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Ixekizumab recaptures response after withdrawal and flare

These findings provide important information regarding treatment interruption

INTRODUCTION

Spondyloarthritis (often shortened to SpA) is an umbrella term for several conditions that share many features and symptoms. These conditions include axial and peripheral spondyloarthritis, psoriatic arthritis, and reactive arthritis. Axial spondyloarthritis (axSpA) primarily affects the spine. Peripheral spondyloarthritis primarily affects non-spinal joints in the body, such as the knees, ankles, shoulders, feet, or hands. AxSpA is further divided into two groups. Radiographic axSpA is axial spondyloarthritis with abnormal pelvic X-rays. Non-radiographic axSpA is axial spondyloarthritis with normal X-rays of the sacroiliac joints – but sometimes people with non-radiographic axSpA might have signs of inflammation on magnetic resonance imaging (MRI) of their sacroiliac joint, where the pelvis links with the lower spine.

People with axSpA experience a high burden of disease and rely on long-term therapy to control their disease, and prevent joint damage or worsening. A group of drugs called the tumour necrosis factor inhibitors (shortened to TNFi) are used in axSpA. TNFi are part of a class of medicines called biologic disease-modifying drugs (bDMARDs). These work by targeting specific molecules that cause inflammation. A key goal for people with axSpA is remission. This is when there are no signs or symptoms of the disease. Previous studies suggest that TNFi need to be taken continuously to maintain response, and that stopping and restarting treatment may lead to the drugs not working so well. But there are often reasons why people might need to stop therapy for a period – for example, if they have a planned surgery, or if they have an infection. Sometimes, people are also reluctant to continue treatment if they feel well.

Other kinds of bDMARD target different inflammatory molecules. Instead of TNF, ixekizumab targets a molecule called interleukin-17. It is important to know whether these drugs also need to be taken continuously, or if people can recapture efficacy if they stop and start treatment.

WHAT DID THE AUTHORS HOPE TO FIND?

The authors wanted to see how many people with axSpA could recapture response if they stopped taking it when they reached remission, and then restarted if they had a flare. Another aim was to see how many people could remain flare-free when they were taking continuous ixekizumab.

WHO WAS STUDIED?

The study looked at 155 people with radiographic or non-radiographic axSpA who had achieved remission when taking ixekizumab. Everyone had taken part in one of three different studies, and had agreed to go into the long-term extension study.

HOW WAS THE STUDY CONDUCTED?

This was a randomised study. This means that people were assigned by chance to one of two treatment groups. Using chance in this way means that the groups will be similar and will allow the treatment under investigation to be compared objectively.

Everyone had taken part in one of three original studies, and had agreed to go into the long-term extension study. After finishing 52 weeks of treatment in the original study, they were treated with 80 mg ixekizumab either every 2 or 4 weeks for 24 weeks. After this, everyone who achieved remission entered a new phase of the study called the withdrawal phase, where they were randomised to either continue with ixekizumab, or be switched to placebo. During this part of the study, neither patients nor their doctors knew which treatment they were taking. The people who were randomised to ixekizumab were basically continuing with treatment, but those randomised to placebo were having the medicine withdrawn.

During this period, if people on placebo experienced a disease flare, they were re-treated with ixekizumab at the same dose and frequency as they had taken before.

The authors compared the two groups to see how many disease flares there were, how quickly – and, importantly, whether people who flared could recapture their original response when they started taking ixekizumab again.

WHAT WERE THE MAIN FINDINGS OF THE STUDY?

In the withdrawal period, more people taking ixekizumab remained flare-free compared to those taking placebo. Interestingly, nearly 36% of people who stopped taking ixekizumab and were put on placebo did not experience a flare. But in general, the time taken to experience a flare was significantly longer in those taking ixekizumab compared to placebo.

The main finding of the study was that the majority of people (96%) who were switched to placebo and experienced a disease flare in the withdrawal period were able to recapture low disease activity, and 71% could even get back to inactive disease when they were re-treated with ixekizumab.

ARE THESE FINDINGS NEW?

Yes, in part. The analysis of recapture of response at Week 104 is novel and builds on what has been previously reported from this study at Week 64.

WHAT ARE THE LIMITATIONS OF THE STUDY?

One limitation is that different studies use different definitions of flare and remission, which limits what comparisons can be made.

In addition, the way that active treatment was discontinued contrasts with what is recommended . In clinical practice, it is recommended that these kinds of medicines should be gradually withdrawn in a process called tapering, rather than just abruptly stopped.

WHAT DO THE AUTHORS PLAN ON DOING WITH THIS INFORMATION?

No additional studies or analyses are planned.

WHAT DOES THIS MEAN FOR ME?

If you have axial spondyloarthritis, there are several treatment options available. If you are taking ixekizumab, this study suggests that you can interrupt your treatment if you need or want to. You might need to do this if you have a planned surgery, or a period of illness or infection. These findings are reassuring that you may be able to regain response once you re-start on treatment when necessary.

If you have any questions or concerns about your disease or its treatment, you should speak to your doctor.

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