

Novel ADC Therapies for R/R DLBCL: Optimizing Patient Safety With Timely AE Recognition and Management



Important Dosing and Premedication Considerations With Available ADCs in R/R DLBCL¹⁻³

ADC Agent and Dosing



Brentuximab vedotin

IV infusion over 30 min on Day 1 every 3 wk

- In combination with lenalidomide/rituximab for R/R LBCL: 1.2 mg/kg up to a maximum of 120 mg every 3 wk

- Avoid use in patients with moderate to severe hepatic impairment or severe renal impairment
- Reduce dose for mild hepatic impairment
- Advise patients of reproductive potential to use effective contraception during treatment and for 2 mo after the last dose (4 mo for male patients)



Loncastuximab tesirine

IV infusion over 30 min on Day 1 every 3 wk

- 0.15 mg/kg every 3 wk for 2 cycles
- 0.075 mg/kg every 3 wk for additional cycles

- Starting the day before loncastuximab tesirine-lpyl, patients should receive premedication with 4 mg of dexamethasone (oral or IV) twice daily for 3 days
- Avoid breastfeeding
- Advise patients of reproductive potential to use effective contraception during treatment and for 10 mo after the last dose (7 mo for male patients)



Polatuzumab vedotin

IV infusion over 90 min every 3 wk

- 1.8 mg/kg in combination with bendamustine and rituximab every 21 days for 6 cycles
- Subsequent infusions may be administered over 30 min if previous infusions were well tolerated

- Patients should receive premedication with antihistamine and antipyretic
- Avoid breastfeeding
- Advise patients of reproductive potential to use effective contraception during treatment and for 3 mo after the last dose

ADC, antibody–drug conjugate; LBCL, large B-cell lymphoma; R/R, relapsed/refractory.

Other Considerations

- Brentuximab vedotin and polatuzumab vedotin drug interactions: closely monitor patients receiving strong CYP3A4 inhibitors because coadministration increases exposure to MMAE potentially increasing the risk of AEs; avoid concomitant use of bleomycin because of pulmonary toxicity.
- Loncastuximab tesirine drug interactions: no significant drug interactions known or reported.

Key AEs Associated With ADCs in R/R DLBCL¹⁻⁵

Common Grade ≥ 3 AEs for ADCs in Patients With R/R DLBCL, %		ADC		
		Brentuximab Vedotin*	Loncastuximab Tesirine ⁵	Polatuzumab Vedotin [†]
	Fatigue	10	10 [†]	5

**Common Grade ≥3 AEs for
ADCs in Patients With R/R DLBCL, %**

		ADC		
		Brentuximab Vedotin*	Loncastuximab Tesirine ⁵	Polatuzumab Vedotin [‡]
	Myelosuppression			
	• Neutrophil decrease	49	26	39
	• Lymphocyte decrease	38	5	12
	• Platelet decrease	29	18	23
	• Hemoglobin decrease (or anemia)	19	10	14
	Pericardial effusion and/or edema	--	2/3 [‡]	--
	Febrile neutropenia	19	3	13
	Neuropathy			
	• Peripheral sensory neuropathy	4	--	2.3
	• Peripheral motor neuropathy	--	1 [†]	--
	Diarrhea	5	2 [†]	8
	Pneumonia	21		6
	Infections (including upper respiratory)	3	<1	<1
	Serious cutaneous/dermatologic reactions (rash/pruritus)	3	2 ^{‡§}	<1
	γ-glutamyl transferase increased	--	15 [†]	--

*In combination with lenalidomide and rituximab. †No grade 4 occurred. ‡Combined with bendamustine and rituximab. §Includes patients with photosensitive reaction.

- The most common any grade AEs with brentuximab vedotin include peripheral neuropathy (27%-62%), fatigue (46%), diarrhea (31%), constipation (17%), nausea (15%), pyrexia (15%), vomiting (26%), alopecia (26%), anemia (66%), stomatitis (11%), lymphocytes decrease (65%), and mucositis (30%).
- The most common any grade AEs with loncastuximab tesirine include thrombocytopenia (58%), γ-glutamyl transferase increased (57%), neutropenia (52%), anemia (51%), hyperglycemia (48%), aspartate aminotransferase/alanine aminotransferase increase (41%/34%), fatigue (38%), rash (30%), edema (28%), nausea (23%), and musculoskeletal pain (23%).
- The most common any grade AEs with polatuzumab vedotin include neutropenia (49%), thrombocytopenia (49%), anemia (47%), peripheral neuropathy (40%), fatigue (40%), diarrhea (45%), pyrexia (30%), decreased appetite (29%), and pneumonia (13%).



Brentuximab Vedotin

AE	Patient Considerations and Monitoring Recommendations
✓ Progressive multifocal leukoencephalopathy	Although rare, fatal cases of PML caused by John Cunningham virus infection have been reported. Onset is approximately 3 mo from initial exposure and more likely in patients who are immunocompromised. If patients develop signs and symptoms of CNS abnormalities, consider workup/diagnosis of PML, hold dose, and discontinue the drug if a PML diagnosis is confirmed. Patients (or anyone close to them) should immediately report neurologic, cognitive, or behavioral signs and symptoms (ie, changes in mood or behavior, confusion, trouble thinking, or loss of memory). Additional symptoms include change in vision, speech, or walking, or weakness/decreased strength on one side of the body.
✓ Peripheral neuropathy	Monitor patients for symptoms of neuropathy. Dose reductions or delays may be required and are recommended by experts. Patients should report numbness or tingling in the hands/feet or any muscle weakness to their care team.
✓ Infusion reactions/anaphylaxis	Infusion-related reactions (ie, fever, chills, rash, or breathing problems within 24 hr of infusion), including anaphylaxis, may occur. Consider premedication with acetaminophen, antihistamine, and a corticosteroid. Advise patients to contact their care team if/as soon as signs/symptoms of infusion reaction develop.
✓ Hyperglycemia	Patients may experience new-onset hyperglycemia and potentially fatal ketoacidosis or experience worsening of preexisting diabetes mellitus. More likely to develop if high BMI or if diabetic. Grade 3/4 hyperglycemia often occurs at a median of 1 mo after treatment. Monitor serum glucose and administer antihyperglycemic as clinically indicated.
✓ Hematologic toxicities	Fatal and serious cases of febrile neutropenia have been reported. Monitor CBCs and manage hematological toxicities with treatment dose delays, dose reductions, and growth factor support. Consider treatment discontinuation for grade 3/4 neutropenia; also consider G-CSF prophylaxis.
✓ Serious dermatologic reactions	Discontinue if Stevens-Johnson syndrome or toxic epidermal necrolysis occurs and administer appropriate medical therapy.

Loncastuximab Tesirine

AE	Patient Considerations and Monitoring Recommendations
✓ Effusion and edema	Monitor patients for new or worsening signs of serious effusion and edema. Consider diagnostic imaging in patients developing symptoms of pleural effusion or pericardial effusion (dyspnea, chest pain, bloating, or swelling in the abdomen). Patients should notify their care team for new or worsening swelling (or puffiness), weight gain, chest pain, shortness of breath, or trouble breathing.
✓ Myelosuppression	Treatment may result in low blood cell counts which in some cases may be serious or severe. Monitor CBCs throughout treatment, hold or reduce dose, or discontinue treatment as needed. Consider prophylactic G-CSF. Patients should notify their care team immediately if they experience a fever $\geq 100.4^{\circ}\text{F}$ (38°C) or if they experience any bleeding or bruising.
✓ Infections	Serious infections, including leading to death, have been reported. Monitor patients for signs and symptoms of infection and treat promptly. Patients should notify their care team immediately if they experience any new or worsening fever, chills, headache, breathing problems, or red/warm/swollen/painful cuts or scrapes, any flu-like symptoms including cough, tiredness, weakness, and body aches and pains.

AE	Patient Considerations and Monitoring Recommendations
✓ Cutaneous reactions	Serious cutaneous reactions have been reported. Monitor patients for new or worsening cutaneous reaction, including photosensitivity reactions. Patients also should be advised to minimize or avoid exposure to sunlight (natural or artificial) including exposure through glass. Patients may use skin protective means such as sunscreen and wearing sun-protective clothing. In the event of a skin reaction or rash, consider a dermatologic consult. Patients should notify their care team immediately if they experience any new or worsening skin reactions, sensitivity to sunlight, rash, peeling, redness, or irritation. Also, patients receiving this treatment may experience severe sunburn more easily.
✓ Embryofetal toxicity	Advise patients of risk about embryo-fetal toxicity and to use effective contraception throughout treatment and for 10 mo after last dose (up to 7 mo in male patients).

Polatuzumab Vedotin

AE	Patient Considerations and Monitoring Recommendations
✓ Progressive multifocal leukoencephalopathy	Although rare, fatal cases of PML have been reported. Consider workup/diagnosis of PML, hold dose, and discontinue the drug if a PML diagnosis is confirmed. Patients (or anyone close to them) should immediately report neurologic, cognitive, or behavioral signs and symptoms (ie, changes in mood or behavior, confusion, trouble thinking, or loss of memory). Additional symptoms include change in vision, speech, or walking, or weakness/decreased strength on one side of the body.
✓ Peripheral neuropathy	Neuropathy may present during the first cycle of treatment. Monitor patients for symptoms of neuropathy. Dose reductions or delays may be required. Advise patients to report numbness or tingling in the hands/feet or any muscle weakness.
✓ Infusion reactions	Infusion-related reactions (ie, fever, chills, rash, or breathing problems within 24 hr of infusion), including anaphylaxis, may occur. Consider premedication with acetaminophen, antihistamine, and a corticosteroid. Advise patients to contact the care team if/as soon as signs/symptoms of infusion-related reaction develop.
✓ Myelosuppression	Severe or serious myelosuppression can occur (eg, neutropenia, thrombocytopenia, anemia). Monitor CBCs during treatment and consider prophylactic G-CSF. Patients should immediately report new signs/symptoms of bleeding/infection to care team.
✓ Infections (serious and opportunistic)	Monitor patients for signs of infection during treatment and implement prophylaxis measures as clinically indicated. Advise patients to contact the care team for fever $\geq 100.4^{\circ}\text{F}$ (38°C) or if they experience any chills, cough, or any signs of infection.
✓ Tumor lysis syndrome	Patients with high-tumor burden may potentially develop tumor lysis syndrome; monitor closely and take appropriate measures, including prophylaxis for tumor lysis syndrome. Patients to seek immediate medical attention if they experience nausea, vomiting, diarrhea, and lethargy.
✓ Hepatotoxicity	Serious cases of hepatotoxicity consistent with hepatocellular injury, including increased transaminases and/or bilirubin. Risk for hepatotoxicity is increased for patients with preexisting liver disease, and elevated liver enzymes at baseline. Advise patients to contact the care team for any signs of liver injury (ie, fatigue, anorexia, right upper abdominal pain, dark urine, or jaundice).

CBC, complete blood count; CNS, central nervous system; G-CSF, granulocyte colony-stimulating factor; PML, progressive multifocal leukoencephalopathy.

References

1. Brentuximab vedotin PI.
2. Loncastuximab tesirine PI.
3. Polatuzumab vedotin PI.
4. Bartlett. JCO. 2025;43:1061.
5. Caimi. Lancet Oncol. 2021;22:790.