Incorporating Scientific Advances into Myelofibrosis Treatment Plans

A SHARED DECISION-MAKING SUPPORT TOOL

What Is Shared Decision-Making?

Shared decision-making (SDM) occurs when a healthcare provider and a patient work together to make a healthcare decision that is best for the patient. Optimal decision making takes into account evidence-based information about available options; the provider's knowledge and experience; and the patient's values, goals, and preferences. Patients and their families/caregivers who are engaged in an SDM process are more likely to arrive at a treatment decision that works best for all those involved.

The AXIS 6 Ease ("Es") to SDM

ENSURE

Ensure you see and treat the patient as an individual not a disease.

ELEVATE

Elevate the patient-centric experience and improve satisfaction with care.

ENABLE

Enable a long-term personal connection with your patients.

ESTABLISH

Establish co-created treatment plans that align medical evidence with patient preferences to foster adherence and optimize outcomes.

ELICIT

Elicit patient/caregiver preferences, values, and goals for therapy.

EVALUATE

Evaluate the risk/benefits and costs of treatment so that they are aligned with patient expectations.

Myelofibrosis Symptom Tracking

Myeloproliferative neoplasms (MPNs) commonly cause an array of symptoms that can often be severe and negatively impact quality of life. Measuring and tracking MPN symptoms is important for assessing prognosis, developing treatment plans, and identifying medication dosing. Several symptom assessment tools are available and include:

- MPN-10
- MFSAF revised
- MFSAF v2.0
- MFSAF v4.0

Risk Stratification of Myelofibrosis

Risk stratification of myelofibrosis is important for determining which types of treatment are best for each patient's disease. Several scoring models are available that consider age, hemoglobin levels, white blood cell counts, circulating blast cells, and constitutional symptoms. Different prognostic models will also consider other disease features, like platelet counts, red blood cell transfusion dependence, and the presence of mutations. Commonly used prognostic risk models are:

• MIPSS-70 • MIPSS-70+ Version 2.0 • DIPSS • DIPSS-Plus • MYSEC-PM

The JAK-STAT Pathway in Myelofibrosis

• JAK-STAT pathway plays a central role in cell proliferation, differentiation, and survival

• JAK2 V617F mutation is present in about 50% of patients with primary myelofibrosis

Key Efficacy Data of JAK Inhibitors

	RUXOLITINIB	FEDRATINIB		PACRITINIB	MOMELOTINIB
Trial	COMFORT-1	JAKARTA	JAKARTA2	PERSIST-2	MOMENTUM
Patient population	Int-2 or high-risk MF PMF, PPV-MF, or PET-MF PLT count ≥100,000 Palpable spleen ≥5 cm PB <10% ECOG PS ≤3 Refractory, intolerant to, or not candidates for available therapy n = 155	Intermediate or high-risk MF PLT count ≥50 × 10^9/L ECOG PS scores ≤2 n = 96	Ruxolitinib R/R or intolerant n = 79	Myelofibrosis with platelet count ≤100 x 10^9/L Neutrophil >0.5 Palpable spleen ≥5 cm TSS ≥13 PB <10% ECOG PS ≤3 n = 149	Previously treated with JAKi TSS ≥10 Hgb <10 g/dL PLT count ≥25 x 10^9 n = 130
Key Outcomes	≥35% SVR = 41.9% ≥50% TSS reduction = 45.9%	≥35% SVR = 47% ≥50% TSS reduction = 40%	≥35% SVR = 30% ≥50% TSS reduction = 27%	≥35% SVR = 18% ≥50% TSS reduction = 25% Clinical improvements in hemoglobin = 25%	≥35% SVR = 23.1% TSS response rate = 24.6% TI response rate = 30.8%
Notes	Approximately 50% of patients lose response to ruxolitinib by 3 years. Presence of *RAS/CBL* mutations are predictive of treatment resistance.	Boxed warning for encephalopathy including Wernicke's. Thiamine monitoring is recommended. GI mitigation strategy includes prophylactic antiemetics and treatment with antidiarrhea mediations.		Conversion to TI can occur after several months on treatment.	Not yet approved.

JAK Inhibitors

	RUXOLITINIB	FEDRATINIB	PACRITINIB	MOMELOTINIB
Approved for treatment of:	Myelofibrosis – 1st line Polycythemia vera – 2nd line	Myelofibrosis – 1st line and 2nd line	Myelofibrosis with platelet count <50 x 10^9/L and/or cytopenia 1st line and 2nd line	Seeking approval
Mechanism of action	Inhibits JAK1 and JAK2	JAK2-selective inhibitor	Inhibits JAK2, ACVR1, and IRAK1	Inhibits JAK1, JAK2, and ACVR1
Administration route	Oral	Oral	Oral	Oral
Dosing	Myelofibrosis – depends on baseline platelet count: >200 x 10^9/L: 20 mg twice daily 100 to 200 x 10^9/L: 15 mg twice daily 50 to <100 x 10^9/L: 5 mg twice daily Polycythemia vera: 10 mg twice daily	400 mg once daily	200 mg twice daily	MOMENTUM trial dosing: 200 mg once daily
Common side effects	• Thrombocytopenia • Anemia • Bruising • Dizziness • Headache • Diarrhea	• Diarrhea • Nausea • Anemia • Vomiting	• Diarrhea • Thrombocytopenia • Nausea • Anemia • Peripheral edema	• Diarrhea • Blood creatinine increased • Pyrexia
Sides effects of special interest	• Thrombocytopenia, anemia, neutropenia • Infection • Non-melanoma skin cancer • Lipid elevation • Major adverse cardiovascular events • Thrombosis • Secondary malignancies	• Anemia, thrombocytopenia • Gastrointestinal toxicity • Hepatic toxicity • Amylase and lipase elevation • Major adverse cardiovascular events • Thrombosis • Secondary malignancies • Decreased thiamine levels leading to Wernicke's encephalopathy	• Hemorrhage • Diarrhea • Thrombocytopenia • Prolonged QT interval • Major adverse cardiovascular events • Thrombosis • Secondary malignancies • Infection	• Thrombocytopenia, anemia, neutropenia • Hemorrhage • Major adverse cardiovascular events • Asthenia • Fatigue
Drug interactions	• Fluconazole • CYP3A4 inhibitors	• CYP3A4 inhibitors • CYP3A4 inducers • CUP3A4, CYP2C19, CYP2D6 substrates • OCT2 and MATE1/2-K substrates	• CYP3A4 inhibitors • CYP3A4 inducers • P-gp, BCRP, or OCT1 substrate concentrations can be impacted by coadministration	• Not known at this time

Abbreviations

ACVR1: activin A receptor type 1

DIPSS: Dynamic International Prognostic Score System

ECOG: Eastern Cooperative Oncology Group

IRAK: interleukin receptor-associated kinase

JAK: Janus-associated kinase

MF: myelofibrosis

MFSAF: myelofibrosis symptom assessment form

MIPSS: Mutation-Enhanced International Prognostic Score System

MPN: myeloproliferative neoplasm

MYSEC-PM: MYelofibrosis SECondary to PV and ET prognostic model

PB: peripheral blast

PLT: platelet

PMF: post-myelofibrosis

PPV-MF: post-polycythemia vera myelofibrosis

PET-MF: post-essential thrombocythemia myelofibrosis

R/R: relapsed/refractory

SVR: spleen volume reduction

TI: transfusion independence

TSS: total symptom score

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