Pralatrexate

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Approved indication: lymphoma

Folotyn (Mundipharma)
vials containing 20 mg/mL
Australian Medicines Handbook section 14.1.3, Antimetabolites

One of the less frequent forms of lymphoma is peripheral T-cell lymphoma. Patients often present with advanced disease and have a poor prognosis even after stem-cell transplantation. As the cancer may be resistant to chemotherapy, there is a need for new treatments.

Pralatrexate is an analogue of the antifolate drug methotrexate. It inhibits the enzyme dihydrofolate reductase. The resulting depletion of folate disrupts DNA synthesis leading to the death of tumour cells.

Unlike methotrexate, pralatrexate has to be given by intravenous infusion over 3–5 minutes. The drug has a half-life of 12–18 hours with 31% being excreted unchanged in the urine. There is uncertainty about how the rest of a dose is eliminated, but pralatrexate is not thought to be metabolised by the cytochrome P450 system. Renal and hepatic function should be monitored during treatment. Caution is advised if the estimated glomerular filtration rate is below 60 mL/min and pralatrexate should not be used in patients with end-stage kidney disease.

Clinical trial data are limited. The main trial was open-label, non-randomised and uncontrolled. This trial enrolled 115 patients with peripheral T-cell lymphoma that had progressed despite at least one previous treatment. They were given weekly infusions for six weeks followed by one week of rest before the cycle was repeated. The median duration of treatment was 70 days. Based on clinical findings and imaging, the overall response rate (in 109 evaluable patients) was 29%. Only 11% achieved a complete response. Progression-free survival was 3.5 months with an overall survival of 14.5 months.[1]

Antifolate drugs can cause frequent and serious adverse effects. In the trial 23% of the patients stopped treatment because of adverse effects, others had to reduce their dose. Common adverse effects included mucositis, altered liver function, thrombocytopenia, anaemia, fever, neutropenia and epistaxis.[1] Full blood counts should be measured weekly. There is a potential for serious skin reactions which may be fatal.

Although some patients will respond to pralatrexate, its efficacy is uncertain as it was not directly compared with any other treatment or placebo. The outcomes may be better, but come with the risk of potentially fatal toxicity. There is a need to research whether pralatrexate could be combined with other drugs. At present its indication is limited to treating patients with peripheral T-cell lymphoma after other therapy has failed.

T T manufacturer provided additional useful information

REFERENCES

1. O'Connor OA, Pro B, Pinter-Brown L, Bartlett N, Popplewell L, Coiffier B, et al. Pralatrexate in patients with relapsed or refractory peripheral T-cell lymphoma: results from the pivotal PROPEL study. J Clin Oncol 2011;29:1182-9. https://doi.org/10.1200/JCO.2010.29.9024

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.