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POSTER ABSTRACTS

624.HODGKIN LYMPHOMAS AND T/NK CELL LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Cumulative Incidence of Myeloid Neoplasms in Patients with Nodal T-Follicular Helper Cell Lymphoma

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Introduction:
Certain T-cell lymphomas (TCL), in particular nodal T-follicular helper (TFH) cell lymphomas, including angioimmunoblastic TCL (AITL), commonly develop on a background of mutations identified in clonal hematopoiesis (CH). Divergent clonal evolution can result in both nodal TFH cell lymphomas and myeloid neoplasms (MN). As peripheral TCLs are commonly treated with combination and dose intensive chemotherapy, there is a risk that these therapies could promote an evolution to MN. The frequency at which this occurs is unclear.

Methods:
We conducted a retrospective search for any patient with an International Classification of Disease (ICD) code referring to a TCL. Then, we identified patients with a concomitant ICD code referring to either myelodysplastic syndromes (MDS), acute-myeloid leukemia (AML), or a myeloproliferative neoplasm (MPN). Once the initial query was performed, we individually reviewed each patient and included only patients meeting the following criteria: (1) A histologically-confirmed diagnosis of either peripheral TCL, not otherwise specified (PTCL-NOS) or nodal TFH cell lymphoma by an MSK hematopathologist between 1/1/02 and 7/1/23; (2) Presentation to MSK at lymphoma diagnosis; (3) At least 6 months of follow-up (unless death from lymphoma); (4) if relevant, a histologically-confirmed diagnosis of a MN by an MSK hematopathologist.
Histological diagnoses were recorded as documented in the pathology electronic record in accordance with the WHO criteria in place *at the time* of diagnosis. In particular, at our center, prior to 2016, cases of PTCL-NOS were not routinely assessed for TFH phenotype, as nodal TFH cell lymphoma was only added to the WHO classification in 2016. Cases documented herein as PTCL-NOS were not re-reviewed to determine TFH phenotype. Only patients who received systemic treatment were included (systemic steroids were *not* considered systemic treatment). CI of MN was evaluated using the reverse Kaplan-Meier method treating death as a competing risk.

Results:
We identified a total of 376 patients with either PTCL-NOS (N=178) or nodal TFH cell lymphoma (N=198; AITL N=184; nodal TFH cell lymphoma, NOS N=13; nodal TFH cell lymphoma, follicular-type=1). In total, 24 patients with a MN and either PTCL-NOS or nodal TFH cell lymphoma were identified. Nine had a MN that preceded the TCL diagnosis (AML: 2; MDS: 1; myelofibrosis: 2; CMML: 2; MDS/MPN: 1; polycythemia vera: 1)-these patients were excluded for CI calculation. Fifteen patients were diagnosed with a MN *subsequent* to lymphoma diagnosis and treatment (AML: 5; MDS: 8; CMML: 1; chronic neutrophilic leukemia: 1). Of the 198 patients with nodal TFH cell lymphoma, nine developed a MN. The CI of developing a MN among all patients at 2, 5, 10, and 15 years was 1.1%, 4.4%, 4.8%, and 5.8%. The CI of developing a MN among those with known nodal TFH cell lymphoma at the same timepoints were 1.6%, 4.5%, 5.3% and 7.1%. The median follow up among survivors was 4.1 years (range: 0.5-18).
The median age at MN diagnosis was 72.6 years (range: 45-81), and the median time from lymphoma diagnosis to MN diagnosis was 2.6 years (range: 0.3-10.4). Four patients had either prior RT or chemotherapy for non-lymphoma conditions. Prior to MN diagnosis, ten patients (67%) received etoposide and seven patients (47%) received autologous stem cell transplant (ASCT) (six with BEAM, one with cyclophosphamide plus total body irradiation). The median number of therapies (including ASCT) prior to MN diagnosis was 2 (range: 1-5). At the time of MN diagnosis, 10 patients had relapsed TCL and were receiving

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lymphoma therapy. No patients had undergone alloSCT prior to the diagnosis of a MN. Next generation mutational profiling with MSK-IMPACT-Heme had previously been performed for eight of the 15 patients (on lymphoma tissue). All except one had mutations in *TET2* and/or *DNMT3A*.

Conclusions:

Herein we report the CI of MN in a cohort of patients with TCL, with particular attention to nodal TFH cell lymphomas given known CH mutations and the genotoxic stress of combination chemotherapy. As more patients have prolonged survival after initial therapy for TCL, further analysis, including baseline genetics and prospective characterization for clonal expansion and acquired mutations during therapy, could identify those at highest risk for developing a MN. Further characterization of our cohort and comparison to patients who did not develop a MN is ongoing.

Disclosures Dogan: *Seattle Genetics:* Consultancy; *Physicians' Education Resource:* Consultancy, Honoraria; *EUSA Pharma:* Consultancy; *Loxo:* Consultancy; *Peer View:* Honoraria; *Incyte:* Consultancy; *Takeda:* Other: Research Funding; *Roche:* Other: Research Funding. **Epstein-Peterson:** *Amgen:* Research Funding; *OncLive:* Honoraria; *Kymera:* Research Funding; *Viracta:* Research Funding; *WebMD:* Honoraria. **Ghione:** *Kite, A Gilead Company:* Research Funding; *Kyowa Hakko Kirin:* Consultancy; *Secura Bio:* Consultancy; *AstraZeneca Pharmaceuticals:* Consultancy. **Johnson:** *Myeloid Therapeutics:* Consultancy. **Lewis:** *United States Drug Testing Laboratories:* Consultancy, Membership on an entity's Board of Directors or advisory committees. **Moskowitz:** *Merck:* Honoraria, Research Funding; *Seattle Genetics:* Honoraria, Research Funding; *Bristol-Myers Squibb:* Research Funding; *Incyte:* Research Funding; *Beigene:* Research Funding; *ADC Therapeutics:* Research Funding. **Shah:** *Beyond Spring:* Research Funding; *BMS:* Research Funding; *Janssen:* Research Funding; *Amgen:* Research Funding; *ArcellX:* Other: DSMB. **Scordo:** *Angiocrine Bioscience, Inc.:* Research Funding; *Amgen, Inc.:* Research Funding; *Omeros Corporation:* Consultancy, Research Funding; *Medscape, LLC:* Honoraria; *CancertNetwork (Intellisphere LLC):* Honoraria. **Horwitz:** *Trillium Therapeutics:* Consultancy, Research Funding; *Takeda:* Consultancy, Research Funding; *Affimed:* Research Funding; *Tubulis:* Consultancy; *Yingli Pharma Limited:* Consultancy; *ADC Therapeutics:* Research Funding; *Celgene:* Research Funding; *Auxilius Pharma:* Consultancy; *Shoreline Biosciences, Inc.:* Consultancy; *SecuraBio:* Consultancy; *ONO Pharmaceuticals:* Consultancy; *Kyowa Hakko Kirin:* Consultancy, Research Funding; *Daiichi Sankyo:* Consultancy, Research Funding; *Cimieo Therapeutics:* Consultancy; *Abcuro Inc.:* Consultancy; *Crispr Therapeutics:* Research Funding; *Millenium:* Research Funding; *Seattle Genetics:* Research Funding; *Verastem/SecuraBio:* Research Funding.

Table 1. Cumulative Incidence of Myeloid Neoplasm in Peripheral T-cell Lymphoma.

Years since lymphoma diagnosis	All	Nodal TFH Cell Lymphoma
2	0.0112 (0.00422-0.0298)	0.0164 (0.00531-0.0508)
5	0.0439 (0.0256-0.0751)	0.0445 (0.0213-0.0927)
10	0.0480 (0.0286-0.0806)	0.0533 (0.0267-0.1061)
15	0.0580 (0.0337-0.0997)	0.0709 (0.0350-0.1437)

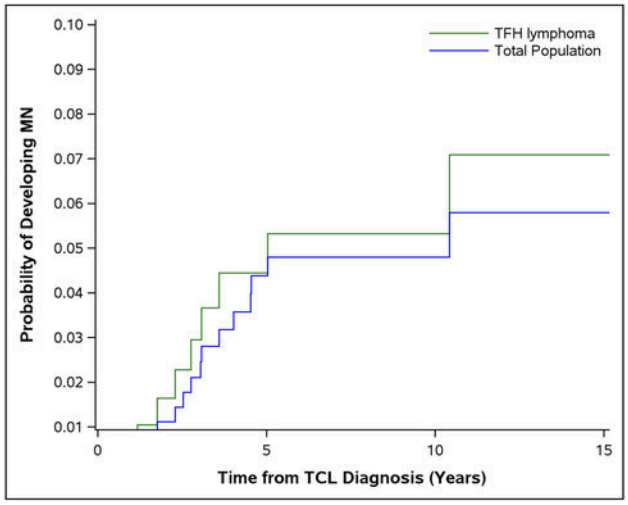

Figure 1

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