Facts about Myelofibrosis

Overview
Myelofibrosis (MF) is a potentially life-threatening blood cancer characterized by bone marrow failure, enlarged spleen (splenomegaly) and debilitating symptoms. MF has a poor prognosis and limited treatment options.¹,²

The exact prevalence of MF is uncertain, and estimates vary widely. In the US, MF affects about 16,000-18,500 people.³ MF is typically diagnosed in people between 50 to 80 years of age, but can occur at any age.⁴ The average survival of people with primary MF is about five years.⁴

Symptoms and Diagnosis
A physician may consider a diagnosis of MF when a routine medical examination shows an enlarged spleen (found in almost all patients) and abnormal blood counts.⁴

Patients may also report the following symptoms:¹,⁴
- Weakness, fatigue, shortness of breath on exertion (e.g., exercise)
- Weight loss
- Night sweats
- Itching
- Unexplained bruising, easy bleeding
- Increased likelihood of getting an infection
- Abdominal pain
- Severe upper left shoulder pain (reflecting referred pain from the spleen, sometimes due to inadequate blood flow)
- Bone pain, especially in the lower extremities

What Causes Myelofibrosis?
In MF, substances called cytokines – small proteins released by cells that affect how cells interact – increase in the marrow, stimulating blood cell production, inflammation and fibrosis.⁴ While the exact sequence of molecular events leading to MF is not fully understood, researchers do know that the condition results from dysregulation of a cell signaling pathway called the JAK (Janus kinase) pathway that may be caused by a number of genetic mutations.⁵ While not all MF patients have one of the mutations currently known to lead to overactive JAK signaling, it is believed that the JAK pathway is nonetheless overactive in all patients with MF.⁵,⁶

The JAK pathway involves a number of JAK proteins: JAK1, JAK2, JAK3 and tyrosine kinase 2. These proteins are key players in many important biological processes, including the regulation of immune function and the formation and development of blood cells.⁷

Normally, the JAK pathway is tightly controlled to ensure normal blood cell production and function. However, in patients with MF, the JAK pathway is overactive. Generally, blood cell growth factors work through JAK2 and pro-inflammatory cytokines work though JAK1.⁸ Since overactive JAK signaling can affect both JAK1 and JAK2, it is associated with both overproduction of blood cells and inflammation.
Treatment Options
The treatment options for MF have been limited. Jakafi™ (ruxolitinib) is the first and only therapy approved by the FDA for MF. Jakafi is an oral, JAK1 and JAK2 inhibitor for the treatment of patients with intermediate or high-risk MF, including primary MF, post–polycythemia vera MF and post–essential thrombocythemia MF. Intermediate and high-risk patients represent 80% to 90% of all MF patients and include anyone over the age of 65 or who have or have had any of the following: anemia, constitutional symptoms, elevated white blood cell or blast counts or platelet counts less than 100 X 10⁹/L.⁸,⁹ Jakafi has been shown to reduce the enlarged spleen and improve symptoms seen in many patients with MF.

Important Safety Information
Treatment with Jakafi can cause hematologic adverse reactions, including thrombocytopenia, anemia and neutropenia, which are each dose-related effects, with the most frequent being thrombocytopenia and anemia. A complete blood count must be performed before initiating therapy with Jakafi. Complete blood counts should be monitored as clinically indicated and dosing adjusted as required.

The three most frequent non-hematologic adverse reactions were bruising, dizziness and headache.

Patients with platelet counts <200 X 10⁹/L at the start of therapy are more likely to develop thrombocytopenia during treatment. Thrombocytopenia was generally reversible and was usually managed by reducing the dose or temporarily withholding Jakafi. If clinically indicated, platelet transfusions may be administered.

Patients developing anemia may require blood transfusions. Dose modifications of Jakafi for patients developing anemia may also be considered.

Neutropenia (ANC <0.5 X 10⁹/L) was generally reversible and was managed by temporarily withholding Jakafi.

Patients should be assessed for the risk of developing serious bacterial, mycobacterial, fungal and viral infections. Active serious infections should have resolved before starting Jakafi. Physicians should carefully observe patients receiving Jakafi for signs and symptoms of infection (including herpes zoster) and initiate appropriate treatment promptly.

A dose modification is recommended when administering Jakafi with strong CYP3A4 inhibitors or in patients with renal or hepatic impairment [see Dosage and Administration]. Patients should be closely monitored and the dose titrated based on safety and efficacy.

There are no adequate and well-controlled studies of Jakafi in pregnant women. 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 breast-feed. Discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.


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References


