

New option for treating active rheumatoid arthritis

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Chemical structure of upadacitinib (ABT494, ABT-494). CC BY-SA 4.0 by jmorris0x0. Wikimedia Commons.



In a large-scale, international study led by renowned rheumatologist Josef Smolen from the Department of Medicine III, a still-to-be-approved drug containing the selective janus kinase inhibitor upadacitinib has proved itself to be a new option for treating active rheumatoid arthritis (RA). It was found that between 12.5 percent and 20 percent of patients who were given the drug on a daily basis experienced so-called "sustained remission"—a state that is almost like being cured. The results of the study have now been published in top journal *The Lancet*.

Janus kinases (JAK) play an important role in intracellular signal transmission and are necessary to forward signals from various receptors to the cell nucleus. In rheumatism, however, they are responsible for <u>inflammatory responses</u>. These are curbed by JK inhibitors. There are ready two other JAK inhibitors (tofacitinib and baricitinib), which are also used for treating <u>rheumatoid arthritis</u>—but mostly as combination therapy with the standard therapy methotrexate.

However, in the current study involving more than 600 patients, the researchers led by Josef Smolen were able to show that a significant improvement can be achieved with upadacitinib as monotherapy: "With a daily dose of 15 mg, more than one third of patients achieved low disease activity, and, at 30 mg, the proportion was nearly 50 percent," says the MedUni Vienna researcher, summarizing the results. "12.5 percent of the group on the low dose and around 20 percent on the higher dose achieved so-called sustained remission, that is to say complete disappearance of disease activity. And that was after only three months."





A hand affected by rheumatoid arthritis. Credit: James Heilman, MD/Wikipedia

This <u>treatment option</u> is so important because RA patients are initially treated with the standard antirheumatic agent methotrexate for six months, and indeed many of them respond very well to this. However, if they do not respond and no remission or at least reduction in disease activity can be achieved, they are given a combined treatment of methotrexate and a biologic agent—frequently anti-TNF, such as e.g. adalimumab, administered by injection, which involves risk factors.

However, treatment with janus kinase inhibitors has already been described by rheumatism experts at MedUni Vienna as being equally good and it has the advantage that it does not involve an injection but is given in the form of a daily tablet, making it a simpler form of treatment. Additional effect of upadacitinib: "It works extremely



quickly—a good response is noticeable after only two to four weeks," says Smolen, who is the second-most frequently cited rheumatism expert in the world.

Approximately 80,000 Austrians have rheumatoid arthritis

Around 3 percent of the world's population have a form of inflammatory rheumatism (hence around 250,000 people in Austria) and around 1 percent have rheumatoid arthritis (approx. 80,000 people in Austria).

More information: Josef S Smolen et al. Upadacitinib as monotherapy in patients with active rheumatoid arthritis and inadequate response to methotrexate (SELECT-MONOTHERAPY): a randomised, placebocontrolled, double-blind phase 3 study, *The Lancet* (2019). DOI: 10.1016/S0140-6736(19)30419-2

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