Poster
PCR130

Health-Related Quality of Life (HRQoL) of Large B-cell Lymphoma (LBCL) and Follicular Lymphoma (FL) Patients Treated with Axicabtagene Ciloleucel (Axi-cel) in Clinical Trials and the Real-World: A Targeted Literature Review

Gribben J,[1] Palivela M,[2] Kanters S,[3] Wade SW,[4] Lakzadeh P,[3] Yang L,[3] Shah GL[5,6]

1. Barts Cancer Institute, Queen Mary University of London, London, England; 2. Kite, A Gilead Company, Santa Monica, CA, USA; 3. RainCity Analytics, Vancouver, BC, Canada; 4. Wade Outcomes Research and Consulting, Salt Lake City, Utah, USA; 5. Adult Bone Marrow Transplant Service, Memorial Sloan Kettering Cancer Center, New York, NY, USA; 6. Department of Medicine, Weill Cornell Medical College, New York, NY

BACKGROUND

- In 2017, axicabtagene ciloleucel (axi-cel), an autologous anti-CD19 chimeric antigen receptor (CAR) T-cell therapy, was the first of its class to receive regulatory approval for the treatment of relapsed/refractory (R/R) LBCL following two or more prior lines of therapy (3L+) in the United States (US) and Europe. Since then, its approval has been extended to include 2L+ R/R LBCL and to 3L+ follicular lymphoma (FL). [1,2]
- Results from both clinical trials and real-world settings have demonstrated that these treatments have statistically and clinically meaningful impact on clinical outcomes, most importantly overall survival.[3]
- Nonetheless, LBCL and FL can negatively affect patients' daily life and well-being, whether through progressive disease symptoms or common treatment-related adverse events. This impact is commonly reflected in evaluations of patient HRQoL.[4]
- Recent real-world studies have reported improvements in HRQoL from baseline among patients treated with axi-cel, suggesting enhanced well-being following treatment.[5]
- The current study sought to identify the published HRQoL evidence among patients treated with axi-cel in either the clinical trial or real-world settings with a targeted literature review (TLR).

OBJECTIVES

- The study objectives were to identify and describe the evidence base of HRQoL outcomes among patients treated with axi-cel in the clinical trial and the real-world settings.

METHODS

- We conducted a targeted literature review using a multipronged approach to identify the evidence base. This included:
  1. A systematic search conducted in Embase on September 19, 2024;
  2. A manual search of select conference abstracts and presentations;
  3. A snowball approach employed on the evidence identified in steps 1 and 2
- Eligible studies met the following criteria:
  - Study design – either real-world observational studies or clinical trials
  - Reporting on HRQoL or cognitive measures
  - As it was unclear whether there would be extensive evidence, we chose to include studies that reported on groups at least 60% axi-cel patients.
  - There were no geographic restrictions, but searches were limited to 2017 to present
  - Only studies published in English were eligible.
- Two reviewers extracted study characteristics, population characteristics, and outcomes into a standardized, piloted data extraction template.
- Discrepancies between reviewers were resolved through discussion or, if necessary, arbitration by a third reviewer.
- Study mapping was conducted to ensure patients were not double counted. While selection was conducted at the publication-level, understanding how many distinct studies were in the evidence base was key.
- The findings from this study were summarized in both tabular and graphical formats. No statistical analyses were conducted under this project.

RESULTS

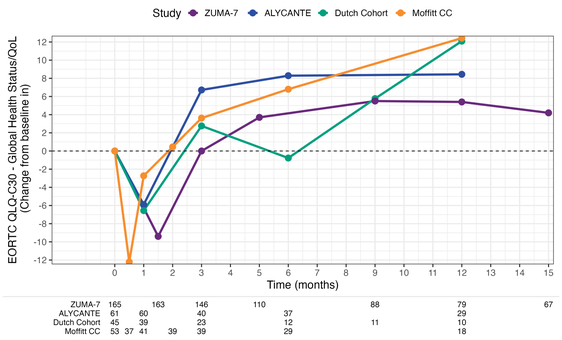
- From a total of 541 identified references, the identified evidence base consisted of 19 publications reporting on 11 eligible studies, including three trials (ALYCANTE, ZUMA-1, and ZUMA-7) and eight real-world cohort studies.
- The characteristics of the included studies are presented in **Table 1**. Most studies were among 3L+ patients with 100% ax-cel use.

Table 1. Characteristics of studies in the evidence base

Study name	Study design	Target population	Sample size	Axi-cel %	Country	HRQoL instrument
ALYCANTE	Trial	2L R/R LBCL	61	100%	France	EORTC QLQ-C30
CARAMA	Cohort	3L+ R/R LBCL	59	63%	France	EQ-5D-5L & VAS, FACT-G, -Lym & -Cog, FACIT-F, HADS
Dutch CAR-T Cohort	Cohort	3L+ R/R LBCL	145	100%	Nether-lands	EORTC QLQ-C30, EQ-5D-5L
Hospital St Louis	Cohort	3L+ R/R BCL	27	63%	France	HADS, QMRP
Mass General Hospital	Cohort	Mixed	100	13%	US	FACT-G
MD Anderson Cancer Center	Cohort	3L+ R/R LBCL	60	86%	US	EQ-5D-5L,PROMIS-29,MDASI
Moffitt Cancer Centre	Cohort	3L+ R/R NHL	118	87-100%	US	PROMIS-29, ECog, SF-36, PRO-CTCAE, RBANS, EORTC QLQ-C30
Stanford University	Cohort	3L+ R/R LBCL	16	100%	US	SF-36, GAD-7, PHQ-9
University of Nebraska MC	Cohort	R/R DLBCL	14	100%	US	Neuro-QoL
ZUMA-1	Trial	3L+ R/R LBCL	34	100%	US and France	EQ-5D-5L
ZUMA-7	Trial	2L R/R LBCL	165	100%	Multi-national	EORTC QLQ-C30, EQ-5D-5L &-VAS, Q-TWiST, WPAI

DLBCL: Diffused large B-cell lymphoma; ECog: Everyday cognition; EORTC: European Organisation for Research and Treatment of Cancer; EQ-5D-5L: EuroQol-5 dimensions - 5 levels; FACIT-F: Functional Assessment of Chronic Illness Therapy – Fatigue; FACT: Functional Assessment of Cancer Therapy; GAD-7: General Anxiety Disorder scale 7; HADS: Hospital Anxiety and Depression Scale; HRQoL: Health-related Quality of Life; LBCL: Large B-cell lymphoma; MDASI: MD Anderson Symptom Inventory; Neuro-QOL: Quality of Life in Neurological Disorders; NHL: Non-Hodgkin Lymphoma; PHQ-9: Patient Health Questionnaire 9; PRO-CTCAE: Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events; PROMIS: Patient-Reported Outcomes Measurement Information System; Q-TWiST: Quality-adjusted Time Without Symptoms or Toxicity; WPAI: Work Productivity and Activity Impairment; R/R: Relapsed or refractory; RBANS: Repeatable Battery for the Assessment of Neuropsychological Status; SF-36: 36 item Short Form Survey; US: United States; VAS: Visual analogue scale

Figure 1. Mean change from baseline in HRQoL using the EORTC QLQ-C30 Global Health Status among axi-cel patients



- A wide range of HRQoL instruments were used across the studies but the most common were the European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire Core 30 (QLQ C30) and the EuroQoL-5 dimensions - 5 levels EQ-5D-5L.
- **Figure 1** presents the change from baseline in global health status (GHS) among axi-cel patients across the four studies reporting longitudinal GHS results. All four studies displayed an initial transient decline in GHS status followed by a rapid recovery and eventual improvement above baseline values.

Table 2. Cross-instrument evaluation of global health and functional domains

	Measure	N	No. of Measurements	Max timepoint (months)	Global Health Status	Physical Functioning	Social Functioning	Emotional Functioning	Role Functioning	Cognitive Functioning
ALYCANTE	EORTC QLQ-C30	61	5	12	↑			↑		
	EQ-5D VAS	61	5	12	↑	–	–		–	–
CARAMA	FACT-Lym	59	4	12	↑	↑		↑		
	FACT-G	59	4	12	↑		–			–
	EQ-5D VAS	59	4	12	↑					
Dutch CAR-T Cohort	EORTC QLQ-C30	145	6	12	↑	↑		↑		
	EQ-5D VAS	145	6	12	↑					
MD Anderson Cancer Center	EQ-5D VAS	60	3	3+	↓					
	PROMIS-29	60	3	3+		↑				
	MDASI	60	3	3+		↑	–	↑		
Moffitt Cancer Centre	EORTC QLQ-C30	53	6	12	↑	⇑	⇑	⇑	⇑	
	PROMIS-29	103	2	12		↑				
ZUMA-1	EQ-5D-5L	165	4	6	–					
ZUMA-7	EORTC QLQ-C30	165	7	15	⇑		↑	↑		
	EQ-5D VAS	165	7	15	↑	–				–
	EQ-5D-5L	165	7	15	↑					

Legend: ↑ Statistically significant improvement in change from baseline; ⇑ Statistically non-significant improvement in change from baseline; ⇓ Statistically non-significant decline in change from baseline; ↓ Statistically significant decline in change from baseline; – Return to baseline

EORTC: European Organisation for Research and Treatment of Cancer; EQ-5D-5L: EuroQol-5 dimensions - 5 levels; FACT-F: Functional Assessment of Chronic Illness Therapy – Fatigue; FACT: Functional Assessment of Cancer Therapy; MDASI: MD Anderson Symptom Inventory; PROMIS: Patient-Reported Outcomes Measurement Information System; QLQ-C30: Quality of Life Questionnaire Core 30; VAS: Visual analogue scale

Table 3. Cross-instrument evaluation of symptoms

	QoL Instrument	N	No. of Measurements	Max timepoint (months)	Fatigue	Insomnia	Pain	Anxiety	Depression	Nausea and vomiting	Appetite loss	Constipation	Diarrhea
ALYCANTE	EORTC QLQ-C30	61	2	3	⇑	⇑	↑			–	⇑	–	–
CARAMA	FACIT-F	59	4	12	↑								
	HADS	59	4	12				↑	⇑				
Hospital St-Louis	HADS	27	2	7.6				⇑	–				
MD Anderson Cancer Center	MDASI-Core	60	3	3+	↑	–	↑		⇑	⇑	↑		
	PROMIS-29	60	3	3+	↑	↓	⇑	⇑	–				
Moffitt Cancer Center	EORTC QLQ-C30	53	7	12	⇑	⇑	⇑				↑	⇑	
	PROMIS-29	103	2	NR	↑		↑	↓	⇑				
	PRO-CTCAE	103	5	3	–						⇑		
ZUMA-7	EORTC	165	7	15	↑	⇑	↑			–	⇑	⇑	–

Legend: ↑ Statistically significant improvement in change from baseline; ⇑ Statistically non-significant improvement in change from baseline; ⇓ Statistically non-significant decline in change from baseline; ↓ Statistically significant decline in change from baseline; – Return to baseline

EORTC: European Organisation for Research and Treatment of Cancer; FACIT-F: Functional Assessment of Chronic Illness Therapy – Fatigue; HADS: Hospital Anxiety and Depression Scale; MDASI: MD Anderson Symptom Inventory; PRO-CTCAE: Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events; PROMIS: Patient-Reported Outcomes Measurement Information System; QLQ-C30: Quality of Life Questionnaire Core 30

- These four studies (presented in **Figure 1**) spanned America and Europe and include 2L and 3L+ studies. Despite these differences between studies, the results were fairly homogenous.
- Trends of results across the various instruments that measure common functional domains are presented in **Table 2**. The summary on the right-hand side shows the general trend.
- For GHS, statistically significant improvements were observed in most studies and across five instruments. Evidence of improvements from baseline were observed in physical and emotional domains while social and cognitive domains more often showed return to baseline values.
- For the symptom scales, the most common outcome was a non-significant improvement from baseline over time (**Table 3**). Fatigue, pain, and appetite loss were the symptoms with the strongest evidence for numeric improvements from baseline, while other symptoms had a mixture of return to baseline or some improvement.

DISCUSSION

- Our TLR found a growing literature on the HRQoL and symptom experiences of patients using axi-cel to treat lymphoma.
- The evidence was cohesive despite the use of various HRQoL instruments to assess the same domains and symptoms. HRQoL improvements were observed across multiple dimensions, including physical functioning, emotional well-being, and global health, indicating a holistic recovery and enhancement in patient quality of life.
- Strengths of this study include extensive search approach and consistency of results across HRQoL instruments.
- Limitations of this study include the targeted nature of the review, heterogeneity of the populations included in the evidence base, the heterogeneity of HRQoL measures used across studies and lack of to CAR T-cell therapy specific HRQoL instruments.

CONCLUSIONS

- This TLR highlights the clinically meaningful improvements in HRQoL achieved by patients treated with axi-cel. While some patients may face early challenges due to treatment-related adverse events, the symptoms burden return to baseline or are reduced relative to baseline values.
- Importantly, the HRQoL outcome patterns observed in the broader populations in real-world studies demonstrated similar trends to those observed in clinical trials.

REFERENCES

1. Neelapu SS, Locke FL, Bartlett NL, et al. Comparison of 2-year outcomes with CAR T cells (ZUMA-1) vs salvage chemotherapy in refractory large B-cell lymphoma. Blood Adv. Oct 26 2021;5(20):4149-4155.
2. Ghione P, Palomba ML, Patel AR, et al. Comparative effectiveness of ZUMA-5 (axi-cel) vs SCHOLAR-5 external control in relapsed/refractory follicular lymphoma. Blood. Aug 25 2022; 140(8):851-860.
3. Jacobson CA, Munoz J, Sun F, et al. Real-World Outcomes with Chimeric Antigen Receptor T Cell Therapies in Large B Cell Lymphoma: A Systematic Review and Meta-Analysis. Transplant Cell Ther. Jan 2024;30(1):77 e71-77 e15.
4. Elsawy M, Chavez JC, Avivi I, et al. Patient-reported outcomes in ZUMA-7, a phase 3 study of axicabtagene ciloleucel in second-line large B-cell lymphoma. Blood. 45620 2022;140(21):2248-2260.
5. Johnson PC, Bailey A, Ma Q, et al. Real-world evaluation of health-related quality of life in patients with diffuse large B-cell lymphoma based on a multinational survey. Front Oncol. 2024;14:1402992.

DISCLOSURES

This study was funded by Kite Pharma, a Gilead Company. **SK, PL** and **LY**, current employment at RainCity Analytics; **MP** and **SWW**, current employment at and holding stock and stock options from Kite, a Gilead company; **JG**, reports receiving consulting fees from AbbVie, Acerta Group Limited/AstraZeneca, Bristol Myers Squibb/ Celgene Corporation, Janssen, Kite/Gilead, research funding from Acerta Group Limited/AstraZeneca, Bristol Myers Squibb/Celgene Corporation, and Janssen; **GLS,** has research funding to the institution from Jansen, Amgen, BMS, Beyond Spring, GPCR, and Recordati, and is on the DSMB for Arcellx