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Efficacy, safety, and survival with ruxolitinib in patients with myelofibrosis: results of a median 3-year follow-up of COMFORT-I

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A complete list of the COMFORT-I investigators appears in the Appendix.

ABSTRACT

In the phase III COMFORT-I study, the Janus kinase 1 (JAK1)/JAK2 inhibitor ruxolitinib provided significant improvements in splenomegaly, key symptoms, and quality-of-life measures and was associated with an overall survival benefit relative to placebo in patients with intermediate-2 or high-risk myelofibrosis. This planned analysis assessed the long-term efficacy and safety of ruxolitinib at a median follow-up of 149 weeks. At data cutoff, approximately 50% of patients originally randomized to ruxolitinib remained on treatment whereas all patients originally assigned to placebo had discontinued or crossed over to ruxolitinib. At week 144, mean spleen volume reduction was 34% with ruxolitinib. Previously observed improvements in quality-of-life measures were sustained with longer-term ruxolitinib therapy. Overall survival continued to favor ruxolitinib despite the majority of placebo patients crossing over to ruxolitinib (hazard ratio 0.69 [95% confidence interval: 0.46-1.03]; P=0.067). Exploratory analyses suggest that crossover may have contributed to an underestimation of the true survival difference between the treatment groups. Ruxolitinib continued to be generally well tolerated; there was no pattern of worsening grade ≥3 anemia or thrombocytopenia with longer-term ruxolitinib exposure. These longer-term data continue to support the efficacy and safety of ruxolitinib in patients with myelofibrosis. The study is registered at clinicaltrials.gov: NCT00952289.

Introduction

Myelofibrosis (MF) is a Philadelphia chromosome–negative myeloproliferative neoplasm that may occur as primary myelofibrosis (PMF) or develop from progression of polycythemia vera or essential thrombocythemia (post-polycythemia vera or post-essential thrombocythemia MF, respectively).1 The clinical hallmarks of MF are splenomegaly, cytopenias, and debilitating symptoms associated with a hypercatabolic state and systemic inflammation.2,3 Allogeneic stem cell transplantation is the only potentially curative therapy for MF. However, this therapy is recommended only for a limited number of patients because of the high risk of treatment-related morbidity and mortality as well as the poor medical condition of patients.4 Dysregulation of the Janus kinase (JAK)–signal transducer and activator of transcription (STAT) pathway is central to the pathogenesis of MF5,6 Approximately 65% of patients with PMF carry the JAK2V617F gain-of-function mutation and 5% to 10% carry mutations in the thrombopoietin receptor gene (MPL).7,8 Additional mutations leading to dysregulation of the JAK-STAT signaling pathway have been characterized in patients with PMF and other myeloproliferative neoplasms, suggesting a high degree of complexity and heterogeneity in disease pathogenesis.9,10 Recently, mutations in the CALR gene encoding calreticulin were detected in approximately 67%11 to 82%12 of patients with essential thrombocythemia and in 80%13 to 88%14 of patients with PMF who did not have JAK2 or MPL mutations. The high frequency of CALR mutations in these patients, along with evidence linking aberrant calreticulin activity to JAK-STAT activation, supports a role for calreticulin in the pathogenesis of myeloproliferative neoplasms.15 Despite the range of mutations, the central role of the JAK-STAT pathway in myeloproliferative neoplasms has provided the rationale for the development of targeted therapies that inhibit JAK-STAT signaling.16,17

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The oral JAK1 and JAK2 inhibitor ruxolitinib has been evaluated in two phase III clinical trials in patients with intermediate-2 or high-risk PMF (according to the International Prognostic Scoring System) or post-polycythemia vera MF or post-essential thrombocythemia MF (according to the 2008 World Health Organization criteria): the randomized, double-blind Controlled Myelofibrosis Study with Oral JAK Inhibitor Treatment (COMFORT)-I study (www.clinicaltrials.gov: NCT00952289) and the randomized, open-label COMFORT-II study (www.clinicaltrials.gov: NCT00934544), which compared the effects of ruxolitinib with placebo or best available therapy, respectively. Both studies showed that ruxolitinib treatment significantly reduced splenomegaly and provided marked improvements in MF-related symptoms and quality-of-life (QOL) measures compared with controls, regardless of JAK2 V617F mutational status. The clinical benefit and safety of ruxolitinib treatment in COMFORT-I and COMFORT-II have been maintained with subsequent longer-term follow-up. As anticipated, the effect of JAK2 inhibition on hematopoiesis resulted in dose-dependent anemia and thrombocytopenia. The majority of these cytopenias occurred in the first 8 to 12 weeks of treatment, and they were generally manageable with dose reductions and/or red blood cell transfusions. Subsequently, mean platelet counts stabilized and mean hemoglobin levels gradually returned to a new steady state just below baseline levels. Additionally, longer-term follow-up of the COMFORT studies showed that ruxolitinib treatment was associated with an overall survival advantage, despite the crossover design of these studies. The objective of the current analysis is to provide an update on the efficacy, focusing on overall survival, and safety of ruxolitinib in patients enrolled in COMFORT-I at a median follow-up of approximately 3 years (149 weeks).

Methods

Patients and study design
Detailed inclusion and exclusion criteria for the COMFORT-I trial have been described previously. Briefly, patients with intermediate-2 or high-risk PMF or post-polycythemia vera MF or post-essential thrombocythemia MF and splenomegaly were randomized 1:1 to receive ruxolitinib or placebo orally twice a day (BID). The starting dose of ruxolitinib was based on baseline platelet count: 15 mg BID or 20 mg BID for baseline platelet counts of 100-200×10^9/L or >200×10^9/L, respectively. Doses could be modified per protocol. Crossover from the placebo arm to ruxolitinib was allowed prior to the primary analysis based on defined criteria for worsening splenomegaly. Upon completion of the primary analysis, the study was unblinded and all remaining patients receiving placebo were allowed to cross over to ruxolitinib. Each participating site’s institutional review board approved the protocol. The study sponsor analyzed and interpreted the data in collaboration with the investigators. All authors had access to the aggregate data and any additional analyses upon request. The study was conducted in accordance with the International Conference on Harmonization guidelines for Good Clinical Practice. All patients provided written informed consent.

Assessments
Timing and methods of assessment of spleen volume, symptom burden, QOL measures, and adverse events, described previously, are detailed in the Online Supplementary Appendix.

Statistical analysis
This prospectively defined analysis was to occur when all patients either reached the 144-week assessment or discontinued participation in the study. Changes from baseline in spleen volume and palpable spleen length were based on observed cases and summarized descriptively. Durability of spleen volume reduction was evaluated using the Kaplan-Meier method in patients who achieved a ≥35% reduction from baseline. Loss of a ≥35% spleen volume reduction was defined as the first <35% spleen volume reduction from baseline that was also a ≥25% increase from nadir. Overall survival was assessed using the Kaplan-Meier method for the intent-to-treat population with patients assessed according to their original randomized treatment. Survival time was measured from the start of the study to last known status of the patient and was not censored at time of discontinuation from randomized treatment. The Cox proportional hazards model and log-rank test were used to calculate the hazard ratio with 95% confidence interval (CI) and P-value, respectively. The incidences of new-onset or worsening grade ≥2 anemia and thrombocytopenia, and of new-onset or worsening grade ≥3 non-hematologic adverse events, were calculated using the life table method. Additional details on safety assessments are discussed in the Online Supplementary Appendix.

To better understand the effect of crossover to ruxolitinib on survival measurements, two exploratory analyses were performed. The first used the rank-preserving structural failure time (RPSFT) method, a statistical method used in oncology trials to adjust for a possible crossover effect. The second analysis was a parametric statistical modeling of overall survival using the generalized Gamma distribution, which fitted a three-parameter regression model to the observed survival data to calculate the corresponding hazard of death for patients originally randomized to ruxolitinib or placebo. Full details and description of the exploratory analyses are described in the Online Supplementary Appendix.

Results

Patient disposition
At a median follow-up of 149 weeks (range, 19-175 weeks), 77 of the 155 patients (49.7%) originally randomized to ruxolitinib were still receiving ruxolitinib therapy. A total of 111 of the 154 patients originally randomized to placebo crossed over to ruxolitinib therapy. Of these 111 patients, 57 (51.4%) patients were still receiving ruxolitinib therapy (Figure 1). In patients originally randomized to ruxolitinib, discontinuation rates estimated using the Kaplan-Meier method were 21% at year 1, 35% at year 2, and 51% at year 3. Reasons for discontinuation included disease progression (23.1%), adverse events (19.2%), death (19.2%), and withdrawal of consent (15.4%) (Figure 1).

The median exposure to ruxolitinib was 145 weeks for patients originally randomized to ruxolitinib; for these patients, the mean dose of ruxolitinib remained stable after initial dose adjustments in the first 8 to 12 weeks of therapy (Figure 2). For patients originally randomized to placebo, the median exposure to placebo was 57 weeks. For patients who crossed over to ruxolitinib from placebo, the median time to crossover was 41 weeks. The median exposure to ruxolitinib for patients who crossed over over 105 weeks, which, at the time of this analysis, was nearly three times longer than their exposure to placebo.
Efficacy

Reductions in spleen size were durable with longer-term treatment with ruxolitinib. The mean percentage change from baseline in spleen volume was $-31.6\%$ at week 24 (median $-33.0\%$) and $-34.1\%$ at week 144 (median $-38.4\%$) (Figure 3A). The mean percentage change from baseline in palpable spleen length was $-43.4\%$ at week 24 (median $-41.2\%$) and $-49.4\%$ at week 144 (median $-50.0\%$) (Figure 3A). Assessment of palpable spleen response using the International Working Group for Myelofibrosis Research and Treatment (IWG-MRT) and European LeukemiaNet (ELN) consensus criteria showed that a palpable spleen response was achieved in $31.6\%$ of ruxolitinib-treated patients compared with $2.0\%$ of patients in the placebo arm at week 24. At week 144, palpable spleen response was achieved in $24.5\%$ of patients originally randomized to ruxolitinib. Fifty-nine percent of patients (91/155) originally randomized to ruxolitinib achieved a $\geq 35\%$ reduction in spleen volume at any time during the study follow-up. The majority of
patients achieved a ≥35% reduction from baseline in spleen volume by week 12, the time of the first spleen volume assessment; in these patients, the probability of maintaining a ≥35% spleen volume reduction for at least 132 weeks corresponded to 144 weeks on therapy. In this analysis, the probability of maintaining a ≥35% spleen volume reduction for at least 132 weeks was 0.53. Over the course of follow-up, more than 80% of patients who achieved a ≥35% reduction in spleen volume maintained a reduction of at least 10% (Figure 3B), a reduction that has been shown to be associated with meaningful improvements in QOL and MF-related symptoms.21 Although the modified MF Symptom Assessment Form version 2.0 was only assessed through week 24, improvements in QOL measures, as assessed by the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLC-C30), were maintained with longer-term therapy, including improvements in global health status/QOL, fatigue, role functioning, and physical functioning scales (Figure 4).

**Overall survival**

At the time of this analysis, 42 patients randomized to ruxolitinib and 54 randomized to placebo had died. A list of causes of death is provided in Online Supplementary Table S1. With median follow-ups of 149.1 and 149.3
weeks for the ruxolitinib and placebo arms, respectively, the hazard ratio for overall survival continued to favor patients originally randomized to ruxolitinib compared with those originally randomized to placebo [hazard ratio 0.69 (95% CI: 0.46-1.03); P=0.067] (Figure 5A). Although the hazard ratio continued to favor ruxolitinib, the P-value no longer reached nominal significance at the P=0.05 level. Therefore, exploratory analyses were conducted to assess the potential impact of crossover and substantially longer exposure to ruxolitinib than placebo among patients originally randomized to placebo. The RPSFT method estimated a hazard ratio of 0.36 (95% CI: 0.204-1.035) (Figure 5B). Exploratory modeling of survival using a generalized Gamma distribution showed that the hazard of death in patients originally randomized to placebo was initially higher than that in patients randomized to ruxolitinib. This hazard subsequently decreased over time, corresponding with an increased proportion of patients who crossed over to ruxolitinib (Online Supplementary Figure S1).

Safety

As expected given the role of JAK2 in erythropoietin and thrombopoietin signaling, anemia and thrombocytopenia were the most common adverse events observed with ruxolitinib therapy. The incidence of new-onset or worsening grade 3 or 4 anemia and thrombocytopenia were highest during the first 6 months of therapy and decreased with longer-term ruxolitinib treatment (Figure 6A). Consistent with this observation, mean hemoglobin levels and platelet counts in ruxolitinib-treated patients decreased in the first 8 to 12 weeks. Mean hemoglobin levels reached a nadir in this time frame, then subsequently increased to a new steady-state level by week 24 and remained stable through the course of longer-term follow-up. Mean platelet counts remained stable with longer-term follow-up after the initial decrease (Figure 6B). Since the last reported analysis at a median follow-up of 102 weeks, no additional patients have discontinued the study because of anemia or thrombocytopenia.

The most common non-hematologic adverse events that occurred more frequently with ruxolitinib than with placebo in the primary analysis were ecchymosis (18.7%), dizziness (14.8%), and headache (14.8%). When adjusted for exposure to ruxolitinib, the incidence of these adverse events as well as other non-hematologic events decreased with longer-term therapy (Table 1), as did rates of grade ≥3 adverse events (Online Supplementary Table S2). Urinary tract infections and herpes zoster infections that occurred in patients receiving ruxolitinib during randomized treatment, however, no increase in incidence was noted with long-term ruxolitinib therapy. A comprehensive analysis of MedDRA preferred terms associated with these infections showed that the incidence of urinary tract infections per the life table method was 10.5% (n=15) for 0 to <12 months, 6.7% (n=7) for 12 to <24 months, 7.7% (n=6) for 24 to <36 months, and 6.0% (n=2) for ≥36 months in patients originally randomized to ruxolitinib. Two urinary tract infections were grade ≥3, one occurring between months 12 and 24 and one occurring between months 24 and 36. The incidences of herpes zoster were 2.1% (n=3) for 0 to <12 months, 3.5% (n=4) for 12 to <24 months, 3.4% (n=3) for 24 to <36 months, and 0% for ≥36 months in patients originally randomized to ruxolitinib; all herpes zoster infections were grade 1 or grade 2. No other opportunistic infections occurred with long-term ruxolitinib therapy. The overall pattern of adverse events observed after treatment interruption or discontinuation continued to support the absence of a specific withdrawal effect (Online Supplementary Tables S3 and S4).

Four new cases of acute myeloid leukemia have been reported since the previous analysis (two in patients originally randomized to ruxolitinib; two in patients originally randomized to placebo who developed acute myeloid leukemia after crossing over to ruxolitinib), for a total of eight cases since the study was started (four in patients originally randomized to ruxolitinib; four in patients originally randomized to placebo). The rate of leukemic transformation per person-year of ruxolitinib exposure was 0.0121/person-year and 0.0233/person-year in patients originally randomized to ruxolitinib or placebo, respectively.

Discussion

In this planned analysis of the COMFORT-I study with a median follow-up of 149 weeks, ruxolitinib treatment continued to be associated with durable reductions in spleen volume and improvements in QOL measures. Longer-term follow-up revealed a slight decline in QOL measures. However, this may be related to the well-described phenomenon of “response shift,” which reflects the changes in patients’ perspective on key QOL domains owing to repeated testing over the course of treatment. Despite this potential for response shift, the EORTC QLQ-C30 scales indicated that QOL was still improved.
relative to baseline with longer-term ruxolitinib treatment.

The hazard ratio for overall survival continued to favor ruxolitinib compared with placebo despite the majority of patients having crossed over from placebo to ruxolitinib, although statistical significance was not maintained. Although the rate of discontinuation from randomized treatment was higher in the placebo group than in the ruxolitinib group at the primary analysis, follow-up for overall survival was well balanced between the two treatment arms. The exposure to ruxolitinib in patients who crossed over from placebo was substantially longer than their exposure to placebo (105 weeks versus 37 weeks for median exposure to ruxolitinib and placebo, respectively), thus confounding the comparison of overall survival between the two treatment groups in favor of the placebo arm. To understand the effect of crossover to active treatment in placebo-controlled studies, several statistical methods have been developed. The exploratory analysis of overall survival using the RPSFT showed that crossover from placebo may have led to an underestimation of overall survival difference. This is consistent with findings from other oncology trials using this method, in which crossover to active treatment may also have led to an underestimation of the survival difference between placebo and active treatment. Consistent with the RPSFT analysis, the exploratory analysis using the generalized Gamma function showed that the probability of death in the placebo group was initially higher than in the original ruxolitinib-treated group, and that this probability decreased over time as patients originally assigned to placebo crossed over to receive ruxolitinib treatment. This finding is expected for a crossover trial in which the active treatment has a positive impact on survival. Although the specific mechanism underlying the prolonged survival observed in patients originally randomized to ruxolitinib in COMFORT-I is unknown, the reductions in spleen volume and improvements in functional status and QOL measures may have had a modulatory effect on the common causes of death not related to disease progression in patients with MF.

Consistent with our findings, a separate report of the COMFORT-II study showed that long-term ruxolitinib therapy was associated with an overall survival advantage relative to best available therapy at 5 years of follow-up [hazard ratio 0.48 (95% CI: 0.25-0.86); P=0.009]. Similar to what was observed in COMFORT-I, this analysis is likely biased against ruxolitinib as a result of the patients crossing over from best available therapy. However, in COMFORT-II the confounding effect of crossover is less severe than in COMFORT-I because of the longer exposure to best available therapy prior to crossover to ruxolitinib (median time of follow-up at primary analysis: 52 weeks in COMFORT-II and 32 weeks in COMFORT-I). Additionally, a pre-specified analysis of overall survival from pooled data from COMFORT-I and COMFORT-II supports an overall survival benefit of ruxolitinib compared with controls [hazard ratio 0.65 (95% CI: 0.46-0.90); P=0.01]. Further exploratory RPSFT analysis of pooled survival data from the COMFORT studies suggests an under-estimation of the survival difference between treatment groups because of the effect of crossover [RPSFT-corrected hazard ratio 0.29 (95% CI: 0.13-0.65); P=0.01].

In this 3-year update of COMFORT-I, ruxolitinib treatment demonstrated durable efficacy at doses that were stable over the course of long-term follow-up. Dose adjust-

Figure 4. Mean change in quality-of-life (QOL) measures assessed using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30. The figures shown are global health status, two functional domains (role and physical functioning), and symptom scores for fatigue, a key symptom affecting QOL in patients with myelofibrosis. Arrows indicate improvement.
Events occurred primarily in the first 8 to 12 weeks of the study, particularly in patients with baseline platelet counts between 100×10⁹/L and 200×10⁹/L who received a starting dose of 15 mg BID. By week 24, the median titrated dose was 10 mg BID for this subgroup of patients and 20 mg BID for those with a baseline platelet count >200×10⁹/L; doses stabilized with longer-term treatment.24

Overall, no unexpected safety or tolerability issues were detected during longer-term ruxolitinib treatment. As expected, anemia and thrombocytopenia mainly occurred early in the course of treatment, and there was no pattern of worsening of these events with longer-term exposure to ruxolitinib in patients who remained in the study. An additional analysis of the incidence of new-onset or worsening grade ≥3 anemia and thrombocytopenia that counted patients who experienced both grade 3 and 4 events in each grade yielded similar results.24 As previously noted, the initial increases in anemia and thrombocytopenia observed in the first 6 months of treatment and the subsequent decline in the incidence of these events was consistent with the timing of ruxolitinib dose adjustments. In ruxolitinib-treated patients, the rate of red blood cell transfusions increased in the first 8 weeks of treatment and later declined to levels similar to those in the placebo arm by week 36 and remained stable thereafter. This was consistent with the observed pattern of hemoglobin levels, which initially decreased and subsequently stabilized at a new steady state.24 Although cases of urinary tract infections and herpes zoster infections were observed in patients randomized to ruxolitinib, the incidence of these infections did not increase with longer-term therapy. As previously described, systematic review of the pattern of adverse events observed after treatment interruption or discontinuation in this analysis fails to support a specific withdrawal syndrome other than return to baseline disease.19,21

Longer-term ruxolitinib treatment did not affect the risk of transformation to acute myeloid leukemia. The rates of leukemic transformation per person-year of ruxolitinib exposure in patients originally randomized to ruxolitinib (0.0121/person-year) and in those originally randomized to placebo after they crossed over to ruxolitinib (0.0233/person-year) showed no evidence of an increased

**Figure 5.** (A) Overall survival in the intent-to-treat population as assessed by the Kaplan-Meier method. (B) Overall survival in the intent-to-treat population as assessed by the rank-preserving structural fail time (RPSFT) method. CI: confidence interval; HR: hazard ratio.
risk of leukemic transformation when compared with the rate derived from a historical control population of 310 patients with MF (0.038/person-year).\textsuperscript{35}

In summary, patients receiving ruxolitinib treatment for a median of 3 years in the COMFORT-I study maintained durable reductions in spleen volume and meaningful improvements in QOL measures. Overall survival continued to favor those patients originally randomized to ruxolitinib compared with those originally randomized to placebo despite the majority of those assigned to placebo crossing over to ruxolitinib treatment. This crossover may have contributed to an underestimation of the true survival difference between the two treatment arms. Ruxolitinib treatment continued to be generally well tolerated, and the incidence of new-onset grade 3 or 4 anemia and thrombocytopenia decreased with longer-term therapy. Collectively, long-term analyses from COMFORT-I and COMFORT-II continue to support the sustained efficacy and safety of ruxolitinib and provide evidence to support a meaningful ability of ruxolitinib to improve overall survival in patients with MF, and possibly modify the course of the disease.

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Appendix

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References