Outcomes of patients with refractory Peripheral T-cell lymphoma, Angioimmunblastic and other nodal lymphomas of T follicular helper-cell origin (OPerA)

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Introduction

Peripheral T cell lymphoma not otherwise specified (PTCL-NOS) and angioimmunoblastic T cell lymphoma (AITL) are the 2 most common T-cell lymphoma (TCL) subtypes in the US, accounting for 45% of diagnoses. Primary refractory disease is common, occurring in 25-30% of patients (pts). Even amongst initial responders, relapses are numerous and survival after relapse or progression (R/P) is typically measured in months despite new therapies (Chihara D, et al. *Br J Haem.* 2017). The aim of our study was to determine outcomes in a well-defined group of pts with either primary refractory PTCL-NOS or TFH lymphoma.

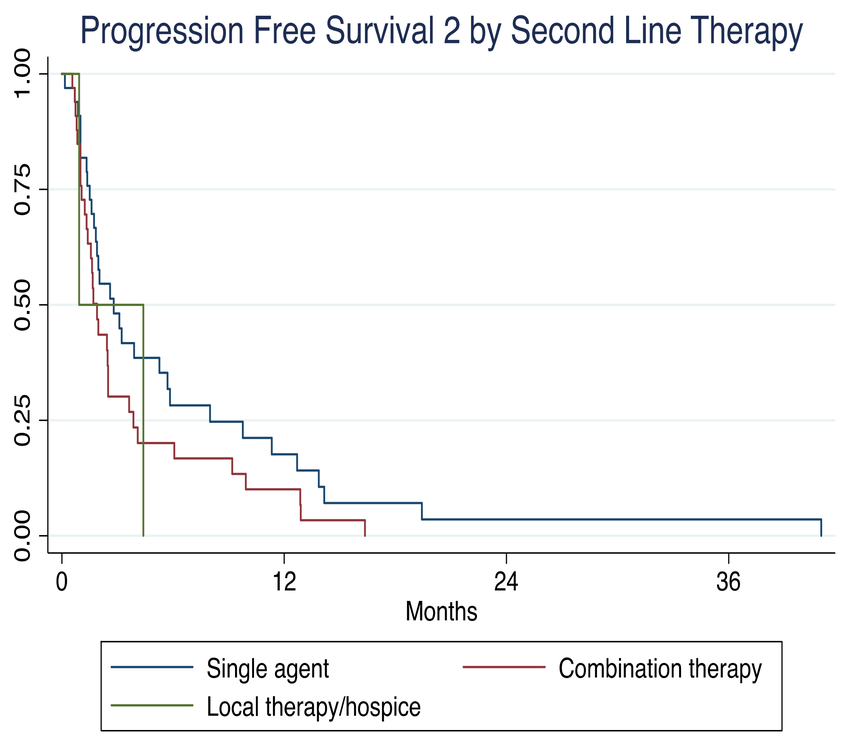
Methods

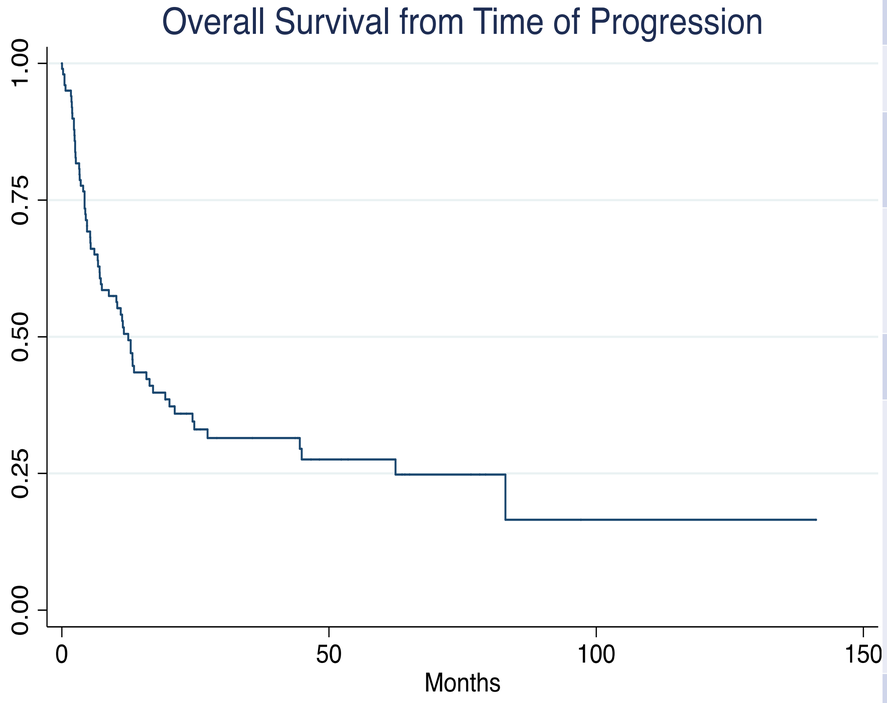
Study Design: We performed a multi-center retrospective study to determine outcomes to 2nd line therapy for adults diagnosed between 1.1.09-6.30.18 with PTCL-NOS or TFH lymphoma, who were primary refractory to initial anthracycline-containing therapy, defined by either induction failure, less than CR, or relapse within 6 months (mo) of completing initial therapy.

Statistical Analysis: PFS 2 was defined as time from 2nd line therapy to progression. Time to event analysis for PFS and OS was calculated using Kaplan-Meier method and comparisons made using log-rank test. Cox regression models were used to determine risk factors of interest. All other statistics were descriptive.

Baseline characteristics (n=107)		At relapse/progression (n=107)
Sex	64% Male 36% Female	
Histologic Subtype	61% PTCL-NOS 39% TFH lymphoma	
Age	65 (21-92)	66(21-92)
Time to treatment	8 days (3-187)	165 days (0-434)
LDH elevated	79%	65%
Platelets <150K	27%	45%
Stage	I: 2% II: 4% III: 32% IV: 62%	I: 4% II: 4% III: 30% IV: 62%
ECOG ≥2	27%	37%
BM involvement	41%	25%
≥2 sites non-BM nodal disease	22%	18%
B Symptoms	55%	32%
Treatment	CHOP: 47% CHOEP: 28% HCVAD: 3% Other: 22%	Romidepsin: 26% Brentuximab vedotin: 17% ICE: 12% ESHAP: 2% Belinostat: 3% Other: 40%
Response to treatment	CR: 47% PR: 13% SD: 8% PD: 32%	CR: 33% PR: 11% SD: 5% PD: 51%
Consolidative HCT	Autologous: 10% Allogeneic: 1%	Autologous: 4% Allogeneic: 4%
Number of subsequent therapies		1 (0-6)

Results





Results

	Progression free survival 2			Overall survival		
	Log Rank test	P-value	Cox Proportional Hazard Multivariate Analysis	Log Rank test	P-value	Cox Proportional Hazard Multivariate Analysis
Age at diagnosis (≤60 vs. ≥61)	57 vs. 75 d	0.14		19 vs. 16.2 mo	0.78	
Sex	59 vs. 75 d	0.95		14.6 vs. 19.4 mo	0.16	
Histologic subtype	74 vs. 55 d	0.74		17.5 vs. 19.4 mo	0.22	
LDH at diagnosis	109 vs. 57 d	0.21		37.2 vs. 16 mo	0.04	
Stage at diagnosis	I: NR II: 51 d III: 93 d IV: 59 d	0.33		I: 16.1 mo II: NR III: 19.4 mo IV: 16 mo	0.97	
ECOG ≥2 at diagnosis	61 vs. 73 d	0.70		18.2 vs. 12.2 mo	0.45	
Platelets <150K at diagnosis	73 vs. 57 d	0.23		18.6 vs. 15.7 mo	0.95	
Bone marrow involvement at diagnosis	78 vs. 49 d	0.93		19.4 vs. 14 mo	0.50	
≥2 site of extranodal disease at diagnosis	61 vs. 51 d	0.30		18.9 vs. 18.2 mo	0.75	
B symptoms at diagnosis	**117 vs. 55 d**	**0.01**	HR 2.2 (1.2-3.81)	19.2 vs. 13.6 mo	0.08	
Initial Treatment	CHOP: 97d CHOEP: 55 d HCVAD: 30 d Other: 47 d	0.42		CHOP: 25.4 mo CHOEP: 16.1 mo HCVAD: NR Other: 13.6 mo	0.53	
Consolidation with transplant	**75 vs. 40 d**	**0.002**	HR 2.08 (0.93-4.63)	18.2 vs. 12.6 mo	0.86	
Age at progression (≤60 vs. ≥61)	57 vs. 75 d	0.21		19 vs. 16.2 mo	0.93	
Elevated LDH at progression	78 vs. 73 d	0.03	HR 1.12 (0.64-1.98)	19.4 vs. 14.6 mo	0.13	
Platelets <150K at progression	75 vs. 59 d	0.68		18.6 vs. 16.1 mo	0.96	
≥2 site of extranodal disease at progression	**75 vs. 40 d**	**0.02**	**HR 3.08 (1.46-6.55)**	**19.2 vs. 11.4 mo**	**0.017**	**HR 2.05 (1.04-4.01)**
B symptoms at progression	78 vs. 47 d	0.19		19.2 vs. 13.5 mo	0.27	
ECOG ≥2 at progression	55 vs. 93 d	0.74		19.2 vs. 12.3 mo	0.075	HR 1.5 (0.97-2.66)
Second line treatment category	Single agent: 84 d Combination: 57 d Local/hospice: 28 d	0.25		Single agent: 19 mo Combination: 18.2 mo Local/hospice: 10.5 mo	0.28	HR 1.36 (0.92-2.03)

Conclusions

Outcomes in this large, well-defined population of primary refractory PTCL-NOS and TFH lymphoma were poor, but better compared to other series in R/R TCL. The presence of EN disease at R/P, B symptoms, and ECOG PS ≥ 2 may predict for poor outcomes. Our findings suggest that single agent therapy following R/P in primary refractory pts and transplant may be beneficial, though our statistical power is limited due to small sample size.

Conflicts of Interest

Rhodes: DAVA Oncology: Honoraria. Olszewski: Spectrum Pharmaceuticals: Research Funding; Genentech: Research Funding; Adaptive Biotechnologies: Research Funding; TG Therapeutics: Research Funding. Brammer: Verastem, Inc: Research Funding; Viracta Therapeutics, Inc.: Research Funding; Bioniz Therapeutics, Inc.: Research Funding. Ghosh: TG Therapeutics: Consultancy, Honoraria, Research Funding; Celgene: Consultancy, Research Funding; Janssen: Consultancy, Honoraria, Research Funding, Speakers Bureau; Forty Seven Inc: Research Funding; AstraZeneca: Honoraria, Speakers Bureau; Pharmacyclics LLC, an AbbVie Company: Consultancy, Honoraria, Research Funding, Speakers Bureau; Genentech: Research Funding; SGN: Consultancy, Honoraria, Research Funding, Speakers Bureau; Bristol-Myers Squibb: Honoraria, Speakers Bureau; Gilead: Consultancy, Honoraria, Speakers Bureau. Dwivedy Nasta: Merck: Membership on an entity's Board of Directors or advisory committees; Roche: Research Funding; 47 (Forty Seven): Research Funding; Rafael: Research Funding; Celgene: Honoraria; ATARA: Research Funding; Aileron: Research Funding; Debiopharm: Research Funding; Millenium/Takeda: Research Funding; Pharmacyclics: Research Funding. Barta: Celgene: Research Funding; Janssen: Membership on an entity's Board of Directors or advisory committees; Mundipharma: Honoraria; Seattle Genetics: Honoraria, Research Funding; Takeda: Research Funding; Celgene: Research Funding; Janssen: Membership on an entity's Board of Directors or advisory committees; Bayer: Consultancy, Research Funding; Mundipharma: Honoraria; Merck: Research Funding.

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Lymphoma/CLL

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