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/treatment-options-for-ruxolitinib-intolerance-or-resistance-in-myelofibrosis/26506/

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

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

Treatment Options for Ruxolitinib Intolerance or Resistance 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. Hobbs:
Hello. This is CME on ReachMD, and I'm Dr. Gabriela Hobbs. Today, I'm going to review and evaluate different treatment options for patients with myelofibrosis who experience intolerance or resistance to ruxolitinib.

Today, I'm going to review the different JAK inhibitors that are approved. So we now have 4 FDA-approved JAK inhibitors, starting with ruxolitinib, the first approved agent, followed by fedratinib, pacritinib, and momelotinib. So let's review some key data on these agents.

Fedratinib was approved in 2019 based on the JAKARTA studies. The JAKARTA-1 study compared fedratinib to placebo, and JAKARTA-2 compared fedratinib to placebo in patients that had been previously treated with ruxolitinib. What's important to notice from the JAKARTA studies is specifically the results of the JAKARTA-2 studies for patients that had been previously treated with ruxolitinib, and that is that patients treated with fedratinib after failing ruxolitinib can still be salvaged with a JAK inhibitor. And so about 1/3 of patients experienced spleen volume reduction as well as symptom burden reduction.

In terms of side effects, fedratinib does have a black box warning for Wernicke's encephalopathy, but this is easily mitigated and prevented by checking thiamine levels as well as giving thiamine repletion for patients receiving this agent. Really the more practical side effects to manage and monitor and be aware of are the GI side effects that occur with this agent, specifically diarrhea, vomiting, and nausea that occur, in particular, in the first month, but can be easily managed with supportive agents.

So now let's talk about pacritinib. Pacritinib was approved based on the PERSIST studies. And what these studies demonstrated was that pacritinib was more efficacious at improving spleen volume response as well as symptom improvement in patients receiving full-dose pacritinib of 200 mg twice daily compared to patients receiving best available therapy. The majority of patients on the best available therapy arm, should be noted, had therapy with low-dose ruxolitinib. So not only did pacritinib lead to improvements in spleen volume response and total symptom score improvement, but about 1/4 of patients on the pacritinib arm experienced an improvement in hemoglobin, and about 20% to 25% of patients also experienced reduced transfusion burden, which really was not seen in the best available therapy arms.

In terms of side effects, the most common side effects of pacritinib are GI, but these can be easily mitigated with supportive care at the beginning of treatment.

After the PERSIST studies, there was the PAC203 study that included risk mitigation factors to make this agent more well tolerated and also to find the most optimal dose of this agent. And what this study demonstrated was that the 200-mg BID dose was the most efficacious dose, and this is the FDA dose that's currently used.

Now let's move on to momelotinib. So momelotinib was approved based on the MOMENTUM study, that was a phase 3 study that

randomized patients receiving momelotinib to danazol. And these were patients that had previously been treated with a JAK inhibitor. About 1/3 of patients on the momelotinib arm experienced transfusion independence compared to 20% of patients on the danazol arm. In addition, more patients on the momelotinib arm experienced an improvement in symptoms compared to those treated with danazol.

Similar to the other agents, the more common adverse events seen with momelotinib included GI side effects like diarrhea and nausea, but cytopenias were also common side effects.

In summary, there are now 4 FDA-approved JAK inhibitors for the treatment of myelofibrosis. Fedratinib is approved for treatment in first or second line and has shown efficacy in improving SVR [spleen volume reduction] and TSS [total symptom score] in first and, importantly, in second line. Pacritinib is FDA-approved in first line for patients with platelets of less than 50, but it can be used with higher platelet counts in second line. Pacritinib is the least myelosuppressive of the JAK inhibitors, and can be used at full dose regardless of cytopenias. Momelotinib is FDA-approved for myelofibrosis patients with anemia, and it's approved in a line-agnostic fashion. It is important to recognize that most JAK inhibitors have GI toxicity that occurs frequently at the initiation of therapy but generally can be easily mitigated with some supportive care.

I'm glad I had the opportunity to share this data with you. Thank you so much 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.