Every step of **your first-line DLBCL** treatment matters

PLAN YOUR PATH WITH POLIVY®

Images do not depict actual patients.

Visit POLIVY.COM for more 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).

Select Important Safety Information

The serious to fatal side effects of POLIVY treatment include nerve problems in your arms and legs, infusion-related reactions, low blood cell counts, infections, rare and serious brain infections, tumor lysis syndrome, liver problems, infusion site injury, and potential harm to your unborn baby.

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

Please see full Prescribing Information, as well as additional Important Safety Information throughout this brochure.

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*POLIVY is given in combination with 4 other medicines called rituximab product, cyclophosphamide, doxorubicin (also called Adriamycin), and prednisone (R-CHP), which also help to fight your cancer. Together with POLIVY, they will be referred to as POLIVY plus R-CHP from here on.

Please see full Prescribing Information, as well as additional Important Safety Information throughout this brochure.

Not an actual patient; image edited with AI.

Getting Started With POLIVY®

You or a loved one has recently been diagnosed with diffuse large B-cell lymphoma (DLBCL). As a first-line DLBCL treatment, your healthcare provider has prescribed POLIVY in combination with a rituximab product and chemotherapy.* You may have a lot of questions about the treatment journey ahead. This brochure will help you learn about DLBCL, the POLIVY regimen, and available support resources.

The information provided in this brochure is meant for educational purposes only. It is not meant to replace medical advice. Please contact your healthcare team with any questions that you may have about DLBCL and your treatment.

*Chemotherapy = cyclophosphamide, doxorubicin (also called Adriamycin), and prednisone.

Please see full Prescribing Information, as well as additional Important Safety Information throughout this brochure.

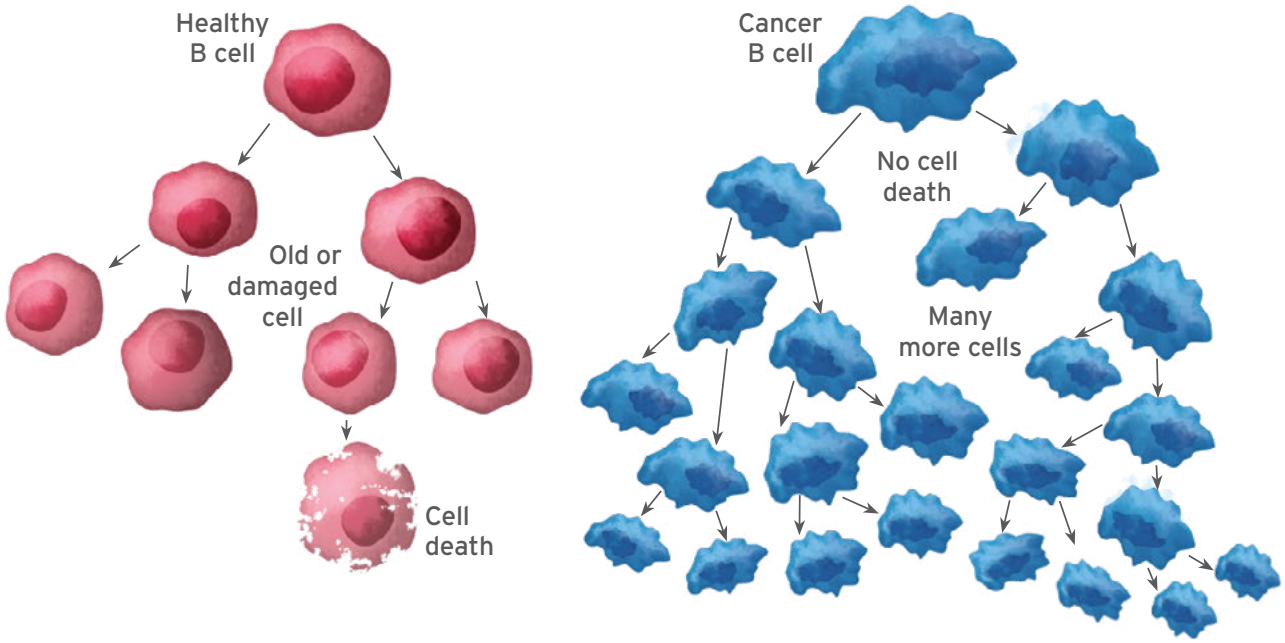
What is DLBCL?

DLBCL is an aggressive (fast-growing) blood cancer

Your blood contains 2 major types of cells: red and white blood cells. B cells are white blood cells that protect your body from infection and disease.

In DLBCL, some B cells become cancerous when changes cause them to grow and multiply uncontrollably or survive for longer than usual.

DLBCL is the most common form of lymphoma* (a type of blood cancer).



a) Healthy B cells grow, divide, and die as they become old or damaged.

b) In DLBCL, B cells either grow and multiply uncontrollably or survive for longer than usual.

DLBCL is an aggressive (fast-growing) blood cancer. Although it can occur at any age, its incidence increases with age. Most people are first diagnosed between the ages of 65 and 74.

DLBCL affects both men and women, but is slightly more common in men. The cause of DLBCL is unknown.

Talk with your healthcare provider to learn more about your specific diagnosis and risk factors.

*DLBCL belongs to a diverse group of blood cancers called non-Hodgkin lymphoma (NHL) that affect different types of white blood cells. In addition to DLBCL, high-grade B-cell lymphoma (HGBL) is a subset of NHL.

Please see full Prescribing Information, as well as additional Important Safety Information throughout this brochure.

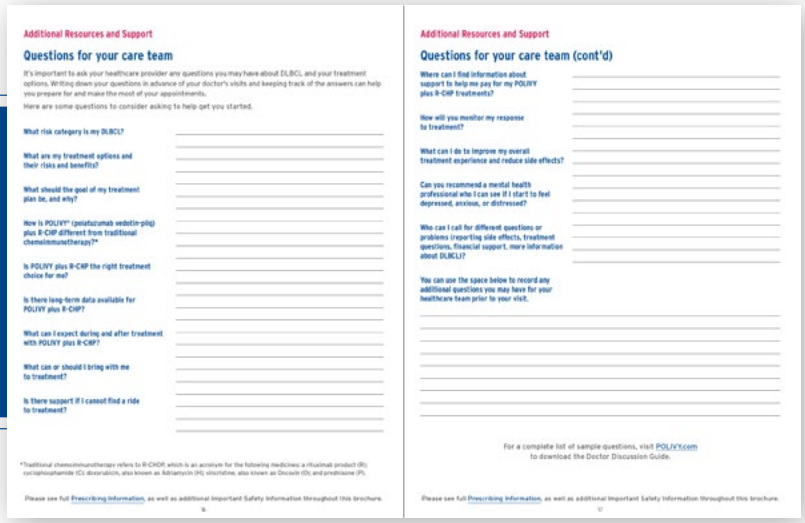
Treatment Considerations in DLBCL

About 30-40% of people with newly diagnosed DLBCL are at risk of their cancer worsening or returning after treatment with traditional chemoimmunotherapy.† When subsequent therapy for DLBCL is needed, the course of the disease has a worse outlook. This is why the first treatment choice is a vital decision.

When evaluating your treatment options with your healthcare team, it is important to understand how well the treatment works and the possible side effects of the treatment.

† R-CHOP is the traditional chemoimmunotherapy regimen that has been historically used in the treatment of newly diagnosed DLBCL. R-CHOP is an acronym for the following medicines: a rituximab product (R); cyclophosphamide (C); doxorubicin, also known as Adriamycin (H); vincristine, also known as Oncovin (O); and prednisone (P).

For a sample list of questions to help you prepare for your next doctor's visit and understand your treatment options, please see pages 16-17 of this brochure.



Additional Resources and Support

Questions for your care team

It's important to ask your healthcare provider any questions you may have about DLBCL and your treatment options. Writing down your questions in advance of your doctor's visits and keeping track of the answers can help you prepare for and make the most of your appointments.

Here are some questions to consider asking to help get you started.

What risk category is my DLBCL?

What are my treatment options and their risks and benefits?

What should the goal of my treatment plan be, and why?

How is POLIVY® (polatuzumab vedotin-piiq) plus R-CHP different from traditional chemoimmunotherapy?*

Is POLIVY plus R-CHP the right treatment choice for me?

Is there long-term data available for POLIVY plus R-CHP?

What can I expect during and after treatment with POLIVY plus R-CHP?

What can or should I bring with me to treatment?

Is there support if I cannot find a ride to treatment?

*Traditional chemoimmunotherapy refers to R-CHOP, which is an acronym for the following medicines: a rituximab product (R); cyclophosphamide (C); doxorubicin, also known as Adriamycin (H); vincristine, also known as Oncovin (O); and prednisone (P).

Please see full Prescribing Information, as well as additional Important Safety Information throughout this brochure.

Additional Resources and Support

Questions for your care team (cont'd)

Where can I find information about support to help me pay for my POLIVY plus R-CHP treatments?

How will you monitor my response to treatment?

What can I do to improve my overall treatment experience and reduce side effects?

Can you recommend a mental health professional who I can see if I start to feel depressed, anxious, or distressed?

Who can I call for different questions or problems (reporting side effects, treatment questions, financial support, more information about DLBCL)?

You can use the space below to record any additional questions you may have for your healthcare team prior to your visit.

For a complete list of sample questions, visit POLIVY.com to download the Doctor Discussion Guide.

Please see full Prescribing Information, as well as additional Important Safety Information throughout this brochure.

Chemoimmunotherapy is a type of treatment that combines chemotherapy and **immunotherapy.**

Chemotherapy is a type of medicine that kills cells that grow and divide rapidly, including both cancer cells and normal cells.

Immunotherapy is a type of targeted treatment that helps your immune system recognize and fight cancer. It may also affect healthy cells.

Remission is the reduction in (partial) or disappearance of (complete) signs and symptoms of cancer in response to treatment.

Please see full Prescribing Information, as well as additional Important Safety Information throughout this brochure.

How Is POLIVY Designed to Work?

POLIVY® (polatuzumab vedotin-piiq) is a targeted treatment

POLIVY is designed to deliver the anticancer agent specifically to B cells, including cancerous B cells.

POLIVY is a type of targeted treatment made up of an antibody attached to an active anticancer agent (also known as an antibody-drug conjugate). Although POLIVY is designed to find and kill dividing B cells, it may also affect some healthy cells in your body.

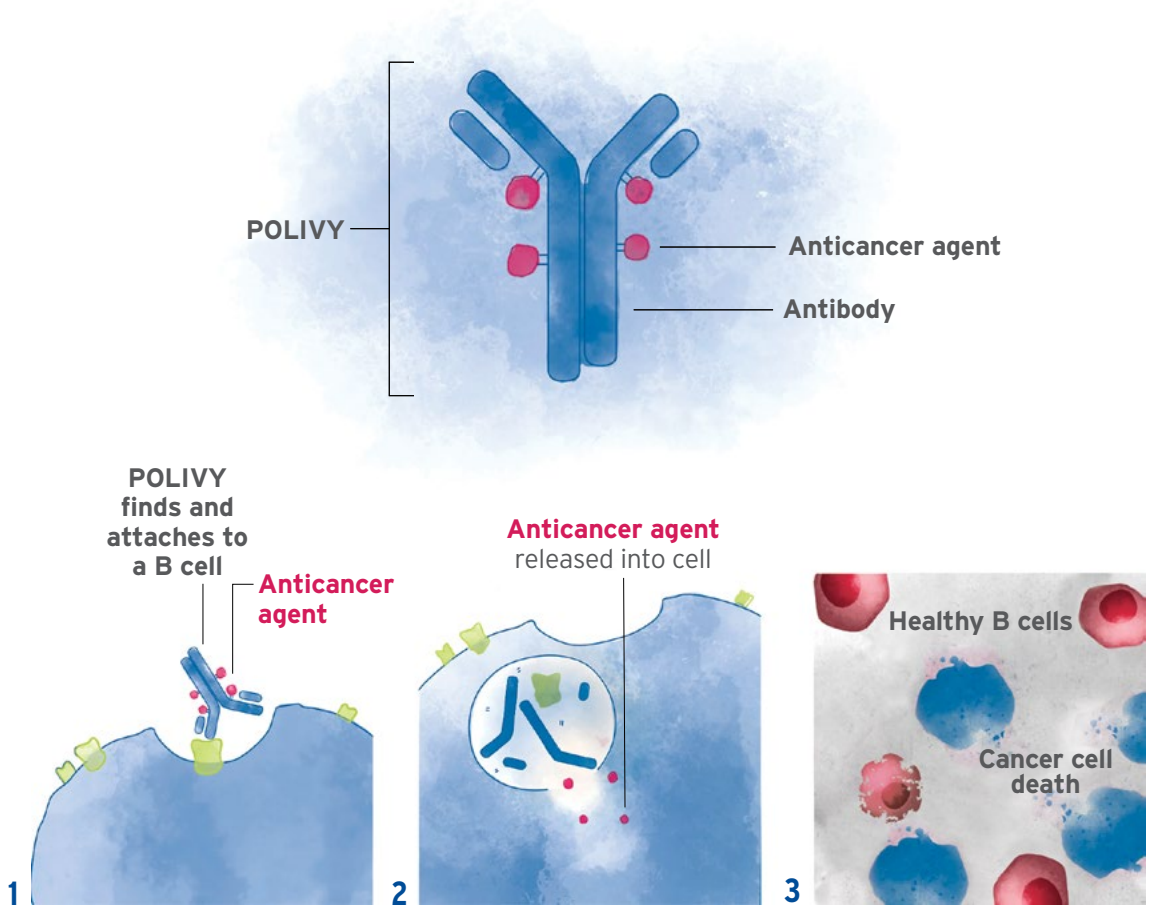


Illustration of how POLIVY works in the body.

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.**

Please see full Prescribing Information, as well as additional Important Safety Information throughout this brochure.

How Is POLIVY Designed to Work?

Why have I been prescribed POLIVY plus R-CHP?

POLIVY is part of an FDA-approved treatment regimen for adults with certain types of newly diagnosed DLBCL. In addition to POLIVY, this regimen contains **4 other medicines**: a rituximab product (R); cyclophosphamide (C); doxorubicin (H); and prednisone (P).

What does R-CHP do?

R-CHP also helps fight cancer. These medicines may also affect healthy cells.

Rituximab product (R) is an immunotherapy that works differently than POLIVY. It is designed to identify B cells (including cancerous B cells) and either destroys these cells on its own or helps the immune system to destroy them.

Cyclophosphamide (C) and **doxorubicin (H)** are chemotherapy treatments that are designed to kill fast-growing cells in your body, including cancer cells.

Prednisone (P) is used in cancer treatment to reduce inflammation and lower the body's immune response. Prednisone is also used alone or with other drugs to prevent or treat certain conditions related to cancer.

The full treatment regimen is usually referred to as POLIVY plus R-CHP (pronounced "AR-chip").

Talk to your healthcare team about possible side effects. Please also see the accompanying full Prescribing Information for a complete list of possible side effects.

Important Safety Information (cont'd)

Possible serious side effects (cont'd)

- **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

Please see full Prescribing Information, as well as additional Important Safety Information throughout this brochure.

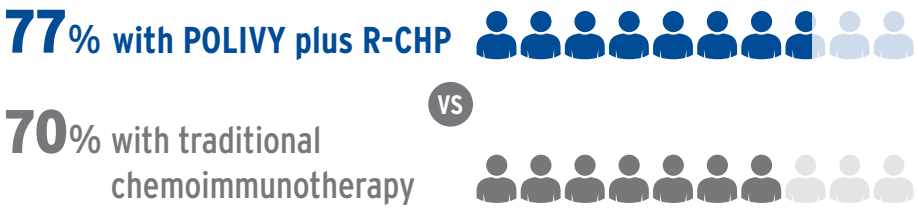
How Effective Is POLIVY Plus R-CHP?

POLIVY® (polatuzumab vedotin-piiq) plus R-CHP is clinically proven to be more effective than traditional chemoimmunotherapy (R-CHOP)

27% **POLIVY plus R-CHP reduced the risk of people's cancer worsening or returning by 27% compared with traditional chemoimmunotherapy.**

POLIVY plus R-CHP was compared with traditional chemoimmunotherapy in a large clinical trial of 879 people with newly diagnosed moderate to high risk large B-cell lymphoma (LBCL), including DLBCL, not otherwise specified (NOS), HGBL and other subtypes of DLBCL. In the study, 440 people were randomly assigned to treatment regimen with POLIVY plus R-CHP, and 439 to traditional chemoimmunotherapy.

Another analysis from the study measured the number of people who did not have their disease worsen or return at 2 years with POLIVY or traditional chemoimmunotherapy*:



*There are limitations with this 2-year data. The results are descriptive, which means that researchers looked at what happened in the clinical trial without determining a definitive benefit. Your experience may differ. Talk to your healthcare provider about how to best understand these results.

POLIVY plus R-CHP is the first FDA-approved treatment since 2006 to delay the worsening or returning of cancer in certain types of newly diagnosed DLBCL patients.

People treated with POLIVY plus R-CHP continued to be followed in the study to see how they did over a longer period of time. Talk to your healthcare provider to learn more about these long-term results.

Important Safety Information (cont'd)

Possible serious side effects (cont'd)

- **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

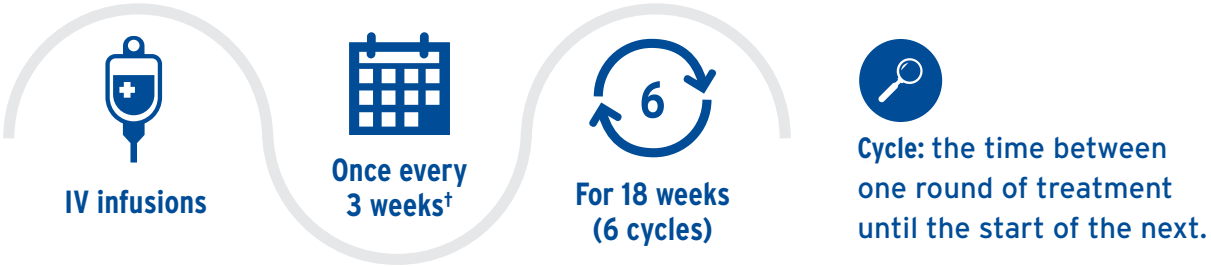
Please see full Prescribing Information, as well as additional Important Safety Information throughout this brochure.

How Is POLIVY Plus R-CHP Given?

Six cycles. Once every 3 weeks.

POLIVY plus R-CHP is prescribed by your healthcare provider and is usually given in a clinic or infusion center.

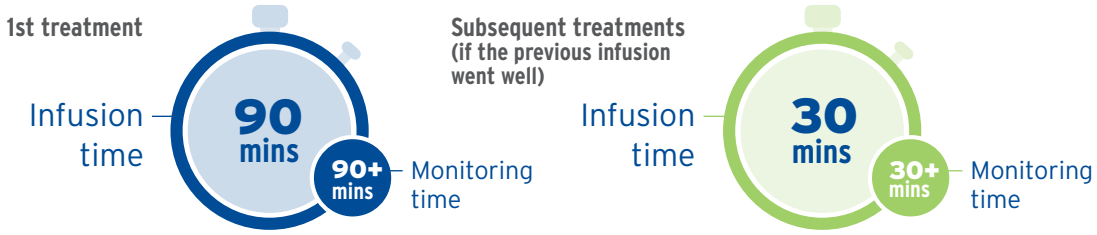
POLIVY is given as an intravenous (IV) infusion during the same treatment visit with R-CHP.



Your healthcare provider may have you take additional medicines ahead of time to prepare you for your infusions.

How long will each treatment cycle last?

POLIVY infusion times may vary from person to person, depending on response to treatment. A typical POLIVY infusion may follow this schedule‡:



Typically, you will have 21 days before the next treatment cycle begins. However, your healthcare team will decide how long you should wait between each cycle and how many cycles you need. Talk to your healthcare team about how you will receive POLIVY plus R-CHP.

†On days 1-5 of each cycle.

‡The infusion times for rituximab, cyclophosphamide, and doxorubicin vary by regimen. Prednisone tablets are given on days 1-5 of each treatment cycle.

Important Safety Information (cont'd)

Possible serious side effects (cont'd)

- **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

Please see full Prescribing Information, as well as additional Important Safety Information throughout this brochure.

Possible side effects of POLIVY® (polatuzumab vedotin-piiq) plus R-CHP

Serious side effects

Your healthcare team will closely monitor your response to the treatment for signs of serious side effects. These possible serious side effects are detailed in the Important Safety Information (on pages 14-15) and may include nerve problems in your arms and legs, infusion-related reactions, low blood cell counts, infections, rare and serious brain infections, tumor lysis syndrome, liver problems, infusion site injury, and potential harm to your unborn baby.

Common side effects

In the clinical trial, some of the most common side effects seen in patients who received POLIVY plus R-CHP were nerve problems in arms and legs, nausea, tiredness or lack of energy, diarrhea, constipation, hair loss, and 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.

Talk to your healthcare team. They are familiar with the possible side effects and can help you manage them.

These may not be all the side effects that you experience with POLIVY. Your healthcare team will help you identify and manage your side effects, so please be sure to inform them of any symptoms and take all necessary tests. More information on side effects can be found on *pages 14-15*.

Side Effects and Tips to Help Manage

To help you cope with some of the common side effects of your treatment, here are some tips you may try.

Nausea

Nausea is when you feel sick to the stomach.

- Relaxation techniques, such as focused breathing or visualization of a positive image or scene, can help
- Avoid foods that are greasy, fried, fatty, sweet, or spicy if you feel sick after eating them
- Try foods that do not have strong odors and cool them down before eating

Diarrhea

When you have diarrhea, your bowel movements are frequent (occurring 3 or more times a day) and are watery or loose.

- Stay hydrated by drinking plenty of water throughout the day to help replenish the fluids that you are losing. Try to drink water at room temperature
- Eat smaller, more frequent meals and snacks that are low in fiber
- Ask your healthcare team about medications that can help with diarrhea

Constipation

Constipation means difficulty having bowel movements.

- Drink plenty of water and eat high-fiber foods such as whole-grain bread and cereals, fruits and vegetables, and nuts and seeds
- Ask your healthcare team about exercises that may be right for you to keep active

Lack of energy

Lack of energy is the feeling of being tired or exhausted and may affect your ability to perform normal activities.

- Plan naps or rest breaks in your day and try to get around 7 to 8 hours of sleep every night
- Ask your care team about exercises you can safely do to help reduce stress and fatigue
- Participate in activities during the time of day when you have the most energy
- Do your most important tasks first

Hair loss

Also called alopecia, hair loss may happen on any part of the body. It may happen suddenly or a little at a time and may cause hair to become thin, dry, or dull.

- Use a mild shampoo, and try not to wash your hair every day
- Avoid perming, curling, straightening, or blow-drying with high heat
- Protect your scalp by applying a broad-spectrum sunscreen, or by covering your scalp with a sun protective hat or scarf when outside

Redness and sores of the lining of the mouth, lips, throat, and digestive tract

These symptoms are also known as mucositis.

- Pick foods that do not require much chewing
- Avoid foods that are spicy, acidic, dry, salty, or coarse
- Drink through a straw to avoid irritating your mouth sores
- Brush your teeth gently several times a day with a fluoride toothpaste. You may use an oral sponge on a stick instead of a toothbrush if your mouth sores are severe

Remember, the tips mentioned above may not work for everyone. Be sure to talk with your healthcare provider before trying any of these tips.

Please see full Prescribing Information, as well as additional Important Safety Information throughout this brochure.

Preparing for Treatment

Your healthcare team is your key partner and best source of information throughout your lymphoma treatment journey. Here are some of the activities the team will help you navigate, leading up to the first treatment:

Tests

Your healthcare team will order a series of tests to confirm that your body is ready for treatment. The tests may be repeated during treatment to ensure that it is safe to continue.

Pretreatment medicines

To help your body prepare for your cancer treatment, you are likely to receive pretreatment medications.

Financial and other support resources

Your healthcare team can help you identify financial support options for POLIVY® (polatuzumab vedotin-piiq). They can also identify organizations that may help support you through your journey.

If you are looking for sample questions to get the conversation started around treatment planning and expectations, please refer to pages 16-17.

To help you keep track of who is on your team and their contact details, please record your healthcare team details on pages 22-23.

POLIVY plus R-CHP may not be for everyone. Talk to your healthcare team if you are (or think you might be) pregnant, planning to become pregnant, or breastfeeding.

What are the signs and symptoms of infusion-related reactions?

Side effects called infusion-related reactions can occur during or within 24 hours after an infusion. Tell your healthcare provider immediately if you experience any side effects, including symptoms of an infusion-related reaction.

Infusion-related reactions may include:

- Fever
- Chills
- Rash
- Breathing problems
- Low blood pressure
- Hives

These may not be all the side effects you may experience with POLIVY. Your healthcare provider will help you identify and manage your side effects, so please be sure to inform your healthcare team of any symptoms and take all necessary tests. More information on side effects can be found on pages 14-15.

Tips to Prepare for Your Treatment

POLIVY plus R-CHP treatment cycles may be lengthy, especially the first one. Here are a few tips to help you plan ahead:

- ✓ Eat a light meal before your appointment to help avoid nausea (feeling sick) during or after your treatment. You may also want to bring along a snack in case you get hungry
- ✓ Drink plenty of water to keep hydrated for your appointment
- ✓ Wear comfortable, loose-fitting clothes for easier infusion access. A blanket may help keep you comfortable if the infusion center is chilly
- ✓ Keep yourself occupied with reading material or an audio device. Your care team may also allow you to bring a friend or family member along for support
- ✓ Arrange transport home prior to your appointment, as you may find it difficult to travel on your own
- ✓ Plan to rest after each treatment cycle, as you may be feeling tired

Indication and Important Safety Information

What does POLIVY® (polatuzumab vedotin-piiq) 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.

Please see full Prescribing Information, as well as additional Important Safety Information throughout this brochure.

Indication and Important Safety Information

Important Safety Information (cont'd)

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.

Questions for your care team

It's important to ask your healthcare provider any questions you may have about DLBCL and your treatment options. Writing down your questions in advance of your doctor's visits and keeping track of the answers can help you prepare for and make the most of your appointments.

Here are some questions to consider asking to help get you started.

What risk category is my DLBCL?

What are my treatment options and their risks and benefits?

What should the goal of my treatment plan be, and why?

How is POLIVY® (polatuzumab vedotin-piiq) plus R-CHP different from traditional chemoimmunotherapy?*

Is POLIVY plus R-CHP the right treatment choice for me?

Is there long-term data available for POLIVY plus R-CHP?

What can I expect during and after treatment with POLIVY plus R-CHP?

What can or should I bring with me to treatment?

Is there support if I cannot find a ride to treatment?

*Traditional chemoimmunotherapy refers to R-CHOP, which is an acronym for the following medicines: a rituximab product (R); cyclophosphamide (C); doxorubicin, also known as Adriamycin (H); vincristine, also known as Oncovin (O); and prednisone (P).

Please see full Prescribing Information, as well as additional Important Safety Information throughout this brochure.

Questions for your care team (cont'd)

Where can I find information about support to help me pay for my POLIVY plus R-CHP treatments?

How will you monitor my response to treatment?

What can I do to improve my overall treatment experience and reduce side effects?

Can you recommend a mental health professional who I can see if I start to feel depressed, anxious, or distressed?

Who can I call for different questions or problems (reporting side effects, treatment questions, financial support, more information about DLBCL)?

You can use the space below to record any additional questions you may have for your healthcare team prior to your visit.

For a complete list of sample questions, visit POLIVY.com to download the Doctor Discussion Guide.

Informational sites and support groups

Support groups, such as advocacy groups, work with patients, their caregivers, and their families to ensure they have access to the support and resources needed. You can learn more about cancer by calling or visiting the websites below:

Information and Patient-to-Patient Support

Lymphoma Research Foundation*
1-800-500-9976
www.lymphoma.org

Blood Cancer United*
1-800-955-4572
www.bloodcancerunited.org

American Cancer Society*
1-800-ACS-2345 (1-800-227-2345)
www.cancer.org

Cancer*Care*, Inc.*
1-800-813-Hope (1-800-813-4673)
www.cancercare.org

Cancer Hope Network*
1-877-HOPENET (1-877-467-3638)
www.cancerhopenetwork.org

Cancer Support Community
1-888-793-WELL (1-888-793-9355)
www.cancersupportcommunity.org

National Cancer Institute*
1-800-4-CANCER (1-800-422-6237)
www.cancer.gov

Patient Advocate Foundation
1-800-532-5274
www.patientadvocate.org

*Support available in English and Spanish.

Treatment Guidelines

National Comprehensive Cancer Network
215-690-0300
www.nccn.org/patients

Many of these groups have local chapters that can help you along your treatment journey and beyond. Your healthcare team may also recommend helpful local resources.

Genentech is neither affiliated with nor endorses any of these third-party organizations. Genentech does not make any representation or guarantee as to the accuracy of the information on sites not controlled by Genentech. These links are provided for informational purposes only.

Additional Resources and Support

Financial assistance options for people taking POLIVY® (polatuzumab vedotin-piiq)

We believe every person should get the Genentech medicine their doctor prescribed, and we offer programs to help make this happen.

Genentech Oncology Co-pay Assistance Program	Eligible patients[†] with commercial insurance[‡] could pay as little as $0 per treatment for POLIVY. The program may be able to assist with your co-pay or co-insurance up to $25,000 in assistance per calendar year.
Genentech Patient Foundation	If you don't have health insurance coverage or have financial concerns and meet eligibility criteria, you may be able to get free medicine from the Genentech Patient Foundation.[§]
Independent Co-pay Assistance Foundations	An independent co-pay assistance foundation is a charitable organization providing financial assistance to patients with specific disease states, regardless of treatment.[‖] Patients who are commercially or publicly insured, including those covered by Medicare and Medicaid, can contact the foundations directly to request assistance.

For help understanding health insurance coverage and costs, contact The Genentech Patient Support Team at (877) GENENTECH (436-3683) or visit POLIVY.com/Support to learn more.

[†]Eligibility criteria and benefit limits apply. Not valid for patients whose prescriptions are reimbursed under any federal or state government programs to pay for their Genentech medicine. Patients must be taking the Genentech medicine for an FDA-approved indication. Please visit the Co-pay Program website for full list of Terms and Conditions.

[‡]This might be a plan you get through your employer or one you purchased through a Health Insurance Marketplace.

[§]If you have health insurance, you should try to get other types of financial assistance, if available. You also need to meet income requirements. If you do not have insurance or if your insurance does not cover your Genentech medicine, you must meet a different set of income requirements. Genentech reserves the right to modify or discontinue the program at any time and to verify the accuracy of information submitted.

[‖]Independent co-pay assistance foundations have their own rules for eligibility. Genentech has no involvement or influence in independent foundation decision-making or eligibility criteria and does not know if a foundation will be able to help you. We can only refer you to a foundation that supports your disease state. Genentech does not endorse or show preference for any particular foundation. The foundations we refer you to may not be the only ones that might be able to help you.

Please see full Prescribing Information, as well as additional Important Safety Information throughout this brochure.

Your care team

It's often more than just your primary care physician and your cancer doctor (oncologist).

While you were most likely diagnosed by a primary care physician or an oncologist, other healthcare providers may be involved at different stages in your journey. You may also hear your care team being called your "cancer care team" or a "multidisciplinary team."
You may not see all these individuals, but they may be a part of your journey.

Primary care physician

The doctor who you see at regular checkups and who you call first when you feel ill. They refer you to specialists, if needed.

Oncologist

Also known as the hematologic oncologist (or heme-onc), a doctor who specializes in diagnosing and treating blood cancers and may lead your care team by working closely with all the other healthcare providers.

Pathologist

Works directly with your oncologist and helps determine the results of your diagnostic tests. They play an important role in figuring out the type and severity of the cancer.

Nurse

Healthcare professionals with whom you might have the most interaction during your treatment. Nurses help you talk to your doctor so you can make informed decisions, and they may help you set up appointments or medical tests.

Case manager

A professional who guides you through the healthcare system. They may assist you with financial, social, legal, or insurance-related aspects of your healthcare needs.

Your care team (cont'd)

Infusion center staff

A multidisciplinary group of healthcare professionals that provides supportive and palliative care during your treatment cycles.

Pharmacist

Fills prescriptions, addresses questions about how to take medicine, and advises you about any necessary precautions.

Nutritionist

Helps you find ways to eat and hydrate appropriately and maintain your health during and after your cancer treatment.

Social worker

Assists with the emotional and social aspects of dealing with cancer and can connect you with community, support services, and other resources to help you cope with difficult transitions.

Psychologist/therapist/counselor

Coaches you on ways to talk about your feelings and cope with them in order to better handle stress and anxiety.

Home health aide

A licensed professional who provides personal care to people at home and can help with bathing, dressing, and other daily chores.

It may be hard at first to keep track of your healthcare team. You may want to use the next page to write down the names and contact information of some of your care team members.

Your care team (cont'd)

Fill in the section below to keep the names and contact details of your healthcare team handy.

Hospital/clinic/contact details:

Hematology ward:

Business hours helpline:

_____

Out-of-office hours helpline:

_____

Patient support line:

Name: _____

Phone: _____

Email: _____

My primary care physician:

Name: _____

Phone: _____

Email: _____

My hematologist/oncologist:

Name: _____

Phone: _____

Email: _____

My nurse:

Name: _____

Phone: _____

Email: _____

My infusion center:

Name: _____

Phone: _____

Email: _____

My pharmacy/pharmacist:

Name: _____

Phone: _____

Email: _____

My nutritionist:

Name: _____

Phone: _____

Email: _____

My social worker:

Name: _____

Phone: _____

Email: _____

My psychologist/therapist/counselor:

Name: _____

Phone: _____

Email: _____

Your care team (cont'd)

My case manager:

Name: _____

Phone: _____

Email: _____

My home health aide:

Name: _____

Phone: _____

Email: _____

Emergency contact (for your side effects management):

Name: _____

Phone: _____

Email: _____

Emergency contact (caretaker/family member/friend):

Name: _____

Phone: _____

Email: _____

Glossary

Antibody: A special protein made by the immune system (B cells) to help protect from harmful invaders like viruses or bacteria.

Antibody-drug conjugate (ADC): A manufactured drug containing an antibody attached to an active anticancer agent. The ADC attaches to and enters targeted cells and kills them without harming other cells in the body.

B cell: A type of white blood cell in your immune system that helps protect your body from infection and disease.

Chemoimmunotherapy: A type of treatment regimen that combines chemotherapy and immunotherapy.

Chemotherapy: A type of medicine that kills cells that grow and divide rapidly, including both cancer cells and normal cells.

Cycle: The time between one round of treatment until the start of the next.

Diffuse large B-cell lymphoma (DLBCL): A type of aggressive blood cancer that affects B cells. It is the most common form of non-Hodgkin's lymphoma. DLBCL, **not otherwise specified (NOS)**, refers to a form of DLBCL that cannot be categorized into a more specific subtype.

Immunotherapy: A type of targeted treatment that helps your immune system recognize and fight cancer. It may also affect healthy cells.

Non-Hodgkin lymphoma: A diverse group of blood cancers that affect different types of white blood cells. B cells are the most common type, and the most common subtype is DLBCL.

R-CHP: R-CHP (pronounced "AR-chip") is an acronym that represents the following medicines: a rituximab product (R); cyclophosphamide (C); doxorubicin, also known as Adriamycin (H); and prednisone (P). In addition to POLIVY® (polatuzumab vedotin-piiq), R-CHP also helps fight cancer.

R-CHOP: R-CHOP is an acronym for the following medicines: a rituximab product (R); cyclophosphamide (C); doxorubicin, also known as Adriamycin (H); vincristine, also known as Oncovin (O); and prednisone (P). R-CHOP is the traditional chemoimmunotherapy regimen that has been historically used in the treatment of newly diagnosed DLBCL.

Remission: The reduction in (partial) or disappearance of (complete) signs and symptoms of cancer in response to treatment.

Notes:

Find frequently asked questions and additional up-to-date information at POLIVY.com.

Please see full Prescribing Information, as well as additional Important Safety Information throughout this brochure.

The Patient Resource Center is here to guide you and your care partner to the right resources

To speak with a representative,
call **(877) GENENTECH (436-3683)**
Monday-Friday, 6 AM-5 PM PST

Learn more at **www.POLIVY.com**

Please see full Prescribing Information, as well as additional Important Safety Information throughout this brochure.

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

M-US-00017874(v2.0) 04/26

Genentech
A Member of the Roche Group

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)	3/2026
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: 3/2026

FULL PRESCRIBING INFORMATION: CONTENTS*

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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 Sterile Water for Injection, USP, using the volume provided in Table 4, into the POLIVY vial, with the stream directed 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 Sterile Water for Injection, USP 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 refrigerated at 2°C to 8°C (36°F to 46°F) for up to 48 hours or at room temperature (9°C to 25°C, 47°F to 77°F) up to a maximum of 8 hours prior to dilution. Discard vial when cumulative storage time prior to dilution exceeds 48 hours.

Dilution

- Dilute polatuzumab vedotin-piiq to a final concentration of 0.72–2.7 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 as specified in Table 5. Discard if storage time exceeds these limits. *Do not freeze or expose to direct sunlight*.

Table 5 Diluted POLIVY Solution Storage Conditions

Diluent Used to Prepare Solution for Infusion	Diluted POLIVY Solution Storage Conditions[a]
0.9% Sodium Chloride Injection, USP	Up to 36 hours refrigerated at 2°C to 8°C (36°F to 46°F) or up to 4 hours at room temperature (9°C to 25°C, 47°F to 77°F)
0.45% Sodium Chloride Injection, USP	Up to 18 hours refrigerated at 2°C to 8°C (36°F to 46°F) or up to 4 hours at room temperature (9°C to 25°C, 47°F to 77°F)
5% Dextrose Injection, USP	Up to 36 hours refrigerated at 2°C to 8°C (36°F to 46°F) or up to 6 hours at room temperature (9°C to 25°C, 47°F to 77°F)

[a] To ensure product stability, do not exceed specified storage durations.

- Limit transportation to 30 minutes at 9°C to 25°C or 24 hours 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 5.
- 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 6 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 6 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 7 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 7 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 8. 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 8 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 9 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 9 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.

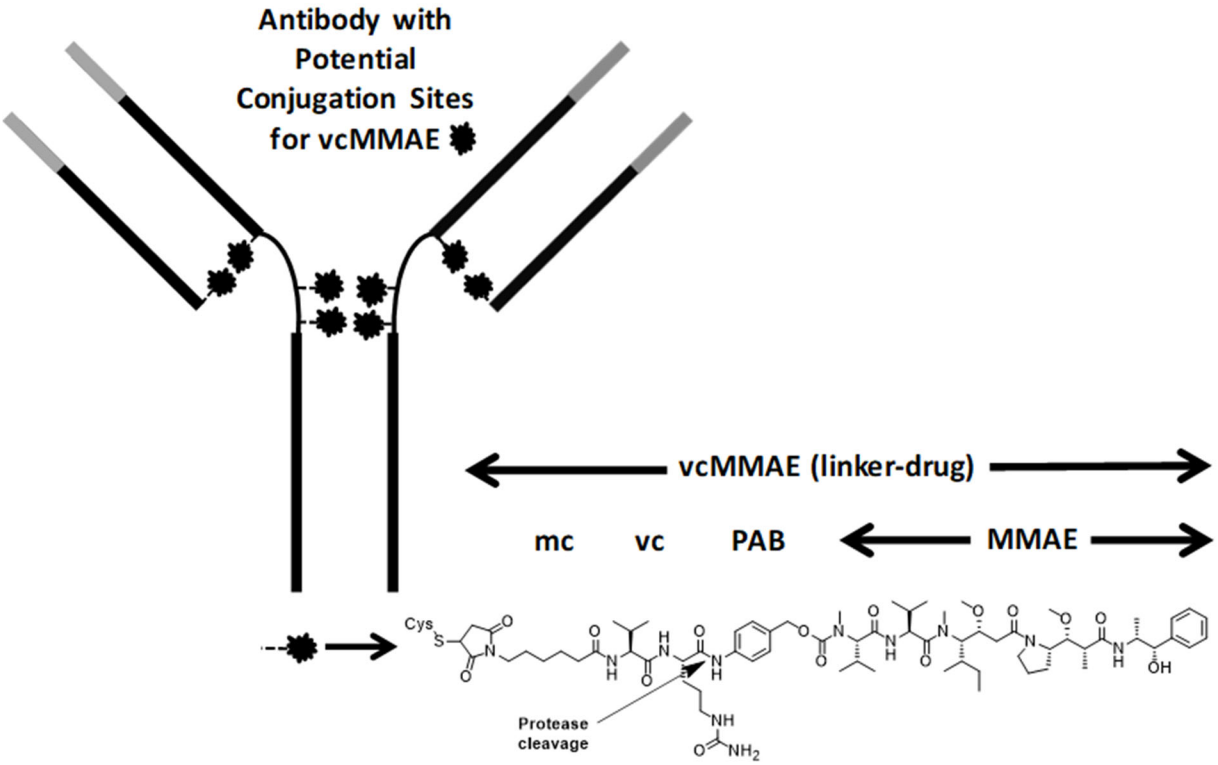
8.6 Hepatic Impairment

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 Sterile Water for Injection, USP, 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 (3.80 mg), succinic acid (8.27 mg), and sucrose (288 mg). After reconstitution with 7.2 mL of Sterile Water for Injection, USP, 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 10. 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 10 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.

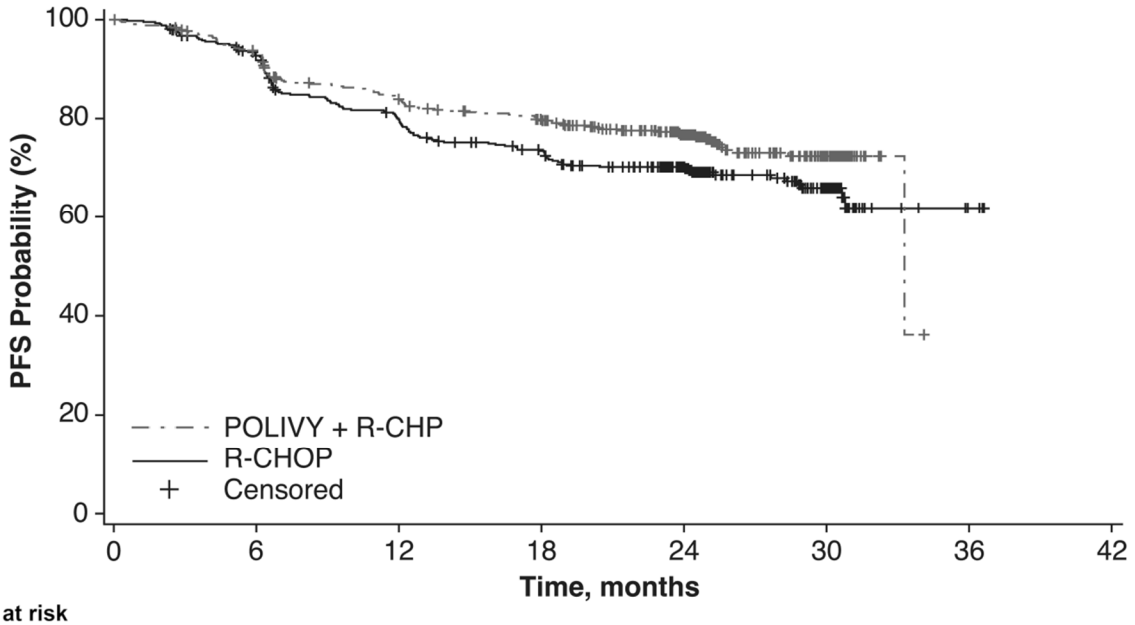
Efficacy was based on investigator-assessed progression-free survival (PFS). Other efficacy measures included modified event-free survival. Efficacy results are summarized in Table 11 and in Figure 1.

Table 11 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 12.

Table 12 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] (95% CI)	18 (45) (29, 62)	7 (18) (7, 33)
CR (95% CI)	16 (40) (25, 57)	7 (18) (7, 33)
Difference in CR rates, % (95% CI)[c]	22 (3, 41)	
Best Overall Response of CR or PR[d] (95% CI)	25 (63) (46, 77)	10 (25) (13, 41)
Best Response of CR (95% CI)	20 (50) (34, 66)	9 (23) (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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