LETTER TO THE EDITOR

Polytypic B cells, monotypic/monoclonal B-cell proliferations, and neoplastic T cells diverge from *TET2-/DNMT3A*-mutant clonal hematopoiesis in follicular helper T-cell lymphomas

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Supplemental materials

Supplemental Table 1. Genomics of follicular helper T-cell lymphomas, polytypic B cells, monotypic/monoclonal B cell proliferations, and myeloid compartments in 25 follicular helper T-cell lymphoma patients

		T-Cell Lymphoma							B Cells/Monotypic/Monoclonal B Cell Proliferations								Myeloid Cells						
Patient	Variant	VAF	TCL Type	Genotyping Assay Utilized	Sample Type	Flow Sorted	Neoplastic T Cells in Sample	TCR Gene Rearrangement	VAF	B Cell Type	Genotyping Assay Utilized	EBV	Sample Type	Flow Sorted	Combined Myeloid and Neoplastic T Cells in Sample	IgH/TCR Gene Rearrangement (Method)	VAF	Myeloid Cell Type	Genotyping Assay Utilized	Sample Type	Flow Sorted	Combined B and Neoplastic T Cells in Sample	IgH/TCR Gene Rearrangement (Method)
1	DNMT3A p.R882H	0.52	TFHL-AI	MSK-IMPACT	BM	Y	NA	NT	0.49	Polytypic	MSK-IMPACT	Neg	BM	Y	NA	IgH: NT	0.46	Myeloid Cells	MSK-IMPACT	BM	Y	NA	NA
	TET2 p.M1333Nfs*6	0.49							0.10								0.06						
	TET2 p.G1145Vfs*7	0.45							0.00								0.00						
	RHOA p.G17L	0.51							0.00								0.00						
	IDH2 p.R172K	0.54							0.00								0.00						
2	DNMT3A p.W795C	0.49	TFHL-AI	ddPCR*	BM	Y	NA	Pos	0.04	Polytypic	ddPCR*	Pos	BM	Y	NA	IgH: NT	0.07	Monocytes	ddPCR*	BM	Y	NA	NA
	TET2 p.Y1337*	0.55							0.01								0.00						
	RHOA p.G17V	0.49							0.00								0.00						
	TET2 p.H1904Y	0.00							0.11								0.00						
3	TET2 p.Y592fs	0.51	TFHL-AI	ddPCR*	PB	Y	NA	Pos^	0.06	Polytypic	ddPCR*	Pos	PB	Y	NA	IgH: NT	0.01	Monocytes	ddPCR*	PB	Y	NA	NA
	DNMT3A exon11 splicing variant (c.1279+1G>A)	0.47							0.03								0.00						
	RHOA p.G17V	0.48							0.00								0.00						
	IDH2 p.R172K	0.49							0.00								0.00						
4	TET2 p.E1106Vfs*23	0.56	TFHL-AI	MSK-IMPACT	LN	Y	NA	NT	0.02	Polytypic	MSK-IMPACT	Neg	LN	Y	NA	IgH: NT	NT						
	TET2 p.S280*	0.44							0.00														
	RHOA p.G17V	0.46							0.00														
	IDH2 p.R172K	0.46							0.00														
5	TET2 p.P570fs	0.13	TFHL-AI	MSK-IMPACT	LN	N	10%	NT	0.15	Polytypic	ddPCR*	NA	PB	Y	NA	IgH: NT	0.22	Monocytes	ddPCR*	PB	Y	NA	NA
	RHOA p.G17V	0.06							0.00								0.00						
	IDH2 p.R172G	0.04							0.00								0.00						
	TET2 p.I873fs	0.06							NT								NT						
	PIK3CG p.V74M	0.13							NT								NT						
6	TET2 p.C973fs	0.07	TFHL-AI	MSK-IMPACT[#]	LN	N	10-15%	Pos	0.27	Polytypic	ddPCR*	Pos	PB	Y	NA	IgH: NT	0.00	Monocytes	ddPCR*	PB	Y	NA	NA
	TET2 p.R1216*	0.08							0.07								0.00						
	RHOA p.G17V	0.05							0.00								0.00						
	IDH2 p.R172S	0.06							0.00								0.00						
7	TET2 N427Vfs*4	0.47	TFHL-NOS	MSK-IMPACT[#]	LN	Y	NA	Pos	0.13	Polytypic	MSK-IMPACT[#]	Pos	LN	Y	NA	IgH: NT	0.43	Granulocytes	MSK-IMPACT[#]	BM	Y	NA	NA
	TET2 X1268_splice	0.44							0.13								0.47						
	STAT5A p.N398K	0.47							0.00								0.00						
8	TET2 p.Q1537*	0.12	TFHL-AI	MSK-IMPACT[#]	LN	N	20%	Pos^	0.00	Polytypic	MSK-IMPACT[#]	Neg	LN	Y	NA	IgH: NT	NT						
	TET2 p.N1610Ifs*6	0.11							0.00														
	DNMT3A p.I681M	0.10							0.00														
	TP53 p.MA160IS	0.01							0.00														
9	TET2 p.M1656Ifs*36	0.44	TFHL-AI	MSK-IMPACT	LN	Y	NA	Pos	0.00	Polytypic	MSK-IMPACT	Pos	LN	Y	NA	IgH: NT	0.00	Granulocytes	MSK-IMPACT	PB	Y	NA	NA
	TET2 p.G1154D	0.30							0.00								0.00						
	DNMT3A p.C557*	0.46							0.00								0.00						
	RHOA p.G17V	0.46							0.00								0.00						
	IDH2 p.R172S	0.39							0.00								0.00						
	IDH2 p.R172S	0.07							0.00								0.00						
	CD28 p.T195P	0.41							0.01								0.00						
10	TET2 p.Q1539*	0.51	TFHL-AI	MSK-IMPACT	LN	Y	NA	Pos^	0.00	Polytypic	MSK-IMPACT	Pos	LN	Y	NA	IgH: NT	NT						
	RHOA p.G17V	0.51							0.00														
11	TET2 p.Q1138Kfs*14	0.48	TFHL-AI	MSK-IMPACT[#]	PB	Y	NA	NT	0.00	Polytypic	MSK-IMPACT[#]	Pos	PB	Y	NA	IgH: NT	0.00	Myeloid Cells	MSK-IMPACT[#]	PB	Y	NA	NA
	TET2 p.C1271Wfs*29	0.46							0.00								0.00						
	RHOA p.G17V	0.59							0.00								0.00						
	ARID5B p.E456Kfs*23	0.32							0.00								0.00						
	CDK12 p.I873dup	0.41							0.00								0.00						
12	TET2 p.Q778*	0.42	TFHL-AI	MSK-IMPACT[#]	LN	N	15%	NT	0.43	LBCL-like MBP	MSK-IMPACT[#]	Pos	GE junction	N	≤5%	IgH/TCR: NT	0.48	Bulk BM	MSK-IMPACT[#]	BM	N	≤5%	IgH/TCR: NT
	TET2 p.D1384N	0.28							0.41								0.45						
	DNMT3A p.V296M	0.41							0.39								0.48						
	RHOA p.G17V	0.07							0.00								0.00						
	IDH2 p.R172S	0.06							0.00								0.00						
	NCOR2 p.A989T	0.07							0.00								0.00						
	SETD1B p.E612*	0.05							0.00								0.00						
	XBP1 p.S52N	0.00							0.25								0.00						
	BCR p.G6D	0.00							0.25								0.00						
	ACTG1 p.S60T	0.00							0.22								0.00						
13	TET2 p.W1233*	0.31	TFHL-AI	MSK-IMPACT[#]	BM	Y	NA	Pos	0.28	LBCL-like MBP	MSK-IMPACT[#]	Pos	Skin	N	≤5%	IgH/TCR: NT	0.07	Myelomonocytic cells	MSK-IMPACT[#]	BM	Y	NA	NA
	TET2 p.Q674*	0.33							0.22								0.00						
	DNMT3A p.V872F	0.29							0.27								0.08						
	RHOA p.G17V	0.24							0.00								0.00						
	CTNNB1 p.G48C	0.32							0.01								0.00						
	CTNNB1 p.S45F	0.30							0.00								0.00						
	GRIN2A p.X336_splice	0.24							0.00								0.00						
	EPHA7 p.A816V	0.00							0.20								0.00						

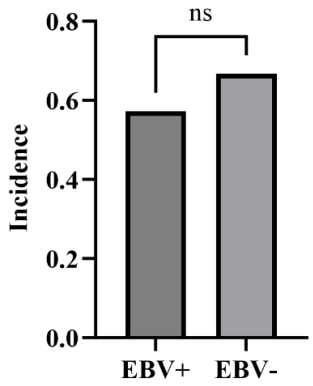
14	TET2 p.N427fs	0.17	TFHL-AI	MSK-IMPACT[#]	LN	N	15%	Pos	0.10	LBCL-like MBP	MSK-IMPACT[#]	Pos	Skin/Subq	N	≤5%	IgH/TCR: NT	0.05	Bulk BM	28 gene panel	BM	N	≤1%	IgH and TCR: Neg (PCR)
	TET2 p.Q745X	0.16							0.09								0.06						
	DNMT3A p.M801V	0.21							0.12								0.14						
	IDH2 p.R172G	0.04							0.00								0.00						
	TNFAIP3 p.R271*	0.18							0.00								NT						
	PAK7 p.P442Q	0.12							0.00								NT						
	MED12 p.R1343S	0.08							0.00								NT						
	TSC2 p.P542L	0.08							0.00								NT						
	BRAF p.K601N	0.03							0.00								NT						
	ATM p.P2842T	0.00							0.10								NT						
	BCORL1 p.V866F	NT							0.10								NT						
	DTX1 p.A120T	NT							0.07								NT						
	CD58 p.P125Hfs*5	NT							0.05								NT						
15	TET2 p.Y1661*	0.44	TFHL-AI	MSK-IMPACT	LN	N	40%	Pos	0.42	LBCL-like MBP	MSK-IMPACT	Neg	Skin/Subq	N	≤10%	IgH/TCR: NT	0.38	Bulk PB	MSK-IMPACT	PB	N	≤5%	IgH/TCR: NT
	TET2 p.I1873T	0.22							0.03								0.00						
	TET2 p.T1554Sfs*16	0.11							0.06								0.00						
	PRDM1 p.Q171*	0.00							0.30								0.00						
	KMT2D p.S2910Rfs*32	0.00							0.25								0.00						
	TET2 p.N1746Kfs*5	0.00							0.23								0.00						
	SF3B1 p.K666N	0.00							0.00								0.05						
	TP53 p.H193R	0.00							0.00								0.03						
16	TET2 p.R1452*	0.85	TFHL-AI	MSK-IMPACT	PB	Y	NA	Neg^	0.00	LBCL-like MBP	MSK-IMPACT	Pos	PB[†]	Y	NA	IgH: NT	NT						
	TET2 p.L1276Wfs*87	0.00							0.45														
17	TET2 p.S631*	0.45	TFHL-NOS	MSK-IMPACT[#]	PB	Y	NA	Pos^	0.49	Polymorphic MBP	MSK-IMPACT[#]	Pos	PB[‡]	Y	NA	IgH: NT	0.11	Myeloid Cells	MSK-IMPACT[#]	PB	Y	NA	NA
	TET2 p.G641W	0.49							0.47								0.13						
	DNMT3A p.K455*	0.47							0.50								0.18						
	TET2 p.V1232Gfs*21	0.00							0.48								0.09						
	PIK3C3 p.S460P	0.00							0.52								0.09						
	TET3 p.C693G	0.52							0.00								0.00						
	TET3 p.C695Y	0.47							0.00								0.00						
	MAP2K1 p.K57N	0.08							0.00								0.00						
	MAP2K1 p.Q45_E62del	0.02							0.00								0.00						
	SPEN p.S147*	0.07							0.00								0.00						
	FAT1 M1?	0.08							0.00								0.00						
	CCND3 p.R271Pfs*53	0.27							0.00								0.00						
	HNF1A p.M154I	0.21							0.00								0.00						
	CHEK2 p.C284*	0.00							0.00								0.03						
	PTCH1 p.L39Cfs*41	0.00							0.00								0.03						
	TET2 p.Q1030*	0.00							0.00								0.01						
18	TET2 p.L1740*	0.38	TFHL-AI	MSK-IMPACT[#]	LN	N	10%	Pos	0.27	Polymorphic MBP	MSK-IMPACT	Pos	LN	N	≤10%	IgH: Pos (PCR, NGS)^, TCR: NT	NT						
	DNMT3A p.X518_splice	0.40							0.28														
	RHOA p.G17V	0.06							0.00														
	CTNNB1 p.S45F	0.06							0.00														
	TBX3 p.A280T	0.06							0.00														
19	TET2 p.S577Pfs*3	0.37	TFHL-AI	MSK-IMPACT[#]	LN	N	60%	Pos	0.39	Polymorphic MBP	MSK-IMPACT[#]	Pos	LN	N	≤10%	TCR: Neg (PCR), TCRg: Pos (NGS, 0.1%), IgH: NT	0.43	Bulk BM	MSK-IMPACT[#]	BM	N	≤1%	TCRg: Pos (NGS, 0.09%), IgH: NT
	TET2 p.F1300V	0.07							0.28								0.47						
	TET2 p.C1289F	0.24							0.02								0.00						
	CUX1 p.E555L	0.30							0.00								0.00						
	SETBP1 p.L1421P	0.30							0.00								0.00						
	VAV1 p.Y174C	0.33							0.00								0.00						
	CHEK2 p.D134G	0.02							0.28								0.44						
	CBFB p.I102F	0.00							0.14								0.00						
	KRAS p. A146T	0.00							0.13								0.01						
	SETD1A p.G444R	0.01							0.13								0.00						
	SETD5 p.A232V	0.00							0.12								0.00						
	SOCS1 p.NQ5K*	0.00							0.11								0.00						
	SOCS1 p.F79_Y80delinsLH	0.00							0.10								0.00						
	ARID1B p.G357dup	0.00							0.09								0.00						
	DNMT3A p.R736H	0.01							0.05								0.00						
	SRSF2 p.P95H	0.00							0.11								0.48						
	FBXO11 p.Y692H	0.01							0.09								0.44						
20	TET2 p.Q324Hfs*23	0.33	TFHL-NOS	MSK-IMPACT[#]	LN	Y	NA	Pos	0.47	Polymorphic MBP	MSK-IMPACT[#]	Pos	LN	Y	NA	IgH: Pos (PCR)	0.01	Bulk saliva and nails	MSK-IMPACT	Saliva and nails	N	NA	IgH/TCR: NT
	TET2 p.Q831*	0.38							0.46								0.00						
	SOCS1 p.R179P	0.37							0.00								0.00						
	TET2 p.L1276Sfs*22	0.05							0.00								0.00						
	DTX1 p.G58V	0.01							0.47								NT						
	FAT1 p.I1302M	0.00							0.15								0.00						
	DAXX p.F79L	0.00							0.09								0.00						
	RPTOR p.R616H	0.00							0.08								0.00						

21	TET2 p.A1373E	0.10	TFHL-AI	MSK-IMPACT[#]	LN	N	20%	NT	0.00	Polymorphic MBP	MSK-IMPACT[#]	Pos	PB[†]	Y	NA	IgH: NT	0.00	Granulocytes	MSK-IMPACT[#]	PB	Y	NA	NA
	TET2 p.V1136Cfs*6	0.06							0.00								0.00						
	DNMT3A p.P700L	0.10							0.00								0.00						
	RHOA p.G17V	0.09							0.00								0.00						
	CD28 p.T195P	0.10							0.00								0.00						
	SOCS1 p.I194N	0.08							0.00								0.00						
	PLCG1 p.D1169G	0.06							0.00								0.00						
	TET2 p.C1271*	0.00							0.38								0.00						
	TBX3 p.G218V	0.00							0.06								0.00						
22	TET2 p.H1382D (C>G)	0.45	TFHL-NOS	MSK-IMPACT[#]	LN	Y	NA	Pos^	0.00	Polymorphic MBP	MSK-IMPACT[#]	Pos	PB[†]	Y	NA	IgH: Pos (PCR)^	0.00	Bulk BM	49 gene panel	BM	N	≤5%	IgH: Pos (PCR), TCR: NT
	TET2 p.S1494* (C>A)	0.47							0.00								0.00						
23	TET2 p.Y1628*	0.40	TFHL-AI	MSK-IMPACT	LN	Y	NA	NT	0.56	FL-like MBP, grade 3B	MSK-IMPACT	Neg	LN	Y	NA	IgH: NT	0.97	Bulk BM	MSK-IMPACT	BM	N	≤5%	IgH and TCR: Neg (PCR)
	TET3 p.T35Sfs*45	0.21							0.32								0.47						
	RHOA p.G17V	0.14							0.00								0.00						
	KRAS p.A146V	0.01							0.26								0.06						
	NRAS p.G12V	0.00							0.10								0.09						
	ARID2 p.R13Efs*22	0.00							0.00								0.06						
24	TET2 p.R1400*	0.48	TFHL-AI	MSK-IMPACT[#]	LN	Y	NA	Pos	0.00	FL-like MBP, grade 3A	MSK-IMPACT[#]	Pos	LN	Y	NA	IgH: Neg (PCR)	0.26	Bulk saliva	MSK-IMPACT	Saliva	N	NA	IgH/TCR: NT
	SRSF2 p.P95H	0.46							0.00								0.36						
	TET2 p.R1465*	0.43							0.00								0.02						
	TET2 p.Q734*	0.04							0.00								0.00						
	ARID1A p.G105Efs*8	0.00							0.28								0.00						
	BCL2 p.E13D	0.00							0.43								0.00						
	CRLF2 p.C180Y	0.00							0.51								0.00						
	CSF1R p.V38L	0.00							0.39								0.00						
	DTX1 p.G58D	0.00							0.49								0.00						
	DTX1 p.V70L	0.01							0.52								0.00						
	EPHA7 p.I11N	0.00							0.52								0.00						
	KMT2D p.Q3961*	0.01							0.35								0.00						
	KSR2 p.S184I	0.00							0.46								0.00						
	LTB p.V36L	0.00							0.46								0.00						
	MEF2B p.D83V	0.00							0.99								0.00						
	PIM1 p.S75P	0.00							0.47								0.00						
	PTCH1 p.P299L	0.01							0.45								0.00						
	TNFAIP3 p.R136Qfs*3	0.02							0.34								0.00						
	TNFAIP3 p.L324Qfs*7	0.00							0.30								0.00						
	TNFRSF14 p.G60D	0.00							0.69								0.00						
	TNFRSF14 p.N116Rfs*117	0.00							0.18								0.00						
25	TET2 p.Y1128*	0.46	TFHL-AI	MSK-IMPACT[#]	BM	Y	NA	Pos	0.00	MM	MSK-IMPACT[#]	Neg	BM	Y	NA	IgH: Pos (PCR)	0.05	Bulk PB	49 gene panel	PB	N	≤1%	IgH/TCR: NT
	TET2 p.Q810*	0.46							0.00								0.05						
	DNMT3A p.R736C	0.48							0.00								0.07						
	RHOA p.G17V	0.46							0.00								NT						
	IDH2 p.R172K	0.41							0.00								0.00						
	ATR p.D1409N	0.21							0.00								NT						
	KMT2B p.Q757*	0.25							0.00								NT						
	BRCA2 p.A2306S	0.00							0.48								NT						
	BTG1 p.K29*	0.00							0.48								NT						
	EPHA5 p.G1033E	0.00							0.23								NT						
	KMT2D p.H1525Pfs*37	0.00							0.25								NT						
	SETD5 p.Y987F	0.00							0.35								NT						

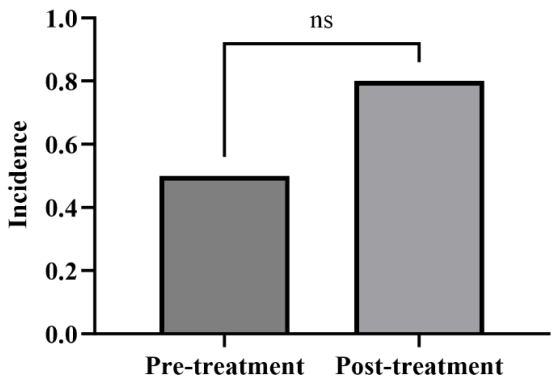
Footnote: Targeted next-generation sequencing (NGS)-based mutational analysis was performed using Memorial Sloan Kettering laboratory-developed hybrid-capture-based 400 or 410 gene panels (MSK-IMPACT) with or without a matched germline control (minimum depth of coverage 100x) or microdroplet amplicon-based 28 or 49 gene panels (minimum depth of coverage 500x), all containing at least 28 genes commonly mutated in hematopoietic neoplasms. Mutations with allele frequencies (VAFs) ≤0.02 are included here but were not included in the final analysis. Percentages of neoplastic T-, total B-, and/or myeloid cells in a sample (based on morphology, immunohistochemistry, flow cytometry, and/or gene rearrangement analysis) are reported only for unsorted samples. Variants with VAFs >2x the percentage of neoplastic T- and myeloid cells combined in bulk monotypic/monoclonal B cell proliferation (MBP) samples and of neoplastic T- and total B cells in bulk blood (PB) or bone marrow (BM) samples were considered present in MBP or myeloid compartments, respectively, as variants at those levels would generally be too high to be explained by the T/myeloid or T/B cells alone and would most likely be present in the remaining compartment (MBP or myeloid, respectively). Clonality assessment was performed during clinical case work up using polymerase chain reaction (PCR)-based (T cell receptor [TCR] gamma [TCRg] and beta, immunoglobulin heavy chain [IgH]) and/or NGS-based (TCRg, IgH) gene rearrangement assays. IgH gene rearrangement results are reported on all polytypic B cell and MBP samples (to provide clonality evaluation) and on bulk myeloid samples (to provide sample purity evaluation). TCR gene rearrangement results are reported on T-cell lymphoma (TCL) samples (PCR only) (to provide clonality evaluation) and on bulk MBP and myeloid samples (to provide purity evaluation). For TCR gene rearrangement studies using NGS, the percentage indicates the percentage of clonal reads of all rearranged TCR reads. *Droplet digital polymerase chain reaction (ddPCR) was performed utilizing custom primers targeting mutated genes detected by targeted NGS performed on corresponding bulk TCL samples (see Figure 2 for genes evaluated). For patients 2 and 3, the targeted NGS was performed on a separate TCL sample (data not shown). ^Performed on a separate similar sample. [#]Matched germline control (nails or saliva) utilized. [†]The histologic type of MBP was determined on a concurrent or recent (obtained within 3 months) tissue sample that demonstrated the same B cell immunophenotype by flow cytometry and/or immunohistochemistry as the immunophenotypically abnormal B cell population identified in the genotyped PB sample by flow cytometry. [‡]Only a PB sample was available for evaluation, which showed an abnormal, light chain restricted B cell population with plasmacytic differentiation by flow cytometry and a lack of a significant population of large lymphocytes on the PB smear. EBV indicates Epstein-Barr virus; FL, follicular lymphoma; GE, gastroesophageal; LBCL, large B-cell lymphoma; LN, lymph node; MM, plasma cell myeloma; N, no; NA, not applicable; Neg, negative; NT, not tested; Pos, positive; TFHL-AI, follicular helper T-cell lymphoma, angioimmunoblastic type; TFHL-NOS, follicular helper T-cell lymphoma, not otherwise specified; Subq, subcutaneous tissue; Y, yes.

Supplemental Figure 1

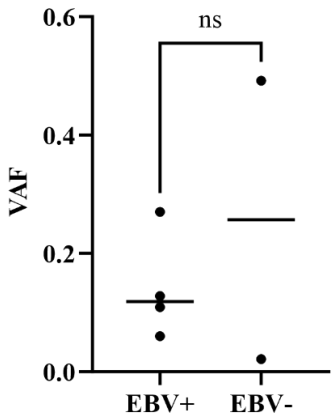
A Incidence of shared mutations in PolyBCs and TFHLs, EBV+ vs EBV-



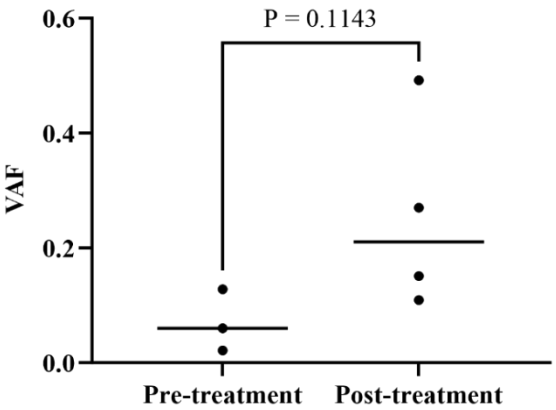
B Incidence of shared mutations in PolyBCs and TFHLs, pre- vs post-treatment



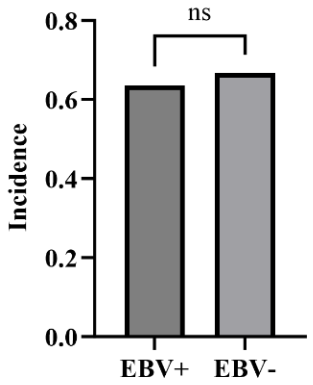
C VAFs of *TET2*/*DNMT3A* mutations in PolyBCs, EBV+ vs EBV-



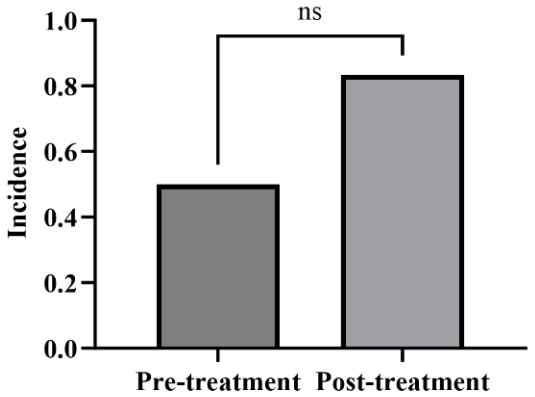
D VAFs of *TET2*/*DNMT3A* mutations in PolyBCs, pre- vs post-treatment



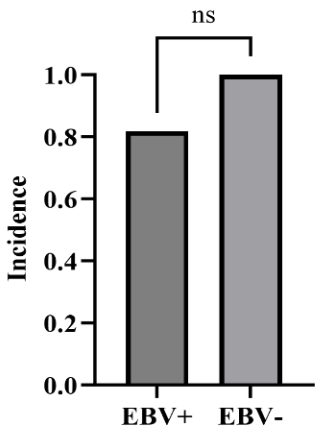
E Incidence of shared mutations in MBPs and TFHLs, EBV+ vs EBV-



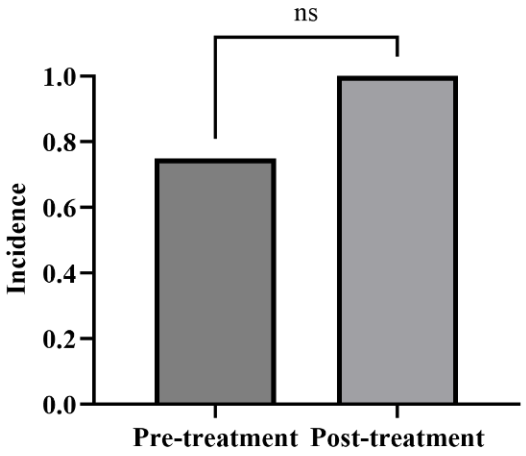
F Incidence of shared mutations in MBPs and TFHLs, pre- vs post-treatment



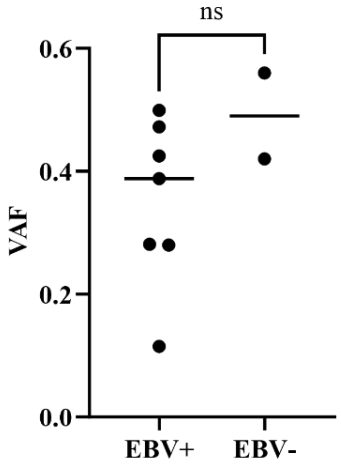
G Incidence of private mutations in MBPs EBV+ vs EBV-



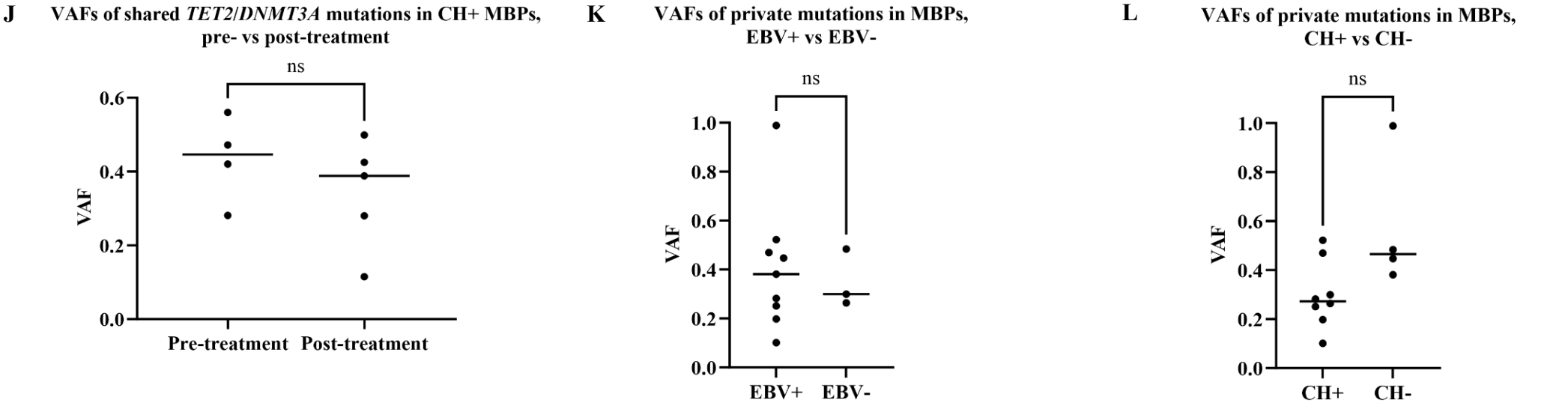
H Incidence of private mutations in MBPs, pre- vs post-treatment



I VAFs of shared *TET2*/*DNMT3A* mutations in CH+ MBPs, EBV+ vs EBV-

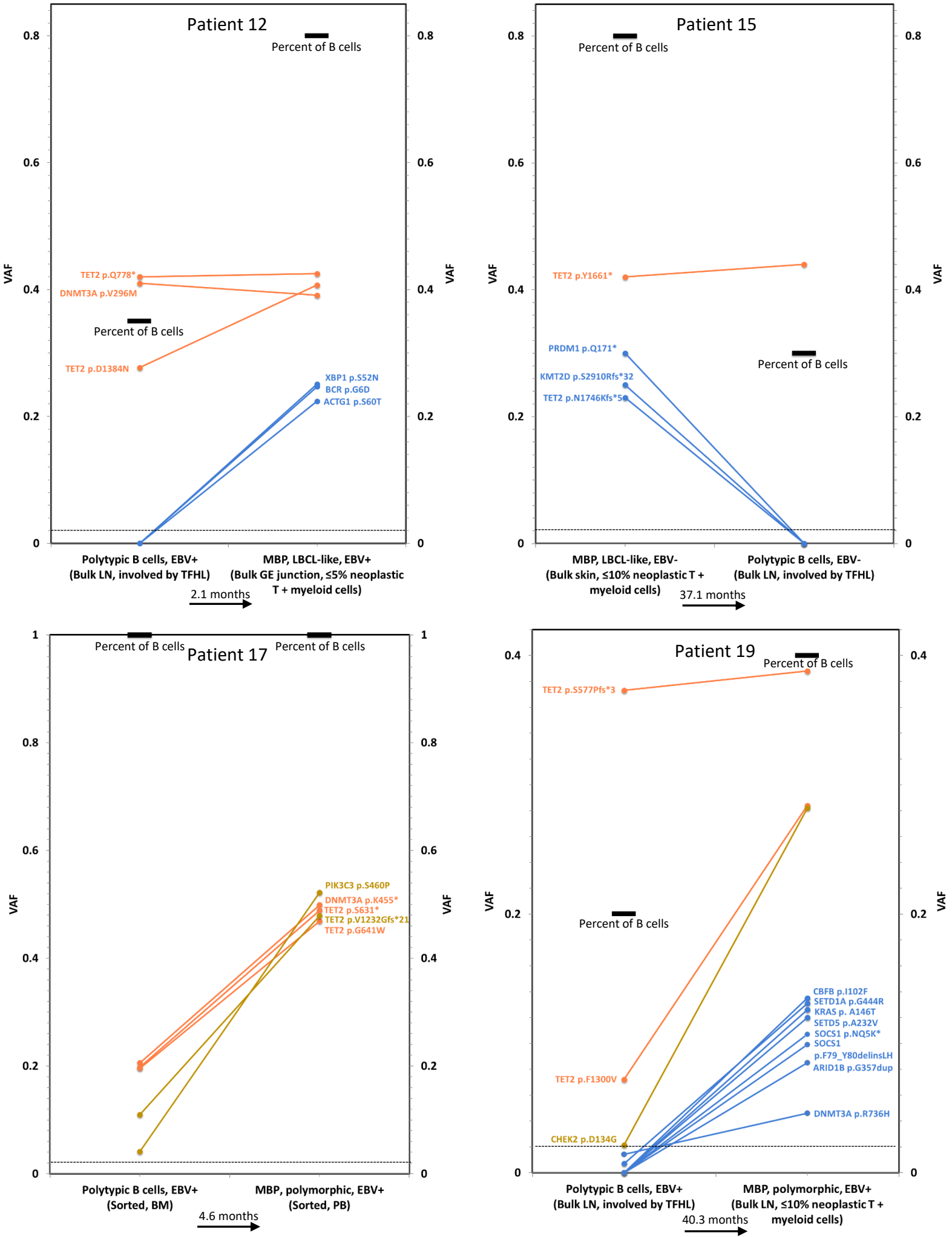


Supplemental Figure 1, Continued



Supplemental Figure 1. Comparisons of the incidences and allele frequencies of shared and/or private mutations in polytypic B cells and monotypic/monoclonal B cell proliferations among various groups. (A) The proportion of patients with shared mutations in polytypic B cells **(**PolyBCs) and follicular helper T-cell lymphomas (TFHLs) was not significantly different among Epstein-Barr virus-positive (EBV+) and EBV-negative (EBV-) patients or (B) among those with PolyBCs sampled pre- and post-treatment. (C) The allele frequencies (VAFs) of the *TET2*/*DNMT3A* mutations in PolyBCs did not significantly differ among EBV+ and EBV- patients harboring those mutations. (D) A trend towards lower VAFs was present among samples obtained pre-treatment. (E) The incidence of shared mutations in monotypic/monoclonal B cell proliferations (MBPs) and TFHLs did not significantly differ among EBV+ and EBV- MBPs or (F) among MBP samples obtained pre- and post-treatment. (G, H) The incidence of private mutations in MBPs also did not differ among these groups. (I) Among clonal hematopoiesis-positive (CH+) MBPs (those that shared mutations with corresponding TFHLs), no significant difference in VAFs of the shared *TET2*/*DNMT3A* mutations was seen among EBV+ and EBV- MBPs or (J) among pre- and post-treatment samples. (K) Private mutant VAFs in MBPs did not significantly differ among EBV+ and EBV- cases or (L) among CH+ and CH-negative (CH-) MBPs. Horizontal lines in (C-D) and (I-L) indicate medians; ns, not significant.

Supplemental Figure 2



Supplemental Figure 2, Continued

Supplemental Figure 2. Comparison of mutations detected in samples containing high levels of polytypic B cells and monotypic/monoclonal B cell proliferations obtained from the same patients. Separate samples containing high levels of polytypic B cells (PolyBCs) from 4 monotypic/monoclonal B cell proliferation (MBP) patients (12, 15, 17, 19) were sequenced. Such samples consisted of lymph node (LN) involved by follicular helper T-cell lymphoma (TFHL) (patients 12, 15, 19) or bone marrow (BM) (patient 17), which either pre-dated (patients 12, 17, 19) or followed (patient 15) MBP development at time intervals ranging from 2.1 to 40.3 months. Each patient received interval systemic therapy in-between the PolyBC- and MBP-containing samples. At PolyBC sampling, 3 patients were Epstein-Barr virus-positive (EBV+) (patients 12, 17, 19) and 1 EBV-negative (EBV-) (patient 15), the same EBV status as each patient's corresponding MBP. As the samples containing PolyBCs from patients 12, 15, and 19 were sequenced in bulk, determination of whether the shared mutations were present in the PolyBCs could not be performed. However, the private mutations seen in the corresponding MBPs were not identified despite high levels of PolyBCs in these samples. The *CHECK2* mutation in patient 19's PolyBC-containing sample was present at a low allele frequency (VAF) just below our cutoff (0.02) and whether it was present in background myeloid cells or in the PolyBCs could not be determined in this bulk sample. The PolyBCs from patient 17 were flow cytometry-sorted and harbored both the shared and private mutations detected in the MBP but at significantly lower VAFs. The PolyBC sample predated the MBP sample by a short time interval (4.6 months) in this case. The Y axes indicate the VAFs of the mutations detected as well as the fraction of B cells among total cells in each sample (horizonal black bars). The sample descriptions (including tissue site, EBV status, flow cytometry sorted vs bulk, and degree of involvement by other cell types) are indicated on the X axes with the time in-between the samples indicated on the bottom. Dotted lines indicate the VAF cut off of >0.02 used in this study for variant calling. Mutations in orange indicate those shared among the MBPs, TFHLs, and myeloid compartments, those in blue indicate private mutations found in MBPs and not in corresponding TFHLs or myeloid cells, while those in yellow indicate mutations detected in MBPs and myeloid cells but not in TFHLs. Private mutations detected in the TFHLs are not displayed. GE indicates gastroesophageal; LBCL, large B-cell lymphoma; PB, peripheral blood.