Biologic drugs for the treatment of psoriasis

**Overview:** Psoriasis is a skin condition in which skin cells reproduce too quickly, causing red, flaky, crusty patches with silvery scales. It affects about 2% of the UK population and is a chronic condition that often goes through cycles and can return at any time. There are several clinical variants of psoriasis, including plaque, guttate, erythrodermic and pustular. Plaque type is the most common form, accounting for 80% of cases. Psoriasis runs in families, although the exact role of genetics in the condition is unclear. The inflammatory processes of psoriasis are not fully understood but it is known that levels of tumour necrosis factor-alpha (TNF-alpha) are elevated in the skin of people with the condition.

**Current treatment:** There is no cure for psoriasis but several treatments are available to relieve symptoms, including creams and ointments, ultraviolet light (phototherapy) or oral and injected medication. Some biologic medications work by lowering levels of TNF-alpha, thus modifying the inflammatory processes.

NICE recommends the use of biologic drugs infliximab, adalimumab and etanercept when psoriasis is severe and has failed to respond to standard systemic therapies such as methotrexate.

There is accredited guidance on the diagnosis and management of psoriasis and psoriatic arthritis in adults from SIGN.

**New evidence:** Tumour necrosis factor (TNF-alpha) inhibitors are expensive drugs (£8,000-£10,000 a year), which have tended to be evaluated against placebo rather than active comparators.

A network meta-analysis was used to produce a quantitative comparison of all currently licensed biologics, providing estimates on comparative effectiveness and a suggested ranking of treatments (Reich et al. 2011).

Comparative effectiveness was estimated based on the reported response rates according to the percentage reduction in the Psoriasis Area and Severity Index (PASI), an assessment tool to record the severity of a patient's psoriasis.

Twenty trials involving patients with a mean disease duration of 18-22 years were included in the meta-analysis. The analysis suggests a ranking of treatments in terms of effectiveness, the highest being infliximab, followed by ustekinumab, adalimumab, etanercept and efalizumab.

In a separate study, Barker et al carried out an open-label, active-controlled, randomized trial to compare the efficacy and safety of infliximab with methotrexate, in patients with moderate-to-severe plaque psoriasis (Barker et al. 2011).

The primary efficacy endpoint was PASI75 response at week 16, which means that the person's PASI score dropped by 75% as a result of the psoriasis treatment. At week 16, patients with <PASI50 response could switch treatment groups.

The primary endpoint was achieved by a significantly greater proportion of infliximab patients (78%, 509/653) than methotrexate patients (42%, 90/215). Overall adverse event incidence was comparable.
between groups, but incidence of serious and severe adverse events was slightly higher in the infliximab group.

As this is the first study to make a direct comparison of infliximab and methotrexate additional research is needed to confirm the results.

Commentary: "Public health authorities, physicians and patients need results from good comparative effectiveness research for common diseases such as psoriasis (Naldi and Raho, 2009), so the two studies in this month's Eyes on Evidence are welcome (Barker et al. 2011; Reich et al. 2011).

"Barker et al. demonstrated the superiority of infliximab over methotrexate in achieving 75% reduction in the Psoriasis Area and Severity Index (PASI) score at 16 weeks. The magnitude of the observed difference appears large enough to consider the superiority likely, although the absolute value of the difference and its 95% confidence interval was not given. There were further concerns about possible biases that could have led to overestimating the difference such as lack of blinding, methotrexate-naive but not biologics-naive patients who might select good responders to biologics, and the 3 to 1 randomisation.

"Network meta-analysis is a useful new tool for comparative effectiveness research because it uses data from existing trials to make indirect comparisons which would otherwise require new trials. The meta-analysis by Reich et al. focused on biologics. Despite few trials and a large variety of outcomes (Spuls et al. 2011), enlarging this meta-analysis to include studies of other systemic agents for psoriasis such as methotrexate would have been of interest. The limitations in the included trials were, as expected, also found in the meta-analysis and include a too-short time for evaluating efficacy and long-term and rare adverse effects in the context of a chronic disease and non-curative treatments.

"Infliximab is the most effective treatment in these two studies but results of some observational cohort studies suggested it might also be the most frequent inducer of severe adverse effects (Tubach et al. 2005).

"Further comparative efficacy and long-term safety studies are already in progress. The two studies highlighted in this issue do not support changing the current recommendations that biologics are indicated when psoriasis is severe and has failed to respond to standard systemic therapies such as methotrexate and that the choice of biologic is based on cost, patient preference and physician preference (SIGN GUIDELINE 121, 2010). - Professor Olivier Chosidow, Dr Emilie Sbidian, Assistant Professor and Dr Laurence Le Cleach senior lecturer, Department of Dermatology Hôpital Henri-Mondor, Créteil, France

About this article: This article appeared in the February 2012 issue of the Eyes on Evidence newsletter. This free monthly newsletter from NICE Evidence outlines interesting new evidence and what it means for current practice. They do not constitute formal NICE guidance. The opinions of contributors do not necessarily reflect the views of NICE.

To receive the Eyes on Evidence e-bulletin, please complete the online registration form.

Visit Evidence Search

Copyright © 2012 National Institute for Health and Care Excellence. All Rights Reserved.