Supportive Care Bispecific Antibodies Strategies

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Disclosures

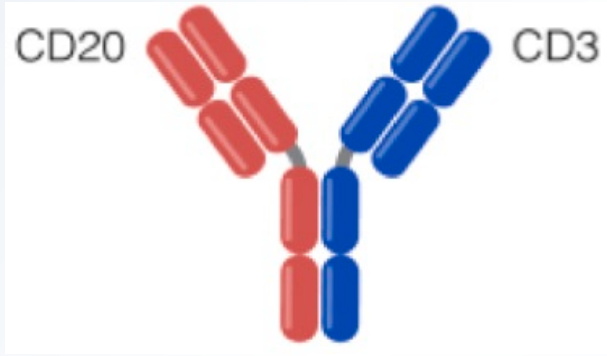
- No relevant conflicts of interest to disclose

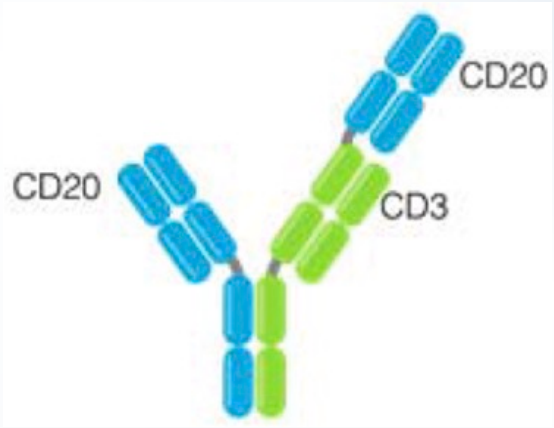
Objectives

- Understand the supportive care of the FDA approved bispecific antibodies in Non-Hodgkin lymphoma

- Review mitigation strategies to minimize toxicity

NHL CD20 Targeted Bispecific T-cell Engagers





Mosunetuzumab

- Knob-in-holes technology with 1:1 ratio
- CD20 type 1 epitope identical to rituximab

Epcoritamab

- DuoBody technology with 1:1 ratio
- CD20 type 1 epitope shared by ofatumomab

Glofitamab

- CrossMab technology with 1:2 ratio
- CD20 type 2 epitope identical to obinutuzumab

Falchi L, Vardhana SA, Salles GA. Bispecific antibodies for the treatment of B-cell lymphoma: promises, unknowns, and opportunities. *Blood*. 2023;141(5):467-480.

Infusion/Injection Related Reactions

Bispecific T-cell engagers are created using humanized antibodies

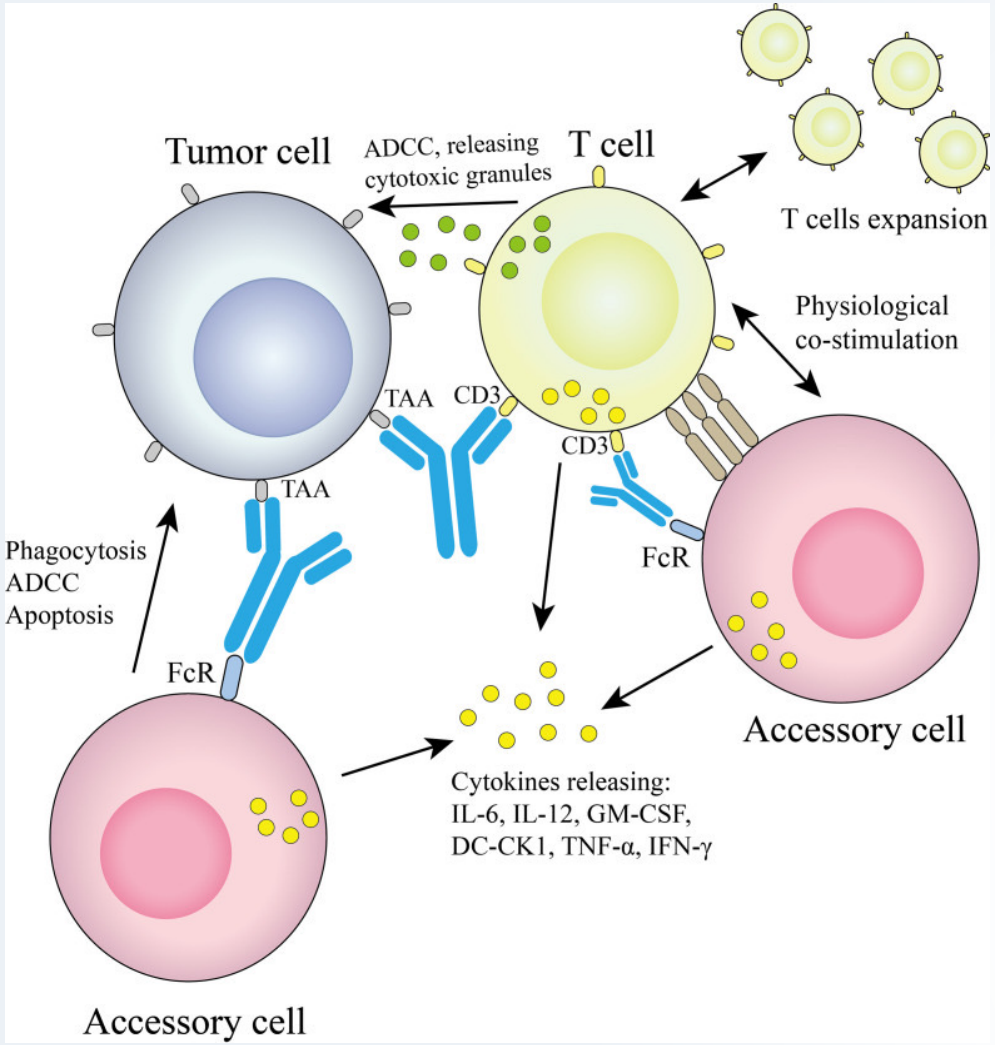
- Mosunetuzumab: < 10% infusion-related reactions
- Epcoritamab: 27% injection-site reactions (Grade 3+: 0%)
- Glofitamab: < 10% infusion-related reactions

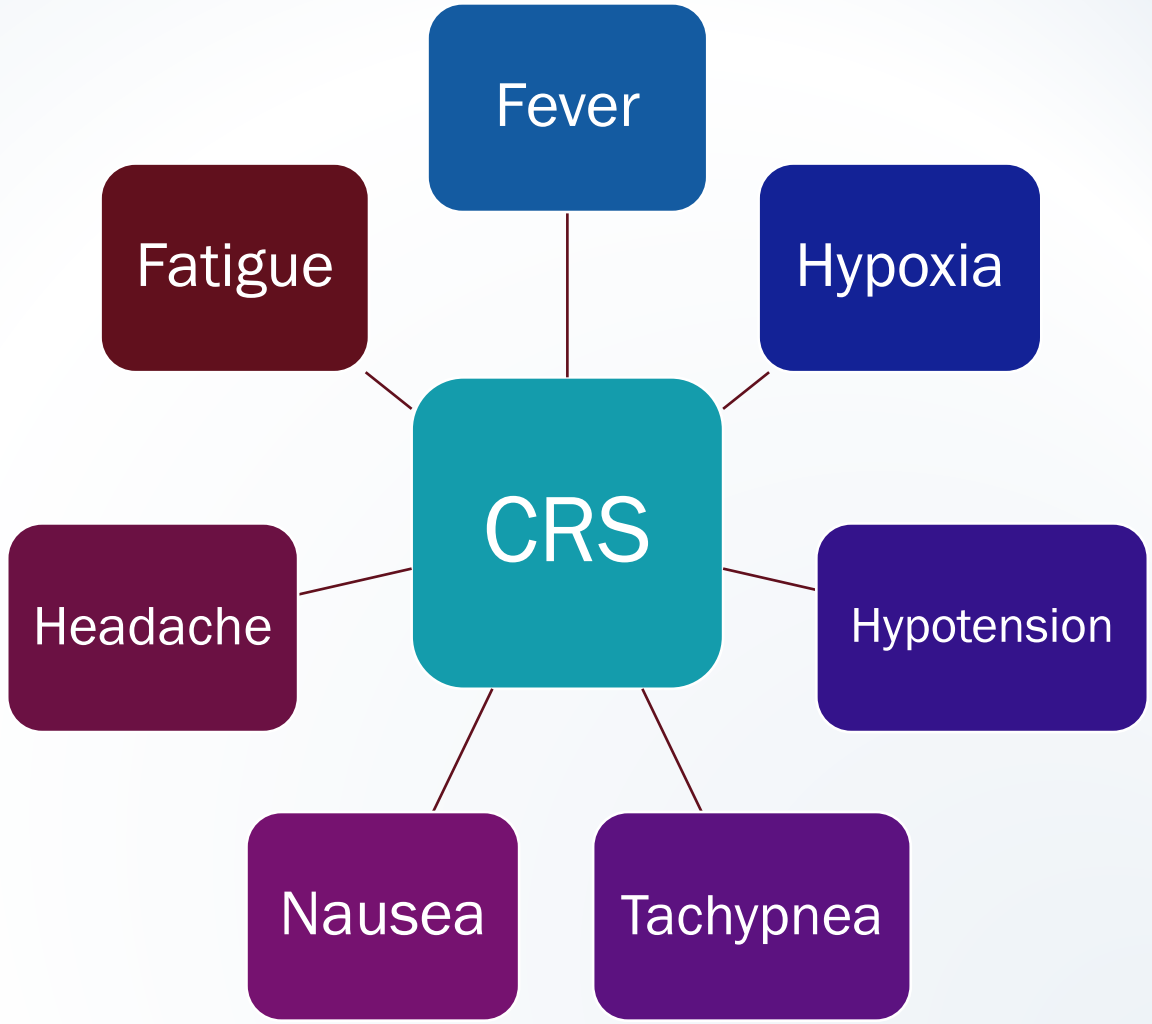
Mosunetuzumab	Epcoritamab	Glofitamab
Acetaminophen 650-1000 mg **Diphenhydramine** 50 mg	**Acetaminophen** 650-1000 mg **Diphenhydramine** 50 mg	**Acetaminophen** 650-1000 mg **Diphenhydramine** 50 mg
All Cycle 1 and Cycle 2	All Cycle 1	All cycles
At least 30 minutes prior to infusion	30-120 minutes prior to administration	At least 30 minutes prior to infusion

Glofitamab [package insert]. Genetech US, Inc. Epcoritamab [package insert]. Genmab US, Inc.LUNSUMIO™ [package insert]. Genentech, Inc.

Cytokine Release Syndrome (CRS) and Neurotoxicity

Cytokine Release Syndrome (CRS)





Crombie JL, Graff T, Falchi L, et al. Consensus Recommendations on the Management of Toxicity Associated with CD3xCD20 Bispecific Antibody Therapy. *Blood*. Published online January 22, 2024.

ASTCT Grading of CRS

CRS Parameter	CRS Grade 1	CRS Grade 2	CRS Grade 3	CRS Grade 4
Fever	Temperature ≥38°C	Temperature ≥38°C	Temperature ≥38°C	Temperature ≥38°C
	With either:			
Hypotension	None	Not requiring vasopressors	Requiring one vasopressor (with or without vasopressin)	Requiring multiple vasopressors (excluding vasopressin)
	And/or			
Hypoxia	None	Requiring lowflow nasal cannula (≤ 6L/min) or blow-by	Requiring high-flow nasal cannula (> 6L/min), facemask, non-rebreather mask, or Venturi mask	Requiring positive pressure (e.g. CPAP, BiPAP, intubation and mechanical ventilation)

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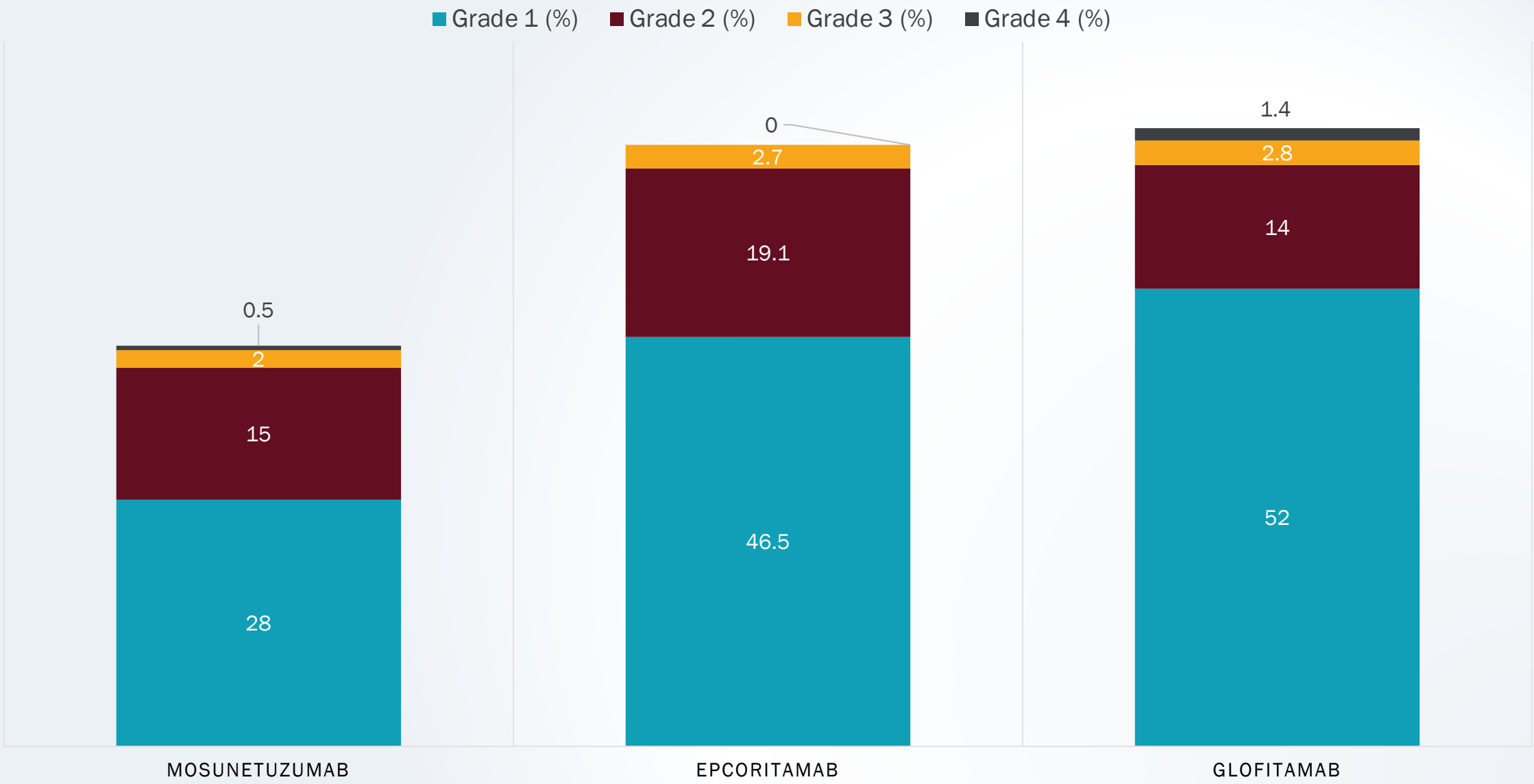
Average CRS Grade



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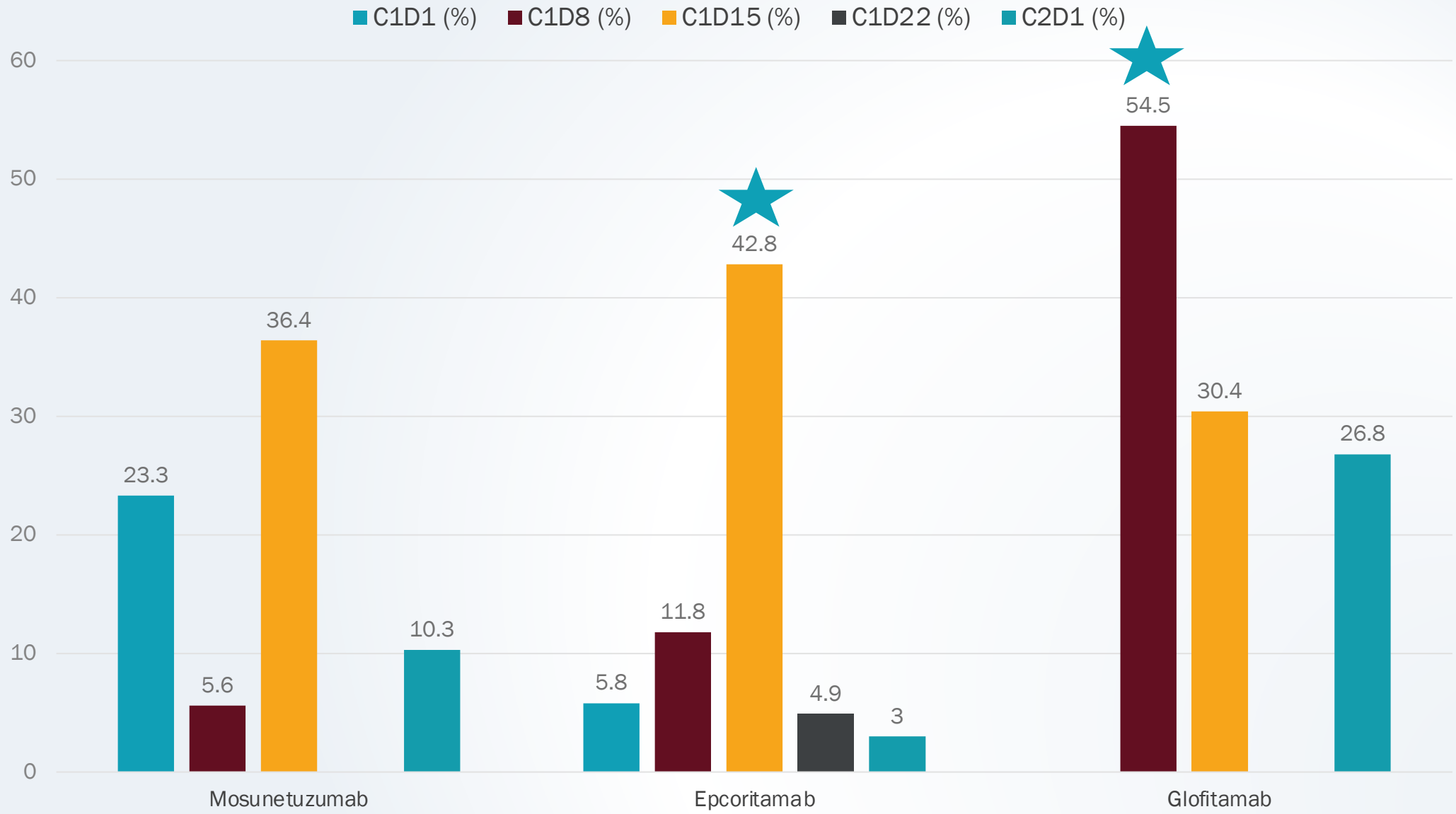
Time Course for CRS Onset



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Median Time and Duration of CRS

Bispecific T-cell Engager	Median Time to CRS	Median Duration of CRS
Mosunetuzumab	C1D1: 5 hours C1D8: 20 hours C1D15: 27 hours C2D1: 38 hours	3 days (1-29 days)
Epcoritamab	All doses except below: 24 hours *C1D15: 20 hours	2 days (1-27 days)
Glofitamab	*C1D8: 13.5 hours (6-52 hours)	30.5 *hours* (0.5-317 *hours*)

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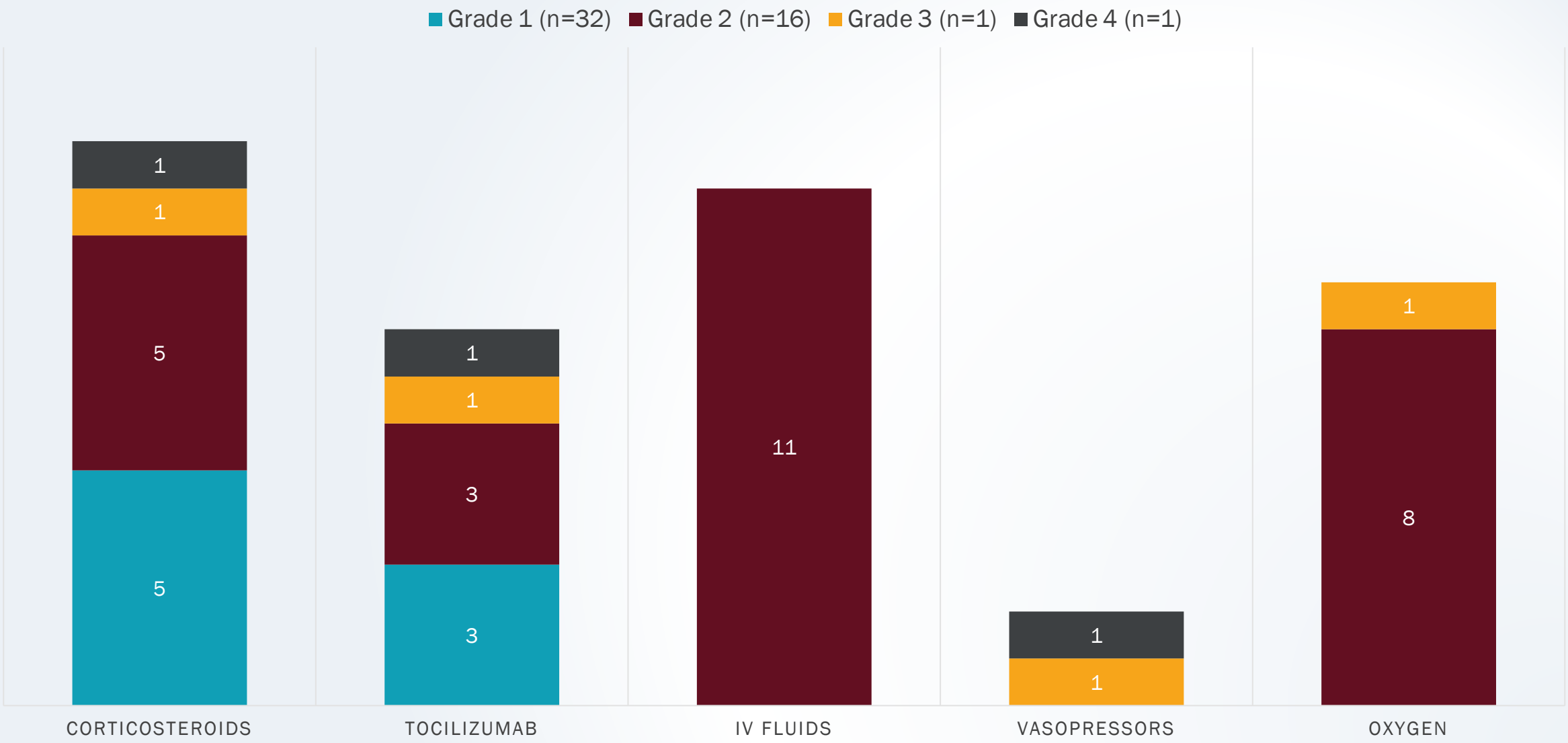
Mosunetuzumab CRS Management



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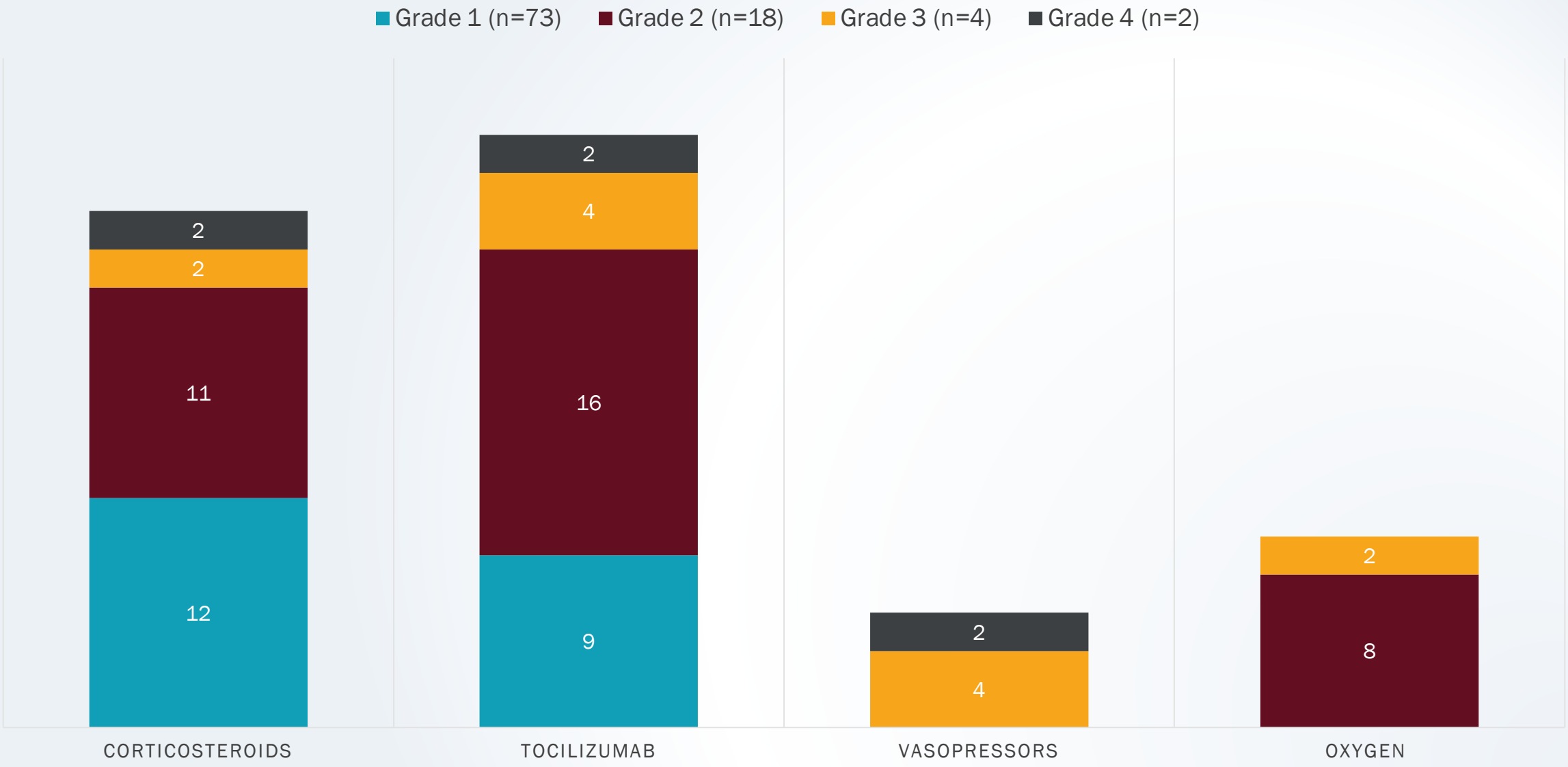
Glofitamab CRS Management



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CRS Management

Slow infusion rate?

Inpatient CRS monitoring?

Grade 1

- Acetaminophen 650-1000 mg PO
  - Repeat if recurrent fever 6-8 hours later if clinically stable
- Aggressive oral hydration
- Continue to check temperature every 1-2 hours and other vitals if able
- If symptoms are persistent:
  - Evaluate in clinic or ED

Grade 2

- Evaluate patient in clinic or ED
- Acetaminophen 650-1000 mg Q6-8 hours
- Start Dexamethasone 10 mg PO Q12H
- Administer IV fluids/supplemental oxygen as appropriate
- If symptoms are persistent:
  - Tocilizumab 8 mg/kg (max 800 mg)

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CRS Management

Hospitalize for next dose

Permanently discontinue!

Grade 3

- Emergent inpatient admission
- Acetaminophen 650-1000 mg Q 6-8 hours as needed
- Dexamethasone 10 mg IV Q 6 hours
- Tocilizumab 8 mg/kg (max 800 mg)
- If refractory hypotension/hypoxia admit to ICU
  - Consider anakinra or siltuximab

Grade 4

- Inpatient admission to ICU
- Acetaminophen 650-1000 mg Q 6-8 hours as needed
- Dexamethasone 20 mg IV Q 6 hours
- Tocilizumab 8 mg/kg (max 800 mg)
  - Consider anakinra or siltuximab if refractory

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CRS Mitigation

- Weekly step-up dosing strategy
- Prophylactic dexamethasone

Mosunetuzumab

Dexamethasone 20 mg

Cycle 1 and Cycle 2

Epcoritamab

Dexamethasone 15 mg
- Day 1 through and including Day 4

Cycle 1 only

Glofitamab

Dexamethasone 20 mg

Cycle 1, Cycle 2 and Cycle 3

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Potential Risk Factors for CRS

- High tumor burden (Bulky disease, elevated LDH, elevated uric acid)
- History of CRS with CAR-T or with previous step-up doses
- High baseline CPR and ferritin
- Frailty
- Comorbidities (cardiac or pulmonary)

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The Question of Outpatient CRS Monitoring

- IV hydration with each step-up dose
- Ensure medications and thermometer at home
- Check temperature at home three times a day for 48 hours post dose
- Hold blood pressure medication for 48 hours
- Consider a 24-hour post dose phone call
- Develop a bispecific CRS monitoring team
- Distance of patient to hospital with tocilizumab

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Average Neurotoxicity Grade

Bispecific T-cell Engager	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Mosunetuzumab	3%	3%	0%	0%	0%
Epcoritamab	4.5%	1.3%	0%	0%	0.6%
Glofitamab	5%	5%	3%	3%	0%

Common neurologic toxicities of any grade: Headache, dizziness or vertigo, peripheral neuropathy, mental status changes

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Cytopenias and Infection Risk

Neutropenia and Bispecific T-cell Engagers

Bispecific T-cell engager	Neutropenia (%)	Infection (%) Clinical Trials
Mosunetuzumab	All grade: 58% Grade 3+: 40%	All grade: 17% Grades 3-4: 14% Fatal: 0.9%
Epcoritamab	All grade: 56% Grade 3+: 26%	All grade: 15% Grades 3-4: 14% Fatal: 1.3%
Glofitamab	All grade: 38% Grade 3+: 27%	All grade: 16% Grades 3-4: 10% Fatal: 4.8%

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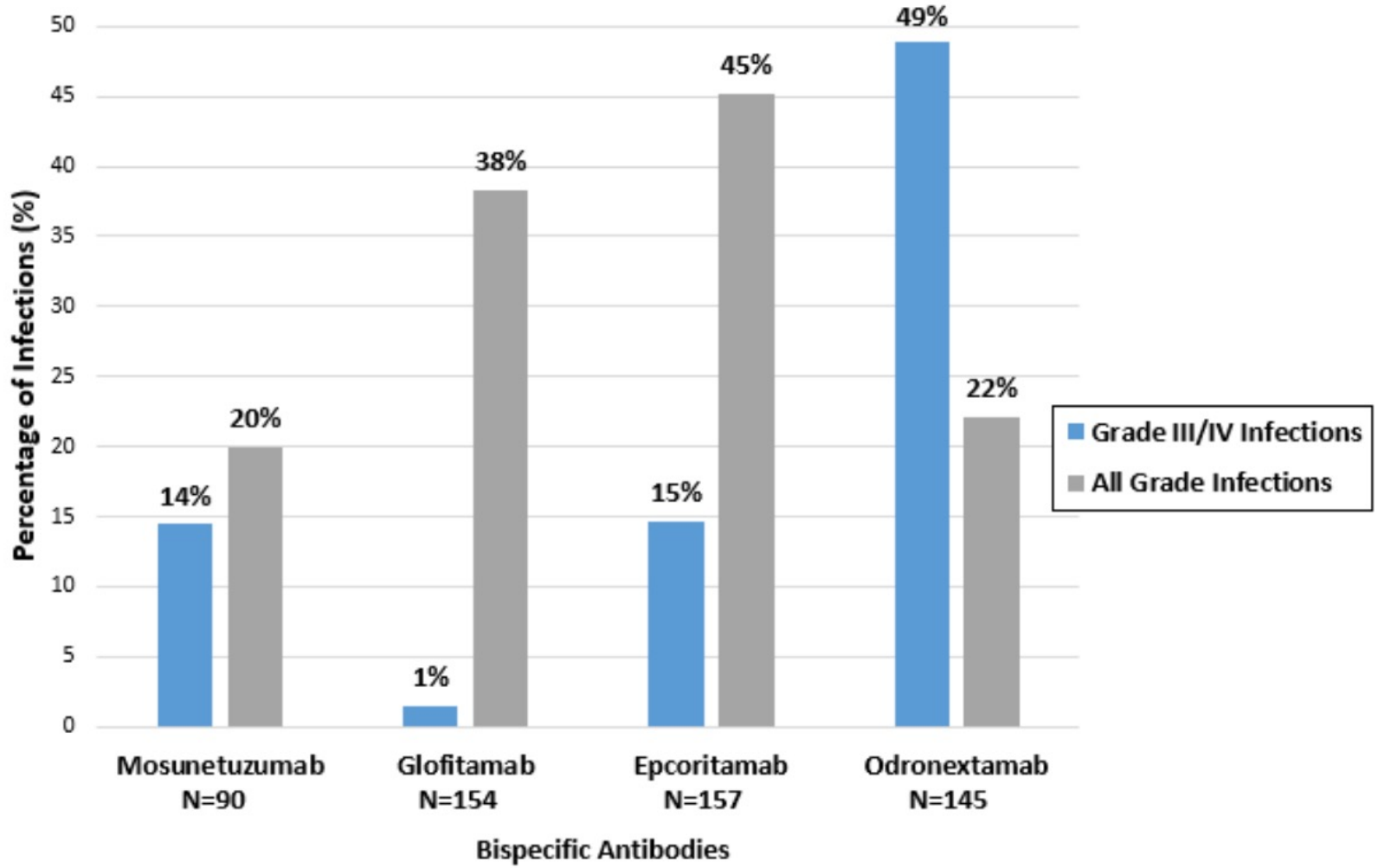
Infections and Bispecific T-cell Engagers

Figure 1: Incidence of Infections with BsAbs for B-cell NHL



ASH Abstract: #2329 Incidence of Infections Associated with the Use of BsAbs in B-cell Non Hodgkin Lymphoma

Infections and Bispecific T-cell Engagers

- Recommend prophylactic antimicrobials against *Pneumocystis jirovecii* pneumonia (PJP) and varicella zoster virus (VZV)
- Withhold treatment for patients with active infection and treat accordingly
- Consider secondary GCSF prophylaxis if concurrently neutropenic (ANC < 500/mm^3)
- Consider evaluating hypogammaglobinaemia and eligibility for IVIG depending on recurrent infection and institutional standards

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Other toxicities

Mosunetuzumab

- Fatigue, rash, pruritus, diarrhea, nausea, musculoskeletal pain, arthralgia, cough, increased GGT, hepatotoxicity, increased uric acid, increased glucose, anemia, thrombocytopenia

Epcoritamab

- Fatigue, musculoskeletal pain, diarrhea, nausea, vomiting, rash, decreased appetite, cardiac arrythmias, hepatotoxicity, anemia, thrombocytopenia, increase creatinine

Glofitamab

- Musculoskeletal pain, fatigue, constipation, diarrhea, nausea, tumor flare, anemia, thrombocytopenia, increased uric acid, increased GGT

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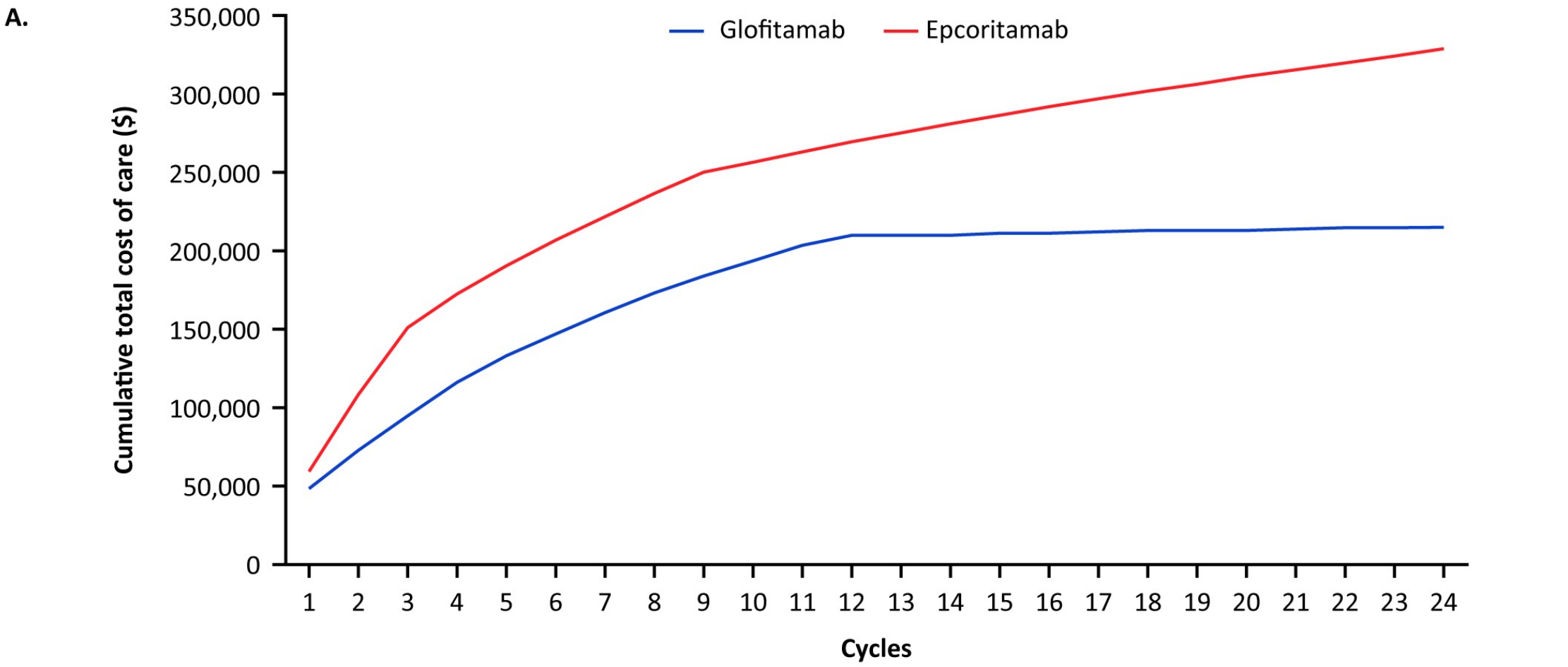
Financial Care

Figure: (A) Cumulative total cost of care for glofitamab versus epcoritamab over 24 treatment cycles and **(B)** differences in total costs of care between glofitamab and epcoritamab across various time horizons.



ASH abstract: 3703 Glofitamab Results in Cost Savings Versus Epcoritamab in Diffuse Large B-Cell Lymphoma (DLBCL): A Total Cost of Care Analysis. 2023

In Summary

- A low rate of Infusion/injection reactions were noted in clinical trials
- The majority of CRS was Grade 1-2 with the bispecific T-cell engagers
- There’s a gray area with moving all CRS monitoring outpatient or admitting for 24 hours as recommended
- Be aware of neutropenia and infections with the bispecific T-cell engagers
- Remember to consider individualizing treatment for the patient

Questions?

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