Retreatment with Polivy

This article responds to your request for information on Polivy® (polatuzumab vedotin) and retreatment. This response was developed according to the principles of evidence-based medicine and summarizes data from clinical trials and published medical literature.

Roche does not have any recommendations regarding retreatment with Polivy. Any decision on using Polivy for retreatment will be at the discretion of the treating physician taking into consideration individual risk-benefit.

In brief

Considerations for retreatment with Polivy:

- Dedicated clinical studies evaluating the risk-benefit balance of retreatment with Polivy have not been conducted.
- In a trial amongst patients with R/R aggressive LBCL, two patients were retreated with Polivy and mosunetuzumab. One patient experienced a CR and one a PR for six months before progression.
- In vitro, Polivy-resistant cells were used to assess the combinaed efficacy of Polivy and rituximab. The authors concluded that retreatment with this combination could be a therapeutic option for Polivy-resistant tumors.
- In a retrospective study amongst patients with R/R B-cell lymphomas, a patient receiving bridging therapy was retreated with five cycles of Polivy-BR after failure of CAR T-cell therapy. The patient achieved a PR, enabling them to undergo consolidative alloHCT.
- Polivy dosing beyond six cycles was permitted in phase 1 and 2 trials, but was capped to six or eight cycles in subsequent trials due to the cumulative nature of PN.
- A time-to-event analysis of Polivy-induced PN, suggested that capping Polivy treatment duration to six to eight cycles at doses of 1.8–2.4 mg/kg would result in PN incidences comparable to other antimicrotubule agents.

Abbreviations

alloHCT=allogeneic hematopoietic cell transplantation

CAR-T=chimeric antigen receptor T-cell

CDC=complement dependent cytotoxicity

CR=complete response

DLBCL=diffuse large B cell lymphoma

LBCL=large b cell lymphoma

MMAE=mono-methyl auristatin E

Polivy-BR=polatuzumab vedotin, bendamustine, and rituximab

PN=peripheral neuropathy

PR=partial response

R/R=relapsed/refractory

Experience from clinical trials

A phase 1b/2 trial evaluated mosunetuzumab in combination with Polivy in R/R aggressive LBCL.[1] Patients with an initial CR, who subsequently progressed, were permitted to receive retreatment with Polivy and mosunetuzumab. Two patients were retreated this way; one experienced another CR and one a PR. Both responses lasted more than six months before progression. Additionally, five patients were retreated with Polivy in combination with other anti-lymphoma therapies, however retreatment outcomes for these patients were not reported.

Experience from pre-clinical trials

In vitro, Polivy resistant cells were used to assess the combined efficacy of Polivy and rituximab.[2] Pretreatment with Polivy enhanced rituximab-induced CDC sensitivity in two Polivy-resistant cells with distinct mechanisms of resistance: increased MDR1 or decreased Bim expression. Combination treatment of Polivy with rituximab enhanced antitumor activity in STR-428-Pola-R xenografted mice. The authors concluded that retreatment with Polivy in combination with rituximab could be a therapeutic option in patients with Polivy-resistant tumors.

Published reports of retreatment with Polivy

A retrospective multicenter study evaluated Polivy as a salvage and bridging treatment in adults with R/R LBCL who had failed at least two lines of therapy.[3] A patient receving bridging therapy was retreated with Polivy after failure of CAR T-cell therapy. Patient initially received three cycles of Polivy-BR, achieved a PR, started CAR T-cell therapy but relapsed after two months. The patient was retreated with five cycles of Polivy-BR and achieved a PR again, enabling him to undergo consolidative alloHCT.

Retreatment considerations

In Phase 1 and 2 trials with Polivy in DLBCL, dosing of Polivy beyond six cycles was permitted.[4,5] However, ongoing and future trials are limited to six or eight Polivy cycles because of the

- apparent cumulative nature of peripheral neuropathy leading to study treatment discontinuation, and
- supportive exposure-response and time-to-event analysis.

A time-to-event analysis concluded that the risk of grade ≥2 PN increased with increasing exposure to antibody-conjugated MMAE and treatment duration.[6] The model-estimated PN incidence suggested that capping treatment duration to six to eight Polivy cycles at doses of 1.8–2.4 mg/kg would result in PN incidences comparable to other antimicrotubule agents.

References

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