POLIVY™
polatuzumab vedotin-piiq
INJECTION FOR INTRAVENOUS USE 140 MG

POLIVY + bendamustine + a rituximab product (BR)

Advance the possibilities in R/R DLBCL, NOS, after at least 2 prior therapies[1]

Granted accelerated approval. Additional studies are needed to establish clinical benefit.

NCCN GUIDELINES® PREFERRED TREATMENT (CATEGORY 2A)[2]

*NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) recommend polatuzumab vedotin-piiq (POLIVY) + bendamustine + rituximab (BR) as a preferred treatment option, after at least 2 prior therapies, for patients with relapsed or refractory diffuse large B-cell lymphoma who are not candidates for transplant (Category 2A).[2]**

CLICK HERE to learn more

*See the NCCN Guidelines for detailed recommendations. The National Comprehensive Cancer Network® (NCCN®) makes no warranties of any kind whatsoever regarding their content, use, or application and disclaims any responsibility for their application or use in any way.
R/R=relapsed or refractory; DLBCL=diffuse large B-cell lymphoma; NOS=not otherwise specified.

Indication

POLIVY in combination with bendamustine and a rituximab product is indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, after at least 2 prior therapies.

Accelerated approval was granted for this indication based on complete response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

Important Safety Information

Serious and sometimes fatal adverse reactions can occur with POLIVY treatment. Peripheral neuropathy, infusion-related reactions, myelosuppression, serious and opportunistic infections, progressive multifocal leukoencephalopathy (PML), tumor lysis syndrome, hepatotoxicity, and embryo-fetal toxicity can occur with POLIVY treatment.

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POLIVY+BR was studied in the first and only pivotal, randomized trial in R/R DLBCL vs BR[1]

Study GO29365: a randomized, phase II, open-label study in patients with R/R DLBCL (N=80)[1,3]

Patients with R/R DLBCL not candidates for HSCT
(N=80)

Randomized
1:1

POLIVY 1.8 mg/kg + BR
Every 21 days for 6 cycles (n=40)

BR
Every 21 days for 6 cycles (n=40)

Following premedication with an antihistamine and an antipyretic, POLIVY was given by intravenous (IV) infusion at 1.8 mg/kg on Day 2 of cycle 1 and on Day 1 of cycles 2 to 6.* Bendamustine was dosed at 90 mg/m^2 intravenously on Days 2 and 3 of cycle 1 and on Days 1 and 2 of cycles 2 to 6.

A rituximab product was administered at a dose of 375 mg/m^2 intravenously on Day 1 of cycles 1 to 6. Each cycle was 21 days in length.

The primary endpoint was CR at EOT as assessed by IRC.[1]

POLIVY+BR was studied in a broad range of patients with R/R DLBCL, including those who were primary refractory and/or double expressors[1,3]

Eighty patients were randomized to receive POLIVY+BR (n=40) or BR alone (n=40).

In the POLIVY+BR arm:
The median age was 67 years (range: 33-86 years) and 70% were male. Most patients (95%) had DLBCL, NOS, and 27.5% were double expressors (*MYC* and *BCL2* overexpression).† The primary reasons patients were not candidates for HSCT included age (32.5%), insufficient response to salvage therapy (30%), and prior transplant failure (25%). The median number of prior therapies was 2 (range: 1-7), with 27.5% receiving 1 prior therapy, 27.5% receiving 2 prior therapies, and 45% receiving 3 or more prior therapies. Seventy-five percent of patients had refractory disease to last therapy and 52.5% were primary refractory.[1,3]

In the BR arm:
The median age was 71 years (range: 30-84 years) and 62.5% were male. All patients (100%) had DLBCL, NOS, and 15% were double expressors (*MYC* and *BCL2* overexpression).† The primary reasons patients were not candidates for HSCT included age (47.5%), insufficient response to salvage therapy (22.5%), and prior transplant failure (15%). The median number of prior therapies was 2 (range: 1-5), with 30% receiving 1 prior therapy, 22.5% receiving 2 prior therapies, and 47.5% receiving 3 or more prior therapies. Eighty-five percent of patients had refractory disease to last therapy and 67.5% were primary refractory.[1,3]

*Dosing protocol in Study GO29365.
†Of patients tested for *MYC*/*BCL2* overexpression, POLIVY+BR had 11 patients with double-expressor lymphoma (DEL) and 12 patients with non-DEL; BR had 6 patients with DEL and 13 patients with non-DEL. Not all patients were assessed for DEL.
HSCT=hematopoietic stem cell transplantation; CR=complete response; EOT=end of treatment; IRC=independent review committee.
Please see full Prescribing Information and additional information in this brochure for recommended dosing schedule.

POLIVY is a first-in-class CD79b-directed antibody-drug conjugate engineered for targeted activity against dividing B cells[1,3]

Important Safety Information (cont'd)

Peripheral Neuropathy

POLIVY can cause severe peripheral neuropathy. Peripheral neuropathy occurs as early as the first cycle of treatment and is cumulative. POLIVY may exacerbate preexisting peripheral neuropathy.

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. The peripheral neuropathy was Grade 1 in 26% of cases, Grade 2 in 12%, and Grade 3 in 2.3%. Peripheral neuropathy resulted in POLIVY dose reduction in 3% 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 time to resolution 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.

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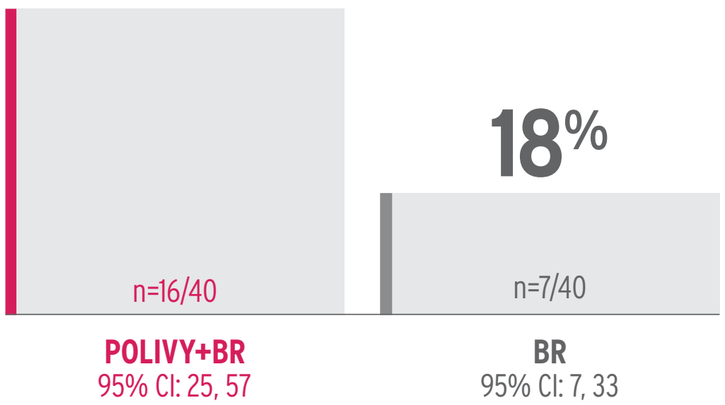
Twice the response and double the duration for POLIVY+BR vs BR[1]

Complete response at EOT*



Duration of response†

DoR calculated based on the 63% of patients who achieved a best overall response at any point in the study (n=25/40)

48% POLIVY+BR (n=12/25) DoR of at least 12 months

64% POLIVY+BR (n=16/25) DoR of at least 6 months

In the BR arm, 25% of patients achieved a best overall response at any time in the study, with 20% attaining a DoR ≥12 months and 30% attaining a DoR ≥6 months.

Objective response rate at EOT*

45% (95% CI: 29, 62; n=18/40) with POLIVY+BR vs 18% (95% CI: 7, 33; n=7/40) with BR

*EOT was defined as 6 to 8 weeks after Day 1 of cycle 6 or last study treatment. All endpoints were assessed by IRC.
†DoR was based on best overall response, which was defined as having a CR or PR at any time in the study.[4]
DoR=duration of response; PR=partial response.

Important Safety Information (cont'd)

Infusion-Related Reactions

POLIVY can cause severe infusion reactions. Delayed infusion-related reactions as late as 24 hours after receiving POLIVY have occurred. 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 67% of patients, Grade 2 in 25%, and Grade 3 in 8%. Symptoms included fever, chills, flushing, dyspnea, hypotension, facial swelling, and urticaria.

Administer an antihistamine and an 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.

Myelosuppression

Treatment with POLIVY can cause serious or severe myelosuppression, including neutropenia, thrombocytopenia, and anemia. In patients treated with POLIVY plus bendamustine and a rituximab product (BR) (n=45), 42% received primary prophylaxis with granulocyte colony-stimulating factor. Grade 3 or higher hematologic adverse reactions included neutropenia (42%), thrombocytopenia (40%), anemia (24%), lymphopenia (13%), and febrile neutropenia (11%). 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. Consider prophylactic granulocyte colony-stimulating factor administration.

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.

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POLIVY offers a predictable safety profile[1]

Select Grade 3 or higher adverse reactions in both study arms

The safety of POLIVY+BR (n=45) is based on the safety run-in stage of the trial (n=6) and the randomized cohort (n=39) comparing treatment with BR alone (n=39) in patients with R/R DLBCL.

The types of adverse events reported in Study GO29365 were consistent compared to control.

Adverse Reaction by Body System	POLIVY+BR (n=45)	BR (n=39)
Blood and lymphatic system disorders		
Neutropenia	**42%**	**36%**
Thrombocytopenia	**40%**	**26%**
Anemia	**24%**	**18%**
Lymphopenia	**13%**	**8%**
Nervous system disorders		
Peripheral neuropathy	**0%**	**0%**
Gastrointestinal disorders		
Diarrhea	**4.4%**	**5%**
Vomiting	**2.2%**	**0%**

Adverse Reaction by Body System	POLIVY+BR (n=45)	BR (n=39)
General disorders		
Infusion-related reaction	**2.2%**	**0%**
Pyrexia	**2.2%**	**0%**
Decreased appetite	**2.2%**	**0%**
Infections		
Pneumonia	**16%***	**2.6%†**
Investigations		
Weight decreased	**2.2%**	**2.6%**
Metabolism and nutrition disorders		
Hypokalemia	**9%**	**2.6%**
Hypoalbuminemia	**2.2%**	**0%**
Hypocalcemia	**2.2%**	**0%**

The table includes a combination of grouped and ungrouped terms. Events were graded using NCI CTCAE version 4.[5]

*Includes 2 events with fatal outcome.
†Includes 1 event with fatal outcome.
NCI CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events.

The adverse drug reactions (all grades; >10% incidence and ≥5% more in the POLIVY+BR arm) occurring in patients with R/R DLBCL treated with POLIVY+BR or BR were neutropenia (49% vs 44%), thrombocytopenia (49% vs 33%), anemia (47% vs 28%), peripheral neuropathy (40% vs 8%), diarrhea (38% vs 28%), pyrexia (33% vs 23%), decreased appetite (27% vs 21%), pneumonia (22% vs 15%), vomiting (18% vs 13%), infusion-related reaction (18% vs 8%), weight decreased (16% vs 8%), hypokalemia (16% vs 10%), hypoalbuminemia (13% vs 8%), upper respiratory tract infection (13% vs 8%), dizziness (13% vs 8%), lymphopenia (13% vs 8%), and hypocalcemia (11% vs 5%).

- Fatal adverse reactions occurred in 7% in the POLIVY+BR arm 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+BR included pneumonia (16%), febrile neutropenia (11%), pyrexia (9%), and sepsis (7%)

Important Safety Information (cont'd)

Serious and Opportunistic Infections (cont'd)
Grade 3 or higher infections occurred in 32% (55/173) of patients treated with POLIVY. 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.

Progressive Multifocal Leukoencephalopathy (PML)
PML has been reported after treatment with POLIVY (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.

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POLIVY+BR has a fixed treatment duration of 6 cycles that can be administered in an outpatient setting, such as an infusion center[1]

Recommended dosing schedule for POLIVY*

Day 1
POLIVY
1.8 mg/kg IV
Bendamustine
90 mg/m² IV
Rituximab product
375 mg/m² IV

Day 2
Bendamustine
90 mg/m² IV

Wait 3 weeks
between infusions

Repeat
for a total of
6 cycles

*See additional dosing information below.

POLIVY, bendamustine, and a rituximab product can be administered in any order on Day 1 of each cycle. Dilute POLIVY to a final concentration of 0.72 to 2.7 mg/mL in an IV 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.

Start treatment quickly with a predictable treatment course. POLIVY is ready for infusion for adult patients with R/R DLBCL, NOS, after at least 2 prior therapies. Learn more at POLIVY.com/hcp/dosing

Administration requirements

- Do not mix POLIVY with or administer through the same infusion line as other medicinal products
- If a planned dose of POLIVY is missed, administer as soon as possible. Adjust schedule of administration to maintain a 21-day interval between doses
- See full Prescribing Information for complete dosing and administration requirements
- See full Prescribing Information for bendamustine and a rituximab product prior to initiation

Important Safety Information (cont'd)

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

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 in Study GO29365 (n=173), Grade 3 and 4 transaminase elevations of AST and/or ALT developed in 1.9% and 1.9%, respectively. Laboratory values suggestive of drug-induced liver injury (both an ALT or AST greater than 3 times upper limit of normal [ULN] and total bilirubin greater than 2 times ULN) occurred in 2.3% of patients.

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

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. When administered to rats, the small molecule component of POLIVY, monomethyl auristatin E, 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 at least 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 at least 5 months after the last dose.

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Resources for POLIVY

Click below for resources related to POLIVY

Dosing and Administration Guide

Comprehensive steps on how to administer POLIVY to eligible patients with R/R DLBCL.

Patient Financial Support

Financial assistance for eligible patients.

Expert Videos

In-depth promotional videos about POLIVY presented by clinical experts.

Reach a Representative

Genentech Representatives are available to you and can provide more information on POLIVY.

Visit POLIVY.com/hcp for more information on POLIVY and patient resources

Important Safety Information (cont'd)

The Most Common Adverse Reactions

The most common adverse reactions (≥20%) included neutropenia, thrombocytopenia, anemia, peripheral neuropathy, fatigue, diarrhea, pyrexia, decreased appetite, and pneumonia.

Lactation

Advise women not to breastfeed during treatment with POLIVY and for at least 2 months after the last dose.

You may report side effects to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Genentech at 1-888-835-2555.

References: 1. POLIVY Prescribing Information. South San Francisco, CA: Genentech, Inc.; June 2019. **2.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for B-Cell Lymphomas V.1.2020. © National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed January 27, 2020. To view the most recent and complete version of the guideline, go online to NCCN.org. **3.** Sehn LH, Herrera AF, Flowers CR, et al. Polatuzumab vedotin in relapsed or refractory diffuse large B-cell lymphoma. *J Clin Oncol*. 2020;38(2):155-165. **4.** Data on File. South San Francisco, CA: Genentech, Inc. 2018. **5.** National Cancer Institute. Common Terminology Criteria for Adverse Events (CTCAE) V4. 2009. https://evs.nci.nih.gov/ftp1/CTCAE/CTCAE_4.03/CTCAE_4.03_2010-06-14_QuickReference_5x7.pdf. Accessed March 23, 2020.

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Complete and durable response in R/R DLBCL, NOS, after at least 2 prior therapies[1]

Twice the response

CR rate at EOT*

40%
POLIVY+BR
(n=16/40)
95% CI: 25, 57

18%
BR
(n=7/40)
95% CI: 7, 33

Double the duration

Nearly half of patients who responded achieved a DoR ≥12 months. In patients achieving a best overall response (63%; n=25/40)

48%
DoR ≥12 months
(n=12/25)

64%
DoR ≥6 months
(n=16/25)

with POLIVY+BR†

In the BR arm, 25% of patients achieved a best overall response, with 20% (n=2/10) attaining a DoR ≥12 months and 30% (n=3/10) attaining a DoR ≥6 months.

Predictable safety profile

The types of adverse events observed and their management are consistent with those of a familiar rituximab product-containing regimen

Select Grade 3 or higher adverse reactions in both study arms (POLIVY+BR vs BR): neutropenia (42% vs 36%), thrombocytopenia (40% vs 26%), anemia (24% vs 18%), lymphopenia (13% vs 8%), peripheral neuropathy (0% vs 0%), diarrhea (4.4% vs 5%), vomiting (2.2% vs 0%), infusion-related reaction (2.2% vs 0%), pyrexia (2.2% vs 0%), decreased appetite (2.2% vs 0%), pneumonia‡ (16% vs 2.6%), weight decreased (2.2% vs 2.6%), hypokalemia (9% vs 2.6%), hypoalbuminemia (2.2% vs 0%), hypocalcemia (2.2% vs 0%).

*EOT was defined as 6 to 8 weeks after Day 1 of cycle 6 or last study treatment. All endpoints were assessed by IRC.
†DoR was based on best overall response, which was defined as having a CR or PR at any time in the study.[4]
‡Includes 2 events with fatal outcome in the POLIVY+BR study arm and 1 event with fatal outcome in the BR study arm.

Indication

POLIVY in combination with bendamustine and a rituximab product is indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, after at least 2 prior therapies.

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Please see the full Prescribing Information for additional Important Safety Information.

Genentech
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Learn more at POLIVY.com/hcp

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