Evaluation and Management of Cytokine Release Syndrome and Neurotoxicity Rates in Hematologic Malignancy Patients Treated with Bispecific Antibodies in Community Oncology Practice

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Background

- **Bispecific T-cell engaging antibodies (bispecifics)** enhance immune-mediated cytotoxicity for hematologic malignancies.
- **Adverse effects (AEs):** Cytokine Release Syndrome (CRS) & Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS), ranging from mild to severe.
- **Comparison to CAR T-cell therapy:** Similar AEs but require different management strategies.
- **Current management:** Corticosteroids, tocilizumab, and emerging outpatient care to reduce hospitalizations and improve quality of life.
- **Study focus:** Frequency & severity of CRS/neurotoxicity in bispecific-treated patients to optimize safety, balance inpatient vs. outpatient care, and improve clinical strategies in community oncology.

Introduction

Study Objectives

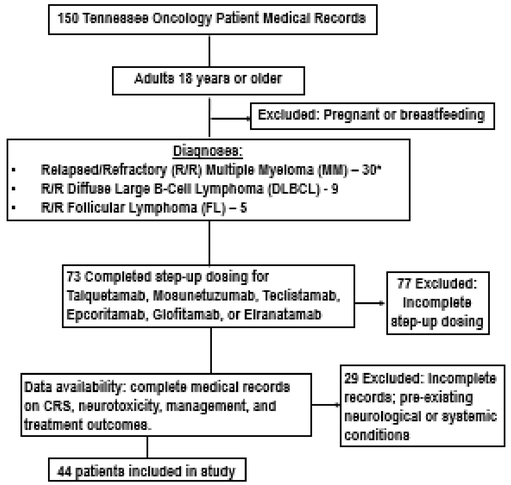
- Evaluate the frequency, severity, and management of CRS and neurotoxicity in patients receiving bispecifics.
- Assess the feasibility of outpatient treatment in community oncology settings.
- Optimize patient safety, resource utilization, and clinical outcomes.

Methodology

Study Design and Setting

- Retrospective, multicohort study; outpatient, community oncology clinic and hospital.

Inclusion/Exclusion Criteria



*One patient was treated with two bispecifics at different time periods

Methodology (continued)

Baseline Characteristics

Characteristic	All n= 44
R/R MM	68%
Predominant Sex (Female)	52%
Average Age at Treatment Onset	68.75 years old
Average Number of Prior Lines of Therapy	4.96
Average Prior Stem Cell Transplant	33%
Average Prior Monoclonal Antibody Treatment	84%

Data Collection

- **Data Source:** Medical record reports used to identify patients treated with hematologic bispecifics from December 2022 to December 2024.
- **Data Abstraction Fields:**
  - Patient MRN, sex, diagnosis
  - Bispecific therapy details (agent, setting)
  - Step-up/treatment doses before AE onset
  - CRS and neurotoxicity onset, severity, and intervention strategies
    - Hospitalization (duration, interventions)
    - Outpatient management (medications, supportive care)
  - Time to resolution or escalation

Primary Objectives and Statistical Analysis

- **Frequency of CRS and Neurotoxicity:** Determine incidence rates using EMR data.
  - $\textbf{Incidence Rate} = \frac{\text{Number of Patients with CRS or Neurotoxicity}}{\text{Total Number of Patients Receiving Bispecifics}} \text{ X } 100$
- **Management Strategies:** Evaluate hospitalization vs. outpatient care for CRS and neurotoxicity.
  - $\textbf{Proportion Hospitalized} = \frac{\text{Number of Hospitalized Cases}}{\text{Total Cases with CRS\Neurotoxicity}} \text{ X } 100$
  - $\textbf{Proportion Outpatient} = \frac{\text{Number of Outpatient Cases}}{\text{Total Cases with CRS\Neurotoxicity}} \text{ X } 100$
  - **Severity Comparison: Compare management strategies by AE grade.**

Secondary Objectives and Statistical Analysis

- **Feasibility in Community Oncology:** Assess the feasibility of managing CRS and neurotoxicity, including tocilizumab, corticosteroids, or ICU care.
  - $\textbf{Proportion Requiring Escalation} = \frac{\text{Cases Transferred to Hospital}}{\text{Total CRS\Neurotoxicity Cases}} \text{ X } 100$

Subgroup Analyses

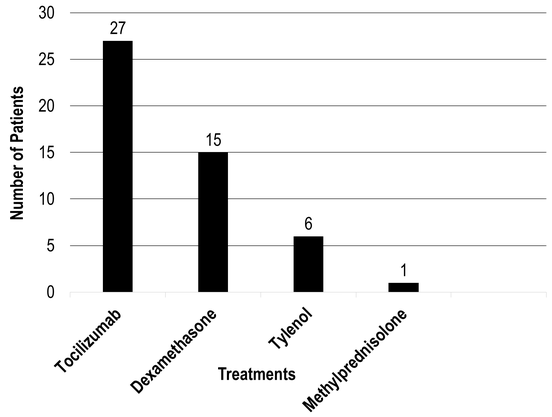
- **By Bispecific Therapy Type:** Analyze AE incidence and compare with chi-square test.
- **By Malignancy Type:** Compare AE frequency and grade.
- **By Severity:** Calculate incidence rates for each AE grade and compare treatment outcomes.

Results

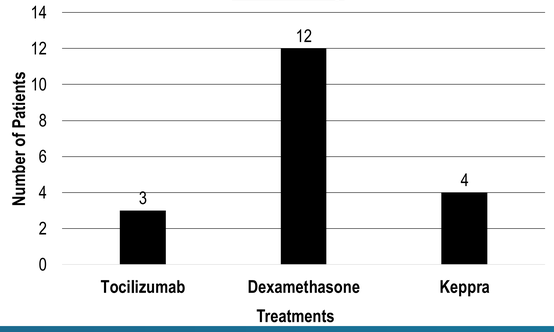
Primary Objectives

Primary Objectives n= 44	Outcome (%)
Incidence Rate of CRS or Neurotoxicity	29
Proportion Hospitalized	89
Proportion Outpatient	11

CRS



Neurotoxicity



Results (continued)

Primary Objectives (continued)

Comparison of Severity (Number of Occurrences) Grade	CRS	Neurotoxicity
1	14	10
2	24	2
3	1	2
Unknown	1	2

Secondary Objectives

- **Time to Intervention:** On average, interventions were implemented for patients experiencing CRS or neurotoxicity **< 1 day** after onset of symptoms.
- **Transition of Care: 3 out of 44** patients transferred from outpatient to higher-level of care.
- **Escalation Proportion: 6.8%** of patients were transitioned from outpatient to hospital level of care.

Subgroup Analyses

Bispecific	CRS (%)	Neurotoxicity (%)	p-Value
Talquetamab	5.07	1.93	0.863
Teclistamab	16.66	6.34	
Elranatamab	7.24	2.76	
Glofitamab	2.90	1.10	
Epcoritamab	4.34	1.66	
Mosunetuzumab	5.79	2.21	

Characteristic (%)		R/R MM n=30*	R/R FL n= 5	R/R DLBCL n=9
CRS		1.21	1	0.89
Neurotoxicity		0.38	0.2	0.11
Grade 1	P-Value: 0.016	0.45	0.6	0.22
Grade 2		0.55	0.2	0.78
Grade 3		--	0.2	--
Outpatient		3	40	22
Hospital	P-Value: 0.004	97	60	78

Conclusion

- CRS/neurotoxicity common with bispecifics, requiring close monitoring
- Incidence aligns with known toxicity profiles
- 9/10 patients hospitalized during observation, highlighting severity and resource demands
- Patients required 24-48 hours of care, exceeding Tennessee Oncology's capacity
- No significant link between bispecific type and toxicity
- Low outpatient management suggests most patients need hospitalization

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WIRB-Copernicus Group Institutional Review Board Approved-Study No. 1387984

References: