Transcript Details
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Managing Anemia in Patients With Myelofibrosis

ReachMD Voiceover:
Welcome to ReachMD.

This medical industry feature, titled “Managing Anemia in Patients With Myelofibrosis,” is sponsored by Incyte Corporation. This program is intended for healthcare professionals only. The speaker is presenting on behalf of, and is being compensated by, Incyte Corporation. Before we begin, let’s take a moment to review the Indications and Usage for Jakafi®.

INDICATIONS AND USAGE
Jakafi® (ruxolitinib) is indicated for treatment of intermediate or high-risk myelofibrosis (MF), including primary MF, post-polycythemia vera MF and post-essential thrombocythemia MF in adults.

Please stay tuned for additional Important Safety Information included later in this program.

Here’s your host, Dr. Ruben Mesa.

Dr. Mesa:
My name is Dr Ruben Mesa and I'm a hematologic oncologist.

Today, I’d like to talk about how I manage anemia in my patients with myelofibrosis, whether it be disease- or treatment-related.

We know that patients with myelofibrosis require active management at the time of diagnosis. Many clinicians may have concerns about initiating Jakafi therapy in patients with anemia. However, anemia is not a reason for me to delay treatment with Jakafi in appropriate patients.

In my practice, there is no hemoglobin level that precludes me from starting my appropriate patients with MF on Jakafi. Anemia is not a contraindication and therefore is not a barrier when initiating Jakafi.

And the COMFORT-I study gives me the confidence to not only initiate Jakafi at diagnosis for my patients with MF who have anemia at baseline, but also manage through that anemia while on treatment. And we see in the data that the benefits of Jakafi may balance the potential concerns around anemia, especially because the hemoglobin gradually recovers over time with appropriate management.

The COMFORT-I study was a phase 3 study that enrolled patients with intermediate-2 or high-risk myelofibrosis. The study was designed to assess spleen volume reduction of at least 35% at week 24 in patients treated with Jakafi vs placebo.

It’s important to note that in this study, 46% of patients in the Jakafi group had anemia at baseline, with a mean hemoglobin of 9.2 g/dL and a range of 6.6 to 13.7 gram per deciliter, which is typically what I see in my patients.

The study found that 42% of patients receiving Jakafi achieved the primary endpoint at week 24 compared with less than 1% receiving placebo.

As I mentioned earlier, patients with baseline anemia were included in this study, so it was interesting to see that after initiating Jakafi, patients with new-onset grade 3 or 4 anemia still had comparable efficacy to patients without anemia. And this is consistent with what I see in my practice, as well.

For me, the benefits of Jakafi are clear, not only from a spleen perspective, but also when it comes to its impact on total symptom score.

In the COMFORT-I study, we saw that 46% of patients on Jakafi achieved a 50% or greater improvement in total symptom scores at

week 24. And these improvements were reported regardless of whether patients presented with new-onset grade 3 or 4 anemia.

Knowing that these outcomes were not affected by hemoglobin levels gives me the confidence to initiate and continue use of Jakafi in my appropriate MF patients, regardless of anemia.

In the COMFORT-I study, we also saw that there was a mean decrease in hemoglobin levels, which reached a nadir of approximately 1.5 to 2 grams per deciliter below baseline in the first 8 to 12 weeks of therapy. However, the hemoglobin did gradually recover to reach a new steady state that was approximately 1 gram per deciliter below baseline.

While 60% of Jakafi patients required red blood cell transfusions, that requirement did decrease over time.

And although 96% of patients on Jakafi experienced anemia, less than 1% of patients discontinued from the study due to anemia. Which tells me that the anemia can generally be managed.

When I do have a patient with anemia, I first educate them that a decrease in hemoglobin is to be expected, typically within the range of 1.5 to 2 grams per deciliter. This decrease is typically front-loaded; however, it is often transient.

I also explain that a decrease in hemoglobin levels may not limit the impact or long-term outcomes of Jakafi. For me, the net benefit of being on Jakafi reinforces the importance of managing through the anemia, when appropriate.

In my clinical practice, I start Jakafi at the label-recommended dose of 15-20 mgs twice daily based on the platelets. I may use a couple red blood cell transfusions to manage these patients, as the anemia tends to recover over time. And in 4-6 months, we will re-evaluate the situation.

Overall, the safety and efficacy results from the COMFORT-I study give me the confidence to initiate Jakafi at diagnosis in my appropriate patients with MF, regardless of baseline anemia. In most cases, if it should occur, I am able to manage new-onset anemia in my patients with MF while on Jakafi.

Let's take the opportunity to review the safety information for Jakafi.

Female:
INDICATIONS AND USAGE

Jakafi® (ruxolitinib) is indicated for treatment of intermediate or high-risk myelofibrosis (MF), including primary MF, post-polycythemia vera MF and post-essential thrombocythemia MF in adults.

IMPORTANT SAFETY INFORMATION

- Treatment with Jakafi® (ruxolitinib) can cause thrombocytopenia, anemia and neutropenia, which are each dose-related effects. Perform a pre-treatment complete blood count (CBC) and monitor CBCs every 2 to 4 weeks until doses are stabilized, and then as clinically indicated
- Manage thrombocytopenia by reducing the dose or temporarily interrupting Jakafi. Platelet transfusions may be necessary
- Patients developing anemia may require blood transfusions and/or dose modifications of Jakafi
- Severe neutropenia (ANC <0.5 × 10^9/L) was generally reversible by withholding Jakafi until recovery
- Serious bacterial, mycobacterial, fungal and viral infections have occurred. Delay starting Jakafi until active serious infections have resolved. Observe patients receiving Jakafi for signs and symptoms of infection and manage promptly. Use active surveillance and prophylactic antibiotics according to clinical guidelines
- Tuberculosis (TB) infection has been reported. Observe patients taking Jakafi for signs and symptoms of active TB and manage promptly. Prior to initiating Jakafi, evaluate patients for TB risk factors and test those at higher risk for latent infection. Consult a physician with expertise in the treatment of TB before starting Jakafi in patients with evidence of active or latent TB. Continuation of Jakafi during treatment of active TB should be based on the overall risk-benefit determination
- Progressive multifocal leukoencephalopathy (PML) has occurred with Jakafi treatment. If PML is suspected, stop Jakafi and evaluate
- Herpes zoster infection has been reported in patients receiving Jakafi. Advise patients about early signs and symptoms of herpes zoster and to seek early treatment. Herpes simplex virus reactivation and/or dissemination has been reported in patients receiving Jakafi. Monitor patients for the development of herpes simplex infections. If a patient develops evidence of dissemination of herpes simplex, consider interrupting treatment with Jakafi; patients should be promptly treated and monitored according to clinical guidelines
- Increases in hepatitis B viral load with or without associated elevations in alanine aminotransferase and aspartate aminotransferase have been reported in patients with chronic hepatitis B virus (HBV) infections. Monitor and treat patients with chronic HBV infection

according to clinical guidelines
- When discontinuing Jakafi, myeloproliferative neoplasm-related symptoms may return within one week. After discontinuation, some patients with myelofibrosis have experienced fever, respiratory distress, hypotension, DIC, or multi-organ failure. If any of these occur after discontinuation or while tapering Jakafi, evaluate and treat any intercurrent illness and consider restarting or increasing the dose of Jakafi. Instruct patients not to interrupt or discontinue Jakafi without consulting their physician. When discontinuing or interrupting Jakafi for reasons other than thrombocytopenia or neutropenia, consider gradual tapering rather than abrupt discontinuation
- Non-melanoma skin cancers (NMSC) including basal cell, squamous cell, and Merkel cell carcinoma have occurred. Perform periodic skin examinations
- Treatment with Jakafi has been associated with increases in total cholesterol, low-density lipoprotein cholesterol, and triglycerides. Assess lipid parameters 8-12 weeks after initiating Jakafi. Monitor and treat according to clinical guidelines for the management of hyperlipidemia
- Another JAK-inhibitor has increased the risk of major adverse cardiovascular events (MACE), including cardiovascular death, myocardial infarction, and stroke (compared to those treated with tumor TNF blockers) in patients with rheumatoid arthritis, a condition for which Jakafi is not indicated. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with Jakafi particularly in patients who are current or past smokers and patients with other cardiovascular risk factors. Patients should be informed about the symptoms of serious cardiovascular events and the steps to take if they occur
- Another JAK-inhibitor has increased the risk of thrombosis, including deep venous thrombosis (DVT), pulmonary embolism (PE), and arterial thrombosis (compared to those treated with TNF blockers) in patients with rheumatoid arthritis, a condition for which Jakafi is not indicated. In patients with myelofibrosis (MF) and polycythemia vera (PV) treated with Jakafi in clinical trials, the rates of thromboembolic events were similar in Jakafi and control treated patients. Patients with symptoms of thrombosis should be promptly evaluated and treated appropriately
- Another JAK-inhibitor has increased the risk of lymphoma and other malignancies excluding NMSC (compared to those treated with TNF blockers) in patients with rheumatoid arthritis, a condition for which Jakafi is not indicated. Patients who are current or past smokers are at additional increased risk. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with Jakafi, particularly in patients with a known secondary malignancy (other than a successfully treated NMSC), patients who develop a malignancy, and patients who are current or past smokers
- In myelofibrosis and polycythemia vera, the most common nonhematologic adverse reactions (incidence ≥15%) were bruising, dizziness, headache, and diarrhea. In acute graft-versus-host disease, the most common nonhematologic adverse reactions (incidence >50%) were infections (pathogen not specified) and edema. In chronic graft-versus-host disease, the most common nonhematologic adverse reactions (incidence >20%) were infections (pathogen not specified) and viral infections
- Avoid concomitant use with fluconazole doses greater than 200 mg. Dose modifications may be required when administering Jakafi with fluconazole doses of 200 mg or less, or with strong CYP3A4 inhibitors, or in patients with renal or hepatic impairment. Patients should be closely monitored and the dose titrated based on safety and efficacy
- Use of Jakafi during pregnancy is not recommended and should only be used if the potential benefit justifies the potential risk to the fetus. Women taking Jakafi should not breastfeed during treatment and for 2 weeks after the final dose

Please view Full Prescribing Information for Jakafi at:

https://www.jakafi.com/pdf/prescribing-information.pdf

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Be Part of the Knowledge.

References:

1. Jakafi Prescribing Information. Wilmington, DE: Incyte Corporation.
2. Verstovsek S, Mesa RA, Gotlib J, et al. A double-blind, placebo-controlled trial of ruxolitinib for myelofibrosis. *N Engl J Med* . 2012;366(9):799-807.
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4. Verstovsek S, Mesa RA, Gotlieb J, et al. Efficacy, safety, and survival with ruxolitinib in patients with myelofibrosis results of a median 3-year follow-up of COMFORT-I. *Haematologica* . 2015;100(4):479-488.

5. Verstovsek S, Mesa RA, Gotlieb J, et al. Efficacy, safety, and survival with ruxolitinib in patients with myelofibrosis: results of a median 2-year follow-up of COMFORT-I. *Haematologica*. 2013;98(12):1865-1871. © 2023

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