Blinatumomab (Blincyto®) Care Guideline

Inclusion Criteria: Patients receiving blinatumomab
Exclusion Criteria: Patients not eligible to receive blinatumomab

Interventions

- Labs:
  - CBC, CMP
    - Requirements to start cycle: ANC > 750, platelet > 75,000 (or per provider discretion).
    - IgG level – monitor monthly, starting after the first blinatumomab cycle and continuing through maintenance until levels stabilize within the normal range.
- Admit to oncology.
- If scheduled for lumbar puncture on day of admission, start blinatumomab infusion *after* procedure. Hydrate with a NS bolus 10 mL/kg to infuse over 1 hour and then change rate to TKO until the blinatumomab is hung.
- Dosing:
  - Dexamethasone 5 mg/m^2 PO/IV within 30 minutes of starting blinatumomab infusion.
  - For Down Syndrome patients only – anti-seizure prophylaxis:
    - Levetiracetam 10 mg/kg/dose (Max = 1000 mg) IV/PO q12h, start 12 hours prior to the start of blinatumomab infusion and continue until completion of blinatumomab infusion.
  - Blinatumomab: 15 mcg/m^2/day x 28 days (wt. < 45 kg) or 28 mcg/day (fixed dose wt. > 45 kg).
  - Relapsed/refractory ALL patients may get step dosing: 5 mcg/m2 or 9 mcg for Day 1 to 7, then 15 mcg/m^2 or 28 mcg Day 8 to 28.
  - Inpatients will have 24 hour bags of blinatumomab (will-call pharmacy each day)
- Nursing ratio 1:2 for first 24 hours.
- Vital signs q15 minutes x 1 hour then q2 hours for first 24 hours, then routine if stable. Monitor for neuro changes with each vital sign check.
- Continuous cardiac monitoring for first 24 hours.
- Neuro checks q shift:
  - Daily finger-nose, writing sample test, or utilize child life to assist with age appropriate assessment for neuro changes/tremors.
- Labs 1 - 2 times during admission (daily labs not indicated during blinatumomab infusion).
- Diet and activity as tolerated.
  - Patients must remain on the unit while blinatumomab is infusing

Recommendations/Considerations

- Ensure line is secured using securement garment (CareAline® , Gus Gear®) or other securement strategies.
- Implanted ports:
  - Recommend access with Deltec Gripper needle or other needle with polyurethane tubing.
- Attempt to perform required lab draws with bag change to minimize interruptions to blinatumomab infusion and line entries.
- For lab draws (including blood cultures) they can be drawn by pausing the blinatumomab and withdrawing 4 - 5 cc of blood as a discard. Then draw sample, flush with saline, and reconnect blinatumomab.
- Monitor for Cytokine Release Syndrome (CRS) *see Table 1* – most common in first 24 - 48 hours.
  - Severity of CRS is associated with degree of tumor burden.
- Monitor for neurotoxicities *see Table 2* – can happen anytime throughout infusion, but most common within the first 2 weeks.
- Fever management:
  - Pause blinatumomab, draw cultures from central line.
  - Daily Ceftriaxone may be given via blinatumomab line (pause Blina during antibiotic infusion). Dosage: 75 mg/kg (max dose 2g) daily.
- If blinatumomab is paused for ≥ 4 hours, patient must receive another dose of dexamethasone.
- Administer IVIG based on individual symptoms and patient-specific patient conditions, rather than universally for low IgG levels.
- Per CHOC's Blood Culture Algorithm - avoid drawing blood cultures in asymptomatic patients who have inadvertent CVAD disconnection and/or broken or cracked CVAD.

CHOC Blood Culture Algorithm

Discharge Criteria

- Afebrile, no s/s of CRS or neurotoxicities
- Blinatumomab education completed
- 7 day bag must be connected to home Curlin pump
- Provider to sign CHOC Blinatumomab After Hours ONC PowerPlan
- For issues with pump while at home, see *Blina Issues After Hours and Weekends Provider Workflow*.

Day of Discharge

- 7 day bag connected to Curlin pump
- Send patient with batteries and power cord to change every other day
- Calendar with follow-up appointment and battery change reminders.
- Patient Education
  - PFE handouts:

Blinatumomab Infusion Problems

Curlin Pump Guide

Common Side Effects with Blinatumomab

- Consider line protection strategies (sleeve/wrap, Aquaguard for showers)
- ***Patients should not drive during*** blinatumomab ***infusion***

Approved Evidence Based Medicine Committee
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Table 1: Managing Cytokine Release Syndrome (CRS)		
Grade	**Symptoms**	**Management**
1	Temperature ≥ 38.3° C	• Vigilant supportive care • Assess for infection with blood cultures • Begin broad spectrum antibiotics • Acetaminophen as needed
2	Temperature ≥ 38.3° C ***with*** hypotension not requiring vasopressors ***and/or*** hypoxia requiring low-flow nasal cannula or blow-by	• Do all above as for Grade 1 • Supplemental O_2 • NS bolus 10-20 mL/kg
3	Temperature ≥ 38.3° C ***with*** hypotension requiring vasopressors ***with or without*** hypoxia requiring high-flow nasal cannula or by OxyMask	• Do above as for Grade 2 • If refractory hypotension occurs after 2 NS boluses, transfer to PICU and start vasopressors • Stop blina infusion • Start dexamethasone 5mg/m_2 (max dose – 8 mg) every 8 hours IV or PO for up to 3 days and taper thereafter over 4 days. When CRS is resolved restart blina (see below)
4	Temperature ≥ 38.3° C ***with*** hypotension requiring multiple vasopressors (excluding vasopressin ***and/or*** hypoxia requiring positive pressure (e.g. CPAP, BiPAP, intubation and mechanical ventilation)	• Do above as for Grade 3 • Discontinue blinatumomab permanently • Continue to administer dexamethasone
• Grade 3 CRS will require stopping blinatumomab infusion, administering dexamethasone then restarting at a lower dose (5 mcg/m^2/day or 9 mcg/day based on patient's weight) if CRS resolves to Grade 1. • Escalation to 15 mcg/m^2/day or 28 mcg/day based on patients weight after 7 days in subsequent cycle.		

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Table 2: Neurological Grading per National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE)				
Neurological Symptom	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**
Confusion	Mild disorientation	Moderate disorientation; limiting instrumental ADL	Severe disorientation limiting self-care ADL	Life-threatening consequences; urgent intervention
Dizziness	Mild unsteadiness or sensation of movement	Moderate disorientation; limiting instrumental ADL	Severe unsteadiness or sensation of movement; limiting self-care ADL	- - - - - - -
Dysethesia	Mild sensory alteration	Moderate sensory alteration; limiting ADL	Severe sensory alteration; limiting self-care ADL	- - - - - -
Dysphasia	Awareness of receptive or expressive characteristics; not impairing ability to communicate	Moderate receptive or expressive characteristic's impairing ability to communicate spontaneously	Severe receptive or expressive characterics; impairing ability to read, write or communicate intelligibly	- - - - - -
Edema, Cerebral	- - - - - - -	- - - - - - -	New onset; worsening from baseline	Life threatening consequences; urgent intervention required
Encephalopathy	Mild symptoms	Moderate symptoms; limiting instrumental ADL	Severe symptoms; limiting self-care ADL	Life-threatening consequences; urgent intervention indicated
Headache	Mild pain	Moderate pain; limiting instrumental ADL	Severe pain; limiting self-care ADL	- - - - - -
Seizure	Brief partial seizure and no loss of consciousness	Brief generalized seizure	New onset seizures; multiple seizures despite medical intervention	Life-threatening consequences; prolonged repetitive seizures
Tremor	Mild symptoms	Moderate symptoms; limiting instrumental ADL	Severe symptoms; limiting self-care ADL	- - - - - -

CNS Toxicity (Grade 1-4, including Seizures)

- Seizure and other CNS toxicities require prompt supportive care, including anti-convulsant therapy and dexamethasone, along with appropriate imaging and diagnostic evaluation (e.g., LP) as clinically indicated.
- Anti-convulsant therapy should be initiated if seizures occur and continue for the duration of the blinatumomab infusion. For subsequent cycles, consider initiating anti-convulsant prophylaxis at least 24-48 hours prior to infusion and continuing throughout the treatment cycle.

Management by Grade:

- Grade 1-2 CNS Toxicity (including seizures); Manage supportively as above.
- Grade 3 CNS Toxicity: Hold blinatumomab infusion and administer dexamethasone. Once toxicity resolves to Grade 1, restart at 5 mcg/m2/day. Dose escalation to 15 mcg/m2/day may be considered after 7 days in the subsequent cycle.
- Grade 4 CNS Toxicity (including seizures): Stop blinatumomab and administer dexamethasone. Permanently discontinue blinatumomab.

Additional Seizure-Specific Guidance:

- Patients who experience a Grade 1-3 seizure should not undergo dose escalation beyond 5 mcg/m2/day (max 9 mcg/day) in subsequent cycles.

References

Bergeron, S. (2019). Launching an innovative home administration program for the delivery of a unique targeted agent treating relapsed or refractory b-cell acute lymphoblastic leukemia. Administrative Tidbits, *APHON Counts*, *33(2).* (Level V)

Bhojwani, D., Bansal, R., & Wayne, A. S. (2021). Managing therapy-associated neurotoxicity in children with ALL. Hematology. American Society of Hematology. Education Program, 2021(1), 376–383. https://doi.org/10.1182/hematology.2021000269 (Level V)

Hogan, L. E., Brown, P. A., Ji, L., Xu, X., Devidas, M., Bhatla, T., Borowitz, M. J., Raetz, E. A., Carroll, A., Heerema, N. A., Zugmaier, G., Sharon, E., Bernhardt, M. B., Terezakis, S. A., Gore, L., Whitlock, J. A., Hunger, S. P., & Loh, M. L. (2023). Children's oncology group AALL1331: phase III trial of blinatumomab in children, adolescents, and young adults with low-risk b-cell ALL in first relapse. *Journal of Clinical Oncology, 41(25)*, 4118–4129. https://doi.org/10.1200/JCO.22.02200 (Level II)

Montgomery, K. E., Zupanec, S., Yun, C., Okada, M., Kubaney, H., Feehily, E., & Withycombe, J. S. (2024). A quality approach to blinatumomab delivery in pediatric oncology: A children's oncology group study. *Journal of Pediatric Hematology/Oncology Nursing*, *41*(5), 324–335. https://doi.org/10.1177/27527530241267303 (Level V)

Withycombe, J. S., Kubaney, H. R., Okada, M., Yun, C. S., Gupta, S., Bloom, C., Parker, V., Rau, R. E., & Zupanec, S. (2024). Delivery of Care for Pediatric Patients Receiving Blinatumomab: A Children's Oncology Group Study. *Cancer Nursing*, *47*(6), 451–459. https://doi.org/10.1097/NCC.0000000000001309 (Level III)