Baricitinib

We **recommend** baricitinib in AE patients, who are candidates for systemic treatment.	↑↑	100%  (15/15) Evidence and consensus based, see Evidence Report

baricitinib: in licence for adults;
dosage adults: 4 mg per day, reduction to 2 mg per day possible, depending on treatment response

Certainty of evidence[1, 2]:

Short term (8-16 weeks) vs placebo (NMA medications used in clinical practice or likely to be approved soon)

⊕⊕⊕⊕ HIGH for mean difference/ standardized mean difference **EASI, change in signs, POEM, peak pruritus NRS, DLQI, QoL, itch**

⊕⊕◯◯ LOW - ⊕◯◯◯ VERY LOW for undesirable effects

Mechanisms of action and efficacy

Baricitinib is an oral selective JAK1 and JAK2 inhibitor. The drug has been tested in one phase 2 and several phase 3 trials in adults with moderate-to-severe AE at 1mg, 2mg and 4mg once daily against placebo, showing significant improvement with regard to EASI from baseline to 16 weeks, in particular in the two higher doses (2 mg daily (mean difference, 5.6-point reduction; 95% CI, 0.4-10.9 [GRADE assessment: moderate certainty]) and 4 mg daily (mean difference, 5.2-point reduction; 95% CI, 0.1-10.4 [GRADE assessment: moderate certainty]).[3] Similar efficacy has been shown in these studies with regard to the IGA and itch scores. The concomitant use of topical corticosteroids was allowed in one trial.[4]

Dosage: acute flare, short term, long term

At present, Baricitinib data is available up to 52 weeks follow up[5], demonstrating sustained efficacy. There is no study that has looked at acute flare treatment and the paediatric study programme is still underway[6] and no clear dosing guidance for paediatric patients is currently available.

Safety

The most common side effects with baricitinib in clinical trials include an increase in LDL cholesterol, upper respiratory tract infections, and headache. Acne is less common than with other JAK inhibitors. Infections reported with baricitinib include herpes simplex. However, the rate of these events reported in a recent combined safety study including 2531 patients from 8 RCTs who were given baricitinib for 2247 patient-years (median duration 310 days) was overall low: eczema herpeticum (n = 11), cellulitis (n = 6) and pneumonia (n = 3). There were four opportunistic infections reported.[7] A transient increase of CPK may be seen, especially after extensive bodily exercise. No malignancies, gastrointestinal perforations, positively adjudicated cardiovascular events or tuberculosis were reported in the placebo-controlled period in baricitinib-treated patients. The frequency of herpes simplex was higher in the 4 mg group (6.1%) compared to the 2 mg (3.6%) and placebo groups (2.7%). Long-term safety

data beyond 16 weeks is available from an integrated data base covering mostly rheumatoid arthritis patients for up to 9.3 years of treatment.[8]

Monitoring

For baseline screening, the manufacturer advises that patients with suspected hepatitis B consult a liver specialist for advice before initiation of treatment. Lipid and liver profiles need to be regularly monitored following treatment initiation. Screening for any haematological abnormalities is also advised.

In practice, we recommend the same baseline screening and treatment monitoring investigations for all JAK inhibitors. For baseline screening this is a full blood count, renal, liver and lipid profile as well as creatinine phosphokinase levels and hepatitis and TB screen, including a chest radiograph.

For monitoring purposes, we recommend a full blood count, renal, liver and lipid profile as well as creatinine phosphokinase level at four weeks into treatment and then three-monthly while on therapy.

Combination with other treatments

No studies assessing the use of baricitinib with other systemic therapies in AE patients have been published to date, but the combination therapy with MTX is an established combination regimen in the management of rheumatoid arthritis.[9]

Special considerations

AE patients with concomitant inflammatory diseases, such as rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis are likely to experience benificial effects. Baricitinib is already licensed for this indication.

References

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