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Interim analysis of safety and efficacy of ruxolitinib in patients with myelofibrosis and low platelet counts

Moshe Talpaz[1*], **Ronald Paquette**[2], **Lawrence Afrin**[3], **Solomon I Hamburg**[4], **Josef T Prchal**[5], **Katarzyna Jamieson**[6], **Howard R Terebelo**[7], **Gregory L Ortega**[8], **Roger M Lyons**[9], **Ramon V Tiu**[10], **Elliott F Winton**[11], **Kavita Natrajan**[12], **Olatoyosi Odenike**[13], **David Claxton**[14], **Wei Peng**[15], **Peter O'Neill**[15], **Susan Erickson-Viitanen**[15], **Lance Leopold**[15], **Victor Sandor**[15], **Richard S Levy**[15], **Hagop M Kantarjian**[16] and **Srdan Verstovsek**[16]

* Corresponding author: Moshe Talpaz mtalpaz@med.umich.edu

For all author emails, please log on.

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Abstract

Background

Ruxolitinib, a Janus kinase 1 and 2 inhibitor, demonstrated improvements in spleen volume, symptoms, and survival over placebo and best available therapy in intermediate-2 or high-risk myelofibrosis patients with baseline platelet counts ≥100 × 10^9/L in phase III studies. The most common adverse events were dose-dependent anemia and thrombocytopenia, which were anticipated because thrombopoietin and erythropoietin signal through JAK2. These events were manageable, rarely leading to treatment discontinuation. Because approximately one-quarter of MF patients have platelet counts <100 × 10^9/L consequent to their disease, ruxolitinib was evaluated in this subset of patients using lower initial doses. Interim results of a phase II study of ruxolitinib in myelofibrosis patients with baseline platelet counts of 50-100 × 10^9/L are reported.

Methods

Ruxolitinib was initiated at a dose of 5 mg twice daily (BID), and doses could be increased by 5 mg once daily every 4 weeks to 10 mg BID if platelet counts remained adequate. Additional dosage increases required evidence of suboptimal efficacy. Assessments included measurement of spleen volume by MRI, MF symptoms by MF Symptom Assessment Form v2.0 Total Symptom Score [TSS]), Patient Global Impression of Change (PGIC); EORTC QLQ-C30, and safety/tolerability.

Results

By week 24, 62% of patients achieved stable doses ≥10 mg BID. Median reductions in spleen volume and TSS were 24.2% and 43.8%, respectively. Thrombocytopenia necessitating dose reductions and dose interruptions occurred in 12 and 8 patients, respectively, and occurred mainly in patients with baseline platelet counts ≤75 × 10^9/L. Seven patients experienced platelet count increases ≥15 × 10^9/L. Mean hemoglobin levels remained stable over the treatment period. Two patients discontinued for adverse events: 1 for grade 4 retroperitoneal hemorrhage secondary to multiple and suspected pre-existing renal artery aneurysms and 1 for grade 4 thrombocytopenia.

Conclusions

Results suggest that a low starting dose of ruxolitinib with escalation to 10 mg BID may be appropriate in myelofibrosis patients with low platelet counts.

Trial registration

ClinicalTrials.gov: NCT01348490.

Keywords: Janus kinase inhibitor; Myelofibrosis; Phase II; Platelet count; Ruxolitinib; Spleen volume; Total symptom score