Real-world outcomes of lisocabtagene maraleucel in patients with Richter transformation from the Center for International Blood and Marrow Transplant Research (CIBMTR)

CLL-189

Abu-Sayeef Mirza, MD, MPH,[1] Allison Winter, MD,[2] Sushma Bharadwaj, MD,[3] Alex F. Herrera, MD,[4] Chaitanya Iragavarapu, MD,[5] M. Lia Palomba, MD,[6] Sagar S. Patel, MD,[7] Mecide Gharibo, MD,[8] David Bernasconi, MSc,[9] Tracy Krimmel, MSN, DNP,[8] Fei Fei Liu, GDCE, MBA,[8] Debasmita Roy, PhD,[8] Marcelo C. Pasquini, MD, MS[10]

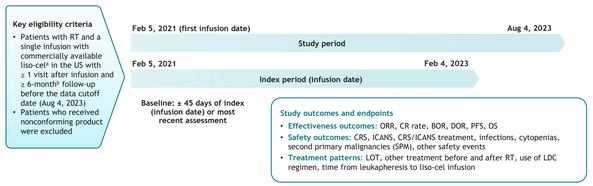
[1]Moffitt Cancer Center, Tampa, FL, USA; [2]Cleveland Clinic Taussig Cancer Institute, Cleveland, OH, USA; [3]Stanford University School of Medicine, Stanford, CA, USA; [4]City of Hope Medical Center, Duarte, CA, USA; [5]University of Kentucky College of Medicine, Lexington, KY, USA; [6]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [7]Huntsman Cancer Institute at the University of Utah, Salt Lake City, UT, USA; [8]Bristol Myers Squibb, Princeton, NJ, USA; [9]Celgene, a Bristol-Myers Squibb Company, Boudry, Switzerland; [10]Center for International Blood & Marrow Transplant Research, Medical College of Wisconsin, Milwaukee, WI, USA

Background

- Up to 1% of patients with CLL experience Richter transformation (RT), with up to 95% of cases transforming to DLBCL[1]
- These patients have poor prognosis and a high unmet need with no standard of care[1,2]
- Here, we report real-world clinical effectiveness and safety of commercial lisocabtagene maraleucel (liso-cel) in patients in the United States (US) with RT to large B-cell lymphoma (LBCL) based on data collected at the Center for International Blood and Marrow Transplant Research (CIBMTR)

Methods

Figure 1. Study design



[a]Recently FDA-approved new product specifications for liso-cel in the US are harmonized for use across all FDA-approved indications (R/R LBCL, CLL, FL, and MCL); [b]Due to data entry delays, not all patients had a 6-month follow-up in the analysis set.
BOR, best overall response; CRS, cytokine release syndrome; DOR, duration of response; ICANS, immune effector cell-associated neurotoxicity syndrome; LDC, lymphodepleting chemotherapy; LOT, line of therapy.

- Retrospective, observational study of patients in the US enrolled in the CIBMTR Cellular Therapy Registry and treated with liso-cel through August 4, 2023 (**Figure 1**)
- The first patient was infused with liso-cel on February 5, 2021, and the analysis included patients with infusions through February 4, 2023, and follow-up through August 4, 2023

Results

Table 1. Patient demographics and disease characteristics

	Total (N = 30)
Median (range) age, y	66 (42–82)
Median (range) time from CLL diagnosis to RT, mo	49 (0[a]–180)
Median (range) time from RT to liso-cel infusion, mo	11 (1–110)
Histology,[b] n (%)	
DLBCL	27 (90)
Germinal center B cell / activated B-cell type / not otherwise specified	3 (10) / 13 (43) / 10 (33)
HGBCL	2 (7)
Molecular abnormalities, n/N (%)	
TP53 mutated at infusion	6/15 (40)
Del17p at infusion	10/28 (36)
CD19[+] at CLL diagnosis[c]	15/17 (88)
Disease status at infusion, n (%)	
Refractory / relapse / in remission	12 (40) / 16 (53) / 2 (7)
ECOG PS of 0–1 / 2, n (%)[d]	27 (93) / 2 (7)
Comorbidities, n (%)	
Types (> 10%): pulmonary[e] / cardiac[f] / hepatic[e]	11 (37) / 6 (20) / 4 (13)
Active CNS involvement at liso-cel infusion, n (%)	2 (7)
Elevated LDH at infusion, n/N (%)	12/27 (44)
Median (range) LDH level at liso-cel infusion, U/L	241 (117–15,971)
IPI score before liso-cel infusion, n (%)	
0–2 / 3–5	21 (70) / 9 (30)

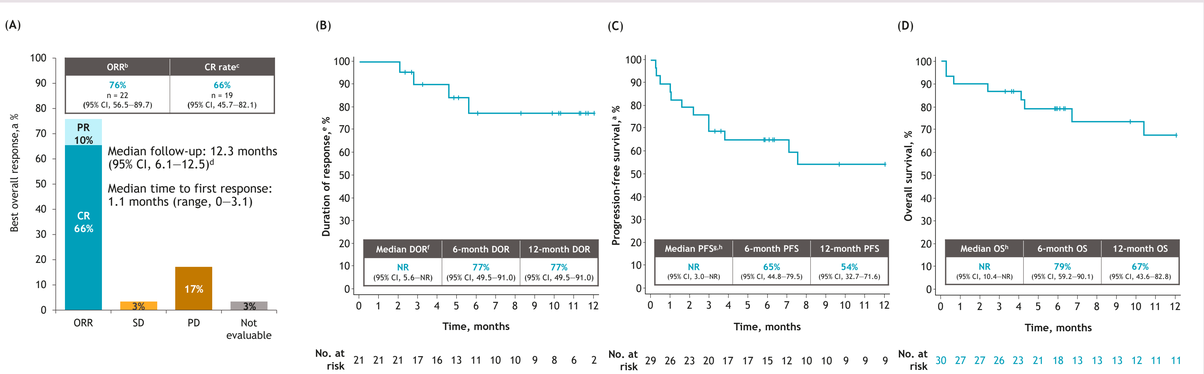
[a]Diagnosis of CLL and RT were done at the same time in 2 patients; [b]One patient had primary cutaneous DLBCL, leg type; [c]Data not available at liso-cel infusion; [d]N = 29; [e]Includes moderate and severe comorbidities; [f]Includes cardiac, cerebrovascular, and heart valve disease.
HGBCL, high-grade B-cell lymphoma; IPI, International Prognostic Index.

Patient demographics and disease characteristics

- Thirty patients who met the eligibility criteria were included
- Patient demographics and baseline disease characteristics of the 30 patients with RT are shown in **Table 1**
- Most patients (90%) had DLBCL
- Of patients who had samples available for molecular analysis, 6/15 (40%) had *TP53* mutated at infusion
  - 10/28 (36%) had del17p at infusion
  - 15/17 (88%) were CD19[+] at CLL diagnosis
- Two (7%) patients had active CNS involvement at liso-cel infusion

Results from this large, multicenter, real-world study showed patients with RT who received liso-cel had high ORR with deep and durable responses, and promising survival

Figure 2. (A) ORR, CR rate, and BOR; (B) DOR; (C) PFS; and (D) OS



[a]Among evaluable patients (n = 29); [b]Continued complete remission + CR + PR; [c]Continued complete remission + CR; [d]Estimated using the reverse Kaplan-Meier method; [e]Responders with available DOR data; [f]Median follow-up for DOR was 9.9 months (95% CI, 4.9–11.3); [g]Patients with available PFS data; [h]Median follow-up for PFS and OS was 12.3 months (95% CI, 6.1–12.5).
NR, not reached; SD, stable disease.

Table 2. Treatment history

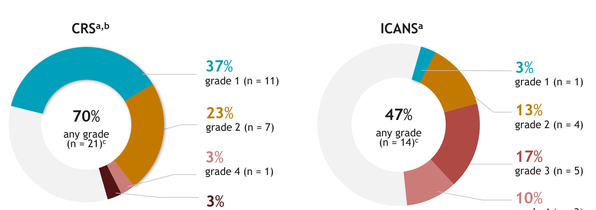
	Total (N = 30)	
Median (range) number of prior LOTs		
From CLL diagnosis to liso-cel infusion	4 (1–11)	
For CLL	2[a] (0[b]–9)	
After RT	3[c] (1–7)	
Received treatment for CLL before RT, n (%)	23 (77)	
Received treatment for RT before liso-cel infusion, n (%)	30 (100)	
HSCT, n (%)		
Autologous	3 (10)	
Allogeneic	2 (7)	
Received prior treatment with the following agents, n/N (%)	**For CLL**	**After RT**
BTKi (ibrutinib, acalabrutinib, pirtobrutinib)	13/28 (46)	8/29 (28)
BCL2i (venetoclax)	7/28 (25)	9/30 (30)
Anti-CD20–targeted agent	16/27 (59)	30/30 (100)
Chemoimmunotherapy	16/27 (59)	29/30 (97)
Dual-class exposed (BTKi + BCL2i), n/N (%)	10/28 (36)	
Refractory to last LOT before liso-cel infusion, n/N (%)	24/29 (83)	
Refractory to BTKi, n/N (%)	12/28 (43)	
Received bridging therapy, n/N (%)	13/27 (48)	
Received standard LDC (FLU/CY), n (%)	26 (87)	
Median (range) time from leukapheresis to liso-cel infusion, d	35 (28–63)	

[a]Median of 1.5 was rounded to nearest integer; [b]Diagnosis of CLL and RT was done at the same time in 2 patients and no therapy for CLL was reported for 1 patient; [c]Median of 2.5 was rounded to nearest integer.
BCL2i, B-cell lymphoma 2 inhibitor; BTKi, Bruton tyrosine kinase inhibitor; CY, cyclophosphamide; FLU, fludarabine.

Treatment history

- Patients received a median of 4 prior lines of therapy from CLL diagnosis to liso-cel infusion (**Table 2**)
- Twenty-three (77%) patients had received treatment for CLL before RT
- Of patients with available data:
  - 10/28 (36%) patients had been dual-class exposed to both BTKi and BCL2i
  - 13/27 (48%) had received bridging therapy

Figure 3. CRS and ICANS

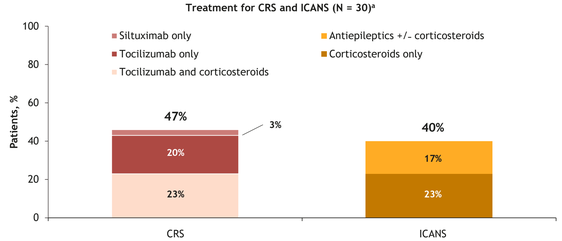


[a]Summed percentages for grouped grades within each graph may not equal the any-grade percentage due to rounding; [b]CRS was graded based on the Lee 2014 criteria. There was high concordance on CRS grading per Lee 2014 and the American Society for Transplantation and Cellular Therapy criteria; [c]One patient had an event with no grade reported.

Safety

- A total of 21 patients experienced CRS, of whom 11 and 7 patients had grade 1 and 2 events, respectively (**Figure 3**)
- Fourteen patients experienced ICANS, of whom 1 and 4 patients had grade 1 and 2 events, respectively; 8 patients had grade 3 or 4 events and none had grade 5 events

Figure 4. Treatment for CRS and ICANS



[a]Summed percentages may not equal individual treatment percentage due to rounding.

- Fourteen patients were treated for CRS, with most patients receiving both tocilizumab and corticosteroids or tocilizumab only (**Figure 4**)
- Twelve patients were treated for ICANS; all patients received either corticosteroids only or a combination of antiepileptics and/or corticosteroids

Table 3. Other AEs of special interest (AESI)

AESI	N (%)
Prolonged cytopenias[a]	5 (17)
Clinically significant infections[b]	13 (43)
Hypogammaglobulinemia	22 (73)
SPM	1 (3)
Grade 3/4 organ toxicity	2 (7)

[a]Defined as grade 4 thrombocytopenia and/or neutropenia persistent at 30 days after infusion; [b]Defined as any infection requiring treatment.

- Rates of AESIs (**Table 3**) were consistent with prior liso-cel studies
- One patient experienced an SPM of the gastrointestinal tract; no secondary hematologic malignancies were reported

Deaths

- Eight patients died during the study period
  - Seven patients died due to progression of primary disease
  - One patient died due to CRS (patient also had hemophagocytic lymphohistiocytosis)

Conclusions

- This is the largest, multicenter, real-world study of patients with RT who received commercial liso-cel in the US
- One-time infusion of liso-cel demonstrated high ORR with deep and durable responses in patients with RT, the majority of whom had previously been treated for their CLL disease
  - The probability of 1-year survival after infusion was 67%
- A total of 70% of patients experienced any-grade CRS; the incidence of grade ≥ 3 CRS was low (7%)
- A total of 47% of patients experienced any-grade ICANS; the incidence of grade ≥ 3 ICANS was 27%
- The meaningful clinical benefit of liso-cel and observed safety profile in patients with difficult-to-treat RT disease is promising
  - Longer follow-up in a larger cohort is needed to fully characterize the benefit of liso-cel in this patient population

References

1. Bajwa A, et al. *Curr Hematol Malig Rep* 2024;19:45–55.
2. Eyre TA. *Hematology Am Soc Hematol Educ Program* 2023;2023:427–432.

Acknowledgments

- We would like to thank the patients, caregivers, investigators, and study personnel
- This study was funded by Bristol Myers Squibb
- CIBMTR is a research collaboration between the Medical College of Wisconsin and NMDP. The CIBMTR operates the Cellular Immunotherapy Data Resource (CIDR) (NCI U24 CA233032; NIH [NHLBI, NCI, NIAID] Resource for HCT and CT [U24CA076518]), which funded the development and implementation of the Cellular Therapy Registry
- All authors contributed to and approved the presentation; writing and editorial assistance were provided by Emily Burke, PhD, CMPP, of The Lockwood Group (Stamford, CT, USA), funded by Bristol Myers Squibb

Scientific Content on Demand

To request a copy of this poster:

Scan QR code via a barcode reader application

QR codes are valid for 90 days after the congress presentation date.

Copies of this poster obtained through QR (Quick Response) and/or text key codes are for personal use only and may not be reproduced without written permission of the authors.