Selected Abstracts

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Blood (ASH Annual Meeting Abstracts) 120: 800.

Abstract 1 of 1 **Oral Sessions**

634. Myeloproliferative Syndromes - Clinical: Myeloproliferative neoplasms - Novel Therapies II

Long-Term Outcome of Ruxolitinib Treatment in Patients with Myelofibrosis: Durable Reductions in Spleen Volume, Improvements in Quality of Life, and Overall Survival Advantage in COMFORT-I

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Background: Ruxolitinib (RUX), an oral JAK1/JAK2 inhibitor, reduced spleen volume (SV), improved myelofibrosis (MF)-associated symptoms and quality of life (QoL), and appeared to exhibit a survival advantage over placebo (PBO) in patients (pts) with MF regardless of JAK2V617F mutation status in the phase III COMFORT-I study. We describe long-term efficacy and safety of RUX from COMFORT-I, with 1 year of additional follow up beyond previously published data.

Methods: Eligible pts (N=309) were randomized (1:1) to RUX or PBO. The primary analysis occurred when all pts completed 24 weeks (wks) and when half the pts completed 36 wks of treatment. All pts receiving PBO were eligible for crossover to RUX after the primary analysis; crossover before wk 24 was permitted if pts met protocol-defined criteria for worsening splenomegaly. The proportion of pts with ≥35% SV reduction at 24 wks (primary endpoint) and durability of SV response were assessed. Although symptom burden (measured daily using the modified MF Symptom Assessment Form v2.0) was only measured up to wk 24, QoL continued to be evaluated beyond wk 24 (every 24 wks) using the EORTC QoL Questionnaire-Core 30 (QLQ-C30). Overall survival (OS) was assessed according to original randomized treatment.

Results: In this updated analysis, median follow-up of pts randomized to RUX was 102 wks. All pts receiving PBO completed crossover or discontinued within 3 months of the primary analysis. Of 134 pts randomized to RUX who remained on treatment after the primary data analysis, 100 continue on study. Mean SV reduction in pts randomized to RUX was 31.6% at wk 24 and has remained stable with additional follow up through wk 96 (Table). In pts who achieved a ≥35% SV reduction, response was durable, with a median response duration of 108 wks. RUX treatment was also associated with durable improvements in the Global Health Status/QoL (Table) and the 5 functional domains of the EORTC QLQ-C30. Twenty-seven (27) pts randomized to RUX and 41 pts randomized to PBO died, representing a continued OS benefit in favor of RUX (HR=0.58; 95% CI: 0.36, 0.95; $P = 0.028$; Fig 1) similar in magnitude to that previously reported. OS favored RUX across subgroups including starting dose as well as baseline risk status and hemoglobin (Hgb).

Of 34 pts randomized to RUX who discontinued after the primary analysis, 4 discontinued for an adverse event (AE). In pts who continued on RUX, anemia and thrombocytopenia remained the most frequently reported AEs. New onset of grade 3 or 4 anemia and thrombocytopenia was reported in only 12 and 5 pts, respectively. One pt discontinued for anemia. Overall, among all pts randomized to RUX, Grade 3 and 4 anemia regardless of baseline Hgb was reported in 37.4% and 14.8% of pts, respectively. Similarly, Grade 3 and 4 thrombocytopenia was reported in 11.0% and 5.2% of pts, respectively. These rates were similar to those reported in the primary analysis. By wk 36, the proportion of pts receiving red blood cell transfusions decreased to the level seen with PBO and remained stable thereafter (Fig 2). Rates of nonhematologic AEs adjusted for increased follow-up duration remain similar to those seen at the time of the primary data analysis. No additional cases of acute myeloid leukemia (AML) in pts randomized to RUX were reported. Two pts originally randomized to PBO developed AML, 21 and 178 days after crossover to RUX. There continued to be no reports of a withdrawal syndrome after RUX discontinuation.

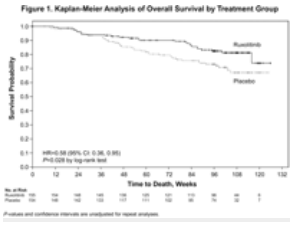
Conclusions: RUX provides durable reductions in SV and improvements in QoL. Although all pts randomized to PBO crossed over to RUX shortly after the primary analysis, with 1 year of additional follow up, RUX continues to be associated with a survival advantage over PBO. RUX continues to be well tolerated; the AE profile with long-term treatment is consistent with that previously reported. The proportion of pts receiving transfusions decreased over time to rates similar to PBO, and there were no reports of a specific withdrawal syndrome or cytokine rebound phenomenon after RUX discontinuation.

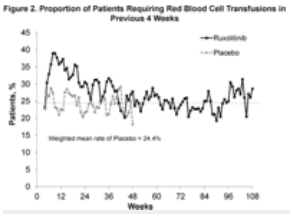
Table. Efficacy of RUX on SV and QoL

		RUX	PBO
Mean % change in SV ± SEM			
Wk	24	□31.6 ± 1.6	8.2 ± 1.5
	36	□31.9 ± 1.9	8.6 ± 1.8
	48	□31.6 ± 2.1	NA
	60	□32.9 ± 2.4	NA
	72	□34.1 ± 2.5	NA
	96	□34.9 ± 3.0	NA
Mean change in EORTC QLQ-C30 Global Health Status/QoL ± SEM*			
Wk	24	12.3 ± 2.2	□3.7 ± 2.1
	48	13.6 ± 2.2	NA
	72	14.1 ± 2.5	NA
	96	13.0 ± 2.4	NA

* Improvements >10 are clinically significant.

NA, not available; SEM, standard error of the mean.





Disclosures: Verstovsek: *Incyte Corporation:* Research Funding. **Mesa:** *Incyte:* Research Funding; *Lilly:* Research Funding; *Sanofi:* Research Funding; *NS Pharma:* Research Funding; *YM Bioscience:* Research Funding. **Gotlib:** *Incyte:* Consultancy, travel to congress Other. **Levy:** *Incyte:* Employment, Equity Ownership. **Gupta:** *Incyte:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Novartis:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Celgene:* Research Funding; *YM Biosciences:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Sanofiå]Aventis:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Research Funding. **Catalano:** *Incyte:* Consultancy. **Deininger:** *Bristol-Myers Squibb:* Consultancy, Research Funding; *Novartis:* Consultancy; *Ariad:* Consultancy. **Miller:** *Novartis:* Consultancy, Research Funding, Speakers Bureau, development of educational presentations Other; *Incyte:* development of educational presentations, development of educational presentations Other. **Talpaz:** *Novartis:* Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *B.M.S.:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *Ariad:* Research Funding; *Sanofi:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *Teva:* Membership on an entity's Board of Directors or advisory committees; *Pfizer:* Membership on an entity's Board of Directors or advisory committees. **Winton:** *Incyte:* Consultancy, Honoraria. **Arcasoy:** *Incyte:* Research Funding. **Lyons:** *Incyte:* Consultancy, Research Funding; *Amgen:* Consultancy, Research Funding; *Novartis:* Research Funding; *Telik:* Research Funding. **Paquette:** *Incyte:* Consultancy. **Vaddi:** *Incyte:* Employment, Equity Ownership. **Erickson-Viitanen:** *Incyte:* Employment, Equity Ownership. **Sun:** *Incyte Corporation:* Employment, Equity Ownership. **Sandor:** *Incyte Corporation:* Employment, Equity Ownership. **Kantarjian:** *Incyte:* grant support Other.

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 Online ISSN: 1528-0020