Transcript Details

This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting:
https://reachmd.com/programs/cme/managing-treatment-related-toxicities-with-jak-inhibitor-therapy-in-myelofibrosis/26511/

Released: 07/19/2024
Valid until: 07/19/2025
Time needed to complete: 47m

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Managing Treatment-Related Toxicities With JAK Inhibitor Therapy in Myelofibrosis

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Mascarenhas:
This is CME on ReachMD, and I'm Dr. John Mascarenhas. Today, I'm reviewing common JAK inhibitor-related toxicities and practical considerations for managing these in your practice.

So let's start with ruxolitinib. Ruxolitinib, of course, is dose based on platelet count, so you start off at a lower dose and titrate up based on the platelet count. And there is a nomogram that can be used as part of the package insert, and that's the only one of the JAK inhibitors that's dosed in that way. One needs to be aware of the on-target expected cytopenias that can occur, usually up front, nadiring of the hemoglobin within the first 3 months, so you can dose through that and transfuse patients if needed. And then the platelet count usually decreases by about median a 40%, so keep an eye on the platelet count. Lipid elevation and weight gain can be seen with ruxolitinib. In some patients that's a welcomed side effect. And as an immunosuppressive compound, there can be an increased risk of infections, particularly viral infections. So make sure that you're vaccinating your patients with the dead vaccines, not the live attenuated vaccines.

And there may be an increased risk of skin cancer, particularly non-melanoma skin cancer, based on studies that we've done prospectively, but also retrospective reports. So skin exams, at least yearly, if not twice yearly.

And if you're stopping ruxolitinib, please don't stop abruptly for a potential for cytokine rebound, which can be associated with significant symptom burden, changes in blood counts, and even hemodynamics. So taper when possible or switch directly from ruxolitinib to the next JAK inhibitor the following day.

Now fedratinib, another JAK inhibitor that is selected for JAK2 and FLT3, is given at 400 mg once daily, with or without food. I do think it does better with food. And I do think it's tolerated better at night. One can expect, based on the fact that it's a FLT3 inhibitor, GI toxicity. So prophylax those patients with antiemetics and antidiarrheals. And there is a black box warning for thiamine deficiency, Wernicke's encephalopathy. So check the thiamine level, vitamin B1, and supplement as needed.

Lastly, we have momelotinib, which is dosed at 200 mg once daily, again with or without food. Most adverse events were related to myelosuppression, but also complications such as hemorrhage, bacterial infection, fatigue, and dizziness. So monitor for signs and symptoms of infection, follow the blood counts, thrombocytopenia and neutropenia, you may need to dose reduce, and follow liver function tests, as well. There's a sufficient amount of phase 3 safety data from momelotinib from 3 different trials that suggest that it's a well-tolerated drug over a prolonged period of administration and associated with anemia responses as well.

Pacritinib in myelofibrosis also has practical considerations. It's dosed at 200 mg twice daily, importantly not based on platelet count like ruxolitinib. So even in these patients with low platelets, you can start at the full dose at 200 mg twice daily. It is a FLT3 inhibitor, so it

does have some GI toxicity, much like, fedratinib. Prophylax the patients with an antiemetic and antidiarrheal. It's usually in the first 2 months, usually low grade, easy to manage, rarely leads to discontinuation. QTc prolongation can be an issue with pacritinib, as well as the other JAK inhibitors, so I get a baseline, EKG and I monitor those patients as well. And I would discontinue therapy or hold therapy for a QTc greater than 500 milliseconds. We have sufficient, long-term follow-up and comparison studies of toxicity profile of pacritinib versus best available therapy, including ruxolitinib, which would show a lower rate of non-melanoma skin cancer malignancies, viral infections, and zoster specifically.

So in summary, we have 4 effective JAK inhibitors that can help spleen symptom burden across many different patient profiles, but there are some differences based on the kinome profile in terms of toxicity. I'll just enumerate some of the most important ones to consider. Ruxolitinib is a JAK1/2 inhibitor, cytopenias, so follow the blood counts and vaccinate with a dead viral vaccine. For FLT3 inhibitors like fedratinib and pacritinib, antiemetics and antidiarrheals when needed, usually within the first 2 months in half the patients, easy to manage, rarely a reason for discontinuation. Black box warning for fedratinib of Wernicke's encephalopathy. Check the vitamin B1 level and replete. I check it every 3 months, so I just put them on a B1 complex vitamin, which is very easy to do, rarely an issue. And then lastly, with momelotinib, also may need to check blood counts and follow liver enzymes. With all of these drugs, I would get an EKG at baseline and follow the EKG intermittently, holding for QTc greater than 500 milliseconds.

Our time is up. I hope this information will be useful for you in your clinical practice. Thanks for listening.

Announcer:
You have been listening to CME on ReachMD. This activity is provided by TotalCME, LLC. and is part of our MinuteCE curriculum.

To receive your free CME credit, or to download this activity, go to ReachMD.com/CME. Thank you for listening.