Recognizing the Profound Impact on Quality of Life:

Emerging Therapy Options for Patients with Myelofibrosis

Timeline of JAK Inhibitor Therapies for MF

2011 — **Ruxolitinib** (JAKAFI)
Adults with intermediate or high-risk MF, including primary MF, post-PV MF and post-ET MF

2019 — **Fedratinib** (INREBIC)
Adults with intermediate-2 or high-risk primary or secondary (post-PV or post-ET) MF

2022 — **Pacritinib** (VONJO)
Adults with intermediate or high-risk primary or secondary (post-PV or post-ET) MF with a platelet count below 50 × 10^9/L

2023 — **Momelotinib** (OJJAARA)
Adults with anemia and intermediate or high-risk MF, including primary MF or secondary MF (post-PV and post-ET)

Management of MF with JAK Inhibitors

Generic (Brand Name)	MOA	Dosage and Administration	Indication (For Adults)	Pivotal Trials (Click on the link for more information)
Ruxolitinib (JAKAFI)	JAK 1 JAK 2	Starting dose based on patient's baseline platelet count: • > 200 × 109/L: 20 mg PO BID • 100 × 109/L to 200 × 109/L: 15 mg PO BID • 50 × 109/L to less than 100 × 109/L: 5 mg PO BID Monitor complete blood counts every 2 to 4 weeks until doses are stabilized, and then as clinically indicated. Modify or interrupt dosing for thrombocytopenia.	Intermediate or high-risk MF, including primary MF, post-PV MF and post-ET MF	COMFORT-1 COMFORT-2
Fedratinib (INREBIC)	JAK2 FLT3	400 mg PO QD with or without food for patients with a baseline platelet count of greater than or equal to 50 x 109/L	Intermediate-2 or high-risk primary or secondary (post-PV or post-ET) MF	JAKARTA JAKARTA2 FREEDOM FREEDOM2
Pacritinib (VONJO)	JAK2 FLT3 IRAK1	200 mg PO BID with or without food	Intermediate or high-risk primary or secondary (post-PV or post-ET) MF with a platelet count below 50 × 109/L	PERSIST-1 PERSIST-2 PACIFICA PAC203
Momelotinib (OJJAARA)	JAK1 JAK2 ACVR1	200 mg PO QD with or without food Reduce the starting dose to 150 mg PO QD for severe hepatic impairment (Child-Pugh Class C)	Anemia and intermediate or high-risk MF, including primary MF or secondary MF (post-PV and post-ET)	SIMPLIFY-1 SIMPLIFY-2 MOMENTUM

ACVR1, activin receptor type 1; BID, twice daily; ET, essential thrombocythemia; FLT, FMS-like tyrosine kinase 3; IRAK, interleukin 1 receptor associated kinase-1; JAK, Janus associated kinase 2; MF, myelofibrosis; PO, orally; PV, polycythemia vera; QD, once daily.
U.S. Prescribing Information.

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Monitoring of Patients for Disease and Treatment-Related Adverse Events

Dosing and administration
- Consider the impact of dose adjustments and tapering on patient quality of life

Treatment failure
- Assess previous therapies and response when making a therapeutic change
- Counsel patients regarding symptomatic relapse, worsening splenomegaly, and potentially life-threatening AEs

Hematologic toxicities
- Weigh the symptomatic burden on quality of life between anemia, thrombocytopenia, and severe neutropenia
- Assess individualized physical function, tiredness, and fatigue

Nonhematologic toxicities
- Conduct frequent checkups for hepatic and renal function to prevent further complications

Infections
- Prevent opportunistic infection for patients who are high risk
- Test patients for HBV before treatment
- Treat patients with suspected herpes zoster and COVID-19 infection according to clinical guidelines

Secondary cancers
- Discuss increased risk of developing a secondary cancer as well as other patient- and disease-related risk factors (age, history of arterial thrombosis, ruxolitinib, hydroxyurea, and alkylating agents)

For Further Information

1. The infection risks of JAK inhibition
2. Incidence and risk factors for second malignancies among patients with myeloproliferative neoplasms
3. Anemia-related response end points in myelofibrosis clinical trials: current trends and need for renewed consensus
4. Myeloproliferative neoplasms (MPNs) – Part 2: A nursing guide to managing the symptom burden of MPNs

Feliciano J, et al.. Age, history of arterial thrombosis, ruxolitinib, hydroxyurea, and alkylating agents may increase the risk of second cancersJCO 34, e18260-e18260(2016). Reynolds SB & Pettit K. He*matol-ogy Am Soc Hematol Educ Program* 2022; 2022 (1): 235–244.