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No significant difference between advanced therapies for RA

Individualised care should be based on clinical judgement and consideration of patient preferences.

INTRODUCTION

Rheumatoid arthritis is a chronic inflammatory disease that can affect a person's joints, and may cause pain and disability. Rheumatoid arthritis affects people of all ages, and is more common in women than men.

The goal of treatment is often remission – a state in which there is no or minimal inflammation in the joints and the body. There are a lot of different treatment options for people with rheumatoid arthritis. Usually, the first treatment will be a traditional medicine called a conventional synthetic disease-modifying antirheumatic drug (shortened to csDMARD). This group includes methotrexate and leflunomide.

If csDMARDs do not work well, then people may receive newer therapies such as a biologic (also called a bDMARD) or a targeted synthetic DMARD (tsDMARD). Targeted synthetic DMARDs include JAK inhibitors (short for Janus kinase inhibitor), which work by blocking cell signalling involved in inflammation. It is not known if it matters which order this second group of drugs are given in after people have tried csDMARDs.

WHAT DID THE AUTHORS HOPE TO FIND?

The authors wanted to find out whether it matters which of the newer therapies are tried first after csDMARDs. They also wanted to see whether some patient characteristics would be associated with better response to one of the two treatment groups. For example, whether women or men might respond differently, or if some treatments might work better for some groups depending on age, race, weight, or any other diseases people might have.

WHO WAS STUDIED?

The study looked at nearly 5,000 people with rheumatoid arthritis. Everyone was over the age of 18, and had been enrolled in Corrona – a large registry database in the US that has been collecting information on more than 45,000 people with rheumatoid arthritis over the last 20 years. All the people included were receiving routine care for their condition and had data recorded in the registry approximately every 6 months.

HOW WAS THE STUDY CONDUCTED?

The authors wanted to answer their question by looking at people in a real-world setting, without the strict rules imposed in a clinical trial. Using the Corrona database they identified the records of people who had been treated with traditional csDMARDs such as methotrexate, but not reached remission, and who had then been started on one of the newer medicines. The newer medicines were divided into two groups. The first group included biologic medicines that target a molecule called *tumour necrosis factor* (often shortened to TNF). This included adalimumab, etanercept, certolizumab, golimumab, and infliximab. The second group include other biologics and targeted medicines, specifically abatacept, tocilizumab, rituximab, anakinra, and tofacitinib (non-TNF).

The authors then compared how well the two groups were doing 1 year later by measuring several aspects of the disease. The authors particularly wanted to take into account what matters for the rheumatologist and for people with rheumatoid arthritis. This included levels of inflammation, swollen joints, painful joints, fatigue, sleep quality, length of morning stiffness, and quality of life.

WHAT WERE THE MAIN FINDINGS OF THE STUDY?

There was no notable difference in how well people did after 1 year based on which type of new treatment was tried first after csDMARDs. This means the main finding was that for people who have not done well on csDMARDs, it does not matter which kind of advanced treatment they try next: both TNF and non-TNF biologics and targeted DMARDs will work just as well. This was true for achievement of low disease activity or remission, and problems with sleep and anxiety. No specific characteristics affected the treatment outcomes. These findings support guidelines that recommend individualised care for people with rheumatoid arthritis.

ARE THESE FINDINGS NEW?

Similar findings have been shown before. But this study used a very large registry and included a lot of patients, which makes the results more robust. These results also add an important real-world perspective to the body of evidence that suggests that the differences in effectiveness of current treatments for rheumatoid arthritis are relatively small.

WHAT ARE THE LIMITATIONS OF THE STUDY?

When comparing two different treatments, ideally the people in each group should be very similar. This can be achieved with randomisation, the way it is done in randomised clinical trials. However, in this study – as in every study that uses real-world registry data – the people were not randomised. It is therefore possible that there were some differences that may have influenced the choice of treatment, or the chance of responding to that treatment. However, the authors used statistical methods that mimic the results of a randomized clinical trial, and they are confident that the people included in these analyses are as similar as possible.

WHAT DO THE AUTHORS PLAN ON DOING WITH THIS INFORMATION?

In the future, a larger number of people may make it possible to compare individual treatments, rather than broad treatment categories.

WHAT DOES THIS MEAN FOR ME?

If you have rheumatoid arthritis, there are a lot of good treatment options available to you. These findings suggest that all newer treatments work well.

The right treatment for you will depend on your own personal circumstances. Current guidelines recommend that people with rheumatoid arthritis get individualised care based on clinical judgement and consideration of their particular preferences.

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

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From: Pappas DA, *et al*. Comparative effectiveness of first-line tumour necrosis factor inhibitor versus non-tumour necrosis factor inhibitor biologics and targeted synthetic agents in patients with rheumatoid arthritis: results from a large US registry study. *Ann Rheum Dis* 2021;80:96–102. doi:10.1136/annrheumdis-2020-217209