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Supplemental information

Robust SARS-CoV-2 T cell responses with common TCR$\alpha\beta$ motifs toward COVID-19 vaccines in patients with hematological malignancy impacting B cells

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SUPPLEMENTAL INFORMATION

Robust T cell responses with common TCRαβ motifs towards COVID-19 vaccines in haematological malignancy patients with impacted B cell immunity

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Supplementary Tables

Table S1. Cohort demographics and clinical summary, refer to Figure 1.

	Healthy individuals	Haematology patients	BNT162b2, mRNA-1273	ChAdOx1
Number of individuals, *n*	58	95	25	70
Age, mean (range)	44 (20-80)	65 (19-91)	51 (19-80)	70 (51-91)
Female, *n* (%)	41 (71%)	28 (29%)	-	-
Vaccine (2 doses), *n* (%)			-	-
ChAdOx1 (AstraZeneca)	26 (45%)	70 (74%)	-	-
Age, mean (range)	51 (20-80)	70 (51-91)		
BNT162b2 Comirnaty (Pfizer)	32 (55%)	24 (25%)	-	-
Age, mean (range)	38 (23-60)	50 (19-80)		
mRNA-1273 (Moderna)	0	1 (1%)	-	-
Vaccine (3rd dose), *n* (%)			-	-
ChAdOx1 (AstraZeneca)	1 (2%)	5 (5%)	-	-
BNT162b2 Comirnaty (Pfizer)	20 (34%)	63 (66%)	-	-
mRNA-1273 (Moderna)	1 (2%)	10 (11%)	-	-
Novavax	1 (2%)	0 (0%)	-	-
Unknown due to lost follow-up	35 (60%)	17 (18%)	-	-
Cellular therapy, *n* (%)	-	33 (34%)	17 (68%)	16 (23%)
Allogeneic SCT		5 (5%)	4 (16%)	1 (1%)
Autograft	-	21(22%)	9 (36%)	12 (17%)
CAR T-cell	-	7 (7%)	4 (16%)	3 (5%)
Days post-cellular therapy, mean (range)	-	177 (45-393)	185 (45-393)	167 (73-337)
Malignancy/treatment, *n* (%)				
CLL/naive	-	14 (15%)	2 (8%)	12 (17%)
CLL/venetoclax	-	5 (5%)	1 (4%)	4 (6%)
CLL/zanubrutinib	-	25 (26%)	1 (4%)	24 (34%)
WM/naive	-	1 (1%)	0	1 (1%)
WM/zanubrutinib	-	10 (11%)	1 (4%)	9 (13%)
Myeloma	-	7 (7%)	3 (12%)	4 (6%)
Previous SARS-CoV-2 infection, *n*	1	0	0	0
SARS-CoV-2 infection during the study, *n*	8	12	5	7

Abbreviations: CAR T-cell, chimeric antigen receptor T-cell; CLL, chronic lymphocytic leukemia; SCT, stem cell transplantation; WM, Waldenstrom macroglobulinemia. Clinical information and limited immune data have been described for a subset of CLL patients.[41]

SUPPLEMENTARY FIGURES

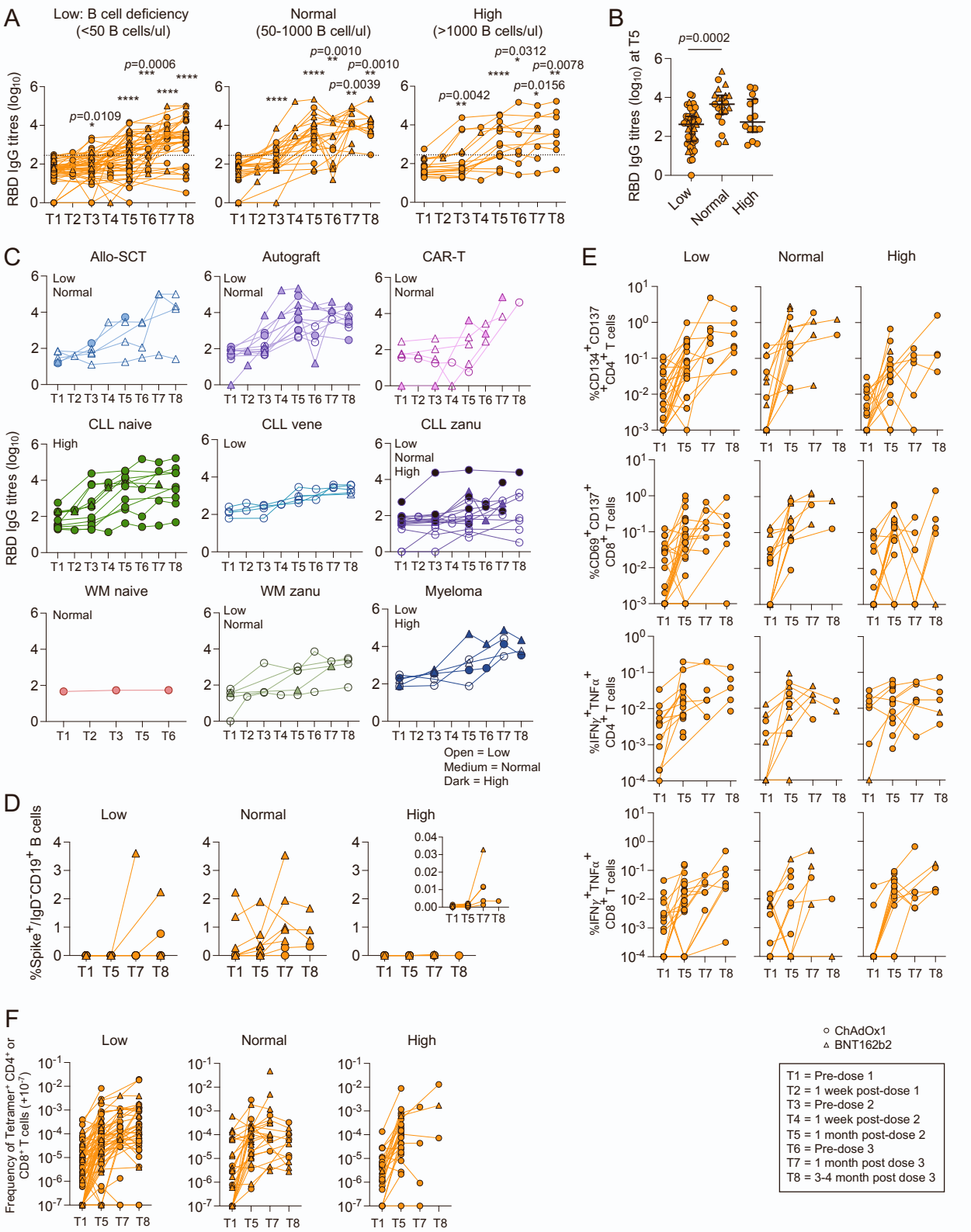


Figure S1. Haematology patients grouped by low, normal or high B cell numbers. End-point IgG titres of ancestral RBD antibodies (A) across sampling timepoints, (B) at T5, and (C) per malignancy and treatment group. (D) Spike-specific memory B cells in haematology patients grouped by low, normal or high B cell numbers. (E) AIM and ICS frequencies and (F) tetramer^{+} spike-specific CD4^{+} and CD8^{+} T cells grouped by low, normal or high B cell numbers. Due to limited sample availability, experiments were performed once for each sample. Related to Figure 1, 3, 4.

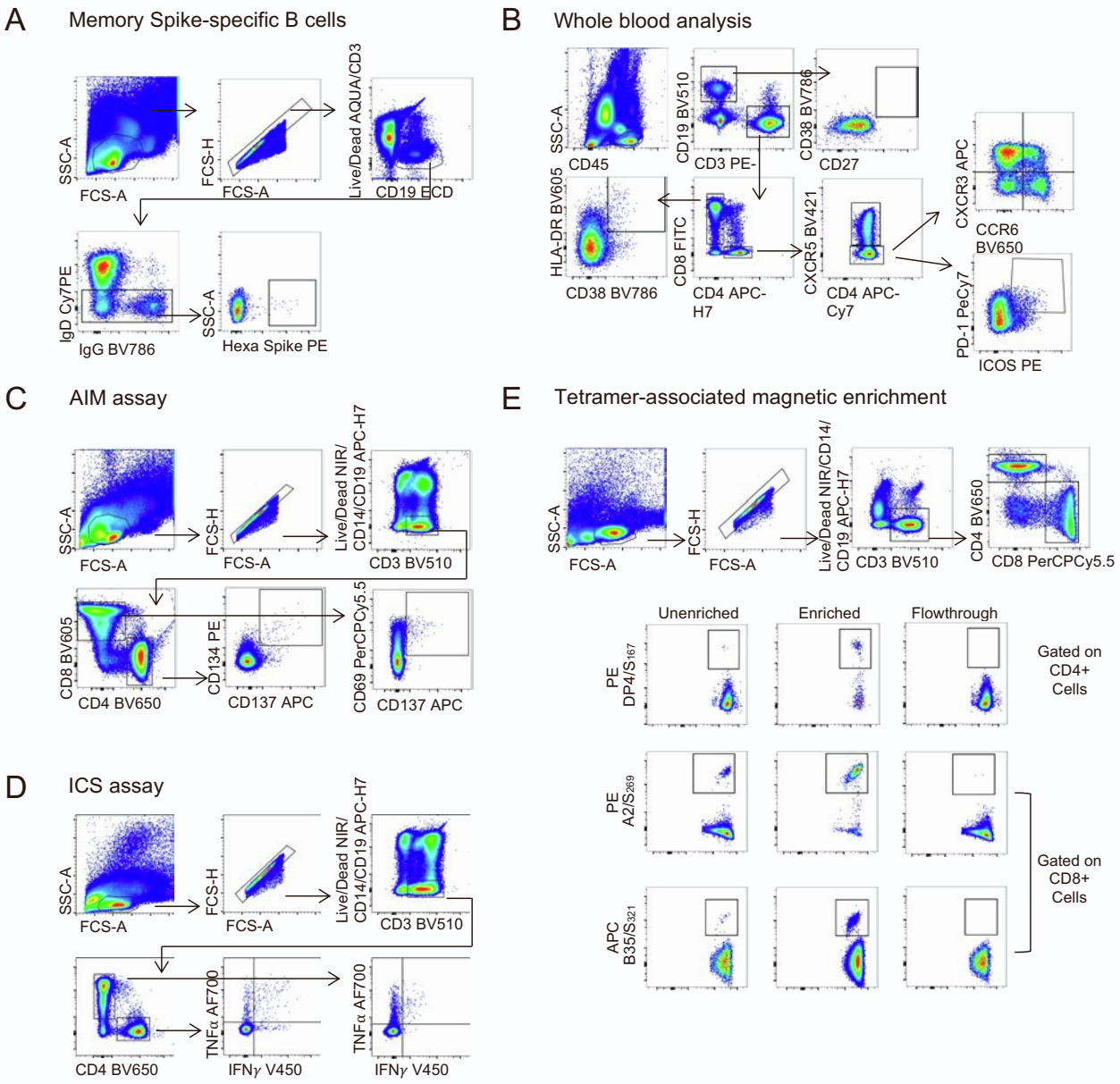


Figure S2. FACS gating strategies to measure cellular vaccine responses. Gating strategy for (A) memory spike-specific B cells, (B) whole blood analysis, (C) AIM and (D) ICS assay, and (E) TAME. Related to Figure 1, 2, 3 and 4.

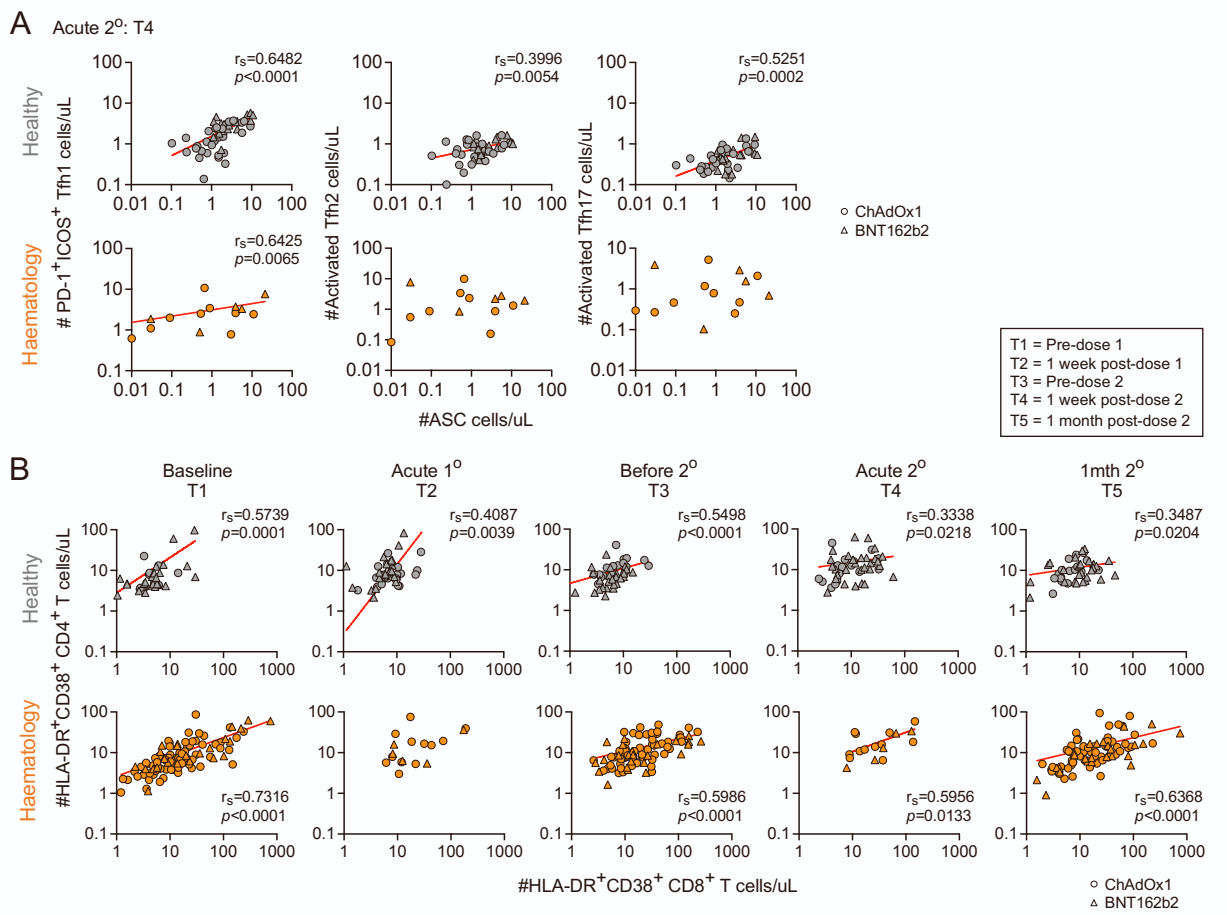


Figure S3. Correlations of whole blood subsets. (A) Spearman's correlation (r_s) of ASCs and Tfh1, Tfh2 and Tfh17 subsets at T4. (B) Spearman's correlation (r_s) of activated $CD4^+$ and $CD8^+$ T cells at T1-T5. Due to limited sample availability, experiments were performed once for each sample. Related to Figure 2.

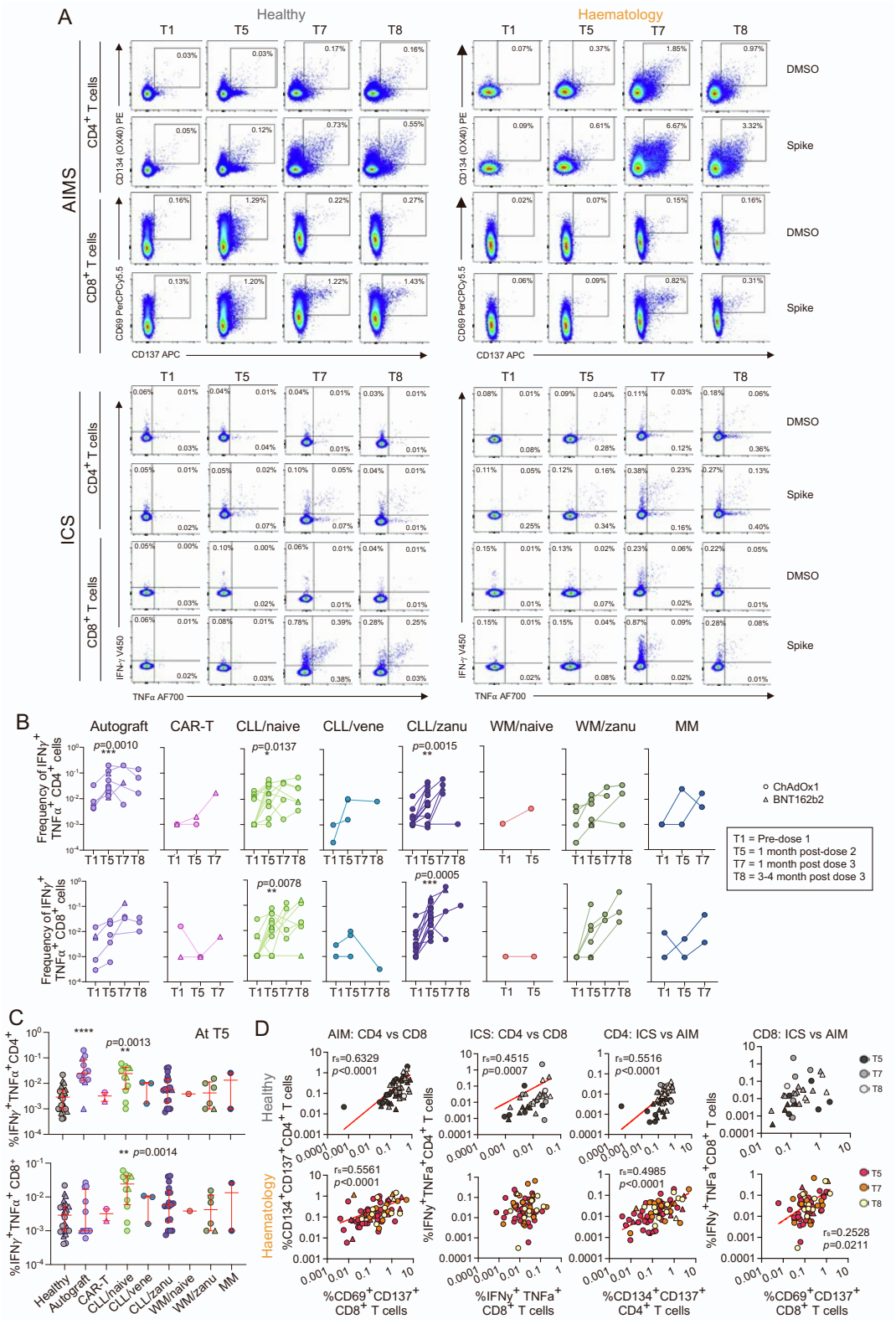


Figure S4. Functional spike-specific CD4$^+$ and CD8$^+$ T cell responses in haematology patients and healthy individuals. (A) Representative AIM and ICS FACS plots including DMSO controls. (B) ICS frequency per malignancy and treatment group at all timepoints measured and (C) at T5 where median and IQR are shown. Statistical significance determined by Dunn's multiple comparisons set on healthy versus all other disease groups. (D) Spearman correlations of CD4$^+$ and CD8$^+$ T cell responses via AIM and ICS assays. Statistical significance determined by Wilcoxon test for timepoint comparisons against T1 (floating values). Exact p values 0.0001<0.05 are shown except p<0.0001=****. Due to limited sample availability, experiments were performed once for each sample. Related to Figure 3.

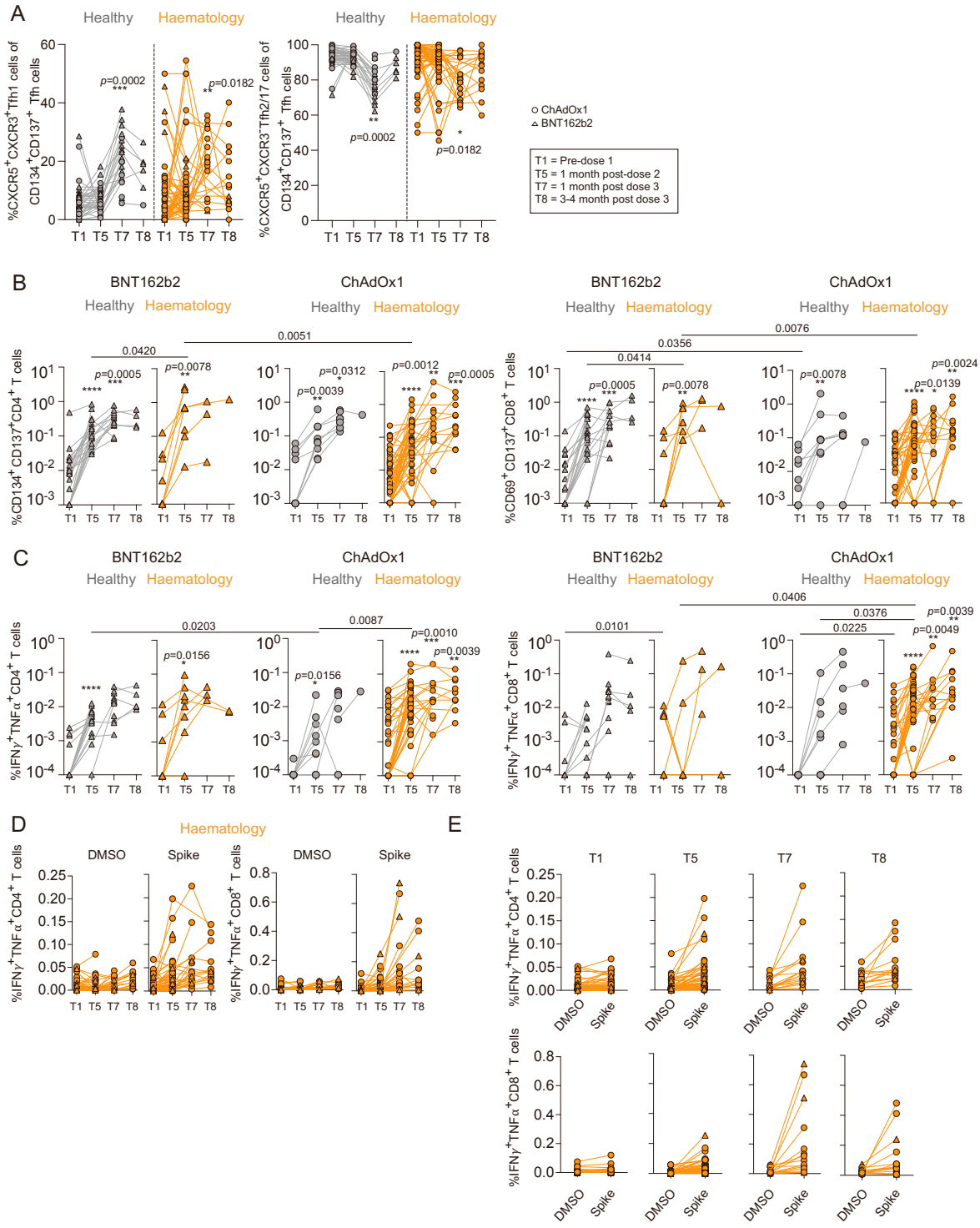


Figure S5. Spike-specific CD4$^+$ and CD8$^+$ T cell responses by vaccine type. (A) Frequency of Tfh1 and Tfh2/17 AIM$^+$ responses of total AIM$^+$ CXCR5$^+$CD4$^+$ Tfh cell response. (B) AIM and (C) ICS frequencies of CD4$^+$ and CD8$^+$ T cells in healthy and haematology per vaccine type. (D, E) Raw percentages of IFNγ$^+$TNF$^+$ in DMSO and spike ICS cultures. Statistical significance determined by Wilcoxon test for timepoint comparisons against T1 (floating values) or by Mann-Whitney for comparisons between healthy and patient timepoints or between vaccine type (connecting line). Exact p values 0.0001<0.05 are shown except p<0.0001=****. Due to limited sample availability, experiments were performed once for each sample. Related to Figure 3.

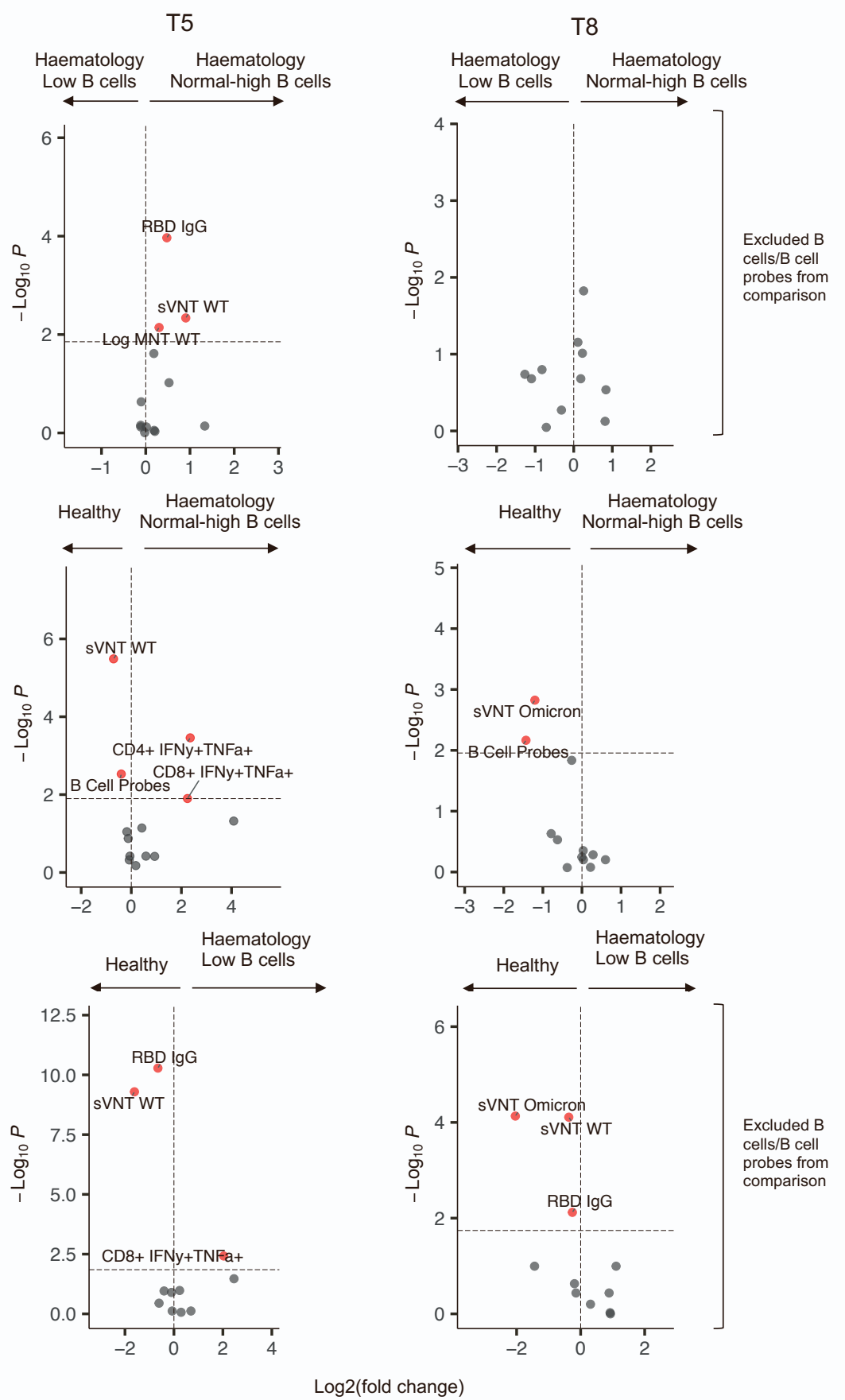


Figure S6. Volcano plots comparing healthy individuals and haematology patients. Related to Figure 3.

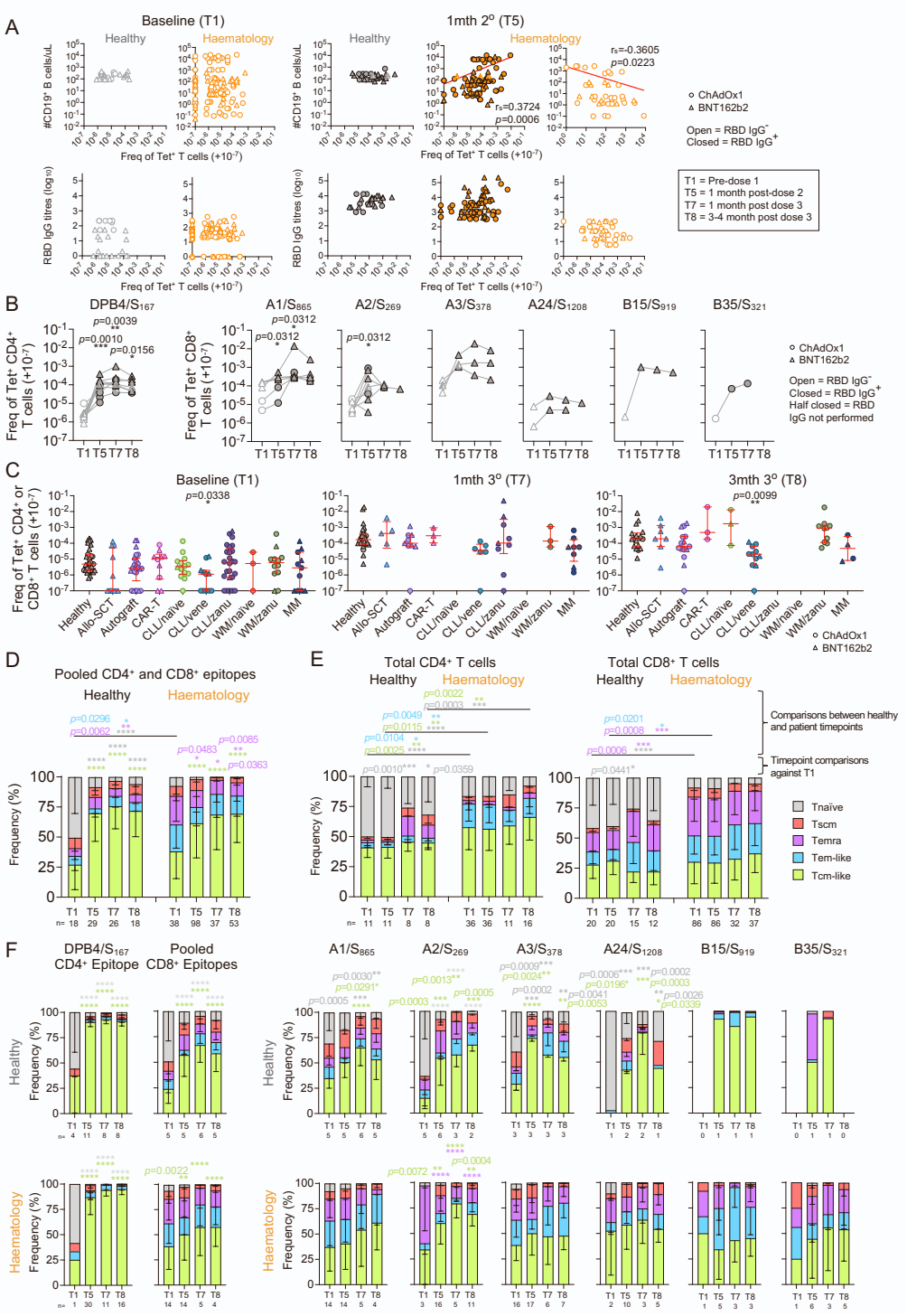


Figure S7. *Ex vivo* SARS-CoV-2-specific tetramer$^+$ T cell responses following COVID-19 vaccination. (A) Spearman's correlation (r_s) of tetramer frequencies versus B cell numbers and RBD IgG titres at T1 and T5. (B) Tetramer CD4$^+$ and CD8$^+$ T cell frequencies of healthy individuals per SARS-CoV-2 epitope. (C) Tetramer frequencies at T1, T7 and T8 where median and IQR are shown. (D) Phenotype profiles of pooled tetramer$^+$ cells, (E) total CD4$^+$ T cells and CD8$^+$ T cells and (F) per SARS-CoV-2 epitope. The frequency of tetramer$^+$ cells have been right-shifted by 10^{-7} (i.e. no detected tetramer$^+$ events displayed as 10^{-7}) to allow for visibility on the logarithmic y axis. Only samples with 10 or more tetramer$^+$ events are included in the phenotypic analysis (Figure D, E and F). Statistical significance determined by Wilcoxon test for timepoint comparisons against T1 ((B) floating values), Dunn's multiple comparisons set on healthy versus all other disease groups (c), Tukey's multiple comparison test (floating values are timepoint comparisons against T1; connecting line are comparisons between healthy and patient timepoints) (D,E), and Dunnett's multiple comparison test for timepoint comparisons against T1 (F). Exact p values 0.0001<0.05 are shown except p<0.0001=****. Due to limited sample availability, experiments were performed once for each sample. Related to Figure 4.

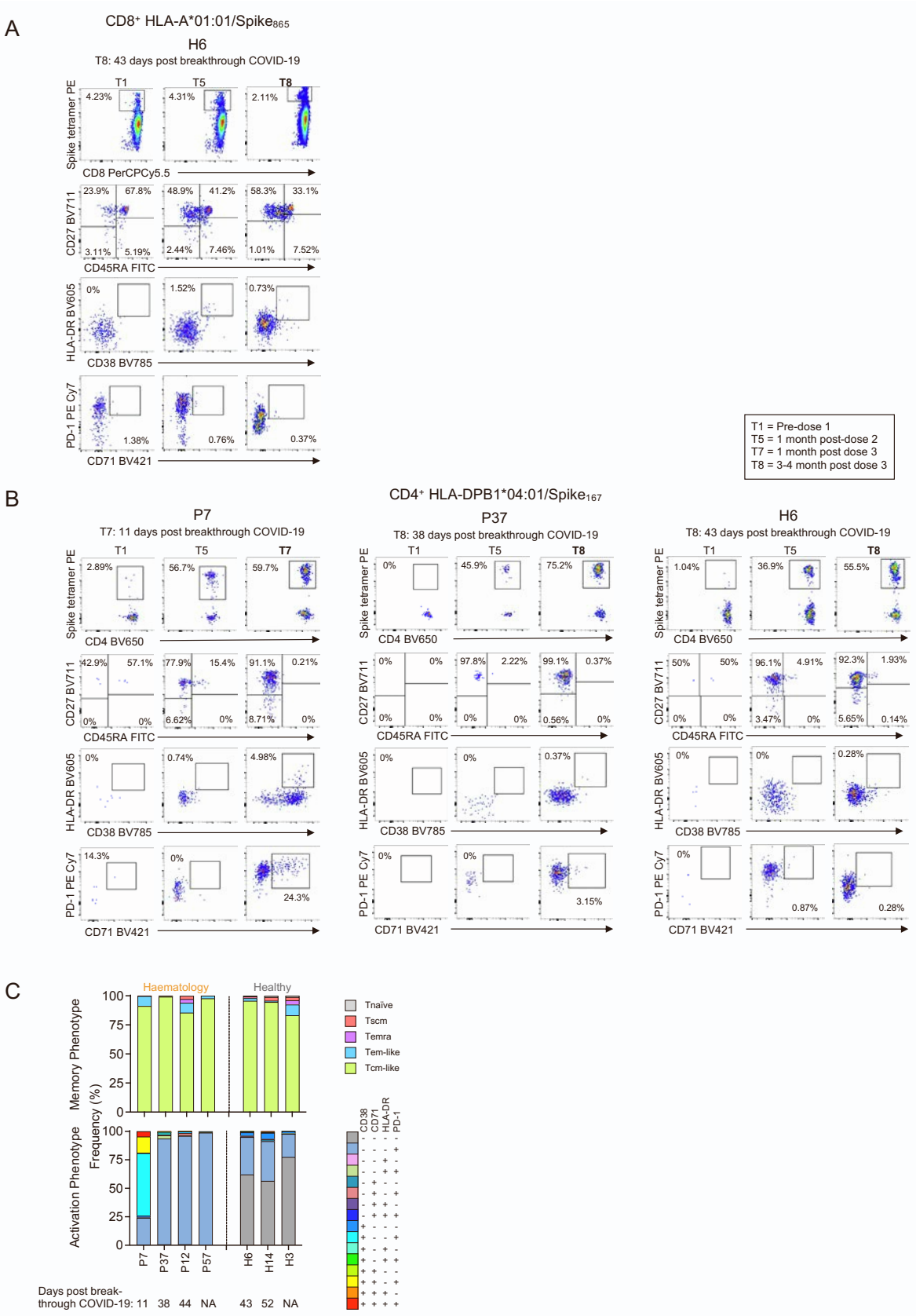


Figure S8. Vaccine responses in donors with breakthrough SARS-CoV-2 infections. Representative TAME enriched FACS plots gated on $CD8^+$ (A) and $CD4^+$ (B) T cells depicting tetramer, and memory and activation phenotypes. (C) Memory and activation phenotypes of DPB4/S_{167}-specfic $CD4^+$ T cells from individuals with breakthrough COVID-19. Due to limited sample availability, experiments were performed once for each sample. Related to Figure 5.

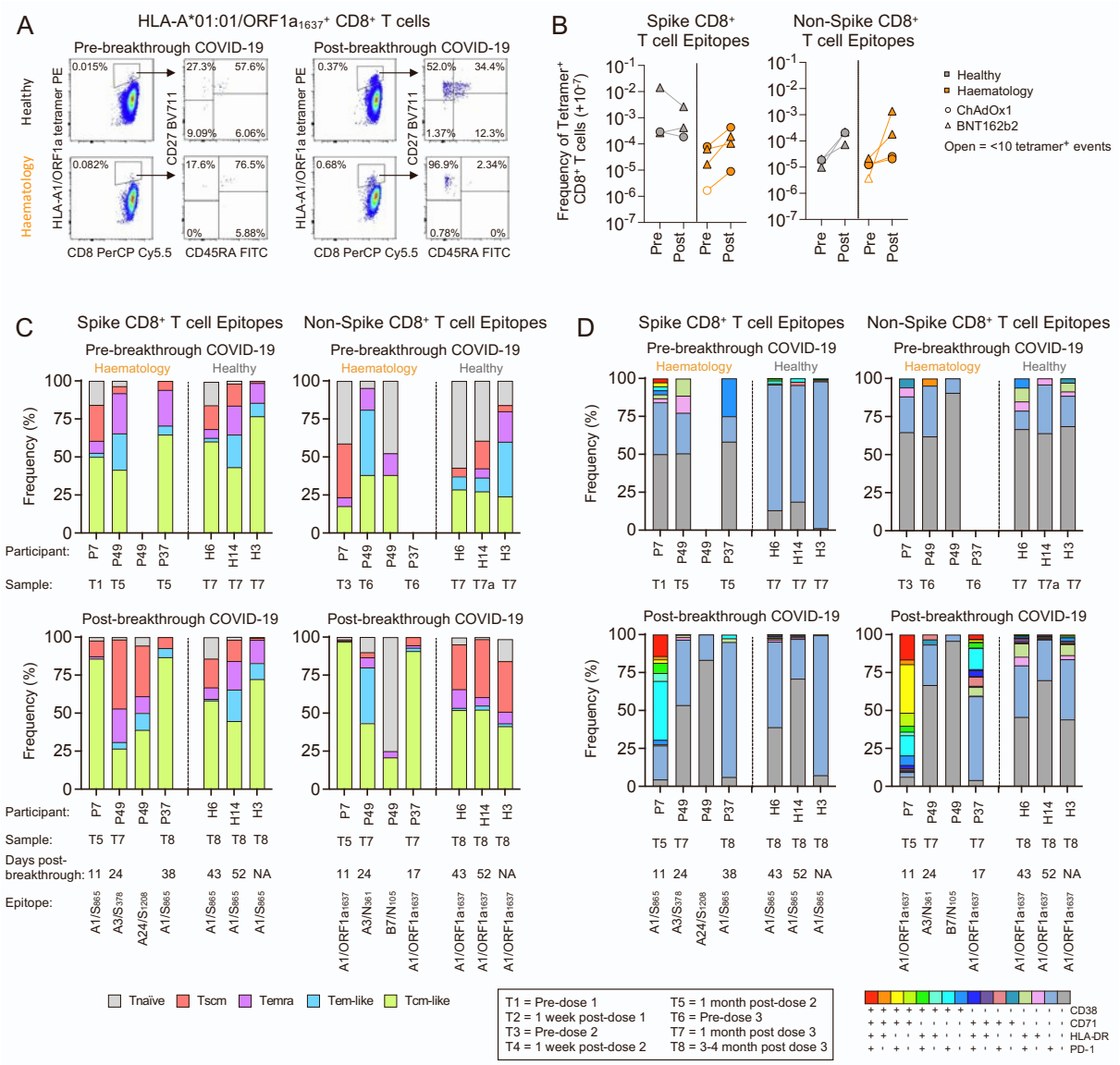


Figure S9. *Ex vivo* paired spike and non-spike-specific tetramer$^+$ CD8$^+$ T cell responses following breakthrough COVID-19. (A) Representative FACS plots of TAME-enriched non-spike-specific CD8$^+$ tetramer populations. (B) Paired tetramer CD8$^+$ T cell frequencies of healthy and haematology participants pre- and post-COVID-19 breakthrough. Any samples with <10 tetramer$^+$ events are shown as open symbols. (C) Memory and (D) activation phenotype profiles for spike and non-spike-specific CD8$^+$ T cells for individuals with breakthrough COVID-19. The frequency of tetramer$^+$ cells have been right-shifted by 10^{-7} (i.e. no detected tetramer$^+$ events displayed as 10^{-7}) to allow for visibility on the logarithmic y axis. Only samples with 10 or more tetramer$^+$ events are included in the phenotypic analysis (Figure C and D). Due to limited sample availability, experiments were performed once for each sample. Related to Figure 5.

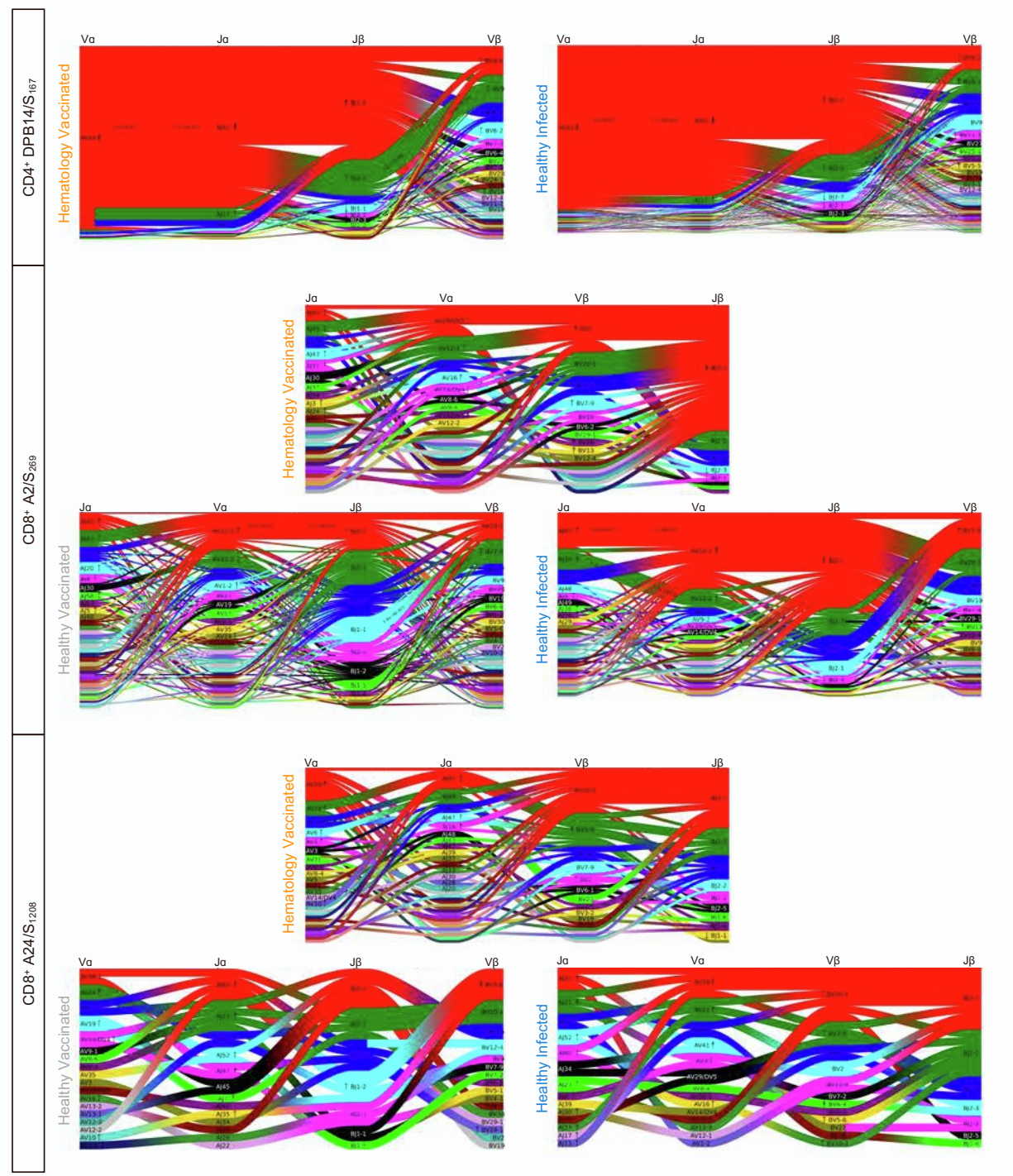


Figure S10. V and J gene segment usage and covariation in epitope-specific responses. Gene-gene pairing landscapes are depicted by curves between vertical gene segment stacks (thickness proportional to the number of TCRs with the gene pairing). Vertical arrows indicate the enrichment of gene segments relative to background frequencies, each arrowhead indicates a 2-fold enrichment. The clonally expanded TCRs were reduced to a single data point for this analysis. Genes are coloured based on frequency: red (most frequent), green (second most frequent), blue, cyan, magenta, and black, followed by assorted colours for rare frequencies. Related to Figure 6.

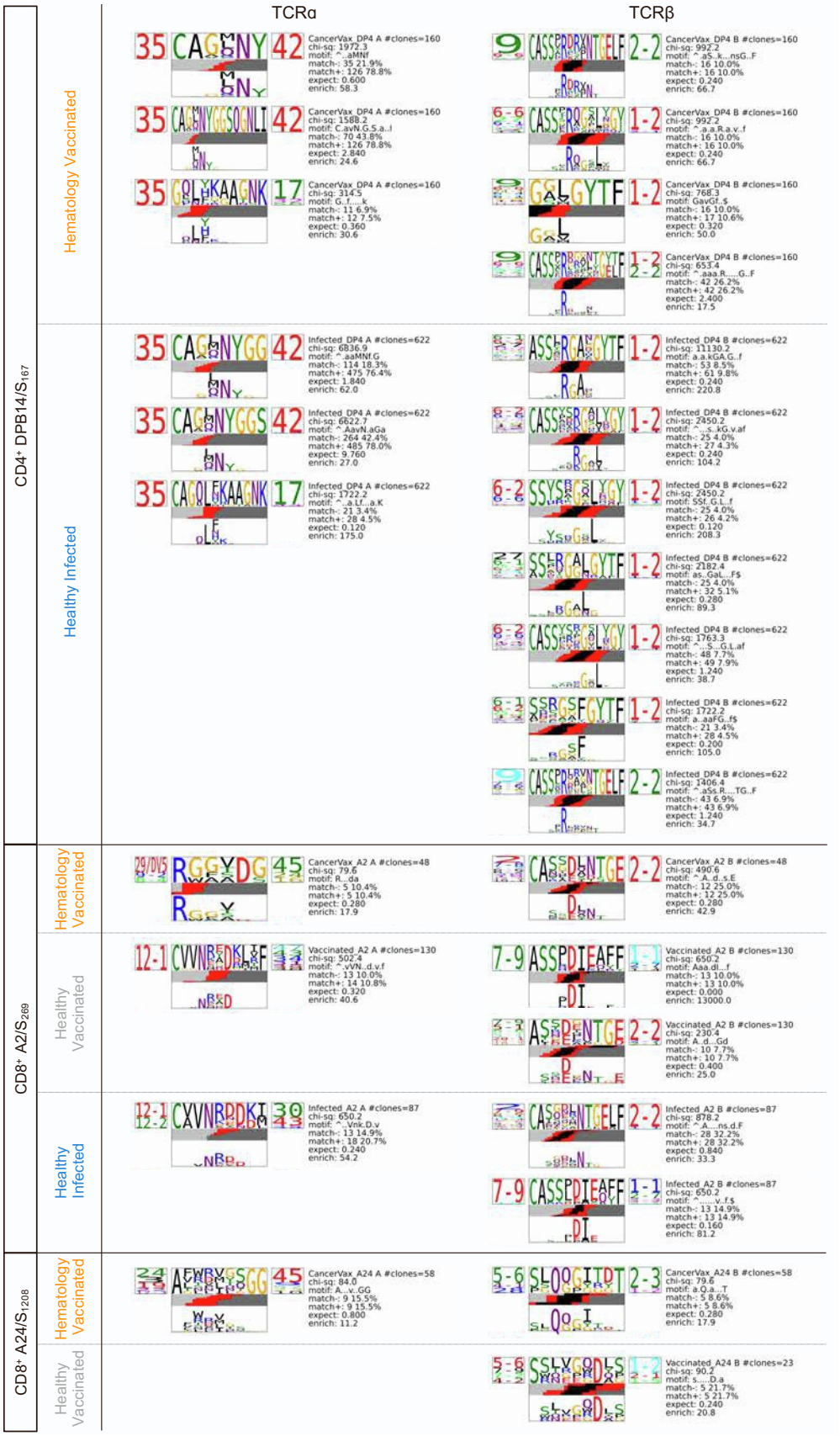
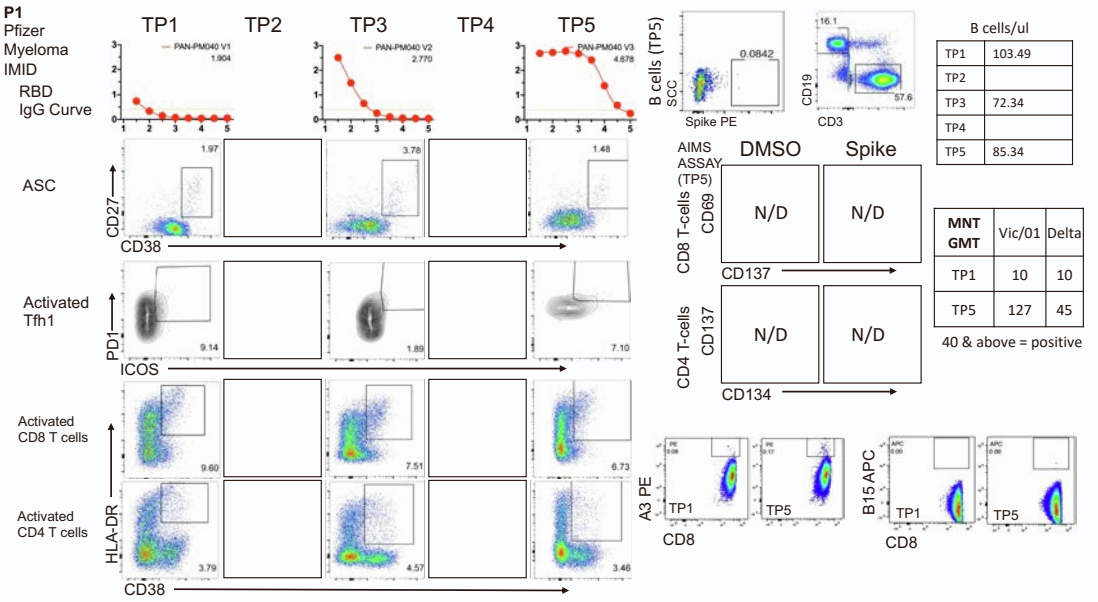


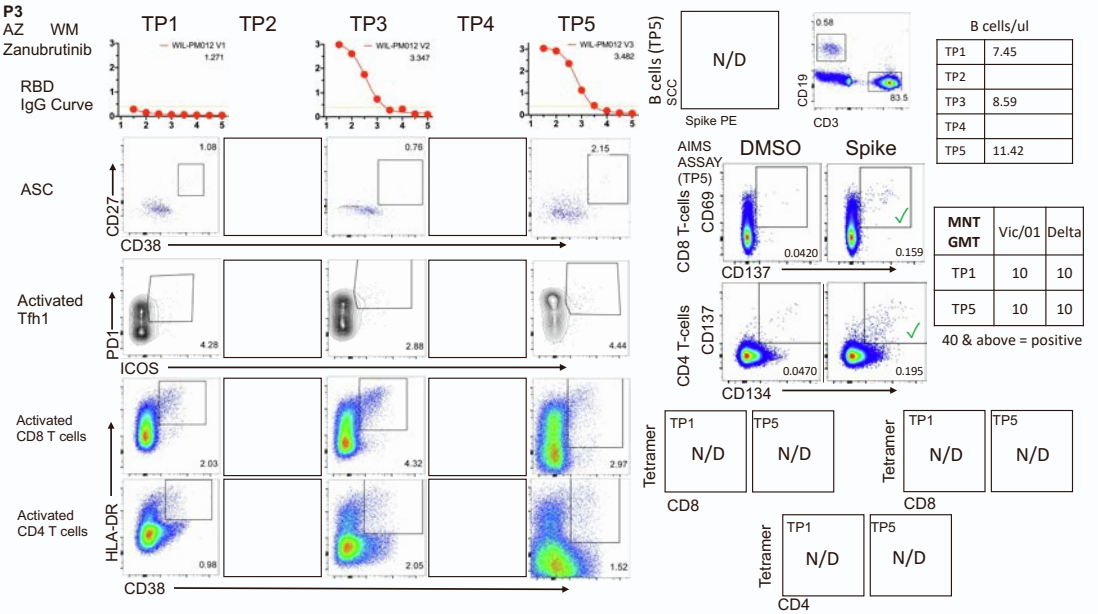
Figure S11. TCR logo representations of CDR3α and β sequence motifs for DPB4/S$_{167}$, A2/S$_{269}$ and A24/S$_{1208}$. Each TCR motif depicts the V (left side) and J (right side) gene frequencies, the CDR3 amino acid sequence (middle), and the inferred rearrangement structure (bottom bars coloured by source region; V-region, light grey; insertions, red; diversity (D)-region, black; and J-region dark grey). The motif scores with chi-squared values greater than 90 were considered highly significant. Related to Figure 6.



B cells/ul	
TP1	103.49
TP2	
TP3	72.34
TP4	
TP5	85.34

MNT GMT	Vic/01	Delta
TP1	10	10
TP5	127	45

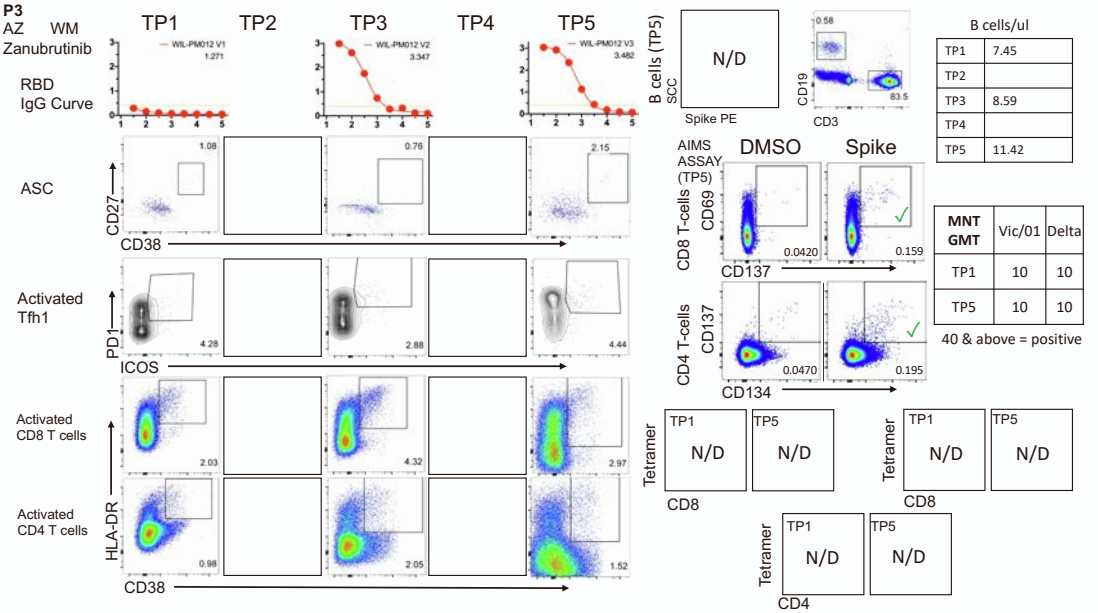
40 & above = positive



B cells/ul	
TP1	7.45
TP2	
TP3	8.59
TP4	
TP5	11.42

MNT GMT	Vic/01	Delta
TP1	10	10
TP5	10	10

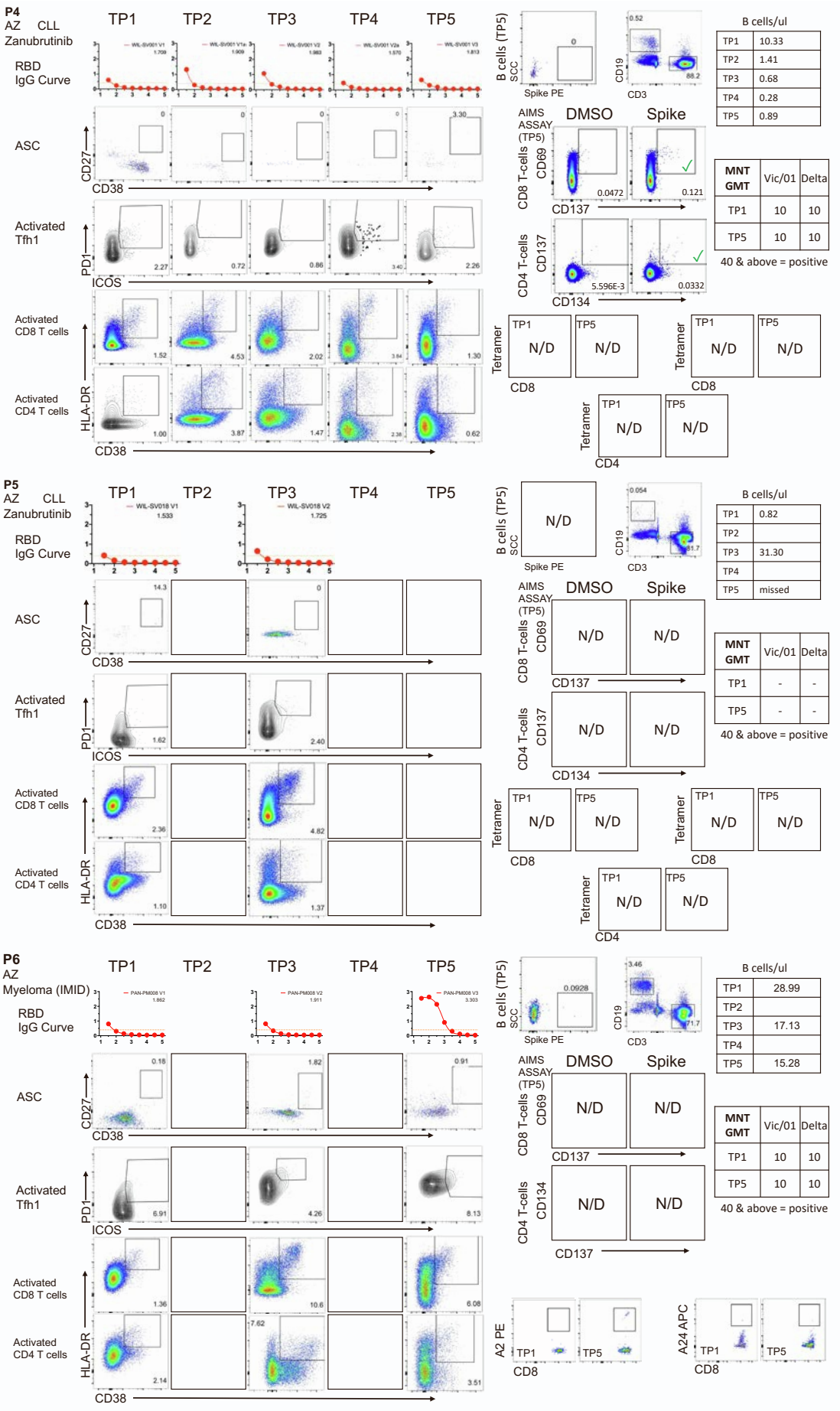
40 & above = positive

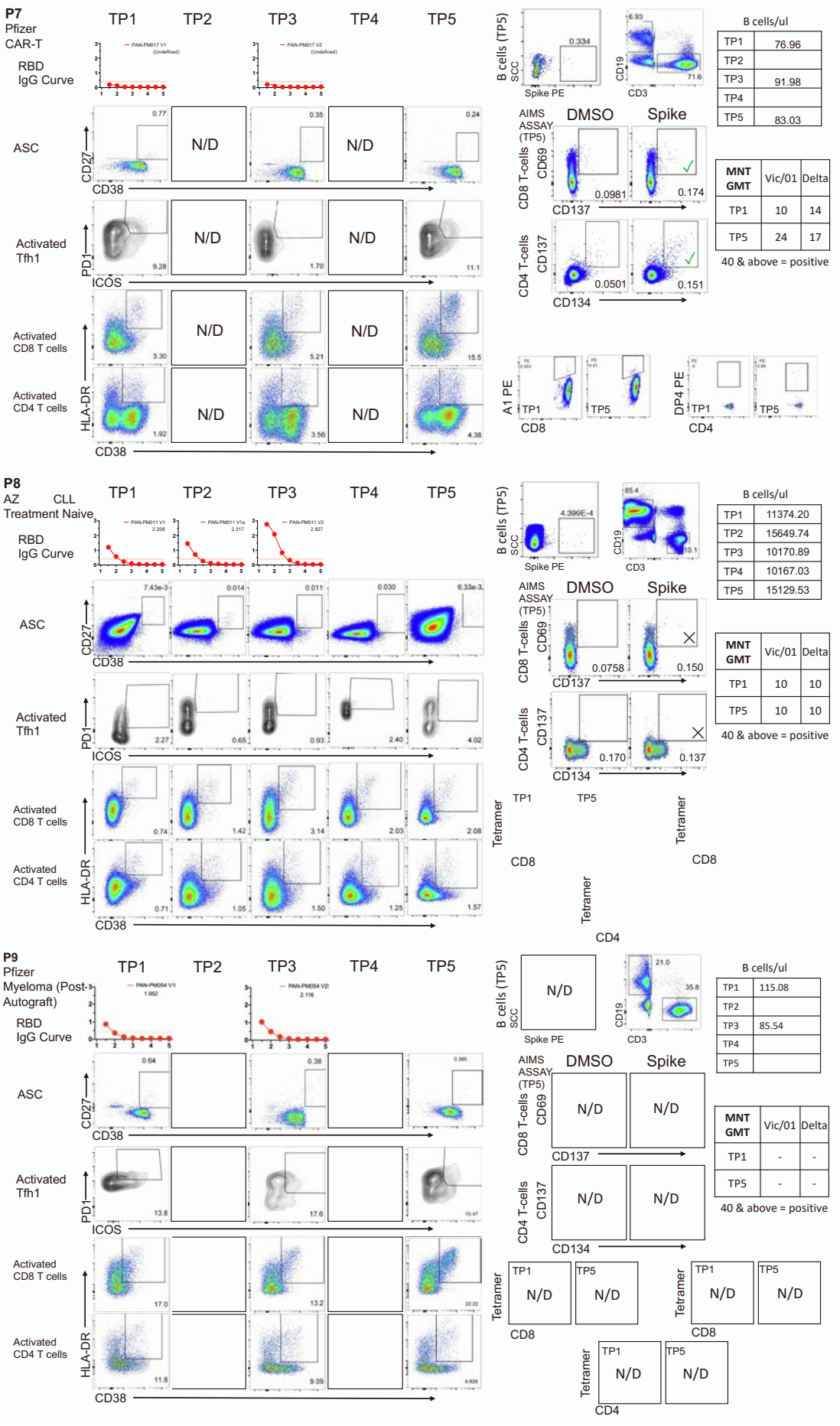


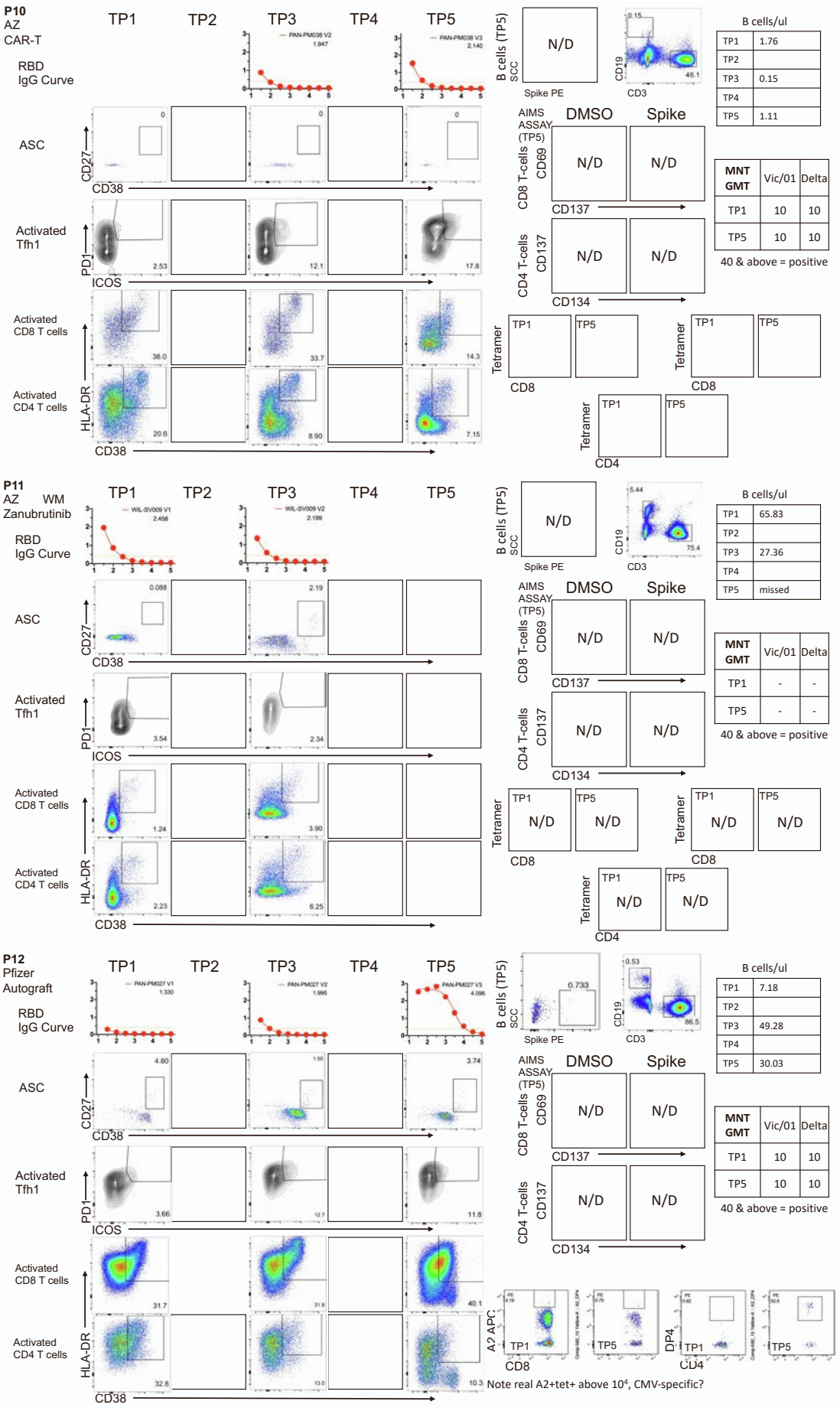
B cells/ul	
TP1	7.45
TP2	
TP3	8.59
TP4	
TP5	11.42

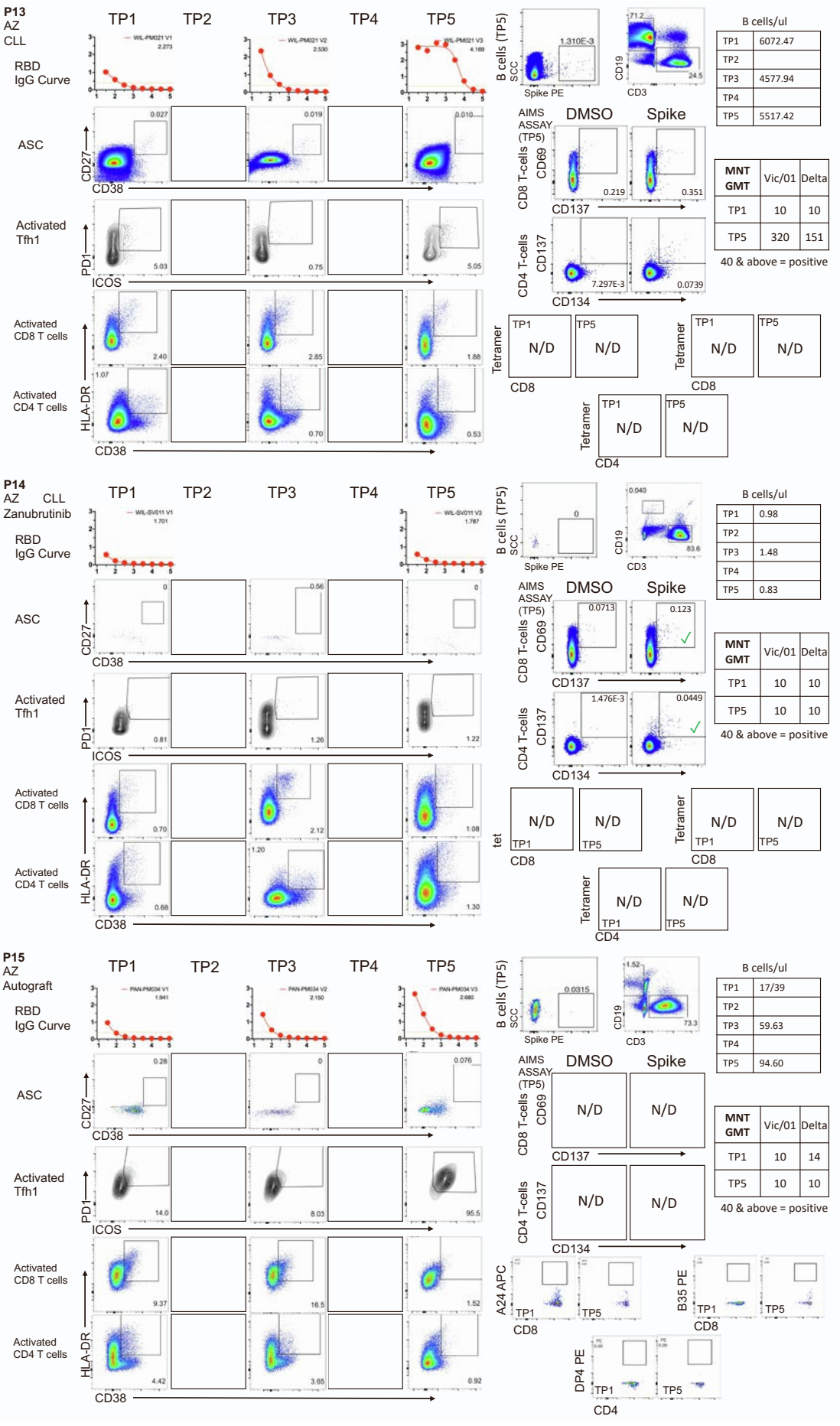
MNT GMT	Vic/01	Delta
TP1	10	10
TP5	10	10

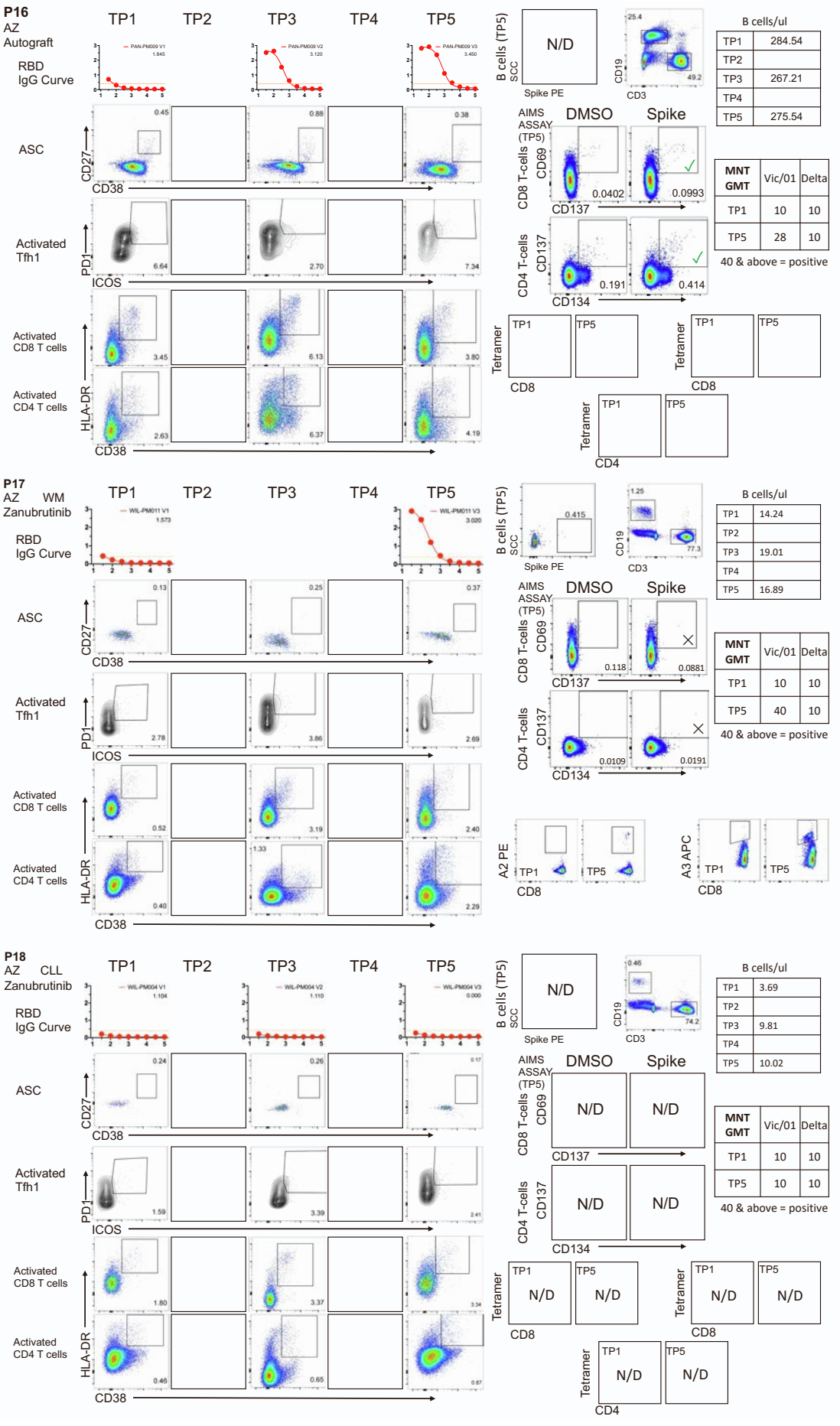
40 & above = positive

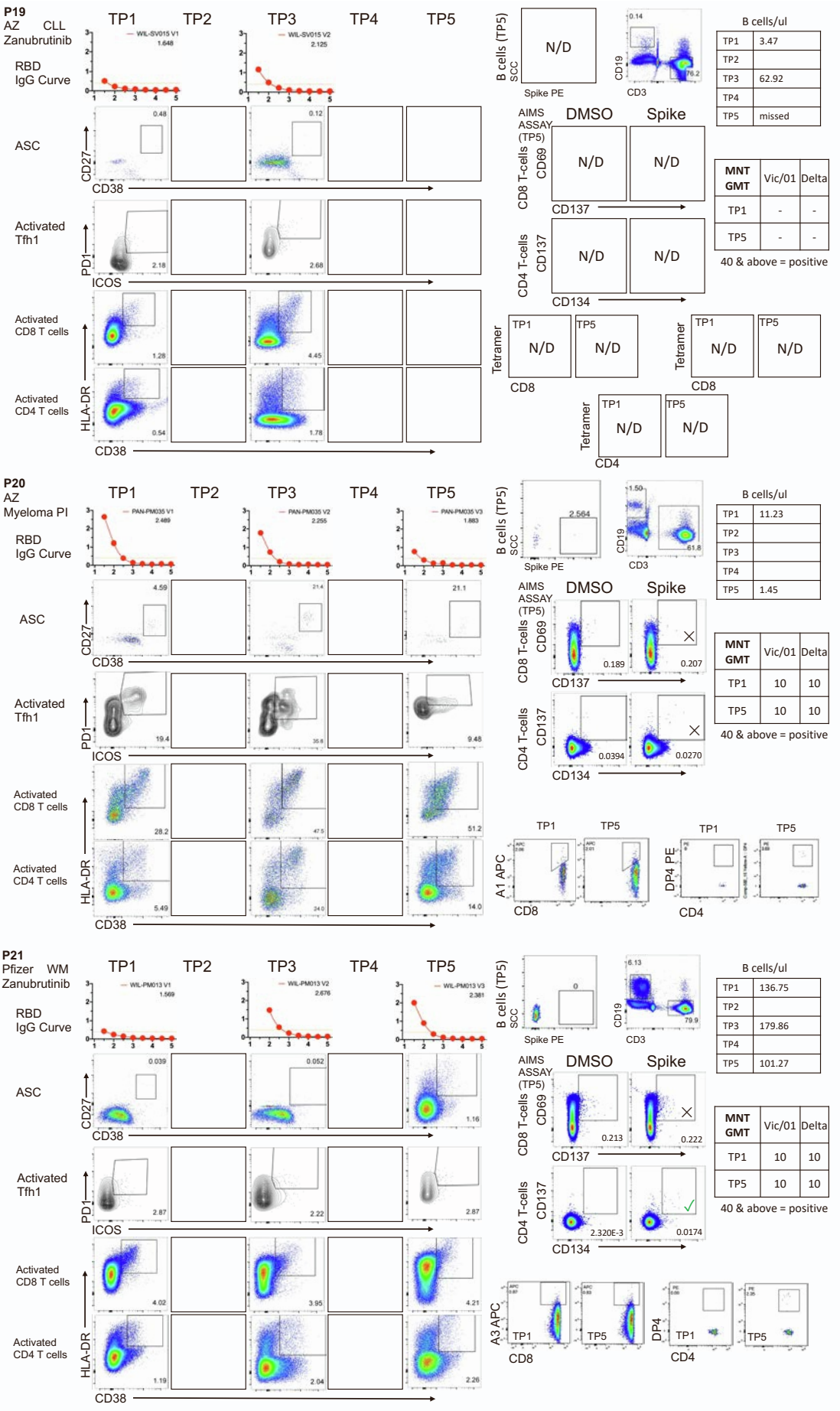

P4
AZ CLL
Zanubrutinib
TP1 TP2 TP3 TP4 TP5
RBD IgG Curve
ASC
CD27
CD38
Activated Tfh1
PD1
ICOS
Activated CD8 T cells
Activated CD4 T cells
HLA-DR
B cells (TP5)
SCC
Spike PE
CD19
CD3
AIMS ASSAY (TP5)
DMSO
Spike
CD8 T-cells CD69
CD137
CD4 T-cells CD137
CD134
B cells/ul
TP1 10.33
TP2 1.41
TP3 0.68
TP4 0.28
TP5 0.89
MNT GMT Vic/01 Delta
TP1 10 10
TP5 10 10
40 & above = positive
Tetramer
CD8
CD4
N/D
P5
AZ CLL
Zanubrutinib
TP1 0.82
TP2
TP3 31.30
TP4
TP5 missed
P6
AZ
Myeloma (IMID)
TP1 28.99
TP2
TP3 17.13
TP4
TP5 15.28
A2 PE
A24 APC


P7
Pfizer
CAR-T
TP1
TP2
TP3
TP4
TP5
RBD
IgG Curve
ASC
CD27
CD38
N/D
Activated
Tfh1
PD1
ICOS
Activated
CD8 T cells
Activated
CD4 T cells
HLA-DR
B cells (TP5)
SCC
Spike PE
CD19
CD3
B cells/ul
TP1 76.96
TP2
TP3 91.98
TP4
TP5 83.03
AIMS
ASSAY
(TP5)
DMSO
Spike
CD8 T-cells
CD69
CD137
CD4 T-cells
CD134
MNT GMT | Vic/01 | Delta
TP1 | 10 | 14
TP5 | 24 | 17
40 & above = positive
A1 PE
DP4 PE
CD8
CD4
P8
AZ CLL
Treatment Naive
TP1 11374.20
TP2 15649.74
TP3 10170.89
TP4 10167.03
TP5 15129.53
TP1 | 10 | 10
TP5 | 10 | 10
Tetramer
P9
Pfizer
Myeloma (Post-Autograft)
TP1 115.08
TP2
TP3 85.54
TP4
TP5
TP1 - | -
TP5 - | -

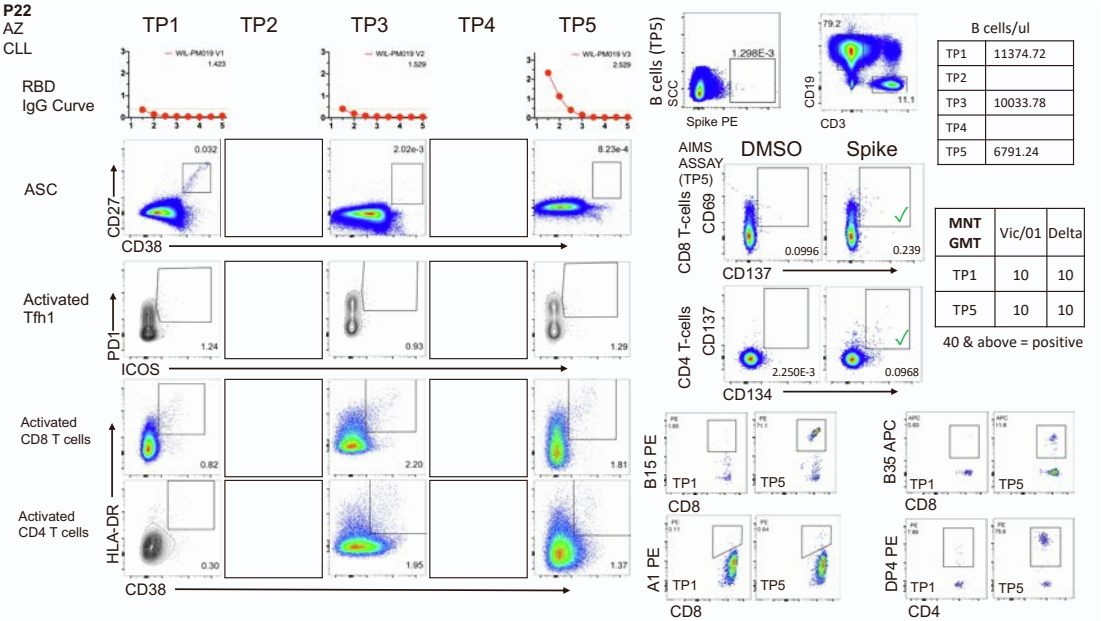

P10
AZ
CAR-T
TP1
TP2
TP3
TP4
TP5
RBD
IgG Curve
ASC
CD27
CD38
Activated
Tfh1
PD1
ICOS
Activated
CD8 T cells
Activated
CD4 T cells
HLA-DR
B cells (TP5)
SCC
Spike PE
CD19
CD3
N/D
B cells/ul
TP1 1.76
TP2
TP3 0.15
TP4
TP5 1.11
AIMS
ASSAY
(TP5)
DMSO
Spike
CD8 T-cells
CD69
CD137
CD4 T-cells
CD134
MNT GMT | Vic/01 | Delta
TP1 | 10 | 10
TP5 | 10 | 10
40 & above = positive
Tetramer
CD8
CD4
P11
AZ WM
Zanubrutinib
B cells/ul
TP1 65.83
TP2
TP3 27.36
TP4
TP5 missed
MNT GMT | Vic/01 | Delta
TP1 | - | -
TP5 | - | -
40 & above = positive
P12
Pfizer
Autograft
B cells/ul
TP1 7.18
TP2
TP3 49.28
TP4
TP5 30.03
MNT GMT | Vic/01 | Delta
TP1 | 10 | 10
TP5 | 10 | 10
40 & above = positive
A2 APC
DP4
Note real A2+tet+ above 10⁴, CMV-specific?


P13
AZ
CLL
RBD IgG Curve
TP1
TP2
TP3
TP4
TP5
ASC
CD27
CD38
Activated Tfh1
PD1
ICOS
Activated CD8 T cells
Activated CD4 T cells
HLA-DR
B cells (TP5)
SCC
Spike PE
CD19
CD3
B cells/ul
TP1 6072.47
TP2
TP3 4577.94
TP4
TP5 5517.42
AIMS ASSAY (TP5)
DMSO
Spike
CD8 T-cells CD69
CD137
CD4 T-cells CD137
CD134
MNT GMT | Vic/01 | Delta
TP1 | 10 | 10
TP5 | 320 | 151
40 & above = positive
Tetramer
CD8
CD4
N/D
P14
AZ CLL
Zanubrutinib
P15
AZ
Autograft
A24 APC
B35 PE
DP4 PE


P16
AZ
Autograft
TP1
TP2
TP3
TP4
TP5
RBD
IgG Curve
ASC
CD27
CD38
Activated
Tfh1
PD1
ICOS
Activated
CD8 T cells
Activated
CD4 T cells
HLA-DR
CD38
B cells (TP5)
SCC
N/D
Spike PE
CD19
CD3
B cells/ul
TP1 284.54
TP2
TP3 267.21
TP4
TP5 275.54
AIMS
ASSAY
(TP5)
DMSO
Spike
CD8 T-cells
CD69
CD137
0.0402
0.0993
CD4 T-cells
CD137
CD134
0.191
0.414
MNT GMT | Vic/01 | Delta
TP1 | 10 | 10
TP5 | 28 | 10
40 & above = positive
Tetramer
TP1
TP5
CD8
CD4
P17
AZ WM
Zanubrutinib
0.415
1.25
77.3
0.118
0.0881
0.0109
0.0191
B cells/ul
TP1 14.24
TP2
TP3 19.01
TP4
TP5 16.89
MNT GMT | Vic/01 | Delta
TP1 | 10 | 10
TP5 | 40 | 10
40 & above = positive
A2 PE
A3 APC
P18
AZ CLL
Zanubrutinib
0.46
74.2
B cells/ul
TP1 3.69
TP2
TP3 9.81
TP4
TP5 10.02
MNT GMT | Vic/01 | Delta
TP1 | 10 | 10
TP5 | 10 | 10
40 & above = positive


P19
AZ CLL
Zanubrutinib
TP1 TP2 TP3 TP4 TP5
RBD IgG Curve
ASC
CD27
CD38
Activated Tfh1
PD1
ICOS
Activated CD8 T cells
Activated CD4 T cells
HLA-DR
CD38
B cells (TP5)
SCC
Spike PE
CD19
CD3
N/D
AIMS ASSAY (TP5)
DMSO
Spike
CD8 T-cells CD69
CD137
CD4 T-cells CD137
CD134
Tetramer
CD8
CD4
B cells/ul
TP1 3.47
TP2
TP3 62.92
TP4
TP5 missed
MNT GMT | Vic/01 | Delta
TP1 - -
TP5 - -
40 & above = positive
P20
AZ
Myeloma PI
TP1 TP2 TP3 TP4 TP5
RBD IgG Curve
ASC
Activated Tfh1
Activated CD8 T cells
Activated CD4 T cells
CD38
B cells (TP5)
SCC
Spike PE
CD19
CD3
2.564
AIMS ASSAY (TP5)
DMSO
Spike
CD8 T-cells CD69
CD137
0.189
0.207
CD4 T-cells CD137
CD134
0.0394
0.0270
B cells/ul
TP1 11.23
TP2
TP3
TP4
TP5 1.45
MNT GMT | Vic/01 | Delta
TP1 10 10
TP5 10 10
40 & above = positive
A1 APC
DP4 PE
CD8
CD4
P21
Pfizer WM
Zanubrutinib
TP1 TP2 TP3 TP4 TP5
RBD IgG Curve
ASC
Activated Tfh1
Activated CD8 T cells
Activated CD4 T cells
CD38
B cells (TP5)
SCC
Spike PE
CD19
CD3
AIMS ASSAY (TP5)
DMSO
Spike
CD8 T-cells CD69
CD137
0.213
0.222
CD4 T-cells CD137
CD134
2.320E-3
0.0174
B cells/ul
TP1 136.75
TP2
TP3 179.86
TP4
TP5 101.27
MNT GMT | Vic/01 | Delta
TP1 10 10
TP5 10 10
40 & above = positive
A3 APC
DP4
CD8
CD4

P22
AZ
CLL



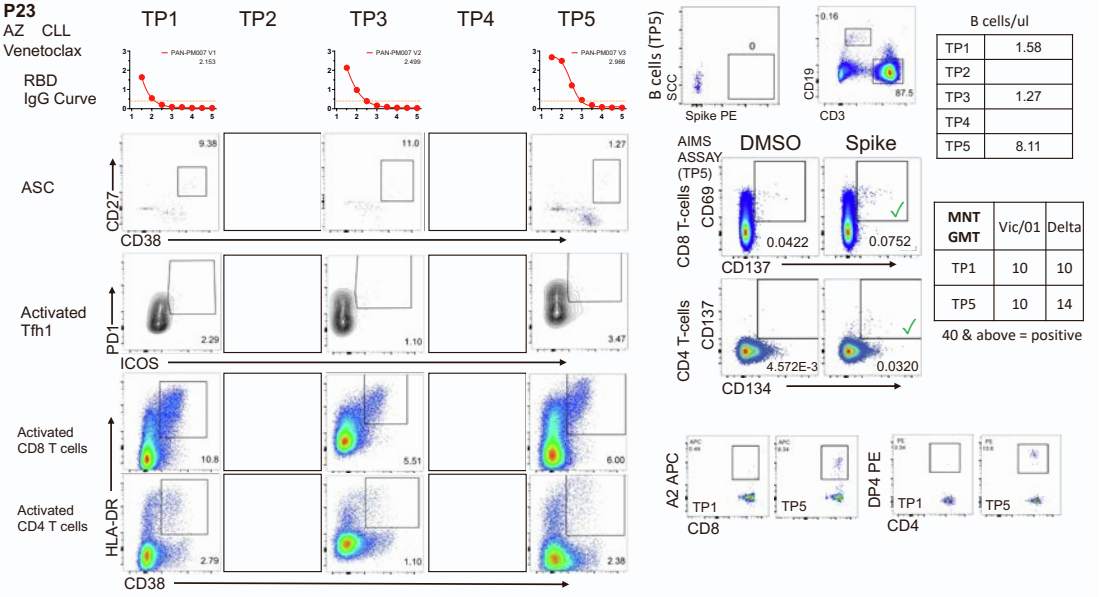
B cells/ul

TP1	11374.72
TP2	
TP3	10033.78
TP4	
TP5	6791.24

MNT GMT	Vic/01	Delta
TP1	10	10
TP5	10	10

40 & above = positive

P23
AZ CLL
Venetoclax



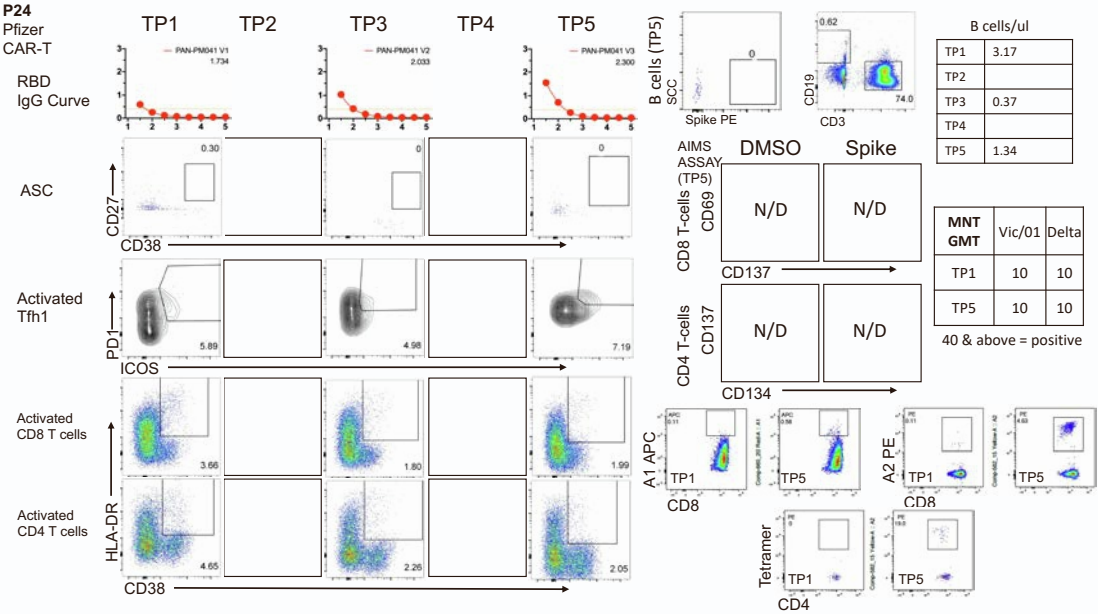
B cells/ul

TP1	1.58
TP2	
TP3	1.27
TP4	
TP5	8.11

MNT GMT	Vic/01	Delta
TP1	10	10
TP5	10	14

40 & above = positive

P24
Pfizer
CAR-T

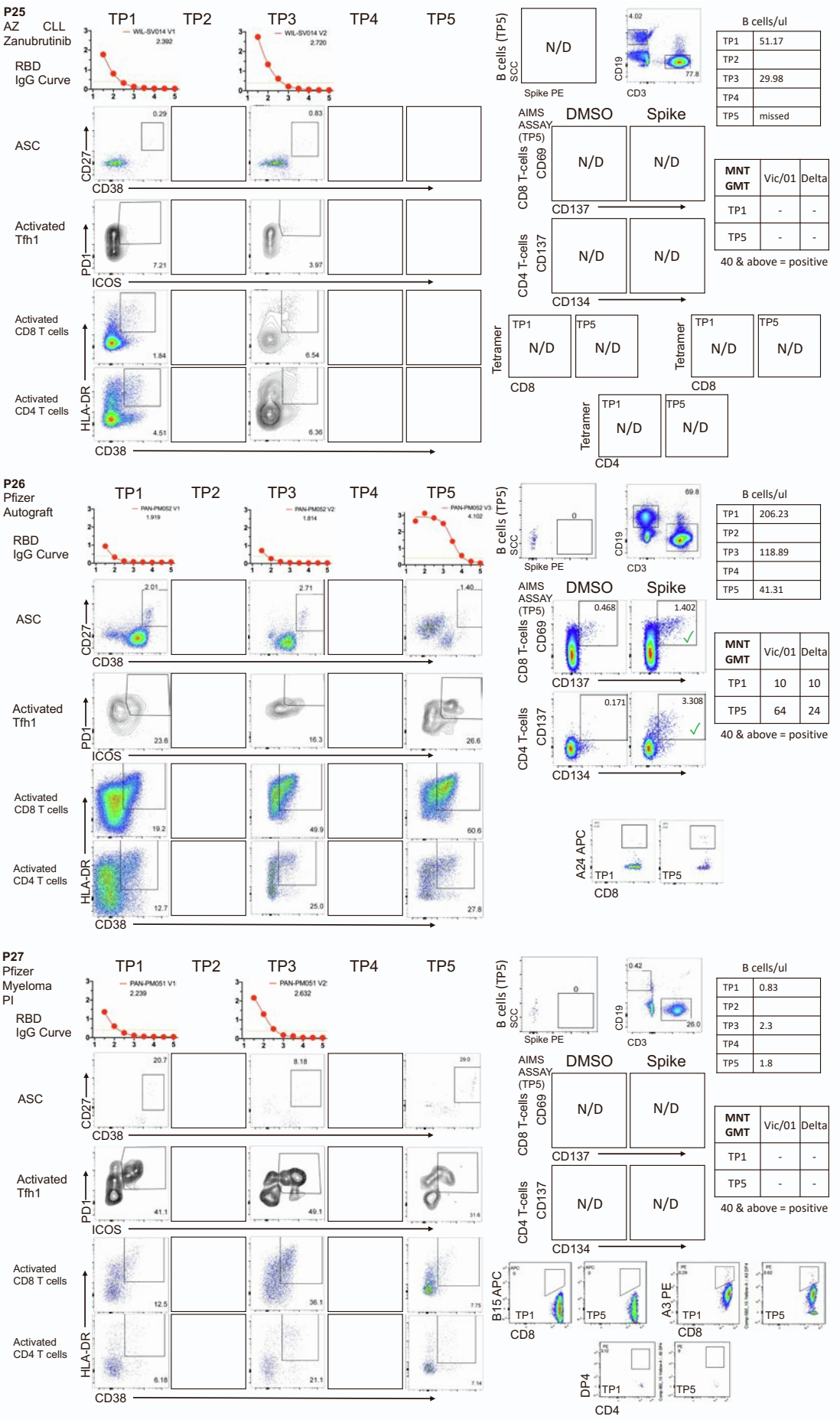


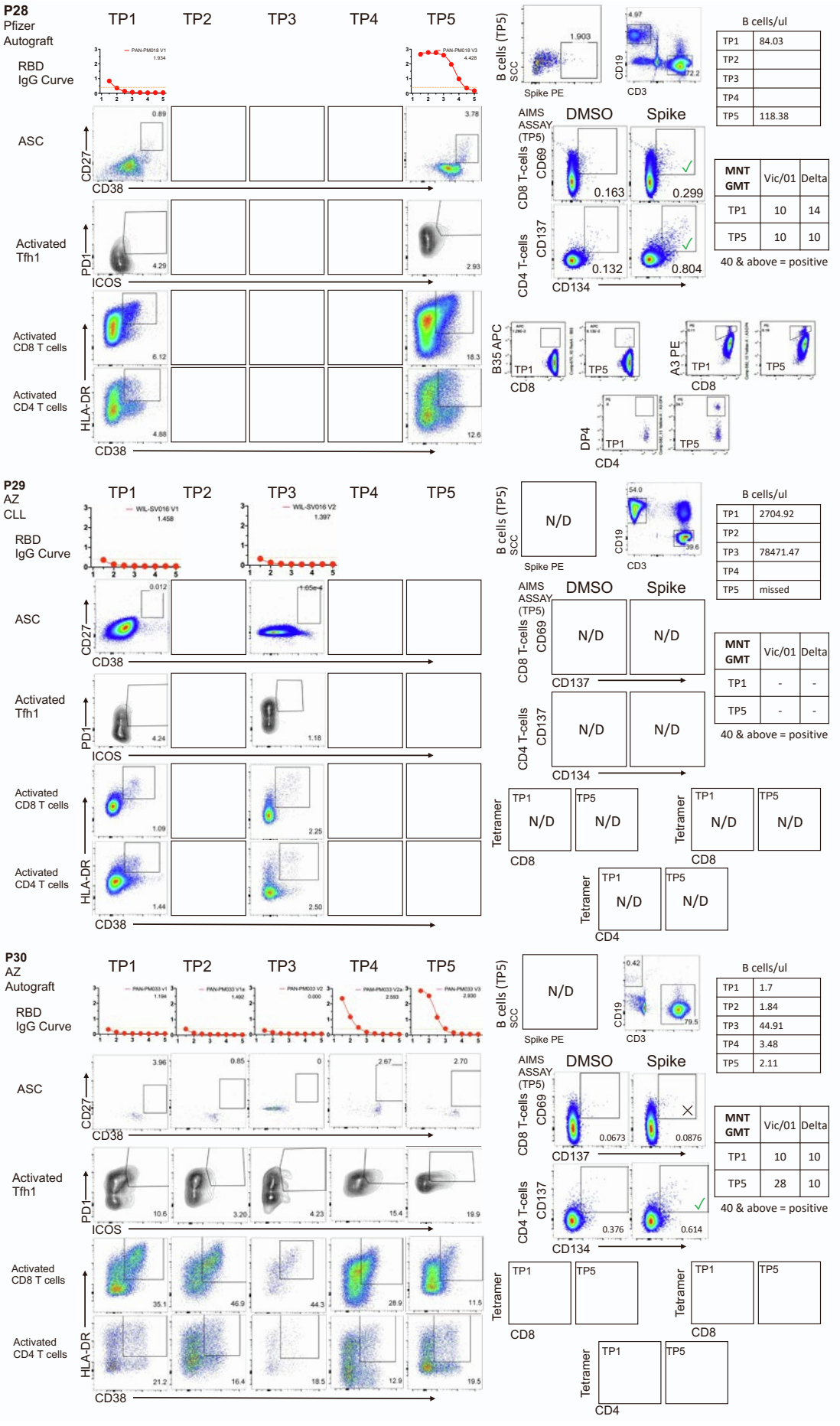
B cells/ul

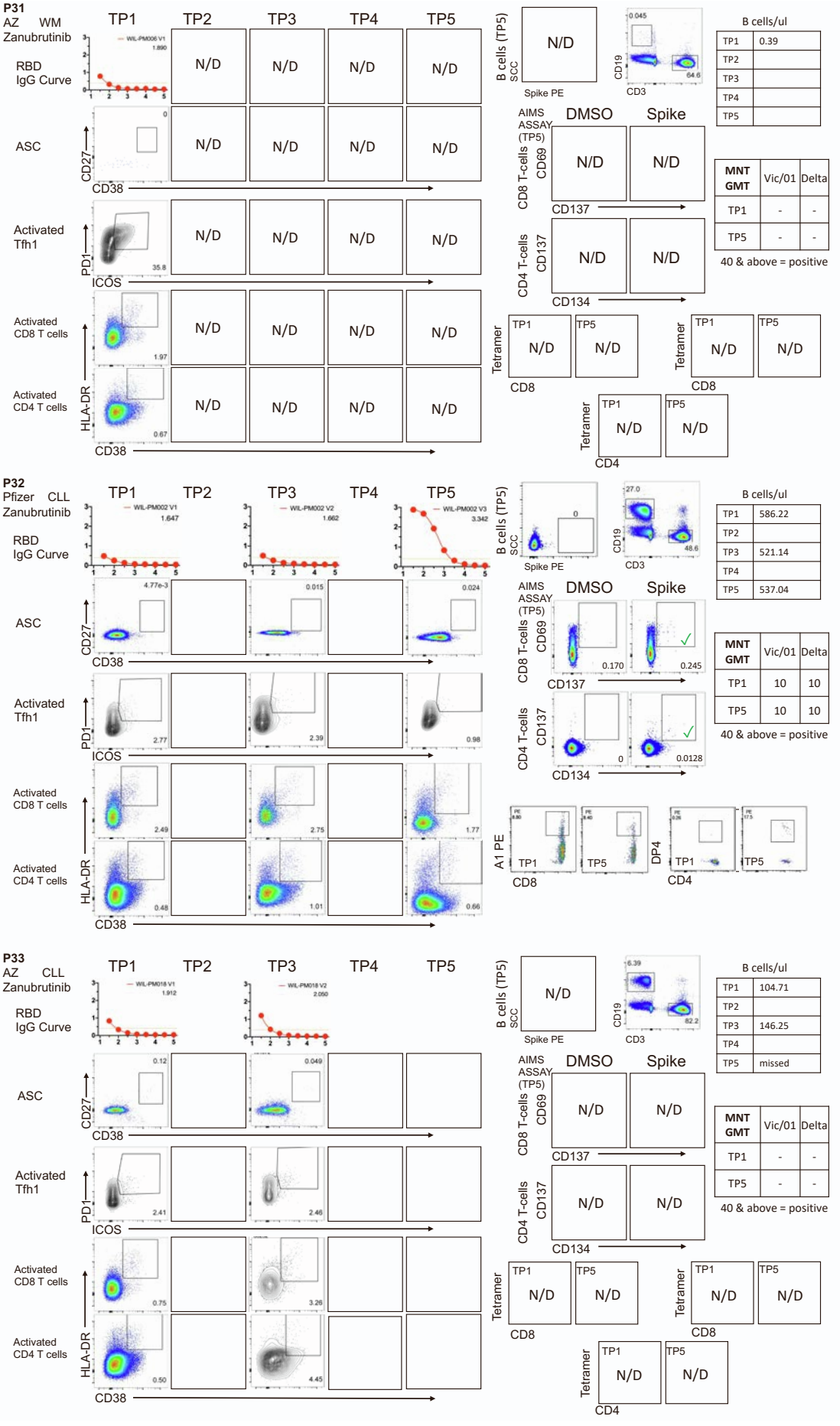
TP1	3.17
TP2	
TP3	0.37
TP4	
TP5	1.34

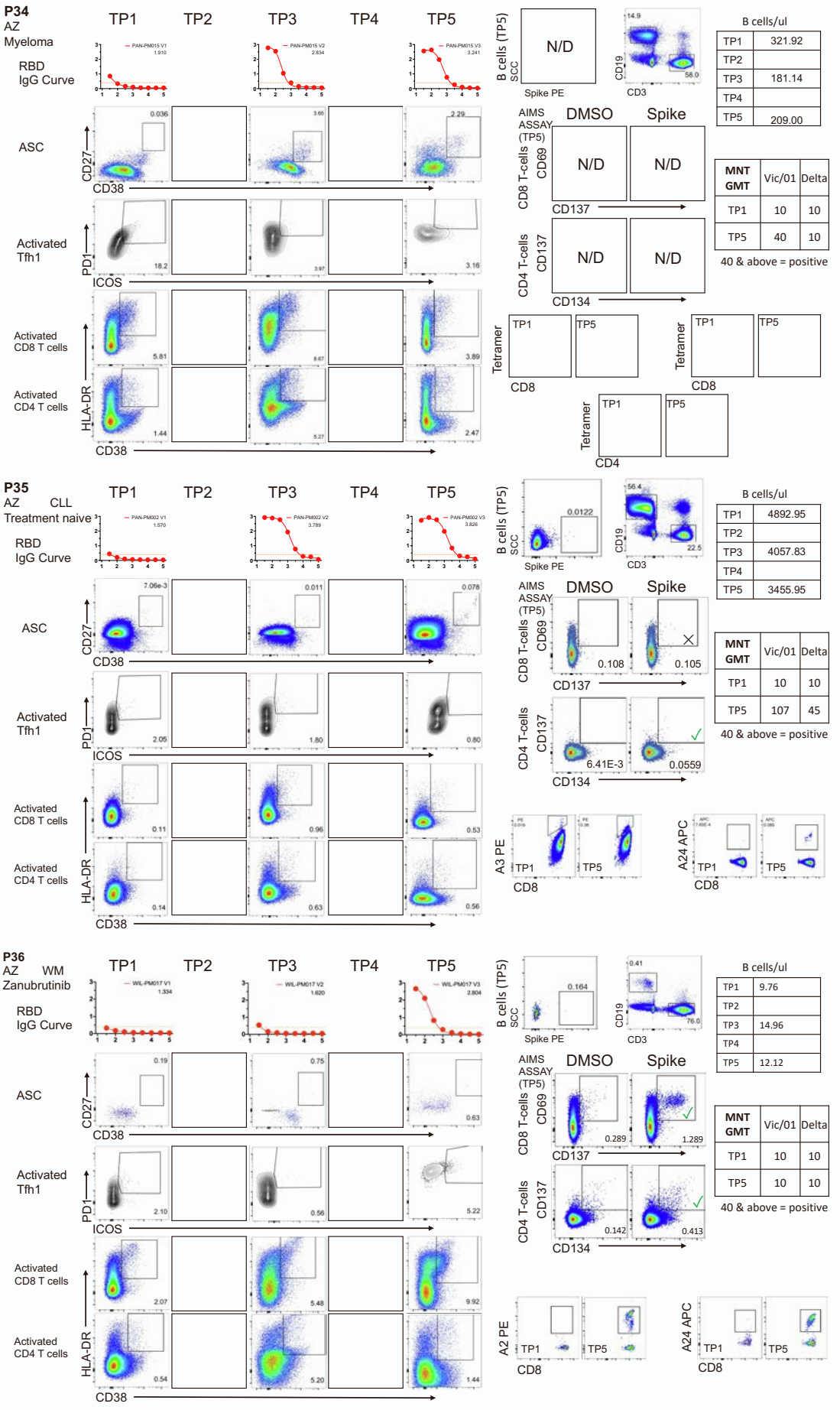
MNT GMT	Vic/01	Delta
TP1	10	10
TP5	10	10

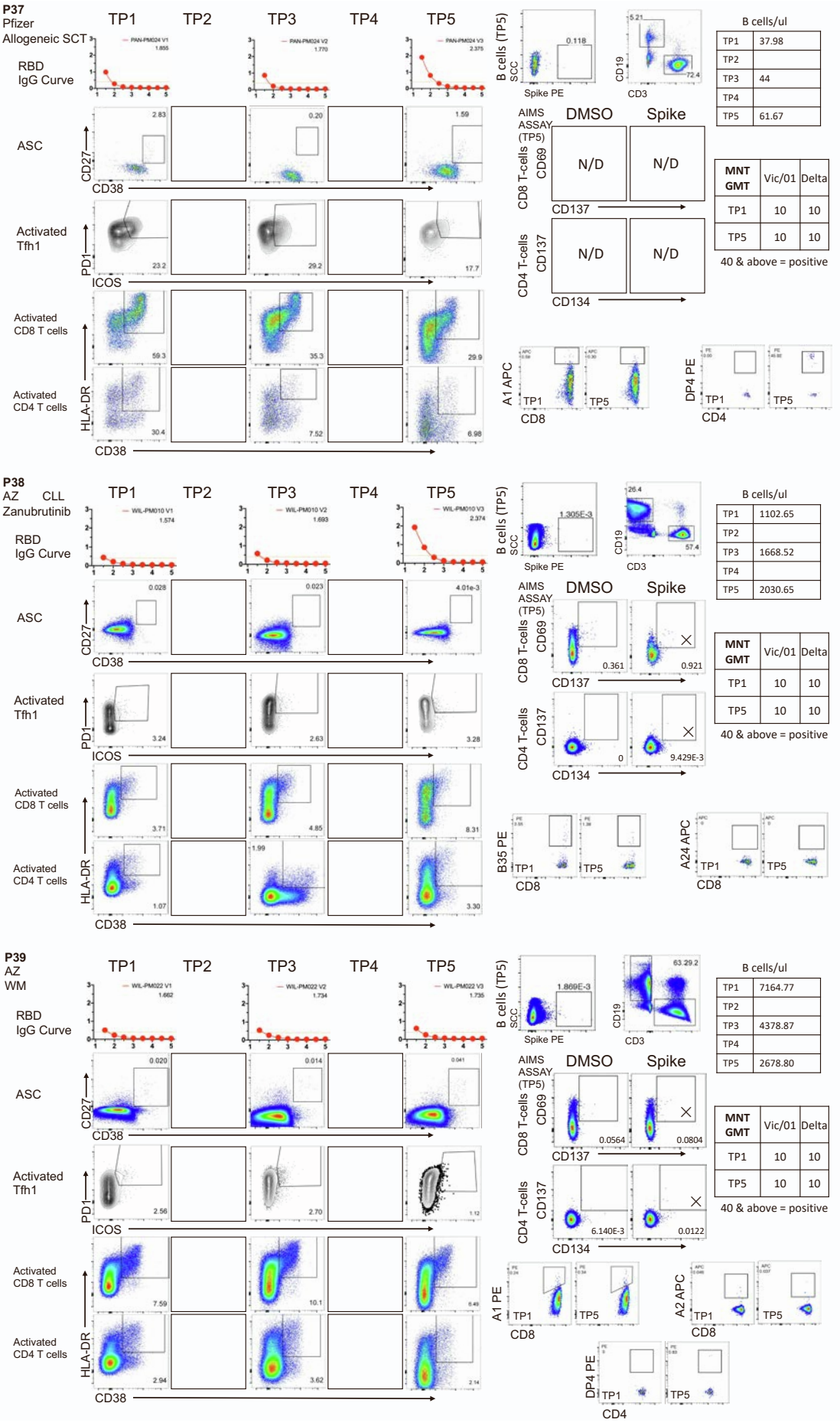
40 & above = positive

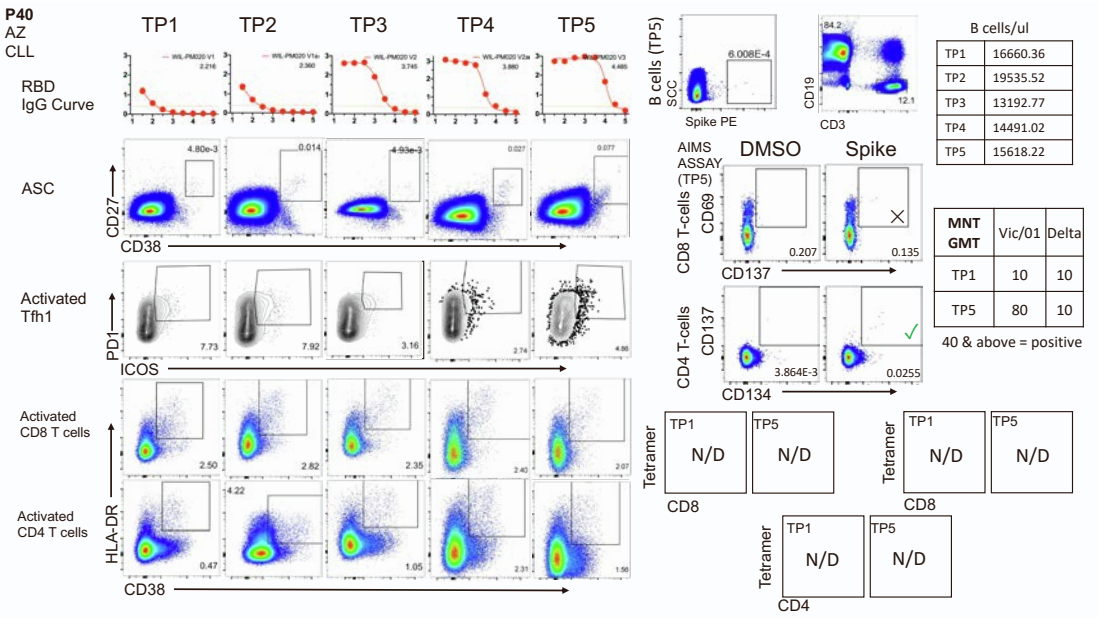

P25
AZ CLL
Zanubrutinib
RBD IgG Curve
ASC
Activated Tfh1
Activated CD8 T cells
Activated CD4 T cells
TP1 TP2 TP3 TP4 TP5
CD27
CD38
PD1
ICOS
HLA-DR
B cells (TP5)
SCC
Spike PE
CD19
CD3
N/D
B cells/ul
TP1 51.17
TP2
TP3 29.98
TP4
TP5 missed
AIMS ASSAY (TP5)
DMSO
Spike
CD8 T-cells CD69
CD137
CD4 T-cells CD137
CD134
MNT GMT | Vic/01 | Delta
TP1 - -
TP5 - -
40 & above = positive
Tetramer
CD8
CD4
P26
Pfizer
Autograft
RBD IgG Curve
ASC
Activated Tfh1
Activated CD8 T cells
Activated CD4 T cells
B cells/ul
TP1 206.23
TP2
TP3 118.89
TP4
TP5 41.31
0.468
1.402
0.171
3.308
MNT GMT | Vic/01 | Delta
TP1 10 10
TP5 64 24
40 & above = positive
A24 APC
P27
Pfizer
Myeloma
PI
RBD IgG Curve
ASC
Activated Tfh1
Activated CD8 T cells
Activated CD4 T cells
B cells/ul
TP1 0.83
TP2
TP3 2.3
TP4
TP5 1.8
MNT GMT | Vic/01 | Delta
TP1 - -
TP5 - -
40 & above = positive
B15 APC
A3 PE
DP4


P28
Pfizer
Autograft
TP1
TP2
TP3
TP4
TP5
RBD
IgG Curve
ASC
CD27
CD38
Activated
Tfh1
PD1
ICOS
Activated
CD8 T cells
Activated
CD4 T cells
HLA-DR
CD38
B cells (TP5)
SCC
Spike PE
CD19
CD3
B cells/ul
TP1 84.03
TP2
TP3
TP4
TP5 118.38
AIMS
ASSAY
(TP5)
DMSO
Spike
CD8 T-cells
CD69
CD4 T-cells
CD137
CD134
MNT GMT Vic/01 Delta
TP1 10 14
TP5 10 10
40 & above = positive
B35 APC
A3 PE
CD8
DP4
CD4
P29
AZ
CLL
N/D
P30
AZ
Autograft
Tetramer


P31
AZ WM
Zanubrutinib
TP1 TP2 TP3 TP4 TP5
RBD IgG Curve
ASC
Activated Tfh1
Activated CD8 T cells
Activated CD4 T cells
CD27
CD38
PD1
ICOS
HLA-DR
N/D
B cells (TP5)
SCC
Spike PE
CD19
CD3
AIMS ASSAY (TP5)
DMSO
Spike
CD8 T-cells CD69
CD137
CD4 T-cells CD137
CD134
Tetramer
CD8
CD4
B cells/ul
TP1 0.39
TP2
TP3
TP4
TP5
MNT GMT | Vic/01 | Delta
TP1 - -
TP5 - -
40 & above = positive
P32
Pfizer CLL
Zanubrutinib
WIL-PM002 V1 1.647
WIL-PM002 V2 1.662
WIL-PM002 V3 3.342
TP1 586.22
TP2
TP3 521.14
TP4
TP5 537.04
TP1 10 10
TP5 10 10
A1 PE
DP4
P33
AZ CLL
Zanubrutinib
WIL-PM018 V1 1.912
WIL-PM018 V2 2.050
TP1 104.71
TP2
TP3 146.25
TP4
TP5 missed


P34
AZ
Myeloma
TP1
TP2
TP3
TP4
TP5
RBD
IgG Curve
ASC
CD27
CD38
Activated
Tfh1
PD1
ICOS
Activated
CD8 T cells
Activated
CD4 T cells
HLA-DR
B cells (TP5)
SCC
Spike PE
CD19
CD3
N/D
AIMS
ASSAY
(TP5)
DMSO
Spike
CD8 T-cells
CD69
CD137
CD4 T-cells
CD134
Tetramer
CD8
CD4
B cells/ul
TP1 321.92
TP2
TP3 181.14
TP4
TP5 209.00
MNT GMT | Vic/01 | Delta
TP1 | 10 | 10
TP5 | 40 | 10
40 & above = positive
P35
AZ CLL
Treatment naive
B cells/ul
TP1 4892.95
TP2
TP3 4057.83
TP4
TP5 3455.95
MNT GMT | Vic/01 | Delta
TP1 | 10 | 10
TP5 | 107 | 45
40 & above = positive
A3 PE
A24 APC
P36
AZ WM
Zanubrutinib
B cells/ul
TP1 9.76
TP2
TP3 14.96
TP4
TP5 12.12
MNT GMT | Vic/01 | Delta
TP1 | 10 | 10
TP5 | 10 | 10
40 & above = positive
A2 PE
A24 APC

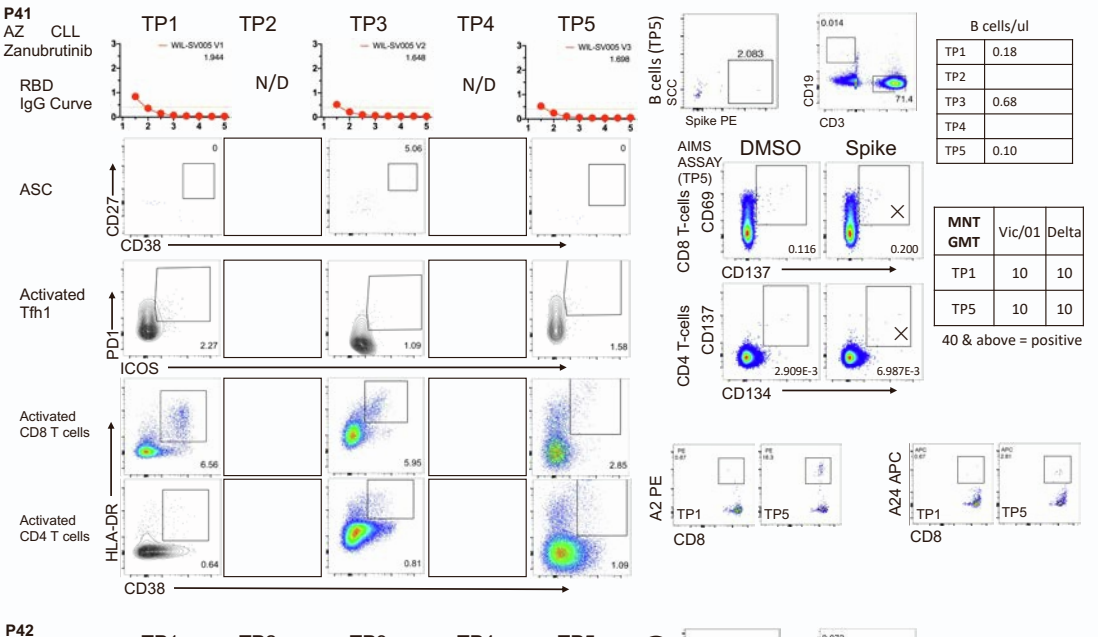

P37
Pfizer
Allogeneic SCT
TP1
TP2
TP3
TP4
TP5
RBD
IgG Curve
ASC
CD27
CD38
Activated
Tfh1
PD1
ICOS
Activated
CD8 T cells
Activated
CD4 T cells
HLA-DR
CD38
B cells (TP5)
SCC
Spike PE
CD19
CD3
AIMS
ASSAY
(TP5)
DMSO
Spike
CD8 T-cells
CD69
CD137
N/D
CD4 T-cells
CD134
A1 APC
CD8
DP4 PE
CD4
B cells/ul
TP1 37.98
TP2
TP3 44
TP4
TP5 61.67
MNT GMT | Vic/01 | Delta
TP1 | 10 | 10
TP5 | 10 | 10
40 & above = positive
P38
AZ CLL
Zanubrutinib
B35 PE
A24 APC
B cells/ul
TP1 1102.65
TP2
TP3 1668.52
TP4
TP5 2030.65
P39
AZ
WM
A1 PE
A2 APC
B cells/ul
TP1 7164.77
TP2
TP3 4378.87
TP4
TP5 2678.80



B cells/ul	
TP1	16660.36
TP2	19535.52
TP3	13192.77
TP4	14491.02
TP5	15618.22

MNT GMT	Vic/01	Delta
TP1	10	10
TP5	80	10

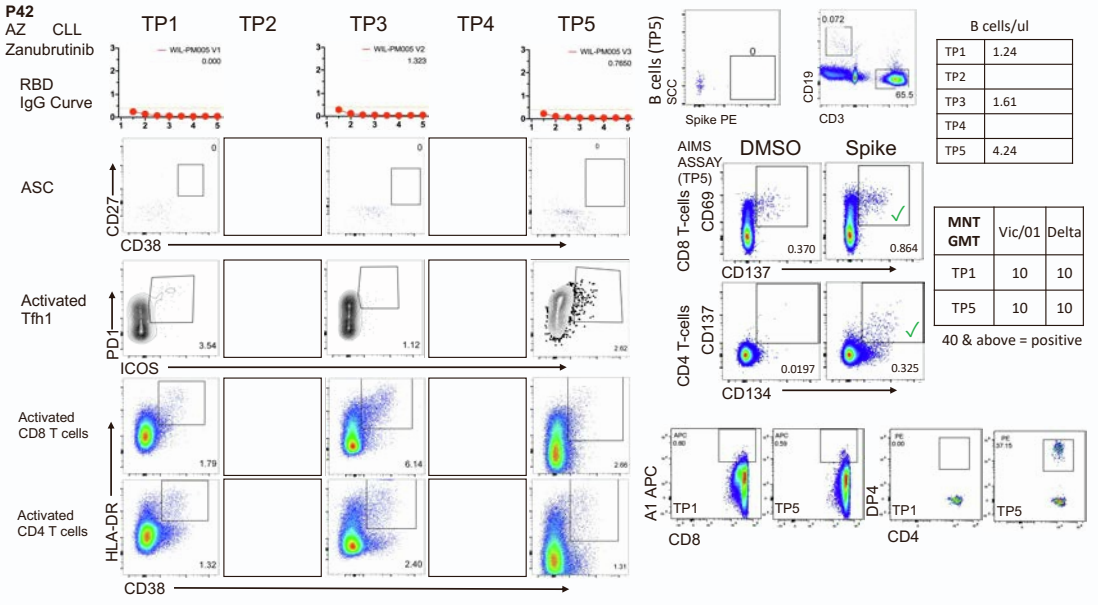
40 & above = positive



B cells/ul	
TP1	0.18
TP2	
TP3	0.68
TP4	
TP5	0.10

MNT GMT	Vic/01	Delta
TP1	10	10
TP5	10	10

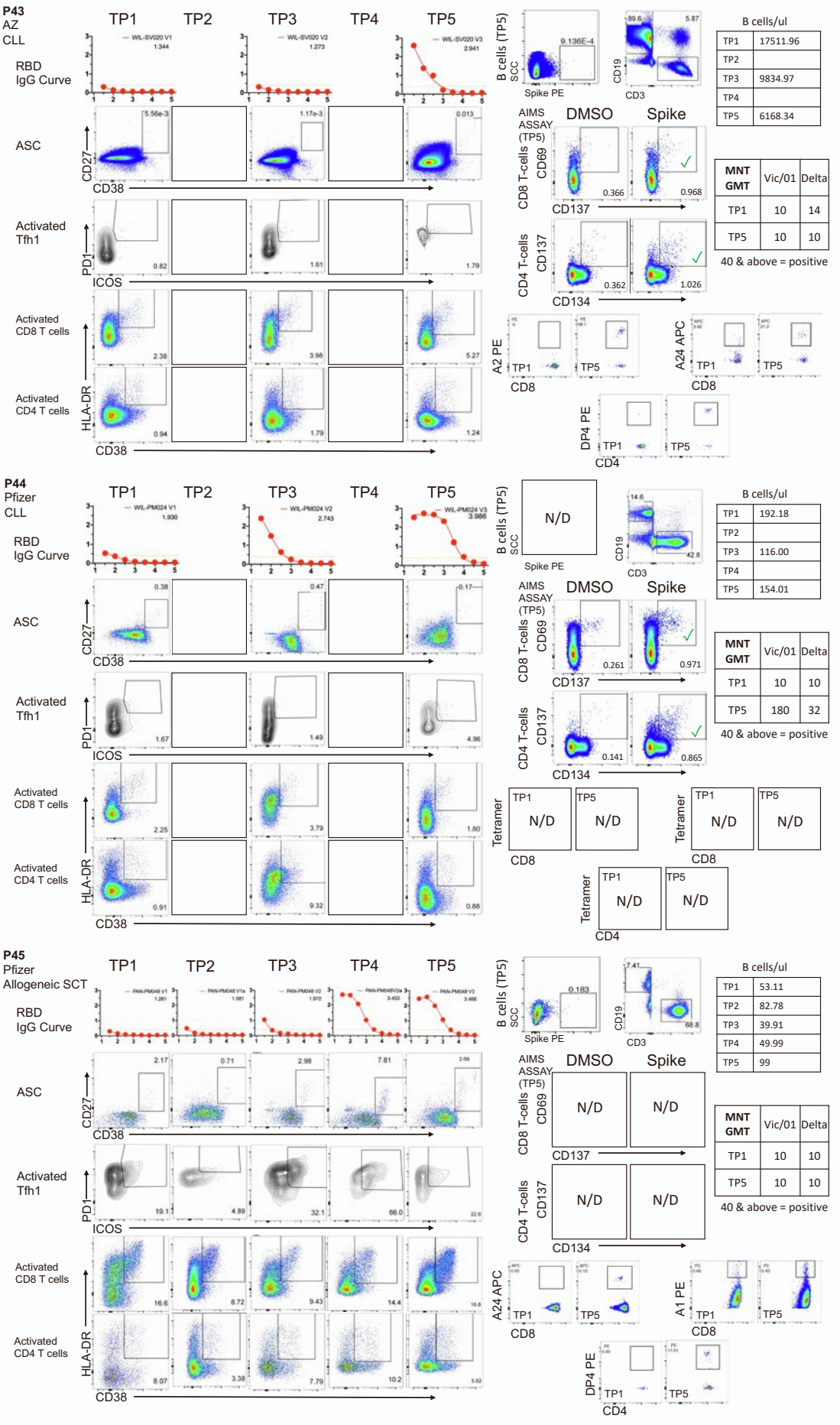
40 & above = positive

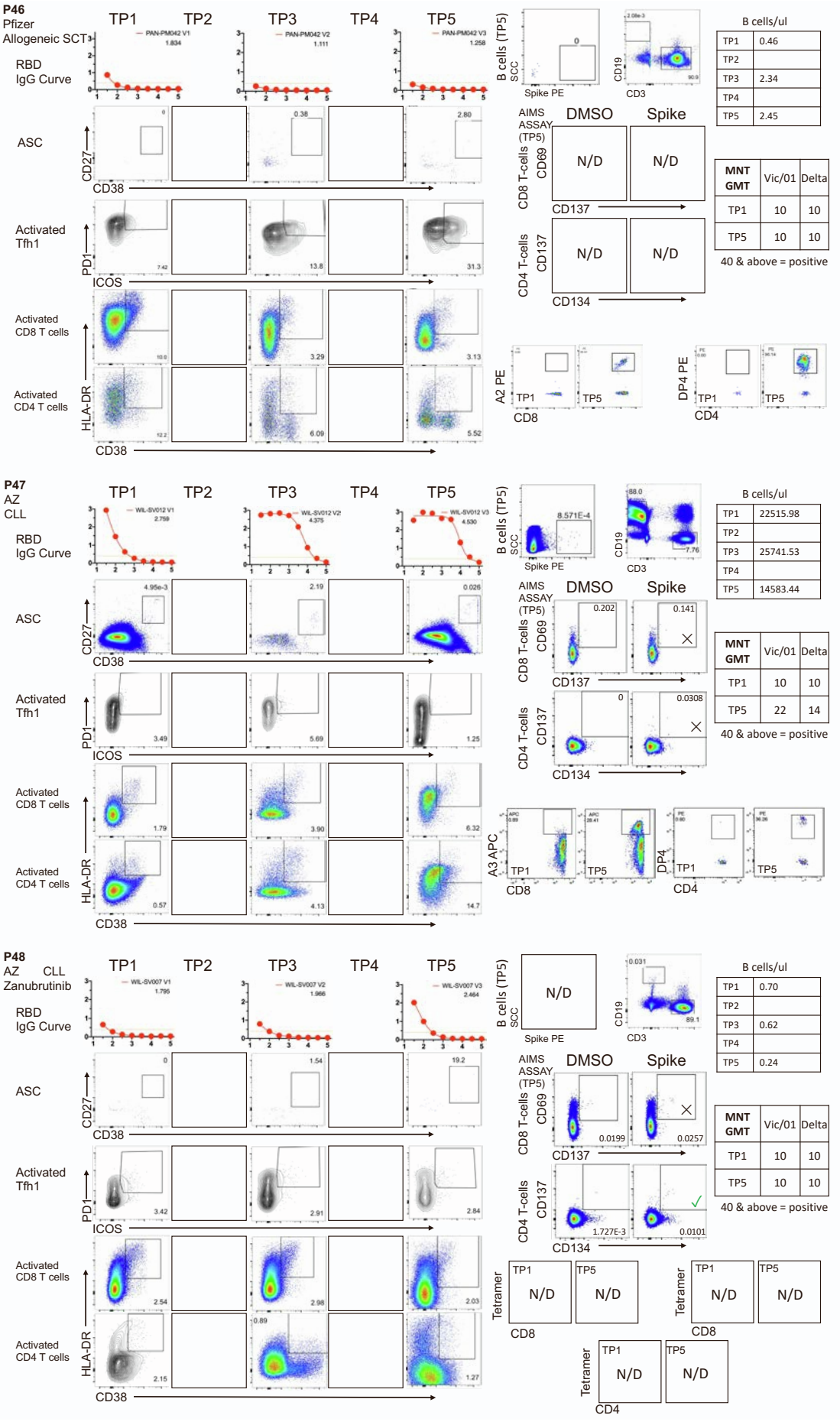


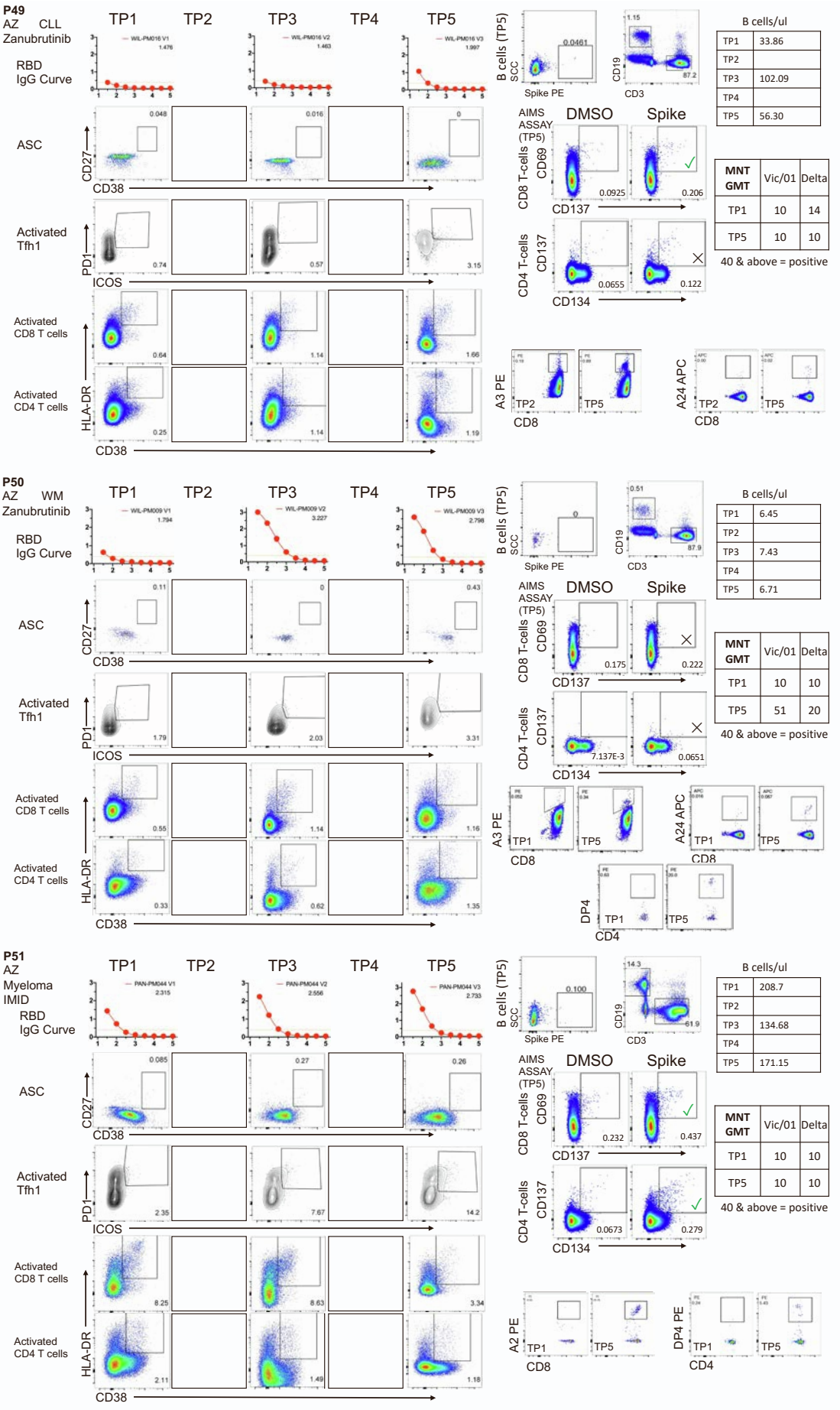
B cells/ul	
TP1	1.24
TP2	
TP3	1.61
TP4	
TP5	4.24

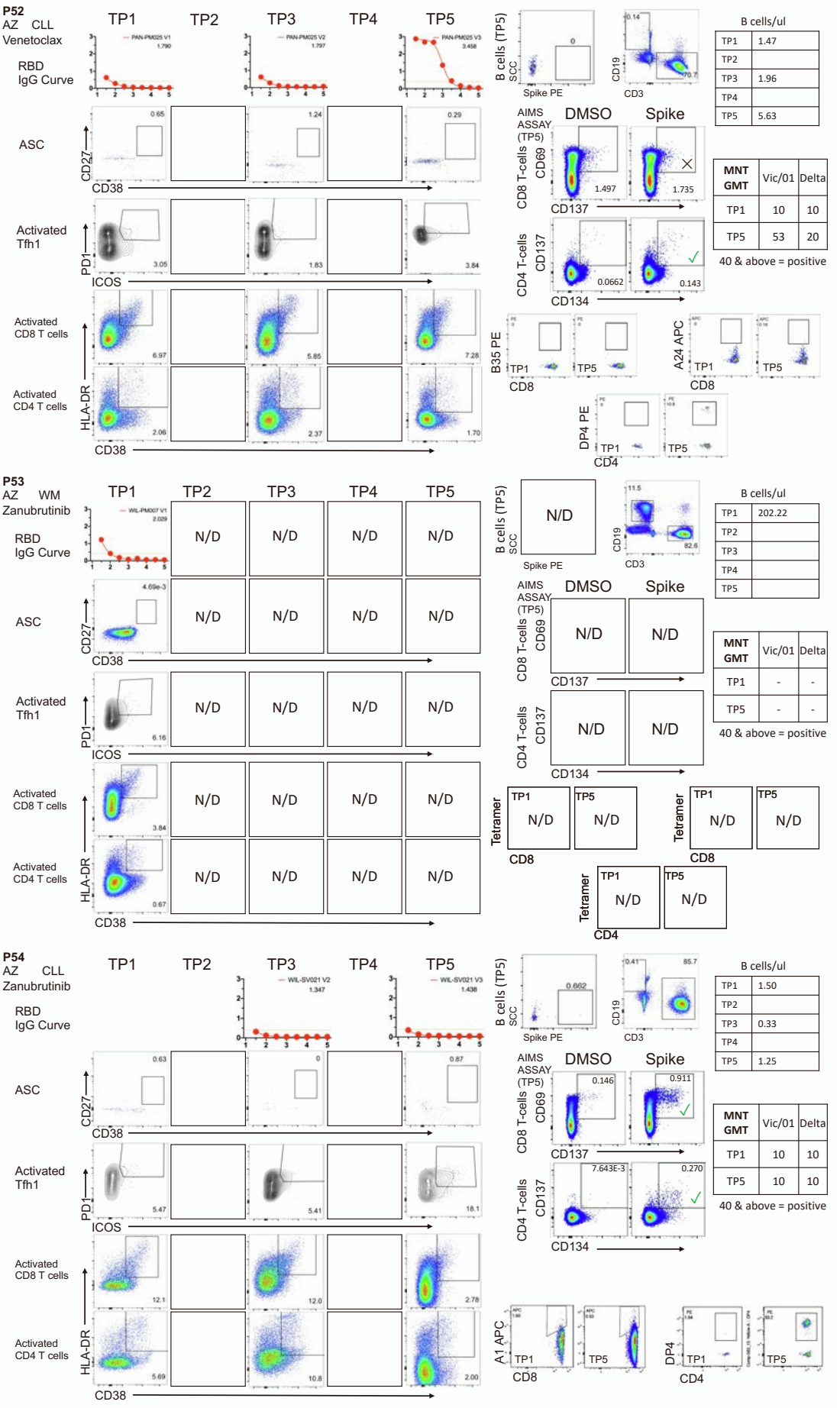
MNT GMT	Vic/01	Delta
TP1	10	10
TP5	10	10

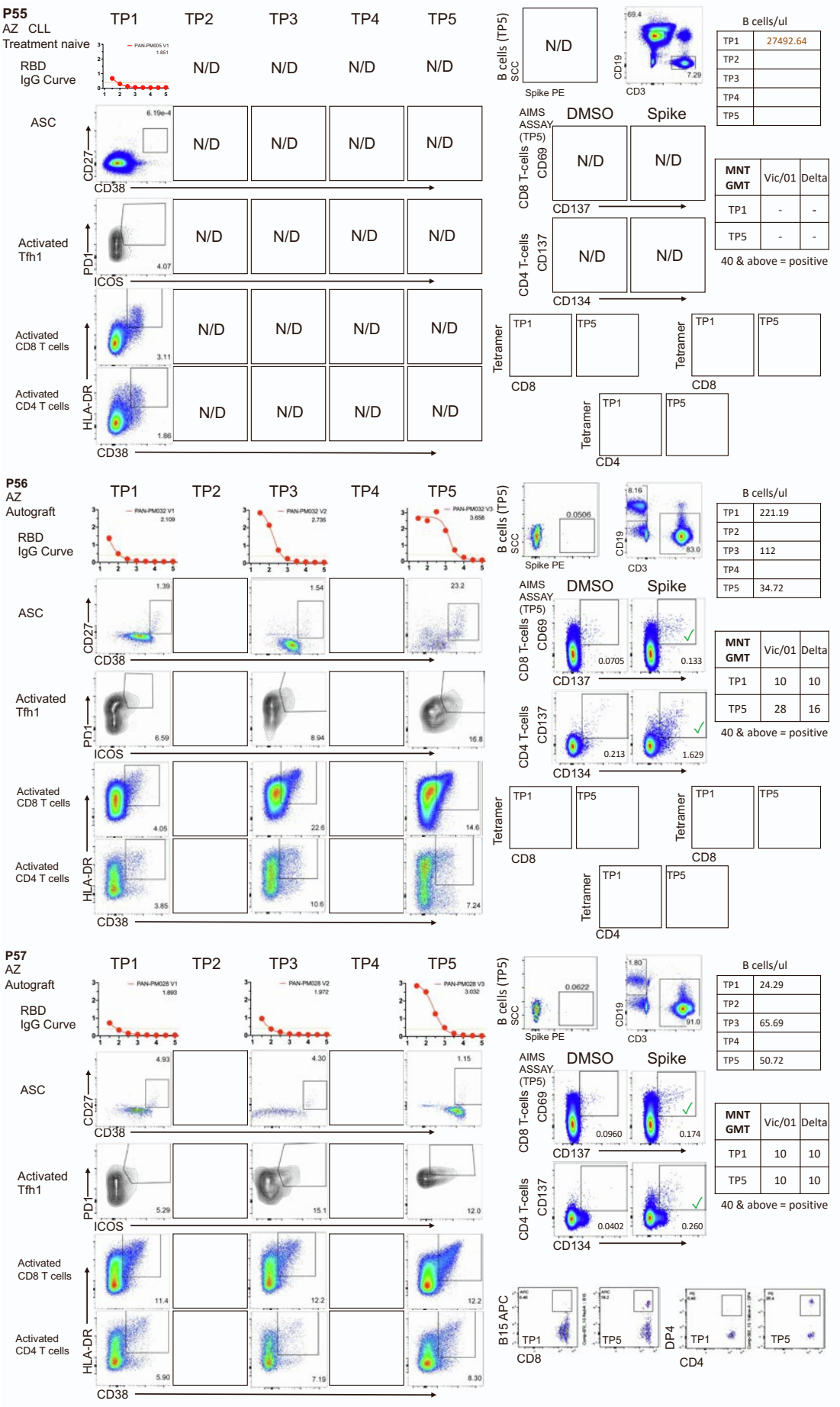
40 & above = positive

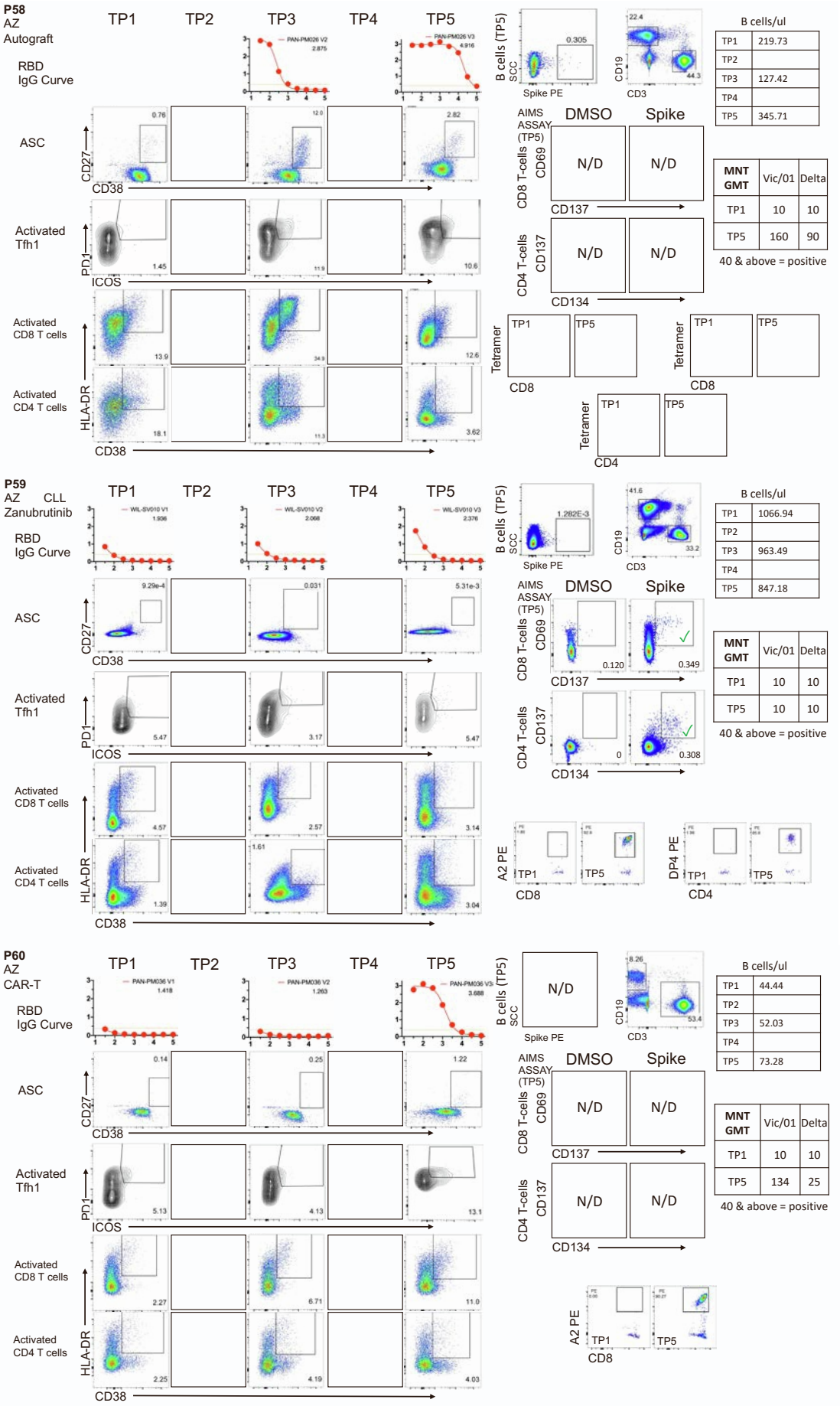

P43
AZ
CLL
RBD IgG Curve
ASC
Activated Tfh1
Activated CD8 T cells
Activated CD4 T cells
TP1
TP2
TP3
TP4
TP5
CD27
CD38
PD1
ICOS
HLA-DR
B cells (TP5)
SCC
Spike PE
CD19
CD3
AIMS ASSAY (TP5)
DMSO
Spike
CD8 T-cells CD69
CD137
CD4 T-cells CD137
CD134
A2 PE
A24 APC
CD8
DP4 PE
CD4
B cells/ul
TP1 17511.96
TP2
TP3 9834.97
TP4
TP5 6168.34
MNT GMT | Vic/01 | Delta
TP1 | 10 | 14
TP5 | 10 | 10
40 & above = positive
P44
Pfizer
CLL
TP1 192.18
TP2
TP3 116.00
TP4
TP5 154.01
N/D
Tetramer
MNT GMT | Vic/01 | Delta
TP1 | 10 | 10
TP5 | 180 | 32
40 & above = positive
P45
Pfizer
Allogeneic SCT
TP1 53.11
TP2 82.78
TP3 39.91
TP4 49.99
TP5 99
A1 PE
MNT GMT | Vic/01 | Delta
TP1 | 10 | 10
TP5 | 10 | 10
40 & above = positive

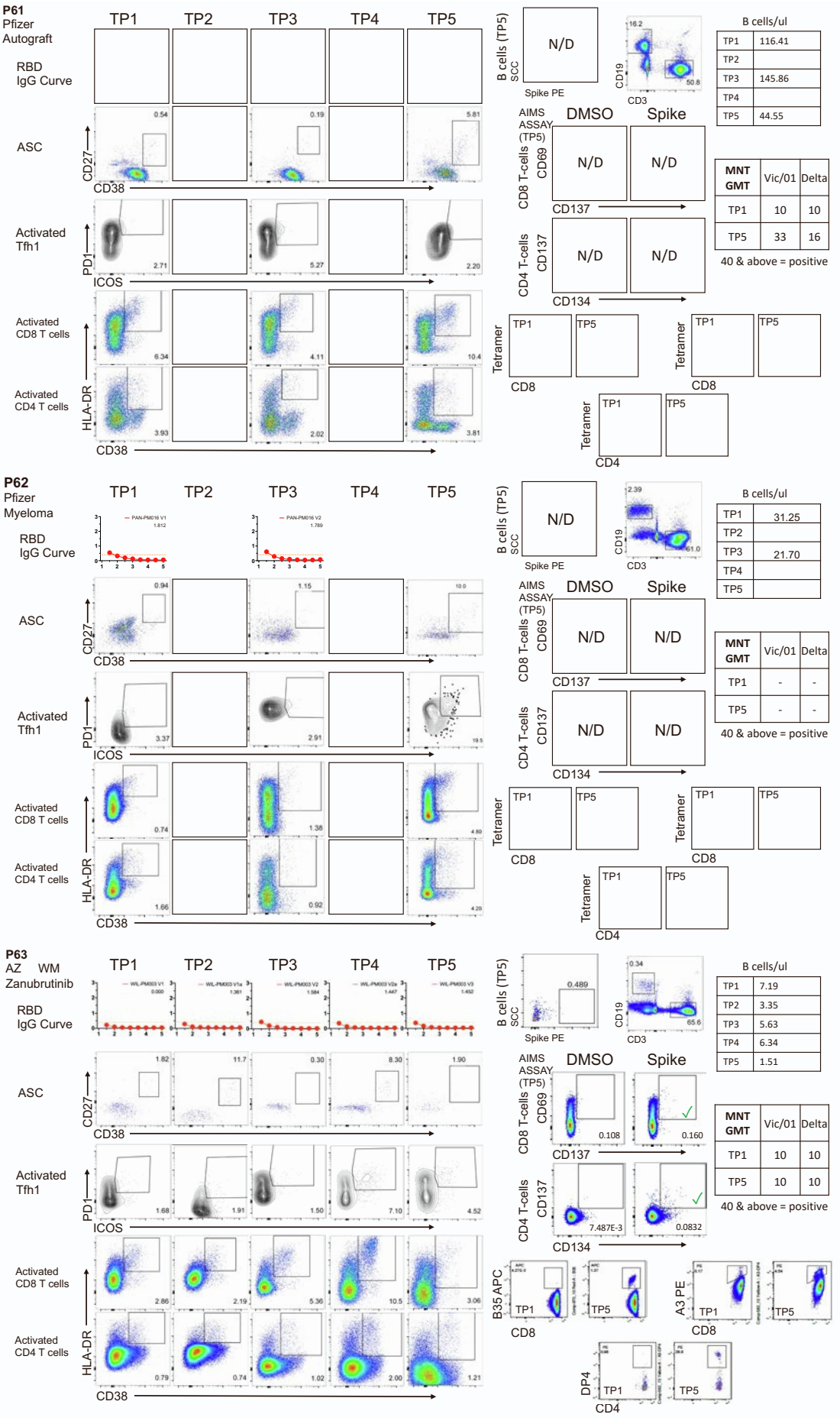

P46
Pfizer
Allogeneic SCT
TP1
TP2
TP3
TP4
TP5
RBD
IgG Curve
ASC
CD27
CD38
Activated
Tfh1
PD1
ICOS
Activated
CD8 T cells
Activated
CD4 T cells
HLA-DR
CD38
B cells (TP5)
SCC
Spike PE
CD19
CD3
AIMS
ASSAY
(TP5)
DMSO
Spike
CD8 T-cells
CD69
CD137
N/D
CD4 T-cells
CD134
B cells/ul
TP1 0.46
TP2
TP3 2.34
TP4
TP5 2.45
MNT GMT
Vic/01
Delta
TP1 10 10
TP5 10 10
40 & above = positive
A2 PE
CD8
DP4 PE
CD4
P47
AZ
CLL
0.571E-4
0.202
0.141
0.0308
TP1 22515.98
TP3 25741.53
TP5 14583.44
TP1 10 10
TP5 22 14
A3 APC
P48
AZ CLL
Zanubrutinib
TP1 0.70
TP3 0.62
TP5 0.24
0.0199
0.0257
1.727E-3
0.0101
Tetramer

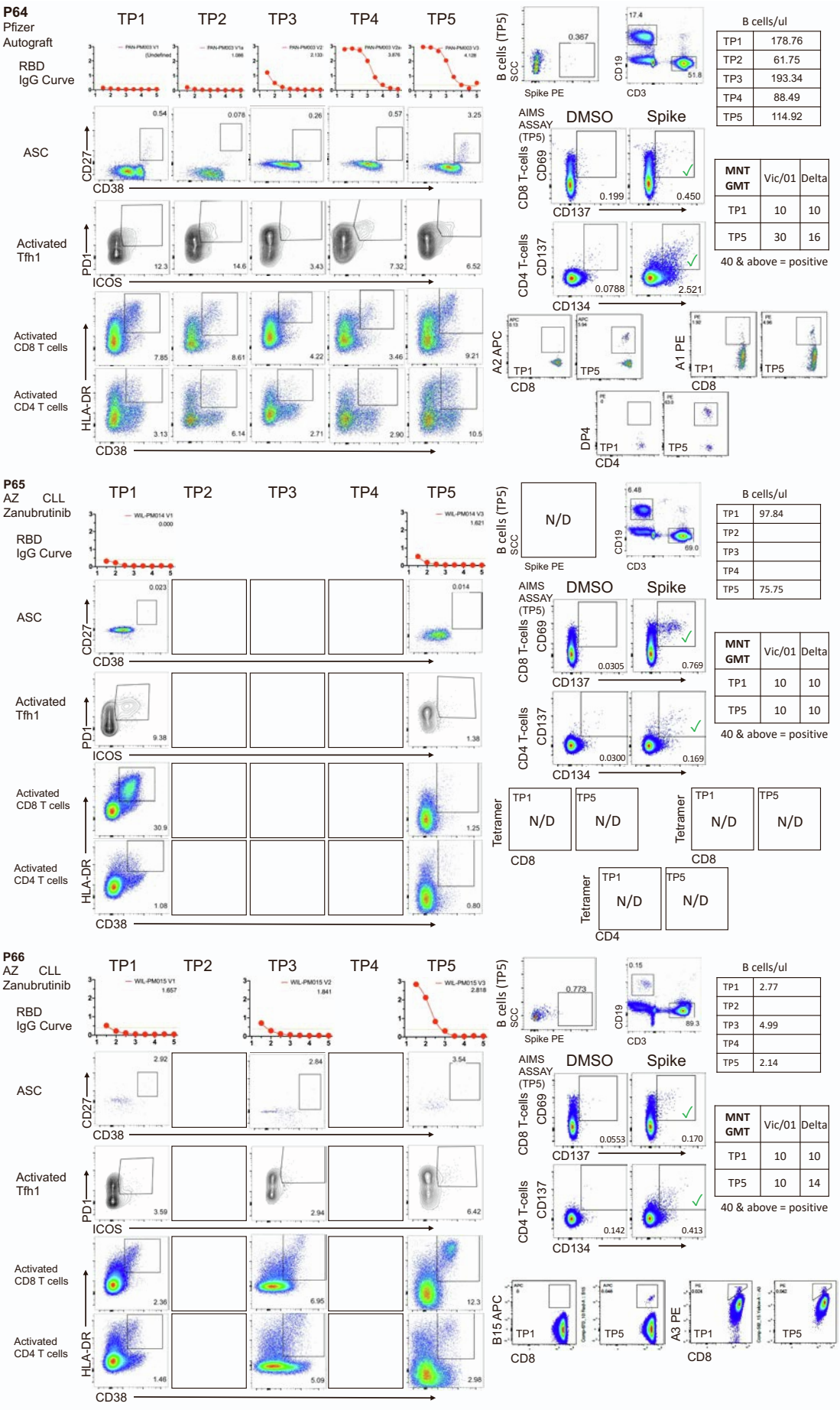

P49
AZ CLL
Zanubrutinib
TP1 TP2 TP3 TP4 TP5
RBD IgG Curve
ASC
CD27
CD38
Activated Tfh1
PD1
ICOS
Activated CD8 T cells
Activated CD4 T cells
HLA-DR
CD38
B cells (TP5)
SCC
Spike PE
CD19
CD3
AIMS ASSAY (TP5)
DMSO
Spike
CD8 T-cells
CD69
CD137
CD4 T-cells
CD137
CD134
A3 PE
A24 APC
CD8
TP2
TP5
B cells/ul
TP1 33.86
TP2
TP3 102.09
TP4
TP5 56.30
MNT GMT | Vic/01 | Delta
TP1 | 10 | 14
TP5 | 10 | 10
40 & above = positive
P50
AZ WM
Zanubrutinib
RBD IgG Curve
ASC
Activated Tfh1
Activated CD8 T cells
Activated CD4 T cells
DP4
CD4
TP1
TP5
B cells/ul
TP1 6.45
TP2
TP3 7.43
TP4
TP5 6.71
MNT GMT | Vic/01 | Delta
TP1 | 10 | 10
TP5 | 51 | 20
40 & above = positive
P51
AZ
Myeloma
IMID
RBD IgG Curve
ASC
Activated Tfh1
Activated CD8 T cells
Activated CD4 T cells
A2 PE
DP4 PE
B cells/ul
TP1 208.7
TP2
TP3 134.68
TP4
TP5 171.15
MNT GMT | Vic/01 | Delta
TP1 | 10 | 10
TP5 | 10 | 10
40 & above = positive

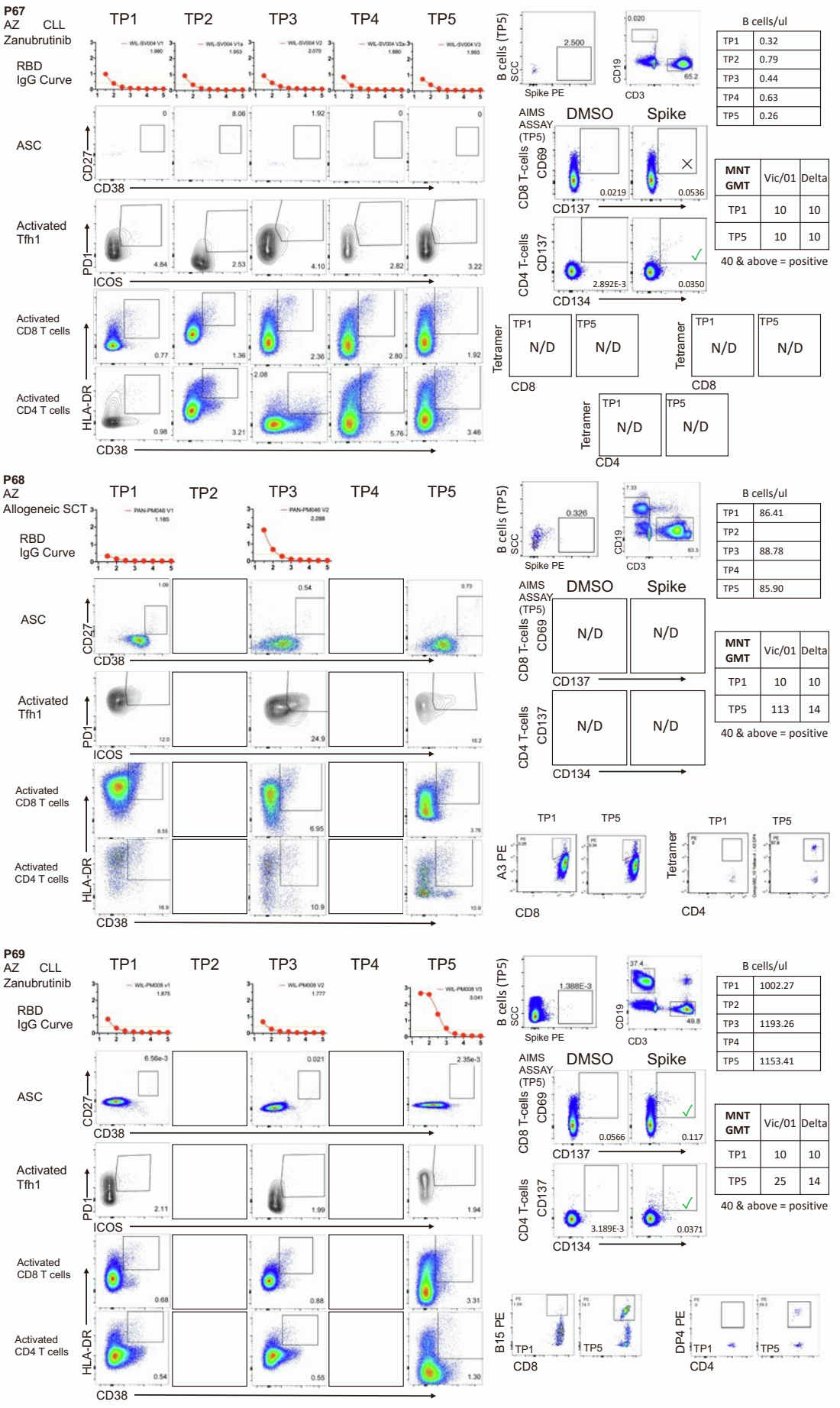

P52
AZ CLL
Venetoclax
TP1
TP2
TP3
TP4
TP5
RBD
IgG Curve
ASC
CD27
CD38
Activated
Tfh1
PD1
ICOS
Activated
CD8 T cells
Activated
CD4 T cells
HLA-DR
B cells (TP5)
SCC
Spike PE
CD19
CD3
AIMS
ASSAY
(TP5)
DMSO
Spike
CD8 T-cells
CD69
CD137
CD4 T-cells
CD134
B35 PE
A24 APC
CD8
DP4 PE
CD4
B cells/ul
TP1 1.47
TP2
TP3 1.96
TP4
TP5 5.63
MNT GMT | Vic/01 | Delta
TP1 | 10 | 10
TP5 | 53 | 20
40 & above = positive
P53
AZ WM
Zanubrutinib
N/D
B cells/ul
TP1 202.22
TP2
TP3
TP4
TP5
MNT GMT | Vic/01 | Delta
TP1 | - | -
TP5 | - | -
40 & above = positive
Tetramer
P54
AZ CLL
Zanubrutinib
B cells/ul
TP1 1.50
TP2
TP3 0.33
TP4
TP5 1.25
MNT GMT | Vic/01 | Delta
TP1 | 10 | 10
TP5 | 10 | 10
40 & above = positive
A1 APC
DP4

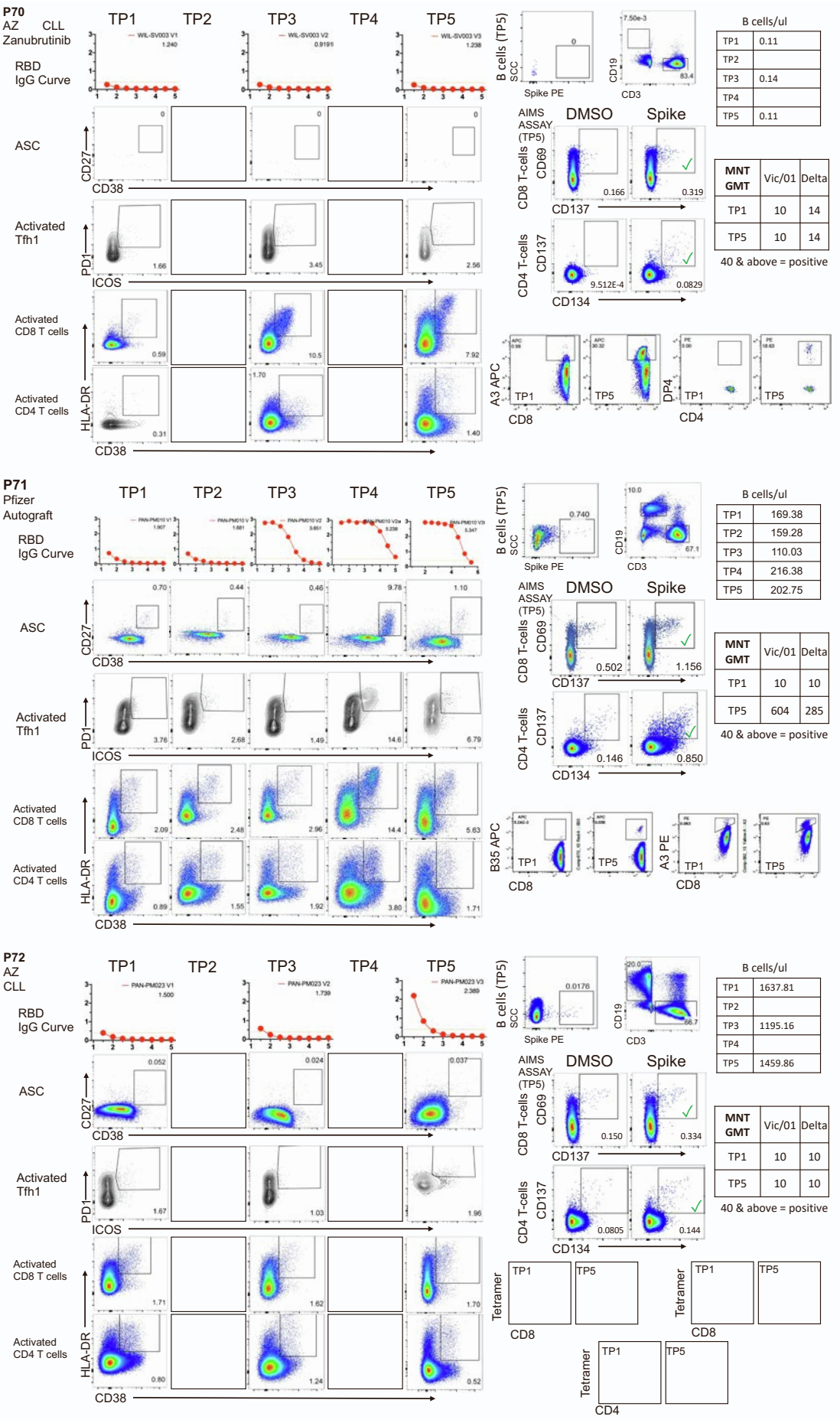

P55
AZ CLL
Treatment naive
TP1
TP2
TP3
TP4
TP5
RBD IgG Curve
ASC
CD27
CD38
Activated Tfh1
PD1
ICOS
Activated CD8 T cells
Activated CD4 T cells
HLA-DR
N/D
B cells (TP5)
SCC
Spike PE
CD19
CD3
AIMS ASSAY (TP5)
DMSO
Spike
CD8 T-cells
CD69
CD137
CD4 T-cells
CD134
Tetramer
CD8
CD4
B cells/ul
TP1 27492.64
TP2
TP3
TP4
TP5
MNT GMT | Vic/01 | Delta
TP1 - -
TP5 - -
40 & above = positive
P56
AZ
Autograft
TP1 221.19
TP2
TP3 112
TP4
TP5 34.72
TP1 10 10
TP5 28 16
P57
AZ
Autograft
TP1 24.29
TP2
TP3 65.69
TP4
TP5 50.72
TP1 10 10
TP5 10 10
B15 APC
DP4

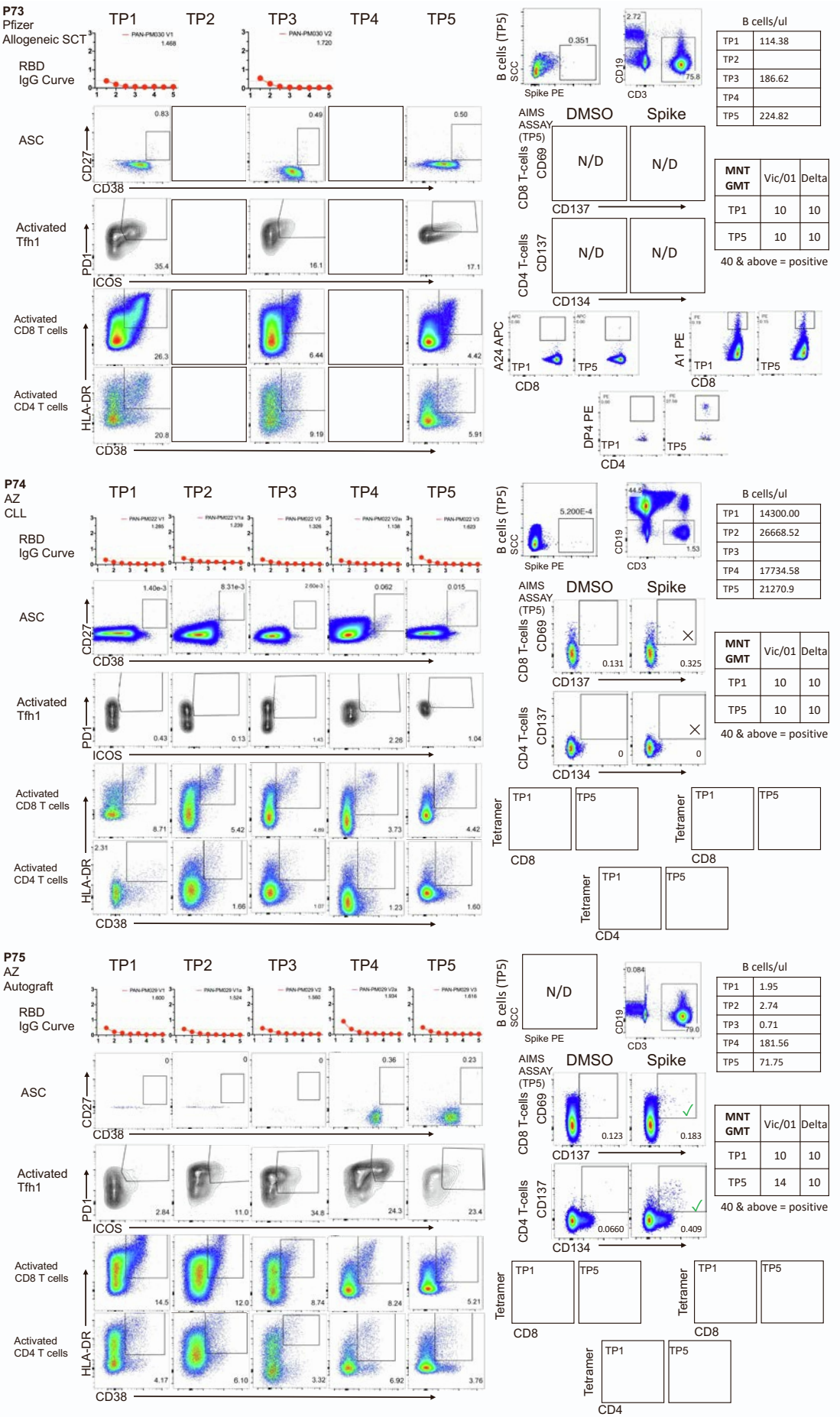

P58
AZ
Autograft
TP1
TP2
TP3
TP4
TP5
RBD
IgG Curve
ASC
CD27
CD38
Activated
Tfh1
PD1
ICOS
Activated
CD8 T cells
Activated
CD4 T cells
HLA-DR
B cells (TP5)
SCC
Spike PE
CD19
CD3
B cells/ul
TP1 219.73
TP2
TP3 127.42
TP4
TP5 345.71
AIMS
ASSAY
(TP5)
DMSO
Spike
CD8 T-cells
CD69
CD137
N/D
CD4 T-cells
CD134
MNT GMT | Vic/01 | Delta
TP1 | 10 | 10
TP5 | 160 | 90
40 & above = positive
Tetramer
CD8
CD4
P59
AZ CLL
Zanubrutinib
B cells/ul
TP1 1066.94
TP2
TP3 963.49
TP4
TP5 847.18
MNT GMT | Vic/01 | Delta
TP1 | 10 | 10
TP5 | 10 | 10
40 & above = positive
A2 PE
DP4 PE
P60
AZ
CAR-T
B cells/ul
TP1 44.44
TP2
TP3 52.03
TP4
TP5 73.28
MNT GMT | Vic/01 | Delta
TP1 | 10 | 10
TP5 | 134 | 25
40 & above = positive

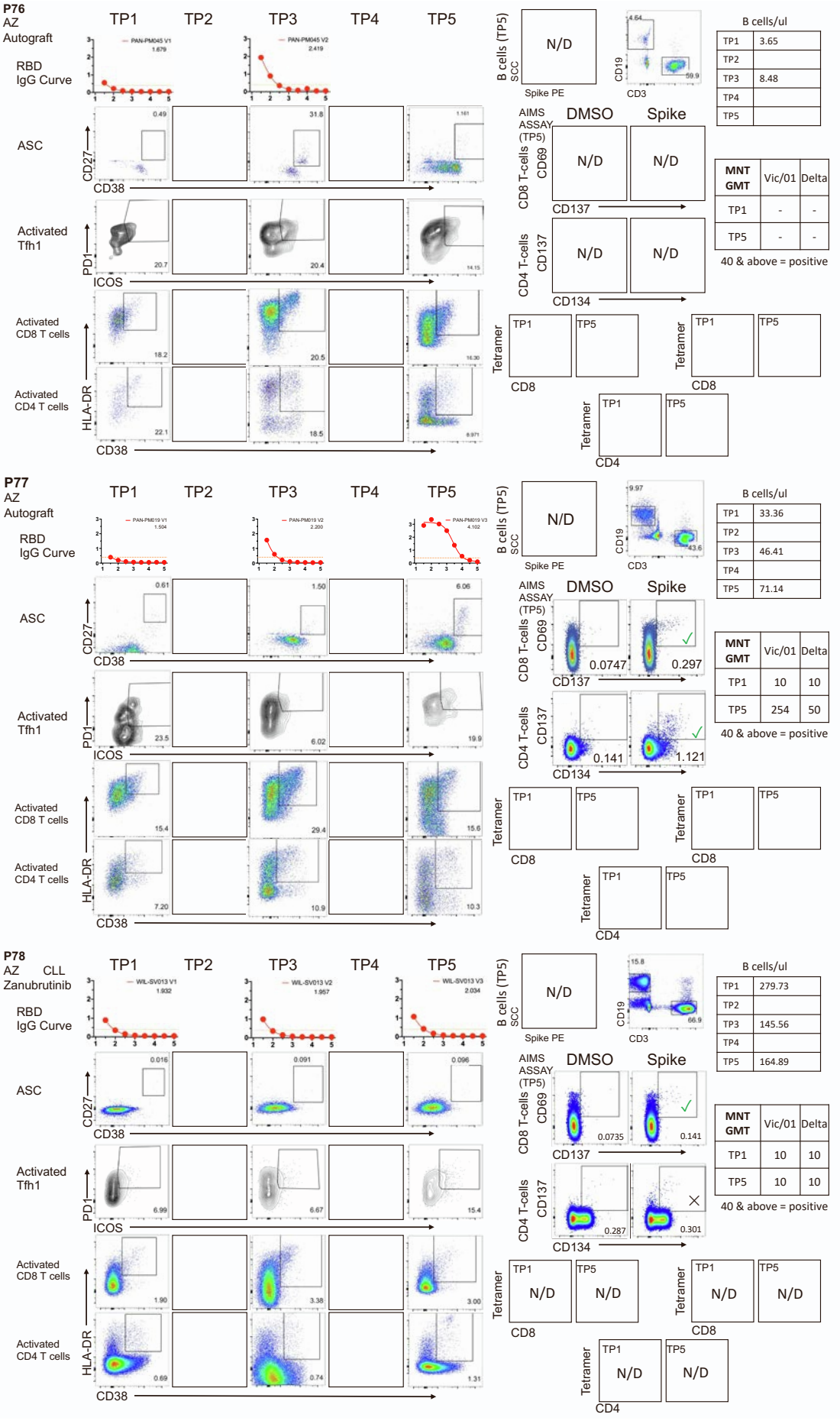

P61
Pfizer
Autograft
TP1
TP2
TP3
TP4
TP5
RBD
IgG Curve
ASC
CD27
CD38
Activated
Tfh1
PD1
ICOS
Activated
CD8 T cells
Activated
CD4 T cells
HLA-DR
CD38
B cells (TP5)
SCC
N/D
Spike PE
CD19
CD3
B cells/ul
TP1 116.41
TP2
TP3 145.86
TP4
TP5 44.55
AIMS
ASSAY
(TP5)
DMSO
Spike
CD8 T-cells
CD69
CD137
N/D
CD4 T-cells
CD137
CD134
MNT GMT Vic/01 Delta
TP1 10 10
TP5 33 16
40 & above = positive
Tetramer
TP1
TP5
CD8
CD4
P62
Pfizer
Myeloma
P63
AZ WM
Zanubrutinib
B35 APC
A3 PE
DP4

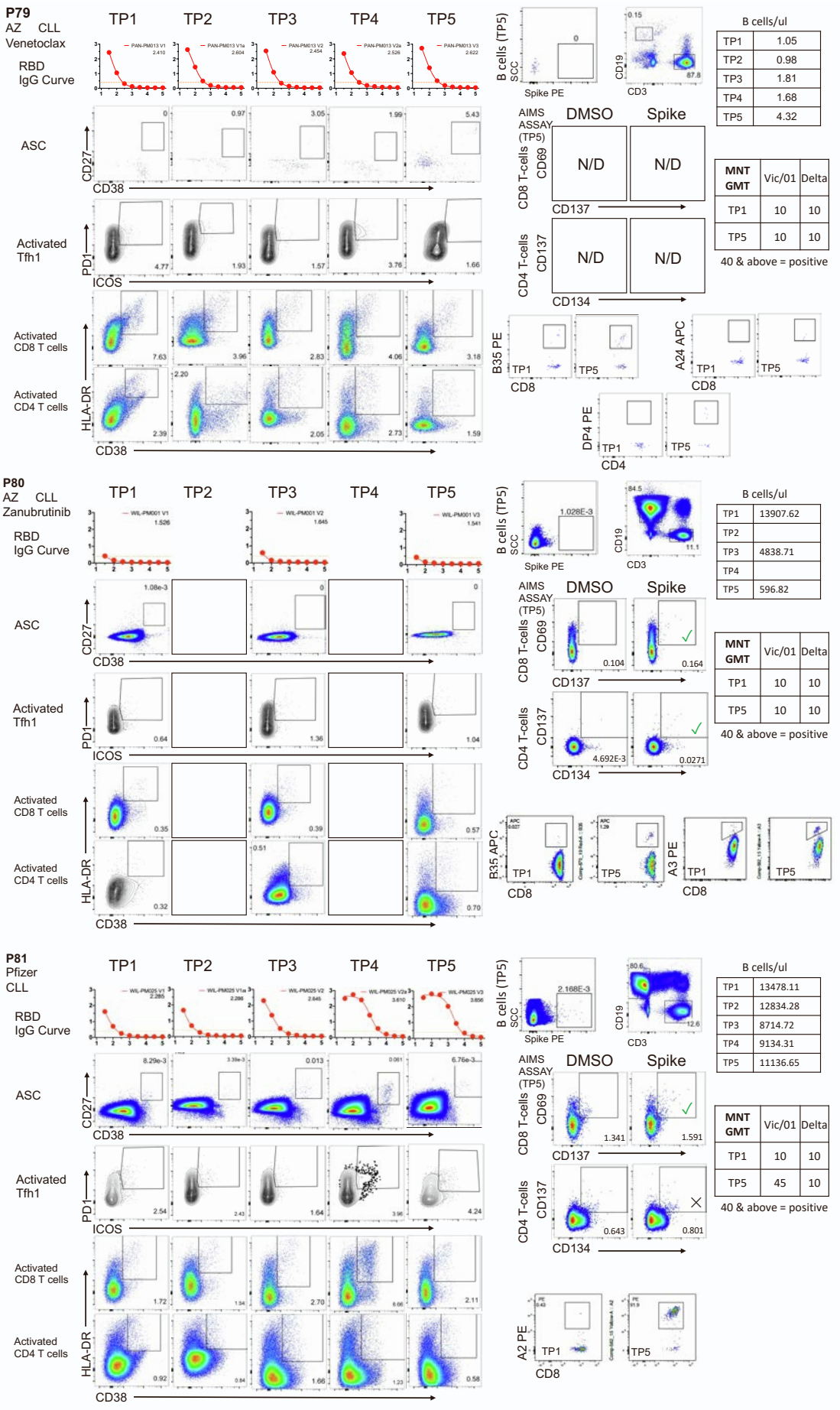

P64
Pfizer
Autograft
TP1
TP2
TP3
TP4
TP5
RBD
IgG Curve
ASC
CD27
CD38
Activated
Tfh1
PD1
ICOS
Activated
CD8 T cells
Activated
CD4 T cells
HLA-DR
B cells (TP5)
SCC
Spike PE
CD19
CD3
B cells/ul
TP1 178.76
TP2 61.75
TP3 193.34
TP4 88.49
TP5 114.92
AIMS
ASSAY
(TP5)
DMSO
Spike
CD8 T-cells
CD69
CD137
0.199
0.450
CD4 T-cells
CD137
CD134
0.0788
2.521
MNT GMT | Vic/01 | Delta
TP1 | 10 | 10
TP5 | 30 | 16
40 & above = positive
A2 APC
A1 PE
CD8
DP4
CD4
P65
AZ CLL
Zanubrutinib
N/D
B cells/ul
TP1 97.84
TP2
TP3
TP4
TP5 75.75
0.0305
0.769
0.0300
0.169
MNT GMT | Vic/01 | Delta
TP1 | 10 | 10
TP5 | 10 | 10
40 & above = positive
Tetramer
P66
AZ CLL
Zanubrutinib
0.773
B cells/ul
TP1 2.77
TP2
TP3 4.99
TP4
TP5 2.14
0.0553
0.170
0.142
0.413
MNT GMT | Vic/01 | Delta
TP1 | 10 | 10
TP5 | 10 | 14
40 & above = positive
B15 APC
A3 PE

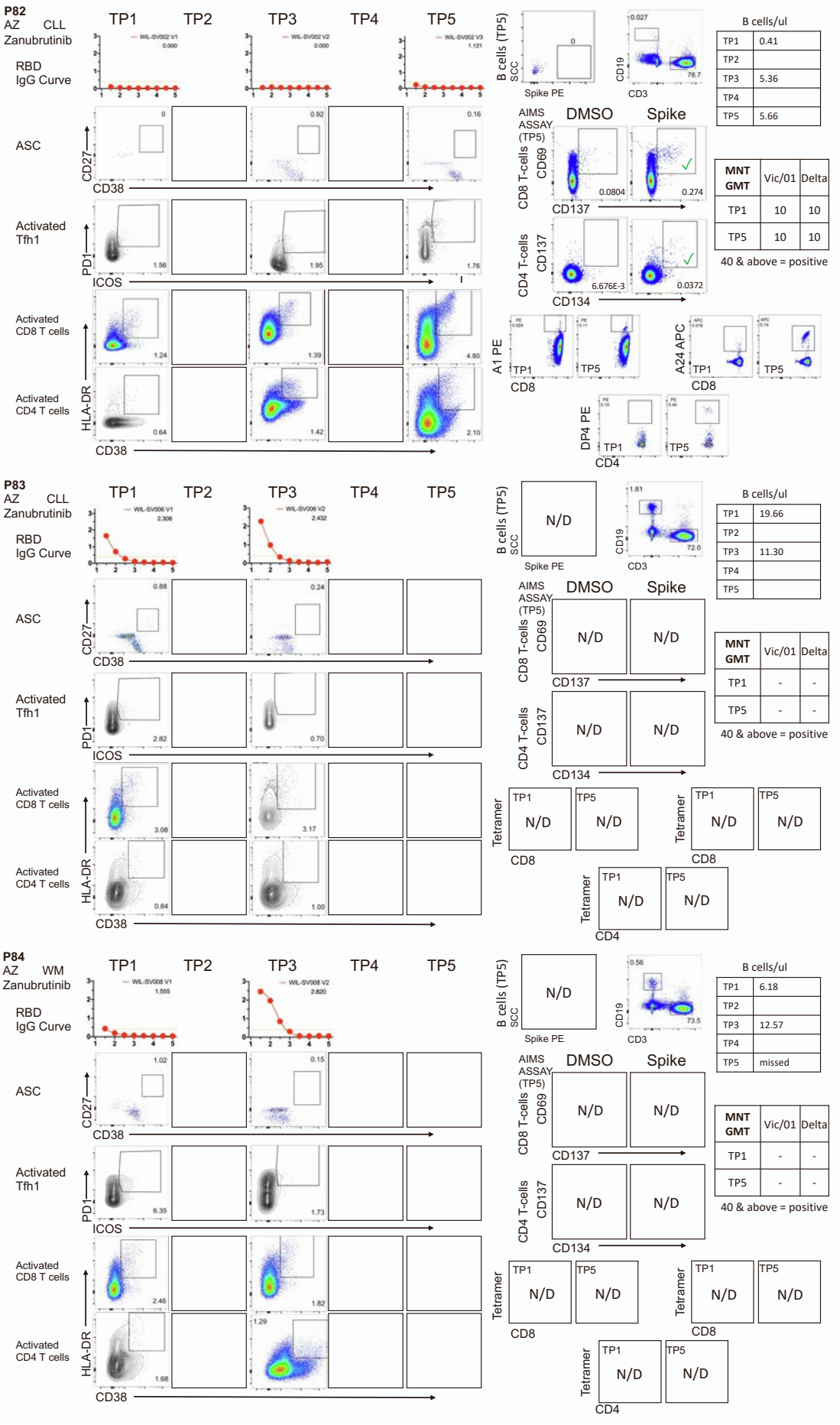

P67
AZ CLL
Zanubrutinib
TP1 TP2 TP3 TP4 TP5
RBD IgG Curve
ASC
CD27
CD38
Activated Tfh1
PD1
ICOS
Activated CD8 T cells
Activated CD4 T cells
HLA-DR
CD38
B cells (TP5)
SCC
Spike PE
CD19
CD3
AIMS ASSAY (TP5)
DMSO
Spike
CD8 T-cells CD69
CD137
CD4 T-cells CD137
CD134
Tetramer
CD8
CD4
N/D
B cells/ul
TP1 0.32
TP2 0.79
TP3 0.44
TP4 0.63
TP5 0.26
MNT GMT | Vic/01 | Delta
TP1 10 10
TP5 10 10
40 & above = positive
P68
AZ
Allogeneic SCT
TP1 86.41
TP2
TP3 88.78
TP4
TP5 85.90
MNT GMT | Vic/01 | Delta
TP1 10 10
TP5 113 14
40 & above = positive
A3 PE
P69
AZ CLL
Zanubrutinib
TP1 1002.27
TP2
TP3 1193.26
TP4
TP5 1153.41
MNT GMT | Vic/01 | Delta
TP1 10 10
TP5 25 14
40 & above = positive
B15 PE
DP4 PE

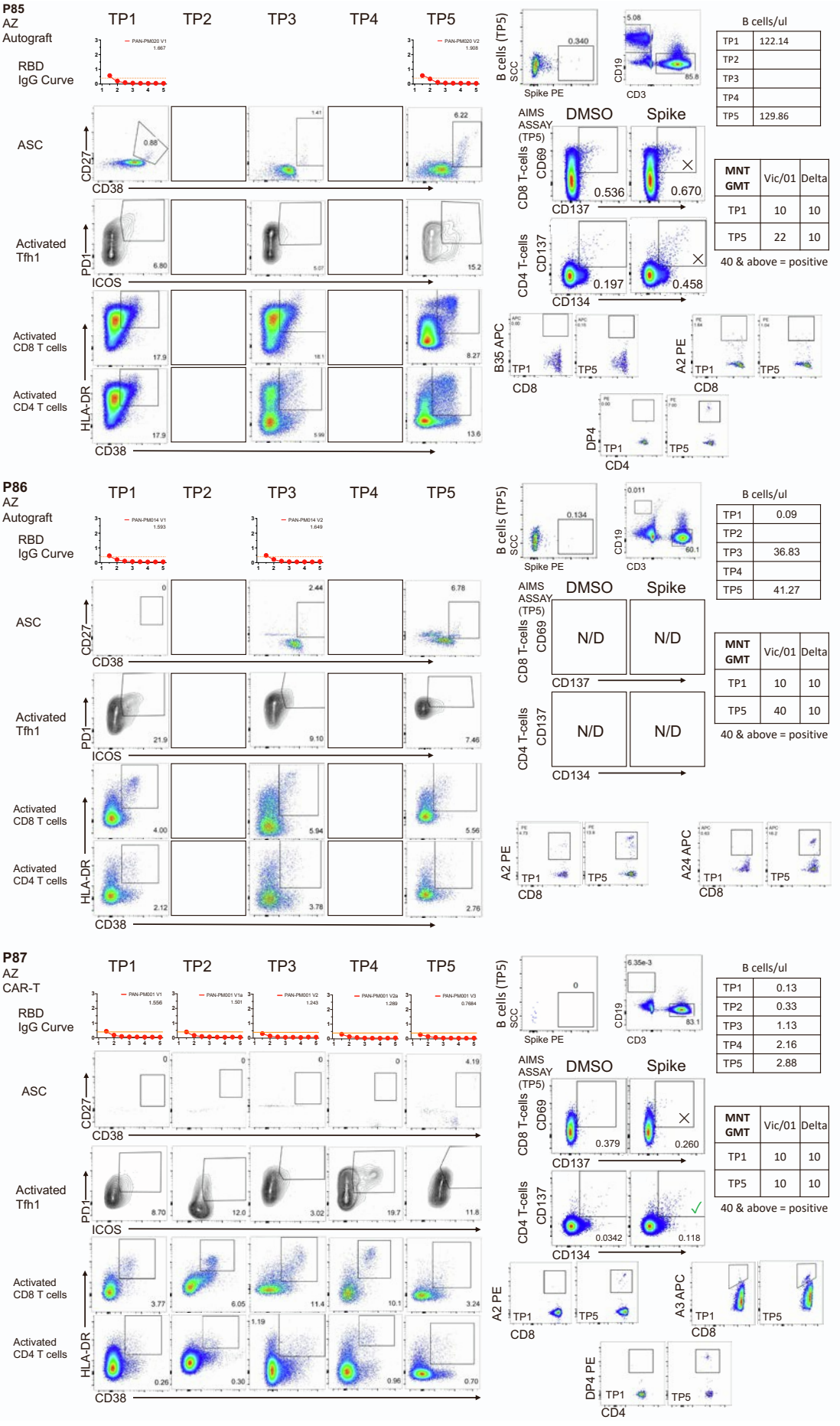

P70
AZ CLL
Zanubrutinib
TP1 TP2 TP3 TP4 TP5
RBD IgG Curve
ASC
CD27
CD38
Activated Tfh1
PD1
ICOS
Activated CD8 T cells
Activated CD4 T cells
HLA-DR
CD38
B cells (TP5)
SCC
Spike PE
CD19
CD3
AIMS ASSAY (TP5)
DMSO
Spike
CD8 T-cells
CD69
CD137
CD4 T-cells
CD137
CD134
A3 APC
CD8
DP4
CD4
B cells/ul
TP1 0.11
TP2
TP3 0.14
TP4
TP5 0.11
MNT GMT | Vic/01 | Delta
TP1 | 10 | 14
TP5 | 10 | 14
40 & above = positive
P71
Pfizer
Autograft
RBD IgG Curve
ASC
Activated Tfh1
Activated CD8 T cells
Activated CD4 T cells
B35 APC
A3 PE
B cells/ul
TP1 169.38
TP2 159.28
TP3 110.03
TP4 216.38
TP5 202.75
MNT GMT | Vic/01 | Delta
TP1 | 10 | 10
TP5 | 604 | 285
40 & above = positive
P72
AZ
CLL
RBD IgG Curve
ASC
Activated Tfh1
Activated CD8 T cells
Activated CD4 T cells
Tetramer
B cells/ul
TP1 1637.81
TP2
TP3 1195.16
TP4
TP5 1459.86
MNT GMT | Vic/01 | Delta
TP1 | 10 | 10
TP5 | 10 | 10
40 & above = positive

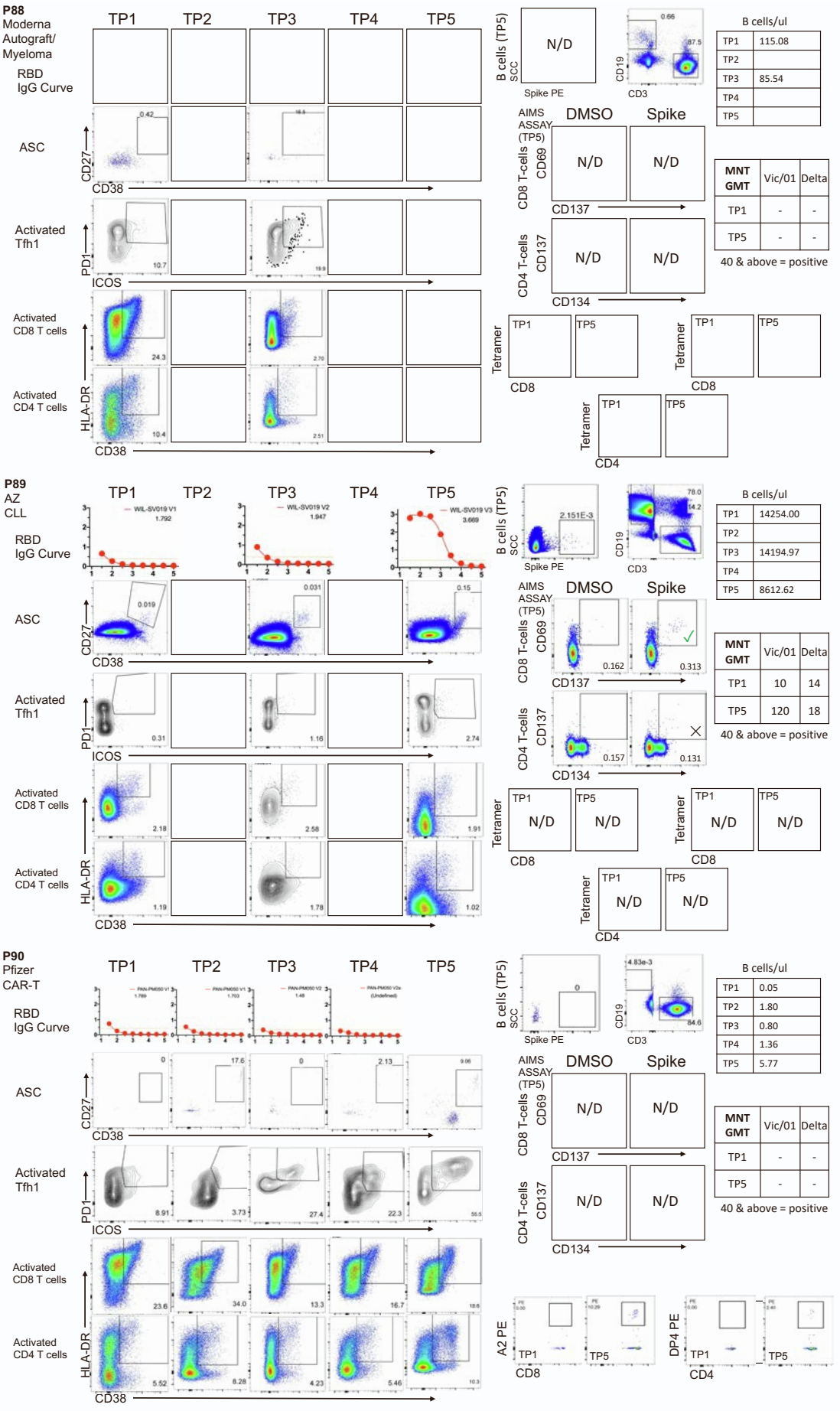

P73
Pfizer
Allogeneic SCT
TP1
TP2
TP3
TP4
TP5
RBD
IgG Curve
ASC
CD27
CD38
Activated
Tfh1
PD1
ICOS
Activated
CD8 T cells
Activated
CD4 T cells
HLA-DR
B cells (TP5)
SCC
Spike PE
CD19
CD3
AIMS
ASSAY
(TP5)
DMSO
Spike
CD8 T-cells
CD69
CD137
N/D
CD4 T-cells
CD134
A24 APC
A1 PE
CD8
DP4 PE
CD4
B cells/ul
TP1 114.38
TP2
TP3 186.62
TP4
TP5 224.82
MNT GMT | Vic/01 | Delta
TP1 | 10 | 10
TP5 | 10 | 10
40 & above = positive
P74
AZ
CLL
B cells/ul
TP1 14300.00
TP2 26668.52
TP3
TP4 17734.58
TP5 21270.9
Tetramer
P75
AZ
Autograft
B cells/ul
TP1 1.95
TP2 2.74
TP3 0.71
TP4 181.56
TP5 71.75

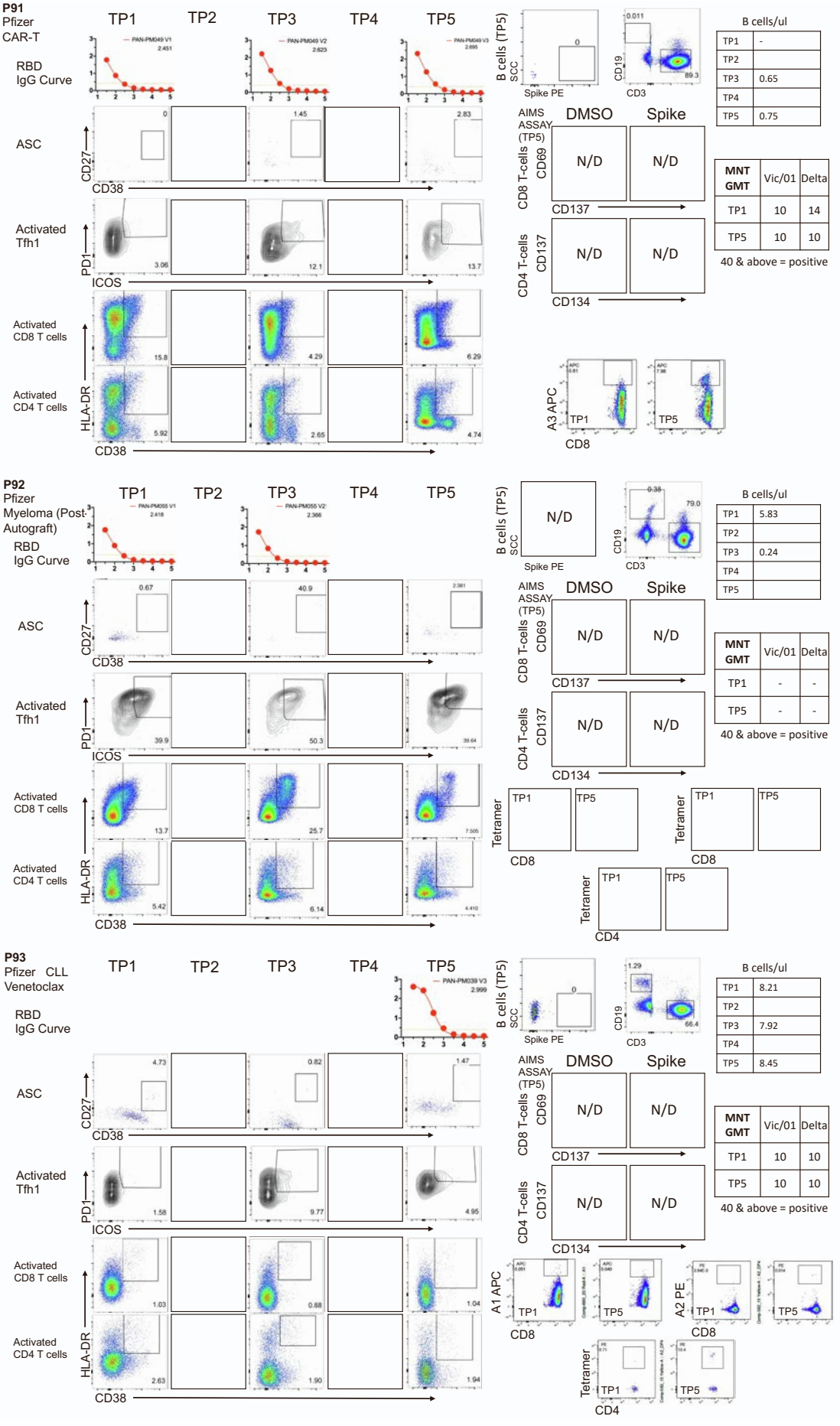

P76
AZ
Autograft
TP1
TP2
TP3
TP4
TP5
RBD
IgG Curve
ASC
CD27
CD38
Activated
Tfh1
PD1
ICOS
Activated
CD8 T cells
Activated
CD4 T cells
HLA-DR
B cells (TP5)
SCC
N/D
Spike PE
CD19
CD3
B cells/ul
TP1 3.65
TP2
TP3 8.48
TP4
TP5
AIMS
ASSAY
(TP5)
DMSO
Spike
CD8 T-cells
CD69
CD137
CD4 T-cells
CD134
MNT GMT | Vic/01 | Delta
TP1 - -
TP5 - -
40 & above = positive
Tetramer
CD8
CD4
P77
AZ
Autograft
TP1 33.36
TP2
TP3 46.41
TP4
TP5 71.14
0.0747
0.297
0.141
1.121
MNT GMT | Vic/01 | Delta
TP1 10 10
TP5 254 50
40 & above = positive
P78
AZ CLL
Zanubrutinib
TP1 279.73
TP2
TP3 145.56
TP4
TP5 164.89
0.0735
0.141
0.287
0.301
MNT GMT | Vic/01 | Delta
TP1 10 10
TP5 10 10
40 & above = positive


P79
AZ CLL
Venetoclax
TP1 TP2 TP3 TP4 TP5
RBD IgG Curve
ASC
CD27
CD38
Activated Tfh1
PD1
ICOS
Activated CD8 T cells
Activated CD4 T cells
HLA-DR
CD38
B cells (TP5)
SCC
Spike PE
CD19
CD3
AIMS ASSAY (TP5)
DMSO
Spike
CD8 T-cells CD69
CD137
N/D
CD4 T-cells CD137
CD134
B35 PE
A24 APC
DP4 PE
TP1
TP5
CD8
CD4
B cells/ul
TP1 1.05
TP2 0.98
TP3 1.81
TP4 1.68
TP5 4.32
MNT GMT | Vic/01 | Delta
TP1 10 10
TP5 10 10
40 & above = positive
P80
AZ CLL
Zanubrutinib
TP1 TP2 TP3 TP4 TP5
RBD IgG Curve
ASC
Activated Tfh1
Activated CD8 T cells
Activated CD4 T cells
CD38
B cells (TP5)
SCC
Spike PE
CD19
CD3
AIMS ASSAY (TP5)
DMSO
Spike
CD8 T-cells CD69
CD137
CD4 T-cells CD137
CD134
B35 APC
A3 PE
TP1
TP5
CD8
B cells/ul
TP1 13907.62
TP2
TP3 4838.71
TP4
TP5 596.82
MNT GMT | Vic/01 | Delta
TP1 10 10
TP5 10 10
40 & above = positive
P81
Pfizer
CLL
TP1 TP2 TP3 TP4 TP5
RBD IgG Curve
ASC
Activated Tfh1
Activated CD8 T cells
Activated CD4 T cells
CD38
B cells (TP5)
SCC
Spike PE
CD19
CD3
AIMS ASSAY (TP5)
DMSO
Spike
CD8 T-cells CD69
CD137
CD4 T-cells CD137
CD134
A2 PE
TP1
TP5
CD8
B cells/ul
TP1 13478.11
TP2 12834.28
TP3 8714.72
TP4 9134.31
TP5 11136.65
MNT GMT | Vic/01 | Delta
TP1 10 10
TP5 45 10
40 & above = positive


P82
AZ CLL
Zanubrutinib
RBD IgG Curve
TP1 TP2 TP3 TP4 TP5
ASC
CD27
CD38
Activated Tfh1
PD1
ICOS
Activated CD8 T cells
Activated CD4 T cells
HLA-DR
B cells (TP5)
SCC
Spike PE
CD19
CD3
B cells/ul
TP1 0.41
TP2
TP3 5.36
TP4
TP5 5.66
AIMS ASSAY (TP5)
DMSO
Spike
CD8 T-cells CD69
CD137
CD4 T-cells CD137
CD134
MNT GMT | Vic/01 | Delta
TP1 | 10 | 10
TP5 | 10 | 10
40 & above = positive
A1 PE
A24 APC
CD8
DP4 PE
CD4
P83
AZ CLL
Zanubrutinib
N/D
P84
AZ WM
Zanubrutinib
missed
Tetramer


P85
AZ
Autograft
TP1
TP2
TP3
TP4
TP5
RBD
IgG Curve
ASC
CD27
CD38
Activated
Tfh1
PD1
ICOS
Activated
CD8 T cells
Activated
CD4 T cells
HLA-DR
B cells (TP5)
SCC
Spike PE
CD19
CD3
AIMS
ASSAY
(TP5)
DMSO
Spike
CD8 T-cells
CD69
CD137
CD4 T-cells
CD134
B35 APC
A2 PE
CD8
DP4
CD4
B cells/ul
TP1 122.14
TP2
TP3
TP4
TP5 129.86
MNT GMT | Vic/01 | Delta
TP1 | 10 | 10
TP5 | 22 | 10
40 & above = positive
P86
AZ
Autograft
TP1 0.09
TP2
TP3 36.83
TP4
TP5 41.27
N/D
MNT GMT | Vic/01 | Delta
TP1 | 10 | 10
TP5 | 40 | 10
40 & above = positive
A24 APC
P87
AZ
CAR-T
TP1 0.13
TP2 0.33
TP3 1.13
TP4 2.16
TP5 2.88
MNT GMT | Vic/01 | Delta
TP1 | 10 | 10
TP5 | 10 | 10
40 & above = positive
A3 APC


P88
Moderna
Autograft/
Myeloma
RBD
IgG Curve
ASC
Activated
Tfh1
Activated
CD8 T cells
Activated
CD4 T cells
TP1
TP2
TP3
TP4
TP5
CD27
CD38
PD1
ICOS
HLA-DR
B cells (TP5)
SCC
Spike PE
CD19
CD3
N/D
B cells/ul
TP1 115.08
TP2
TP3 85.54
TP4
TP5
AIMS
ASSAY
(TP5)
DMSO
Spike
CD8 T-cells
CD69
CD137
CD4 T-cells
CD134
MNT GMT | Vic/01 | Delta
TP1 | - | -
TP5 | - | -
40 & above = positive
Tetramer
CD8
CD4
P89
AZ
CLL
WIL-SV019 V1
WIL-SV019 V2
WIL-SV019 V3
2.151E-3
B cells/ul
TP1 14254.00
TP2
TP3 14194.97
TP4
TP5 8612.62
0.162
0.313
0.157
0.131
MNT GMT | Vic/01 | Delta
TP1 | 10 | 14
TP5 | 120 | 18
40 & above = positive
P90
Pfizer
CAR-T
4.83e-3
B cells/ul
TP1 0.05
TP2 1.80
TP3 0.80
TP4 1.36
TP5 5.77
MNT GMT | Vic/01 | Delta
TP1 | - | -
TP5 | - | -
40 & above = positive
A2 PE
DP4 PE


P91
Pfizer
CAR-T
TP1
TP2
TP3
TP4
TP5
RBD
IgG Curve
ASC
CD27
CD38
Activated
Tfh1
PD1
ICOS
Activated
CD8 T cells
Activated
CD4 T cells
HLA-DR
CD38
B cells (TP5)
SCC
Spike PE
CD19
CD3
B cells/ul
TP1 -
TP2
TP3 0.65
TP4
TP5 0.75
AIMS
ASSAY
(TP5)
DMSO
Spike
CD8 T-cells
CD69
CD137
N/D
CD4 T-cells
CD134
MNT GMT | Vic/01 | Delta
TP1 | 10 | 14
TP5 | 10 | 10
40 & above = positive
A3 APC
CD8
P92
Pfizer
Myeloma (Post-Autograft)
B cells/ul
TP1 5.83
TP2
TP3 0.24
TP4
TP5
MNT GMT | Vic/01 | Delta
TP1 | - | -
TP5 | - | -
40 & above = positive
Tetramer
CD8
CD4
P93
Pfizer CLL
Venetoclax
B cells/ul
TP1 8.21
TP2
TP3 7.92
TP4
TP5 8.45
MNT GMT | Vic/01 | Delta
TP1 | 10 | 10
TP5 | 10 | 10
40 & above = positive
A1 APC
A2 PE

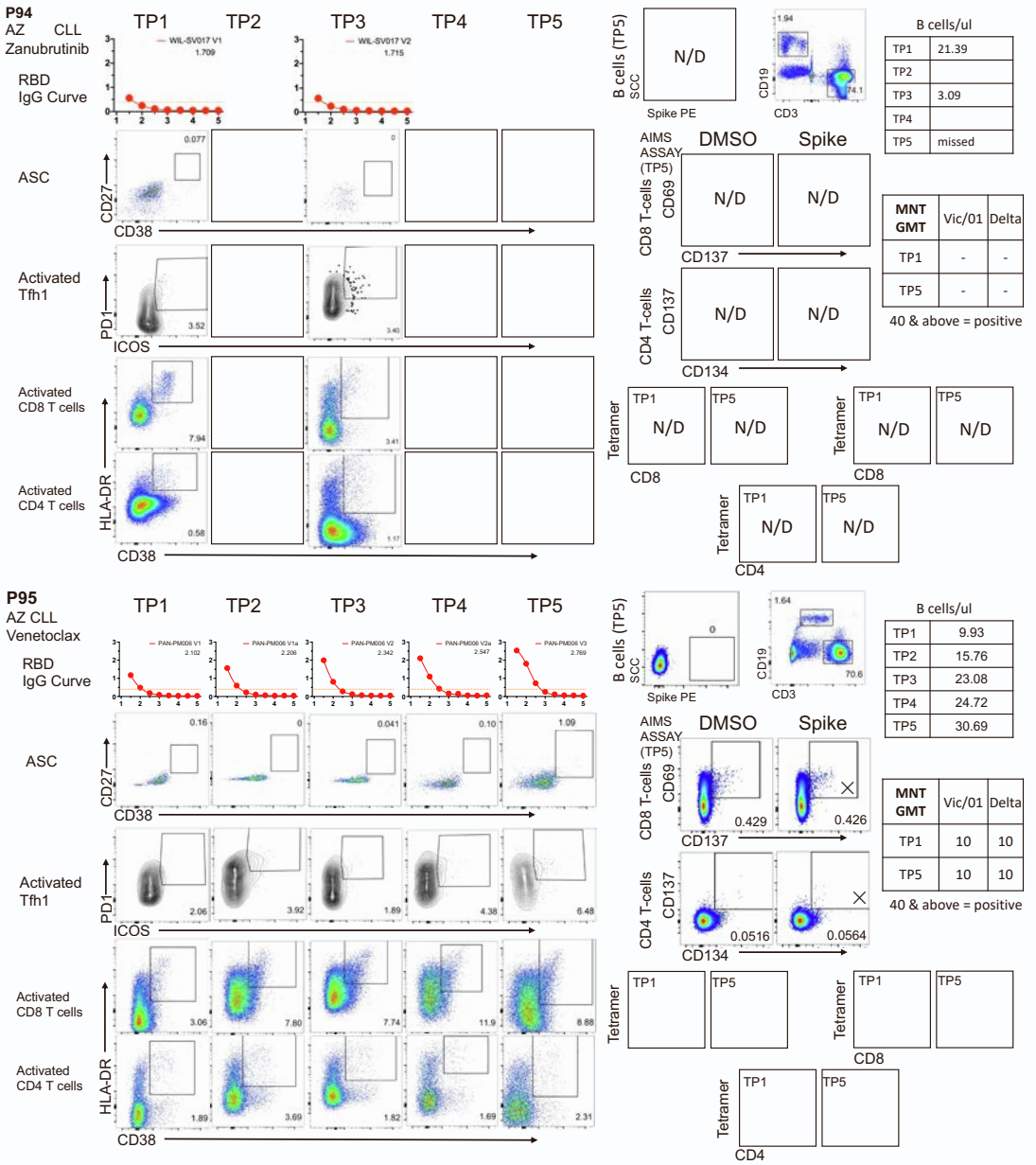


Figure S12. Individual patient's immune response following COVID-19 vaccination. T1=baseline, T2=acute response after first dose, T3=1 month post first dose, T4= acute response after second dose and T5=1 month post second dose. Due to limited sample availability, experiments were performed once for each sample. Related to Figure 1, 2, 3 and 4.