

### No new safety signals with long-term use of tofacitinib



Side effects with tofacitinib are generally stable over time and there are no new safety signals with long-term use

#### INTRODUCTION

Rheumatoid arthritis is a chronic inflammatory disease that affects a person's joints, causing pain and disability. It can also affect internal organs. Rheumatoid arthritis is more common in older people, but there is also a high prevalence in young adults, adolescents and even children, and it affects both men and women.

Tofacitinib is a fairly new drug for rheumatoid arthritis. It belongs to a group of medicines called JAK (janus kinase) inhibitors or targeted synthetic disease-modifying antirheumatic drugs (DMARDs), which you may see shortened to tsDMARDs. Tofacitinib is different from biologic DMARDs (also called biologics or bDMARDs). Tofacitinib works by targeting a specific pathway inside cells, blocking JAK signaling and helping to reduce inflammation throughout the body and in the joint.

The approved dose of tofacitinib in most countries is 5 mg taken two times a day as an oral pill, although there is an 11 mg once daily formulation available in some countries, such as the US. In clinical trials, tofacitinib has shown that it works well and that it is well tolerated in people with rheumatoid arthritis.

#### WHAT DID THE AUTHORS HOPE TO FIND?

The authors wanted to see whether there was any important safety information about the long-term use of tofacitinib from the drug's development programme.

#### WHO WAS STUDIED?

The study looked at 6194 people with rheumatoid arthritis who had taken part in one of the tofacitinib clinical trials and received at least one dose of tofacitinib. People could have been treated with tofacitinib on its own (monotherapy) or in combination with another DMARD such as methotrexate. People were not allowed to take part in the studies if they had an untreated tuberculosis infection or other serious infection, or if they had previously had some types of cancers or malignancies. Overall, people taking tofacitinib were followed for as long as 8.5 years.

#### HOW WAS THE STUDY CONDUCTED?

This was a pooled analysis of 19 trials of tofacitinib. This means that the authors looked back on data that had already been collected in several groups of people. They then used this information to work out how many people had infections (like tuberculosis or herpes zoster) that can affect people when their immune systems are weakened, as well as how many people got malignancies or cancers, had cardiovascular events or who got perforations (holes) in their guts after taking tofacitinib. They used this information to work out how many times these side effects would happen if someone took the drug for 100 years (called the incidence rates), and worked out whether these incidence rates changed over time.

#### WHAT WERE THE MAIN FINDINGS OF THE STUDY?

The most common side effects were nasopharyngitis (symptoms like a common cold) and infections of the upper respiratory or urinary tracts. The most common serious infections were pneumonia, herpes zoster (shingles), urinary tract infections and cellulitis (skin infection). Rates of serious infections, herpes zoster, opportunistic infections and malignancies did not increase over time. The study also found that how often the side effects happened, how often people had to stop taking tofacitinib and how often people died were similar for both doses of the drug.

#### ARE THESE FINDINGS NEW?

This is the first publication of pooled data for tofacitinib in people with rheumatoid arthritis for as long as 8.5 years. However, the types and rates of side effects were similar to what has already been seen in clinical trials of the drug.

### WHAT ARE THE LIMITATIONS OF THE STUDY?

There are several limitations to these data. In some of the studies people received a placebo (dummy) drug for comparison, but this was only for a very short period of time, so we cannot compare the long-term results for tofacitinib to people taking placebo. Also, this study gave results for the two different tofacitinib doses; however, comparison of incidence rates by dose is limited for several reasons. Firstly, there was an imbalance in the number of patients receiving 10 mg or 5 mg in the long-term extension study, and patients could have changed their dose during the study. Also, people in the two groups came from different countries, which might mean they cannot be compared. Finally, people who developed serious side effects stopped taking the drug and withdrew from the trials, which means we cannot see how they would have done over a longer period of time.

### WHAT DO THE AUTHORS PLAN ON DOING WITH THIS INFORMATION?

Additional studies collecting safety information are still ongoing. The safety database will be updated with final long-term extension data and additional study data when it becomes available.

### WHAT DOES THIS MEAN FOR ME?

If you have rheumatoid arthritis, there are a lot of treatment options available and new ones in development. If you are concerned that your current medicine is not working, or if you are getting side effects, you should talk to your doctor about different options that might be suitable for you.

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