touch™ HAEMATOLOGY

Tailoring treatment in myelofibrosis: Addressing anaemia and thrombocytopenia

Practice aid for myelofibrosis

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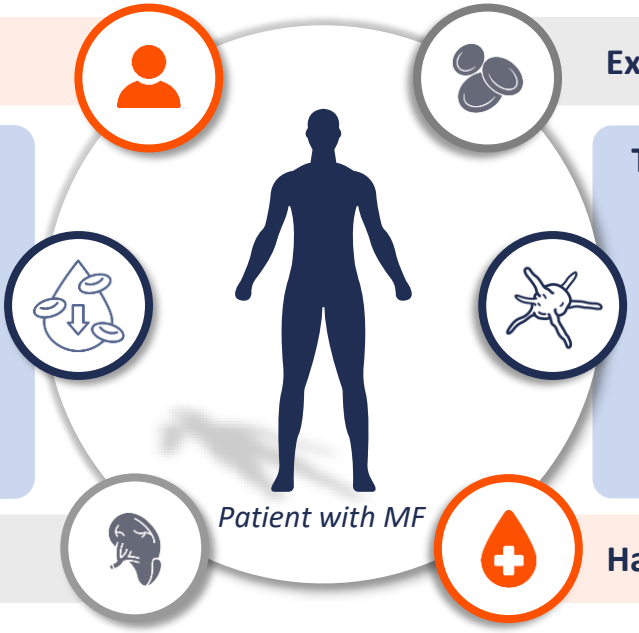
Burden of myelofibrosis

Systemic or constitutional symptoms
e.g. fatigue, night sweats, weight loss[1,2]

Extramedullary haematopoiesis[4]

Anaemia (Hb <100 g/L)[1,3]
- Rates at diagnosis: 35–38%
- A marker for advanced disease and a hallmark of MF
- Associated with fatigue, poor QoL and daily functioning
- **Anaemia is a negative prognostic factor for survival**

Thrombocytopenia (PC <100 x 10^9/L)[6,7]
- Rates at diagnosis: 16–26%
- Significantly influences treatment decisions
- **Associated with poor prognosis (OS and LFS)**



Splenomegaly/hepatomegaly[4,5]

Haemorrhagic[1]

Transfusions as supportive care

RBC transfusions[3]

- Patients with severe anaemia* must rely on **frequent transfusions** to temporarily improve or maintain Hb levels
- While transfusions may temporarily relieve anaemia-related symptoms, they **negatively impact QoL** and **survival** and represent an additional **healthcare burden**

Reported **RBC transfusions** to be 'extremely' or 'quite a bit' **inconvenient**[†8]

Treatments that reduce RBC transfusion dependency and anaemia severity may improve outcomes and prolong survival in patients with MF[9]

Platelet transfusions[4]

- For patients with thrombocytopenia and evidence of bleeding, or PC <10 x 10^9/L
- Provides **short-term benefit only**, to mitigate risk of serious bleeding

*Severe anaemia is defined as Hb <80 g/L and/or transfusion dependence; † Data from a global online survey collected between October 2023 and February 2024 from patients with symptomatic MF and prior JAK inhibitor treatment (N=155).

JAK inhibitor treatment targets and indications for MF[10–14]

Ruxolitinib	Fedratinib	Momelotinib	Pacritinib
JAK1 and **JAK2** inhibitor	**JAK2** and **FLT3** inhibitor	**JAK1**, **JAK2** and **ACVR1** inhibitor	**JAK2**, **FLT3** and **IRAK1** inhibitor
For the treatment of **disease-related splenomegaly or symptoms** in adults with primary MF, PPV-MF or PET-MF	for the treatment of **disease-related splenomegaly or symptoms** in adults with primary MF, PPV-MF or PET-MF; JAK inhibitor naïve or previously treated with ruxolitinib	For the treatment of **disease-related splenomegaly or symptoms** in adults with **moderate to severe anaemia** with primary MF, PPV-MF or PET-MF; JAK inhibitor naïve or previously treated with ruxolitinib	For the treatment of adults with **intermediate or high-risk** primary MF, PPV-MF or PET-MF with **PC <50 x 10^9/L** *Not approved in Europe or Japan*
Recommended **starting dose depends on PC** (ranging from **5–25 mg BID**)	Recommended **dose 400 mg QD**	Recommended **dose 200 mg QD**	Recommended **dose 200 mg BID**
Consider reducing dose if PC decreases during treatment* Treatment should be **discontinued if PC <50 x 10^9/L** Consider **dose modifications or interruptions** for **anaemia** **CBC monitored** as clinically indicated and dose adjusted as required	Reduce dose if PC decreases during treatment and for haematologic and non-haematologic toxicities* **Interrupt** treatment if **PC <50 x 10^9/L or grade 3 or 4 anaemia** **Discontinue treatment** if **recurrence** of **grade 4 haematologic toxicities**	Reduce dose if PC decreases during treatment* **Interrupt** treatment if **PC <20 x 10^9/L** Interrupt treatment for other haematologic and non-haematologic toxicities*	Dose modifications recommended for non-haematologic toxicities* **Discontinue treatment** 7 days **prior to elective surgery or invasive procedures** **Monitor PC** before starting treatment and as clinically indicated

*Full details provided in the Summary of Product Characteristics.

Special warnings and precautions for JAK inhibitors*[11–14]

Ruxolitinib	Fedratinib	Momelotinib	Pacritinib
Myelosuppression Infections Herpes zoster Progressive multifocal leukoencephalopathy Lipid abnormalities/elevations **MACE** **Thrombosis** **Second primary malignancies**	Encephalopathy, including Wernicke's Anaemia, thrombocytopenia and neutropenia GI events Hepatic toxicity Elevated amylase/lipase Elevated creatinine Interactions with CYP3A4 and CYP2C19 inhibitors; agents that are renally excreted via OCT2 and MATE1/2-K **MACE** **Thrombosis** **Secondary malignancies**	Infections Thrombocytopenia and neutropenia Hepatic monitoring **MACE** **Thrombosis** **Secondary malignancies** Interactions with CYP3A4 inhibitors	Haemorrhage Diarrhoea Thrombocytopenia Prolonged QT Interval **MACE** **Thrombosis** **Secondary malignancies** Risk of infection Interactions with CYP3A4 inhibitors or inducers

Strategies to mitigate, identify and manage specific non-haematologic toxicities

Ruxolitinib: Periodic skin examination is recommended for patients who are at increased risk for **skin cancer**.[11]

Fedratinib: Measure **thiamine levels** before and during treatment. **Interrupt treatment** if levels below normal range; **discontinue** if signs and symptoms of **WE**. Administer **100 mg oral thiamine prophylactically** in all patients.[12]

Momelotinib: Monitor for **signs and symptoms of infection**, including reactivation of **hepatitis B**, and initiate appropriate **treatment promptly**.[13]

Pacritinib: Avoid treatment in patients with **baseline QTc >480 msec**. Interrupt treatment and reduce dose in patients with **QTcF >500 msec**. **Correct hypokalaemia** prior to and during treatment.[14]

*Special warnings/precautions in bold are common to all treatments

Abbreviations and references

Abbreviations

ACVR1, activin A receptor type I; BID, twice daily; CBC, complete blood count; FLT3, FMS-related receptor tyrosine kinase 3; GI, gastrointestinal; Hb, haemoglobin; IRAK1, interleukin 1 receptor-associated kinase 1; JAK, Janus kinase; LFS, leukaemia-free survival; MACE, major adverse cardiac events; MATE, multidrug and toxin extrusion protein; MF, myelofibrosis; OS, overall survival; PC, platelet count; PET-MF, post-essential thrombocythemia MF; PPV-MF, post-polycythaemia vera MF; OCT, organic cation transporter; QD, once daily; QoL, quality of life; QTc, corrected QT interval; QTcF, QTc by Fridericia's cube root formula; RBC, red blood cell; SmPC, Summary of Product Characteristics; WE, Wernicke's encephalopathy.

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