Cumulative incidence and factors associated with subsequent myeloid neoplasms in patients with nodal T-follicular helper cell lymphomas

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Supplementary Table 1. Individual Patient Characteristics.

Pt	Other PMH	TFHL subtype	Baseline BM & CBC findings at TFHL diagnosis	Treatment prior to MN	Myeloid Neoplasm (MN)	Time from TFHL to MN, y	Subsequent Course (after MN diagnosis)
73/M	localized prostate cancer (monitored)	AITL	BM: <5% AITL; hypocellular 10-20%; mature trilineage hematopoiesis CBC: WBC 10.2, HGB 10.7, MCV 80, RDW 13.4, PLT 379	CHOEP, BEAM ASCT, romidepsin, duvelisib/bortezomib, EZH2 inhibitor	WHO: MDS-LB ICC: MDS, NOS	8.5	active TFHL and MDS, pursued supportive care, died of disease
72/M	—	AITL	BM: no lymphoma; normocellular 30%; mature trilineage hematopoiesis CBC: WBC 4.0, HGB 12.6, MCV 84, RDW 14.6, PLT 139	CHOEP, romidepsin/ carfilzomib/lenalidomide	WHO: MDS-IB1 -> AML, MR; ICC: MDS-EB -> AML, NOS progression from MDS	3.1	no evidence of TFHL, trial of azacitidine for MDS -> AML, died of disease
63/F	—	AITL	BM: no baseline bone marrow CBC: WBC 5.9, HGB 12.3, MCV 92, RDW 13.1, PLT 205	CHOEP, BEAM ASCT, belinostat, azacytidine	WHO: AML, MR ICC: AML with MR gene mutation	2.6	active TFHL and AML, trial of azacitidine for both, died of disease
74/M	EBV+ B-cell LPD	AITL	BM: no lymphoma; limited specimen, mature trilineage hematopoiesis CBC: WBC 6.6, HGB 13.9, MCV 86, RDW 13.3, PLT 125	lenalidomide-CHOEP, BEAM ASCT, cerdulatinib	WHO/ICC: CMML-1	2.8	CMML observed/not treated, active TFHL and progressive EBV+ B-cell LPD treated with rituximab, died of disease
72/M	IgG λ MM	AITL	BM: <5% AITL; 20% MM; hypercellular 50%, mature trilineage hematopoiesis w/o dysplasia CBC: WBC 6.8, HGB 7.3, MCV 97, RDW 22.2, PLT 224	CHOP	WHO: MDS-IB2 ICC: MDS/AML	2.2	no evidence of TFHL, MDS observed/not treated, progressive DLBCL treated with rituximab, died of disease and infection
81/F	—	TFHL, NOS	BM: +flow TFHL, NOS; mildly hypercellular, mature trilineage hematopoiesis w/ occasional small hypolobated megakaryocytes	mini-CHOP, romidepsin/duvelisib, investigational SIRPα-IgG1 Fc (anti-CD47)	WHO: AML, MR ICC: AML, NOS	1.8	AML treated with azacitidine/venetoclax with CR, then progressive TFHL, died of disease

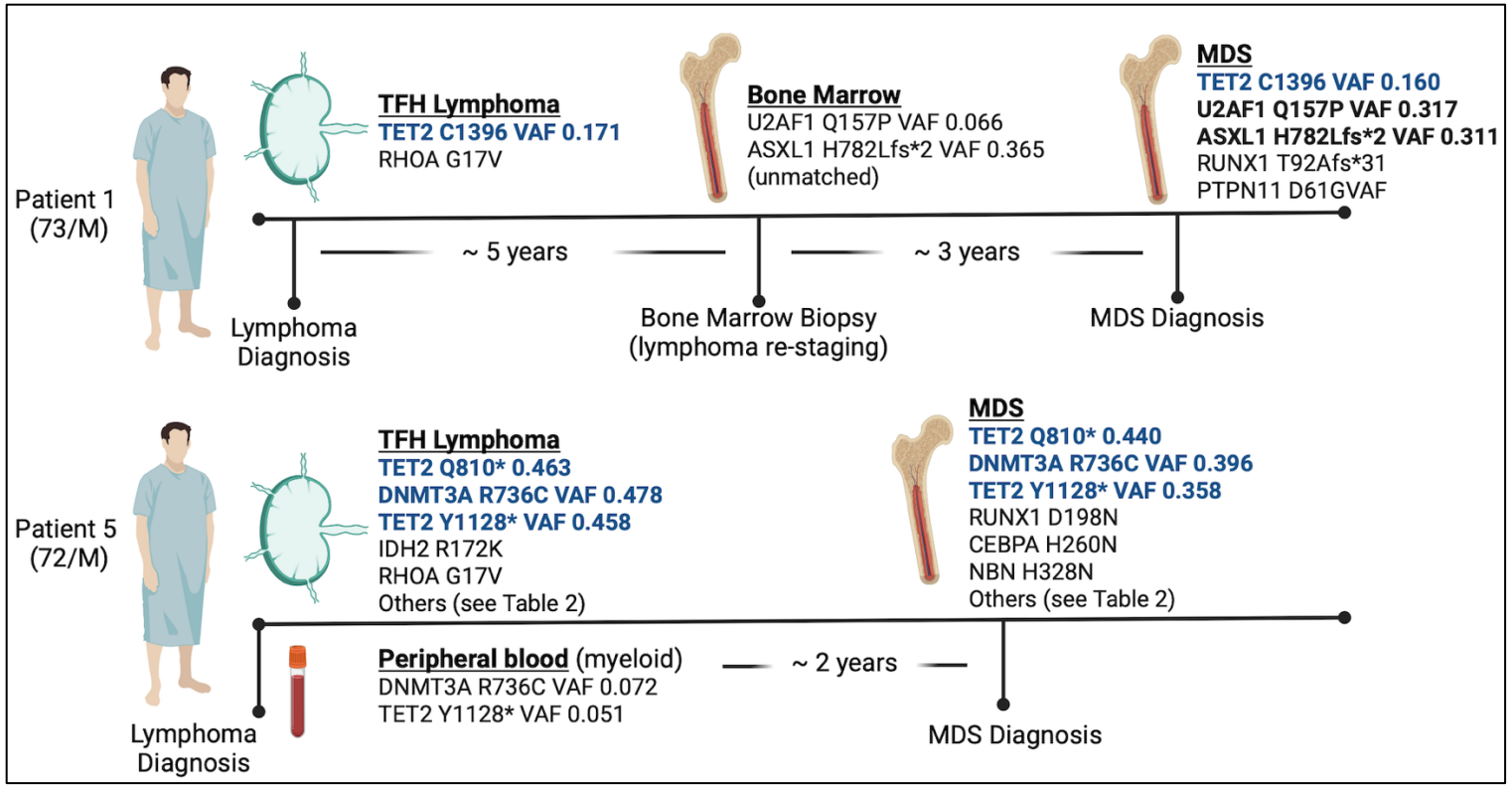
			CBC: WBC 9.6, HGB 10.1, MCV 96, RDW 14.7, PLT 360				
55/M	psoriasis, prior adalimumab	AITL	BM: limited specimen with crush artifact, involved w/ AITL; no overt dysplasia CBC: missing baseline values (started treatment outside of institution)	CHOEP/CHOP (CHOEP x 1, then CHOP), BEAM ASCT, romidepsin	WHO: MDS-LB ICC: MDS, NOS	1.2	active TFHL and MDS, pursued supportive care, died of disease and infection
71/F	breast ca s/p TAC 12 y pre-T-cell dx	AITL	BM: no baseline bone marrow CBC: WBC 7.3, HGB 12.5, MCV 89, RDW 13.9, PLT 331	BV-CEP, romidepsin/duvelisib, EZH2 inhibitor	WHO/ICC: CNL	2.2	CNL observed, active TFHL, pursued supportive care, died of disease
58/M	—	AITL	BM: <5% AITL; hypercellular 60%, mature trilineage hematopoiesis, unremarkable myeloid and megakaryocytic elements CBC: WBC 8.6, HGB 6.4, MCV 89, RDW 15.1, PLT 216	CHOEP, BEAM ASCT	WHO: AML, MR ICC: AML with MR gene mutation	1.3	no evidence of TFHL, AML treated with FLAG-IDA, died post-allogeneic transplant for AML
74/M	head/neck SCC s/p RT 7 m pre T-cell dx	AITL	BM: 10-15% AITL; hypercellular 90% w/ mature trilineage hematopoiesis; mildly hyperplastic myeloid lineage without frank dysplasia or morphologic evidence of MN CBC: missing baseline values (started treatment outside of institution)	CHOP, ruxolitinib/duvelisib, azacitidine	WHO: MDS-LB ICC: MDS, NOS	1.0	active TFHL and MDS, continued treatment with azacitidine, died of disease

AITL, angioimmunoblastic type; AML, acute myeloid leukemia; ASCT, autologous stem cell transplant; BV, brentuximab vedotin; BEAM, carmustine, etoposide, cytarabine, melphalan; CBC, complete blood count; CHOEP, cyclophosphamide, doxorubicin, vincristine, etoposide, prednisone; CHOP, cyclophosphamide, doxorubicin, vincristine, prednisone; CMML, chronic myelomonocytic leukemia; CNL, chronic neutrophilic leukemia; DLBCL, diffuse large B-cell lymphoma; dx, diagnosis; EB, excess blasts; EBV, Epstein-Barr virus; FLAG-IDA, fludarabine, cytarabine, granulocyte colony stimulating factor, idarubicin; IB, increased blasts; HGB, hemoglobin, g/dL; LB, low blasts; LPD, lymphoproliferative disorder; MDS, myelodysplastic syndrome; M, male; MCV, mean corpuscular volume, fL; MM, multiple myeloma; MR, MDS related; NOS, not otherwise specified; PLT, platelets, K/mcL; PMH, past medical history; RDW, red blood cell distribution width, %; RT, radiotherapy; SCC, squamous cell carcinoma; TAC, docetaxel, doxorubicin, cyclophosphamide; TFH, T-follicular helper cell; w/, with; w/o, without; WBC, white blood cell count, K/mcL; y, years.

Supplementary Table 2. Univariate Analysis for Patient- and Treatment-Related Factors.

Variable	UVA HR (95% CI)	P Value
Age at diagnosis > 60	1.2 (0.3-5.8)	0.8
Sex		
Male	1.8 (0.5-6.8)	0.4
Female	Ref.	
Induction		
CHOP	Ref.	0.5
Etoposide-based	0.6 (0.2-2.1)	
BV-CHP	—	
Other	—	
Observation	—	
ASCT		
Yes	1.5 (0.4-5.2)	0.5
No	Ref.	
Etoposide use (any time)	0.9. (0.2-3.3)	0.8

ASCT, autologous stem cell transplant; BV, brentuximab vedotin; CHOP, cyclophosphamide, doxorubicin, vincristine, prednisone; UVA HR, univariate analysis hazard ratio.



Supplementary Figure 1. Schematic representation of two representative patients. Patient 1 was a 73-year-old male with TFH lymphoma who subsequently developed myelodysplastic syndrome (MDS) eight years after lymphoma diagnosis. At baseline, this patient had *TET2* and *RHOA* mutations detected in lymphoma. Five years after diagnosis, restaging bone marrow for lymphoma treatment purposes showed new *U2AF1* and *ASXL1* mutations (note that this was an unmatched sample). This marrow was without morphological evidence of MDS. Three years later, the patient was diagnosed with MDS, which showed the same *TET2* mutation detected eight years prior in the lymphoma, as well as the *U2AF1* and *ASXL1* mutations detected in the bone marrow three years prior. Patient 2 was a 72-year-old male with TFH lymphoma who subsequently developed MDS two years later. At baseline, this patient had two TET2 mutations and a DNMT3A mutation (among others) in lymphoma. In the peripheral blood, there was a shared TET2 and DNMT3A mutation, though at elevated VAF consistent with presence in the myeloid component, as there was only a minute abnormal T-cell population detected by flow cytometry. Two years later, the patient was diagnosed with MDS, which showed the same TET2 and DNMT3A mutations which had been previously detected, in addition to several other mutations.