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Bispecifics for LBCL: Focus on Management of Toxicities in the Community

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Disclosures

- Consulting: Seagen, MorphoSys, Incyte, Kite, ADC Therapeutics, Regeneron
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Outline

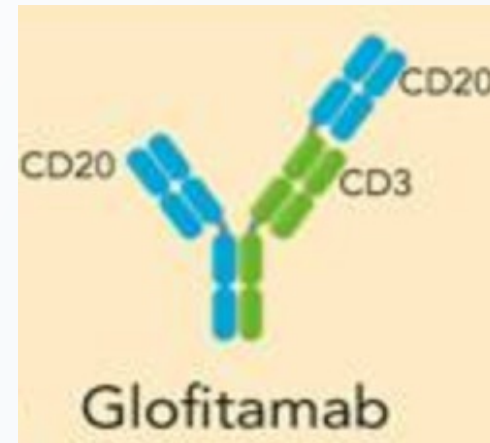
- CD3xCD20 bispecific antibodies for DLBCL
- Key toxicities
- Use of bispecifics antibodies in a range of clinical settings
- Management of toxicities

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Bispecific antibodies for DLBCL

- Epcoritamab
 - 1:1 CD20xCD3 binding
 - SC administration
 - Continuous dosing
 - Steroid prophylaxis for CRS
- Glofitamab
 - 2:1 CD20xCD3 binding
 - IV administration
 - Obinutuzumab pre-treatment
 - Time-limited therapy



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Important side effects with bispecifics

- Cytokine release syndrome (CRS)
- Neurologic toxicity
- Tumor flare
- Cytopenias
- Infectious complications

Determining the severity of CRS

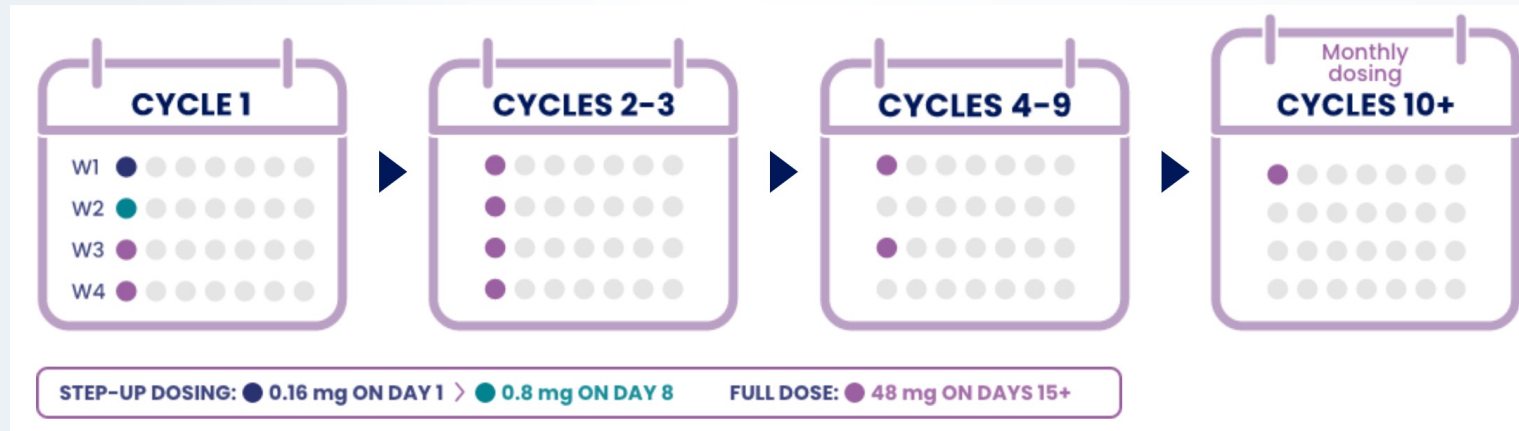
ASTCT Grading				
CRS Parameter	Grade 1	Grade 2	Grade 3	Grade 4
Fever*	Temperature $\geq 38^{\circ}\text{C}$	Temperature $\geq 38^{\circ}\text{C}$	Temperature $\geq 38^{\circ}\text{C}$	Temperature $\geq 38^{\circ}\text{C}$
		With		
Hypotension	None	Not requiring vasopressors	Requiring a vasopressor with or without vasopressin	Requiring multiple vasopressors (excluding vasopressin)
		And/or ^{††}		
Hypoxia	None	Requiring low-flow nasal cannula [‡] or blow-by	Requiring high-flow nasal cannula [‡] , facemask, nonrebreather mask, or Venturi mask	Requiring positive pressure (i.e., CPAP, BiPAP, intubation and mechanical ventilation)

Toxicities with eporitamab

- Epcoritamab
 - **CRS (50%):** G1: 32%, G2: 15%, G3: 2.5%
 - Fever (24%), fatigue (23%), low white blood count (22%), diarrhea (20%), nausea (20%)
 - ICANS: 6% (1% G3+)

When does CRS occur with epcoritamab?

- C1D1: 5.8%
- C1D8: 11.8%
- **C1D15: 42.8% **** Hospitalization recommended
- C1D22: 4.9%
- C2D1+: 3%
- Median time to onset: 24 hours



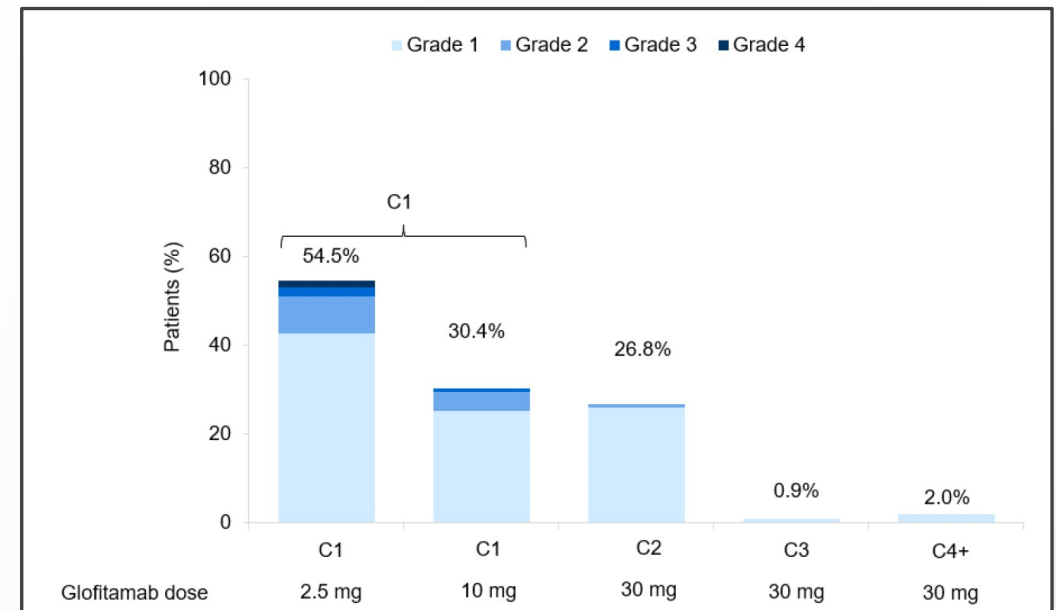
Toxicities with glofitamab

- Glofitamab
 - **CRS (63%):** G1: 47%, G2: 12%, G3: 3%, G4: 1%
 - Low white blood count (38%), low red blood cells (31%), low platelets (25%), musculoskeletal pain (20%), fatigue (20%)
 - ICANS: 8% (3% G3)

When does CRS occur with glofitamab?

- **C1D8: 54.5% **Hospitalization recommended**
- C1D15: 30.4%
- C2: 26%
- C3+: 0.9%
- Median time to onset: 13.5 hours

Cycle	Day	Dose of Glofitamab	
Cycle 1	Day 1	Obinutuzumab 1000 mg	
	Day 8	Step-up dose	2.5 mg
	Day 15	Step-up dose	10 mg
Cycle 2-12	Day 1	30 mg	



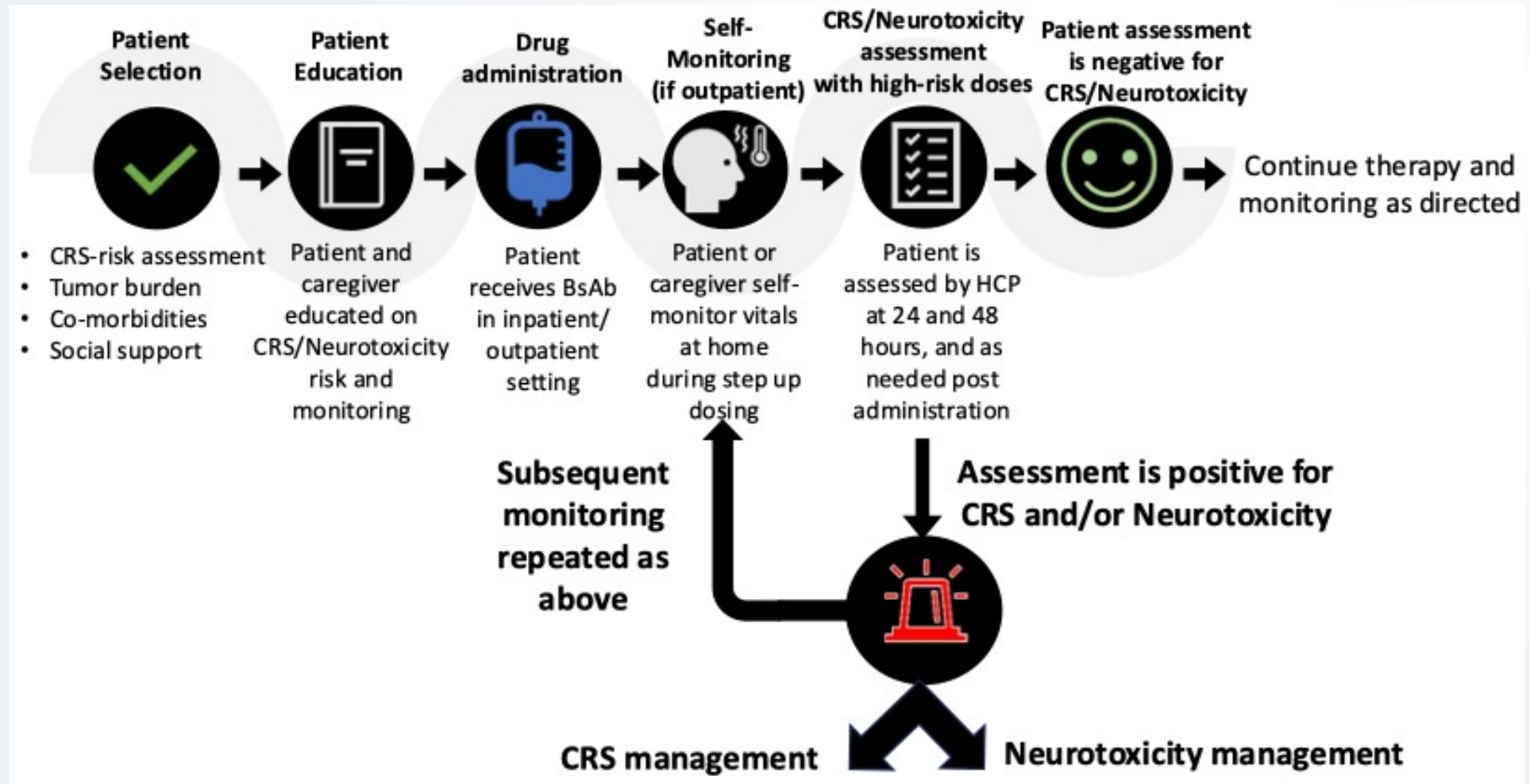
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How can we expand safe use in the community?

- Consensus recommendations for management of toxicity (Crombie, Graff, Falchi, Karimi et al., Blood, 2024)
- Continued evaluation of toxicities
 - Toxicities in real world setting
 - Success of management strategies in various settings
 - Risk stratification and mitigation strategies
- Alternative mechanisms to monitor patients after outpatient treatment being explored

Toxicity Management Overview



Pre-treatment Planning

- Treatment team
 - Patient assessment
 - Identify nearby hospital with ICU and tocilizumab
 - Identify care team comfortable with bispecific therapy/CRS
 - Educate emergency room staff
- Patient and caregiver
 - Education
 - Ensure ability to measure vitals (temperature)
 - Carry wallet card

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Management of Grade 1 CRS

Home:

- Acetaminophen
- Oral hydration
- Monitor temperature (and other vitals if able) every 1-2 hours

Home versus outpatient/ED evaluation:

- If recurrent fever, consider dexamethasone 10 mg once
- Consider earlier administration of steroids and immediate in-person evaluation for patients with multiple disease risk factors or comorbidities
- Consider daily dexamethasone with persistent symptoms

Additional management:

- Tocilizumab with protracted fever (e.g. >48 hours despite corticosteroids).
- Early tocilizumab after trial of dexamethasone should be considered in patients with multiple medical risk factors

Management of Grade 2 CRS

- Evaluation in-person
- Recommend inpatient management for most cases of Grade 2 CRS unless qualified outpatient day hospital/infusion center and no hypoxia.
- Tylenol
- Dexamethasone 10 mg every 12 hours
- IVF/O2
- Administer tocilizumab if symptoms persist despite IV fluids and dexamethasone (approximately 4-6 hours after dosing) or if clinically unstable. Consider alternative agent (e.g. anakinra or siltuximab) if persistent symptoms despite maximal dosing

Management of Grade 3 CRS

- Emergent inpatient admission (floor or ICU)
- Tylenol
- Dexamethasone (e.g. 10 mg IV Q 6 hours), until resolution to grade ≤ 1 , followed by taper
- Evaluate for sepsis and consider empiric antibiotics
- Administer tocilizumab and consider alternative agent (e.g. anakinra or siltuximab) if persistent grade 3 CRS despite maximal dosing

Management of Grade 4 CRS

- Inpatient admission to ICU
- Acetaminophen
- Dexamethasone (e.g. 20 mg IV Q 6 hours), until resolution to grade ≤ 1 , followed by taper
- Administer tocilizumab and if repeated doses of tocilizumab have been utilized, consider alternative agent (e.g. anakinra or siltuximab) if persistent grade 4 CRS despite maximal dosing of first agent.

Neurologic toxicity is rare

- No driving restrictions for patients who feel well
- No need for ongoing neurologic monitoring
- If toxicity occurs, can manage as ICANs
- Consider alternative causes

Other toxicities

- Tumor flare
 - Consider inpatient treatment
 - Steroids
- Cytopenias
 - Growth factor as needed
- Infections
 - PCP and VZV prophylaxis recommended
 - Risk of viral infections (ie COVID-19)
 - Monitor for hypogammaglobulinemia, IVIG as needed

Thank you
