Transcript Details
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Addressing the Urgency of Myelofibrosis (MF) With Thrombocytopenia

Ms. Faysman:
Hello, my name is Karolina Faysman and I'm an Advanced Oncology Certified Nurse Practitioner, specializing in the care of patients living with myelofibrosis.

VONJO® (pacritinib) is indicated for the treatment of adults with intermediate or high-risk primary or secondary (post-polycythemia vera [PPV] or post-essential thrombocythemia [PET]) myelofibrosis (MF) with a platelet count below 50 x 10^9 per liter. 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.

I'd like to share with you today why I believe VONJO is more than just another JAK inhibitor for MF, because it was studied to treat a challenging form of MF, MF with severe thrombocytopenia. And that's why our patient, Carl is here to help us learn about the urgency of MF with thrombocytopenia, with VONJO.

Hi Carl. Thank you for coming in today. Seems like you've noticed some new symptoms and change in your symptoms. It's important that you came in to see me today so we can assess any changes in your disease and determine proper treatment.

MF is a progressive disease. It's important to note that as the condition advances, there are four major pillars of the disease to monitor: spleen volume, symptoms, anemia, and thrombocytopenia.

When you see thrombocytopenia in MF, it can signal that the disease is progressing.

Thrombocytopenia generally arises because of disease or treatment related factors such as bone marrow fibrosis, spleen sequestration, and or the effect of JAK inhibitors.

Patients who present with thrombocytopenia are much more symptomatic. Their quality of life is impacted by their disease in a much more profound way than patients without. They're extremely fatigued, they're extremely unable to perform normal functions. They have very frequent visits to the clinics because of the needs for transfusions.

That's why it's so important you reached out, Carl.

So we can monitor what signs and symptoms may be signaling the change in your disease.

Because when you look at the data, approximately 70% of MF patients will develop moderate to severe thrombocytopenia, which means you have platelet count less than or equal to a hundred thousand per microliter.

That's why we need to keep monitoring your platelet counts.

Ultimately, thrombocytopenia can affect MF patient symptoms and even overall survival.

In a patient survey, patients with MF and thrombocytopenia experienced significantly worse symptom burden than patients without thrombocytopenia.

Carl, that might be why you're experiencing new symptoms such as bruising and symptoms of cytokine release syndrome such as fatigue and night sweats.

In addition, data from a retrospective cohort analysis showed that as thrombocytopenia continued to worsen, overall survival became reduced.

And while anemia is usually the first thing you think of when an MF patient is showing signs of reduced physical function, research has shown that isolated thrombocytopenia has a profound impact on fatigue in the setting of MF.

So Carl, I know you're facing a lot of challenges, but you're strong and you have a strong support system who can help you track your symptoms and report to us any changes that may occur.

Now I would like to share some of the data from PERSIST-2, the phase three clinical trial that led to VONJO accelerated approval. The PERSIST-2 study was a phase 3 clinical trial that enrolled patients with intermediate or high risk, primary or secondary MF with thrombocytopenia, meaning a platelet count less than or equal to 100,000 per microliter and splenomegaly.

Prior JAK inhibitor treatment was also permitted.

And 45% of patients in the study had severe thrombocytopenia; platelet counts under 50,000 per microliter. Since thrombocytopenia is often concomitant with anemia. 59% of VONJO patients in the study were anemic, with hemoglobin level less than 10 grams per deciliter and 23% were red blood cell transfusion dependent.

PERSIST-2 was designed to assess two co-primary endpoints: proportion of patients achieving greater than or equal to 35% SVR, or spleen volume reduction, at week 24, and a reduction of greater than or equal to 50% TSS, or total symptom score, at week 24.

It is important to know that VONJO was tested against best available therapy, or BAT, including ruxolitinib.

It's important because it grounded the trial in a more real-world setting at the time of the study.

In fact, 39% of the patients with platelet count below 50,000 per microliter were on JAK inhibitor ruxolitinib, a standard of care in MF treatment. The other two most common agents in the BAT treatment arm were 32% watch and wait and 26% hydroxyurea.

But before I get into the data, I want to share some important safety information with you.

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 greater than or equal to 3 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 use of VONJO in patients with active bleeding and hold VONJO 7 days prior to any planned surgical or invasive procedures. Assess platelet counts periodically.

Now back to the PERSIST-2 data for VONJO.

VONJO had a strong treatment effect on spleen volume reduction in PERSIST-2, the percentage of patients with platelet counts below 50,000 per microliter achieving greater than or equal to 35% spleen volume reduction was 29% for VONJO versus 3% for BAT.

83% of patients on VONJO with platelet count below 50,000 per microliter experienced any spleen volume reduction, compared to 56% of patients on BAT. And remember, BAT included ruxolitinib.

PERSIST-2 also looked at a reduction of TSS, or total symptoms score, with VONJO.

PERSIST-2 studied reduction in total symptom score in patients with severe thrombocytopenia for VONJO versus BAT. 26% of patients on VONJO versus 9% of patients on BAT had greater than or equal to 50% reduction in TSS using the modified myelofibrosis symptom assessment form version 2.0 from baseline to week 24.

It's important to note that the TSS endpoint was not met and no conclusions regarding the benefit or risk of VONJO can be established based on this data. These results are not included in the VONJO Prescribing Information.

That being said, I want to give you a heads-up on a potential side effect you may experience.

VONJO causes diarrhea in approximately 48% of patients compared to 15% of patients treated on the control arm. The median time to resolution in VONJO-treated patients was 2 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.

In post-hoc analyses of exploratory endpoints, the percentage of patients achieving transfusion independence over any 12-week interval through week 24 was 28% for VONJO versus 8% for BAT. 40% of patients on VONJO achieved greater than or equal to 50% transfusion reduction over any 12-week interval through week 24 versus 12% on BAT.

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.

I want to pause here to give you some important safety information.

VONJO can cause worsening thrombocytopenia. VONJO dosing was reduced due to worsening thrombocytopenia in 2% of patients with preexisting moderate to severe thrombocytopenia (platelet count of less than 100,000 per microliter) and with preexisting severe thrombocytopenia (platelet count 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 7 days. Restart VONJO at 50% of the last given dose once the toxicity has resolved. If toxicity recurs hold VONJO and restart at 50% of the last given dose once toxicity has resolved.

VONJO can cause prolongation of the QTc interval. QTc prolongation of >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.

Other JAK-inhibitors, compared to TNF blockers or BAT, 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.

The safety of VONJO was evaluated in the randomized control PERSIST-2 trial.

The following table summarizes the adverse reactions reported during treatment. The most common adverse reactions reported in the greater than or equal to 20% of patients (N=106) were diarrhea, thrombocytopenia, nausea, anemia, and peripheral edema.

Here are the serious adverse reactions seen in the PERSIST-2 trial.

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

Fatal adverse reactions included events of disease progression and multiorgan failure, cerebral hemorrhage, meningorrhagia, and acute myeloid leukemia.

The most common adverse reactions reported in greater than or equal to 20% of patients included diarrhea, thrombocytopenia, nausea, anemia, and peripheral edema.

Carl, thank you again for coming and helping me walk physicians through the thinking and the data on the urgency of MF with thrombocytopenia.

And the role that VONJO can play in the care of patients like yourself. Keep in contact, especially if symptoms change and get more acute, and we'll keep monitoring the progress.