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Treatment Comparison of Hydroxyurea vs Ruxolitinib in Essential Thrombocythemia: A Matched Cohort Analysis

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Michael R. Grunwald,[1] Ellen Ritchie,[2] Elisa Rumi,[3] Albert Assad,[4] J.E. Hamer-Maansson,[4] Jingbo Yu,[4] Evan Braunstein,[4] Francesco Passamonti[5]

[1]Department of Hematologic Oncology and Blood Disorders, Levine Cancer Institute, Atrium Health, Charlotte, NC, USA; [2]Weill Cornell Medical College and New York Presbyterian Hospital, New York, NY, USA; [3]Department of Molecular Medicine, University of Pavia, Pavia, Italy; [4]Incyte Corporation, Wilmington, DE, USA; [5]Ospedale di Circolo e Fondazione Macchi, Varese, Italy

Introduction

- Essential thrombocythemia (ET) is characterized by uncontrolled platelet production and clonal hematopoiesis leading to increased risk of vascular complications and high symptom burden[1,2]
- In patients with high-risk ET, hydroxyurea (HU) is the preferred first-line cytoreductive treatment; however, many patients are intolerant or refractory to HU[3]
- Ruxolitinib (RUX) has been shown to improve symptoms in patients with ET[4,5]; however, it is unknown whether switching from HU to RUX provides improved clinical benefit

Objective

- This post hoc analysis compared the clinical outcomes of patients with ET who received HU and switched to RUX with those who received HU only

Methods

Study Design

- The study design and patient eligibility criteria are presented in **Table 1**

Table 1. Study Design and Patient Eligibility

Cohort	HU-RUX	HU
Source study for patients	Data from patients with ET from a completed phase 2 interventional study (INCB 18424-256; NCT00726232)[6] of ruxolitinib in patients who were refractory or intolerant to HU	• Patients who received HU only in the **M**yelofibrosis and Essential Thrombocythemia **O**bservational **S**tudy across 124 sites (MOST; NCT02953704) • Data from patient records and physician-reported baseline data (demographics, signs and symptoms, and treatment) were collected as previously characterized during usual-care visits over a planned observation period of 36 months[1]
Inclusion criteria for this analysis	All patients in the study were included for matching	• Patients eligible for this study took only HU prior to enrollment and at least 180 days of HU treatment with no other ET treatment post enrollment

ET, essential thrombocythemia; HU, patients who stayed on hydroxyurea; HU-RUX, patients who switched to ruxolitinib after hydroxyurea.

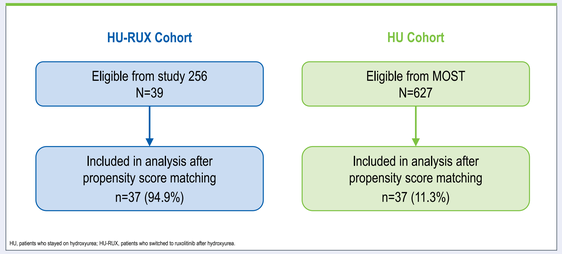
- Patients from MOST and INCB 18424-256 were matched 1:1 using propensity score based on age cohort (<60 years, ≥60 years), sex, body mass index, duration of ET disease, thrombotic event history, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30) global health status score at index (defined as initiation of RUX in HU-RUX cohort and MOST study enrollment in HU cohort)

Results

Patients

- A total of 39 and 627 patients from INCB 18424-256 and MOST, respectively, were eligible for this analysis (**Figure 1**)
  - After propensity score matching, 37 patients from each study were included

Figure 1. Patient Disposition



HU, patients who stayed on hydroxyurea; HU-RUX, patients who switched to ruxolitinib after hydroxyurea.

- A summary of patient demographics and baseline characteristics are presented in **Table 2**
  - The majority of patients were women in both cohorts (HU-RUX, 64.9%; HU, 73.0%)
  - The median duration of disease was similar at 5.7 months in the HU-RUX and 5.3 months in the HU cohorts

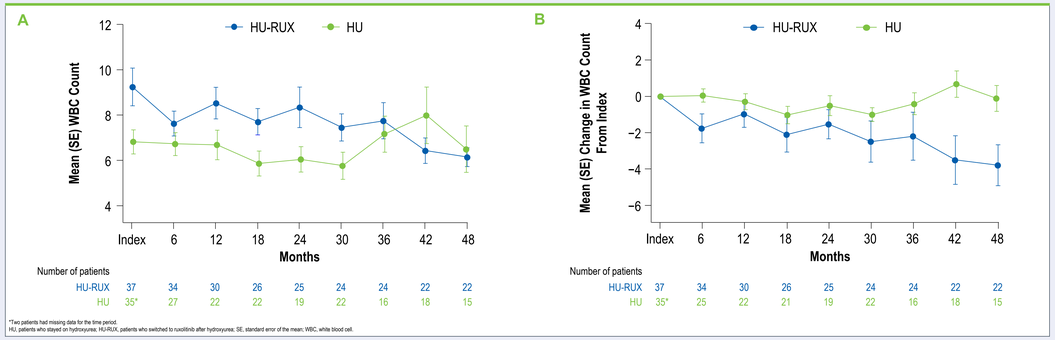
Table 2. Patient Demographics and Baseline Characteristics at Enrollment

Variable	HU-RUX Cohort (N=37)	HU Cohort (N=37)
Age, y		
Median (range)	50.0 (25.0-87.0)	55.0 (39.0-87.0)
≥60, n (%)	10 (27.0)	10 (27.0)
Sex, n (%)		
Women	24 (64.9)	27 (73.0)
Time from ET diagnosis to enrollment, y		
Median (range)	5.7 (0-20.9)	5.3 (0.4-33.5)
History of TEs before enrollment, n (%)	5 (13.5)	4 (10.8)
EORTC QLQ-C30 global health status QoL, n	37	37
Mean (SD)	73.0 (22.9)	78.6 (20.1)
Patients with WBC count (×10^9/L), n*	37	35
Mean (SD)	9.3 (5.1)	6.8 (3.1)
Patients with platelet count (×10^9/L), n*	37	35
Mean (SD)	1027.4 (497.8)	513.9 (154.7)
Patients with palpable spleen, n*,†	30	26
Yes, n (%)	3 (10.0)	0
No, n (%)	27 (90.0)	25 (96.2)

*Two patients in the HU cohort had missing WBC/platelet count data, and 4 and 7 patients in HU and HU-RUX cohorts, respectively, had missing spleen data at enrollment. †One patient in HU cohort reported palpable spleen as indeterminate.
EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; ET, essential thrombocythemia; HU, patients who stayed on hydroxyurea; HU-RUX, patients who switched to ruxolitinib after hydroxyurea; QoL, quality of life; SD, standard deviation; TE, thrombotic event; WBC, white blood cell.

- Mean white blood cell (WBC) count and change in WBC count from index over time are presented in **Figure 2**
  - In the HU-RUX cohort, WBC counts decreased from index to 6 months (mean [standard deviation (SD)] change, −1.8 [4.6]) and continued to decrease, reaching a mean (SD) change from index of −3.8 (5.3) at 48 months
  - In the HU cohort, mean (SD) change in WBC counts from index remained near zero at 6 and 48 months (0 [1.8] and −0.1 [2.7])
  - For the HU-RUX vs HU cohort, the difference in mean WBC count change from index was significant at month 42 (*P*=0.0138) and significance was maintained through month 48 (*P*=0.0182)

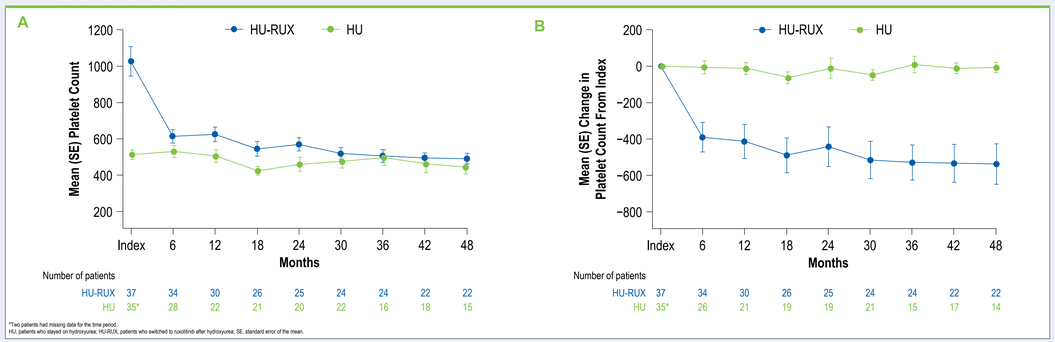
Figure 2. Mean WBC Counts (A) and Mean Change From Index in WBC Counts Over Time (B) in Patients Who Switched to RUX After HU Therapy and of Those Who Were Treated With HU Alone



*Two patients had missing data for the time period.
HU, patients who stayed on hydroxyurea; HU-RUX, patients who switched to ruxolitinib after hydroxyurea; SE, standard error of the mean; WBC, white blood cell.

- Mean platelet count and change in platelet count from index over time are presented in **Figure 3**
  - In the HU-RUX cohort, platelet counts decreased rapidly between index and 6 months (mean [SD] change, −391.7 [472.9]) and declined further thereafter, reaching a mean (SD) change from index of −539.0 (521.8) at 48 months
  - In the HU cohort, platelet counts remained unchanged at 6 and 48 months compared with index (−5.7 [175.3] and −6.9 [105.1])
  - For the HU-RUX vs HU cohort, the difference in mean platelet count change from index was significant at month 6 (*P*=0.0002) and significance was maintained through month 48 (*P*=0.0007).

Figure 3. Mean Platelet Counts (A) and Mean Change From Index in Platelet Counts Over Time (B) in Patients Who Switched to RUX After HU Therapy and of Those Who Were Treated With HU Alone



*Two patients had missing data for the time period.
HU, patients who stayed on hydroxyurea; HU-RUX, patients who switched to ruxolitinib after hydroxyurea; SE, standard error of the mean.

- In HU-RUX, the number of patients with splenomegaly decreased from 3 patients at index to 1 patient at 12 months, and this was maintained through 48 months; no patients in the HU cohort had palpable spleen at baseline
- A summary of thrombotic and hemorrhagic treatment-emergent adverse events in the HU-RUX and HU cohorts is shown in **Table 3**. Analysis adjusting for patient differences is not feasible due to small sample size

Table 3. Thrombotic and Hemorrhagic TEAEs*

Variable	HU-RUX Cohort (N=37)	HU Cohort (N=37)
Thrombotic events, n (%)	3 (8.1)	0
Arterial		
Transient ischemic attack	1 (2.7)	0
Cerebrovascular accident	1 (2.7)	0
Venous		
Pulmonary embolism	1 (2.7)	0
Median (range) time to thrombotic event, mo	39.2 (35.8-39.4)	—
Grade 3/4 hemorrhagic events, n (%)	1 (2.7)	0
Death from thrombotic or hemorrhagic events, n (%)	0	0

*Median (range) follow-up time for patients in HU-RUX and HU cohorts was 93 (4.8-116.6) and 48.3 (10.3-61.4) months, respectively.
HU, patients who stayed on hydroxyurea; HU-RUX, patients who switched to ruxolitinib after hydroxyurea; TEAE, treatment-emergent adverse event.

Conclusions

- **Switching from HU to RUX resulted in improvement in both WBC and platelet counts in patients who were refractory or intolerant to HU**
- **Patients with splenomegaly who switched from HU to RUX also showed a reduction in splenomegaly over time**
- **These results demonstrate that RUX treatment can produce hematologic responses in HU-treated ET patients with abnormal blood counts**

Disclosures

Grunwald: Consulting fees – *AbbVie, Agios/Servier, Amgen, Astellas Pharma, Blueprint Medicines, Bristol Myers Squibb, Cardinal Health, CTI BioPharma, Daiichi Sankyo, Gamida Cell, Genentech, Gilead Sciences, GSK/Sierra Oncology, Incyte Corporation, Invitae Corporation, Jazz Pharmaceuticals, Karius, Novartis, Ono Pharmaceutical Co., Pfizer, Pharmacosmos, Premier Pharma, Sierra Oncology, Stemline Therapeutics*; Research support – *Incyte Corporation, Janssen*; Stock ownership – *Medtronic*. **Ritchie:** Consultancy – *Celgene, Incyte Corporation, Novartis*; Speakers' bureau – *Ariad, Celgene, Incyte Corporation, Novartis*; Research funding – *Astellas Pharma, Bristol Myers Squibb, Novartis, NS Pharma, Pfizer*; Travel support – *Celgene, Novartis*. **Rumi:** Consulting – *Novartis*. **Assad, Hamer-Maansson, Yu, Braunstein:** Current employment, current equity holder in publicly traded company – *Incyte Corporation*. **Passamonti:** Honoraria – *AbbVie, AOP Health, Bristol Myers Squibb, Celgene, Janssen, Karyopharm Therapeutics, Kyowa Kirin, MEI Pharma, Novartis, Roche*; Advisory board – *AbbVie, AOP Health, Bristol Myers Squibb, Celgene, Janssen, Karyopharm Therapeutics, Kyowa Kirin, MEI Pharma, Novartis, Roche*; Research funding – *Bristol Myers Squibb*.

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