

Transcript Details

This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: <https://reachmd.com/programs/living-rheum/beyond-the-black-box-jak-inhibitor-safety-in-ra/70160/>

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Beyond the Black Box: JAK Inhibitor Safety in RA

Announcer:

This is *Living Rheum* on ReachMD. Today, Dr. Roy Fleischmann will be discussing JAK inhibitor safety in rheumatoid arthritis. 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. Here's Dr. Fleischmann now.

Dr. Fleischmann:

All patients with an incomplete response to methotrexate and a TNF inhibitor are candidates for a JAK inhibitor, with few exceptions, in my experience. There are important exceptions, and they are patients with an absolute lymphocyte count below 500, because of the increased risk of a serious infection; a patient with a documented history of diverticulitis or a previous GI perforation, because the JAKs can lead to another perforation; a patient who's planning pregnancy, because you don't really have enough data on the JAK inhibitors in pregnancy. In animal models, there is some increased risk, which may or may not be true in humans. And the last is a patient who has recurrent significant infections. In these patients, I would suggest another mechanism of action.

Because of the results of ORAL surveillance and the subsequent FDA labeling with a black box for MACE, malignancy, serious infections, VTE, and mortality, many rheumatologists think that JAKs increase the risk of these events, which is probably not the case. These events were very rare in oral surveillance study, and the JAK inhibitors probably reduce the risk of these events. But they probably don't reduce them quite as well as TNF inhibitors, and that's why the results of the ORAL surveillance study was what they were. Numerically, there were more events with the JAK inhibitor, but actually, if you look at the statistics, they were very close. Also, ORAL surveillance showed that there was no difference in the risk of these events with JAK inhibitors versus TNF inhibitors if the patient was not at risk for the events. So, if they didn't have a high risk for a past MACE event or high risk of VTE event, there was no difference between the JAK and the TNF.

In the patients who did have an increased risk, events were also increased with a TNF inhibitor, strongly suggesting that patients with increased events should have their risk mitigated no matter what mechanism of action you choose. Since, in the United States, almost all patients one could consider for a JAK inhibitor are TNF incomplete responders, and there's no information on the safety of a JAK versus other biologic DMARDs, I would certainly consider the use of JAK in these patients, but do everything I can to mitigate the risk in patients who do have risk for MACE and VTE.

And, as a last point, uncontrolled disease activity raises the risk of all of these events, and rapid controlled disease activity reduces the risk. JAKs work quicker than the other biologics, and they get the patients under better control in the patients who respond. Therefore, there is a very good risk-benefit ratio of the JAK inhibitors.

Announcer:

You just heard Dr. Roy Fleischmann talking about considerations for JAK inhibitor use in 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!