Baricitinib (Olumiant) is a new oral janus kinase inhibitor licensed for the second-line treatment of moderate to severe active rheumatoid arthritis. This article summarises its efficacy, side-effects and place in therapy.

KEY POINTS

- Baricitinib is an oral janus kinase (JAK) inhibitor that is selective for JAK 1 and 2
- It is licensed as monotherapy or in combination with methotrexate for the treatment of moderate to severe active rheumatoid arthritis in adults who have responded inadequately to, or who are intolerant to, one or more DMARDs
- In placebo-controlled trials, baricitinib slowed disease progression and reduced disease activity, symptoms and disability in patients previously treated with conventional and/or biological DMARDs
- In one trial of combined therapy with methotrexate, it was more effective but less well tolerated than adalimumab
- A month’s treatment with baricitinib costs £805

NICE recommends a combination of conventional disease-modifying antirheumatic drugs (DMARDs), one of which should be methotrexate, for the initial treatment of active rheumatoid arthritis. If this is unsuccessful for patients with severe active rheumatoid arthritis, a biological DMARD such as a TNF inhibitor (adalimumab, certolizumab pegol, etanercept, golimumab, infliximab), an IL-6 inhibitor (tocilizumab) or T cell activation inhibitor (abatacept) is recommended in combination with methotrexate. Adalimumab, etanercept, certolizumab pegol or tocilizumab may also be prescribed as monotherapy for people unable to take methotrexate. If treatment with DMARDs including at least one TNF inhibitor fails, the anti-CD20 monoclonal antibody rituximab (or if this is unsuitable, an alternative biological agent) in combination with methotrexate may be tried.1-4

Baricitinib is a small-molecule janus kinase (JAK) inhibitor, a new class of therapy that inhibits intracellular signalling pathways for cytokines implicated in the pathogenesis of rheumatoid arthritis. It is selective for JAK1 and JAK2, with a weaker effect on JAK3. Unlike the biological therapies, which are given via subcutaneous or intravenous injection or infusion, baricitinib is administered orally.

Indications and dosage

Baricitinib is licensed as monotherapy or in combination with methotrexate for the treatment of moderate to severe active rheumatoid arthritis in adults who have responded inadequately to, or who are intolerant to, one or more DMARDs. Baricitinib is currently being appraised by NICE for the treatment of moderate to severe rheumatoid arthritis, with publication expected in September 2017.

The recommended dosage is 4mg orally once daily, with the possibility of tapering down to 2mg once daily if disease activity allows. A dosage of 2mg once daily is also recommended for patients aged ≥75 years (in whom clinical experience is limited); for patients with a history of chronic or recurrent infections; and for individuals with moderate renal impairment (creatinine clearance 30–60ml/min).

No dose adjustment is recommended for patients with mild or moderate hepatic impairment. Baricitinib is not recommended for patients with severe impairment of renal or hepatic function. Treatment should not be initiated in patients with an absolute lymphocyte count of <0.5 x 10^9 cells/L, an absolute neutrophil count <1 x 10^9 cells/L or haemoglobin <8g/dL.
Efficacy

Three phase 3 trials provide the key evidence for baricitinib: RA BEACON, RA BUILD, and RA BEAM. The primary endpoint was the American College of Rheumatology 20% response (ACR20, a 20% reduction in scores for joints, pain, patient and investigator assessments, and disability). A fourth trial, RA BEGIN, was conducted in patients with little or no prior treatment with DMARDs; they were not selected because a conventional DMARD was unsuitable and therefore they do not fall within the licensed indications.

In RA BEACON, 527 patients with an inadequate response to, or unacceptable side-effects associated with, TNF inhibitor drugs or other biological DMARDs were randomised to treatment with baricitinib 2 or 4mg daily or placebo in addition to established drugs (mostly methotrexate and corticosteroids). This was a heavily pretreated population, 42% of whom had been treated with one biological DMARD, 30% with two and 27% with three.

The ACR20 response rate at 12 weeks was 55% with baricitinib 4mg daily and 27% with placebo (p<0.001). This response was sustained at 24 weeks, supported by reductions in ACR50 and ACR70 (see Figure 1). Treatment history did not significantly affect response rates.

Subsequent analysis of patient-oriented outcomes at 24 weeks showed that baricitinib increased the proportion of patients with normal physical functioning and reduced fatigue, pain and duration of morning stiffness.

A total of 684 patients with an insufficient response or intolerance to a conventional DMARD but no prior treatment with a biological DMARD were randomised to treatment with baricitinib 2 or 4mg daily or placebo in RA BUILD. Most patients were taking methotrexate, alone or with a second DMARD.

The ACR20 response rate at week 12 was 62% with baricitinib 4mg daily and 39% with placebo (p<0.001); again this was associated with improvements in function and reduced disease activity. At 24 weeks, radiographic disease progression was significantly reduced with both doses of baricitinib compared with placebo.

In RA BEAM, 1307 patients with active rheumatoid arthritis despite treatment with methotrexate, but no prior treatment with a biological DMARD, were randomised to treatment with baricitinib 4mg daily, the TNF inhibitor adalimumab 40mg fortnightly or placebo. The ACR20 response rate at 12 weeks was significantly greater with baricitinib (70%) than adalimumab (61%) (p<0.014) or placebo (40%) (p<0.001). Baricitinib slowed disease progression compared with placebo at 24 weeks, and improved function and reduced disease activity and symptoms at 52 weeks more than adalimumab. However, baricitinib appeared to be less well tolerated than adalimumab; by one year, 7.4% of patients taking baricitinib had discontinued treatment compared with 3.9% taking adalimumab.

Adverse effects

In clinical trials, treatment with baricitinib plus methotrexate was associated with serious adverse events in 16% of DMARD-naïve patients, leading to an overall discontinuation rate of 11%.

The most common adverse events included upper respiratory tract infections (14.7%), hypercholesterolaemia (33.6%), nausea (2.8%, or 9.3% when combined with methotrexate in treatment naïve patients), thrombocytosis, and elevated alanine transaminase (ALT). The incidence of all infections was increased with baricitinib compared with placebo (101 vs 83 per 100 patient-years) and these included upper respiratory and urinary tract infection, herpes infection and gastroenteritis. Neutropenia was reported in 0.3% of patients.

References

4. National Institute for Health and Clinical Excellence. Adalimumab, etanercept, infliximab...

Declaration of interests
None to declare.

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