Transcript Details
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Spleen Volume Reduction and Long-Term Survival in Myelofibrosis

ReachMD Voiceover:
Welcome to ReachMD.

This medical industry feature, titled “Spleen Volume Reduction and Long-Term Survival in 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.

Dr. Ruben Mesa will be discussing data from the COMFORT Trials. The COMFORT trials were not designed to compare survival probabilities between the comparator arms. The 5-year overall survival analysis is not included in the Full Prescribing information for Jakafi. Although the 3-year overall survival analysis is presented in the Full Prescribing Information.

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

Here’s your host, Dr. Ruben Mesa.

Dr. Mesa:
Hi, my name is Dr. Ruben Mesa and I'm a hematologic oncologist.

Today, I’d like to talk about how the Jakafi spleen and overall survival data give me the confidence to intervene at diagnosis in my appropriate patients with myelofibrosis, instead of watching and waiting, or initiating hydroxyurea.

When managing patients with MF, my goals include control of the spleen and symptoms, with an ultimate goal of overall survival.

In my practice, the majority of patients present with palpable splenomegaly at diagnosis, which is consistent with literature showing that approximately 90% of patients have a palpable spleen at diagnosis.

Spleen volume is a critical prognostic factor, which is why without question, I always palpate the spleen for a baseline assessment. If it’s not palpable, I typically order an ultrasound and monitor more frequently. Once the spleen is palpable, it’s a significant concern, as we know that new or increasing splenomegaly is considered a sign of disease progression.

And based on a post hoc pooled analysis of the COMFORT trials, we know there is a 14% increase in the risk of death for each additional 5 dL in spleen volume at baseline over 3 years. These increases were seen irrespective of treatment.

Given these data, I actively manage my appropriate patients with MF that have any degree of palpable splenomegaly at diagnosis.

The support for intervening with Jakafi at diagnosis comes from the COMFORT trials, which showed that the impact of Jakafi on spleen volume reduction and overall survival, a secondary endpoint.

Jakafi was studied in 2 phase 3 trials, COMFORT-I and COMFORT-II, in patients with intermediate- or high-risk myelofibrosis.

Jakafi was compared with placebo in COMFORT-I and best available therapy in COMFORT-II.

In the COMFORT-I study, 42% of patients receiving Jakafi achieved the primary endpoint of spleen volume reduction of at least 35% at

week 24 compared with less than 1% on placebo.

And 99% of patients on Jakafi experienced some reduction in spleen volume, which is clinically meaningful.

The other study was the COMFORT-II study. This study compared Jakafi vs best available therapy.

And in the COMFORT-II study, we saw that 29% of patients on Jakafi achieved spleen volume reduction of at least 35% at week 48, compared with 0% on BAT.

It's important to note that approximately 47% of patients on BAT received hydroxyurea. And this is why, in my clinical practice, I don't use hydroxyurea as a treatment option for my patients with MF.

There was a recent post hoc pooled analysis of the COMFORT trials that my colleagues and I shared at the 2021 American Society of Hematology meeting that showed that patients were 2 times more likely to achieve spleen volume reduction if Jakafi was started in the first 12 months of diagnosis, compared to later.

These data inform my decision to intervene at diagnosis in my patients with MF, rather than watching and waiting.

Additionally, COMFORT-I and -II also assessed overall survival as a secondary endpoint.

In COMFORT-I, all patients in the placebo group crossed over to Jakafi at a median of 9 months or discontinued therapy. The 3-year survival probability was 70% for patients originally randomized to Jakafi and 61% for those originally randomized to placebo.

In COMFORT-II study, all patients in the BAT group crossed over at a median of 17 months or discontinued therapy. 3-year survival probability was 79% for patients originally randomized to Jakafi and 59% for those originally randomized to best available therapy.

But what stands out to me is the 5-year overall survival for patients originally randomized to Jakafi, which was 51% in COMFORT-I and 56% in COMFORT-II.

And if we go back to the post hoc pooled analysis of these COMFORT trials, we can see the survival outcomes based on the time of Jakafi initiation.

What we found was that there was a separation of the survival curves. Patients who started on Jakafi earlier had a 5-year survival probability of 63%.

So, the overall survival data available from COMFORT studies give me the confidence of prescribing Jakafi for my appropriate patients at diagnosis and not to delay treatment.

As a clinician, I want a therapy that can meet my treatment goals.

And seeing the impact of Jakafi on spleen volume reduction and overall survival gives me the confidence to intervene with Jakafi at diagnosis, instead of watching and waiting or initiating hydroxyurea.

Let's 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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