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Practical Implication of Multi-Institution Cytokine Release Syndrome and Immune Effector Cell-Associated Neurotoxicity Rates in Lymphoma Targeted Bispecific Antibodies

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Introduction

- Bispecific Antibodies (BsAb) including epcoritamab, glofitamab, and mosunetuzumab are crucial options for the treatment of relapsed/refractory lymphoma
- Known complications of BsAb therapy include cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity (ICANS)
- Currently hospitalization is required or should be considered for the initiation of BsAb therapy
- As these therapies continue to gain traction, practitioners seek to assess the safety and feasibility of outpatient administration and toxicity management

Primary objective: To offer real-world incidence of CRS/ICANS for lymphoma-directed BsAb therapy

Methods

Retrospective, multi-center review of adult patients who received commercial or investigational epcoritamab, glofitamab, or mosunetuzumab for non-Hodgkin's lymphoma

Key secondary outcomes were surrogates for resource utilization including CRS/ICANS management strategies, level of care required, and hospitalization

Descriptive statistics were utilized to summarize patient characteristics, features and rates of CRS/ICANS, and used resources

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Patient Demographics

	N = 87
Median age, years (range)	69 (61-79)
Male, n (%)	57 (66)
Lymphoma Diagnosis, n (%) Diffuse large B-cell Follicular Marginal zone Richter's transformation	 56 (65) 17 (20) 7 (8) 6 (7)
Disease Characteristics, n (%) Stage 3-4 Disease Central Nervous System Involvement	 76 (87) 6 (7)
Treatment History Median number of prior lines (range) Hematopoietic stem cell transplant, n (%) Chimeric receptor antigen T-cell therapy, n (%)	 4 (3-5) 13 (15) 35 (40)
Product Received, n (%) Commercial Epcoritamab Glofitamab Mosunetuzumab	 63 (72) 28 (32) 23 (27) 36 (41)

CRS/ICANS Prophylaxis

Glofitamab

- Cycle 1-3
  - Steroid, Acetaminophen, Antihistamine
- All subsequent infusions
  - Acetaminophen, Antihistamine
  - If patients experienced any grade CRS with the previous dose > Steroid

Epcoritamab

- Cycle 1
  - Steroid, Acetaminophen, Antihistamine
- All subsequent infusions
  - If patients experienced grade 2 or 3 CRS with previous dose > Steroid

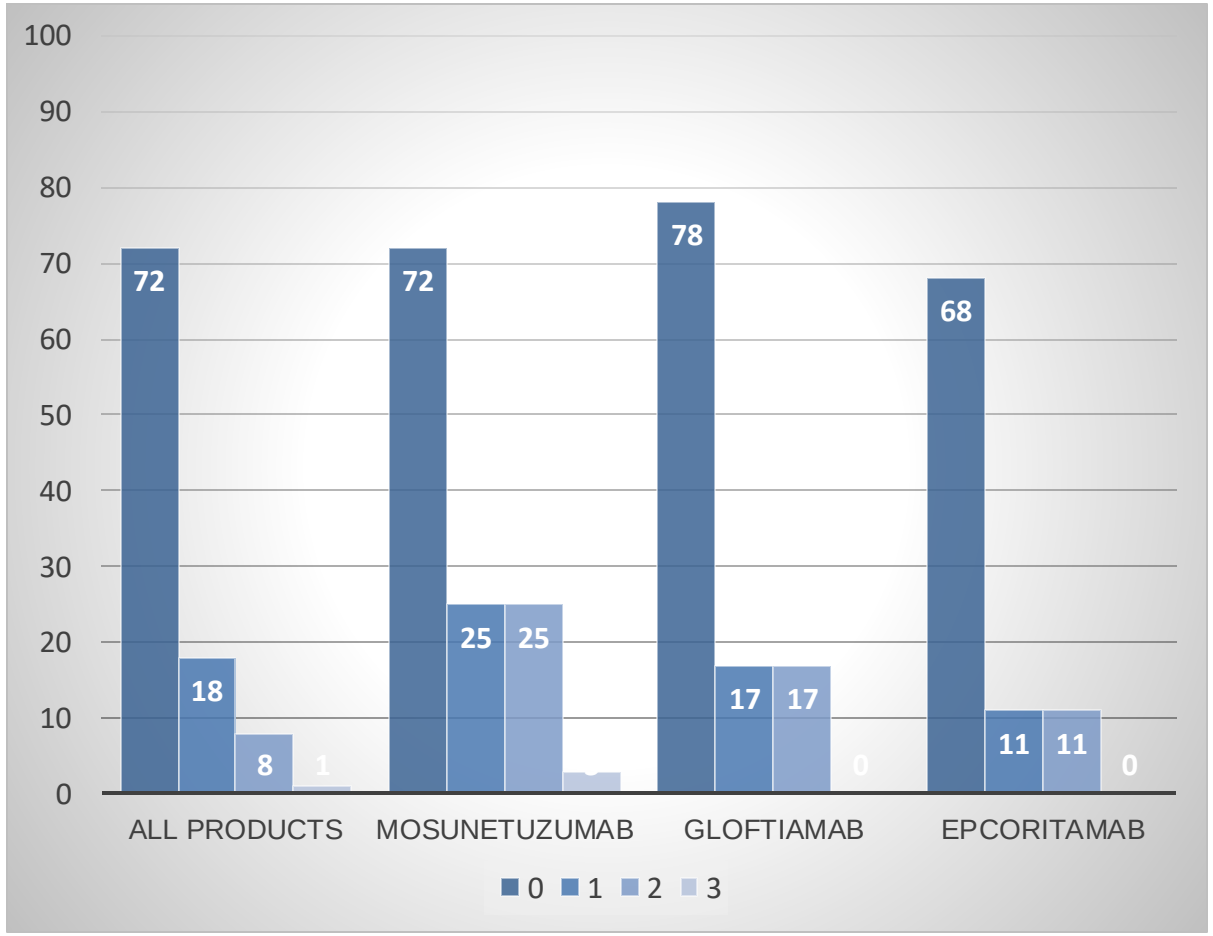
Mosunetuzumab

- Cycle 1 and 2
  - Steroid, Acetaminophen, Antihistamine
- All subsequent infusions
  - If patients experienced any grade CRS with previous dose > Steroid, Acetaminophen, Antihistamine

	N = 87
Steroid Prophylaxis Administered, n (%)	87 (100)
Dosing per Package Insert, n (%)	84 (98)
Additional Pre-Medication Prophylaxis, n (%)*	37 (43)

*Additional pre-medications typically included dexamethasone given at 12, 24, and 48 hours after C1 D1, 8, and 15 or montelukast

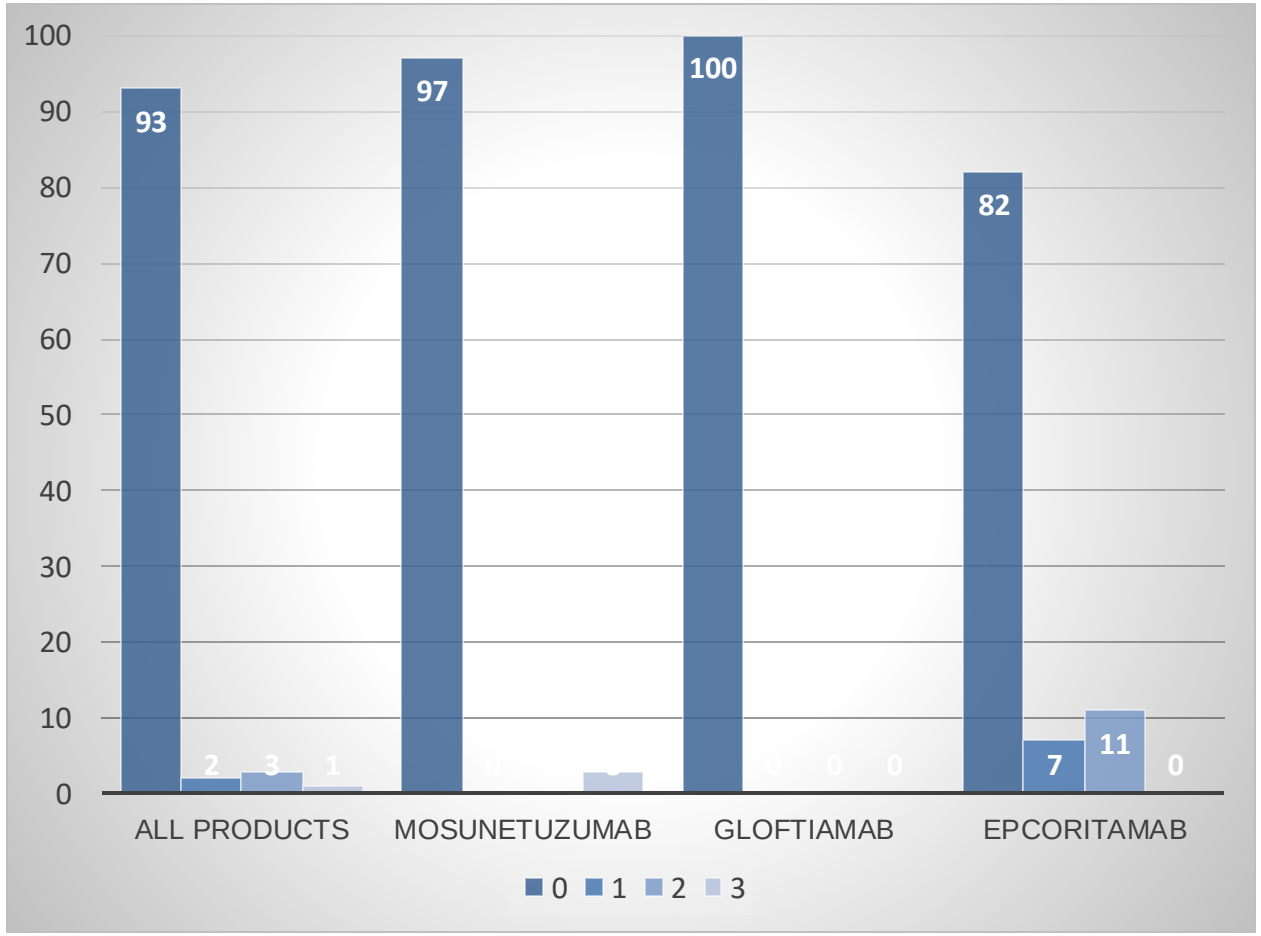
Incidence of CRS



CRS occurred in 24 (28%) patients

- 10 (28%) mosunetuzumab
- 9 (32%) epcoritamab
- 5 (23%) glofitamab

Incidence of ICANS



ICANS occurred in 6 (7%) patients

- 5 (83%) epcoritamab
- 1 (17%) mosunetuzumab

CRS Features

	Total Population (N = 87)
CRS Timing, median (range)	
Onset in Hours	48 (24-73)
Duration in Hours	24 (24-48)
CRS Management, n (%)	
Tocilizumab	9 (10)
Anakinra	0 (0)
Corticosteroids	12 (14)
Vasopressors	1 (1)

ICANS Features

	Total Population (N = 87)
ICANS Timing, median (range) Onset in Hours Duration in Hours	 84 (42-142) 36 (20-108)
ICANS Management, n (%) Corticosteroids	 5 (6)

Resource Utilization

	N = 87
ICU Admission, n (%)	3 (3)
First Dose Outpatient, n (%)	74 (85)
Therapy Discontinuation, n (%)	53 (62)
Patient Expired, n (%)	12 (22)

CRS/ICANS Rates in Pivotal Trials

Mosunetuzumab

- CRS
  - All = 44%
  - Grade 1 = 26%
  - Grade 2 = 17%
  - Grade 3 = 1%
  - Grade 4 = 1%
- ICANS
  - Confusion = 3%
  - Attention disturbance = 1%
  - Cognitive disorder = 1%

Epcoritamab

- CRS
  - All = 50%
  - Grade 1 = 32%
  - Grade 2 = 15%
  - Grade 3 = 3%
  - Grade 4 = 0%
- ICANS
  - All = 6%
  - Grade 1 = 5%
  - Grade 2 = 1%
  - One fatal event

Glofitamab

- CRS
  - All = 63%
  - Grade 1 = 47%
  - Grade 2 = 12%
  - Grade 3 = 3%
  - Grade 4 = 1%
- ICANS
  - All = 8%
  - Grade 3+ = 3%

Limitations

- Retrospective nature and a small patient population included in review
- Comparisons of this data to pivotal trials are limited by lack of homogeneity
- Occurrence of practice change throughout data collection and study period
- Design limits ability to assess long-term outcomes

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Conclusions

1. Low CRS/ICANS rates were seen with the use of lymphoma-directed BsAb
2. Overall incidence of CRS, as well as incidence by grade appeared to be similar or lower than pivotal trials for all 3 BsAbs
3. Overall incidence of ICANS, as well as incidence by grade appeared to be similar or lower than pivotal trials for glofitamab and mosunetuzumab, but this pattern was not seen for epcoritamab
4. The need for CRS/ICANS management, escalation of level of care, and hospitalization in our patients was minimal. This review offers a real-world view of CRS/ICANS incidence, as well as resource utilization that supports the safety and feasibility of outpatient administration

Future Directions

Increased number of BsAb dosing and management in the outpatient and community setting

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