RXADVANCE
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CLINICAL UPDATE

Brand Name	Polivy™
Generic Name	polatuzumab vedotin-piiq
Drug Manufacturer	Genentech, Inc.

Clinical Update

TYPE OF CLINICAL UPDATE

Clinical Update - New Strength

FDA APPROVAL DATE

June 10, 2019 (original); N/A (new strength)

LAUNCH DATE

N/A

REVIEW DESIGNATION

Review Priority N/A; Orphan

TYPE OF REVIEW

Type 5 - New Formulation or New Manufacturer

DISPENSING RESTRICTIONS

Specialty

Overview

INDICATION(S) FOR USE

Polivy™ is a CD79b-directed antibody–drug conjugate indicated in combination with bendamustine and a rituximab product for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma, not otherwise specified, after at least two 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.

MECHANISMS 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.

DOSAGE FORM(S) AND STRENGTH(S)

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

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DOSE & ADMINISTRATION

The recommended dose of Polivy™ is 1.8 mg/kg as an intravenous infusion over 90 minutes every 21 days for 6 cycles in combination with bendamustine and a rituximab product. Subsequent infusions may be administered over 30 minutes if the previous infusion is tolerated.

Premedicate with an antihistamine and antipyretic before Polivy™.

EFFICACY

Approval for Polivy™ was based on results from the Phase Ib/II GO29365 study (NCT02257567). Study GO29365 was an open-label, multi-center clinical trial that included a cohort of 80 patients with relapsed or refractory DLBCL after 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/m2 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/m2 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. 80% 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.

In the study, 40% of patients receiving the Polivy™ plus BR reached a CR, compared with 18% of patients in the BR-alone arm (P = .026). There was also an improvement in the exploratory endpoint of overall survival (OS), with a median OS of 12.4 months versus 4.7 months with BR alone (HR, 0.42; 95% CI, 0.24-0.75; P = .0023). Median DOR was 10.3 months with Polivy™ plus BR arm versus 4.1 months in the BR alone arm (HR, 0.44; 95% CI, 0.20-0.95; P =.0321). Of the people treated with Polivy™ plus BR who achieved a complete or partial response, 64 percent (n=16/25) had a duration of response (DOR) lasting at least six months as compared to 30 percent (n=3/10) of people treated with BR alone. Additionally, 48 percent (n=12/25) of people treated with Polivy™ plus BR had a DOR lasting at least a year, as compared to 20 percent (n=2/10) of people treated with BR alone.

The study also showed that 45 percent of people on Polivy™ plus BR achieved an objective response at the end of treatment (n=18/40; 95 percent CI: 29-62), compared to 18 percent of people treated with BR alone (n=7/40; 95 percent CI: 7-33).

Median follow-up was 37.6 months for the safety cohort, 27.0 months for the expansion cohort, and 22.3 months for the randomized comparison.

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RESPONSE RATES IN PATIENTS WITH RELAPSED OR REFRACTORY DLBCL		
Response per IRC, n (%)	**Polivy + BR N=40**	**BR N=40**
Objective Response at End of Treatment (95%, CI)	18 (45) (29.62)	7 (18) (7,33)
CR (95%, CI)	16 (40) (25, 57)	7 (18) (7,33)
Best Overall Response of CR or PR (95%, CI)	25 (63) (46, 77)	10 (25) (13, 41)
Best Response of CR (95%, CI)	20 (50) (34,66)	9 (23) (11, 38)