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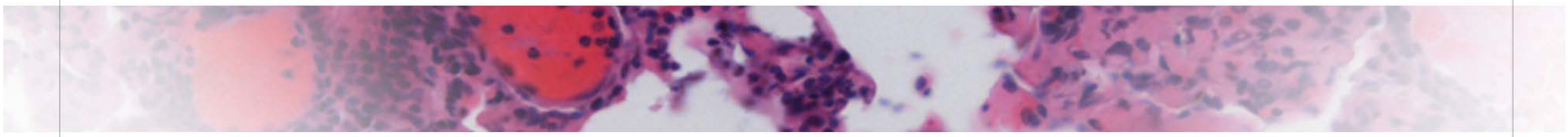

Characteristics and Treatment Patterns of Patients with Relapsed/Refractory Diffuse Large B-cell Lymphoma Who Received ≥3 Lines of Therapies in Post CAR-T Era

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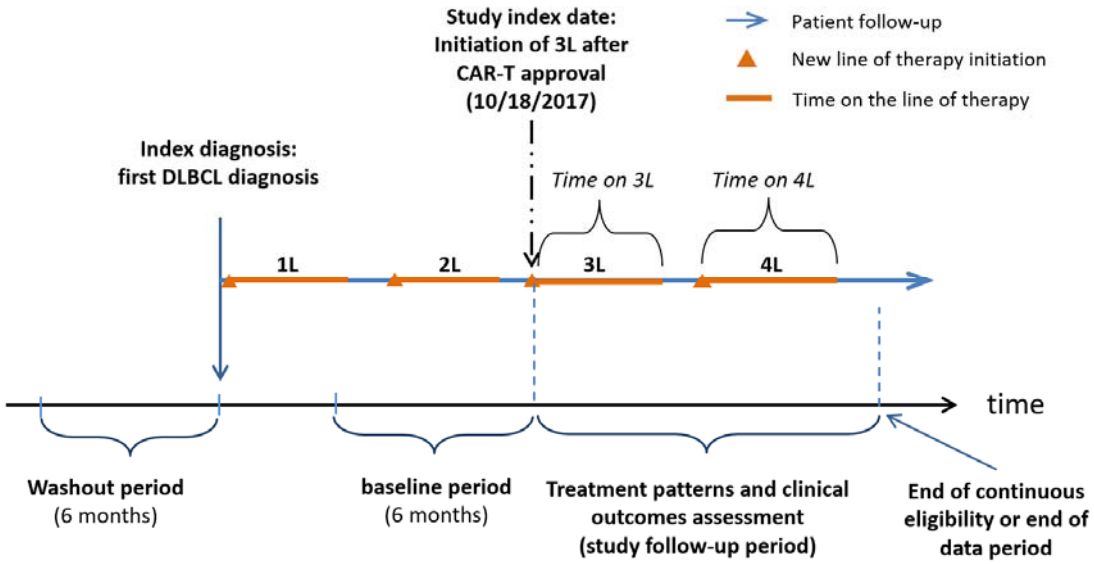
Background and Objectives

- Diffuse large B-cell lymphoma (DLBCL) is an aggressive B-cell malignancy, and the most common form of non-Hodgkin lymphoma (NHL), accounting for approximately one-third of all new cases of NHL[1]
- Approximately 30-40% of patients who undergo first-line treatment relapse or become refractory.[2,3] Patients with refractory/relapse DLBCL (R/R DLBCL) may be treated with salvage therapy, which could be consolidated with autologous stem cell transplant (ASCT) if eligible. However, despite these treatments, the overall prognosis remains poor[2]
- A few novel treatments have been recently approved for the treatment of R/R DLBCL in the ≥3 line setting, such as chimeric antigen receptor T (CAR-T) cell therapy[4,5], polatuzumab, selinexor, and tafasitamab. To date, evidence on the treatment pattern after CAR-T approval is limited
- This study aimed to describe characteristics and treatment patterns of patients with R/R DLBCL who received ≥3 lines of therapy (LOT) using recent real-world data in post CAR-T era (on or after 10/18/2017)

1. American Cancer Society. Types of B-cell lymphoma. https://www.cancer.org/cancer/non-hodgkin-lymphoma/about/b-cell-lymphoma.html
2. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology - B-cell Lymphomas (Version 6.2019)
3. Raut, Lalit S., and Prantar P. Chakrabarti. "Management of relapsed-refractory diffuse large B cell lymphoma." South Asian journal of cancer 3.1 (2014): 66.
4. YESCARTA. Package insert. Kite Pharma, Inc; 2020
5. KYMRIAH. Package insert. Novartis Pharmaceuticals Corporation; 2018

Study Design – A retrospective study using PharMetrics Plus™ administrative claims data (01/01/2014 to 03/31/2020)



A new LOT was indicated by addition of a new drug or re-initiation of the previous LOT after a gap of ≥90 days

- Pharmacologic therapies included
  - Chemotherapy (CT)/chemoimmunotherapy (CIT)
  - Novel agent-based therapy (including brentuximab vedotin, ibrutinib, venetoclax, lenalidomide, obinutuzumab, polatuzumab, nivolumab and pembrolizumab)
- SCT was counted as consolidation therapy instead of a separate line
- CAR-T was counted as a separate line with preparation included (e.g., leukapheresis, bridging therapy, and lymphodepletion)

Results – Sample Selection

≥1 inpatient record or ≥2 outpatient records with a DLBCL diagnosis (**ICD10: C83.3x**) that are ≥60 days apart **between Oct 1, 2015 and Mar 31, 2020 from PharMetrics Plus**
N = 18,223

↓

≥18 years of age on the index diagnosis (*The first DLBCL diagnosis*)
N = 17,955

↓

≥6 months of continuous eligibility prior to the index diagnosis
N = 12,465

↓

No DLBCL diagnosis using ICD-9: 200.7, and no other NHL or other non-NHL hematologic cancers diagnoses before the index diagnosis*
N = 6,171

↓

Removing 31 patients who received SCT only as the 1L treatment without any prior CT/CIT after the index diagnosis
N = 6,140
(Patients with DLBCL)

→

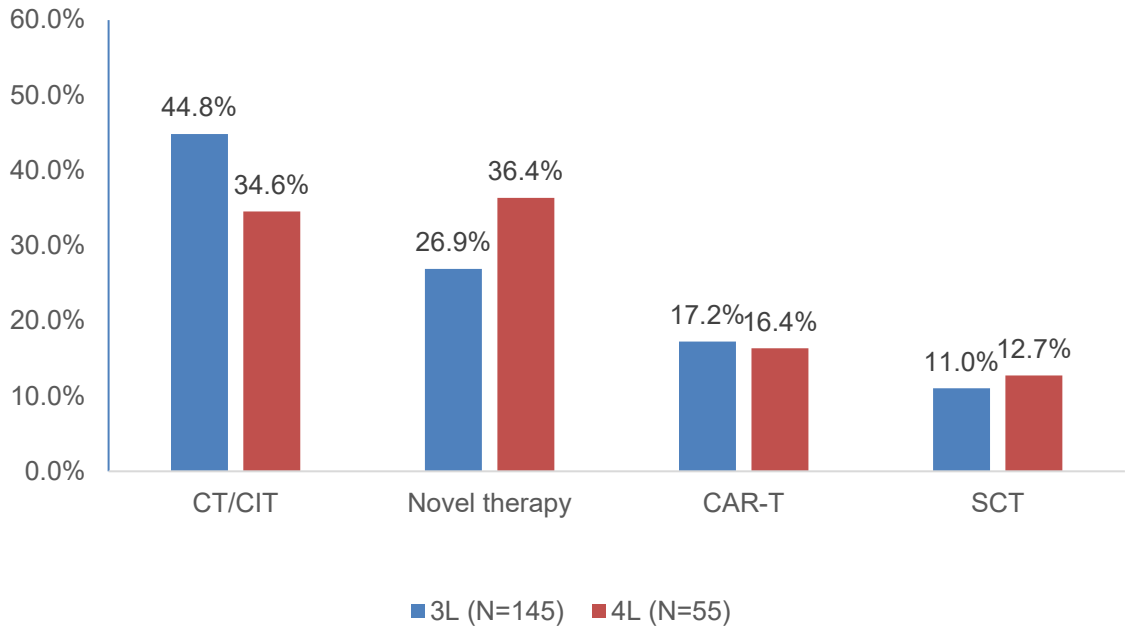
Patients with DLBCL receiving 1L
N=4,172

Receiving 2L
N=675

Receiving 3L after CAR-T approval (10/18/2017)
N=145

* Cancers that can be transformed to DLBCL were allowed before the index diagnosis, including chronic lymphocytic leukemia, marginal zone lymphoma, nodular lymphocyte-predominant Hodgkin's lymphoma, Waldenstrom's macroglobulinemia, and follicular lymphoma.

Results – Treatment distribution in post CAR-T era



- The breakup of pharmacologic (CT/CIT & novel agent) and cell therapy (CAR-T & SCT) were similar in 3L (71.7% vs. 28.3%) and 4L (70.9% vs. 29.1%) settings
- CT/CIT and novel agents were most commonly used in 3L (44.8%) and 4L (36.4%), respectively
- The use of CAR-T and SCT accounted for 17.2% and 11.0% in 3L, and 16.4% and 12.7% in 4L

Results – Baseline characteristics in 3L patients

- CAR-T patients were older (mean age, 58.0), had a relatively lower mean CCI score (3.0), a shorter median time from index diagnosis to index date (12.0 months) and longer median follow-up time (8.0 months)
- SCT patients were younger (mean age, 54.6), had a relatively higher mean CCI score (4.6) and shorter median follow-up time (4.3 months)
- Novel therapy patients had a higher mean CCI score compared with CT/CIT and CAR-T patients.

Patients Characteristics	All patients N = 145	CT/CIT N = 65	Novel therapy N = 39	CAR-T N = 25	SCT N = 16
Age (years), mean (SD)	56.7 (10.8)	56.8 (11.8)	56.5 (10.9)	58.0 (9.3)	54.6 (8.9)
Age ≥ 65 years, %	20.0%	23.1%	18.0%	20.0%	12.5
Gender (female), %	33.8%	33.9%	33.3%	28.0%	43.8%
Time from first diagnosis to 3L (months), median (IQR)	13.6 (9.5, 19.6)	14.8 (9.8, 21.1)	12.5 (8.6, 16.6)	12.0 (10.4, 16.8)	14.4 (10.2, 21.5)
Charlson comorbidity index (CCI), mean (SD)	3.5 (2.6)	3.2 (2.5)	3.7 (2.7)	3.0 (2.0)	4.6 (3.2)
Transformed DLBCL*, %	18.6%	21.5%	20.5%	12.0%	12.5%
Health plan type, %					
Commercial, employer-based insurance	60.0%	70.8%	51.3%	48.0%	56.3%
Commercial, non-employer based insurance	37.2%	26.2%	43.6%	52.0%	43.8%
Medicaid or Medicare or unknown	2.8%	3.1%	5.1%	0.0%	0.0%
Follow-up time (months), median	5.8	6.5	5.5	8.0	4.3

*Transformed DLBCL indicated that patient had one of the following diagnoses during the 6 months before the first DLBCL diagnoses: chronic lymphocytic leukemia, marginal zone lymphoma, nodular lymphocyte-predominant Hodgkin's lymphoma, Waldenstrom's macroglobulinemia, follicular lymphoma

Results – Treatment outcomes in post CAR-T era

Duration on 3L and 4L treatment

Index Treatment Category	3L		4L	
	Sample size, n	Median time on 3L, months (95% CI)	Sample size, n	Median time on 4L, months (95% CI)
Overall	104	2.9 (2.0, 7.1)	39	2.5 (1.5, NR)
CT/CIT	65	2.4 (1.4, NR)	19	1.4 (1.0, NR)
Novel therapy	39	3.2 (2.2, NR)	20	NR

Abbreviation: NR, not reached
Note: Results were based on Kaplan-Meier analysis; patients were censored at the earliest of end of continuous eligibility and end of data period

- The median treatment duration was short for third line and fourth line
- The median treatment duration appeared to be shorter for CT/CIT compared to novel therapy

Percentage of patient initiating 4L during the follow-up time

Index Treatment Category	Total 3L patients, n	Median duration of follow up (months)	Patients initiating 4L, n (%)
All 3L	145	5.8	45 (31.0%)
CT/CIT	65	6.5	19 (29.2%)
Novel therapy	39	5.5	10 (25.6%)
CAR-T	25	8.0	12 (48.0%)
SCT	16	4.3	4 (25.0%)

- About one third of patients initiated a 4L therapy during a short follow-up period

Limitations

- This study was subject to the limitations of retrospective studies based on healthcare claims data, including occasional coding errors or claim omissions
- The 6-month washout period may not be sufficient to ensure that the first observed DLBCL diagnosis is the initial diagnosis
  - However, patients with possible DLBCL diagnosis before the index diagnosis were excluded
- The LOT algorithm developed in this study may cause misclassification
  - However, distribution of non-CAR-T treatments is consistent with that reported in the literature
- The sample size is relatively small, the follow-up period is relatively short
  - Additional analyses with bigger sample and longer follow-up time are warranted to assess the treatment patterns after CAR-T approval
- The current data is limited in capturing the use of recently approved novel agents (e.g., polatuzumab, selinexor, tafasitamab). Future analysis would be warranted

Conclusions

- In patients with R/R DLBCL receiving 3L treatment post CAR-T approval, about 72% were treated with CT/CIT or novel agent-based therapies, though most of the novel agents are not indicated for DLBCL. CAR-T and SCT were used in 17% and 11% of patients, respectively.
- Treatment duration of 3L and 4L CT/CIT or novel agent-based therapies was short.
- A relatively high proportion of 3L patients initiated the next LOT during a short follow-up period.
- These findings highlight the unmet need for more effective treatments among R/R DLBCL patients in 3L and later lines.

Conflict of interest

- Funding for this research was provided by ADC Therapeutics; the study sponsor was involved in all stages of the study research and poster preparation.

- Jipan Xie, Aozhou Wu, Ella Xiaoyan Du, Ahmed Noman, and Yawen Liang are employees of Analysis Group, Inc., which received consultancy fees from ADC Therapeutics for conducting research analysis.

- Laura Liao, Joseph Camardo, and Lei Chen are employees of ADC Therapeutics and own ADC Therapeutics stock or stock options.