Received: 7 July 2022 | Revised: 9 January 2023 | Accepted: 12 January 2023

DOI: 10.1002/cncr.34707

ORIGINAL ARTICLE

Early intervention in myelofibrosis and impact on outcomes: A pooled analysis of the COMFORT-I and COMFORT-II studies

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Funding information
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Abstract

Background: In a pooled analysis of the phase 3 Controlled Myelofibrosis Study With Oral JAK Inhibitor Treatment I (COMFORT-I) and COMFORT-II clinical trials, adult patients with intermediate-2 or high-risk myelofibrosis who received oral ruxolitinib at randomization or after crossover from placebo or best available therapy (BAT) had improved overall survival (OS).

Methods: This post hoc analysis of pooled COMFORT data examined relevant disease outcomes based on the disease duration (≤12 or >12 months from diagnosis) before ruxolitinib initiation.

Results: The analysis included 525 patients (ruxolitinib: ≤12 months, $n = 84$; >12 months, $n = 216$; placebo/BAT: ≤12 months, $n = 66$; >12 months, $n = 159$); the median age was 65.0–70.0 years. Fewer thrombocytopenia and anemia events were observed among patients who initiated ruxolitinib treatment earlier. At Weeks 24 and 48, the spleen volume response (SVR) was higher for patients who initiated ruxolitinib earlier (47.6% vs. 32.9% at Week 24, $p = .0610$; 44.0% vs. 26.9% at Week 48, $p = .0149$). In a multivariable analysis of factors associated with spleen volume reduction, a logistic regression model that controlled for confounding factors found that a significantly greater binary reduction was observed among patients with shorter versus longer disease duration ($p = .022$). At Week 240, OS was significantly improved among patients who initiated ruxolitinib earlier (63% [95% CI, 51%–73%] vs. 57% [95% CI, 49%–64%]; hazard ratio, 1.53; 95% CI, 1.01–2.31; $p = .0430$). Regardless of disease duration, a longer OS was observed for patients who received ruxolitinib versus those who received placebo/BAT.

Conclusions: These findings suggest that earlier ruxolitinib initiation for adult patients with intermediate-2 and high-risk myelofibrosis may improve clinical outcomes, including fewer cytopenia events, durable SVR, and prolonged OS.

This trial was registered at ClinicalTrials.gov (NCT00952289 and NCT00934544).

Plain Language Summary

- Patients with myelofibrosis, a bone marrow cancer, often do not live as long as the general population. These patients may also have an enlarged spleen and difficult symptoms such as fatigue.
- Two large clinical trials showed that patients treated with the drug ruxolitinib lived longer and had improved symptoms compared to those treated with placebo or other standard treatments.
- Here it was examined whether starting treatment with ruxolitinib earlier (i.e., within a year of diagnosis) provided benefits versus delaying treatment.
- Patients who received ruxolitinib within a year of diagnosis lived longer and experienced fewer disease symptoms than those whose treatment was delayed.

KEYWORDS
Janus kinase inhibitor, myelofibrosis, myeloproliferative disorder, ruxolitinib, survival

INTRODUCTION

Myelofibrosis (MF) is a chronic myeloproliferative neoplasm characterized by bone marrow fibrosis, cytopenias, splenomegaly, and activating mutations in *JAK2*, *CALR*, and/or *MPL*.[1] Patients with MF have poor overall survival (OS) compared with the general population,[2,3] with OS shortest for those with intermediate-2 or high-risk MF (a median survival of 2–4 years).[4,5] Patients with MF also experience burdensome symptoms, including fatigue, abdominal discomfort, night sweats, bone pain, and pruritus, which negatively affect the quality of life. Although allogeneic stem cell transplantation is a potentially curative option, transplant-related morbidity and mortality are limiting, and many patients with MF are not eligible for this procedure because of their age and existing comorbidities.[6,7]

Ruxolitinib is a Janus kinase 1 (JAK1)/JAK2 inhibitor approved by the US Food and Drug Administration for patients with intermediate- or high-risk MF, including primary MF (PMF), post–polycythemia vera MF (PPV-MF), and post–essential thrombocythemia MF (PET-MF), and by the European Medicines Agency for treatment of disease-related splenomegaly or symptoms in adult patients with PMF, PPV-MF, or PET-MF.[8,9] In the randomized, phase 3, pivotal Controlled Myelofibrosis Study With Oral JAK Inhibitor Treatment I (COMFORT-I) and COMFORT-II clinical trials, patients with intermediate-2 or high-risk MF who received ruxolitinib at randomization or after crossover from placebo (COMFORT-I) or best available therapy (BAT; COMFORT-II) experienced clinical benefits, including improvements in spleen response, symptom burden, and OS.[10–16] The survival advantage among patients initially randomized to ruxolitinib was greater than among those in the crossover group, suggesting that earlier intervention may provide greater clinical benefits.[12] Additionally, previous reports from real-world and expanded-access settings have shown that patients earlier in their disease course (lower vs. higher risk category or lower vs. higher grade of bone marrow fibrosis) and those who initiated ruxolitinib earlier (≤2 vs. >2 years from diagnosis) had improved responses to ruxolitinib.[17–19]

To date, few studies have investigated whether earlier intervention with targeted MF therapies affects response and OS independent of the prognostic category. The objective of this analysis was to assess the association between MF disease duration before ruxolitinib treatment and disease outcomes by using pooled data from the randomized, phase 3 COMFORT-I and COMFORT-II studies.

MATERIALS AND METHODS

Study design and patients

COMFORT-I (NCT00952289) and COMFORT-II (NCT00934544) were randomized, phase 3 trials of ruxolitinib versus placebo or BAT, respectively, in patients with intermediate-2 or high-risk PMF, PPV-MF, or PET-MF. Eligibility criteria for the COMFORT trials have been described elsewhere[10,11]; briefly, inclusion criteria for both studies were as follows: age ≥ 18 years; diagnosis of PMF, PPV-MF, or PET-MF; intermediate-2 or high-risk MF according to the International Prognostic Scoring System[4]; palpable splenomegaly (≥5 cm below the left costal margin); peripheral blood blast count < 10% and platelet count ≥ 100 × 10^9/L; and Eastern Cooperative Oncology Group performance status ≤ 3 (on a scale of 0–5, with higher scores indicating increasing disability).[20] Patients were randomly assigned to receive oral ruxolitinib at a starting dose of 15 or 20 mg twice daily (based on platelet counts of 100–200 or >200 × 10^9/L, respectively) or a matched placebo (COMFORT-I)[10] or BAT (COMFORT-II).[11] The three most commonly used BATs in COMFORT-II were hydroxyurea (47%), no medication (33%), and prednisone/prednisolone (12%).[12] Patients initially assigned to placebo or BAT meeting protocol-defined worsening splenomegaly were permitted to cross over to ruxolitinib.[10,11] By the 3-year

follow-up, all continuing patients in the control groups had crossed over to ruxolitinib.[13,16]

In this post hoc analysis of COMFORT-I and COMFORT-II, the data from ruxolitinib-randomized patients in both studies were combined (ruxolitinib treatment group), and the data from the placebo and BAT groups were pooled (control group). The ruxolitinib treatment group was limited to those patients who were randomized to ruxolitinib and did not include patients who crossed over from control treatment to receive ruxolitinib. Patient subgroups were defined based on disease duration before randomized study treatment initiation (≤12 or >12 months from the time of diagnosis).

Assessments

The frequency of thrombocytopenia events (platelets < 100×10^9/L or platelet transfusion) and anemia events (hemoglobin < 100 g/L or red blood cell transfusion) was assessed throughout the follow-up period. The spleen volume was assessed by magnetic resonance imaging or computed tomography at baseline and at Weeks 24 and 48. The spleen volume response (SVR) was defined as a ≥35% reduction from baseline to Weeks 24 and 48. The duration of SVR was the time from the first spleen volume measurement that was a ≥35% reduction from baseline to the first measurement that was no longer a ≥35% reduction from baseline and was also a >25% increase from the nadir; patients were censored at their last assessment. Patients who had a ≥25% increase from baseline in spleen volume before their first SVR were not evaluable for the duration of SVR. Symptom response was assessed by the MF-Symptom Assessment Form total symptom score using data strictly from COMFORT-I (the MF-Symptom Assessment Form questionnaire was not used in COMFORT-II). Symptom response was defined as a total symptom score reduction ≥ 50% from baseline (TSS50) at Week 24. OS was defined as the time from randomization to death due to any cause and was evaluated using pooled COMFORT data.

Statistical analyses

Statistical analyses (p values) of differences between MF disease duration subgroups (≤12 vs. >12 months) were generated using log-rank tests for Kaplan–Meier analyses and Fisher exact (proportion of ruxolitinib-treated patients with SVR at Weeks 24 and 48) or χ^2 tests (proportion of ruxolitinib-treated patients with TSS50 at Weeks 24 and 48) for categorical data. OS was assessed using the Kaplan–Meier method, with patients randomized to placebo/BAT included in the control group regardless of crossover to ruxolitinib. For multivariable analyses, a logistic regression model was used to evaluate the effect of the following variables on spleen volume reduction: disease duration (≤12 vs. >12 months); study (COMFORT-I vs. COMFORT-II); age; sex; risk group (high vs. intermediate); baseline hemoglobin level, platelet count, white blood cell count, and spleen volume; and MF subtype (primary vs. post-PV/ET). Statistical significance was determined as p values < .05.

Ethics statement

The study protocols were approved by the institutional review board at each participating institution and were conducted in accordance with the principles of the Declaration of Helsinki. All patients provided written informed consent.

RESULTS

Patients

A total of 525 patients were included in this pooled analysis of patients from COMFORT-I and COMFORT-II (ruxolitinib: ≤12 months, n = 84; >12 months, n = 216; placebo/BAT: ≤12 months, n = 66; >12 months, n = 159; Table 1). The median age across groups ranged from 65.0 to 70.0 years. Baseline clinical characteristics were generally similar across the subgroups.

Ruxolitinib treatment exposure

There was a downward trend in average daily ruxolitinib dose over time in both disease duration groups (Figure 1).

Cytopenias

Among those patients who received ruxolitinib in the COMFORT studies, a numerically smaller percentage of patients experienced thrombocytopenia and anemia events among those who initiated treatment earlier (≤12 vs. >12 months), with differences observed as early as Weeks 4–8 (Figure 1). This trend was observed throughout the observation period.

SVR

The proportion of patients with SVR at Week 24 was numerically higher for patients who initiated ruxolitinib earlier (47.6% vs. 32.9%; p = .0610) and, at Week 48, the difference in the proportion of patients with SVR achieved statistical significance (44.0% vs. 26.9%; p = .0149; Figure 2). Mean reduction from baseline in spleen volume at Weeks 24 and 48 was numerically greater for patients who initiated ruxolitinib at ≤12 versus >12 months.

TABLE 1 Patient demographics and baseline clinical characteristics.

	Ruxolitinib		Placebo/BAT	
Variable	**MF ≤ 12 months[a] (*n* = 84)**	**MF > 12 months[a] (*n* = 216)**	**MF ≤ 12 months[a] (*n* = 66)**	**MF > 12 months[a] (*n* = 159)**
Age, mean (SD), years	64.4 (9.1)	66.6 (9.3)	66.8 (10.6)	67.8 (8.7)
Age, No. (%)				
≤65 years	45 (53.6)	93 (43.1)	28 (42.4)	60 (37.7)
>65 years	39 (46.4)	123 (56.9)	38 (57.6)	99 (62.3)
Male, No. (%)	52 (61.9)	110 (50.9)	38 (57.6)	91 (57.2)
BMI, mean (SD), kg/m^2	25.4 (3.7)	24.4 (4.7)	24.2 (3.9)	23.9 (3.8)
Laboratory parameters, mean (SD)				
Hgb, g/L	113.6 (23.6)	106.9 (19.8)	111.9 (23.0)	102.8 (20.0)
Platelets, Gi/L	320.2 (174.6)	303.5 (191.2)	273.6 (152.3)	279.6 (154.4)
Leukocytes, Gi/L	24.6 (21.9)	19.2 (17.6)	23.0 (16.6)	19.8 (15.7)
Spleen volume, median (range), cm^3	2216 (451–7766)	2539 (461–7462)	2207 (628–8881)	2555 (521–7701)

Abbreviations: BAT, best available therapy; BMI, body mass index; Hgb, hemoglobin; MF, myelofibrosis.
[a]MF disease duration before treatment initiation.

The probability estimate of SVR was higher among those with a shorter versus longer disease course, although the difference did not reach statistical significance (median duration of response, not reached vs. 230 weeks, respectively; hazard ratio, 1.39; 95% CI, 0.72–2.68; $p = .318$; Figure 2).

Symptom response

In an analysis of patients from COMFORT-I, a numerically larger proportion of patients who initiated ruxolitinib at ≤12 versus >12 months achieved TSS50 at Week 24 ($p = .0829$; Figure 3). The mean (SD) percentage change from baseline in TSS at Week 24 was −52.4% (41.6) for patients with shorter disease duration before ruxolitinib initiation (≤12 months) and −43.5% (51.2) for patients with longer disease duration (>12 months). Both TSS50 and mean percentage change from baseline in TSS favored patients treated with ruxolitinib at Week 24 compared with those who received placebo, regardless of MF disease duration.

OS

OS at Week 240 was significantly improved among patients who initiated ruxolitinib within ≤12 versus >12 months of diagnosis (63% [95% CI, 51%–73%] vs. 57% [95% CI, 49%–64%]; hazard ratio, 1.53; 95% CI, 1.01–2.31; $p = .0430$; Figure 4). Longer OS was also observed for patients treated with ruxolitinib versus those receiving placebo or BAT regardless of MF disease duration (placebo/BAT OS at Week 240: ≤12 months, 49% [95% CI, 36%–62%]; >12 months, 41% [95% CI, 32%–49%]).

Multivariable analyses of spleen volume reduction

In a multivariable analysis examining factors associated with spleen volume reduction, a significantly greater binary spleen volume reduction was observed among patients with shorter (≤12 months) versus longer (>12 months) MF disease duration when controlling for individual study, patient age, sex, risk group, baseline blood counts and spleen volume, and MF subtypes ($p = .022$; Table 2). In separate multivariable analyses, significantly smaller binary spleen volume reductions were observed in male versus female patients with disease duration ≤12 months (odds ratio [OR], 0.52 [95% CI, 0.31–0.89]; $p = .016$), but no difference was observed in patients with high-risk versus intermediate-2 MF with disease duration ≤12 months (OR, 0.75 [95% CI, 0.45–1.27]; $p = .29$).

DISCUSSION

In this pooled analysis of data from the COMFORT-I and COMFORT-II studies, earlier initiation of ruxolitinib (≤12 vs. >12 months from diagnosis) in patients with intermediate-2 and high-risk MF was associated with improved clinical outcomes, including significantly improved OS, improvements in spleen and symptom responses, and fewer thrombocytopenia and anemia events. It should be noted that, although all patients had International Prognostic Scoring System scores of 2 (intermediate-2) or ≥3 (high-risk) at study entry, some heterogeneity among patients may have existed regarding their individual disease states. However, the study results were further supported by a multivariable analysis demonstrating that shorter disease duration before ruxolitinib initiation was associated with significantly greater spleen volume reduction. Although younger age

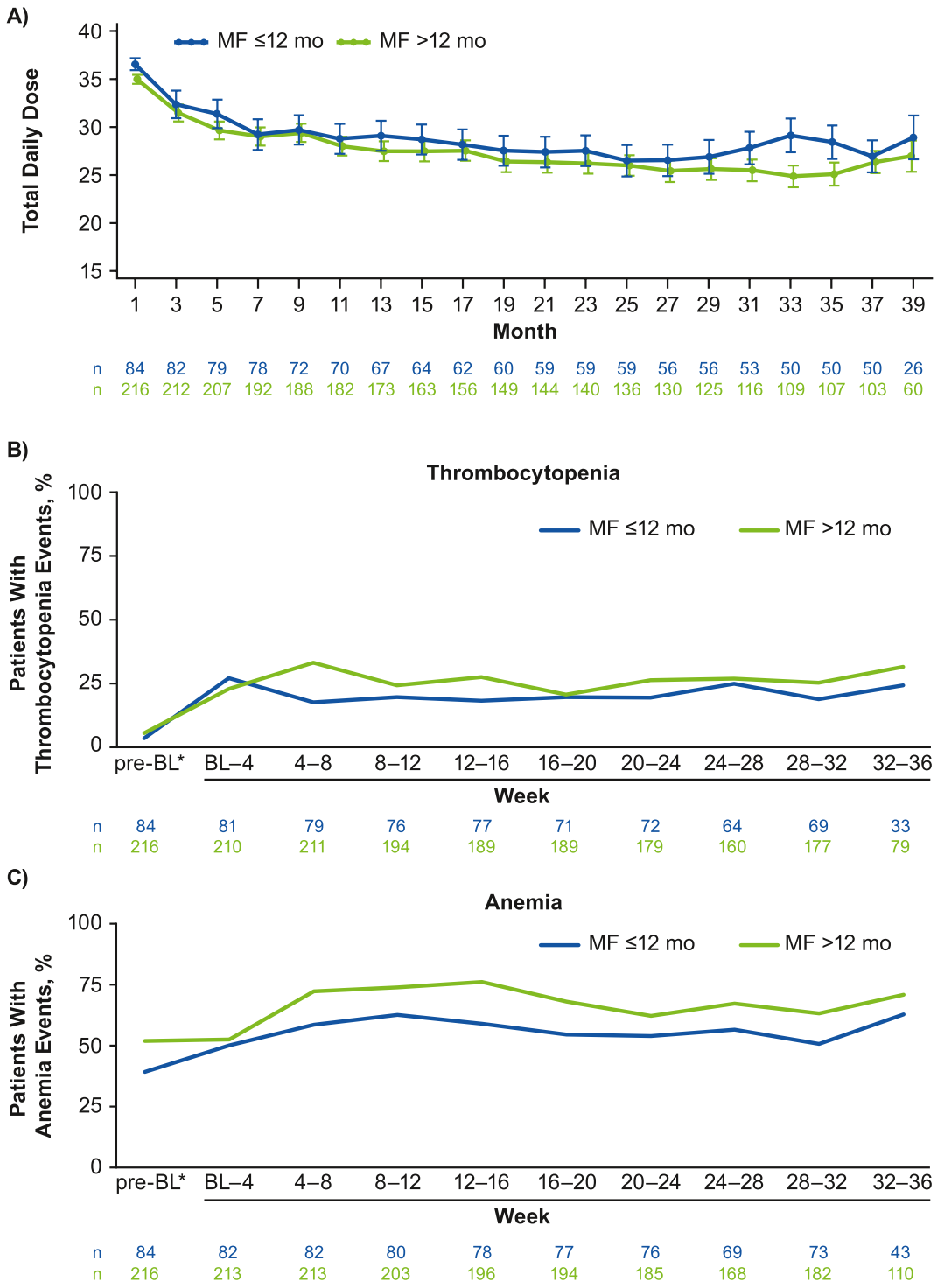

FIGURE 1 Ruxolitinib treatment exposure and cytopenias. (A) Average total daily ruxolitinib dose by disease duration subgroup. (B,C) Pooled COMFORT data for (B) thrombocytopenia events and (C) anemia events by MF disease duration (≤12 vs. >12 months) before ruxolitinib initiation. Thrombocytopenia was defined as a platelet count < 100 × 10^9/L or a platelet transfusion. Anemia was defined as hemoglobin < 100 g/L or a red blood cell transfusion. *Three months before baseline. BL indicates baseline; COMFORT, Controlled Myelofibrosis Study With Oral JAK Inhibitor Treatment; MF, myelofibrosis.

and higher baseline blood counts may have been confounders for improved clinical outcomes in this study, these factors likely reflect an earlier disease stage, and the observed outcomes support the rationale for early intervention in a real-world setting.

The results from this pooled analysis are consistent with earlier studies reporting clinical benefits in patients with MF who were treated with ruxolitinib, including in the COMFORT-I and COMFORT-II clinical trials,[10–16] as well as in real-world

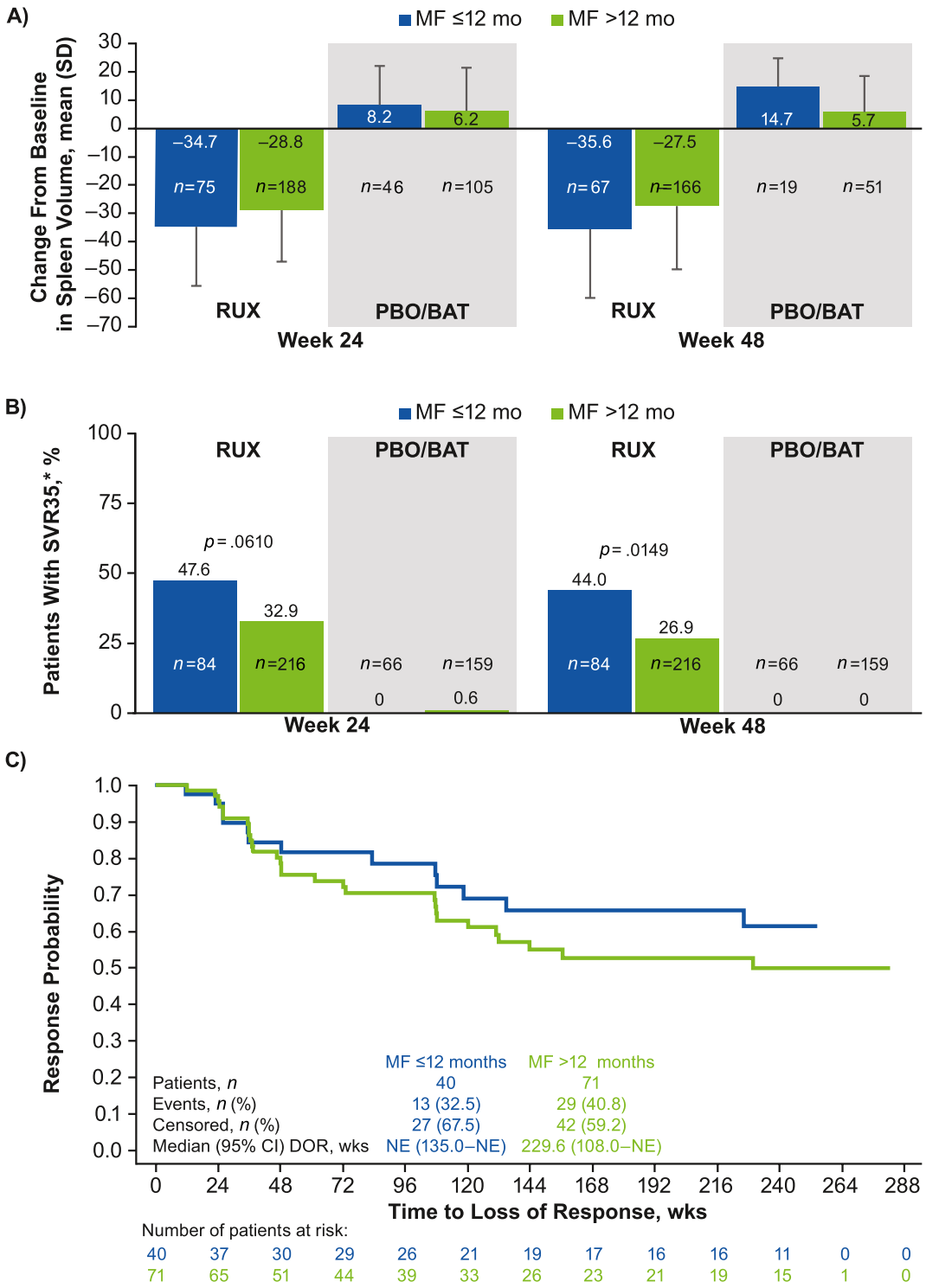

FIGURE 2 Spleen volume response. (A) Percentage change from baseline in spleen volume. (B) Percentage of patients achieving SVR at Weeks 24 and 48. (C) Duration of SVR among patients treated with ruxolitinib by MF disease duration (≤12 vs. >12 months) before treatment initiation. *SVR35 data were missing for 111 patients at Week 24 (RUX ≤12 months, $n = 9$; RUX >12 months, $n = 28$; PBO/BAT ≤12 months, $n = 20$; PBO/BAT >12 months, $n = 54$) and for 222 patients at Week 48 (RUX ≤12 months, $n = 17$; RUX >12 months, $n = 50$; PBO/BAT ≤12 months, $n = 47$; PBO/BAT >12 months, $n = 108$). BAT indicates best available therapy; DOR, duration of response; MF, myelofibrosis; NE; not evaluable; PBO, placebo; RUX, ruxolitinib; SVR, spleen volume response; SVR35, spleen volume reduction ≥ 35% from baseline.

settings.[17,21–23] Because ruxolitinib was approved for first-line treatment of intermediate- or high-risk MF by the US Food and Drug Administration in 2011,[8] and the National Comprehensive Cancer Network guidelines for myeloproliferative neoplasms recommend ruxolitinib as a first-line treatment for patients with higher-risk MF,[6] there is a compelling rationale to treat patients with

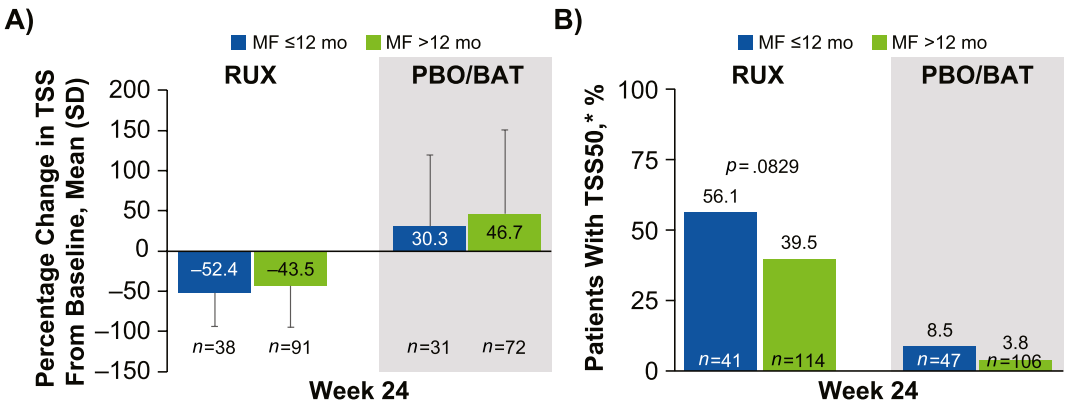

FIGURE 3 Symptom response. (A) Percentage change from baseline in TSS. (B) Proportion of patients achieving TSS50 at Week 24 by MF disease duration (≤12 vs. >12 months) before treatment initiation (COMFORT-I). *TSS50 data were missing for 76 patients (RUX ≤12 months, $n = 3$; RUX >12 months, $n = 23$; PBO/BAT ≤12 months, $n = 16$; PBO/BAT >12 months, $n = 34$). BAT indicates best available therapy; COMFORT, Controlled Myelofibrosis Study With Oral JAK Inhibitor Treatment; MF, myelofibrosis; PBO, placebo; RUX, ruxolitinib; TSS, total symptom score; TSS50, total symptom score reduction ≥50% from baseline.

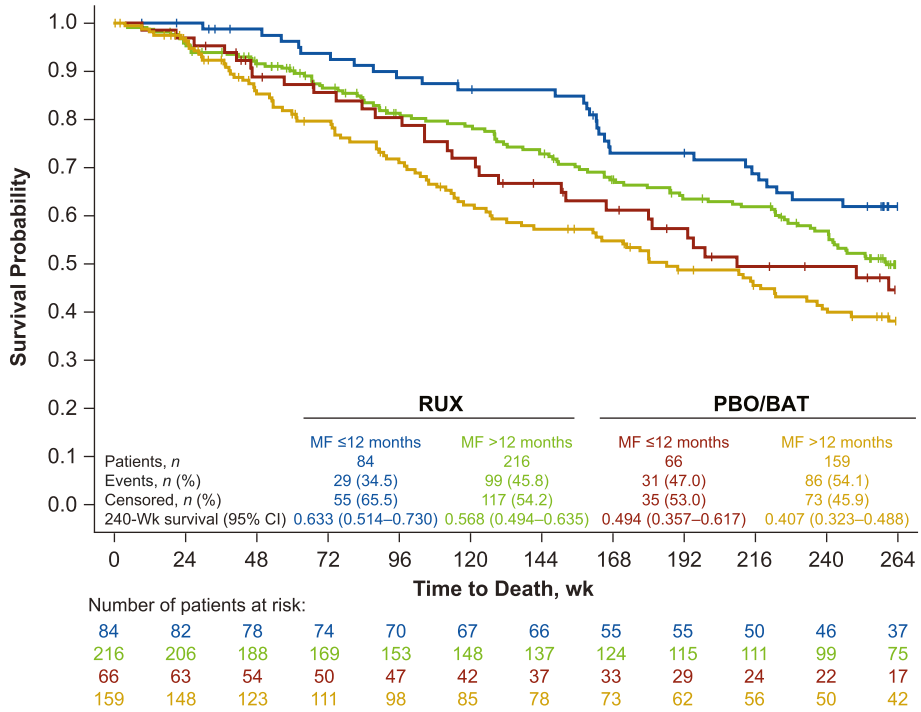

FIGURE 4 Pooled overall survival of patients with MF from COMFORT by MF disease duration (≤12 vs. >12 months) before treatment initiation. BAT indicates best available therapy; COMFORT, Controlled Myelofibrosis Study With Oral JAK Inhibitor Treatment; MF, myelofibrosis; PBO, placebo; RUX, ruxolitinib.

intermediate- or high-risk MF with ruxolitinib. Despite this, real-world treatment patterns indicate that many physicians delay or avoid ruxolitinib treatment, often in favor of hydroxyurea or watchful waiting. In a retrospective study of US veterans with MF in the post–ruxolitinib approval era, only 22.3% of patients with intermediate- or high-risk MF received ruxolitinib.[24] Two other retrospective studies that focused on post–ruxolitinib approval time frames found that hydroxyurea or interferon was used at a similar frequency as ruxolitinib to treat MF, including as a first-line agent and in patients with intermediate-2 disease.[25,26] Moreover, results from the European Registry for Myeloproliferative Neoplasms towards a better understanding of Epidemiology, Survival and Treatment study demonstrated that ruxolitinib may provide better clinical outcomes than hydroxyurea in real-world settings; time to first treatment with hydroxyurea was significantly shorter than for ruxolitinib, but median OS was significantly longer in patients treated with ruxolitinib.[23]

Evidence from several previous analyses provides support for earlier treatment with ruxolitinib. Results from an earlier pooled analysis from the COMFORT studies showed that the survival advantage was lower in patients who crossed over to ruxolitinib from

TABLE 2 Multivariable analysis of factors associated with reduction in spleen volume.

Factor	OR (95% CI)
Disease duration (≤12 vs. >12 months)	2.075 (1.117–3.898)[a]
Study (COMFORT-I vs. COMFORT-II)	1.547 (0.898–2.684)
Age	1.019 (0.987–1.053)
Sex (male vs. female)	0.354 (0.195–0.631)
Risk (high vs. intermediate)	0.477 (0.247–0.904)
Baseline hemoglobin level	1.015 (1.000–1.030)
Baseline platelet count	1.002 (1.001–1.004)
Baseline white blood cell count	1.005 (0.988–1.022)
Baseline spleen volume	1.000 (1.000–1.000)
MF subtype	
Post-PV vs. primary MF	0.982 (0.509–1.871)
Post-ET vs. primary MF	0.847 (0.390–1.806)

Abbreviations: COMFORT, Controlled Myelofibrosis Study With Oral JAK Inhibitor Treatment; ET, essential thrombocythemia; MF, myelofibrosis; OR, odds ratio; PV, polycythemia vera.
[a]Statistically significant ($p = .02$).

placebo or BAT compared with those who were initially randomized to ruxolitinib, suggesting that earlier ruxolitinib use may provide patient benefits.[12] Results from additional studies, including Ruxolitinib Patients With Primary Myelofibrosis, Post Polycythemia Myelofibrosis or Post-essential Thrombocythemia Myelofibrosis (JUMP) and UK ROBUST, suggest that ruxolitinib may induce response rates earlier in the disease course, including in patients with intermediate-1 risk or lower-grade bone marrow fibrosis.[17–19,27] Earlier initiation of ruxolitinib has also been shown to elicit better responses than later initiation,[18,19] similar to what was found in the current pooled analysis. Additionally, use of ruxolitinib as a first-line therapy led to significantly higher spleen responses in a subanalysis of the JUMP study, compared with second- or later-line therapy.[28] Of note in the current analysis, the total daily ruxolitinib dose appeared to be higher in the group who initiated ruxolitinib ≤12 months after diagnosis. This may contribute to the positive outcomes observed in patients who initiated earlier, perhaps as a result of higher dose tolerance.

Taken together, these results suggest that eligible patients would benefit from initiating ruxolitinib earlier rather than undergoing observation or treatment with hydroxyurea first. Although delaying treatment with ruxolitinib may be partially driven by the prevalence of anemia in patients with MF, with or without accompanying treatment with ruxolitinib, results from the Efficacy and Safety of Ruxolitinib in the Treatment of Anemic Myelofibrosis Patients study in patients with MF and anemia demonstrated that an alternative dosing regimen of ruxolitinib was efficacious and well tolerated in this patient population.[29] Additional prospective studies to further evaluate the impact of early intervention with ruxolitinib are warranted to confirm the results of this post hoc analysis presented here and to explore this approach in greater detail.

Several potential limitations of these analyses should be noted. Time from diagnosis may not reflect the true disease latency because of potential delays between disease onset and diagnosis. Additionally, the COMFORT-II study protocol allowed patients in the control arm to receive any commercially available agent as monotherapy or in combination and to change treatment at any time during the study. Consequently, separate subanalyses comparing ruxolitinib with specific BATs could not be performed. Although the results of our analyses suggest that early treatment with ruxolitinib is better than no treatment, future studies will need to be performed to put these results into context with other available MF therapies.

In summary, the findings from this pooled analysis of the COMFORT-I and COMFORT-II studies suggest that earlier ruxolitinib initiation in adult patients with intermediate-2 and high-risk MF is associated with improved clinical outcomes, including fewer cytopenia events, durable SVR, reduced symptom burden, and significantly prolonged OS. Although watch and wait remains a common management approach for newly diagnosed patients, these data suggest that patients with MF may benefit from earlier intervention.

AUTHOR CONTRIBUTIONS

Srdan Verstovsek: Conceptualization, methodology, and writing–review and editing. **Jean-Jacques Kiladjian:** Conceptualization, methodology, and writing–review and editing. **Alessandro M. Vannucchi:** Conceptualization, methodology, and writing–review and editing. **Ruben A. Mesa:** Conceptualization, methodology, and writing–review and editing. **Peg Squier:** Conceptualization, methodology, and writing–review and editing. **J. E. Hamer-Maansson:** Methodology, formal analysis, validation, and writing–review and editing. **Claire Harrison:** Conceptualization, methodology, and writing–review and editing.

ACKNOWLEDGMENTS

The authors thank Dilan Paranagama, PhD, of Incyte Corporation (Wilmington, Delaware) for his statistical consultation. Writing assistance was provided by Cory Pfeiffenberger, an employee of ICON (Blue Bell, Pennsylvania), and was funded by Incyte Corporation. This study was funded by Incyte. The study sponsor collaborated with the authors in the analysis and interpretation of the data and the writing of the manuscript.

CONFLICT OF INTEREST STATEMENT

Srdan Verstovsek has received research support from AstraZeneca, Blueprint Medicines Corporation, Celgene, CTI BioPharma Corp, Genentech, Gilead, Incyte Corporation, ItalPharma, Novartis, NS Pharma, PharmaEssentia, Promedior, Protagonist Therapeutics, Roche, and Sierra Oncology and is a paid consultant for Celgene, Incyte Corporation, Novartis, and Sierra Oncology. Jean-Jacques Kiladjian has served on advisory boards for AbbVie, AOP Orphan Pharmaceuticals, Bristol-Myers Squibb, Incyte Corporation, and Novartis and as a consultant for GlaxoSmithKline. Alessandro M. Vannucchi has received fees for advisory boards/lectures from Bristol-Myers Squibb, Incyte Corporation, and Novartis. Ruben A.

Mesa has served as a consultant for AbbVie, AOP, Blueprint Medicines Corporation, CTI Biopharma, GlaxoSmithKline, Incyte Corporation, La Jolla Pharma, Morphosys, Novartis, Sierra Oncology, and Telios; has served on a data and safety monitoring board for Telios; and has received research funding from AbbVie, Bristol-Myers Squibb, Celgene, CTI BioPharma Corp, Genentech, Gilead, Incyte Corporation, and Sierra Oncology. Peg Squier and J. E. Hamer-Maansson are employees and shareholders of Incyte Corporation. Claire Harrison has served on speakers' bureaus for Celgene, CTI BioPharma Corp, Gilead Sciences, Incyte Corporation, Janssen, Novartis, and Shire; has received research funding (institutional) from Celgene and Novartis; has served as an independent contractor for AbbVie, Bristol-Myers Squibb, and GlaxoSmithKline; and has received honoraria from AOP Orphan Pharmaceuticals, Celgene, CTI BioPharma Corp, Gilead Sciences, Novartis, Promedior, Roche, Shire, and Sierra Oncology.

DATA AVAILABILITY STATEMENT

Incyte Corporation (Wilmington, Delaware) is committed to data sharing that advances science and medicine while protecting patient privacy. Qualified external scientific researchers may request anonymized data sets owned by Incyte for the purpose of conducting legitimate scientific research. Researchers may request anonymized data sets from any interventional study (except phase 1 studies) for which the product and indication have been approved on or after January 1, 2020, in at least one major market (e.g., the United States, the European Union, or Japan). Data will be available upon request after the primary publication or 2 years after the study has ended. Information on Incyte's clinical trial data-sharing policy and instructions for submitting clinical trial data requests are available at https://www.incyte.com/Portals/0/Assets/Compliance%20and%20Transparency/clinical-trial-data-sharing.pdf?ver=2020-05-21-132838-960.

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How to cite this article: Verstovsek S, Kiladjian J-J, Vannucchi AM, et al. Early intervention in myelofibrosis and impact on outcomes: a pooled analysis of the COMFORT-I and COMFORT-II studies. *Cancer*. 2023;1-10. doi:10.1002/cncr.34707