Personalizing JAK Inhibitor Selection in Myelofibrosis: Patient-Specific Safety Signals from FAERS Disproportionality Analysis and Clinical Trial Evidence

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Abstract

Background: Four Janus kinase (JAK) inhibitors are approved for myelofibrosis and are selected by patient phenotype, yet no real-world comparison has separated their drug effects from disease effects.

Methods: We analysed primary-suspect reports for ruxolitinib, fedratinib, pacritinib and momelotinib in the US Food and Drug Administration Adverse Event Reporting System to 2025 with four disproportionality measures, re-tested every signal against a myelofibrosis-restricted background and head-to-head against the other three inhibitors, and triangulated the findings with a meta-analysis of ten randomized trials (2,488 patients).

Results: Of 31,958 reports, 848 preferred terms were signals and 60 survived both restrictions. Restriction removed disease and channelling signals, including ruxolitinib splenomegaly (reporting odds ratio [ROR] 100.06 to 1.10) and momelotinib anaemia (7.37 to 1.11). Drug-specific signals persisted: thiamine depletion with fedratinib (vitamin B1 decreased, ROR 2670.70; median onset 57 days), diarrhoea with pacritinib (ROR 8.48; median onset 1 day; trial risk ratio 5.26), renal impairment (7.82) and peripheral neuropathy (8.34) with momelotinib, and anaemia (9.92) and weight gain (6.10-fold above other inhibitors) with ruxolitinib. Pacritinib was co-reported with contraindicated strong CYP3A4 inhibitors (16 reports), QT-prolonging drugs (12.6%) and antithrombotics (13.9%). Trials confirmed eight of 11 testable signals.

Conclusion: Each inhibitor has a distinct, phenotype-relevant safety fingerprint. Pharmacists can personalize therapy by matching the drug to the patient and monitoring by drug and onset: diarrhoea from day 1 with pacritinib, renal and neuropathy surveillance with momelotinib, thiamine monitoring beyond the first month with fedratinib, and cytopenia and weight monitoring with ruxolitinib. Findings need patient-level confirmation.

Keywords

Disproportionality analysis, FAERS, Janus kinase inhibitors, Myelofibrosis, Personalized medicine, Pharmacovigilance.