Poster 1199

Real-World Outcomes of Axicabtagene Ciloleucel for Treatment of Relapsed or Refractory Large B-Cell Lymphoma in Canada

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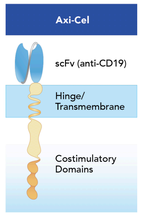
BACKGROUND

- Axicabtagene ciloleucel (axi-cel) is an autologous anti-CD19 CAR T-cell therapy approved for the treatment of relapsed or refractory large B-cell lymphoma (R/R LBCL)[1-3]
- Axi-cel was approved by Health Canada in Feb 2019 for the treatment of R/R LBCL for third or later line settings[3]
  - In the pivotal ZUMA-1 trial, ORR was 82% (CR rate 54%). In a 5-year follow-up analysis of the trial, median OS reached at 25.8 months (5-year OS rate 42.6%), demonstrating its curative potential[4].
  - Real-world data in this population from the United States and Europe have been presented previously, with consistent results compared to those in ZUMA-1[5-9]



OBJECTIVES

- Here, we present the early real-world outcomes of Canadian patients (pts) treated with axi-cel for R/R LBCL

METHODS

Registry-Based Noninterventional Cohort Study

- Real-world data from the observational database of the Center for International Blood and Marrow Transplant Research (CIBMTR®) registry in collaboration with Cell Therapy Transplant Canada (CTTC) for patients receiving commercial axi-cel for R/R LBCL in Canada between Feb 2020 –June 2023[a]
- Data cut-off: Nov 2023[b]

Outcomes of Interest

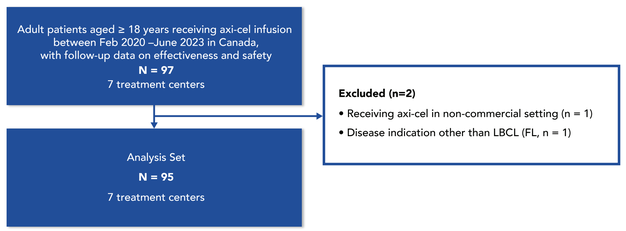
- Effectiveness: ORR, CR rate, DOR, PFS, OS, and REL/PD
- Safety: CRS, ICANS (per ASTCT consensus[10]), prolonged cytopenia, clinically significant infections[c], and NRM

Statistical Analysis

- Dichotomous outcomes summarized using percentages with 95% Clopper-Pearson CI
- TTE outcomes without competing risk summarized using Kaplan-Meier estimator
- TTE outcomes with competing risk summarized using the CIF

[a]Eligible pts must have provided consent and treated with commercial axi-cel in Canada. Outcomes were evaluated in patients who completed 100-day follow-up reporting. [b]Patients who died or discontinued prior to data cutoff were also included. [c]Any infection diagnosed after the initial infusion of axi-cel that requires treatment.

Study Cohort and Patient Disposition



- Median follow-up: 6.4 months (range, 1.2-23.9)

RESULTS

Table 1. Baseline Patient Characteristics

Characteristics, n (%)	Overall (N=95)
Age, median (range), years	60 (22-81)
Age ≥65 years	37 (39)
≥75 years	12 (13)
Sex, male	64 (67)
Disease histology at initial diagnosis	
DLBCL	74 (78)
PMBCL	4 (4)
HGBCL	16 (17)
Monomorphic PTLD	1 (1)
Double/triple hit at initial diagnosis[a]	14 (29)
ECOG performance status 0 or 1 prior to CT	82 (86)
Clinically significant co-morbidity[b]	63 (66)
ZUMA-1 eligibility[c]	58 (61)
Refractory after last line of therapy prior to leukapheresis[d]	60 (79)
Prior history of HSCT	30 (32)
Lines of prior therapy, median (IQR)	2 (2-3)
Bridging therapy[e]	
Any	26 (32)
Systemic	21 (81)
Intrathecal	1 (4)
Radiation	9 (35)
Diagnosis to axi-cel infusion, median (IQR), months	14 (9-28)
<12 months	40 (42)
Time from leukapheresis to infusion (vein-to-vein), days - median (IQR)[f]	32 (28-34)

- 39% of patients would not have met the ZUMA-1 eligibility criteria[c]

[a]Among patients with reported data (n=49). [b]According to Hematopoietic Cell Transplantation Comorbidity Index (HCT-CI) in Sorror M. et al., 2005. [c]Not eligible: organ impairment (n=26), ECOG>1 (n=13), infection (n=5), autoimmune disease (n=3), other BCL (n=1), CNS involvement (n=1). Eligible criteria adapted to available registry data. [d]Among with reported data (n=76). [e]Among patients with reported data on bridging therapy (n=82). Systemic therapy and radiotherapy categories were not mutually exclusive. [f]Time from cell product collection to infusion was not reported in 3 pts.

Figure 1. Response Rates Among all Patients

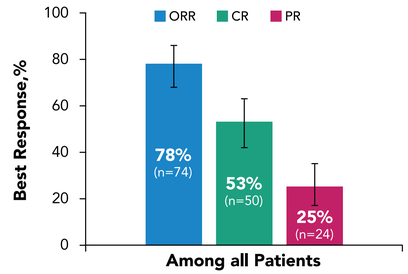
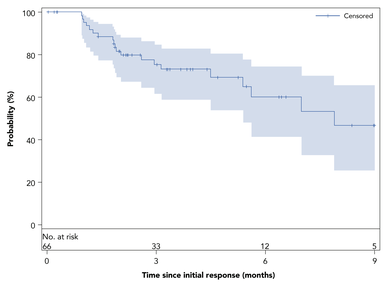


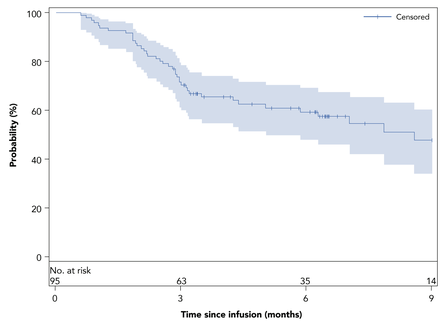
Figure 2. Kaplan-Meier Estimates for DOR[a]



[a]Among pts achieved CR/PR as best response with reported time of response data. Subsequent cellular therapy and HSCT were censored

- At a median follow-up of 6.4 months, best ORR and CR rate among all pts were 78% (95% CI 68−86) and 53% (95% CI 42−63), respectively (Figure 1)
- Among responders with reported time of response data (n = 66), 60% (95% CI 41−74) remained in response for ≥ 6 months (Figure 2)

Figure 3. Kaplan-Meier Estimates of PFS[a]



[a]Subsequent cellular therapy and HSCT were censored.

Figure 4. Kaplan-Meier Estimates of OS

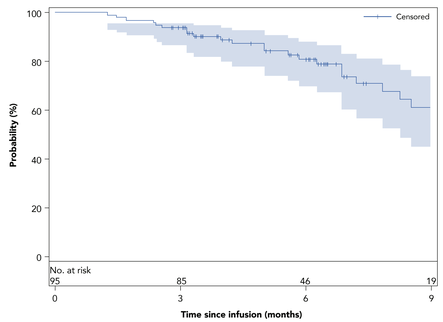
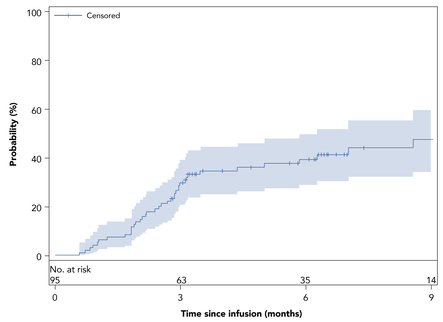


Figure 5. Cumulative Incidence of REL/PD[b]



[b]REL/PD was treated as competing risks.

- Estimated PFS and OS at 6 month were 59% (95% CI 48−69) and 81% (95% CI 70−88), respectively (Figure 3,4)
- At 3 and 6 months, the cumulative incidence of REL/PD were 30% (95% CI 21−39) and 39% (95% CI 29-50) (Figure 5), respectively

Table 2. Adverse Events for CRS and ICANS

Parameter	
Cytokine Release Syndrome (CRS)[a,b]	
Any Grade, %	74
Grade ≥3, %	2
Median time from infusion to CRS onset, days (range)	4 (1-15)
Median time from CRS onset to resolution, days (range)	6 (2-14)
Immune Cell-Associated Neurotoxicity Syndrome (ICANS)[a,b]	
Any Grade, %	30
Grade ≥3, %	8
Median time from infusion to ICANS onset, days (range)	8 (4-15)
Median time from ICANS onset to resolution, days (range)	6 (1-14)
AE Management of CRS/ICANS[c]	
Corticosteroids, n (%)	37 (54)
Tocilizumab, n (%)	57 (83)
Anakinra, n (%)	3 (4)

[a]CRS and ICANS were graded per ASTCT consensus criteria. [b]Among patients with reported data on CRS (n=89) and ICANS (n=86). [c]Among patients who reported any-grade CRS/ICANS.

- Most CRS (97%) and ICANS (100%) resolved within 2 weeks of onset
- No Grade 5 CRS or ICANS were reported

Table 3. Adverse Events of Interest

Adverse Events of Interest, n (%)	All Patients (N=95)
Prolonged Cytopenia (by Day 30)[a]	16 (17)
Neutropenia	10 (11)
Thrombocytopenia	6 (6)
Clinically significant infections[b]	34 (36)
Deaths	**24 (25)**
Primary Causes of Death	
Primary Disease	22 (92)
Pulmonary failure[c]	2 (8)

- Among the 24 (25%) pts who died, primary cause of death was LBCL in 22 pts
  - The time to death for the two cases of non-relapse mortality (pulmonary failures) were 4.2 and 7.9 months[c]

[a]Among patients who survived Day 30. [b]Any infection diagnosed after the initial infusion of axi-cel that requires treatment. [c]One of the causes of death was in the context "refractory hypoxemia" which occurred at 7.9 months.

CONCLUSIONS

- This is the first national registry study of Canadian pts on axi-cel to treat R/R LBCL in real-world settings
- Early results presented here demonstrate effectiveness and safety profiles consistent with those observed internationally and in the ZUMA-1 trial
- This data support ongoing use of axi-cel for the treatment of R/R LBCL in Canada

ABBREVIATIONS

ASTCT, American Society of Transplantation and Cellular Therapy; AE, adverse event; axi-cel, axicabtagene ciloleucel; BCL, B-cell lymphoma; CAR, chimeric antigen receptor; CI, confidence interval; CIBMTR, Center for International Blood and Marrow Transplant Research; CNS, central nervous system; CR, complete response; CTTC, Cell Therapy Transplant Canada; CIF, cumulative incidence function; CRS, cytokine release syndrome; DLBCL, diffused large B-cell lymphoma; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; FL, follicular lymphoma; HGBCL, high grade B-cell lymphoma; HSCT, hematopoietic stem cell transplant; ICANS, immune effector cell-associated neurotoxicity syndrome; IQR, interquartile range; LBCL, large B-cell lymphoma; NRM, non-relapse mortality; OOR, overall response rate; OS, overall survival; PFS, progression-free survival; PMBCL, primary mediastinal large B-cell lymphoma; PR, partial response; PTLD, post-transplant lymphoproliferative disorder; pts, patients; REL/PD, relapse or progressive disease; R/R LBCL, relapsed/refractory large B-cell lymphoma; TTE, time to event

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DISCLOSURES

- Full author disclosures are available through the virtual meeting platform