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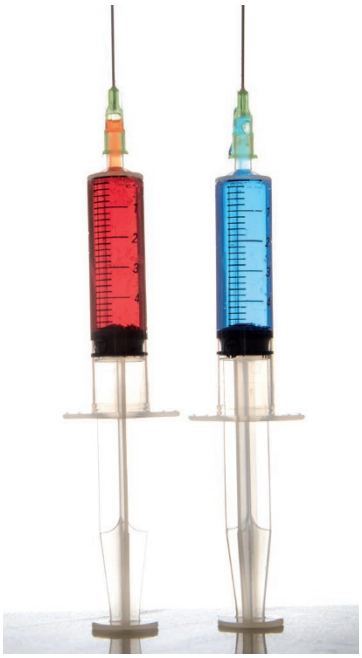
SPONDYLOARTHROPATHIES

Targeting IL-17 in refractory PsA

According to new findings from the SPIRIT-P2 phase III clinical trial, ixekizumab is superior to placebo treatment in improving the signs and symptoms of psoriatic arthritis (PsA) in patients who have previously shown an inadequate response to TNF inhibition. Ixekizumab treatment was associated with improvements in patient-reported physical and mental outcomes, and with the resolution of dactylitis in this difficult-to-treat patient group.



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The term 'inadequate responders' refers to those patients who are either refractory to TNF inhibitor therapy, have demonstrated loss of efficacy of therapy, or are intolerant to TNF inhibitors. Such patients are generally more difficult to treat than biologic-naive patients, with the current alternative treatment options having lower levels of efficacy in inadequate responders. Ixekizumab selectively targets IL-17A, a pro-inflammatory cytokine thought to be involved in the pathogenesis of PsA, and is hence a promising alternative to TNF inhibition.

In this study, patients with active PsA who have had inadequate response to TNF inhibition were recruited from 109 centres across multiple countries and randomly assigned to receive either placebo (n = 118), 80 mg ixekizumab every 4 weeks (n = 122) or 80 mg ixekizumab every 2 weeks (n = 123), following an initial starting dose of 160 mg ixekizumab. Significantly more patients achieved the primary endpoint of at least 20% improvement in the ACR response criteria (ACR-20) at week 24 in either ixekizumab treatment group compared with the placebo group (P<0.0001).

> “Targeting IL-17A represent an alternative strategy to TNF inhibition in patients with active PsA”

Consistent with the role of IL-17A in the immune response to extracellular pathogens, a higher proportion of patients receiving ixekizumab treatment reported *Candida* infection than in the placebo group. Significantly more patients in the ixekizumab treatment group also reported mild-to-moderate injection site reactions. However neither of these adverse events were generally associated with study discontinuation.

These findings are consistent with previous studies of this IL-17A inhibitor, and support the role of IL-17A in PsA pathogenesis. Targeting IL-17A could represent an alternative strategy to TNF inhibition in patients with active PsA.

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ORIGINAL ARTICLE Nash, P. *et al.* Ixekizumab for the treatment of patients with active psoriatic arthritis and an inadequate response to tumour necrosis factor inhibitors: results from the 24-week randomised, double-blind, placebo-controlled period of the SPIRIT-P2 phase 3 trial. *Lancet* http://dx.doi.org/10.1016/S0140-6736(17)31429-0 (2017)
FURTHER READING Lubberts, E. The IL-23–IL-17 axis in inflammatory arthritis. *Nat. Rev. Rheumatol.* **11**, 415–429 (2015).