NEW DRUGS

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Baricitinib

Approved indication: rheumatoid arthritis

Olumiant (Eli Lilly)
2 mg, 4 mg film-coated tablets
Australian Medicines Handbook section 15.1.2, Immunosuppressants

Methotrexate is the drug of choice for most patients with rheumatoid arthritis. However, in some patients, other drugs may be needed to control the disease. There is now a range of options, such as tumour necrosis factor (TNF)-alpha antagonists (e.g. adalimumab) and Janus kinase (JAK) inhibitors (e.g. tofacitinib).[1,2] Baricitinib is another JAK inhibitor that selectively inhibits the enzymes JAK1 and JAK2. As these enzymes are involved in the production of cytokines, inhibiting them has anti-inflammatory effects.[1]

The film-coated tablets are well absorbed. Although there is some metabolism by cytochrome P450 3A4, most of the drug is excreted unchanged in the urine. The half-life is 12.5 hours. Baricitinib is not recommended for patients with severe hepatic or renal impairment (glomerular filtration rate <30 mL/min/1.73 m^2). There are not thought to be any clinically significant pharmacokinetic drug interactions.

A phase II placebo-controlled trial studied baricitinib in daily doses of 1 mg, 2 mg, 4 mg or 8 mg. The 301 patients in this trial had moderate to severe rheumatoid arthritis despite treatment with methotrexate. The primary outcome of the study was the proportion of patients in the 4 mg and 8 mg groups who achieved a 20% response, on the American College of Rheumatology Index (ACR20), after 12 weeks of treatment. This outcome was achieved by 76% of the patients taking baricitinib and 41% of those taking placebo. The benefits of baricitinib were maintained after a further 12 weeks of treatment.[3]

The phase III RA-BEGIN trial studied baricitinib in patients who had not previously been treated with disease-modifying antirheumatic drugs (DMARDs). The 584 patients were randomised to take baricitinib 4 mg once daily, methotrexate weekly, or both drugs. When efficacy was assessed after 24 weeks of treatment, the response to baricitinib monotherapy was statistically superior to methotrexate. In the baricitinib group, 77% of the patients had an ACR20 response versus 62% in the methotrexate group. Combining the two drugs did not improve the response rate more than baricitinib alone. The response was maintained in patients who continued treatment for a total of 52 weeks.[4]

The RA-BUILD trial involved 684 patients who were intolerant of, or had an inadequate response to, at least one DMARD. They were randomised to receive baricitinib 2 mg, baricitinib 4 mg or a placebo for 24 weeks. When efficacy was evaluated after 12 weeks, an ACR20 response had been achieved by 66% of the patients taking 2 mg and 62% of those taking baricitinib 4 mg. These responses were significantly greater than the 39% seen in the placebo group. This advantage was sustained over the next 12 weeks of the trial. After 24 weeks there was radiological evidence of less disease progression in patients taking baricitinib.[5]

The option of using baricitinib instead of adalimumab to treat patients who have had an inadequate response to methotrexate was assessed in the RA-BEAM trial. A total of 1307 patients were randomised to take baricitinib 4 mg daily, adalimumab injections every two weeks, or a placebo. After 24 weeks the patients taking placebo were switched to baricitinib. Efficacy was assessed after 12 weeks, at which time there was an ACR20 response in 70% of the baricitinib group. This was statistically superior to the 61% who responded to adalimumab and the 40% response to placebo. After 52 weeks the ACR20 responses were 71% with baricitinib and 62% with adalimumab. Both drugs reduced radiological progression more than placebo.[6]

The RA-BEACON trial studied 527 patients who had discontinued treatment with, or had been unable to tolerate, TNF antagonists, other biological DMARDs or both. They were randomised to either add baricitinib (2 mg or 4 mg) or a placebo. After 12 weeks 55% of the baricitinib groups had an ACR20 response versus 27% of the placebo group. This advantage was still present after another 12 weeks of treatment. The difference between baricitinib 2 mg and placebo was not significant at 24 weeks for symptoms such as joint swelling and tenderness.[7]

Drugs that modulate the immune system are associated with an increased risk of infections. Patients should be screened for tuberculosis and viral hepatitis before treatment. Reactivation of herpes virus can lead to disseminated herpes zoster. Over 52 weeks, infections were more frequent with baricitinib than with adalimumab (48 vs 44%).[6] There is a possibility that the risk of malignancy could be increased. Baricitinib may also be associated with deep vein thrombosis.

Full blood counts, liver enzymes and lipids should be monitored during treatment. This is because patients can develop anaemia, neutropenia, liver injury and elevated lipids, and treatment may need to be suspended.

Baricitinib is approved for use in patients with moderate to severe arthritis who have had an inadequate response to other treatments. However, it can also be used earlier in treatment if the patient cannot tolerate other drugs. Although the recommended dose is 4 mg daily, a 2 mg dose may help some patients. It is not clear how baricitinib and tofacitinib compare. Tofacitinib appears to cause a reduction in lymphocyte counts more often than baricitinib.

Some of the patients in the clinical trials have continued in an extension study (RA-BEYOND). This should provide more information on the long-term safety and efficacy of baricitinib.

T T manufacturer provided additional useful information

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 European Medicines Agency and the Therapeutic Goods Administration.

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