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Real-world safety of b/tsDMARDS in the ARTIS registry

Currently available b/tsDMARDs have acceptable and on the whole similar safety profiles in a real-world population

INTRODUCTION

Rheumatoid arthritis is a chronic inflammatory disease that mainly affects a person's joints, causing pain and disability. Rheumatoid arthritis can affect people of all ages, but it most often starts between the ages of 40 and 60. It is more common in women than men.

There are many treatments available for rheumatoid arthritis, including disease-modifying antirheumatic drugs (often shortened to DMARDs). The term DMARD includes traditional drugs such as methotrexate, as well as newer biologic and targeted synthetic therapies (b/tsDMARDs). These work by targeting specific molecules that cause inflammation. By doing so, they reduce inflammation in the joints and decrease pain and disease worsening.

All drugs go through clinical trials as part of their development, but they are also closely monitored once, they are approved and available to all patients in normal everyday care. Structured follow-up in registry projects allows researchers to collect real-world data that can play an important role in evaluating safety. Anti-Rheumatic Therapies in Sweden (ARTIS) is a long-standing registry in Sweden that is collecting information on b/tsDMARDs used in clinical practice for people with rheumatoid arthritis.

WHAT DID THE AUTHORS HOPE TO FIND?

The authors wanted to assess and compare rates of key safety outcomes for individual b/tsDMARDs in people with rheumatoid arthritis, and to update previous reports to include newer treatments such as the Janus kinase inhibitors (JAKi).

WHO WAS STUDIED?

The study looked at over 20,000 patients with rheumatoid arthritis. Everyone was living in Sweden, and had been recorded as having started a b/tsDMARD between 2010 and 2020.

HOW WAS THE STUDY CONDUCTED?

This was a nationwide register-based cohort study in Sweden. Everyone taking part was followed through the ARTIS clinical register, which was linked to Sweden's system of national healthcare databases. People in a registry are not randomised to receive any particular drug, but instead are simply observed as they are looked after in normal clinical practice, and their data recorded.

The authors compared the rates of ten selected outcomes between individual b/tsDMARDs. The results were adjusted to take into account demographics, disease characteristics, and any other diseases that people had alongside their rheumatoid arthritis (often called a comorbidity).

The ten outcomes were (1) treatment discontinuation due to side effects, (2) major adverse cardiovascular events such as stroke or heart attacks, (3) serious infections requiring hospitalisation, (4) herpes zoster infection, (5) tuberculosis, (6) liver disease, (7) depression, (8) attempted or completed suicide, (9) any hospitalisation, and (10) all-cause mortality.

WHAT WERE THE MAIN FINDINGS OF THE STUDY?

The main finding was that – with a few exceptions – similarities in safety profile outweighed differences. The safety of b/tsDMARDs has been monitored with regards to many pre-defined outcomes thus making these among the most extensively studied drugs on the market.

There were marked differences in the number of people who stopped taking a drug because of its side effects. The least frequent discontinuations were for rituximab, and the most frequent for tofacitinib, but few significant differences were observed for the serious adverse events under study.

Neither cardiovascular events nor general serious infections were more frequent on baricitinib or tofacitinib versus bDMARDs, but JAKi were associated with higher rates of hospital-treated herpes zoster.

The authors noted that low numbers of events limited some comparisons, in particular for sarilumab and tofacitinib. The scarcity of tuberculosis, liver disease, and suicide also made these results inconclusive.

ARE THESE FINDINGS NEW?

Yes. These findings provide new long-term data for side effects of older drugs, and new short-term data for side effects of newer drugs for the treatment of rheumatoid arthritis.

WHAT ARE THE LIMITATIONS OF THE STUDY?

One key limitation is that due to the study design the results might have certain inaccuracies. Also, despite this study looking at a large number of patients from across Sweden, the small number of people with tuberculosis, liver disease, and suicide made these results inconclusive. It would be good to add to these findings with some more specific studies that can be tailored to special circumstances, time scales, and potentially important factors for individual safety concerns.

WHAT DO THE AUTHORS PLAN ON DOING WITH THIS INFORMATION?

The authors think these findings will be important for updating treatment guidelines for rheumatoid arthritis. They will also be interesting to people involved in making policy decisions, and prescribers in everyday practice who need to make treatment choices for their patients. The authors will continue to monitor the relative safety of current and future treatments in rheumatology.

WHAT DOES THIS MEAN FOR ME?

This study found no new or previously unknown safety concerns. If you have rheumatoid arthritis, these are reassuring findings. There are a lot of different treatments available to you which can help to modify and limit your disease and its impact on your health and wellbeing.

If you have any concerns about your disease or its treatment, you should talk to your doctor or a healthcare professional involved in your care.

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