POLIVY® Infusion Checklist

Here are some suggestions to help you prepare for the infusion experience.

POLIVY®
polatuzumab vedotin-piiq
INJECTION FOR INTRAVENOUS USE 30MG | 140MG

BEFORE YOUR INFUSION

Talk to your doctor about what to expect when planning for your treatment. Take care of these things the week before your infusion.

- ☐ Check with your infusion center to find out if:
  - You can bring food or snacks
  - You can bring a friend or family member along for support
  - There will be other people in the same infusion room
  - You need to visit the center prior to the day of your appointment
- ☐ Plan ahead to have someone drive you home after your treatment in case you feel tired
- ☐ Clear your schedule in the hours after your infusion appointment to rest

THE DAY OF YOUR INFUSION

Plan to arrive early or on time for your appointment.

- ☐ Wear comfortable, loose-fitting clothes for easier infusion access
- ☐ Drink plenty of water to stay hydrated
- ☐ Remember to bring these items with you:
  - Your insurance card/information (and authorization from your insurer, if requested)
  - A list of your medications and doctors
  - Water, food, and snacks to prevent dry mouth (if your infusion center's policy allows them)
  - Things to keep you warm and comfortable, such as a pillow, a blanket, or socks
  - Reading material, an audio device, a smartphone, a tablet, or a game (such as cards) to keep you occupied
- ☐ Eat a light meal before your appointment to help avoid feeling sick during or after your treatment

AFTER YOUR INFUSION

Plan to rest as you may feel tired.

- ☐ Note the date and time of your next infusion appointment
- ☐ Call your doctor or someone on your healthcare team if you experience side effects.

Contact details:

Call the Genentech Patient Resource Center at 1 (877) GENENTECH (1-877-436-3683) for general questions and information about patient resources, financial support options, and understanding your insurance coverage.

To help you make the most of your doctor visits and prepare for your POLIVY treatment, visit POLIVY.com to download the Doctor Discussion Guide.

Please see accompanying full Prescribing Information or visit POLIVY.com, as well as additional Important Safety Information located on the back side.

Indication and Important Safety Information

What does POLIVY® treat?

POLIVY is a prescription medicine used with other medicines (a rituximab product, cyclophosphamide, doxorubicin, and prednisone) as a first treatment for adults who have moderate to high risk diffuse large B-cell lymphoma (DLBCL), not otherwise specified (NOS) or high-grade B-cell lymphoma (HGBL).

Important Safety Information

Possible serious side effects

Everyone reacts differently to POLIVY therapy, so it's important to know what the side effects are. **Some people who have been treated with POLIVY have experienced serious to fatal side effects.** Your doctor may stop or adjust your treatment if any serious side effects occur. **Be sure to contact your healthcare team if there are any signs of these side effects.**

- **Nerve problems in your arms and legs:** This may happen as early as after your first dose and may worsen with every dose. Your doctor will monitor for signs and symptoms, such as changes in your sense of touch, numbness or tingling in your hands or feet, nerve pain, burning sensation, any muscle weakness, or changes to your walking pattern
- **Infusion-related reactions:** You may experience fever, chills, rash, breathing problems, low blood pressure, or hives within 24 hours of your infusion
- **Low Blood Cell Counts:** Treatment with POLIVY can cause severe low blood cell counts. Your doctor will monitor your blood counts throughout treatment with POLIVY
- **Infections:** If you have a fever of 100.4°F (38°C) or higher, chills, cough, or pain during urination, contact your healthcare team. Your doctor may also give you medication before giving you POLIVY, which may prevent some infections
- **Rare and serious brain infections:** Your doctor will monitor closely for signs and symptoms of these types of infections. Contact your doctor if you experience confusion, dizziness or loss of balance, trouble talking or walking, or vision changes
- **Tumor lysis syndrome:** Caused by the fast breakdown of cancer cells. Signs include nausea, vomiting, diarrhea, and lack of energy
- **Potential harm to liver:** Some signs include tiredness, weight loss, pain in the abdomen, dark urine, and yellowing of your skin or the white part of your eyes. You may be at higher risk if you already had liver problems or you are taking other medication
- **Skin damage at or near the infusion site:** POLIVY may leak out of the vein and into the surrounding tissue during the infusion, which can cause skin or tissue damage. Your doctor will closely monitor for signs and symptoms of skin damage during the infusion. Tell your healthcare provider immediately if you see any fluid leaking at or around the infusion site, or if you notice any burning, tingling, pain, discomfort, swelling and redness at the infusion site

Side effects seen most often

The most common side effects during treatment were

- Nerve problems in arms and legs
- Nausea
- Tiredness or lack of energy
- Diarrhea
- Constipation
- Hair loss
- Redness and sores of the lining of the mouth, lips, throat, and digestive tract

POLIVY may lower your red or white blood cell counts and increase uric acid levels.

POLIVY may not be for everyone. Talk to your doctor if you are

- **Pregnant or think you are pregnant:** Data have shown that POLIVY may harm your unborn baby
- **Planning to become pregnant:** Women should avoid getting pregnant while taking POLIVY. Women should use effective contraception during treatment and for 3 months after their last POLIVY treatment. Men taking POLIVY should use effective contraception during treatment and for 5 months after their last POLIVY treatment
- **Breastfeeding:** Women should not breastfeed while taking POLIVY and for 2 months after the last dose

These may not be all the side effects. Talk to your healthcare provider for more information about the benefits and risks of POLIVY treatment.

You may report side effects to the FDA at (800) FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Genentech at (888) 835-2555.

Please see accompanying full Prescribing Information or visit POLIVY.com, as well as additional Important Safety Information located on the back side.

Genentech
A Member of the Roche Group

POLIVY®
polatuzumab vedotin-piiq
INJECTION FOR INTRAVENOUS USE 30 MG | 140 MG

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HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use POLIVY safely and effectively. See full prescribing information for POLIVY.

POLIVY® (polatuzumab vedotin-piiq) for injection, for intravenous use
Initial U.S. Approval: 2019

RECENT MAJOR CHANGES

Dosage and Administration (2.4)	8/2026
Warnings and Precautions (5.8)	3/2026

INDICATIONS AND USAGE

POLIVY is a CD79b-directed antibody and microtubule inhibitor conjugate indicated:

- in combination with a rituximab product, cyclophosphamide, doxorubicin, and prednisone (R-CHP) for the treatment of adult patients who have previously untreated diffuse large B-cell lymphoma (DLBCL), not otherwise specified (NOS) or high-grade B-cell lymphoma (HGBL) and who have an International Prognostic Index score of 2 or greater. (1.1)
- in combination with bendamustine and a rituximab product for the treatment of adult patients with relapsed or refractory DLBCL, NOS, after at least two prior therapies. (1.2)

DOSAGE AND ADMINISTRATION

- The recommended dose of POLIVY is 1.8 mg/kg as an intravenous infusion every 21 days for 6 cycles. (2)
- Administer the initial POLIVY dose over 90 minutes. Subsequent infusions may be administered over 30 minutes if the previous infusion is tolerated. (2)
- Premedicate with an antihistamine and antipyretic before POLIVY. (2)
- See Full Prescribing Information for instructions on preparation and administration. (2.4)

DOSAGE FORMS AND STRENGTHS

For injection: 30 mg or 140 mg of polatuzumab vedotin-piiq as a lyophilized powder in a single-dose vial. (3)

CONTRAINDICATIONS

None. (4)

WARNINGS AND PRECAUTIONS

- Peripheral Neuropathy: Monitor patients for peripheral neuropathy and modify or discontinue dose accordingly. (5.1)
- Infusion-Related Reactions: Premedicate with an antihistamine and antipyretic. Monitor patients closely during infusions. Interrupt or discontinue infusion for reactions. (5.2)
- Myelosuppression: Monitor complete blood counts. Manage using dose delays or reductions and growth factor support. Monitor for signs of infection. (5.3)
- Serious and Opportunistic Infections: Closely monitor patients for signs of bacterial, fungal, or viral infections. (5.4)
- Progressive Multifocal Leukoencephalopathy (PML): Monitor patients for new or worsening neurological, cognitive, or behavioral changes suggestive of PML. (5.5)
- Tumor Lysis Syndrome: Closely monitor patients with high tumor burden or rapidly proliferative tumors. (5.6)
- Hepatotoxicity: Monitor liver enzymes and bilirubin. (5.7)
- Infusion Site Extravasation Injury: Ensure patent venous access prior to initiating the infusion and closely monitor the infusion site throughout administration for any signs of extravasation. Stop the infusion immediately if extravasation occurs. (5.8)
- Embryo-Fetal Toxicity: Can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception during treatment and for 3 months after the last dose. (5.9)

ADVERSE REACTIONS

The most common adverse reactions (≥20%) in patients with large B-cell lymphoma treated with POLIVY in combination with R-CHP, excluding laboratory abnormalities, are peripheral neuropathy, nausea, fatigue, diarrhea, constipation, alopecia, and mucositis. Grade 3 to 4 laboratory abnormalities (≥10%) are lymphopenia, neutropenia, hyperuricemia, and anemia. (6.1)

The most common adverse reaction (≥20%) in patients with relapsed or refractory DLBCL treated with POLIVY in combination with BR are neutropenia, thrombocytopenia, anemia, peripheral neuropathy, fatigue, diarrhea, pyrexia, decreased appetite, and pneumonia. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Genentech at 1-888-835-2555 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

Concomitant use of strong CYP3A inhibitors or inducers has the potential to affect the exposure to unconjugated monomethyl auristatin E (MMAE). (7.1)

USE IN SPECIFIC POPULATIONS

- Hepatic impairment has the potential to increase exposure to MMAE. Monitor patients for adverse reactions. (8.6)
- Lactation: Advise not to breastfeed. (8.2)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 8/2026

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Previously Untreated DLBCL, NOS or HGBL

POLIVY in combination with a rituximab product, cyclophosphamide, doxorubicin, and prednisone (R-CHP) is indicated for the treatment of adult patients who have previously untreated diffuse large B-cell lymphoma (DLBCL), not otherwise specified (NOS) or high-grade B-cell lymphoma (HGBL) and who have an International Prognostic Index score of 2 or greater.

1.2 Relapsed or Refractory DLBCL, NOS

POLIVY in combination with bendamustine and a rituximab product is indicated for the treatment of adult patients with relapsed or refractory DLBCL, NOS, after at least two prior therapies.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage

Patients with Previously Untreated DLBCL, NOS or HGBL

The recommended dosage of POLIVY is 1.8 mg/kg administered as an intravenous infusion every 21 days for 6 cycles in combination with a rituximab product, cyclophosphamide, doxorubicin, and prednisone *[see Clinical Studies (14.1)]*. Administer POLIVY, cyclophosphamide, doxorubicin, and a rituximab product in any order on Day 1 after the administration of prednisone. Prednisone is administered on Days 1–5 of each cycle.

Patients with Relapsed or Refractory DLBCL, NOS

The recommended dosage of POLIVY is 1.8 mg/kg administered as an intravenous infusion every 21 days for 6 cycles in combination with bendamustine and a rituximab product. Administer POLIVY, bendamustine, and a rituximab product in any order on Day 1 of each cycle. The recommended dose of bendamustine is 90 mg/m^2/day on Days 1 and 2 when administered with POLIVY and a rituximab product. The recommended dose of rituximab product is 375 mg/m^2 intravenously on Day 1 of each cycle.

For All Indicated Patients

If not already premedicated, administer an antihistamine and antipyretic at least 30 minutes prior to POLIVY.

If a planned dose of POLIVY is missed, administer as soon as possible. Adjust the schedule of administration to maintain a 21-day interval between doses.

2.2 Management of Adverse Reactions

Previously Untreated DLBCL, NOS or HGBL

Table 1 provides management guidelines for peripheral neuropathy in patients receiving POLIVY plus R-CHP *[see Warnings and Precautions (5.1)]*.

Table 1 Management of Peripheral Neuropathy in Patients Receiving POLIVY Plus R-CHP

Adverse reaction	Grade	Dose modification[a]
Peripheral sensory neuropathy	Grade 1	None
	Grade 2	If resolves to Grade 1 or lower before the next scheduled dose, resume at the same dose level. If Grade 2 persists at the next scheduled dose, reduce one dose level.
	Grade 3	Withhold until Grade 2 or lower and reduce one dose level.
	Grade 4	Permanently discontinue.
Peripheral motor neuropathy	Grade 1	None
	Grade 2 or 3	Withhold until Grade 1 or lower and reduce one dose level.
	Grade 4	Permanently discontinue.
R-CHP should be continued if POLIVY is withheld. If there is concurrent sensory and motor neuropathy, follow the guidance for the most severe neuropathy. If the grade of sensory and motor neuropathy are the same, follow the guidance for motor neuropathy.		

[a] Starting dose for POLIVY is 1.8 mg/kg. First dose reduction level is 1.4 mg/kg. Second dose reduction level is 1 mg/kg. No further dose reduction is recommended beyond 1 mg/kg. If further reduction needed discontinue POLIVY.

Table 2 provides management guidelines for infusion-related reaction and myelosuppression *[see Warnings and Precautions (5.2 and 5.3)]*.

Table 2 Management of Infusion-Related Reaction and Myelosuppression in Patients Receiving POLIVY Plus R-CHP

Adverse Reaction	Dosage Modification[a]
Infusion-Related Reaction **Grade 1–3**	Interrupt POLIVY infusion and give supportive treatment. For the first instance of Grade 3 wheezing, bronchospasm, or generalized urticaria, permanently discontinue POLIVY. For recurrent Grade 2 wheezing or urticaria, or for recurrence of any Grade 3 symptoms, permanently discontinue POLIVY. Otherwise, upon complete resolution of symptoms, infusion may be resumed at 50% of the rate achieved prior to interruption. In the absence of infusion related symptoms, the rate of infusion may be escalated in increments of 50 mg/hour every 30 minutes. For the next cycle, infuse POLIVY over 90 minutes. If no infusion-related reaction occurs, subsequent infusions may be administered over 30 minutes. Administer premedication for all cycles.

Adverse Reaction	Dosage Modification[a]
Infusion-Related Reaction **Grade 4**	Stop POLIVY infusion immediately. Give supportive treatment. Discontinue POLIVY.
Neutropenia[b,c] **Grade 3–4**	Hold all treatment until ANC recovers to greater than or equal to 1,000/microliter. Consider therapeutic G-CSF if neutropenia occurs after prophylactic G-CSF. If ANC recovers to greater than or equal to 1,000/microliter on or before Day 7, resume all treatment without any dose reductions. If ANC recovers to greater than or equal to 1,000/microliter after Day 7: • resume all treatment • administer prophylactic G-CSF in next cycle. If G-CSF was already given, consider a dose reduction of POLIVY.
Thrombocytopenia[b,c] **Grade 3–4**	Hold all treatment until platelets recover to greater than or equal to 75,000/microliter. If platelets recover to greater than or equal to 75,000/microliter on or before Day 7, resume all treatment without any dose reductions. If platelets recover to greater than or equal to 75,000/microliter after Day 7: • resume all treatment and consider a dose reduction of POLIVY.

Toxicity graded per National Cancer Institute (NCI) Common Terminology for Adverse Events (CTCAE) version 4.0.

[a] Starting dose for POLIVY is 1.8 mg/kg. First dose reduction level is 1.4 mg/kg. Second dose reduction level is 1 mg/kg. No further dose reduction is recommended beyond 1 mg/kg. If further reduction needed discontinue POLIVY.
[b] Severity on Day 1 of any cycle.
[c] If primary cause is lymphoma, dosage delay or reduction may not be needed.

Relapsed or Refractory DLBCL, NOS

Table 3 provides management guidelines for peripheral neuropathy, infusion-related reaction, and myelosuppression in patients receiving POLIVY in combination with bendamustine and a rituximab product *[see Warnings and Precautions (5.1, 5.2, 5.3)]*.

Table 3 Management of Peripheral Neuropathy, Infusion-Related Reaction, and Myelosuppression in Patients Receiving POLIVY Plus Bendamustine and a Rituximab Product

Adverse Reaction	Dosage Modification[a]
Peripheral Neuropathy **Grade 2–3**	Hold POLIVY dosing until improvement to Grade 1 or lower. If recovered to Grade 1 or lower on or before Day 14, restart POLIVY with the next cycle at a permanently reduced dose of 1.4 mg/kg. If a prior dose reduction to 1.4 mg/kg has occurred, discontinue POLIVY. If not recovered to Grade 1 or lower on or before Day 14, discontinue POLIVY.

Adverse Reaction	Dosage Modification[a]
Peripheral Neuropathy Grade 4	Discontinue POLIVY.
Infusion-Related Reaction Grade 1–3	Interrupt POLIVY infusion and give supportive treatment. For the first instance of Grade 3 wheezing, bronchospasm, or generalized urticaria, permanently discontinue POLIVY. For recurrent Grade 2 wheezing or urticaria, or for recurrence of any Grade 3 symptoms, permanently discontinue POLIVY. Otherwise, upon complete resolution of symptoms, infusion may be resumed at 50% of the rate achieved prior to interruption. In the absence of infusion related symptoms, the rate of infusion may be escalated in increments of 50 mg/hour every 30 minutes. For the next cycle, infuse POLIVY over 90 minutes. If no infusion-related reaction occurs, subsequent infusions may be administered over 30 minutes. Administer premedication for all cycles.
Infusion-Related Reaction Grade 4	Stop POLIVY infusion immediately. Give supportive treatment. Permanently discontinue POLIVY.
Neutropenia[b,c] Grade 3–4	Hold all treatment until ANC recovers to greater than 1,000/microliter. If ANC recovers to greater than 1,000/microliter on or before Day 7, resume all treatment without any additional dose reductions. Consider granulocyte colony-stimulating factor prophylaxis for subsequent cycles, if not previously given. If ANC recovers to greater than 1,000/microliter after Day 7: • restart all treatment. Consider granulocyte colony-stimulating factor prophylaxis for subsequent cycles, if not previously given. If prophylaxis was given, consider dose reduction of bendamustine. • if dose reduction of bendamustine has already occurred, consider dose reduction of POLIVY to 1.4 mg/kg.
Thrombocytopenia[b,c] Grade 3–4	Hold all treatment until platelets recover to greater than 75,000/microliter. If platelets recover to greater than 75,000/microliter on or before Day 7, resume all treatment without any additional dose reductions. If platelets recover to greater than 75,000/microliter after Day 7: • restart all treatment, with dose reduction of bendamustine. • if dose reduction of bendamustine has already occurred, consider dose reduction of POLIVY to 1.4 mg/kg.

Toxicity graded per NCI CTCAE version 4.0.

[a] Starting dose for POLIVY is 1.8 mg/kg. First dose reduction level is 1.4 mg/kg. Second dose reduction level is 1 mg/kg. No further dose reduction is recommended beyond 1 mg/kg. If further reduction needed discontinue POLIVY.
[b] Severity on Day 1 of any cycle.
[c] If primary cause is lymphoma, dosage delay or reduction may not be needed.

2.3 Recommended Prophylactic Medications

If not already premedicated for a rituximab product, administer an antihistamine and antipyretic at least 30 to 60 minutes prior to POLIVY for potential infusion-related reactions *[see Warnings and Precautions (5.2)]*.

Administer prophylaxis for *Pneumocystis jiroveci* pneumonia and herpesvirus throughout treatment with POLIVY.

Administer prophylactic granulocyte colony-stimulating factor (G-CSF) for neutropenia in patients receiving POLIVY plus R-CHP. Consider prophylactic G-CSF administration for neutropenia in patients receiving POLIVY plus bendamustine and a rituximab product *[see Warnings and Precautions (5.3)]*.

Administer tumor lysis syndrome prophylaxis for patients at increased risk of tumor lysis syndrome *[see Warnings and Precautions (5.6)]*.

2.4 Instructions for Preparation and Administration

Reconstitute and further dilute POLIVY prior to intravenous infusion.

POLIVY is a hazardous drug. Follow applicable special handling and disposal procedures.[1]

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

Reconstitution

- Reconstitute immediately before dilution.
- More than one vial may be needed for a full dose. Calculate the dose, the total volume of reconstituted POLIVY solution required, and the number of POLIVY vials needed.
- Using a sterile syringe, slowly inject one of the following diluents into the POLIVY vial using the volume provided in Table 4:
    - Sterile Water for Injection, USP
    - Bacteriostatic Water for Injection, USP
    - 0.9% Sodium Chloride Injection, USP
    - 0.45% Sodium Chloride Injection, USP
- Direct the stream toward the inside wall of the vial to obtain a concentration of 20 mg/mL of polatuzumab vedotin-piiq.

Table 4 Reconstitution Volumes

Strength	Volume of Diluent Required for Reconstitution
30 mg vial	1.8 mL
140 mg vial	7.2 mL

- Swirl the vial gently until completely dissolved. *Do not shake*.
- Inspect the reconstituted solution for discoloration and particulate matter. The reconstituted solution should appear colorless to slightly brown, clear to slightly opalescent, and free of visible particulates. Do not use if the reconstituted solution is discolored, is cloudy, or contains visible particulates. *Do not freeze or expose to direct sunlight.*
- If needed, store unused reconstituted POLIVY solution prior to dilution according to the storage conditions and maximum durations specified in Table 5 based on the diluent used

for reconstitution. Discard vial when cumulative storage time prior to dilution exceeds 168 hours.

Table 5 Storage of Reconstituted POLIVY Solution

Diluent Used to Prepare Reconstituted Solution	Refrigerated at 2°C to 8°C (36°F to 46°F)	Room Temperature 9°C to 25°C (47°F to 77°F)
Sterile Water for Injection, USP	168 hours	8 hours
Bacteriostatic Water for Injection, USP		4 hours
0.9% Sodium Chloride Injection, USP		4 hours
0.45% Sodium Chloride Injection, USP		5 hours

Dilution

- Dilute polatuzumab vedotin-piiq to a final concentration of 0.72 mg/mL to 2.7 mg/mL in an intravenous infusion bag with a minimum volume of 50 mL containing 0.9% Sodium Chloride Injection, USP, 0.45% Sodium Chloride Injection, USP, or 5% Dextrose Injection, USP.
- Determine the volume of 20 mg/mL reconstituted solution needed based on the required dose.
- Withdraw the required volume of reconstituted solution from the POLIVY vial using a sterile syringe and dilute into the intravenous infusion bag. Discard any unused portion left in the vial.
- Gently mix the intravenous bag by slowly inverting the bag. *Do not shake*.
- Inspect the intravenous bag for particulates and discard if present.
- If not used immediately, store the diluted POLIVY solution according to the storage conditions and maximum durations specified in Table 6 based on the diluents used for reconstitution and infusion. Discard if storage time exceeds these limits. *Do not freeze or expose to direct sunlight*.

Table 6 Storage of Diluted POLIVY Solution

Diluent Used to Prepare Reconstituted Solution	Diluent Used to Prepare Solution for Infusion	Refrigerated at 2°C to 8°C (36°F to 46°F)	Room Temperature 9°C to 25°C (47°F to 77°F)
Sterile Water for Injection, USP	0.9% Sodium Chloride Injection, USP	36 hours	4 hours
	0.45% Sodium Chloride Injection, USP	18 hours	4 hours
	5% Dextrose Injection, USP	36 hours	6 hours
Bacteriostatic Water for Injection, USP	0.9% Sodium Chloride Injection, USP	36 hours	4 hours
	0.45% Sodium Chloride Injection, USP	18 hours	
	5% Dextrose Injection, USP	36 hours	

Diluent Used to Prepare Reconstituted Solution	Diluent Used to Prepare Solution for Infusion	Refrigerated at 2°C to 8°C (36°F to 46°F)	Room Temperature 9°C to 25°C (47°F to 77°F)
0.9% Sodium Chloride Injection, USP	0.9% Sodium Chloride Injection, USP	72 hours	4 hours
	0.45% Sodium Chloride Injection, USP		
	5% Dextrose Injection, USP		
0.45% Sodium Chloride Injection, USP	0.9% Sodium Chloride Injection, USP	72 hours	4 hours
	0.45% Sodium Chloride Injection, USP		
	5% Dextrose Injection, USP		

- Limit transportation to 30 minutes at room temperature (9°C to 25°C) or 24 hours refrigerated at 2°C to 8°C (refer to instructions below). The total storage plus transportation times of the diluted product should not exceed the storage duration specified in Table 6.
- Agitation stress can result in aggregation. Limit agitation of diluted product during preparation and transportation to administration site. Do not transport diluted product through an automated system (e.g., pneumatic tube or automated cart). If the prepared solution will be transported to a separate facility, remove air from the infusion bag to prevent aggregation. If air is removed, an infusion set with a vented spike is required to ensure accurate dosing during the infusion.
- No incompatibilities have been observed between POLIVY and intravenous infusion bags with product-contacting materials of polyvinyl chloride (PVC) or polyolefins (PO) such as polyethylene (PE) and polypropylene (PP). No incompatibilities have been observed with infusion sets or infusion aids with product-contacting materials of PVC, PE, polyurethane (PU), polybutadiene (PBD), acrylonitrile butadiene styrene (ABS), polycarbonate (PC), polyetherurethane (PEU), fluorinated ethylene propylene (FEP), or polytetrafluorethylene (PTFE), or with filter membranes composed of polyether sulfone (PES) or polysulfone (PSU).

Administration

- Administer POLIVY as an intravenous infusion only.
- Confirm patency of the intravenous line prior to infusion. Monitor for extravasation; if extravasation occurs, stop the infusion and manage medically *[see Warnings and Precautions (5.8)]*.
- Administer the initial dose of POLIVY over 90 minutes. Monitor patients for infusion-related reactions during the infusion and for a minimum of 90 minutes following completion of the initial dose. If the previous infusion was well tolerated, the subsequent dose of POLIVY may be administered as a 30-minute infusion and patients should be monitored during the infusion and for at least 30 minutes after completion of the infusion.
- POLIVY must be administered using a dedicated infusion line equipped with a sterile, non-pyrogenic, low-protein-binding in-line or add-on filter (0.2- or 0.22-micron pore size) and a catheter.

- Do not mix POLIVY with or administer as an infusion with other drugs.

3 DOSAGE FORMS AND STRENGTHS

For injection: 30 mg/vial or 140 mg/vial of polatuzumab vedotin-piiq as a white to grayish-white lyophilized powder in a single-dose vial for reconstitution and further dilution.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Peripheral Neuropathy

POLIVY can cause peripheral neuropathy, including severe cases. Peripheral neuropathy occurs as early as the first cycle of treatment and is a cumulative effect *[see Adverse Reactions (6.1)]*. POLIVY may exacerbate pre-existing peripheral neuropathy.

In POLARIX, of 435 patients treated with POLIVY plus R-CHP, 53% reported new or worsening peripheral neuropathy, with a median time to onset of 2.3 months. Peripheral neuropathy was Grade 1 in 39% of patients, Grade 2 in 12%, and Grade 3 in 1.6%. Peripheral neuropathy resulted in dose reduction in 4% of treated patients and treatment discontinuation in 0.7%. Among patients with peripheral neuropathy after POLIVY, 58% reported resolution after a median of 4 months.

In Study GO29365, of 173 patients treated with POLIVY, 40% reported new or worsening peripheral neuropathy, with a median time to onset of 2.1 months. Peripheral neuropathy was Grade 1 in 26% of patients, Grade 2 in 12%, and Grade 3 in 2.3%. Peripheral neuropathy resulted in POLIVY dose reduction in 2.9% of treated patients, dose delay in 1.2%, and permanent discontinuation in 2.9%. Sixty-five percent of patients reported improvement or resolution of peripheral neuropathy after a median of 1 month, and 48% reported complete resolution.

The peripheral neuropathy is predominantly sensory; however, motor and sensorimotor peripheral neuropathy also occur. Monitor for symptoms of peripheral neuropathy such as hypoesthesia, hyperesthesia, paresthesia, dysesthesia, neuropathic pain, burning sensation, weakness, or gait disturbance. Patients experiencing new or worsening peripheral neuropathy may require a delay, dose reduction, or discontinuation of POLIVY *[see Dosage and Administration (2.2)]*.

5.2 Infusion-Related Reactions

POLIVY can cause infusion-related reactions, including severe cases. Delayed infusion-related reactions as late as 24 hours after receiving POLIVY have occurred.

With premedication, 13% of patients (58/435) in POLARIX reported infusion-related reactions after the administration of POLIVY plus R-CHP. The reactions were Grade 1 in 4.4% of patients, Grade 2 in 8%, and Grade 3 in 1.1%.

With premedication, 7% of patients (12/173) in Study GO29365 reported infusion-related reactions after the administration of POLIVY. The reactions were Grade 1 in 4.6% of patients, Grade 2 in 1.7%, and Grade 3 in 0.6%.

Symptoms occurring in ≥1% of patients included chills, dyspnea, pyrexia, pruritus, rash, and chest discomfort. Administer an antihistamine and antipyretic prior to the administration of POLIVY, and monitor patients closely throughout the infusion. If an infusion-related reaction

occurs, interrupt the infusion and institute appropriate medical management *[see Dosage and Administration (2.2)]*.

5.3 Myelosuppression

Treatment with POLIVY can cause serious or severe myelosuppression, including neutropenia, thrombocytopenia, and anemia.

In POLARIX, 90% of patients treated with POLIVY plus R-CHP had primary prophylaxis with G-CSF. Grade 3–4 hematologic adverse reactions included lymphopenia (44%), neutropenia (39%), febrile neutropenia (15%), anemia (14%), and thrombocytopenia (8%) *[see Adverse Reactions (6.1)]*.

In Study GO29365, in patients treated with POLIVY plus BR (n = 45), 42% received primary prophylaxis with G-CSF. Grade 3 or higher hematologic adverse reactions included neutropenia (42%), thrombocytopenia (40%), anemia (24%), lymphopenia (13%), and febrile neutropenia (11%) *[see Adverse Reactions (6.1)]*. Grade 4 hematologic adverse reactions included neutropenia (24%), thrombocytopenia (16%), lymphopenia (9%), and febrile neutropenia (4.4%). Cytopenias were the most common reason for treatment discontinuation (18% of all patients).

Monitor complete blood counts throughout treatment. Cytopenias may require a delay, dose reduction, or discontinuation of POLIVY *[see Dosage and Administration (2.2)]*. Administer prophylactic G-CSF for neutropenia in patients receiving POLIVY plus R-CHP. Consider prophylactic G-CSF administration in patients receiving POLIVY plus bendamustine and a rituximab product.

5.4 Serious and Opportunistic Infections

Fatal and/or serious infections, including opportunistic infections such as sepsis, pneumonia (including *Pneumocystis jiroveci* and other fungal pneumonia), herpesvirus infection, and cytomegalovirus infection have occurred in patients treated with POLIVY *[see Adverse Reactions (6.1)]*.

In POLARIX, Grade 3–4 infections occurred in 14% (61/435) of patients treated with POLIVY plus R-CHP and infection-related deaths were reported in 1.1% of patients.

In Study GO29365, Grade 3 or higher infections occurred in 32% (55/173) of patients treated with POLIVYand infection-related deaths were reported in 2.9% of patients within 90 days of last treatment.

Closely monitor patients during treatment for signs of infection. Administer prophylaxis for *Pneumocystis jiroveci* pneumonia and herpesvirus. Administer prophylactic G-CSF for neutropenia as recommended *[see Dosage and Administration (2.3)]*.

5.5 Progressive Multifocal Leukoencephalopathy (PML)

PML has been reported after treatment with POLIVY plus bendamustine and obinutuzumab in study GO29365 (0.6%, 1/173). Monitor for new or worsening neurological, cognitive, or behavioral changes. Hold POLIVY and any concomitant chemotherapy if PML is suspected, and permanently discontinue if the diagnosis is confirmed.

5.6 Tumor Lysis Syndrome

POLIVY may cause tumor lysis syndrome. Patients with high tumor burden and rapidly proliferative tumor may be at increased risk of tumor lysis syndrome. Monitor closely and take appropriate measures, including tumor lysis syndrome prophylaxis.

5.7 Hepatotoxicity

Serious cases of hepatotoxicity that were consistent with hepatocellular injury, including elevations of transaminases and/or bilirubin, have occurred in patients treated with POLIVY.

In recipients of POLIVY plus R-CHP, Grade 3–4 elevation of ALT and AST developed in 1.4% and 0.7% of patients, respectively.

In Study GO29365, Grade 3 and Grade 4 transaminase elevations each developed in 1.9% of patients.

Preexisting liver disease, elevated baseline liver enzymes, and concomitant medications may increase the risk of hepatotoxicity. Monitor liver enzymes and bilirubin level.

5.8 Infusion Site Extravasation Injury

Cases of tissue damage following infusion site extravasation, including severe events, have been reported in clinical studies and in the postmarketing setting in patients treated with POLIVY. The signs and symptoms of infusion site extravasation occur within hours to weeks and may include a sensation of burning, tingling, pain, discomfort, swelling and redness at the site of injection, and can progress to more severe events like blistering, necrosis, ulceration, and tissue damage such as cellulitis.

To minimize the risk of extravasation, ensure patent venous access prior to initiating the infusion and closely monitor the infusion site throughout administration for any signs of extravasation. If extravasation occurs, stop the infusion and manage medically.

For mild symptoms, the remaining dose may be administered in an alternate limb after establishing patent venous access. For moderate to severe symptoms, the infusion can be restarted in an alternate limb based on the clinical judgment of the treating physician.

5.9 Embryo-Fetal Toxicity

Based on the mechanism of action and findings from animal studies, POLIVY can cause fetal harm when administered to a pregnant woman. The small molecule component of POLIVY, MMAE, administered to rats caused adverse developmental outcomes, including embryo-fetal mortality and structural abnormalities, at exposures below those occurring clinically at the recommended dose.

Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with POLIVY and for 3 months after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with POLIVY and for 5 months after the last dose *[see Use in Specific Populations (8.1, 8.3), Clinical Pharmacology (12.1)]*.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are discussed in greater detail in other sections of the label:

- Peripheral Neuropathy *[see Warnings and Precautions (5.1)]*
- Infusion-Related Reactions *[see Warnings and Precautions (5.2)]*
- Myelosuppression *[see Warnings and Precautions (5.3)]*
- Serious and Opportunistic Infections *[see Warnings and Precautions (5.4)]*
- Progressive Multifocal Leukoencephalopathy *[see Warnings and Precautions (5.5)]*
- Tumor Lysis Syndrome *[see Warnings and Precautions (5.6)]*
- Hepatotoxicity *[see Warnings and Precautions (5.7)]*
- Infusion Site Extravasation Injury *[see Warnings and Precautions (5.8)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared with rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety data described below reflect exposure to POLIVY 1.8 mg/kg in 480 patients with large B-cell lymphoma (LBCL), including those with previously untreated LBCL (POLARIX) and relapsed or refractory DLBCL (GO29365).

Previously Untreated DLBCL, NOS or HGBL

GO39942 (POLARIX)

The safety of POLIVY in combination with R-CHP chemoimmunotherapy was evaluated in POLARIX, a randomized double-blind, placebo-controlled, multicenter study of 873 patients with previously untreated large B-cell lymphoma, 435 of whom received POLIVY plus R-CHP *[see Clinical Studies (14.1)]*.

Patients were randomized 1:1 to receive POLIVY plus R-CHP or to receive R-CHOP for six 21-day cycles followed by two additional cycles of rituximab alone in both arms. Granulocyte colony-stimulating factor (G-CSF) primary prophylaxis was required and administered to 90% of patients in the POLIVY plus R-CHP arm and 93% of patients in the R-CHOP arm. Following premedication with an antihistamine and antipyretic, POLIVY was administered intravenously at 1.8 mg/kg on Day 1 of Cycles 1–6. R-CHP was administered starting on Day 1 of Cycles 1–6. Rituximab monotherapy was administered on Day 1 of Cycles 7–8 *[see Clinical Studies (14.1)]*.

The trial required an absolute neutrophil count ≥1,000/μL, platelet count ≥75,000/μL, creatinine clearance (CLcr) ≥40 mL/min, hepatic transaminases ≤2.5 times the upper limit of normal (ULN), and bilirubin <1.5 times ULN, unless abnormalities were from the underlying disease. The trial excluded patients having age >80, ECOG performance status above 2, known central nervous system (CNS) lymphoma, and Grade 2 or higher peripheral neuropathy.

The median age was 65 years overall (range: 19 to 80 years); 54% of patients were male; 53% were White, 19% were Asian, 2%, Black or African American, and 5% were Hispanic or Latino.

In the POLIVY plus R-CHP group, 92% of patients received 6 cycles of POLIVY, and 94% completed 6 cycles of combination therapy.

Serious adverse reactions occurred in 34% of patients who received POLIVY plus R-CHP, including febrile neutropenia and pneumonia in ≥5% of recipients. Fatal adverse reactions occurred in 3% of recipients of POLIVY plus R-CHP within 90 days of last treatment, primarily from infection including pneumonia (0.9%) and sepsis (0.2%).

Adverse reactions led to dose reduction of POLIVY in 6% of patients, mainly from peripheral neuropathy. Adverse reactions lead to dose interruption of POLIVY in 18% of patients, most commonly from pneumonia and neutropenia, and permanent discontinuation of POLIVY in 4.4% of patients.

Table 7 summarizes adverse reactions in POLARIX. In recipients of POLIVY plus R-CHP, adverse reactions in ≥20% of patients, excluding laboratory abnormalities, were peripheral neuropathy, nausea, fatigue, diarrhea, constipation, alopecia, and mucositis. New or worsening Grade 3 to 4 laboratory abnormalities in ≥10% of patients were lymphopenia, neutropenia, hyperuricemia, and anemia.

Table 7 Select Adverse Reactions Occurring in ≥10% of Patients Treated with POLIVY Plus R-CHP in POLARIX

Adverse Reactions by Body System	POLIVY + R-CHP n = 435		R-CHOP n = 438	
	All Grades, %	Grade 3–4, %	All Grades, %	Grade 3–4, %
Blood and Lymphatic System Disorders[1]				
Lymphopenia	80	44	77	44
Anemia	68	14	67	11
Neutropenia	60	39	60	42
Thrombocytopenia	32	8	33	6
Febrile neutropenia[a]	15	15	9	9
Investigations[1]				
Creatinine increased	66	0.7	64	0.9
Aspartate aminotransferase increased	26	0.7	23	1.1
Alanine aminotransferase increased	25	1.4	27	0.5
Alkaline phosphatase increased	23	0	22	0.5
Uric acid increased	19	18	17	16
Weight decreased	13	0.9	12	0.2
Nervous System Disorders				
Peripheral neuropathy[2,b]	53	1.6	54	1.1
Altered taste	14	0	16	0
Headache	13	0.2	14	0.9
Gastrointestinal Disorders				
Nausea	42	1.1	37	0.5
Diarrhea	31	3.9	20	1.8
Constipation	29	1.1	29	0.2
Mucositis[c]	22	1.4	19	0.5
Abdominal pain[d]	16	1.1	14	1.6
Vomiting	15	1.1	14	0.7
General Disorders				
Fatigue	37	2.5	38	3.0
Pyrexia	16	1.4	13	0
Edema[e]	14	0.5	11	0.2
Infusion-related reaction[f]	13	1.1	16	1.6
Skin and Subcutaneous Tissue Disorders				
Alopecia	24	0	24	0.2
Rash[g]	13	0.7	11	0
Musculoskeletal Disorders				
Musculoskeletal pain[h]	19	0.5	21	1.8
Infections				
Upper respiratory tract infection[i]	17	0.5	16	0.5
Metabolism and Nutrition Disorders				
Decreased appetite	17	1.1	14	0.7

Adverse Reactions by Body System	POLIVY + R-CHP n = 435		R-CHOP n = 438	
	All Grades, %	Grade 3–4, %	All Grades, %	Grade 3–4, %
Respiratory Disorders				
Cough	15	0	14	0
Dyspnea	13	0.9	10	0.9

The table includes a combination of grouped and ungrouped terms. Events were graded using NCI CTCAE version 4.0.

[1] Laboratory values are based on integrated analysis of laboratory and adverse reaction data. Reported investigations exclude electrolytes.
[2] At last assessment, peripheral neuropathy was unresolved in 42% in the POLIVY + R-CHP arm and in 33% in the R-CHOP arm.

[a] Febrile neutropenia includes febrile neutropenia, febrile bone marrow aplasia, and neutropenic sepsis.
[b] Peripheral neuropathy includes all terms containing "neuropathy", neuralgia, dysesthesia, paresthesia, hypoesthesia, peroneal nerve palsy, hypotonia, hyporeflexia, neuromyopathy, and hyperesthesia.
[c] Mucositis includes stomatitis, oropharyngeal pain, mucosal inflammation, mouth ulceration, oral pain, oropharyngeal discomfort, aphthous ulcer, odynophagia, oral discomfort, tongue blistering, and tongue ulceration.
[d] Abdominal pain includes abdominal pain, abdominal discomfort, gastrointestinal pain, epigastric discomfort, and related terms.
[e] Edema includes edema, face edema, swelling face, edema peripheral, fluid overload, fluid retention, pulmonary edema, peripheral swelling, and swelling.
[f] Infusion related reaction is reflective of the combination regimen due to same-day administration.
[g] Rash includes rash, dermatitis, and related terms.
[h] Musculoskeletal pain includes musculoskeletal pain, back pain, musculoskeletal chest pain, neck pain, myalgia, and bone pain.
[i] Upper respiratory tract infection incudes sinusitis, laryngitis, pharyngitis, nasopharyngitis, rhinitis, and specific infections.

Other clinically relevant adverse reactions in <10% of recipients of POLIVY plus R-CHP included:

- **Infections:** pneumonia, herpesvirus infection, sepsis, cytomegalovirus infection
- **Metabolic disorders:** tumor lysis syndrome
- **Renal disorders:** renal insufficiency
- **Respiratory disorders:** pneumonitis

Relapsed or Refractory DLBCL, NOS

GO29365

The data described in this section reflect exposure to POLIVY in Study GO29365, a multicenter clinical trial for adult patients with relapsed or refractory B-cell lymphomas *[see Clinical Studies (14.2)]*. In patients with relapsed or refractory DLBCL, the trial included a single-arm safety evaluation of POLIVY in combination with bendamustine and a rituximab product (BR) (n = 6), followed by an open-label randomization to POLIVY in combination with BR versus BR alone (n = 39 treated per arm).

Following premedication with an antihistamine and antipyretic, POLIVY 1.8 mg/kg was administered by intravenous infusion on Day 2 of Cycle 1 and on Day 1 of Cycles 2–6, with a cycle length of 21 days. Bendamustine 90 mg/m^2 daily was administered intravenously on Days 2 and 3 of Cycle 1 and on Days 1 and 2 of Cycles 2–6. A rituximab product dosed at 375 mg/m^2 was administered intravenously on Day 1 of each cycle. Granulocyte colony-stimulating factor primary prophylaxis was optional and administered to 42% of recipients of POLIVY plus BR.

In POLIVY-treated patients (n = 45), the median age was 67 years (range 33 – 86) with 58% being ≥age 65, 69% were male, 69% were White, and 87% had an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1. The trial required an absolute neutrophil

count ≥1500/µL, platelet count ≥75/µL, creatinine clearance (CLcr) ≥40 mL/min, hepatic transaminases ≤2.5 times ULN, and bilirubin <1.5 times ULN, unless abnormalities were from the underlying disease. Patients with Grade 2 or higher peripheral neuropathy or prior allogeneic hematopoietic stem cell transplantation (HSCT) were excluded.

Patients treated with POLIVY plus BR received a median of 5 cycles, with 49% receiving 6 cycles. Patients treated with BR alone received a median of 3 cycles, with 23% receiving 6 cycles.

Fatal adverse reactions occurred in 7% of recipients of POLIVY plus BR within 90 days of last treatment. Serious adverse reactions occurred in 64%, most often from infection. Serious adverse reactions in ≥5% of recipients of POLIVY plus BR included pneumonia (16%), febrile neutropenia (11%), pyrexia (9%), and sepsis (7%).

In recipients of POLIVY plus BR, adverse reactions led to dose reduction in 18%, dose interruption in 51%, and permanent discontinuation of all treatment in 31%. The most common adverse reactions leading to treatment discontinuation were thrombocytopenia and/or neutropenia.

Table 8 summarizes commonly reported adverse reactions. In recipients of POLIVY plus BR, adverse reactions in ≥20% of patients included neutropenia, thrombocytopenia, anemia, peripheral neuropathy, fatigue, diarrhea, pyrexia, decreased appetite, and pneumonia.

Table 8 Adverse Reactions Occurring in >10% of Patients with Relapsed or Refractory DLBCL and ≥5% More in the POLIVY Plus Bendamustine and Rituximab Product Group in Study GO29365

Adverse Reactions by Body System	POLIVY + BR n = 45		BR n = 39	
	All Grades, %	Grade 3 or Higher, %	All Grades, %	Grade 3 or Higher, %
Blood and Lymphatic System Disorders				
Neutropenia	49	42	44	36
Thrombocytopenia	49	40	33	26
Anemia	47	24	28	18
Lymphopenia	13	13	8	8
Nervous System Disorders				
Peripheral neuropathy	40	0	8	0
Dizziness	13	0	8	0
Gastrointestinal Disorders				
Diarrhea	38	4.4	28	5
Vomiting	18	2.2	13	0
General Disorders				
Infusion-related reaction	18	2.2	8	0
Pyrexia	33	2.2	23	0
Decreased appetite	27	2.2	21	0
Infections				
Pneumonia	22	16[a]	15	2.6[b]
Upper respiratory tract infection	13	0	8	0
Investigations				
Weight decreased	16	2.2	8	2.6
Metabolism and Nutrition Disorders				
Hypokalemia	16	9	10	2.6
Hypoalbuminemia	13	2.2	8	0
Hypocalcemia	11	2.2	5	0

The table includes a combination of grouped and ungrouped terms. Events were graded using NCI CTCAE version 4.
[a] Includes 2 fatalities.
[b] Includes 1 fatality.

Other clinically relevant adverse reactions (<10% or with a <5% difference) in recipients of POLIVY plus BR included:

- **Blood and lymphatic system disorders:** pancytopenia (7%)
- **Musculoskeletal disorders:** arthralgia (7%)
- **Investigations:** hypophosphatemia (9%), transaminase elevation (7%), lipase increased (7%)
- **Respiratory disorders:** pneumonitis (4.4%)

Selected treatment-emergent laboratory abnormalities are summarized in Table 9. In recipients of POLIVY plus BR, >20% of patients developed Grade 3 or 4 neutropenia, leukopenia, or thrombocytopenia, and >10% developed Grade 4 neutropenia (13%) or Grade 4 thrombocytopenia (11%).

Table 9 Select Laboratory Abnormalities Worsening from Baseline in Patients with Relapsed or Refractory DLBCL and ≥5% More in the POLIVY Plus Bendamustine and Rituximab Product Group

Laboratory Parameter[a]	POLIVY + BR n = 45		BR n = 39	
	All Grades, (%)	Grade 3–4, (%)	All Grades, (%)	Grade 3–4, (%)
Hematologic				
Lymphocyte count decreased	87	87	90	82
Neutrophil count decreased	78	61	56	33
Hemoglobin decreased	78	18	62	10
Platelet count decreased	76	31	64	26
Chemistry				
Creatinine increased	87	4.4	77	5
Calcium decreased	44	9	26	0
SGPT/ALT increased	38	0	8	2.6
SGOT/AST increased	36	0	26	2.6
Lipase increased	36	9	13	5
Phosphorus decreased	33	7	28	8
Amylase increased	24	0	18	2.6
Potassium decreased	24	11	28	5

[a] Includes laboratory abnormalities that are new or worsening in grade or with worsening from baseline unknown.

Safety was also evaluated in 173 adult patients with relapsed or refractory lymphoma who received POLIVY, bendamustine, and either a rituximab product or obinutuzumab in Study GO29365, including the 45 patients with DLBCL described above. In the expanded safety population, the median age was 66 years (range 27 – 86), 57% were male, 91% had an ECOG performance status of 0-1, and 32% had a history of peripheral neuropathy at baseline.

Fatal adverse reactions occurred in 4.6% of recipients of POLIVY within 90 days of last treatment, with infection as a leading cause. Serious adverse reactions occurred in 60%, most often from infection.

Table 10 summarizes the most common adverse reactions in the expanded safety population. The overall safety profile was similar to that described above. Adverse reactions in ≥20% of patients were diarrhea, neutropenia, peripheral neuropathy, fatigue, thrombocytopenia, pyrexia, decreased appetite, anemia, and vomiting. Infection-related adverse reactions in >10% of patients included upper respiratory tract infection, febrile neutropenia, pneumonia, and herpesvirus infection.

Table 10 Most Common Adverse Reactions (≥20% Any Grade or ≥5% Grade 3 or Higher) in Recipients of POLIVY and Chemoimmunotherapy for Relapsed or Refractory Lymphoma

Adverse Reaction by Body System	POLIVY + Bendamustine + Rituximab Product or Obinutuzumab n = 173	
	All Grades, %	Grade 3 or Higher, %
Blood and Lymphatic System Disorders		
Neutropenia	44	39
Thrombocytopenia	31	23
Anemia	28	14
Febrile neutropenia[a]	13	13
Leukopenia	13	8
Lymphopenia	12	12
Nervous System Disorders		
Peripheral neuropathy	40	2.3
Gastrointestinal Disorders		
Diarrhea	45	8
Vomiting	27	2.9
General Disorders		
Fatigue	40	5
Pyrexia	30	2.9
Decreased appetite	29	1.7
Infections		
Pneumonia	13	10[b]
Sepsis	6	6[c]
Metabolism and Nutrition Disorders		
Hypokalemia	18	6

The table includes a combination of grouped and ungrouped terms.

[a] Primary prophylaxis with granulocyte colony-stimulating factor was given to 46% of all patients.
[b] Includes 5 fatalities.
[c] Includes 4 fatalities.

Other clinically relevant adverse reactions (<20% any grade) included:

- **General disorders:** infusion-related reaction (7%)
- **Infection:** upper respiratory tract infection (16%), lower respiratory tract infection (10%), herpesvirus infection (12%), cytomegalovirus infection (1.2%)
- **Respiratory:** dyspnea (19%), pneumonitis (1.7%)
- **Nervous system disorders:** dizziness (10%)
- **Investigations:** weight decrease (10%), transaminase elevation (8%), lipase increase (3.5%)
- **Musculoskeletal disorders:** arthralgia (7%)
- **Eye disorders:** blurred vision (1.2%)

7 DRUG INTERACTIONS

7.1 Effects of Other Drugs on POLIVY

Strong CYP3A Inhibitors

Concomitant use with a strong CYP3A4 inhibitor may increase unconjugated MMAE AUC *[see Clinical Pharmacology (12.3)]*, which may increase POLIVY toxicities. Monitor patients for signs of toxicity.

Strong CYP3A Inducers

Concomitant use with a strong CYP3A4 inducer may decrease unconjugated MMAE AUC *[see Clinical Pharmacology (12.3)]*.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Based on findings from animal studies and its mechanism of action *[see Clinical Pharmacology (12.1)]*, POLIVY can cause fetal harm. There are no available data in pregnant women to inform the drug-associated risk. In animal reproduction studies, administration of the small molecule component of POLIVY, MMAE, to pregnant rats during organogenesis at exposures below the clinical exposure at the recommended dose of 1.8 mg/kg POLIVY every 21 days resulted in embryo-fetal mortality and structural abnormalities *(see Data)*. Advise a pregnant woman of the potential risks to a fetus.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2–4% and 15–20%, respectively.

Data

Animal Data

No embryo-fetal development studies in animals have been performed with polatuzumab vedotin-piiq. In an embryo-fetal developmental study in pregnant rats, administration of two intravenous doses of MMAE, the small molecule component of POLIVY, on gestational days 6 and 13 caused embryo-fetal mortality and structural abnormalities, including protruding tongue, malrotated limbs, gastroschisis, and agnathia compared to controls at a dose of 0.2 mg/kg (approximately 0.5-fold the human area under the curve [AUC] at the recommended dose).

8.2 Lactation

Risk Summary

There is no information regarding the presence of polatuzumab vedotin-piiq in human milk, the effects on the breastfed child, or milk production. Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment with POLIVY and for 2 months after the last dose.

8.3 Females and Males of Reproductive Potential

POLIVY can cause embryo-fetal harm when administered to pregnant women *[see Use in Specific Populations (8.1)]*.

Pregnancy Testing

Verify pregnancy status in females of reproductive potential prior to initiating POLIVY *[see Use in Specific Populations (8.1)]*.

Contraception

Females

Advise females of reproductive potential to use effective contraception during treatment with POLIVY and for 3 months after the last dose *[see Nonclinical Toxicology (13.1)]*.

Males

Based on genotoxicity findings, advise males with female partners of reproductive potential to use effective contraception during treatment with POLIVY and for 5 months after the final dose *[see Nonclinical Toxicity (13.1)]*.

Infertility

Females

Based on findings in animal studies with MMAE-containing antibody-drug conjugates (ADCs), POLIVY may impair female fertility. The effect on fertility is reversible *[see Nonclinical Toxicology (13.1)]*.

Males

Based on findings from animal studies, POLIVY may impair male fertility. The reversibility of this effect is unknown *[see Nonclinical Toxicology (13.1)]*.

8.4 Pediatric Use

Safety and effectiveness of POLIVY have not been established in pediatric patients.

8.5 Geriatric Use

Among 435 patients treated with POLIVY plus R-CHP in POLARIX, 227 (52%) were ≥65 years of age. No overall differences in safety or efficacy were observed between patients aged ≥65 years and younger patients.

Among 173 patients treated with POLIVY plus BR in Study GO29365, 95 (55%) were ≥65 years of age. Patients aged ≥65 had a numerically higher incidence of serious adverse reactions (64%) than patients aged <65 (53%). This study did not include sufficient numbers of patients to determine whether efficacy differed in patients aged ≥65 and younger patients.

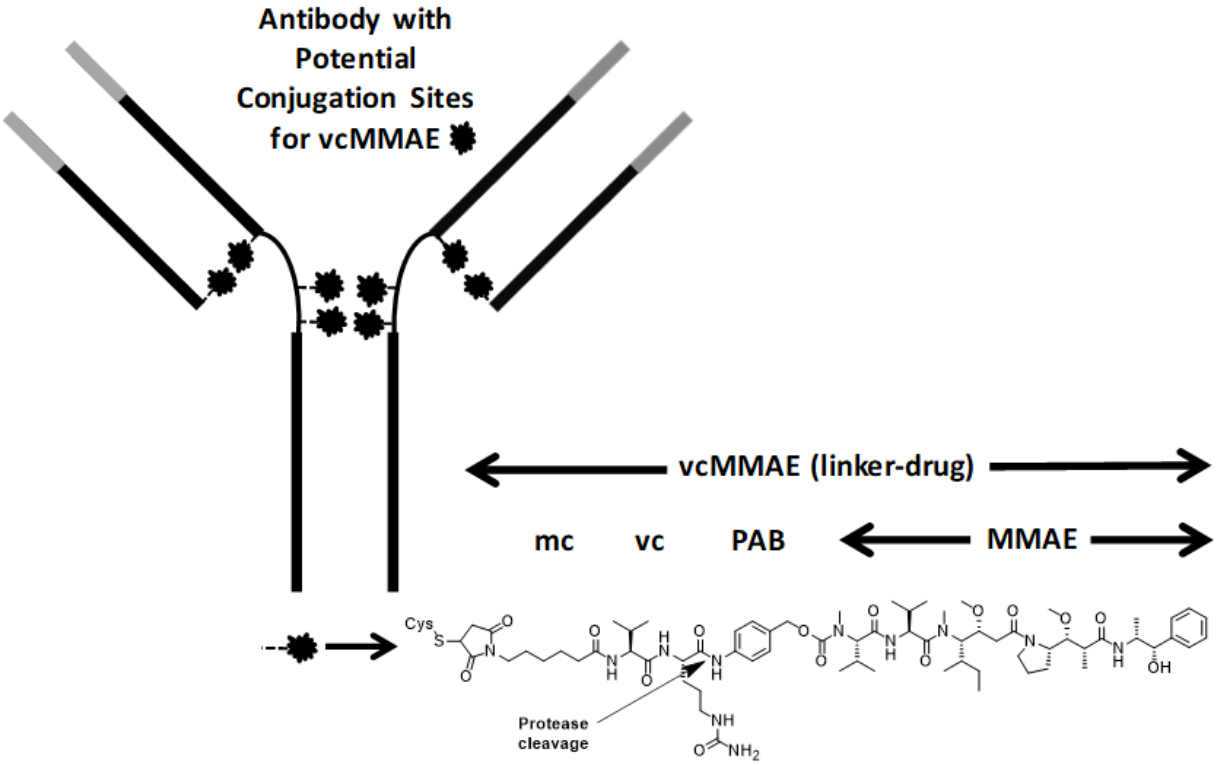
8.6 Hepatic Impairment

Avoid the administration of POLIVY in patients with moderate or severe hepatic impairment (total bilirubin greater than 1.5 × ULN and any AST). Patients with moderate or severe hepatic impairment are likely to have increased exposure to MMAE, which may increase the risk of adverse reactions. POLIVY has not been studied in patients with moderate or severe hepatic impairment *[see Clinical Pharmacology (12.3) and Warnings and Precautions (5.7)]*.

No adjustment in the starting dose is required when administering POLIVY to patients with mild hepatic impairment (total bilirubin 1 to 1.5 × ULN or AST greater than ULN).

11 DESCRIPTION

Polatuzumab vedotin-piiq is a CD79b-directed antibody and microtubule inhibitor conjugate. It consists of three components: 1) the humanized immunoglobulin G1 (IgG1) monoclonal antibody specific for human CD79b; 2) the small molecule anti-mitotic agent MMAE; and 3) a protease-cleavable linker maleimidocaproyl-valine-citrulline-p-aminobenzyloxycarbonyl (mc-vc-PAB) that covalently attaches MMAE to the polatuzumab antibody.



Polatuzumab vedotin-piiq has an approximate molecular weight of 150 kDa. An average of 3.5 molecules of MMAE are attached to each antibody molecule. Polatuzumab vedotin-piiq is produced by chemical conjugation of the antibody and small molecule components. The antibody is produced by mammalian (Chinese hamster ovary) cells, and the small molecule components are produced by chemical synthesis.

POLIVY (polatuzumab vedotin-piiq) for injection is supplied as a sterile, white to grayish-white, preservative-free, lyophilized powder, which has a cake-like appearance, for intravenous infusion after reconstitution and dilution.

Each single-dose 30 mg POLIVY vial delivers 30 mg of polatuzumab vedotin-piiq, polysorbate-20 (1.8 mg), sodium hydroxide (0.82 mg), succinic acid (1.77 mg), and sucrose (62 mg). After reconstitution with 1.8 mL of any of the diluents listed in Table 5, the final concentration is 20 mg/mL with a pH of approximately 5.3.

Each single-dose 140 mg POLIVY vial delivers 140 mg of polatuzumab vedotin-piiq, polysorbate-20 (8.4 mg), sodium hydroxide (3.8 mg), succinic acid (8.27 mg), and sucrose (288 mg). After reconstitution with 7.2 mL of any of the diluents listed in Table 5, the final concentration is 20 mg/mL with a pH of approximately 5.3.

The POLIVY vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Polatuzumab vedotin-piiq is a CD79b-directed antibody-drug conjugate with activity against dividing B cells. The small molecule, MMAE, is an anti-mitotic agent covalently attached to the antibody via a cleavable linker. The monoclonal antibody binds to CD79b, a B-cell specific surface protein, which is a component of the B-cell receptor. Upon binding CD79b, polatuzumab vedotin-piiq is internalized, and the linker is cleaved by lysosomal proteases to enable intracellular delivery of MMAE. MMAE binds to microtubules and kills dividing cells by inhibiting cell division and inducing apoptosis.

12.2 Pharmacodynamics

Over polatuzumab vedotin-piiq dosages of 0.1 to 2.4 mg/kg (0.06 to 1.33 times the approved recommended dosage), higher exposures (AUC and C_{max}) of antibody-conjugated MMAE (acMMAE) and unconjugated MMAE were associated with higher incidence of some adverse reactions (including ≥Grade 3 thrombocytopenia and ≥Grade 3 anemia). Higher exposure (AUC and C_{max}) of unconjugated MMAE was associated with higher incidence of ≥Grade 2 peripheral neuropathy. Lower acMMAE exposure (AUC) was associated with lower efficacy in patients with relapsed or refractory DLBCL.

Cardiac Electrophysiology

Polatuzumab vedotin-piiq did not prolong the mean QTc interval to any clinically relevant extent based on ECG data from two open-label studies in patients with previously treated B-cell malignancies at the recommended dosage.

12.3 Pharmacokinetics

The exposure parameters of acMMAE and unconjugated MMAE (the cytotoxic component of polatuzumab vedotin-piiq) are summarized in Table 11. The plasma exposure of acMMAE and unconjugated MMAE increased proportionally over a polatuzumab vedotin-piiq dose range from 0.1 to 2.4 mg/kg (0.06 to 1.33 times the approved recommended dosage). Cycle 3 acMMAE AUC were predicted to increase by approximately 30% over Cycle 1 AUC, and achieved more than 90% of the Cycle 6 AUC. Unconjugated MMAE plasma exposures were <3% of acMMAE exposures, and the AUC and C_{max} were predicted to decrease after repeated every-3-week dosing.

Table 11 Cycle 1 Exposure of acMMAE and Unconjugated MMAE[a,b]

	R/R DLBCL, NOS		Previously Untreated DLBCL, NOS or HGBL	
	acMMAE	Unconjugated MMAE	acMMAE	Unconjugated MMAE
C_{max} (ng/mL)	688 (15%)	3.19 (57%)	587 (15%)	2.45 (46%)
AUC (day*ng/mL)	2040 (35%)	31.0 (56%)	1690 (22%)	20.8 (50%)

[a] After the first polatuzumab vedotin-piiq dose of 1.8 mg/kg.
[b] Cycle 1 exposures are reported as Geometric Mean (Geometric Coefficient of Variation %).
C_{max}=maximum concentration; AUC=area under the concentration-time curve from time zero to day 21.

Distribution

The acMMAE central volume of distribution is 3.15 L. For humans, MMAE plasma protein binding is 71% to 77% and the blood-to-plasma ratio is 0.79 to 0.98, in vitro.

Elimination

At the end of Cycle 6, the median (min, max) acMMAE terminal half-life was 12.2 days (4.5 to 36.7 days) and the clearance was 0.9 L/day in patients with B-cell malignancies. The median (min, max) unconjugated MMAE terminal half-life was 3.74 days (1.58 to 10.1 days) days after the first polatuzumab vedotin-piiq dose.

Metabolism

Polatuzumab vedotin-piiq catabolism has not been studied in humans; however, it is expected to undergo catabolism to small peptides, amino acids, unconjugated MMAE, and unconjugated MMAE-related catabolites. MMAE is a substrate for CYP3A4.

Specific Populations

No clinically significant differences in the pharmacokinetics of acMMAE or unconjugated MMAE were observed based on age (19 to 89 years), sex (males versus females), race (White 69%, Asian 11%), or mild to moderate renal impairment (CLcr 30 to 89 mL/min).

The effect of severe renal impairment (CLcr 15 to 29 mL/min) or end-stage renal disease with or without dialysis on the pharmacokinetics of acMMAE or unconjugated MMAE is unknown.

Patients with Hepatic Impairment

Compared to patients with normal hepatic function, geometric mean MMAE exposure was 11% higher in patients with previously untreated DLBCL and mild hepatic impairment (total bilirubin 1 to 1.5 × ULN or any AST greater than ULN) and 40% higher in patients with relapsed or refractory DLBCL and mild hepatic impairment. The effect of mild hepatic impairment on MMAE exposure is not expected to have a clinically significant impact.

Mild hepatic impairment was not associated with a significant difference in acMMAE exposure.

The effect of moderate to severe hepatic impairment (total bilirubin greater than 1.5 × ULN and any AST) or liver transplantation on the pharmacokinetics of acMMAE or unconjugated MMAE is unknown.

Drug Interaction Studies

No dedicated clinical drug-drug interaction studies with POLIVY in humans have been conducted.

Physiologically-Based Pharmacokinetic (PBPK) Modeling Predictions:

Strong CYP3A Inhibitor: Concomitant use of polatuzumab vedotin-piiq with ketoconazole (strong CYP3A inhibitor) is predicted to increase unconjugated MMAE AUC by 45%.

Strong CYP3A Inducer: Concomitant use of polatuzumab vedotin-piiq with rifampin (strong CYP3A inducer) is predicted to decrease unconjugated MMAE AUC by 63%.

Sensitive CYP3A Substrate: Concomitant use of polatuzumab vedotin-piiq is predicted not to affect exposure to midazolam (sensitive CYP3A substrate).

Population Pharmacokinetic (popPK) Modeling Predictions:

Bendamustine or Rituximab: No clinically significant differences in the pharmacokinetics of acMMAE or unconjugated MMAE are predicted when polatuzumab vedotin-piiq is used concomitantly with bendamustine or rituximab.

Rituximab, Cyclophosphamide, Doxorubicin, or Prednisone (R-CHP): No clinically significant differences in the pharmacokinetics of acMMAE or unconjugated MMAE are predicted when polatuzumab vedotin-piiq is used concomitantly with R-CHP.

In Vitro Studies Where Drug Interaction Potential Was Not Further Evaluated Clinically:

Cytochrome P450 (CYP) Enzymes: MMAE does not inhibit CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, or CYP2D6. MMAE does not induce major CYP enzymes.

Transporter Systems: MMAE does not inhibit P-gp. MMAE is a P-gp substrate.

12.6 Immunogenicity

The observed incidence of anti-drug antibodies is highly dependent on the sensitivity and specificity of the assay. Differences in assay methods preclude meaningful comparisons of the incidence of anti-drug antibodies in the studies described below with the incidence of anti-drug antibodies in other studies, including those of POLIVY or of other polatuzumab products.

In studies POLARIX and GO29365, 1.4% (6/427) and 6% (8/134) of patients tested positive for antibodies against polatuzumab vedotin-piiq, respectively, of which none were positive for neutralizing antibodies. Because of the low occurrence of anti-drug antibodies, the effect of these antibodies on the pharmacokinetics, pharmacodynamics, safety, and/or effectiveness of polatuzumab products is unknown.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity studies in animals have not been performed with polatuzumab vedotin-piiq or MMAE.

MMAE was positive for genotoxicity in the in vivo rat bone marrow micronucleus study through an aneugenic mechanism. MMAE was not mutagenic in the bacterial reverse mutation (Ames) assay or the L5178Y mouse lymphoma forward mutation assay.

Fertility studies in animals have not been performed with polatuzumab vedotin-piiq or MMAE. However, results of repeat-dose toxicity indicate the potential for polatuzumab vedotin-piiq to impair female and male fertility. In the 4-week repeat-dose toxicity study in rats with weekly dosing of 2, 6, and 10 mg/kg, dose-dependent testicular seminiferous tubule degeneration with abnormal lumen contents in the epididymis was observed. Findings in the testes and epididymis did not reverse and correlated with decreased testes weight and gross findings of small and/or soft testes at recovery necropsy in males given doses ≥2 mg/kg (below the exposure at the recommended dose based on unconjugated MMAE AUC).

MMAE-containing ADCs have been associated with adverse ovarian effects when administered to sexually immature animals. Adverse effects included decrease in, or absence of, secondary and tertiary ovarian follicles after weekly administration to cynomolgus monkeys in studies of 4-week duration. These effects showed a trend towards recovery 6 weeks after the end of dosing; no changes were observed in primordial follicles.

14 CLINICAL STUDIES

14.1 Previously Untreated DLBCL, NOS or HGBL

GO39942 (POLARIX)

The efficacy of POLIVY was evaluated in POLARIX (NCT03274492), a randomized double-blind, placebo-controlled, multicenter trial in patients with previously untreated large B-cell lymphoma. Eligible patients were aged 18–80 and had an International Prognostic Index (IPI) score of 2–5 and ECOG performance status of 0–2. The study excluded patients with transformed lymphoma, primary mediastinal large B-cell lymphoma, known CNS lymphoma, or Grade 2 or higher peripheral neuropathy.

Patients were randomized in a 1:1 ratio to receive POLIVY plus R-CHP or to receive R-CHOP for six 21-day cycles followed by two additional cycles of rituximab alone in both arms. Randomization was stratified by IPI score (2 vs 3–5), presence or absence of bulky disease (lesion ≥7.5 cm), and geographical region. Dosing in each treatment arm was as follows:

- POLIVY + R-CHP arm: POLIVY 1.8 mg/kg intravenously, rituximab 375 mg/m² intravenously, cyclophosphamide 750 mg/m² intravenously, and doxorubicin 50 mg/m² intravenously on Day 1 and prednisone 100 mg orally once daily on Days 1–5 for 6 cycles. Rituximab 375 mg/m^2 was administered intravenously on Day 1 of cycles 7 and 8.
- R-CHOP arm: rituximab 375 mg/m² intravenously, cyclophosphamide 750 mg/m² intravenously, doxorubicin 50 mg/m² intravenously, and vincristine 1.4 mg/m²

intravenously on Day 1 and prednisone 100 mg orally once daily on Days 1–5 for 6 cycles. Rituximab 375 mg/m^2 was administered intravenously on Day 1 of cycles 7 and 8.

Prophylaxis with granulocyte-colony stimulating factor (G-CSF) was mandated for both arms. Dosing in both treatment arms was preceded by premedication.

Of the 879 patients randomized (440 to POLIVY plus R-CHP, 439 to R-CHOP), the median age was 65 years (range 19 to 80 years), 54% were male, 54% were White, 19% were Asian, 1.8% were Black or African American, and 6% were Hispanic or Latino. In total, 38% had an IPI score of 2, 62% had an IPI score of 3–5, 89% had Stage 3 or 4 disease, and 44% had bulky disease. The majority of patients had DLBCL, NOS (84%; n = 740), 11% (n = 93) had HGBL with *MYC* and *BCL2* and/or *BCL6* rearrangements or HGBL, NOS, and 5% had other large B-cell lymphomas.

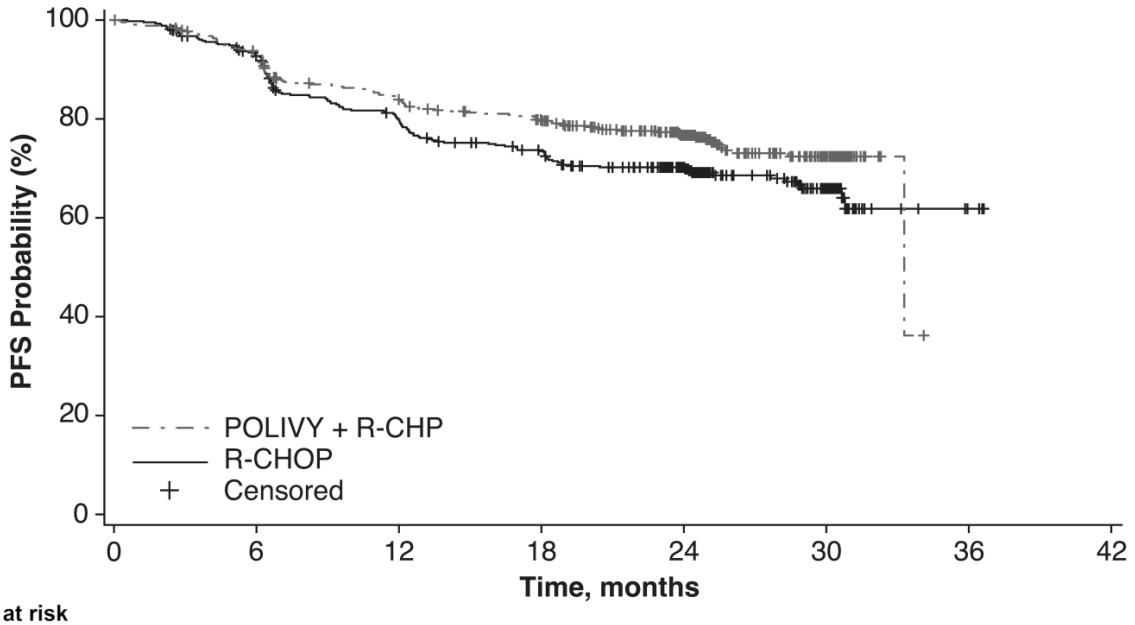
Efficacy was based on investigator-assessed progression-free survival (PFS). Other efficacy measures included modified event-free survival. Efficacy results are summarized in Table 12 and in Figure 1.

Table 12 Summary of Efficacy in POLARIX by Intention-to-Treat Analysis

Outcomes	**POLIVY + R-CHP n = 440**	**R-CHOP n = 439**
Progression-Free Survival per Investigator[a]		
Number (%) of patients with event	107 (24)	134 (31)
Progression	88	114
Death	19	20
HR (95% CI)	0.73 (0.57, 0.95)	
p-value[b]	0.0177	
Modified Event-Free Survival per Investigator[c]		
Number (%) of patients with event	112 (26)	138 (31)
HR (95% CI)	0.75 (0.58, 0.96)	
p-value[b]	0.0244	
Objective Response at End of Treatment[d]		
Objective response rate, % (95% CI)	86 (82, 89)	84 (80, 87)
CR rate, %	78 (74, 82)	74 (70, 78)
Difference in CR rate, % (95% CI)	3.9 (–1.9, 9.7)	
p-value[e]	0.1557	

[a] Estimated median follow-up for PFS was 24.7 months in both arms combined.
[b] Stratified log-rank test, with a two-sided significance boundary of 0.05. The hierarchical testing order was PFS, modified EFS, then CR rate and overall survival.
[c] Modified EFS was defined as time from randomization to the earliest occurrence of disease progression or relapse, death, an efficacy finding that led to non-protocol specified lymphoma treatment, or biopsy positive for residual disease.
[d] By blinded independent central review, per 2014 Lugano response criteria.
[e] Cochran-Mantel-Haenszel chi-squared test, with a two-sided significance boundary of 0.01.
CI=confidence interval; CR=complete response; EFS=event-free survival; HR=hazard ratio; PFS=progression-free survival.

Figure 1 Kaplan-Meier Curve of Investigator-Assessed Progression-Free Survival in POLARIX by Intention-to-Treat Analysis



Patients at risk								
POLIVY + R-CHP	440	404	353	327	246	78	NE	NE
R-CHOP	439	389	330	296	220	78	3	NE

In a prespecified descriptive analysis of the largest lymphoma subgroup, DLBCL, NOS, the PFS HR was 0.75 (95% CI: 0.57, 0.99). In patients with HGBL, the PFS HR was 0.48 (95% CI: 0.21, 1.08). There were insufficient data to evaluate efficacy in other large B-cell lymphomas.

With an estimated median follow-up of 3.3 years, the prespecified final analysis of overall survival (OS) showed no statistically significant difference, with a HR of 0.94 (95% CI: 0.67, 1.33). In a descriptive analysis, the OS HR in patients with DLBCL, NOS was 1.02 (95% CI: 0.70, 1.49). The OS HR in patients with HGBL was 0.42 (95% CI: 0.15, 1.19).

14.2 Relapsed or Refractory DLBCL, NOS

GO29365

The efficacy of POLIVY was evaluated in Study GO29365 (NCT02257567), an open-label, multicenter clinical trial that included a cohort of 80 patients with relapsed or refractory DLBCL after at least one prior regimen. Patients were randomized 1:1 to receive either POLIVY in combination with bendamustine and a rituximab product (BR) or BR alone for six 21-day cycles. Randomization was stratified by duration of response (DOR) to last therapy. Eligible patients were not candidates for autologous HSCT at study entry. The study excluded patients with Grade 2 or higher peripheral neuropathy, prior allogeneic HSCT, active central nervous system lymphoma, or transformed lymphoma.

Following premedication with an antihistamine and antipyretic, POLIVY was given by intravenous infusion at 1.8 mg/kg on Day 2 of Cycle 1 and on Day 1 of Cycles 2–6. Bendamustine was administered at 90 mg/m^2 intravenously daily on Days 2 and 3 of Cycle 1 and on Days 1 and 2 of Cycles 2–6. A rituximab product was administered at a dose of 375 mg/m^2 intravenously on Day 1 of Cycles 1–6. The cycle length was 21 days.

Of the 80 patients randomized to receive POLIVY plus BR (n = 40) or BR alone (n = 40), the median age was 69 years (range: 30–86 years), 66% were male, and 71% were White. Most patients (98%) had DLBCL not otherwise specified. The primary reasons patients were not candidates for HSCT included age (40%), insufficient response to salvage therapy (26%), and prior transplant failure (20%). The median number of prior therapies was 2 (range: 1–7), with

29% receiving one prior therapy, 25% receiving 2 prior therapies, and 46% receiving 3 or more prior therapies. Eighty percent of patients had refractory disease to last therapy.

In the POLIVY plus BR arm, patients received a median of 5 cycles, with 49% receiving 6 cycles. In the BR arm, patients received a median of 3 cycles, with 23% receiving 6 cycles.

Efficacy was based on complete response (CR) rate at the end of treatment and DOR, as determined by an independent review committee (IRC). Other efficacy measures included IRC-assessed best overall response.

Response rates are summarized in Table 13.

Table 13 Response Rates in Patients with Relapsed or Refractory DLBCL

Response per IRC, n (%)[a]	POLIVY + BR n = 40	BR n = 40
Objective Response at End of Treatment[b]	18 (45)	7 (18)
(95% CI)	(29, 62)	(7, 33)
CR	16 (40)	7 (18)
(95% CI)	(25, 57)	(7, 33)
Difference in CR rates, % (95% CI)[c]	22 (3, 41)	
Best Overall Response of CR or PR[d]	25 (63)	10 (25)
(95% CI)	(46, 77)	(13, 41)
Best Response of CR	20 (50)	9 (23)
(95% CI)	(34, 66)	(11, 38)

[a] PET-CT based response per modified Lugano 2014 criteria. Bone marrow confirmation of PET-CT CR was required. PET-CT PR required meeting both PET criteria and CT criteria for PR.
[b] End of treatment was defined as 6–8 weeks after Day 1 of Cycle 6 or last study treatment.
[c] Miettinen-Nurminen method.
[d] PET-CT results were prioritized over CT results.
CR=complete response; PR=partial remission.

In the POLIVY plus BR arm, of the 25 patients who achieved a partial or complete response, 16 (64%) had a DOR of at least 6 months, and 12 (48%) had a DOR of at least 12 months. In the BR arm, of the 10 patients who achieved a partial or complete response, 3 (30%) had a DOR lasting at least 6 months, and 2 (20%) had a DOR lasting at least 12 months.

15 REFERENCES

1. "OSHA Hazardous Drugs." *OSHA*. http://www.osha.gov/SLTC/hazardousdrugs/index.html

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

POLIVY (polatuzumab vedotin-piiq) for injection is a preservative-free, white to grayish-white lyophilized powder, which has a cake-like appearance. POLIVY is supplied as:

Carton Contents	NDC
One 30 mg single-dose vial	NDC 50242-103-01
One 140 mg single-dose vial	NDC 50242-105-01

Storage and Handling

Store refrigerated at 2°C to 8°C (36°F to 46°F) in original carton to protect from light. Do not use beyond the expiration date shown on the carton. Do not freeze. Do not shake.

POLIVY is a hazardous drug. Follow applicable special handling and disposal procedures.[1]

17 PATIENT COUNSELING INFORMATION

Peripheral Neuropathy

Advise patients that POLIVY can cause peripheral neuropathy. Advise patients to report to their healthcare provider any numbness or tingling of the hands or feet or any muscle weakness *[see Warnings and Precautions (5.1)]*.

Infusion-Related Reactions

Advise patients to contact their healthcare provider if they experience signs and symptoms of infusion reactions, including fever, chills, rash, or breathing problems, within 24 hours of infusion *[see Warnings and Precautions (5.2)]*.

Myelosuppression

Advise patients to report signs or symptoms of bleeding or infection immediately. Advise patients of the need for periodic monitoring of blood counts *[see Warnings and Precautions (5.3)]*.

Infections

Advise patients to contact their healthcare provider if a fever of 38°C (100.4°F) or greater or other evidence of potential infection such as chills, cough, or pain on urination develops. Advise patients of the need for periodic monitoring of blood counts *[see Warnings and Precautions (5.4)]*.

Progressive Multifocal Leukoencephalopathy

Advise patients to seek immediate medical attention for new or changes in neurological symptoms such as confusion, dizziness, or loss of balance; difficulty talking or walking; or changes in vision *[see Warnings and Precautions (5.5)]*.

Tumor Lysis Syndrome

Advise patients to seek immediate medical attention for symptoms of tumor lysis syndrome such as nausea, vomiting, diarrhea, and lethargy *[see Warnings and Precautions (5.6)]*.

Hepatotoxicity

Advise patients to report symptoms that may indicate liver injury, including fatigue, anorexia, right upper abdominal discomfort, dark urine, or jaundice *[see Warnings and Precautions (5.7)]*.

Infusion Site Extravasation Injury

Advise patients to contact their healthcare provider if they experience any signs or symptoms of infusion site extravasation such as burning sensation, tingling, pain, discomfort, swelling or redness at or around the infusion site during or after the treatment with POLIVY *[see Warnings and Precautions (5.8)]*.

Embryo-Fetal Toxicity

Advise females of reproductive potential of the potential risk to a fetus. Advise females to contact their healthcare provider if they become pregnant, or if pregnancy is suspected, during treatment with POLIVY *[see Warnings and Precautions (5.9)* and *Use in Specific Populations (8.1)]*.

Females and Males of Reproductive Potential

Advise females of reproductive potential, and males with female partners of reproductive potential, to use effective contraception during treatment with POLIVY and for 3 months and 5 months after the last dose, respectively *[see Use in Specific Populations (8.3)]*.

Lactation

Advise women not to breastfeed while receiving POLIVY and for 2 months after the last dose *[see Use in Specific Populations (8.2)]*.

Infertility

Advise females and males of reproductive toxicity that POLIVY may impair fertility *[See Use in Specific Populations (8.3)]*.

POLIVY® [polatuzumab vedotin-piiq]

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South San Francisco, CA 94080-4990

U.S. License No. 1048

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