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POSTER ABSTRACTS

905.OUTCOMES RESEARCH-LYMPHOID MALIGNANCIES

Use of Prephase Steroids in Older Patients Treated for Diffuse Large B-Cell Lymphoma

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Background

Treatment related morbidity and mortality (TRM) are significant contributors to overall morbidity and mortality for elderly patients with diffuse large B-cell lymphoma (DLBCL). Several studies have shown that TRM is greatest during the first two cycles of treatment. While attenuated doses of standard-of-care treatment regimens (such as R-mini-CHOP) are commonly used to reduce TRM, one additional strategy that has shown promise is the use of glucocorticoids prior to initiation of systemic chemoimmunotherapy (CIT). This approach, defined as *prephase* steroid use, has been evaluated in small studies, primarily single-center and retrospective in nature. However, older patients with comorbidities are both at greatest risk of TRM and less frequently included in clinical trials. Moreover, patient populations may differ across clinical settings. We conducted an analysis of prephase steroid use in a broader, real-world population treated across multiple centers.

Methods

We used longitudinal data from the US nationwide, Flatiron Health electronic health record-derived de-identified database. We included patients aged >60 with a diagnosis of DLBCL treated with CIT. This included high-grade B-cell lymphoma, but omitted diagnoses of Burkitt's or primary CNS lymphoma. We utilized a prespecified data analysis plan to determine whether outcomes differed by our exposure of interest, use of prephase steroids.

The primary outcome measure was the combined endpoint of time to start of next treatment or death (real-world time to next treatment [rwTTNT]). The secondary outcome was real-world overall survival (rwOS). Outcomes were measured from frontline treatment start date. We also assessed rates of dose delays to evaluate whether prephase steroid use facilitates the maintenance of dose intensity.

Prephase steroid use (the exposure) was defined as an order or administration for steroids occurring 5-21 days prior to the start of antineoplastic therapy (excluding steroids used as part of a standard treatment regimen). Patients were stratified by use of anthracycline-based CIT, with sensitivity analyses conducted limited to the anthracycline CIT group. To reduce confounding, we used propensity score-based inverse probability of treatment weighting (IPTW) for the primary analysis. Time to event endpoints were assessed using weighted Kaplan-Meier curves and log-rank tests. Odds of dose delays were assessed using weighted logistic regression.

Results

We included 3587 patients meeting our criteria, of whom 569 (15.9%) received prephase steroids prior to first-line CIT. A greater percentage of patients treated with anthracycline-based CIT received prephase steroids as compared to those treated with non-anthracyline CIT: 16.3% vs 12.4%, respectively (Table 1).

In adjusted analysis using IPTW, there was no significant difference in the rwTTNT by prephase steroid use (p=0.807, Figure 1). Median rwTTNT was 41.2 months (95% CI, 34.6 to 52.4) vs 40.8 months (95% CI, 35.1 to 46.7) with and without prephase steroids, respectively. There was no difference in median rwOS by prephase steroid use: 65.7 months (95% CI, 52.4 to 84.8) vs 74.8 months (95% CI, 67.4 to 82.5) (p=0.707). No differences were seen in sensitivity analyses limiting to patients treated with anthracycline-based CIT.

For dose delays, adjusted analysis showed a numerically lower odds of dose delay in patients administered prephase steroids in the total study population: 40.6% vs 50.7% (OR 0.796; p=0.0569).

Discussion

In this retrospective study of 3587 real-world, elderly patients with DLBCL, prephase steroid use within 21 days of induction CIT did not improve the rwTTNT or rwOS. There was a suggestion that use of prephase steroids may promote maintenance of dose intensity by reducing delays in CIT administration, though this finding did not reach statistical significance.
The strengths of this analysis included use of a large, nationwide, real-world dataset and propensity score methods to control for confounding. Limitations include the retrospective nature of the study and potential for unmeasured confounding. In summary, in a real-world cohort of older patients with DLBCL, use of prephase steroids was not associated either with longer TTNT/death, or with longer OS. However, it may be associated with maintenance of CIT dose intensity. This finding is worth exploring in future studies.

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Table 1. Patient and Disease Characteristics by Prephase Exposure.

	No Prephase (N=3018)	Prephase (N=569)
Age at Diagnosis (years)		
Mean (SD)	72.8 (7.2)	73.4 (6.9)
Disease Subtype		
DLBCL, NOS	2725 (90.3%)	508 (89.3%)
Double-hit lymphoma	178 (5.9%)	34 (6.0%)
Other*	115 (3.8%)	27 (4.7%)
Gender		
F	1340 (44.4%)	247 (43.4%)
M	1676 (55.5%)	322 (56.6%)
Race		
Black or African American	142 (4.7%)	22 (3.9%)
White	2120 (70.2%)	425 (74.7%)
Other Race / Unknown	756 (25.1%)	122 (21.4%)
Ethnicity		
Hispanic/Latino	157 (5.2%)	32 (5.6%)
Not Hispanic/Latino	2270 (75.2%)	444 (78.0%)
Unknown	591 (19.6%)	93 (16.3%)
ECOG Performance Status		
0	710 (23.5%)	148 (26.0%)
1	778 (25.8%)	169 (29.7%)
2	369 (12.2%)	57 (10.0%)
3-4	159 (4.6%)	21 (3.7%)
Unknown	1022 (33.9%)	174 (30.6%)
Insurance Type		
Commercial	1011 (33.5%)	205 (36.0%)
Medicaid	159 (5.2%)	28 (4.9%)
Medicare	435 (14.4%)	106 (18.6%)
Medicare/Commercial	907 (30.1%)	163 (28.6%)
Other	126 (4.2%)	21 (3.7%)
Unknown	380 (12.6%)	46 (8.1%)
Disease Stage (I/II or III/IV)		
I/II	744 (24.7%)	151 (26.5%)
III/IV	1563 (51.8%)	282 (49.6%)
Unknown/Not Documented	711 (23.6%)	136 (23.9%)
Transformation		
No	2460 (81.5%)	468 (82.2%)
Yes	558 (18.5%)	101 (17.8%)
Treatment		
Anthracycline CIT	2643 (87.6%)	516 (90.7%)
Non-Anthracycline CIT	375 (12.4%)	53 (9.3%)
LDH (units/L)		
Median (IQR; Q1,Q3)	255.5 (184.8,445.3)	261 (184.5,466.0)
Missing	1394 (46.2%)	170 (29.9%)
SES Quintile		
1 (lowest SES)	416 (13.8%)	68 (12.0%)
2	529 (17.5%)	99 (17.4%)
3	559 (18.5%)	116 (20.4%)
4	623 (20.6%)	119 (20.9%)
5 (highest SES)	604 (20.0%)	123 (21.6%)
Not Documented	287 (9.5%)	44 (7.7%)

* Other Disease Subtype histology includes: EBV+ DLBCL, Primary cutaneous DLBCL, leg type, Primary mediastinal B-cell lymphoma, T-cell/Histiocyte-rich large B-cell lymphoma. These are combined due to small individual case representation.

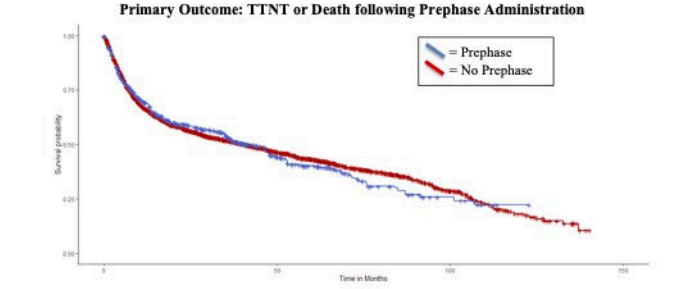

Figure 1. IPTW adjusted Kaplan Meier curve for TTNT or death for all evaluable patients who received CIT. No difference in TTNT or death was seen by prephase steroid exposure.

Figure 1

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