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/durable-hct-control-in-patients-with-polycythemia-vera/14905/

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Durable Hct Control in Patients with Polycythemia Vera

ReachMD Voiceover:
Welcome to ReachMD.

This medical industry feature, titled “Durable Hct Control in Patients With Polycythemia Vera” 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 post-polycythemia vera (PV) in adults who have had an inadequate response to or are intolerant of hydroxyurea.

Dr. Andrew Kuykendall will be discussing data from the RESPONSE Trial. The RESPONSE Composite Primary Endpoint shows that 23% of patients receiving Jakafi achieved Hct control and ≥ 35% spleen volume reduction at week 32 vs <1% of patients receiving BAT.

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

Here’s your host, Dr. Andrew Kuykendall.

Dr. Kuykendall:
Hi, I'm Dr. Andrew Kuykendall. I'm a malignant hematologist, and today we're going to talk about patients with Polycythemia Vera who are unable to maintain strict hematocrit control less than 45% with hydroxyurea and phlebotomy.

So, we know there's some risks when hematocrit levels are above 45%, so we really focus on keeping patients below that number, maybe in a zone between 40 and 45%.

And we'll set some goals. Since we know that hematocrit goes up, we may need to intervene at levels that are below that, maybe 43 or 44%. So, there are certain signs and triggers that we look for that may indicate that we need to change treatment plan.

We do find that in many cases, hydroxyurea may not be optimal for patients. The ways to kind of tell if this is happening is if you're increasing your dose of hydroxyurea repeatedly, and yet patients are still requiring phlebotomies. And when that happens, we frequently run into tolerability issues. And in my experience, this happens around one and a half or two grams of hydroxyurea daily.

And this is very effective at maintaining hematocrit values, but it’s really a temporary solution. It's kind of like bailing water from a leaky boat. And there's some red flags associated with phlebotomy.

Excessive amounts of phlebotomies are different for each patient, but for some it may be three phlebotomies a year, while for others, it may be six phlebotomies a year.

Oftentimes you're running into a situation where it doesn't matter how many buckets you have, you're just not able to keep the water out of the boat or get the water out of the boat fast enough. You're bringing them in weekly, every other week, monthly, for visits just to check their hematocrit and you're doing phlebotomies very frequently.

And certainly, when patients are requiring repeated phlebotomies week after week, month after month, this can be a challenge. It’s inconvenient for patients to do this and it puts them at risk for symptoms associated with iron deficiency.

So, when I have a patient at their maximum tolerated dose of hydroxyurea -- and I have to give more than 3 to 6 phlebotomies a year to strictly maintain hematocrit below 45%. At this point, I would intervene with Jakafi. Jakafi can help me achieve count control when I can't

keep patients in my hematocrit zone using just hydroxyurea and phlebotomy.

I'm confident about using Jakafi to control hematocrit not only from my own clinical experience, but also because of the findings from the RESPONSE trial. Patients enrolled in this trial had polycythemia vera and were resistant to or intolerant of hydroxyurea. They also required phlebotomy to control their hematocrit levels.

The study was designed to look at hematocrit control and reduction in spleen volume of at least 35%. Patients could not become eligible for a phlebotomy between weeks eight and 32 of the trial.

And when we look at the results of the RESPONSE trial, you can see that significantly more patients who received Jakafi were able to achieve the hematocrit control and spleen volume reduction composite endpoint, compared to those who received best available therapy, the majority of which received hydroxyurea.

Investigators also continued to study Jakafi, and it was encouraging to see that there was a 74% probability that patients who achieved primary response would maintain it for at least 5 years.

So, if we focus just on hematocrit control, it was helpful to see that 60% of patients receiving Jakafi achieved hematocrit control at Week 32.

And, those patients who did achieve hematocrit control on Jakafi had a 73% probability of maintaining it at 5 years. That's the kind of durable treatment response I look for, and that helps give me the confidence to prescribe Jakafi for my appropriate patients. And remember: these results were achieved in the absence of phlebotomy eligibility.

So it's important to me as a physician to see this long-term data, because I know that once I put patients on this treatment, that it's not only something that can solve an immediate problem, controlling hematocrit levels, but it may be something that's more of a long-term solution.

In patients where I'm not able to achieve their hematocrit goal of less than 45%, despite maximum tolerated doses of hydroxyurea and frequent phlebotomies, then that's the time where I often need to shift treatment.

And oftentimes that means Jakafi.

Female:
Let's take the opportunity to review the Safety Information for Jakafi.

INDICATIONS AND USAGE

Jakafi® (ruxolitinib) is indicated for treatment of polycythemia vera (PV) in adults who have had an inadequate response to or are intolerant of hydroxyurea.

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

ReachMD Voiceover:
This program was brought to you by Incyte. If you missed any part of this discussion, visit ReachMD.com/industryfeature. This is ReachMD.

Be Part of the Knowledge.

References:

1. Jakafi Prescribing Information. Wilmington, DE: Incyte Corporation.
2. Vannucchi AM, Kiladjian JJ, Griesshammer M, et al; Ruxolitinib versus standard therapy for the treatment of polycythemia vera. *N Engl J Med* . 2015;372(5):426-435.

3. Kiladjian J-J, Zachee P, Hino M, et al. Long-term efficacy and safety of ruxolitinib versus best available therapy in polycythemia vera (RESPONSE): 5-year follow up of a phase 3 study. *Lancet Haematol*. 2020;7(3):e226-e237.
4. Data on file. Incyte Corporation. Wilmington, DE.