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ORAL ABSTRACTS

627.AGGRESSIVE LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

LEO Consortium for Real World Evidence (CReWE): Outcomes after Second-Line Therapy in Large B-Cell Lymphoma By Treatment Era

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Background: Recently, large B-cell lymphomas (LBCLs) have undergone major shifts in classification and treatment paradigm, particularly with the advent of CD19-targeted chimeric antigen receptor T cell therapy (CAR-T). Initially approved as third-line treatment in LBCL in 2017, as of early 2022 CAR-T is indicated for second-line therapy (2L) in patients with relapsed or refractory (R/R) disease within 12 months of frontline treatment or who are not candidates for autologous stem cell transplant (ASCT). Given this quickly changing landscape, we aimed to describe disease characteristics, patterns of care, and survival outcomes in patients with R/R LBCL receiving two or more lines of systemic therapy across modern treatment eras.
Methods: We developed a database of patients with R/R LBCL from 8 U.S. academic centers in the Lymphoma Epidemiology of Outcomes (LEO) Cohort study (NCT02736357) and Consortium for Real World Evidence (CReWE). Unlike the SCHOLAR-1 dataset (M Crump et al, *Blood* 2017), our cohort included any patient receiving 2L, regardless of timing of progression/relapse. For this analysis, eligible patients were aged ≥18 years and received 2L between 2002-2022. Patients with histologic transformation, post-transplant lymphoproliferative disorder, primary CNS lymphoma, primary mediastinal B-cell lymphoma, Burkitt lymphoma, or plasmablastic lymphoma were excluded. Prognostic factors, therapy details (including intent for ASCT and/or CAR-T), and outcomes, including treatment response, event-free survival (EFS), and overall survival (OS), were abstracted for all lines of therapy. Treatment eras were defined as pre-CAR-T (2002-2010), CAR-T available via clinical trial (2011-2017), and post-FDA approval of CAR-T (2018-2022).
Results: Of 1760 patients initiating 2L for R/R disease, 1523 were eligible for analysis. Median age at start of 2L was 62 (interquartile range [IQR] 53-70), and 65% were male; 11% were non-White, and 8% were Hispanic. High-grade subtypes comprised 16% of all cases. IPI was available for 1013 patients at time of 2L therapy, with 54% having IPI 3-5. Median time from diagnosis to 2L was 8.7 months (IQR 5.6-18.5), with 834 patients not having achieved complete response (CR) to 1L, 285 patients relapsing <12 months after 1L, and 404 patients relapsing ≥12 months after 1L. The median number of total lines

of therapy received was 4 (range 2-18), with 586 and 347 receiving ASCT and CAR-T, respectively, at any line of treatment. At a median follow-up of 48 months from the start of 2L, 926 patients (61%) had died. Progressive lymphoma was the primary cause of death in 75% of deceased patients, with 8% of reported deaths due to therapy.

2L was received at an academic medical center in 83% cases, and 209 patients (14%) received 2L on a clinical trial. ASCT and/or CAR-T was planned at 2L for 989 patients (65%), of whom 463 ultimately received ASCT, 88 received CAR-T, and 21 received allogeneic transplant at 2L. 494 patients were not considered for ASCT or CAR-T at 2L, and 40 were unknown for ASCT/CAR-T intent. Breakdown by treatment era (n = 1518 with available treatment start date) is shown in the Table.

Median EFS from start of 2L was 4.2 months (95% confidence interval [CI]: 3.8-4.8). Median OS from start of 2L was 18 months (95% CI: 17-22), and 2- and 5-year OS estimates were 46% (95% CI: 44-49%) and 35% (95% CI: 33-38%), respectively. EFS and OS improved significantly for patients initiating 2L between 2011-2017 compared to 2002-2010. However, EFS and OS in the 2018-2022 era remained similar to 2011-2017 (Figure).

Conclusions: To our knowledge, this study is the first-ever large-scale attempt to describe patterns of care and outcomes in LBCL 2L in the modern era, inclusive of all treatment approaches. The rich and unique LEO CReWE dataset captures evolving practice approaches over time in terms of both intent for and receipt of cellular therapies. Likely reflecting the rapid development of many novel immune effector cell products and bispecific antibodies, we observed increased enrollment on 2L clinical trials in the 2018-2022 period, including a substantial proportion of patients receiving CAR-T in 2L. Importantly, survival increased in treatment eras during which CAR-T was available. Ongoing analyses of factors associated with improved survival will be presented at the meeting.

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Table. Large B-cell lymphoma patient characteristics and outcomes at second-line therapy (2L) by era in the LEO CReWE database.

	2002-2010 (n = 275)	2011-2017 (n = 576)	2018-2022 (n = 667)	All (n = 1518)
Median age at diagnosis (years)	62	60	64	62
Median time from diagnosis (months)	7.7	8.4	8.9	8.4
IPI 3-5 at 2L	59%	48%	58%	54%
High-grade subtype	8%	15%	19%	16%
Achieved <CR to 1L	60%	55%	52%	55%
Achieved CR to 1L	40%	45%	48%	45%
Relapse <12 months from 1L	19%	18%	20%	19%
Relapse ≥12 months from 1L	21%	27%	28%	26%
2L at academic medical center	81%	84%	84%	83%
2L on clinical trial	9%	13%	17%	14%
2L EFS24	22%	28%	22%	24%
EFS HR (95% CI)	1.17 (1.00 – 1.36)	*Ref*	1.15 (1.01 – 1.31)	-
2L OS24	38%	47%	48%	46%
OS HR (95% CI)	1.28 (1.08 – 1.51)	*Ref*	0.91 (0.78 -1.06)	-
Received ASCT in 2L	94 (34%)	203 (35%)	166 (25%)	463 (31%)
2L EFS24	49%	57%	51%	54%
2L OS24	64%	74%	80%	74%
Received CAR-T in 2L	-	4 (0.6%)	84 (13%)	88 (6%)
2L EFS24	-	50%	29%	30%
2L OS24	-	75%	44%	46%
Planned for but did not receive ASCT and/or CAR-T at 2L	50 (18%)	153 (27%)	212 (32%)	417 (27%)
Stem cell collection failure	1	5	5	11
Inadequate response to salvage therapy before ASCT	37	93	105	235
Ultimately did not meet criteria for ASCT	6	15	3	24
CAR-T manufacturing failure	-	-	1	1
Inadequate response to pre-CAR-T bridging	-	1	3	4
Ultimately did not meet criteria for CAR-T	-	2	3	5
Inadequate response to salvage therapy precluded proceeding to ASCT or CAR-T	2	13	53	68
Ultimately did not meet criteria for ASCT or CAR-T	-	1	7	10
2L EFS24	6%	4%	7%	6%
2L OS24	20%	28%	31%	29%
Not intended for ASCT or CAR-T	120 (44%)	188 (33%)	183 (27%)	494 (33%)
2L EFS24	8%	15%	23%	11%
2L OS24	23%	34%	39%	33%

Abbreviations: 1L, first-line therapy; ASCT, autologous stem cell transplant; CAR-T, chimeric antigen receptor T cell therapy; CI, confidence interval; CR, complete response; EFS24, 24-month event-free survival; HR, hazard ratio; IPI, International Prognostic Index; OS24, 24-month overall survival.

Figure.

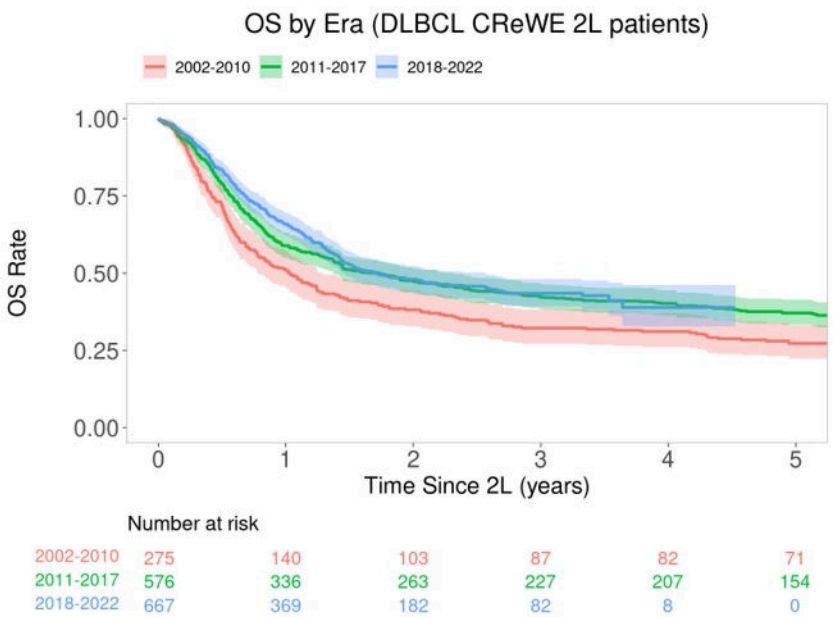

Figure 1