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Brentuximab Vedotin (Adcetris®) Neuropathy and Neutropenia Management

Description:
The purpose of this document is to discuss the clinical considerations and general management of toxicities related to brentuximab vedotin and its use across various indications.

Background:
Brentuximab vedotin is a CD30-directed antibody and microtubule inhibitor conjugate indicated for use in:[1,2,3,4]

- Hodgkin lymphoma:
  - Adult patients with previously untreated Stage III or IV classical Hodgkin lymphoma (cHL), in combination with doxorubicin, vinblastine, and dacarbazine
  - Pediatric patients 2 years and older with previously untreated high risk cHL, in combination with doxorubicin, vincristine, etoposide, prednisone, and cyclophosphamide
  - Adult patients with cHL after failure of auto-HSCT or after failure of at least two prior multi-agent chemotherapy regimens in patients who are not auto-HSCT candidates
- Anaplastic large cell lymphoma:
  - Adult patients with previously untreated systemic anaplastic large cell lymphoma (sALCL) or other CD30-expressing peripheral T-cell lymphomas (PTCL), including angioimmunoblastic T-cell lymphoma and PTCL not otherwise specified (NOS), in combination with cyclophosphamide, doxorubicin, and prednisone
  - Adult patients with sALCL after failure of at least one prior multi-agent chemotherapy regimen
  - Adult patients with primary cutaneous anaplastic large cell lymphoma (pcALCL) or CD30-expressing mycosis fungoides (MF) who have received prior systemic therapy
- Large B-cell lymphoma:
  - Adult patients with relapsed or refractory large B-cell lymphoma (LBCL), including diffuse large B-cell lymphoma (DLBCL) NOS, DLBCL arising from indolent lymphoma, or high-grade B-cell lymphoma (HGBL), after two or more lines of systemic therapy who are not eligible for auto-HSCT or CAR T-cell therapy, in combination with lenalidomide and a rituximab product

Most common adverse reactions (≥ 20%):[1]

- Peripheral neuropathy, nausea, fatigue, musculoskeletal pain, constipation, diarrhea, vomiting, pyrexia, upper respiratory tract infection, mucositis, abdominal pain, and rash
- Laboratory abnormalities (≥ 20%): decreased neutrophils, increased creatinine, decreased hemoglobin, decreased lymphocytes, increased glucose, increased alanine aminotransferase (ALT), and increased aspartate aminotransferase (AST)

PQI Process:

- Neutropenia Prevention and Management
  - Patients initiating front-line therapy with brentuximab vedotin for HL or PTCL should receive granulocyte colony-stimulating factor (G-CSF) beginning with Cycle 1, Day 1

- The choice of G-CSF therapy should follow institutional standards and formulary; the use of long-acting G-CSF agents is appropriate when indicated (14- or 21-day regimens)
- All patients who experience Grade ≥3 neutropenia who did not receive primary G-CSF prophylaxis should receive it with subsequent cycles
- CBC with differential should be assessed prior to each dose of brentuximab vedotin

- Neuropathy Prevention and Management
  - Neuropathies, primarily sensory rather than motor, may be seen in >50% of patients
  - Symptoms of hypo- or hyperesthesia, paresthesia, discomfort, burning sensation, weakness, tingling and neuropathic pain should be assessed with each cycle

Table 1: Dose Adjustments for Neuropathy

Brentuximab Vedotin Dose[1]	**Grade**	**Intervention**
1.8 mg/kg (maximum dose: 180 mg) every 3 weeks in combination with chemotherapy*	2	Sensory: Continue at same dose Motor: Reduce to 1.2 mg/kg (maximum dose: 120 mg)
	3	Sensory: Reduce to 1.2 mg/kg (maximum dose: 120 mg) Motor: Discontinue
	4	Discontinue
1.8 mg/kg (maximum dose: 180 mg) every 3 weeks as single agent**	New or worsening grade 2 or 3	Withhold until improvement to grade 1 or baseline; resume at 1.2 mg/kg (maximum dose: 120 mg)
	4	Discontinue
1.2 mg/kg (maximum dose: 120 mg) every 2 weeks in combination with chemotherapy***	2	Reduce to 0.9 mg/kg (maximum dose: 90 mg)
	3	Hold until recovery to ≤ Grade 2 and restart at 0.9 mg/kg (maximum dose: 90 mg) Consider modifying other neurotoxic chemotherapy agents
	4	Discontinue
1.2 mg/kg (maximum dose: 120 mg) every 3 weeks in combination with lenalidomide and rituximab****	2	Sensory: • *Resolves to ≤ grade 1 prior to next scheduled dose*: continue at same dose • *Persistent grade 2 at next scheduled dose*: Reduce to 0.9 mg/kg (maximum dose: 90 mg) Motor: Reduce to 0.9 mg/kg (maximum dose: 90 mg)
	3	Sensory: Hold until recovery to ≤ Grade 2 and restart at 0.9 mg/kg (maximum dose: 90 mg) Motor: Discontinue
	4	Discontinue

* previously untreated sALCL in combination with cyclophosphamide, doxorubicin, and prednisone; previously treated PTCL in combination with cyclophosphamide, doxorubicin, and prednisone

** relapsed pcALCL, sALCL or MF; R/R HL, or consolidation therapy after autologous hematopoietic cell transplantation

***previously untreated HL in combination with doxorubicin, vinblastine, and dacarbazine

**** DLBCL and HGBL, relapsed or refractory

Patient-Centered Activities:

- Counsel patient and provide written education sheets
- Educate patients to report fevers or signs of an infection such as coughing or congestion immediately
    - Some patients may require supportive care with G-CSF agents for neutropenia; supplemented with antihistamines if associated bone pain occurs (ex. loratadine)
- Many patients (especially those with HL) may under report symptoms due to a concern of diminished efficacy with interventions; building a rapport with these patients and helping them understand the balance between safety and efficacy is important
- Tests to help assess for neuropathy include buttoning a shirt or picking up a coin off of a flat surface
- Colder temperatures may exacerbate the neuropathies
- Counsel patients to report any numbness or tingling in their hands or feet or muscle weakness
- Patient Assistance: NCODA Financial Assistance Tool

References:

1. Adcetris® (brentuximab vedotin) [prescribing information]. Bothell, WA: Seagen Inc; February 2025.
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3. National Comprehensive Cancer Network (NCCN Guidelines®). T-Cell Lymphomas. Version 1.2025. https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf. Accessed May 19, 2025
4. National Comprehensive Cancer Network (NCCN Guidelines®). B-Cell Lymphomas. Version 2.2025. https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed May 19, 2025