also be monitored as life-threatening anaemia has been reported.[7]

Routine monitoring of liver function is recommended and the patient's lipid concentrations will also need to be measured as tofacitinib increases cholesterol concentrations. Although the relationship to tofacitinib is unclear, serious adverse events have included gastrointestinal perforation, interstitial lung disease, lymphoma and skin cancer.

Tofacitinib should not be used in pregnancy or lactation, or by women trying to conceive. It does not affect the pharmacokinetics of combined oral contraceptive pills.

While tofacitinib produces a 20% improvement in ACR criteria for some patients, there is less evidence about its effect on the long-term progression of rheumatoid arthritis. The potential advantages of tofacitinib have to be balanced against the risk of possibly fatal adverse reactions. Whether the risk of harm is greater than with other biological drugs is currently unclear. The combination of tofacitinib with other biological or immunosuppressive drugs is contraindicated. Longer term study will be needed to establish the place of tofacitinib in the treatment of rheumatoid arthritis. It will probably be reserved for specialist use in patients with arthritis that has not responded to other disease-modifying drugs.

T manufacturer provided the AusPAR and the product information

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Vedolizumab

Approved indication: inflammatory bowel disease
Entyvio (Takeda)
vials containing 300 mg powder for reconstitution
Australian Medicines Handbook section 12.6

In Crohn's disease and ulcerative colitis there is an influx of inflammatory cells into the gut. Conventional treatments, such as corticosteroids, aim to reduce this inflammation. The development of biological drugs such as adalimumab and infliximab has increased the options for managing inflammatory bowel disease that has not responded to conventional treatment. Vedolizumab is a monoclonal antibody that binds to a human integrin. It reduces inflammation by inhibiting the adhesion of T lymphocytes to gastrointestinal tissues.

Vedolizumab is given by intravenous infusion. An induction regimen is followed by infusions every eight weeks. The half-life of the antibody is approximately 25 days, but how it is eliminated is uncertain. No studies have been carried out in people with renal or hepatic impairment. There have also been no studies of drug interactions.

The main trial of vedolizumab in ulcerative colitis investigated induction and maintenance therapy in patients whose previous treatments had been unsuccessful. In a double-blind part of the trial, 225 patients were randomised to vedolizumab and 149 to placebo. A second cohort included 521 patients who were given open-label vedolizumab. Induction infusions were given two weeks apart. Patients from either cohort who showed a response to vedolizumab after six weeks were randomised to receive further infusions of vedolizumab every four weeks or eight weeks, or placebo, for up to one year.

In the first cohort, after six weeks, 47.1% of the vedolizumab group and 25.5% of the placebo group had a clinical response. In the second, open-label cohort there was a response in 44.3% of patients. After a year, 41.8% (51/122) of the patients treated every eight weeks and 44.8% (56/125) of those treated every four weeks were in clinical remission. Only 15.9% (20/126) of the placebo group went into remission. Sigmoidoscopy showed mucosal healing in 19.8% of the placebo group, 51.6% of the eight-weekly group and 56% of the four-weekly vedolizumab group.[1]

The main trial of vedolizumab in Crohn's disease had a similar design. It enrolled patients who had not tolerated or not responded to other drugs. One cohort compared vedolizumab and placebo while another took open-label vedolizumab for induction. Patients who responded to vedolizumab after six weeks were then randomised to continue receiving it every four or eight weeks, or to switch to placebo for up to a year.[2]

The response rates for the first cohort at six weeks were 25.7% (38/148) for placebo and 31.4% (69/220) for vedolizumab. In the open-label cohort 34.4% (257/747) had a clinical response. After 52 weeks of maintenance therapy 21.6% (33/153) of the placebo group were in remission. This was significantly less than the remission rate of 39% (60/154) with eight-weekly and 36.4% (56/154) with four-weekly vedolizumab.[2]

Another study in Crohn's disease tried to induce remission in 315 patients who had previously not responded to treatment with tumour necrosis factor (TNF) antagonists. There were also 101 patients in the trial who had not been treated with a TNF antagonist. The patients were infused with vedolizumab or placebo with repeat doses at two and six weeks. This induced remission in 13% of the placebo group and 28.7% of the vedolizumab group after 10 weeks. However, the primary efficacy end point was the remission rate in patients previously treated with TNF antagonists at six weeks. Only 15.2% of these patients achieved remission compared with 12.1% of the placebo group.

The incidence of adverse effects of vedolizumab was similar to the placebo group. Common events included nasopharyngitis, headache, arthralgia, nausea and fatigue.[1,2] Approximately 4% of the patients developed antibodies against vedolizumab. While 4% of the patients had infusion-related reactions, so did 3% of the placebo group. As the rate of infections is increased by vedolizumab, patients should be screened for infections such as tuberculosis before treatment. No cases of progressive multifocal leukoencephalopathy were reported in the trials. Little is known about the safety of vedolizumab in pregnancy and lactation.

Assessing the effectiveness of vedolizumab after six weeks may be too soon, especially in Crohn's disease. In the main trial the response rate at six weeks was not significantly greater than placebo, although the remission rates were (14.5% vs 6.8%).[2] It is therefore recommended to assess the patients 12–14 weeks after starting treatment. If there is no response by then, vedolizumab should be stopped. How long treatment can safely be continued in patients who do respond is currently unknown.

As the patients who are likely to be treated with vedolizumab will have moderate to severe inflammatory bowel disease, there is a need to compare vedolizumab with other biological therapies such as adalimumab and infliximab. Only a few patients with Crohn's disease will have a sustained remission with vedolizumab if they have not previously improved with a TNF antagonist.

[T][T] manufacturer provided additional useful information

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The Transparency score ([T]) is explained in 'New drugs: transparency', Aust Prescr 2014;37:27.

* At the time the comment was prepared, information about this drug was available on the website of the Food and Drug Administration in the USA (www.fda.gov).

† At the time the comment was prepared, a scientific discussion about this drug was available on the website of the European Medicines Agency (www.ema.europa.eu).

A At the time the comment was prepared, information about this drug was available on the website of the Therapeutic Goods Administration (www.tga.gov.au/industry/pm-auspar.htm).