indicate the correlation between Log<sub>2</sub> fold change from baseline (C1D1 predose) of peripheral CD3+ T cells and the administered glofitamab dose (mg) at 6h post-EOI of cycle 2 day 1 (top) and cycle 5 day 1 (bottom). Colors indicate BOR categories. *P*-values >0.05 for complete response (CR) vs partial response/stable disease/progressive disease (PR/SD/PD). (D) Plots show Log<sub>2</sub> fold change from baseline (C1D1 predose) of peripheral CD8+ T-cell subsets measured by flow cytometry on the first day of cycle 4 (C4D1 predose; top panel; n = 37) and the first day of cycle 5 (C5D1 predose; bottom panel; n = 29) for the high dose cohort (4-25 mg). X-axes indicate the BOR. Means of each response category are shown. *P*-values >0.05 for CR vs PR/SD/PD. In panels (B and D) dotted lines indicate baseline levels and dashed lines indicate 2-fold change from baseline. Statistical analysis was not adjusted for log(glofitamab dose) and International Prognostic Index (IPI) category. Data in (A-C) are from n = 119 patients with evaluable flow cytometry data.

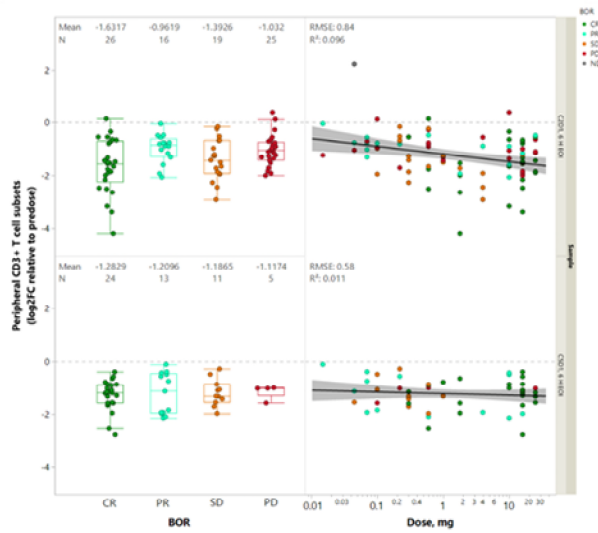
**A**



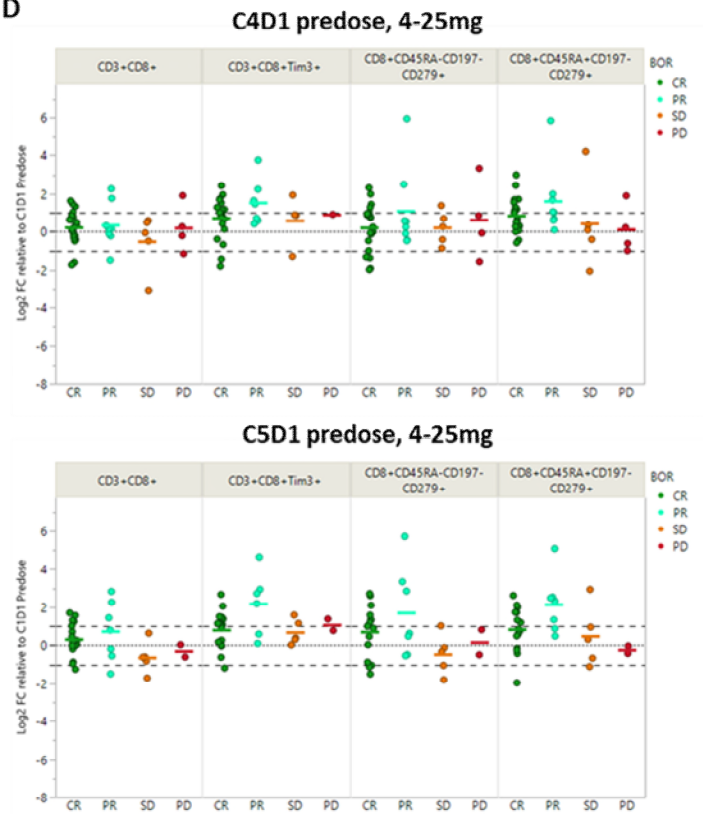
**B**



**C**



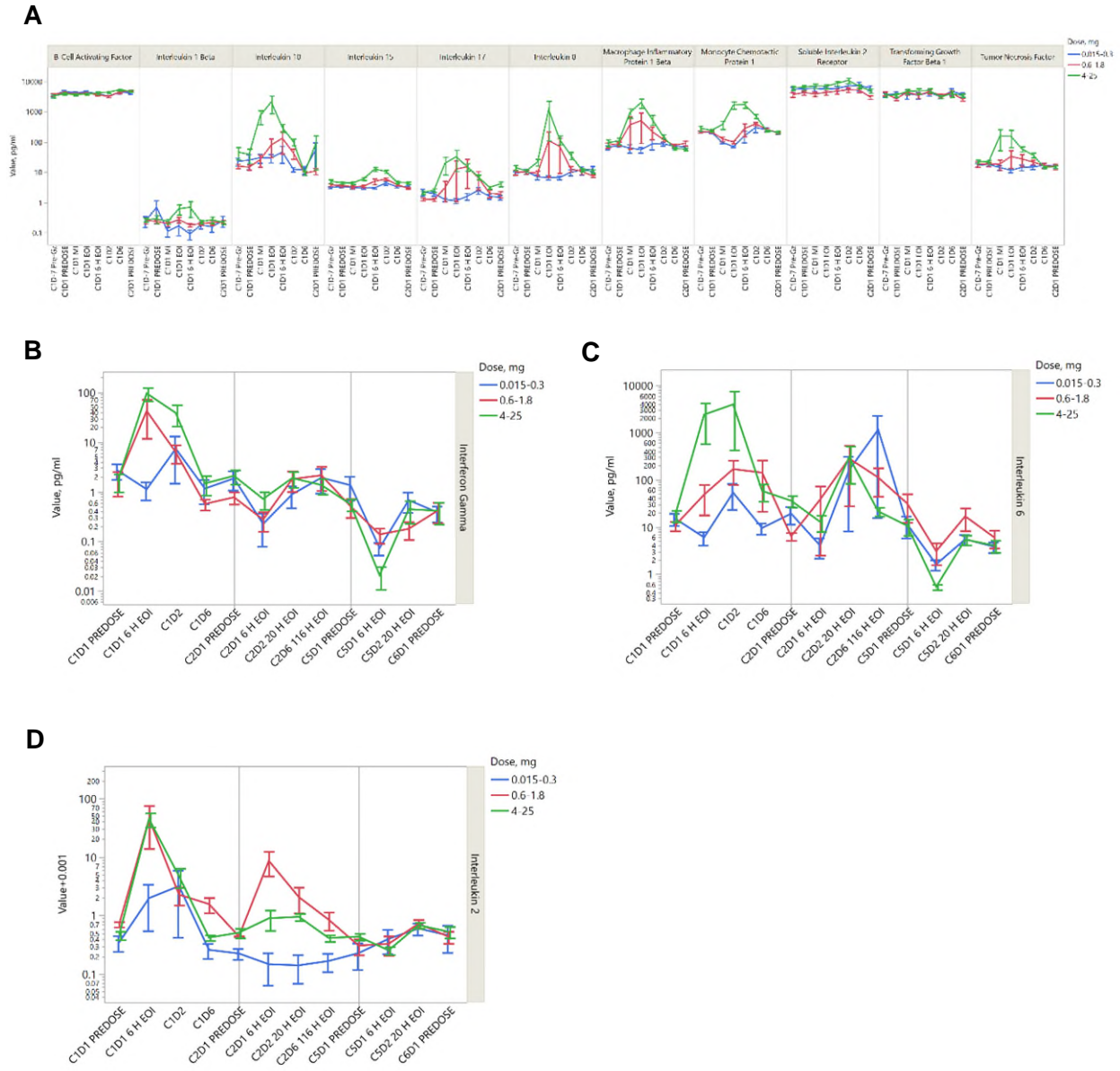
**D**



6H post-EOI, 6 hours post-end of infusion; BOR, best overall response; C, cycle; CR, complete response; D, day; NK, natural killer cells; PD, progressive disease; PR, partial response; SD, stable disease.



**Supplementary Figure 2.** (A) Plasma cytokine concentrations (pg/mL) of B-cell activating factor, IL-1 $\beta$ , IL-10, IL-15, IL-17, IL-8, MIP-1 $\beta$ , MCP1, soluble IL-2R (sCD25), TGF- $\beta$  and TNF- $\alpha$  are shown at indicated timepoints during the first cycle. (A) Plasma cytokine concentrations (pg/mL) of (B) IFN $\gamma$ , (C) IL-6, and (D) IL-2 are shown at indicated timepoints during cycles 1, 2 and 5. In panels (A-D), y-axes are in logarithmic scales and error bars indicate standard error of the mean. Data are generated from n = 119 patients with evaluable cytokine data.



6H post-EOI, 6 hours post-end of infusion; BOR, best overall response; C, cycle; CR, complete response; D, day; MI, mid-infusion; NK, natural killer cells; PD, progressive disease; PR, partial response; pre-Gpt, before obinutuzumab pretreatment; SD, stable disease.

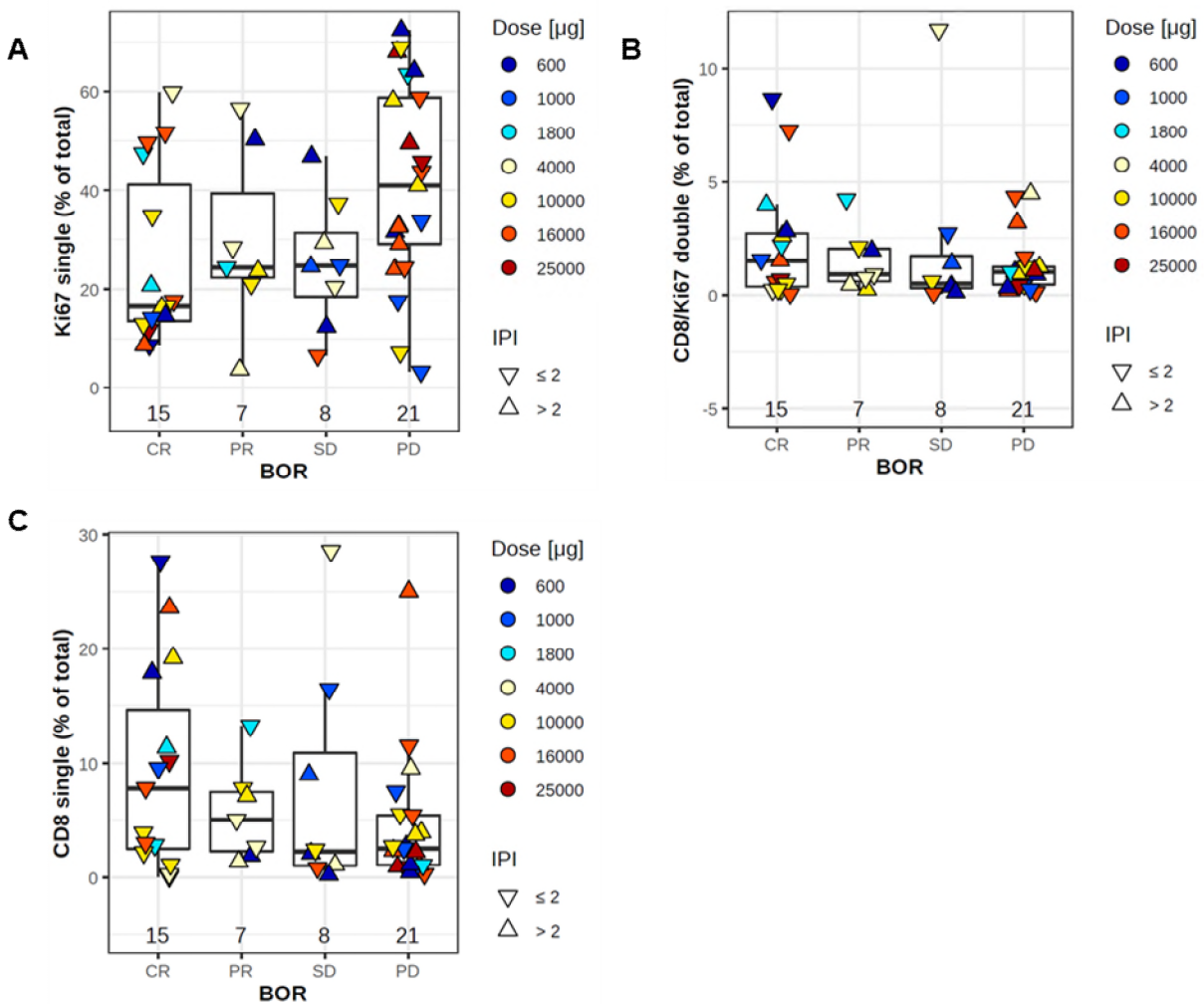
**Supplementary Figure 3.** Box plots demonstrate (A) percentage of total (CD8-) Ki67+ cells, (B) percentage of CD8+Ki67+ cells, and (C) percentage of CD8+Ki67- cells in

baseline tumor biopsies (n = 51) in relation to the best overall response (BOR)

categories. All fractions are shown as of total cells in the tumor area. *P*-values >0.05.

Statistical analyses in panels A-C were performed for complete response (CR) vs partial response/stable disease/progressive disease (PR/SD/PD) and adjusted for log

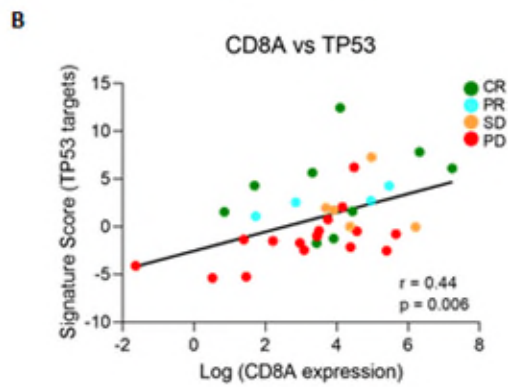
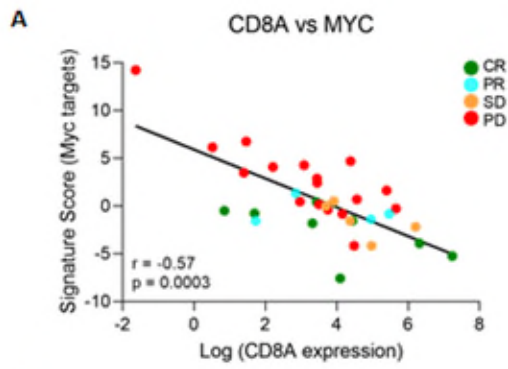
(glofitamab dose) and International Prognostic Index (IPI) category.



BOR, best overall response; CR, complete response; IPI, International Prognostic

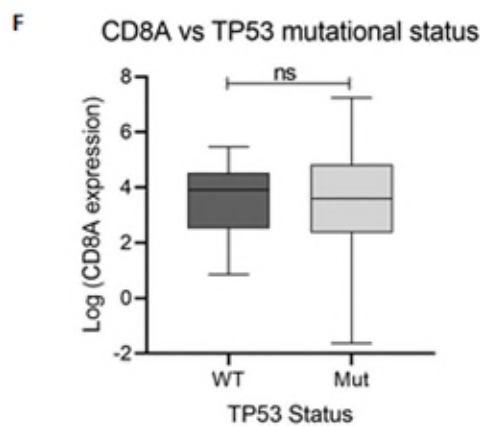
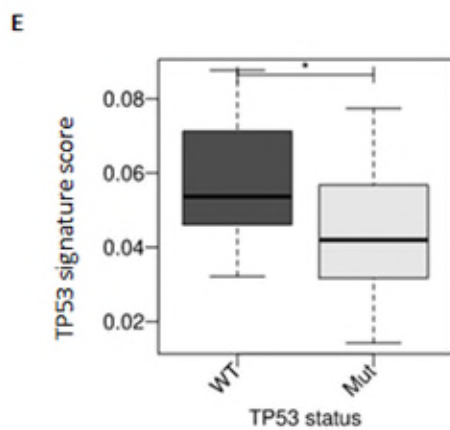
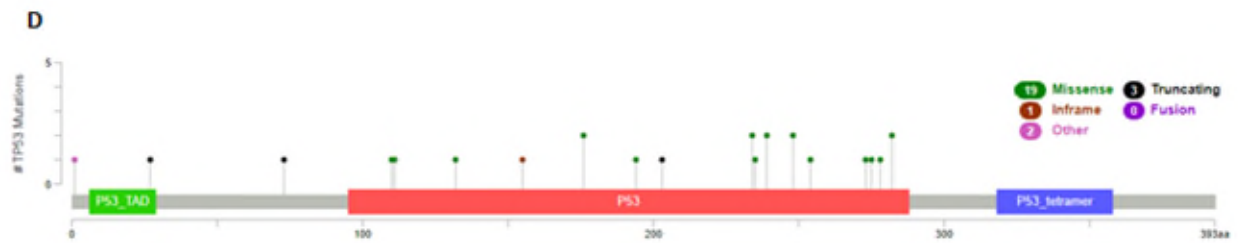
Index; PD, progressive disease; PR, partial response; SD, stable disease.

**Supplementary Figure 4. Scatter plots show correlation between log (CD8A expression) (RNAseq) and (A) MYC targets or (B) TP53 targets signature scores in baseline biopsies.** (C) Table of identified *TP53* mutations in the mutant patient population, and (D) their schematic mapping on TP53 protein. LOF indicates loss-of-function. (E) Box plots represent the TP53 signature score (RNA-seq) for the *TP53* wild-type (WT) and mutant (mut) subsets. Asterisk denotes *P*-value <0.05. (F) Box plots represent the Log (CD8A expression) (RNA-seq) for the TP53 wild-type (WT) and mutant (mut) subsets. TP53 mutation data is generated from n = 33 patients with targeted sequencing data.



**C**

Hugo_Symbol	Protein_Change	Mutation_Type	Biological_Effect	Frequency
TP53	R248Q	Missense_Mutation	LOF (likely)	2
TP53	T155_R156	In_Frame_Del	LOF (likely)	1
TP53	C176R	Missense_Mutation	LOF (likely)	1
TP53	C176Y	Missense_Mutation	LOF (likely)	1
TP53	C275Y	Missense_Mutation	LOF (likely)	1
TP53	I254S	Missense_Mutation	LOF (likely)	1
TP53	K132R	Missense_Mutation	LOF (likely)	1
TP53	L111R	Missense_Mutation	LOF (likely)	1
TP53	L194R	Missense_Mutation	LOF (likely)	1
TP53	M1K	Missense_Mutation	LOF (likely)	1
TP53	N235D	Missense_Mutation	LOF (likely)	1
TP53	N239D	Missense_Mutation	LOF (likely)	1
TP53	N239S	Missense_Mutation	LOF (likely)	1
TP53	P278R	Missense_Mutation	LOF (likely)	1
TP53	R110L	Missense_Mutation	LOF (likely)	1
TP53	R248Q	Missense_Mutation	LOF (likely)	1
TP53	R273H	Missense_Mutation	LOF (likely)	1
TP53	R282P	Missense_Mutation	LOF (likely)	1
TP53	R282W	Missense_Mutation	LOF (likely)	1
TP53	Y234C	Missense_Mutation	LOF (likely)	1
TP53	Y234D	Missense_Mutation	LOF (likely)	1
TP53	P27*	Nonsense_Mutation	LOF (likely)	1
TP53	V203*	Nonsense_Mutation	LOF (likely)	1
TP53	V73*	Nonsense_Mutation	LOF (likely)	1
TP53	splice site 672+1G>T	Splice site variant	Unknown	1



Del, deletion; LOF, loss of function; Mut, mutant; WT, wildtype.