Real World Evidence of Axicabtagene Ciloleucel (Axi-Cel) for the Treatment of Large B Cell Lymphoma in the United States

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Center for International Blood and Marrow Transplant Research® (CIBMTR®), a research collaboration between National Marrow Donor Program®/Be The Match® and Medical College of Wisconsin.

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Background

- Axicabtagene Ciloleucel (Axi-Cel) is approved in the US for the treatment of adult patients with relapsed or refractory large B cell lymphoma (LBCL) and follicular lymphoma after 2 or more lines of systemic therapy.
- A post-marketing study utilizing the infrastructure created by the Center for International Blood and Marrow Transplant Research (CIBMTR) for post-approval safety and efficacy assessment recently completed enrollment of patients with LBCL.

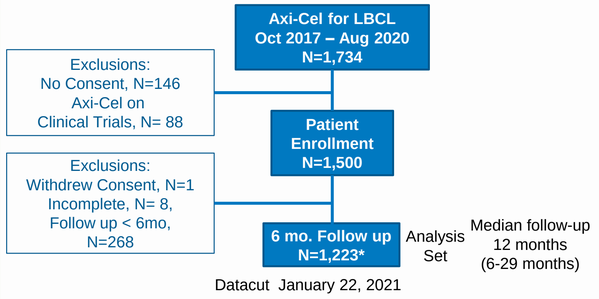
Objectives

- To describe safety and efficacy outcomes of commercial Axi-Cel as part of a post-approval safety study (PASS).
- Analyze efficacy outcomes among patients with at least 6 months follow up and based on disease status prior to Axi-Cel.

Methods

- Patients who received commercial Axi-Cel after the FDA approval date for LBCL and signed informed consent were included in the study.
- Description of patterns of care of commercial Axi-Cel, and analysis of disease response (Overall Response, [ORR], complete remission [CR] + partial remission [PR]), duration of response (DOR), progression-free survival (PFS) and overall survival (OS), cytokine release syndrome (CRS) and immune-effector cell associated neurotoxicity syndrome (ICANS).
- Comparison based on disease status at time of Axi-Cel based on sensitivity to prior therapy (sensitive, refractory or relapse untreated prior to Axi-Cel).
- Landmark analysis of PFS and OS among patients who were in CR at 6 months.
- Causes of death and subsequent neoplasms are also described.

Consort Diagram

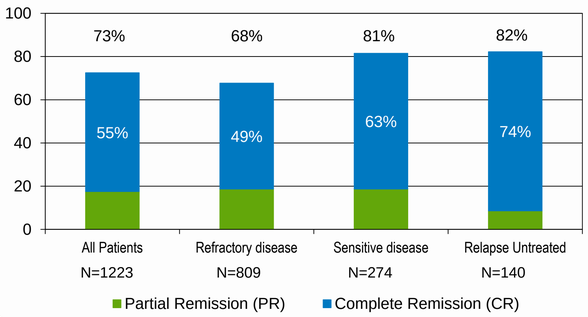


*For PFS, 1,174 patients had complete information on disease progression

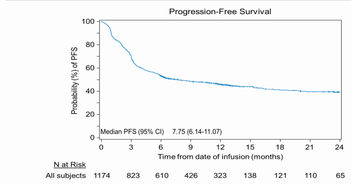
Patient Demographics

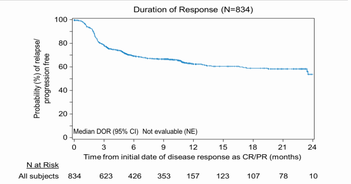
Characteristic	Total
No. of patients	1,223
No. of US centers	76
Median age, years (range)	62 (19-91)
≥65 y	38%
Male	65%
ECOG performance status 0-1	83%
Prior History of Malignancy	16%
Transformed lymphoma	26%
Double/triple hit lymphoma	15%
Chemotherapy resistant disease	66%
Prior auto-HCT	27%
Time from diagnosis to Axi-Cel, median months	14

Disease Overall Response

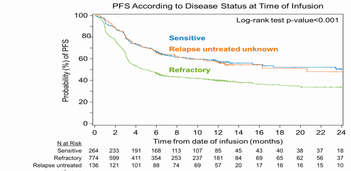


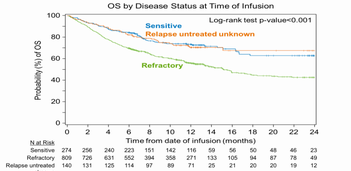
PFS and DOR



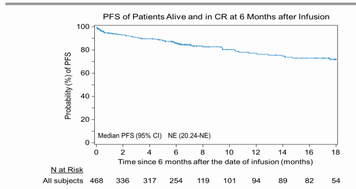


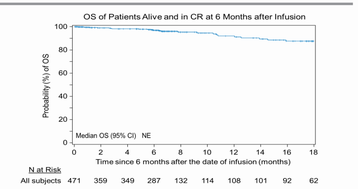
PFS and OS by Disease Status at time of Axi-Cel infusion





Landmark Analysis at 6 Months Among Patients in CR

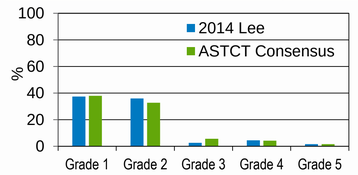


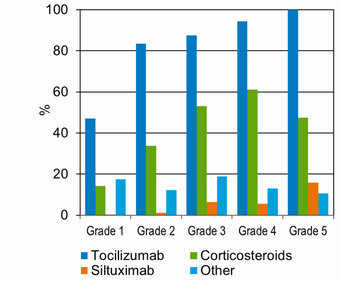


Patients who did not achieve CR within 6 months after Axi-Cel or relapsed/progressed/died within 6 months after Axi-Cel or had less than 6 months of follow-up were excluded.

CRS Grading and Treatment Patterns (N=1,223)

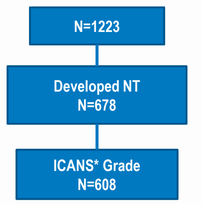
Characteristic	Total
Any CRS / Grade ≥3 [1]	82% / 9%
Time to CRS, median (range) in days	4 (1-28)
CRS resolved by day 14 post Axi-Cel	89%
Duration of CRS, median in days	7

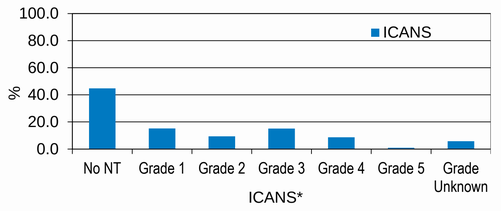




*[1] Lee D et al , Blood 2014; [2] ASTCT Consensus, Lee D et al, BBMT 2018, *Treatment of CRS not mutually exclusive*

Neurologic Toxicity and ICANS* Grading (N=1,223)



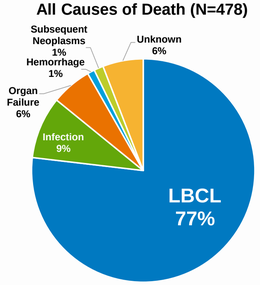


Characteristics	ICANS
Any ICANS / Grade ≥ 3 / Unknown Grade	55% / 24% / 6%
Time from CT to onset, median (range) in days	7 (1-82)
Neurologic toxicity resolution at 21d post Axi-Cel	77%
Duration of Neurologic Toxicity, days – median	9
Corticosteroids, Tocilizumab, Siltuximab	73%/17%/3%

**Immune-effector Cell Associated Neurotoxicity Syndrome, Lee DW et al BBMT 2018*

Subsequent Neoplasms & Causes of Death After Axi-Cel

Subsequent Neoplasms	Total
Myelodysplasia	18
Acute myeloid leukemia	2
GI malignancy	1
Lung cancer	1
Carcinoid tumor - lung	1
Melanoma	2
Non-melanoma skin carcinoma	8
Genitourinary malignancy	2
Other	3
Total (patients)	37



CAR T-Cell Specific Deaths:

- Neurologic Toxicity: N=4
- CRS: N=8
- Hemorrhage:
  - CNS N=3
  - GI N=2

Conclusions

- This is the largest report on Axi-Cel in the real-world setting and demonstrates consistent efficacy outcomes and further characterizes safety outcomes.
- Patients in CR at 6 months have sustained disease control with low number of relapse events.
- Although patients with therapy-sensitive disease experience better outcomes than patients with therapy-resistant, the overall outcomes on both groups of patients are favorable.

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