Study confirms effectiveness of newer arthritis meds

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Newer oral medications for rheumatoid arthritis (RA) do work quite well
in the "real world," despite some doubts that they would, according to a new study.

The study, of 622 adults with RA, found that most were doing well on medications called JAK inhibitors, a relatively new drug class for the arthritic condition. They are taken by mouth, unlike many other RA drugs, which are given by injection or infusion.

Three JAK inhibitors—**tofacitinib** (Xeljanz), **baricitinib** (Olumiant) and **upadacitinib** (Rinvoq)—are approved in the United States. They are specifically for people with RA who do not get relief from, or cannot tolerate, older RA medications.

But while JAK inhibitors have proven effective in [clinical trials](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7557795/), there have been questions about whether that would translate to the [real world](https://www.nature.com/articles/s41591-019-1093-8) —where they are often given to patients whose RA has stubbornly resisted standard treatment.

The new findings—published Nov. 1 in the journal *Rheumatology*—may allay the concerns.

Researchers in Japan found that patients on any of four JAK inhibitors approved there generally fared well.

Overall, about one-third saw their RA go into remission within six months, and over 80% reached the goal of "low disease activity," where symptoms are largely under control.

The takeaway is straightforward, according to a U.S. rheumatologist who was not involved in the research.

"This study confirms the efficacy of JAK inhibitor therapies," said [Dr. Stanley Cohen](https://www.gender-equality.org/), of Rheumatology Associates in Dallas.
It also suggests the different JAK medications have an equal likelihood of working, Cohen said. No trials have compared the drugs head-to-head, he noted, but individual studies of each medication had suggested they are similarly effective.

And "real-world experiences," including the new study, confirm that, Cohen said.

RA is caused by a misguided immune system attack on the body's own joint tissue, leading to pain, swelling and stiffness in the joints. Over time, that systemic inflammation can feed problems in other areas of the body, including the heart, lungs, skin and eyes.

Numerous RA medications can slow the progression of joint damage by targeting parts of the immune response. JAK inhibitors are among them.

However, they are not considered an initial go-to for RA, Cohen said.

He pointed to a 2021 trial that raised safety concerns about JAK inhibitors for some older patients.

That study included RA patients age 50 and up who had at least one risk factor for heart disease or stroke, such as high blood pressure or diabetes. It found that those given the JAK inhibitor tofacitinib had a higher risk of heart attack, stroke and certain cancers, versus patients given a TNF blocker.

TNF blockers are older RA drugs, given by injection or infusion, which include etanercept (Enbrel) and adalimumab (Humira).

Based on those findings, the U.S. Food and Drug Administration added a boxed warning to all JAK inhibitors used for RA. The agency also recommended that doctors only prescribe a JAK inhibitor after patients
have tried at least one TNF inhibitor.

For the new study, researchers led by Dr. Shinya Hayashi of Kobe University in Japan analyzed medical records from 622 RA patients treated at seven medical centers. All received any of four JAK inhibitors approved in Japan.

Researchers found that most patients—around 90%—were still taking their medication six months after starting. And most had gotten symptom relief, or even remission.

That's not the end of the story, though. Six months is a short follow-up, the researchers pointed out, and it's not clear how effective JAK inhibitors are long-term.

Besides effectiveness, people with RA have to consider a treatment's safety, too.

Cohen noted that although JAK inhibitors have been tied to some increased risks versus TNF inhibitors, the overall risks still appear "quite low."

In the trial that spurred the FDA warning, 3.4% of tofacitinib patients had a heart attack or stroke over four years, compared with 2.5% of TNF inhibitor users.

Overall, Cohen said, the risks of JAK inhibitors appear similar to those of TNF blockers and other "biologic" drugs that target the underlying immune activity driving RA.

Because they put the brakes on a portion of the immune response, all of those medications can make people more susceptible to certain infections.
Cohen said JAK inhibitors do seem to carry a higher risk of shingles, which is caused by a reactivation of the chickenpox virus (which, after a person is infected, remains dormant in the body).

But that, Cohen noted, can be countered with shingles vaccination.

The study received no outside funding. Some of Hayashi's co-researchers have received funding from drug companies that make JAK inhibitors.


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