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/medical-industry-feature/myelofibrosis-mf-with-thrombocytopenia-digging-through-the-data/33204/

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

Myelofibrosis (MF) With Thrombocytopenia: Digging Through the Data

Dr. McCloskey:
Hi, my name is Dr. James McCloskey. I'm an expert in the care of people living with myelofibrosis, and I'm an avid gardener.

Believe it or not, caring for a garden can be similar to caring for a person living with myelofibrosis.

Myelofibrosis with thrombocytopenia is very common. A survey of 807 physicians across 12 countries reported that almost 70% of patients with myelofibrosis had thrombocytopenia. That's over two-thirds of patients. The percentage of these patients having moderate thrombocytopenia, 50,000 to 100,000 platelets per microliter, was 34% and 35% had severe thrombocytopenia. Less than 50,000 platelets per microliter.

Thrombocytopenia can be seen at presentation of myelofibrosis and typically worsens over time for most patients.

A retrospective cohort analysis of over a thousand patients with MF and thrombocytopenia showed that 25% of patients had moderate to severe thrombocytopenia at first presentation, with platelet counts less than or equal to 100,000 per microliter.

Results from a retrospective cohort analysis and real-world analysis showed that patients with severe thrombocytopenia, platelet counts less than 50,000 per microliter, were found to be older, have increased rates of anemia, leukopenia, transfusion dependency, blood and bone marrow blasts, unfavorable karyotype, more bleeding manifestations at diagnosis and increased rates of grade three bone marrow fibrosis.

Moreover, thrombocytopenia can affect MF patients' symptoms. A prospective patient survey showed that patients with myelofibrosis and thrombocytopenia experience greater symptom burden than those patients without thrombocytopenia.

A retrospective cohort analysis of 1,269 patients with MF and thrombocytopenia showed that patients with MF and platelet counts greater than 100,000 per microliter had a median overall survival of 57 months. While patients with platelet counts less than or equal to 100,000 per microliter had a significantly reduced median overall survival of only 26 months.

When I meet a patient with severe thrombocytopenia, I'm always concerned about their disease trajectory.

It's made me more proactive with monitoring platelet counts, tracking them more carefully so I'm ready when it presents, not taken by surprise. I'm also going to be ready for a possible change in treatment knowing that almost 70% of my patients with myelofibrosis have, or may have, thrombocytopenia at some point, which will arise from overall disease progression or from a current treatment.

VONJO (pacritinib) is indicated for the treatment of adults with intermediate or high risk, primary or secondary, post polycythemia vera or post-essential thrombocythemia myelofibrosis with a platelet count below 50,000 per microliter. This indication is approved under accelerated approval based on spleen volume reduction, so continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

VONJO is contraindicated in patients concomitantly using strong CYP3A4 inhibitors or inducers.

Serious and fatal hemorrhages have occurred in VONJO-treated patients with platelet counts less than 100,000 per microliter and less than 50,000 per microliter. Grade three or greater bleeding events occurred in 15% of patients treated with VONJO compared to 7% of patients treated on the control arm.

And as a result, VONJO dose reductions, dose interruptions or permanent discontinuations occurred.

Avoid the use of VONJO in patients with active bleeding and hold VONJO seven days prior to any planned surgical or invasive procedures. Assess platelet counts periodically.

VONJO causes diarrhea in approximately 48% of patients compared to 15% of patients treated on the control arm. The median time to resolution of VONJO-treated patients was two weeks. The incidence of reported diarrhea decreased over time. Diarrhea resulted in treatment interruption in 3% of VONJO-treated patients and did not result in treatment discontinuation.

Serious diarrhea adverse reactions occurred in 2% of patients treated with VONJO compared to none in the control arm. Control preexisting diarrhea before starting VONJO treatment. Interrupt or reduce VONJO dose in patients with significant diarrhea.

Now let's take a look at VONJO and the PERSIST-2 data to see how VONJO may help patients challenged by thrombocytopenia in myelofibrosis.

The PERSIST-2 trial showed that with VONJO, almost 10 times the number of patients with severe thrombocytopenia experienced a greater than or equal to 35% spleen volume reduction, and that was against best available therapy, which included Ruxolitinib, watch and wait and hydroxyurea.

83% of patients with severe thrombocytopenia experienced any spleen volume reduction on VONJO, compared to 56% of patients on best available therapy.

The PERSIST-2 study measured reduction of total symptom score in patients with severe thrombocytopenia for VONJO, versus best available therapy.

The post-hoc analysis of severely thrombocytopenic patients with myelofibrosis showed that 26% of VONJO-treated patients experienced greater than or equal to 50% improvement in total symptom score versus best available therapy 9%.

It's important to note that the TSS endpoint was not met and no conclusions regarding the benefits or risks of VONJO can be established based on this data. TSS is not included in the prescribing information.

In post-hoc analyses of exploratory endpoints, the percentage of patients that had transfusion independence over any 12-week interval through Week 24 was 28% for VONJO, versus 8% for best available therapy. 40% of patients on VONJO achieve greater than or equal to 50% transfusion reduction over any 12-week interval through Week 24 versus 12% on best available therapy.

Please note that no conclusions regarding the benefit or risk of VONJO can be established based on the transfusion data as these are post-hoc analyses of exploratory endpoints from the PERSIST-2 trial, and are not appropriately powered. These results are not included in the VONJO Prescribing information.

VONJO can cause prolongation of the QTc interval. QTc prolongation of greater than 500 milliseconds was higher in VONJO-treated patients than in patients in the control arm. Adverse reactions of QTc prolongation were reported for 3.8% of VONJO-treated patients and 2% of control arm patients.

Avoid use of VONJO in patients with a baseline QTc of greater than 480 milliseconds and with drugs with significant potential for QTc prolongation. Correct hypokalemia prior to and during VONJO treatment.

VONJO can cause worsening thrombocytopenia. VONJO dosing was reduced due to worsening thrombocytopenia in 2% of patients with preexisting moderate to severe thrombocytopenia, platelet counts less than 100,000 per microliter, and with preexisting severe thrombocytopenia, platelet counts less than 50,000 per microliter.

Monitor platelet count prior to and during treatment. Interrupt VONJO in patients with clinically significant worsening of thrombocytopenia that lasts for more than seven days, restart VONJO at 50% of the last dose given once the toxicity has resolved.

Other JAK-inhibitors, compared to TNF blockers or best available therapy, increased the risk of the following conditions, for which VONJO is not indicated: lymphoma and other malignancies excluding non-melanoma skin cancer, MACE (Major Adverse Cardiovascular Events) including cardiovascular death, myocardial infarction, and stroke. Patients who are current or past smokers and patients with other cardiovascular risk factors may be at increased risk.

Thrombosis, including deep venous thrombosis, pulmonary embolism, and arterial thrombosis.

Serious infections in patients with myeloproliferative neoplasms. Serious bacterial, mycobacterial, fungal and viral infections may occur in patients treated with VONJO. Delay starting therapy with VONJO until active serious infections have resolved

Co-administration of VONJO with strong CYP3A4 inhibitors or inducers is contraindicated. Monitor for increased adverse reactions of VONJO when administered with moderate CYP3A4 inhibitors.

I think that the availability of VONJO has dramatically changed the way we think about managing patients with myelofibrosis and severe thrombocytopenia.

When I meet a patient with severe thrombocytopenia, I'm always concerned about their disease trajectory. As we saw earlier, these are patients who are more likely to have severe symptoms. They're patients who are more likely to progress and they're patients for whom we've had really limited therapeutic options in the past. And historically I might have been utilizing agents at lower doses maybe that weren't well explored in randomized clinical trials just because I didn't have other options. And I think that the PERSIST-2 trial really changed that landscape.

So now we have treatment options for these patients and I'm reassured that based on the data in that study that I can offer them a safe and effective drug for their specific disease.

These are adverse events that physicians should expect with VONJO as per the PERSIST-2 trial data.

Vonjo was generally well tolerated in PERSIST-2. The following table summarizes the adverse reactions reported during treatment. The most common adverse reactions reported in greater than or equal to 20% of patients, n=106, were diarrhea, thrombocytopenia, nausea, anemia and peripheral edema.

The most frequent serious adverse reactions occurring in greater than or equal to 3% of patients receiving VONJO were anemia, thrombocytopenia, pneumonia, cardiac failure, disease progression, pyrexia and squamous cell carcinoma of the skin.

Fatal adverse reactions included events of disease progression and multi-organ failure, cerebral hemorrhage, menorrhagia, and acute myeloid leukemia.

The most common adverse reactions reported in greater than or equal to 20% of patients (n=106) were diarrhea, thrombocytopenia, nausea, anemia, and peripheral edema.

While every myelofibrosis patient is different, let me walk you through a myelofibrosis patient in terms of monitoring their blood cell counts.

Myelofibrosis is a progressive disease, so we are routinely doing complete blood cell counts, or CBCs, and sometimes genetic testing to track any changes in driver mutations, or high-risk mutations, or even the number of mutations we're seeing.

As MF progresses, it can be hard to determine if the changes we're seeing are due to the disease itself and/or the treatment. It is important to evaluate the patient's platelet counts, spleen size, symptoms and current therapy to determine if the patient is being optimally managed with their current treatment regimen.

For example, in the context of a patient with progressive disease and worsening thrombocytopenia, lowering the dose of a current JAK inhibitor may be a sign that it's time to look for an alternative treatment to still accomplish your goals such as spleen volume reduction. All of that helps us understand how aggressive their myelofibrosis is and when we need to act.

Importantly, the patient helps to guide treatment decisions as they report on how they're feeling and to what extent their spleen volume is becoming an issue for them symptomatically, such as pain under the left rib or early satiety.

Every garden really is unique. I think when you know a friend or know someone, you get to see their garden. It's always interesting to see because it's an expression of them, but each garden also is unique throughout the year.

Even more so than a garden, myelofibrosis patients are each unique in their own way, and I think that can really be a challenge in a community where this is a disease that providers may not see every single day. So appreciating the nuances of each individual patient's presentation can be really challenging. And what that means is that each patient presents to us in a unique way. They also probably need unique approaches to their management, and each patient will sort of do better with a different approach.

When patients encounter thrombocytopenia in their myelofibrosis, and it's more a question of when, than if, the changing symptoms and falling platelet levels can signal that there may be a need to change treatment.