Psoriasis and ixekizumab

Turn first to standard systemic treatments

In a randomised trial in 108 adults with moderate to severe plaque psoriasis who had never received systemic therapy, subcutaneous ixekizumab (an interleukin-17A inhibitor) appeared to have greater efficacy than oral methotrexate in achieving short-term clearance of lesions. However, these results are not robust, due to the lack of blinding and the imbalance in patient characteristics between the groups.

In adults with plaque psoriasis who continue to be badly affected by the disease despite topical treatments and phototherapy, a systemically administered drug is an option. The immunosuppressive drugs methotrexate or ciclosporin, or the retinoid acitretin, are the standard treatments in this situation. TNF alpha antagonists such as adalimumab or etanercept should be reserved for situations in which these systemic drugs have failed. In clinical trials, antibodies directed against interleukins, such as ixekizumab (an interleukin-17A inhibitor), had greater efficacy than TNF alpha antagonists. However, as of early 2021, there is less experience with the use of interleukin inhibitors (1,2).

At the time of its evaluation prior to marketing authorisation (MA), ixekizumab had not been compared to a standard treatment such as methotrexate, ciclosporin or acitretin (1,2). The results of a randomised trial of ixekizumab versus methotrexate were published in 2020 (3).

Possibly more frequent clearance of lesions in the ixekizumab group. This randomised non-blinded trial included 162 adults with moderate to severe plaque psoriasis who had never received systemic treatment. On average, one-quarter of the patients’ body surface was affected. They were randomised to receive, for 24 weeks, either subcutaneous ixekizumab (at the dosage recommended in the MA), or oral methotrexate (aiming for a weekly dose of at least 15 mg), or a drug based on fumaric acid esters. The results in the fumaric acid esters group are not considered here, since this drug is not marketed in France (3,4).

Despite randomisation, the patient characteristics were not the same in the ixekizumab and the methotrexate groups. For example, in the ixekizumab group, more patients had already received phototherapy (52% versus 24%) (3). The potential influence of these differences in unknown, but it increases the uncertainty surrounding interpretation of the results. The level of evidence is also reduced by the absence of blinding.

After 24 weeks of treatment, 91% of patients in the ixekizumab group had a reduction of at least 75% in a score which took into account the extent and nature of the lesions (erythema, thickness and scaling) – the primary endpoint – compared to 70% in the methotrexate group (p=0.014). In the ixekizumab group, 41% of the patients achieved complete clearance of lesions, versus 13% in the methotrexate group (p=0.004) (3).

Infections and injection site reactions. Ixekizumab shares the adverse effect profile of all interleukin-17A inhibitors, with in particular: immunosuppressive effects leading to infections and an increased risk of cancer, injection site and hypersensitivity reactions, and neutropenia (1,5).

During the evaluation of ixekizumab prior to MA, cardiovascular events and Crohn’s disease were mentioned as adverse effects of this drug (1). After the drug was marketed, severe arterial thrombosis (especially in patients with a history of cardiovascular disorders) and serious colonic pathology (not otherwise specified) have been reported with ixekizumab (6).

The trial of ixekizumab versus methotrexate described above does not provide additional information, due to the small number of patients included and the absence of blinding (3).

In practice As of 2021, there is no strong evidence that ixekizumab has greater efficacy than methotrexate in patients with psoriasis. In addition, its adverse effects are less well established than those of standard treatments, particularly in the long term. When systemic therapy is considered, it seems preferable to turn first to methotrexate, acitretin or ciclosporin, rather than ixekizumab.

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