

Transcript Details

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Choosing a JAK Inhibitor for Rheumatoid Arthritis

Announcer:

You're listening to *Living Rheum* on ReachMD. On this episode, we'll learn about selecting a JAK inhibitor for rheumatoid arthritis with Dr. Roy Fleischmann. Dr. Fleischmann is an Adjunct Clinical Professor of Medicine at the University of Texas Southwestern Medical Center. He also serves as Co-Medical Director of the Metroplex Clinical Research Center and Co-Director of the Division of Rheumatology at the Texas Health Presbyterian Hospital in Dallas. Let's hear from Dr. Fleischmann now.

Dr. Fleischmann:

The JAK1 inhibitor that we have in the United States is upadacitinib. We have a pan-JAK with tofacitinib, and then we have a JAK1/2 with baricitinib. The problem with baricitinib is that only the two-milligram dose was approved by the FDA, for reasons that have subsequently been proven not to be reasonable. And the two-milligram baricitinib is really not as effective as the four-milligram, so I rarely, rarely use baricitinib.

So we're really talking about tofacitinib versus upadacitinib. I looked at the integrated safety analysis for both those drugs, as well as for baricitinib four-milligram and filgotinib—which is approved in many countries of the world, but not in the US—and it's interesting that the incidence rate of MACE, VTE, and SIE is almost exactly the same between them. So, although in preclinical studies, JAK1 seems to make more sense—clinically and safety-wise—that has not been borne out.

And then, if you look at efficacy, both tofacitinib and upadacitinib have been approved in multiple patients: methotrexate-naïve patients, patients who failed the methotrexate, and patients who have failed a TNF or a biologic. And both are effective in those populations. In head-to-head studies of upadacitinib versus adalimumab and tofacitinib versus adalimumab—both of which I was the first author on—the upadacitinib study showed that upadacitinib was statistically superior to TNF based on an ACR50 at six months, which is the correct analysis, because it's a head-to-head study, and that should be the ACR50. With tofacitinib, tofacitinib was non-inferior. So the conclusion has been that, because upadacitinib was superior and tofacitinib was non-inferior, upadacitinib must be better. However, the numbers that differentiated that were really relatively small, and there has never been a head-to-head study of tofacitinib versus upadacitinib in that population.

With that being said, what would I suggest to a patient? To a patient, upadacitinib is a once-a-day medication. Tofacitinib has two doses. It has a BID dose and a long-acting once-a-day. The data with upadacitinib is all on the 15 milligrams once a day. With tofacitinib, the five-milligram BID seems to be a little bit more effective than the 11 milligrams once a day. When tofacitinib was approved, it was only the BID dose. And when the 11-milligram was introduced, I did switch patients to the 11-milligram, because once a day is better than twice a day for patients. But about 25 percent of the patients who went to the 11-milligram wanted to go back to the five-milligram BID, because it was a little bit more effective. Now, I usually suggest upadacitinib 15-milligram once a day for that reason. If a patient's willing to take tofacitinib five milligrams BID initially or upadacitinib 15-milligram, to me, they're probably equal.

So, safety-wise, I don't think there's any difference. Efficacy-wise, I think that the once-a-day upadacitinib is a little bit more effective than the once-a-day tofacitinib. But the BID tofacitinib is probably similar to the upadacitinib.

Announcer:

That was Dr. Roy Fleischmann talking about the choice between JAK inhibitors for rheumatoid arthritis. To access this and other episodes in our series, visit *Living Rheum* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!