Myelofibrosis (MF)

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MF risk stratification: A guide to using prognostic scores[1–4]

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JAKAVI® ruxolitinib

JAKAVI® (ruxolitinib) is indicated for the treatment of disease-related splenomegaly or symptoms in adult patients with primary myelofibrosis (also known as chronic idiopathic myelofibrosis), post-polycythaemia vera myelofibrosis or post-essential thrombocythaemia myelofibrosis. JAKAVI® is also indicated for adult patients with polycythaemia vera who are resistant to or intolerant of hydroxyurea.[5]

A guide to optimising your choice of prognostic scoring system in MF[1–4]

MF prognostic scores and their variables[1–4]

Current management approaches for MF are based on clinical phenotype, prognostic group, patient age and performance status with consideration of comorbidities.[6] Risk stratifying patients with MF can help to ensure accuracy and consistency of predicted prognoses and help you determine the most appropriate MF treatment and management pathway for your patients.[1–4,6]

	Three of the most common scoring systems[4]						
Variable (score)	**IPSS[2–4]**	**DIPSS[1–4]**	**DIPSS+[1–4]**	**MYSEC-PM[1–4]**	**MIPSS70+ v2.0[1–4]**	**MTSS[1,2,4]**	**GIPSS[2–4]**
Patient characteristics	Age >65 years (1) Constitutional symptoms (1)	Age >65 years (1) Constitutional symptoms (1)	Age >65 years (1) Constitutional symptoms (1) RBC transfusions needed (1)	Age (0.15 x years) Constitutional symptoms (1)	Constitutional symptoms (2)	Age >57 years (1) Karnofsky score <90% (1) HLA mismatched donor (2)	
Laboratory values	Hb <10 g/dL (1) WCC >25x10^9/L (1) Blasts ≥1% (1)	Hb <10 g/dL (2) WCC >25x10^9/L (1) Blasts ≥1% (1)	Hb <10 g/dL (1) WCC >25x10^9/L (1) Blasts ≥1% (1) PLT <100x10^9/L (1)	Hb <11 g/dL (2) Blasts ≥3% (2) PLT <150x10^9/L (1)	Severe anaemia† (2) Moderate anaemia‡ (1) Blasts ≥2% (1)	WCC >25x10^9/L (1) PLT <150x10^9/L (1)	
Driver mutation				*CALR* absent (2)	Type 1/like *CALR* absent (2)	Non-*CALR/MPL* mutation (1)	Type 1/like *CALR* absent (2)
Myeloid-gene variants					1 HMR§ (2) ≥2 HMR§ (3)	*ASXL1* (1)	*ASXL1* (1) *SRSF2* (1) *U2AF1Q157* (1)
Karyotype			Unfavourable* (1)		Unfavourable‖ (3) Very high risk¶ (4)		Unfavourable (1) Very high risk (2)
Risk, median survival	0 = Low (11.3 y) 1 = Int-1 (7.9 y) 2 = Int-2 (4.0 y) ≥3 = High (2.3 y)	0 = Low (NR) 1–2 = Int-1 (14.2 y) 3–4 = Int-2 (4.0 y) 5–6 = High (1.5 y)	0 = Low (15.4 y) 1 = Int-1 (6.5 y) 2–3 = Int-2 (2.9 y) 4–6 = High (1.3 y)	<11 = Low (NR) 11–13 = Int-1 (9.3 y) 14–16 = Int-2 (4.4 y) >16 = High (2.0 y)	0 = Very low (NR) 1–2 = Low (16.4 y) 3–4 = Int-1 (7.7 y) 5–8 = Int-2 (4.1 y) ≥9 = Very high (1.8 y)	0–2 = Low (83% 5 y OS) 3–4 = Int-1 (64% 5 y OS) 5 = Int-2 (37% 5 y OS) >5 = High (22% 5 y OS)	0 = Low (26.4 y) 1 = Int-1 (8.0 y) 2 = Int-2 (4.2 y) ≥3 = High (2.0 y)
Which score to use when?	**To provide a prognosis at diagnosis – does not evaluate risk factor acquisition[2–4]**	**Evolution of IPSS, developed to be applied at any time during follow-up[2–4]**	**Revision of DIPSS that includes karyotype, platelet count and transfusion status to predict OS[2–4]**	**Independently validated score specifically designed for post-ET/PV MF[2–4]**	**Combines clinical, pathological mutational and cytogenic parameters[2–4]**	**Specifically designed to refine risk stratification of HSCT outcomes[2–4]**	**Purely genetic scoring system proven to be noninferior to the MIPSS70+ and DIPSS[2–4]**

* Complex karyotype or sole or two abnormalities including +8, -7/7q-, i(17q), -5/5q-, 12p-, inv(3) or 11q23 rearrangement.[3] † Hb <8 g/dL in women, Hb <9 g/dL in men.[3] ‡ Hb 8–9.9 g/dL in women, Hb 9–10.9 g/dL in men.[3] § Including *U2AF1Q157*.[3] ‖ Chromosomal abnormalities except "very high-risk" (see below) or sole 13q-, +9, 20q-, chromosome 1 translocation/duplication or sex chromosome alterations including –Y.[3] ¶ Single/multiple abnormalities of -7, i(17q), inv(3)/3q21, 12p-/12p11.2, 11q-/11q23, + 21, or other autosomal trisomies except + 8/9.[3]

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RR6: Assessing JAKAVI® response and prognosis during the first 6 months of treatment[1,3]

Variable	Score
RUX dose <20 mg BID at baseline, Month 3 and Month 6	1
≤30% spleen length reduction at Month 3 and Month 6	1.5
RBC units needed at Month 3 and/or Month 6	1
RBC units needed at baseline, Month 3 and Month 6	1.5
Risk category, score (% of patients)	**OS, months**
Low, 0 (19%) Month	NR
Intermediate, 1–2 (45%)	61
High, ≥2.5 (36%)	33

Adapted from Mora B, et al. Curr Hematol Malig Rep. 2024.

Please refer to the summary of product characteristics (SmPC) for information on posology.

The most frequently reported adverse drug reactions were thrombocytopenia and anaemia.[5]

Haematological adverse drug reactions (any CTCAE grade) included anaemia (83.8%), thrombocytopenia (80.5%) and neutropenia (20.8%).*[5]

The three most frequent non-haematological adverse drug reactions were bruising (33.3%), other bleeding (including epistaxis, post-procedural haemorrhage and haematuria) (24.3%) and dizziness (21.9%).[5]

A complete blood cell count, including a white blood cell count differential, must be performed before initiating therapy with JAKAVI®.[5]

Complete blood count, including a white blood cell count differential, should be monitored every 2–4 weeks until JAKAVI® doses are stabilised, and then as clinically indicated.[5]

* Anaemia, thrombocytopenia and neutropenia are dose-related effects.[5]

BID, twice daily; CTCAE, Common Terminology Criteria for Adverse Events; DIPSS, Dynamic International Prognostic Scoring System; ET, essential thrombocythaemia; GIPSS, Genetically Inspired Prognostic Scoring System; Hb, haemoglobin; HLA, human leukocyte antigen; HMR, high molecular risk; HSCT, haematopoietic stem cell transplantation; Int-1, intermediate-1; Int-2, intermediate-2; IPSS, International Prognostic Scoring System; MF, myelofibrosis; MIPSS70+, Mutation and Karyotype-Enhanced International Prognostic Scoring System for Primary Myelofibrosis in adults 70 and younger; MTSS, Myelofibrosis Transplant Scoring System; MYSEC-PM, Myelofibrosis Secondary to Polycythaemia and Essential Thrombocythaemia-Prognostic Model; NR, not reached; OS, overall survival; PLT, platelet count; PV, polycythaemia vera; RBC, red blood cell; RR6, Response to Ruxolitinib after 6 Months; RUX, ruxolitinib; SmPC, summary of product characteristics; WCC, white cell count; Y, year.

References: 1. McLornan DP, et al. Br J Haematol. 2024;204:127–135. **2.** Duminuco A, et al. J Clin Med. 2023;12:2188. **3.** Mora B, et al. Curr Hematol Malig Rep. 2024;19:223–235. **4.** How J and Hobbs GS. J Natl Compr Canc Netw. 2020;18:1271–1278. **5.** Novartis Pharmaceuticals UK Ltd. JAKAVI® summary of product characteristics. **6.** McLornan DP, et al. Br J Haematol. 2024;204:136–150.

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