ELSEVIER

Blood 142 (2023) 3123–3126

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

627.AGGRESSIVE LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Diagnosis to Treatment Interval (DTI) Informs Outcomes across Subtypes of Aggressive B-Cell Lymphoma

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Background: Shorter diagnosis to treatment interval (DTI) has been shown to be associated with more aggressive disease features and inferior outcomes in diffuse large B-cell lymphoma (DLBCL; Maurer et al, JCO 2018). Additional confirmatory studies have also shown that DTI is related to tumor volume (Alig et al, JCO 2021) and molecular phenotype (Aluaij et al, Blood 2023). Here we evaluate DTI in a large multicenter cohort of patients prospectively enrolled and followed as part of the Lymphoma Epidemiology of Outcome (LEO) cohort.

Methods: Patients were enrolled within 6 months of diagnosis at one the 8 LEO cohort academic medical centers in the United States between 2015 and 2020. Patients in this analysis had aggressive B-cell lymphoma (BCL) treated with anthracycline-based chemotherapy. DTI was defined as the initial lymphoma biopsy date until the start of initial chemotherapy; patients with DTI between 0-100 days were evaluated. Short DTI was defined as DTI $\leq$ 14 days (DTI$\leq$14) as previously described in prior publications (e.g. Maurer et al, JCO 2018) and confirmed via examination of functional forms via splines. Event-free survival (EFS) was defined as the time from start of treatment until progression/relapse, retreatment, or death due to any cause. Overall survival (OS) was defined as the time from start of treatment until death due to any cause.

Results: 2565 patients with aggressive B-cell lymphoma were evaluated. Median age was 62 years (IQR 51-71) and 1469 (57%) were male. 297 patients (12%) were self-reported non-White race and 314 patients (12%) were self-reported Hispanic or Latino. The majority had DLBCL, NOS subtype (N=1927, 75%), while 227 (9%) had high-grade BCL with MYC and BCL2 and/or BCL6 rearrangements (HG, DH) and 90 (4%) had high-grade BCL NOS (HG, NOS). Clinical characteristics are summarized in the **table**. At median follow-up of 49 months (IQR 36-68), 800 patients (31%) had an event and 578 patients (23%) died. EFS at 24 months (EFS24) was 76% (95% CI: 74-77).

Median DTI across all subtypes was 21 days (IQR 12-33) and 845 patients (33%) had DTI$\leq$14. Patients with DTI$\leq$14 were significantly younger (median age 59 years) but there was no association between DTI and gender, race, or ethnicity. Patients with DTI$\leq$14 were more likely to have HG, DH or HG NOS subtypes, ECOG PS 2-4, advanced stage, elevated LDH, CNS involvement, B symptoms, and bulky disease (**see table**). Patients with DTI$\leq$14 were more likely to receive R-EPOCH-based or intensive therapies (41%) and less likely to receive 1L therapy on a clinical trial (3.8%) compared to DTI>14 (26% and 10.1%,

respectively). Consistent with previously reported data, DTI≤14 was associated with inferior EFS (HR=1.62, 95% CI: 1.41-1.87, **figure**), OS (HR=1.73, 95% CI: 1.47-2.04), and EFS24 (OR=1.93, 95% CI: 1.60-2.38). The association between DTI and outcomes remained significant after stratifying for subtype (EFS HR=1.68, 95% CI: 1.46-1.94; OS HR=1.78, 95% CI: 1.50-2.10) and adjustment for IPI (EFS HR=1.43, 95% CI: 1.24-1.65; OS HR=1.47, 95% CI: 1.24-1.74).
In subset analysis, DTI≤14 was significantly associated with inferior outcomes within the subtypes of HG, DH (EFS HR=2.70, 95% CI: 1.82-4.01; OS HR=2.97, 95% CI: 1.92-4.60); HG, NOS (EFS HR=2.07, 95% CI: 0.93-4.60; OS HR=2.36, 95% CI: 1.03-5.43); and DLBCL, NOS (EFS HR=1.51, 95% CI: 1.27-1.78; OS HR=1.52, 95% CI: 1.45-1.85). Analysis was limited in other subtypes due to number of events. Notably, within the subset of patients with DTI>14, there was no significant difference in EFS between subtypes for DLBCL, NOS (EFS24=80%, EFS HR=ref), HG, DH (EFS24=73%, EFS HR=1.26, 95% CI: 0.92-1.73) and HG, NOS (EFS24=83%, EFS HR =0.84, 95% CI: 0.40-1.78), logrank p=0.29; similar results were observed for OS (p=0.22).
Conclusions: Patients requiring early initiation of therapy for aggressive B-cell lymphoma represent a distinct population of patients with more aggressive clinical features and inferior outcomes. In patients with longer DTI, high grade subtypes had similar outcomes to DLBCL, NOS. Efforts should be made to include patients with anticipated short DTI in clinical trials and translational studies to fully capture the spectrum of patients with aggressive B-cell lymphoma.

Disclosures Maurer: *AstraZeneca:* Membership on an entity's Board of Directors or advisory committees; *Adaptive Biotechnology:* Membership on an entity's Board of Directors or advisory committees; *GenMab:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *BMS:* Consultancy, Research Funding; *Roche/Genentech:* Research Funding; *Morphosys:* Research Funding. **Nowakowski:** *F Hoffmann-La Roche Limited:* Consultancy; *Curis:* Consultancy; *Ryvu Therapeutics:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Bantam Pharmaceutical LLC:* Consultancy; *Selvita Inc:* Consultancy; *Genentech:* Consultancy; *Kite Pharma:* Consultancy; *Incyte:* Consultancy; *MorphoSys:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Research Funding; *TG Therapeutics:* Consultancy; *Abbvie:* Consultancy; *Debiopharm:* Consultancy; *Fate Therapeutics:* Consultancy, Membership on an entity's Board of Directors or advisory committees; 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Wellcome Fund: Research Funding; *Eastern Cooperative Oncology Group:* Research Funding; *Cellectis:* Research Funding; *Genmab:* Consultancy; *SeaGen:* Consultancy. **Nastoupil:** *Gilead Sciences/Kite Pharma:* Honoraria, Research Funding; *AstraZeneca:* Honoraria; *Regeneron:* Honoraria; *Genentech, Inc., Genmab, Gilead/Kite, Janssen, Merck, Novartis, Takeda:* Honoraria, Research Funding; *Daiichi Sankyo:* Honoraria, Research Funding; *DeNovo:* Honoraria; *Caribou Biosciences:* Honoraria, Research Funding; *Bristol Myers Squibb/Celgene:* Honoraria, Research Funding; *AbbVie:* Honoraria; *ADC Therapeutics:* Honoraria.

	DTI 15-100 days (N=1720)	DTI 0-14 days (N=845)	Total (N=2565)	p value
Age, median (IQR)	63 (53-72)	59 (45-70)	62 (51-71)	<0.0001
Male (%)	985 (57.3%)	484 (57.3%)	1469 (57.3)	0.99
Non-White Race (%)	201 (11.7%)	96 (11.4%)	297 (11.6%)	0.81
Hispanic/Latino (%)	212 (12.3%)	102 (12.1%)	314 (12.2%)	0.93
Subtype				
Burkitt	24 (1.4%)	49 (5.8%)	73 (2.8%)	
PMBCL	47 (2.7%)	51 (6.0%)	98 (3.8%)	
DLBCL, NOS	1364 (79.3%)	563 (66.6%)	1927 (75.1%)	<0.0001
High Grade DH	134 (7.8%)	93 (11.0%)	227 (8.8%)	
High Grade, NOS	45 (2.6%)	45 (5.3%)	90 (3.5%)	
Other	106 (6.2%)	44 (5.2%)	150 (5.8%)	
ECOG PS 2-4 (%)	201 (12.4%)	208 (26.4%)	409 (17.0%)	<0.0001
Stage III/IV (%)	954 (58.2%)	593 (73.6%)	1547 (63.2%)	<0.0001
>1 Extranodal Site (%)	417 (24.7%)	280 (33.7%)	697 (27.7%)	<0.0001
LDH > ULN (%)	734 (48.6%)	546 (73.0%)	1280 (56.7%)	<0.0001
CNS Involvement (%)	29 (1.7%)	44 (5.2%)	73 (2.8%)	<0.0001
B Symptoms (%)	507 (29.5%)	323 (38.2%)	830 (32.4%)	<0.0001
Bulky Disease (>=7cm, %)	499 (33.0%)	340 (47.4%)	839 (37.6%)	<0.0001
Initial Treatment				
R-CHOP-based	1201 (69.8%)	483 (57.2%)	1684 (65.7%)	
R-EPOCH-based	411 (23.9%)	283 (33.5%)	694 (27.1%)	<0.0001
Intensive	25 (2.0%)	55 (6.5%)	90 (3.5%)	
Other	73 (4.2%)	24 (2.8%)	97 (3.8%)	
Initial Treatment on Clinical Trial (%)	174 (10.1%)	32 (3.8%)	205 (8.0%)	<0.0001

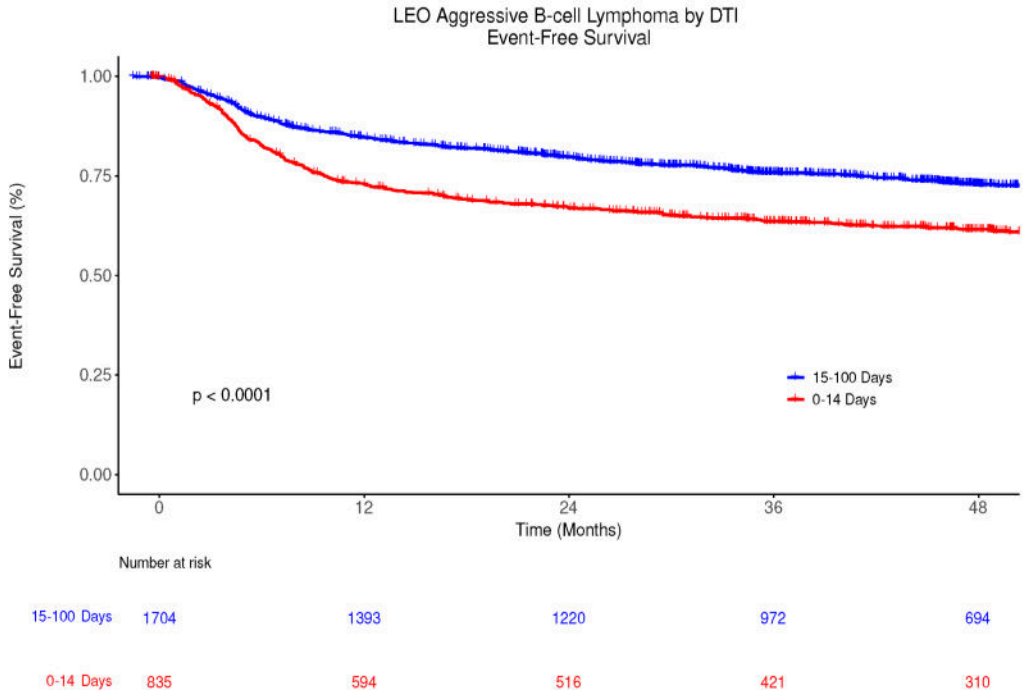

Figure 1

https://doi.org/10.1182/blood-2023-174715