NEW DRUGS

Aust Prescr 2020;43:218–9
https://doi.org/10.18773/austprescr.2020.069
First published 22 October 2020

Polatuzumab vedotin

Approved indication: B-cell lymphoma

Polivy (Roche)
vials containing 140 mg as powder for reconstitution

Diffuse large B-cell lymphoma is the most common type of non-Hodgkin lymphoma. It can be treated with a combination of rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone, but up to 40% of patients relapse or do not respond. They may then be considered for a stem cell transplant. For patients who are unable to have a transplant, polatuzumab vedotin adds to the options for treatment, such as gemcitabine, rituximab and bendamustine.

Polatuzumab vedotin is a combination of a monoclonal antibody and the cytotoxic drug monomethyl auristatin E (MMAE). The monoclonal antibody is aimed at a component of B-cell receptors called CD79b. This is found on the surface of normal and malignant B-cells. After the antibody binds to CD79b, the linkage with MMAE is cleaved and the cytotoxic drug is released inside the B-cell. MMAE has an antimitotic action and induces apoptosis. A similar combination, brentuximab vedotin, has been approved for Hodgkin lymphoma.

Polatuzumab vedotin has to be given intravenously. After it is reconstituted the drug is diluted and infused. The first infusion is given over 90 minutes. If this is well tolerated, subsequent infusions can be given over 30 minutes. Most of the MMAE in the circulation is conjugated to the antibody. This conjugated form has a half-life of about 12 days. The antibody is expected to be catabolised like other proteins with most of the dose probably being eliminated in the faeces. Unconjugated MMAE is a substrate for cytochrome P450 3A4 so inhibitors and inducers of this enzyme could change the concentrations of MMAE. There are limited data about the effect of liver or kidney disease on the pharmacokinetics of polatuzumab vedotin.

There is also limited information about the effectiveness of polatuzumab vedotin in relapsed or refractory diffuse large B-cell lymphoma. The main study of patients who were ineligible for a transplant was an open-label, phase II trial of 80 people.[1] Forty patients were randomised to treatment with polatuzumab vedotin plus bendamustine and rituximab, while the other 40 received bendamustine and rituximab. The polatuzumab vedotin regimen was an infusion every 21 days for up to six cycles. Positron emission tomography identified a complete response in 16 patients compared with seven patients who responded to bendamustine and rituximab. After a median follow-up of 22.3 months, the progression-free survival for the three-drug regimen was 9.5 months versus 3.7 months for bendamustine and rituximab. Adding polatuzumab vedotin reduced the risk of death – median overall survival was 12.4 months compared with 4.7 months for bendamustine and rituximab.[1]

As CD79b is not limited to cancer cells, adding polatuzumab vedotin to bendamustine and rituximab increases toxicity. Myelosuppression is very common and may require treatment to be reduced or stopped. Patients can develop febrile neutropenia, and infections, such as pneumonia, are very common. These infections may be fatal. Peripheral neuropathy is a frequent adverse effect possibly because of the action of unconjugated MMAE in the circulation. This can be another reason to reduce or stop treatment.

Other adverse events that are more frequent when polatuzumab vedotin is added to bendamustine and rituximab include diarrhoea, fever, reduced appetite, hypokalaemia, hypoalbuminaemia and hypocalcaemia. In addition to monitoring the patient's blood count, liver function should be checked as there is a risk of hepatotoxicity. Approximately one third of patients will have an infusion-related reaction. Every patient should be given an antihistamine and an antipyretic before each infusion.

The median survival for patients who have refractory disease or have relapsed and cannot have a stem cell transplant is approximately six months. On the evidence available survival is improved if polatuzumab vedotin is added to bendamustine and rituximab. However, this needs to be confirmed in a larger trial. There have been concerns that the 40 patients given polatuzumab vedotin in the phase II trial had more favourable prognostic factors at baseline than patients in the other group. Treatment will inevitably include managing the serious adverse effects. In the phase II trial 33% of the patients discontinued treatment because of adverse events, compared with 10% of those treated with bendamustine and rituximab. The adverse events were fatal for approximately 23% of the patients taking polatuzumab vedotin with bendamustine and rituximab versus 28% of those taking bendamustine and rituximab.[1]

T manufacturer provided the product information

The new drug commentaries in *Australian Prescriber* are prepared by the Editorial Executive Committee. Some of the views expressed on newly approved products should be regarded as preliminary, as there may be limited published data at the time of publication, and little experience in Australia of their safety or efficacy. However, the Editorial Executive Committee believes that comments made in good faith at an early stage may still be of value. Before new drugs are prescribed, the Committee believes it is important that more detailed information is obtained from the manufacturer's approved product information, a drug information centre or some other appropriate source.

REFERENCES

1. Sehn LH, Herrera AF, Flowers CR, Kamdar MK, McMillan A, Hertzberg M, et al. Polatuzumab vedotin in relapsed or refractory diffuse large B-cell lymphoma. J Clin Oncol 2020;38:155-65. https://doi.org/10.1200/jco.19.00172

The Transparency Score is explained in New drugs: transparency, Vol 37 No 1, Aust Prescr 2014;37:27.

At the time the comment was prepared, information about this drug was available on the websites of the Food and Drug Administration in the USA, and the European Medicines Agency and the Therapeutic Goods Administration.

A:

ANSWERS TO SELF-TEST QUESTIONS

1 False 2 False

Correction

Prescribing medicinal cannabis [Correction]

Aust Prescr 2020;43:219
First published 9 October 2020
https://doi.org/10.18773/austprescr.2020.073

The Table in the medicinal cannabis article by Jonathon Arnold et al. (Aust Prescr 2020;43:152-9) has been amended to clarify Queensland's requirements for prescribing Schedule 8 medicinal cannabis products. View corrected article.

In the 'Documents required' section of the Table, the QLD State Health application cell should have read "No – unless a drug-dependent person" (not "Done simultaneously via TGA online portal").

EDITORIAL OFFICE

For general correspondence such as Letters to the Editor, contact the Editor.

Postal The Editor
Australian Prescriber
GPO Box 266
Canberra, ACT 2600

Telephone +61 2 8217 8700

Email info@australianprescriber.com

Website nps.org.au/australian-prescriber

Twitter @AustPrescriber