Results From the 208-Week (4-Year) Follow-up of the RESPONSE Trial, a Phase 3 Study Comparing Ruxolitinib (Rux) With Best Available Therapy (BAT) for the Treatment of Polycythemia Vera (PV)

Jean-Jacques Kiladjian,[1] Srdan Verstovsek,[2] Martin Griesshammer,[3] Tamas Masszi,[4] Simon Durrant,[5] Francesco Passamonti,[6] Claire N. Harrison,[7] Fabrizio Pane,[8] Pierre Zachee,[9] Keita Kirito,[10] Carlos Besses,[11] Masayuki Hino,[12] Ana Ines Varela,[13] Carole B. Miller,[14] Elisa Rumi,[15] Vittorio Rosti,[16] Igor W. Blau,[17] Ruben A. Mesa,[18] Tuochuan Dong,[19] Nathalie Francillard,[20] Alessandro M. Vannucchi[21]

[1]Hôpital Saint-Louis et Université Paris Diderot, Paris, France; [2]Department of Leukemia, The University of Texas MD Anderson Cancer Center, Houston, Texas, USA; [3]Department of Hematology, Oncology, Hemostaseology and Palliative Care, Johannes Wesling Clinic, Minden, Germany; [4]3rd Department of Internal Medicine, Semmelweis University, Budapest, Hungary; [5]Royal Brisbane & Women's Hospital, Brisbane, Australia; [6]Hematology, Department of Medicine and Surgery, University of Insubria, Varese, Italy; [7]Guy's and St. Thomas' NHS Foundation Trust, London, UK; [8]Division of Hematology, University of Naples Federico II, Naples, Italy; [9]ZNA Stuivenberg, Antwerp, Belgium; [10]Department of Hematology and Oncology, University of Yamanashi, Japan; [11]Haematology Department, Hospital del Mar-IMIM, Universidad Autónoma de Barcelona, Barcelona, Spain; [12]Department of Clinical Hematology and Diagnostics, Osaka University Graduate School of Medicine, Osaka, Japan; [13]Hospital Jose Maria Ramos Mejia, Buenos Aires, Argentina; [14]Saint Agnes Cancer Institute, Baltimore, Maryland, USA; [15]Department of Haematology Oncology, Fondazione IRCCS Policlinico S. Matteo, Pavia, Italy; [16]Center for the Study of Myelofibrosis, IRCCS Policlinico San Matteo Foundation, Pavia, Italy; [17]Medical Department, Division of Hematology, Oncology, and Tumor Immunology, Charité Universitätsmedizin Berlin, Germany; [18]UT Health San Antonio Cancer Center, San Antonio, Texas, USA; [19]Novartis Pharmaceuticals Corporation, East Hanover, New Jersey, USA; [20]Novartis Pharma S.A.S, Rueil Malmaison, France; [21]University of Florence, Florence, Italy
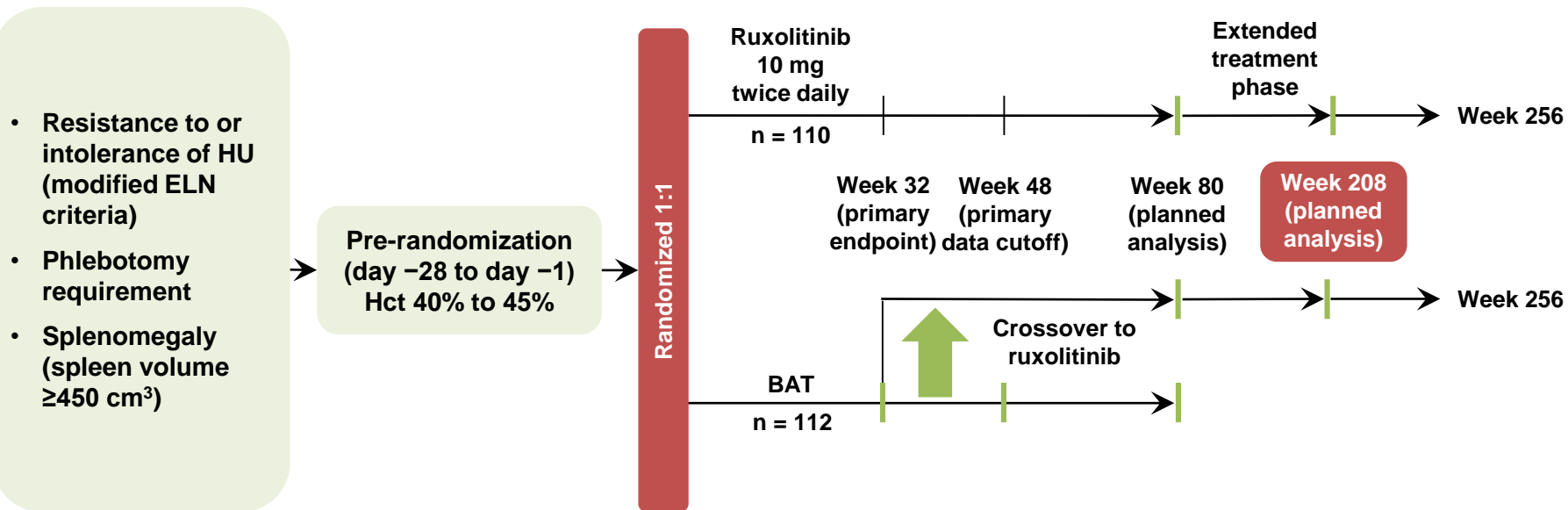
Disclosures

- Novartis, membership on an entity's Board of Directors or Advisory Committees and Research Funding.

- AOP Orphan, membership on an entity's Board of Directors or Advisory Committees and Research Funding.

- Celgene, membership on an entity's Board of Directors or Advisory Committees.

- Study sponsored by Novartis and Incyte.

- Medical Writing support provided by Novartis.

Introduction

- RESPONSE (NCT01243944) is a global, multicenter, open-label, Phase 3 trial comparing the efficacy and safety of ruxolitinib with best available therapy in patients with polycythemia vera (PV) who are resistant to or intolerant of hydroxyurea.[1]

- The primary endpoint of the RESPONSE study was achieved demonstrating that ruxolitinib was superior to best available therapy in controlling hematocrit and reducing spleen volume at week 32.[1]

- This preplanned analysis of the RESPONSE study was conducted to evaluate the long-term safety and durability of efficacy of ruxolitinib after a follow-up of 208 weeks (after last patient has been followed for 208 weeks [4 years]).

  - The study is currently ongoing.

1. Vannucchi AM et al. *N Engl J Med.* 2015;372(5):426-435.

American Society *of* Hematology

RESPONSE Study Design

- **Resistance to or intolerance of HU (modified ELN criteria)**
- **Phlebotomy requirement**
- **Splenomegaly (spleen volume ≥450 cm³)**

Pre-randomization (day −28 to day −1) Hct 40% to 45%

Randomized 1:1

Ruxolitinib 10 mg twice daily
n = 110

Extended treatment phase

Week 256

Week 32 (primary endpoint) **Week 48 (primary data cutoff)** **Week 80 (planned analysis)** **Week 208 (planned analysis)**

Crossover to ruxolitinib

Week 256

BAT
n = 112

- Patients randomized to BAT were permitted to cross over to ruxolitinib at week 32, if they did not meet the primary endpoint or after week 32 in case of phlebotomy eligibility or splenomegaly progression.

BAT; best available therapy; ELN, European LeukemiaNet; Hct, hematocrit; HU, hydroxyurea.

American Society *of* Hematology

Endpoints

Durability of Efficacy

- Durability of efficacy in the ruxolitinib arm, including durability of the primary response, primary response components (hematocrit control and spleen volume reduction), and overall clinicohematologic response (CLHM).

  – Primary endpoint was a composite of (1) hematocrit control and (2) a ≥ 35% reduction in spleen volume as measured by magnetic resonance imaging at Week 32.

  – Complete hematologic response (CHR) was a key secondary endpoint defined as hematocrit control, platelet count ≤ 400 × 10^9/L, and white blood cell count ≤ 10 × 10^9/L.

  – Overall CLHM was a key secondary endpoint defined CHR and spleen volume reduction ≥ 35% by imaging.

- Overall survival was an exploratory endpoint.

Safety

- Adverse events, regardless of causality, were summarized.

Patient Disposition

	Ruxolitinib (n = 110)	BAT* (n = 112)	Ruxolitinib Crossover (n = 98)
Ongoing treatment at database lock, n (%)	41 (37)	0	37 (38)
Completed treatment period	32 (29)	1 (1)	30 (31)
Reasons for discontinuation of treatment, n (%)			
Adverse event	15 (14)	2 (2)	14 (14)
Disease progression	12 (11)	1 (1)	8 (8)
Patient decision	6 (6)	5 (5)	6 (6)
Lack of efficacy	0	100 (89)	0
Others (protocol deviation, lost to follow-up, and physician decision)	3 (3)	2 (2)	3 (3)
Death[†]	1 (1)	0	0
Median treatment exposure, weeks	225	34	189

* Initial BAT included HU (n = 66), IFN/pegylated IFN (n = 13), anagrelide (n = 8), IMIDs (n = 5), pipobroman (n = 2), and observation (n = 17).
For patients who were randomized to BAT and then crossed over to ruxolitinib, the reasons for end of BAT are reported in the "BAT" column.
[†]One patient, determined by the Investigator to have discontinued the study treatment due to AEs, died afterwards.

BAT, best available therapy; HU, hydroxyurea; IFN, interferon; IMIDs, immunomodulators.

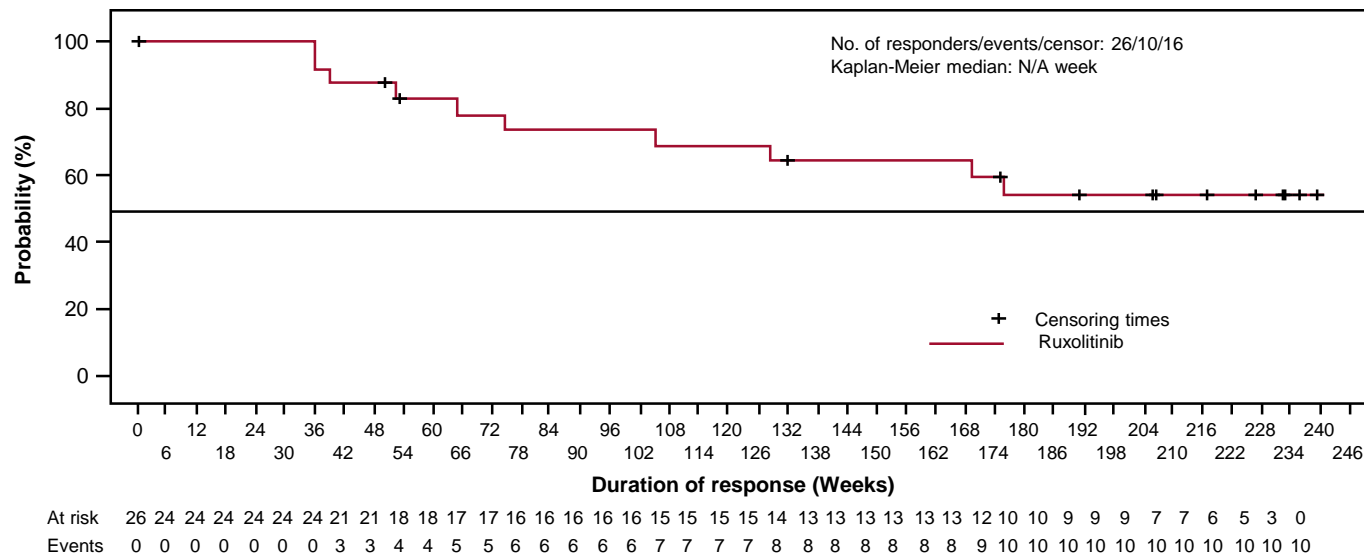American Society *of* Hematology

Durability of Primary Response With Ruxolitinib
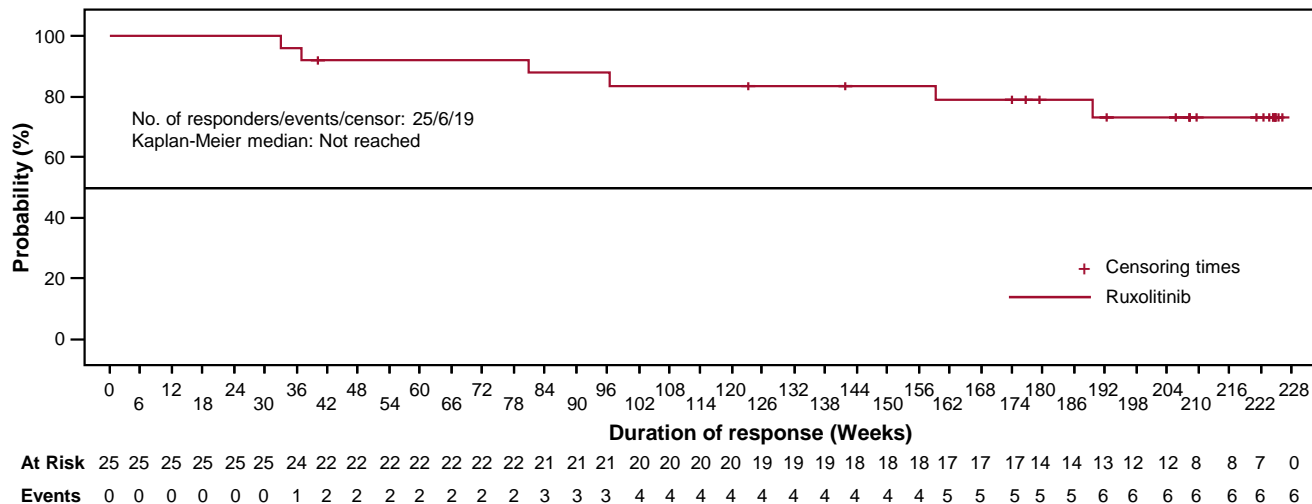
- At the time of analysis in the ruxolitinib arm, 6 of 25 primary responders have progressed.
- The K-M estimate of duration of maintaining primary response for 208 weeks (4 years) was 0.73 (95% CI: 0.49, 0.87).
  - The K-M estimates of duration of hematocrit control for 208 weeks was 0.73 (95% CI: 0.60, 0.83).
  - The K-M estimates of duration of at least 35% reduction in the spleen volume was 0.86 (95% CI: 0.61, 0.95).
- Median duration of primary response has not been reached.
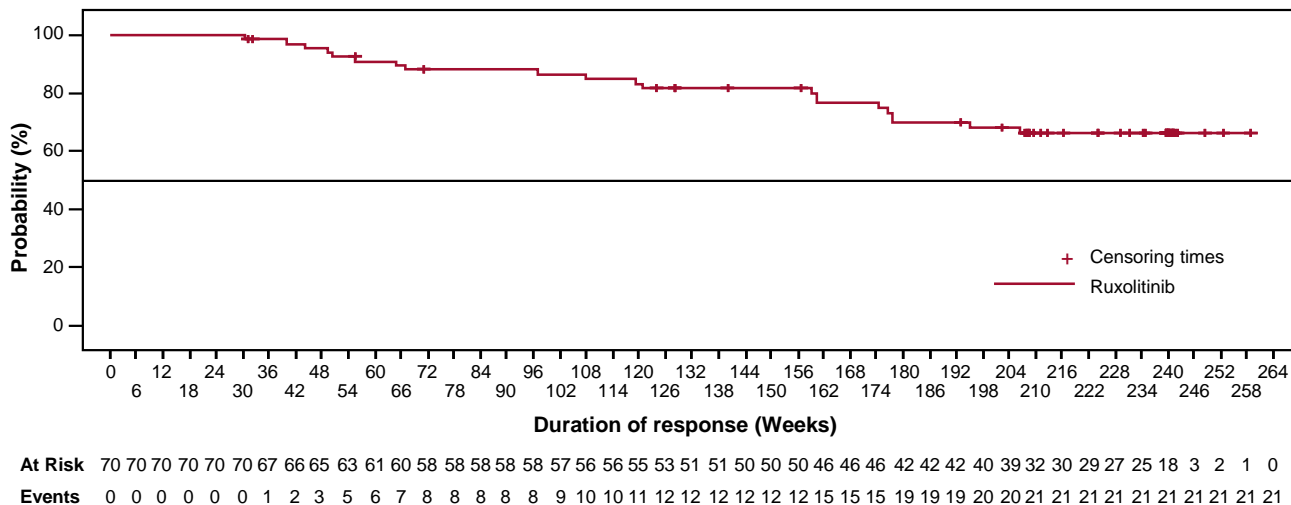
CI, confidence interval; K-M, Kaplan–Meier.

Durability of Complete Hematologic Remission With Ruxolitinib

No. of responders/events/censor: 26/10/16
Kaplan-Meier median: N/A week

Probability (%)

Duration of response (Weeks)

+ Censoring times
— Ruxolitinib

| At risk | 26 24 24 24 24 24 24 21 21 18 18 17 17 16 16 16 16 15 15 15 15 14 13 13 13 13 13 13 12 10 10 9 9 9 7 7 6 5 3 0 |
| Events | 0 0 0 0 0 0 0 3 3 4 4 5 5 6 6 6 6 6 7 7 7 7 8 8 8 8 8 8 8 9 10 10 10 10 10 10 10 10 10 10 |

- The K-M estimate of duration of CHR (hematocrit control, platelet count ≤ 400 × 10^9/L, and WBC count ≤ 10 × 10^9/L) for 208 weeks (4 years) was 0.54 (95% CI: 0.31, 0.72).
  - Of 87 patients with WBC > 10 × 10^9/L at baseline, 42 (48.3%) achieved WBC ≤ 10 × 10^9/L at week 208.
  - Of 54 patients with platelet count > 400 × 10^9/L at baseline, 26 (48.1%) achieved platelet count ≤ 400 × 10^9/L at week 208 .

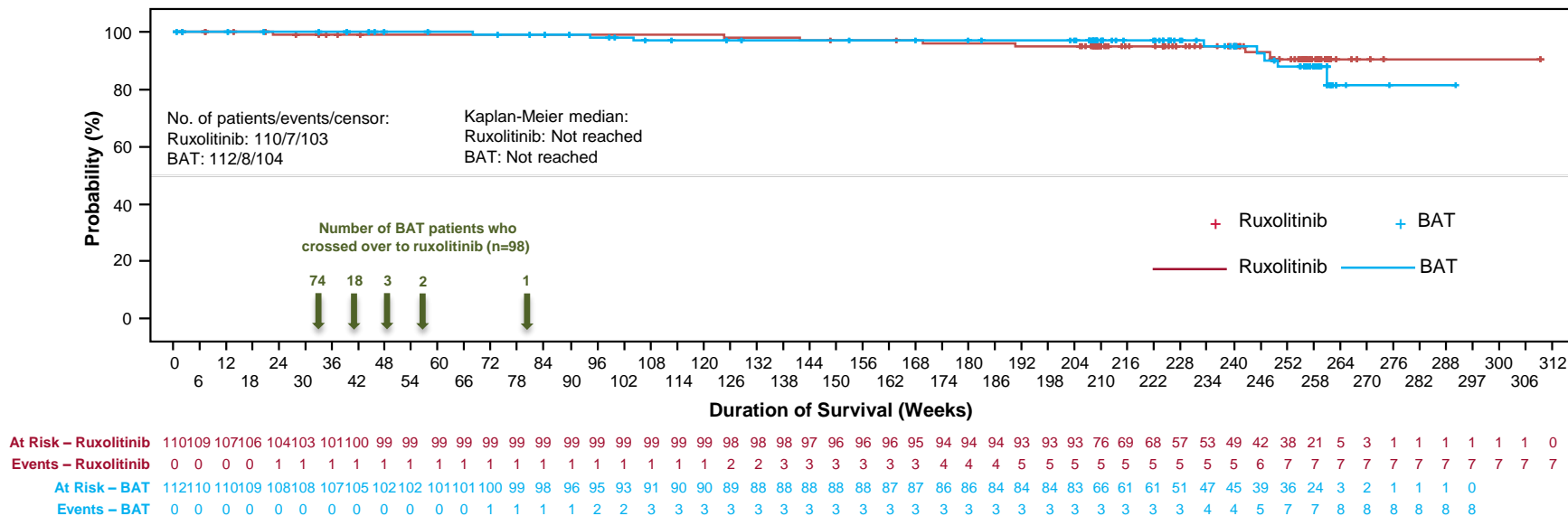CHR, complete hematologic remission; CI, confidence interval; K-M, Kaplan-Meier

American Society *of* Hematology

Durability of Overall Clinicohematologic Response With Ruxolitinib

At Risk   70 70 70 70 70 70 67 66 65 63 61 60 58 58 58 58 58 57 56 56 55 53 51 51 50 50 50 46 46 46 42 42 42 40 39 32 30 29 27 25 18 3 2 1 0

Events   0 0 0 0 0 0 1 2 3 5 6 7 8 8 8 8 8 9 10 10 11 12 12 12 12 12 12 15 15 15 19 19 19 20 20 21 21 21 21 21 21 21 21 21 21

- Of the 70 patients (63.6%) who achieved an overall CLHM response at week 32, twenty-one had progressed by week 208.
- The K-M estimate of duration of maintaining CLHM for 208 weeks (4 years) was 0.67 (95% CI: 0.54, 0.77).
  – Median duration of CLHM response has not been reached.

CLHM, clinicohematologic response; CI, confidence interval; K-M, Kaplan-Meier

American Society *of* Hematology

Overall Survival Analysis in the Intent-to-Treat Population

No. of patients/events/censor:
Ruxolitinib: 110/7/103
BAT: 112/8/104

Kaplan-Meier median:
Ruxolitinib: Not reached
BAT: Not reached

Number of BAT patients who crossed over to ruxolitinib (n=98)

74 18 3 2 1

Probability (%)

Duration of Survival (Weeks)

+ Ruxolitinib   + BAT

Ruxolitinib   BAT

At Risk – Ruxolitinib 110 109 107 106 104 103 101 100 99 99 99 99 99 99 99 99 99 99 99 99 99 99 99 99 98 98 98 97 96 96 96 95 94 94 94 93 93 93 76 69 68 57 53 49 42 38 21 5 3 1 1 1 1 1 1 0
Events – Ruxolitinib 0 0 0 0 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 2 2 3 3 3 3 3 3 4 4 4 5 5 5 5 5 5 5 5 6 7 7 7 7 7 7 7 7 7 7 7 7
At Risk – BAT 112 110 110 109 108 108 107 105 102 102 101 101 100 99 98 96 95 93 91 90 90 89 88 88 88 88 88 87 87 86 86 84 84 84 83 66 61 61 51 47 45 39 36 24 3 2 1 1 1 0
Events – BAT 0 0 0 0 0 0 0 0 0 0 0 0 0 1 1 1 2 2 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 4 4 5 7 7 8 8 8 8 8 8 8

- In the ITT analysis not accounting for crossover, the K-M estimates for overall survival at 5 years was 90.6% (95% CI: 80.1, 95.7) in the ruxolitinib arm and 87.7% (95% CI: 74.8, 94.3) in the BAT arm.
- Patients were allowed to cross over from BAT to ruxoltinib at or after week 32, no patient remained on randomized BAT treatment after week 80.

BAT, best available therapy; CI, confidence interval; CO, crossover; K-M, Kaplan-Meier; ITT, intent- to- treat.

Adverse Events

(Adjusted for Patient-Year Exposure, Regardless of Study Drug Relationship [All Grades, Rate ≥ 5 in Either Arm])

| Rate per 100 Patient-Years of Exposure | 208-Week (4-Year) Analysis | | | |
| | Ruxolitinib n = 110 Exposure, Patient-Years = 409 | | Crossover n = 98 Exposure, Patient-Years = 310 | |
	All Grades	Grade 3 or 4	All Grades	Grade 3 or 4
Hematologic adverse events				
Anemia	9.3	1.0	9.4	0.6
Thrombocytopenia	4.6	1.0	1.3	0.3
Non-hematologic adverse events				
All infections	19.6	3.7	19.7	6.5
Herpes zoster infection	4.9	0.5	4.2	0.6
Pruritus	7.3	0.5	5.8	0
Diarrhea	7.1	0.2	3.2	0
Headache	6.1	0.5	5.5	0
Fatigue	5.1	0.2	4.2	0
Increased weight	5.6	0.7	4.2	0.3
Arthralgia	5.9	0.2	3.2	0.3
Muscle spasms	5.4	0.2	3.2	0
Dizziness	4.2	0.0	6.1	0

Adverse Events

(Adjusted for Patient-Year Exposure, Regardless of Study Drug Relationship [All Grades, Rate ≥ 5 in Either Arm])

Rate per 100 Patient-Years of Exposure	208-Week (4-Year) Analysis				80-Week Analysis			
	Ruxolitinib n = 110 Exposure, Patient-Years = 409		Crossover n = 98 Exposure, Patient-Years = 310		Ruxolitinib n = 110 Exposure, Patient-Years = 227.7		Crossover n = 98 Exposure, Patient-Years = 147.6	
	All Grades	Grade 3 or 4	All Grades	Grade 3 or 4	All Grades	Grade 3 or 4	All Grades	Grade 3 or 4
Hematologic adverse events								
Anemia	9.3	1.0	9.4	0.6	13.2	0.9	14.9	1.4
Thrombocytopenia	4.6	1.0	1.3	0.3	6.1	1.8	2.7	0.7
Non-hematologic adverse events								
All infections	19.6	3.7	19.7	6.5	29.4	4.0	27.8	5.4
Herpes zoster infection	4.9	0.5	4.2	0.6	5.3	0.9	5.4	0.7
Pruritus	7.3	0.5	5.8	0	9.7	0.4	8.8	0
Diarrhea	7.1	0.2	3.2	0	9.7	0	5.4	0
Headache	6.1	0.5	5.5	0	10.5	0.9	8.8	0
Fatigue	5.1	0.2	4.2	0	8.3	0.4	6.8	0
Increased weight	5.6	0.7	4.2	0.3	7.5	0.4	6.8	0
Arthralgia	5.9	0.2	3.2	0.3	6.1	0	4.7	0
Muscle spasms	5.4	0.2	3.2	0	7.9	0.4	3.4	0
Dizziness	4.2	0.0	6.1	0	7.5	0	7.5	0

American Society *of* Hematology

Thromboembolic Adverse Events (SMQ)

(Adjusted for Patient-Year Exposure, Regardless of Study Drug Relationship [All Grades, Rate ≥ 0.2 in Either Arm])

	208-Week (4-Year) Analysis			
	Ruxolitinib n = 110 Exposure, Patient-Years = 409		Crossover n = 98 Exposure, Patient-Years = 310	
n (Rate per 100 Patient-Years of Exposure)	All Grades	Grade 3 or 4	All Grades	Grade 3 or 4
All thromboembolic events[a]	5 (1.2)	3 (0.7)	9 (2.9)	5 (1.6)
Cerebral infarction	1 (0.2)	1 (0.2)	0	0
Ischemic stroke	1 (0.2)	0	1 (0.3)	1 (0.3)
Transient ischemic attack	0	0	2 (0.6)	2 (0.6)
Portal vein thrombosis	1 (0.2)	1 (0.2)	0	0
Pulmonary embolism	1 (0.2)	1 (0.2)	0	0
Retinal vascular thrombosis	1 (0.2)	0	0	0
Myocardial infarction	0	0	2 (0.6)	1 (0.3)
Deep vein thrombosis	0	0	1 (0.3)	0
Thrombophlebitis	0	0	1 (0.3)	0
Thrombosis	0	0	1 (0.3)	0
Bone infarction	0	0	1 (0.3)	0
Coronary artery occlusion	0	0	1 (0.3)	0
Disseminated intravascular coagulation	0	0	1 (0.3)	1 (0.3)

- While on BAT, the rates of all grade and grade 3/4 thromboembolic events per 100 patient-years of exposure were 8.2 (n = 6) and 2.7 (n = 2), respectively.

[a]MedDRA version 19.1 was used to code the events. BAT; best available therapy; SMQ, standardized medical dictionary for regulatory activities (MedDRA) query.

Thromboembolic Adverse Events (SMQ)

(Adjusted for Patient-Year Exposure, Regardless of Study Drug Relationship [All Grades, Rate ≥ 0.2 in Either Arm])

n (Rate per 100 Patient-Years of Exposure)	208-Week (4-Year) Analysis				80-Week Analysis			
	Ruxolitinib n = 110 Exposure, Patient-Years = 409		Crossover n = 98 Exposure, Patient-Years = 310		Ruxolitinib n = 110 Exposure, Patient-Years = 227.7		Crossover n = 98 Exposure, Patient-Years = 147.6	
	All Grades	Grade 3 or 4	All Grades	Grade 3 or 4	All Grades	Grade 3 or 4	All Grades	Grade 3 or 4
All thromboembolic events[a]	**5 (1.2)**	**3 (0.7)**	**9 (2.9)**	**5 (1.6)**	**4 (1.8)**	**2 (0.9)**	**6 (4.1)**	**4 (2.7)**
Cerebral infarction	1 (0.2)	1 (0.2)	0	0	1 (0.4)	1 (0.4)	0	0
Ischemic stroke	1 (0.2)	0	1 (0.3)	1 (0.3)	1 (0.4)	0	0	0
Transient ischemic attack	0	0	2 (0.6)	2 (0.6)	0	0	2 (1.4)	2 (1.4)
Portal vein thrombosis	1 (0.2)	1 (0.2)	0	0	1 (0.4)	1 (0.4)	0	0
Pulmonary embolism	1 (0.2)	1 (0.2)	0	0	0	0	0	0
Retinal vascular thrombosis	1 (0.2)	0	0	0	1 (0.4)	0	0	0
Myocardial infarction	0	0	2 (0.6)	1 (0.3)	0	0	2 (1.4)	1 (0.7)
Deep vein thrombosis	0	0	1 (0.3)	0	0	0	0	0
Thrombophlebitis	0	0	1 (0.3)	0	0	0	0	0
Thrombosis	0	0	1 (0.3)	0	0	0	1 (0.7)	0
Bone infarction	0	0	1 (0.3)	0	0	0	1 (0.7)	0
Coronary artery occlusion	0	0	1 (0.3)	0	0	0	1 (0.7)	0
Disseminated intravascular coagulation	0	0	1 (0.3)	1 (0.3)	0	0	1 (0.7)	1 (0.7)

- While on BAT, the rates of all grade and grade 3/4 thromboembolic events per 100 patient-years of exposure were 8.2 (n = 6) and 2.7 (n = 2), respectively.

[a]MedDRA version 19.1 was used to code the events. BAT; best available therapy; SMQ, standardized medical dictionary for regulatory activities (MedDRA) query.

Other Adverse Events of Interest

(Adjusted for Patient-Year Exposure, Regardless of Study Drug Relationship [All Grades, Rate ≥ 0.5 in Either Arm])

	208-Week (4-Year) Analysis	
	Ruxolitinib n = 110 Exposure, Patient-Years = 409	Crossover n = 98 Exposure, Patient-Years = 310
	n (Rates)	n (Rates)
Disease Progression		
Acute myeloid leukemia	1 (0.2)	1 (0.3)
Myelofibrosis	9 (2.2)	6 (1.9)
Other Malignancies		
Prostate cancer	1 (0.2)	2 (0.6)
Breast cancer	1 (0.2)	0
Chronic myelomonocytic leukemia	1 (0.2)	1 (0.3)
Malignant fibrous histiocytoma	0	0

- While on BAT, no patient progressed to acute myeloid leukemia or myelofibrosis.

BAT; best available therapy.

American Society *of* Hematology

Other Adverse Events of Interest

(Adjusted for Patient-Year Exposure, Regardless of Study Drug Relationship [All Grades, Rate ≥ 0.5 in Either Arm])

	208-Week (4-Year) Analysis		80-Week Analysis	
	Ruxolitinib **n = 110** **Exposure, Patient-Years** **= 409**	**Crossover** **n = 98** **Exposure, Patient-Years** **= 310**	**Ruxolitinib** **n = 110** **Exposure, Patient-Years** **= 227.7**	**Crossover** **n = 98** **Exposure, Patient-Years** **= 147.6**
	n (Rates)	**n (Rates)**	**n (Rates)**	**n (Rates)**
Disease Progression				
Acute myeloid leukemia	1 (0.2)	1 (0.3)	1 (0.4)	1 (0.7)
Myelofibrosis	9 (2.2)	6 (1.9)	3 (1.3)	3 (2.0)
Other Malignancies				
Prostate cancer	1 (0.2)	2 (0.6)	0	2 (1.4)
Breast cancer	1 (0.2)	0	2 (0.9)	0
Chronic myelomonocytic leukemia	1 (0.2)	1 (0.3)	0	1 (0.7)
Malignant fibrous histiocytoma	0	0	0	1 (0.7)

- While on BAT, no patient progressed to acute myeloid leukemia or myelofibrosis.

BAT; best available therapy.

American Society *of* Hematology

Other Adverse Events of Interest

(Nonmelanoma Skin Cancer Adjusted for Patient-Year Exposure)

n (Rate per 100 Patient-Years of Exposure)	208-Week (4-Year) Analysis				80-Week Analysis			
	Ruxolitinib n = 110 Exposure, Patient-Years = 409		Crossover n = 98 Exposure, Patient-Years = 310		Ruxolitinib n = 110 Exposure, Patient-Years = 227.7		Crossover n = 98 Exposure, Patient-Years = 147.6	
Prior history of Nonmelanoma Skin Cancer	**No**	**Yes**	**No**	**Yes**	**No**	**Yes**	**No**	**Yes**
Total events	**13 (3.6)**	**8 (18.6)**	**6 (2.1)**	**2 (9.5)**	**4 (2.0)**	**6 (24.2)**	**2 (1.4)**	**1 (10.6)**
Basal cell carcinoma	10 (2.7)	7 (16.3)	4 (1.4)	1 (4.7)	3 (1.5)	5 (20.2)	1 (0.7)	1 (10.6)
Squamous cell carcinoma of skin	4 (1.1)	4 (9.3)	3 (1.0)	0	1 (0.5)	2 (8.1)	0	0
Bowen's disease	1 (0.3)	1 (2.3)	0	0	0	1 (4.0)	0	0
Carcinoma in situ of skin	0	2 (4.7)	0	0	0	1 (4.0)	0	0
Metastatic squamous cell carcinoma	0	2 (4.7)	0	0	0	1 (4.0)	0	0
Keratoacanthoma	1 (0.3)	0	0	0	0	0	0	0
Squamous cell carcinoma[*]	2 (0.5)	3 (7.0)	2 (0.7)	2 (9.5)	1 (0.5)	4 (16.1)	1 (0.7)	0

[*]Categorized as non-skin squamous cell carcinoma cases.

Deaths

- Since week 80, there were 2 new on-treatment deaths in the **ruxolitinib** arm.
  - Adenocarcinoma gastric (n = 1): The investigator assessed the event to be related to study drug.
  - Neoplasm malignant (n = 1): The investigator assessed the event not related to study drug.
- In the **crossover population**, 4 patients had fatal adverse events leading to 4 on-treatment deaths. These deaths were assessed as not related to ruxolitinib treatment.
  - Pneumonia (n = 2)
  - Central nervous system hemorrhage (n = 1)
  - Hypovolemic shock (n = 1)

Discussion

- In the RESPONSE study, patients with PV who were resistant to or intolerant of hydroxyurea had durable hematocrit control and clinicohematologic response.

  - In both the ruxolitinib arm and crossover population, 66% of patients completed 5 years of study treatment (29%) or were still on treatment (37%).

- With an additional 120 weeks (30 months) of follow-up, the overall safety profile remains unchanged from the 80-week analysis.

- Taken together, these results support ruxolitinib as an effective long-term treatment option for patients with PV who have had an inadequate response to or are intolerant of hydroxyurea.

PV, polycythemia vera.

Acknowledgements

- We thank the patients and investigators of the RESPONSE study, and Incyte Corporation for their contributions to conduct this study.
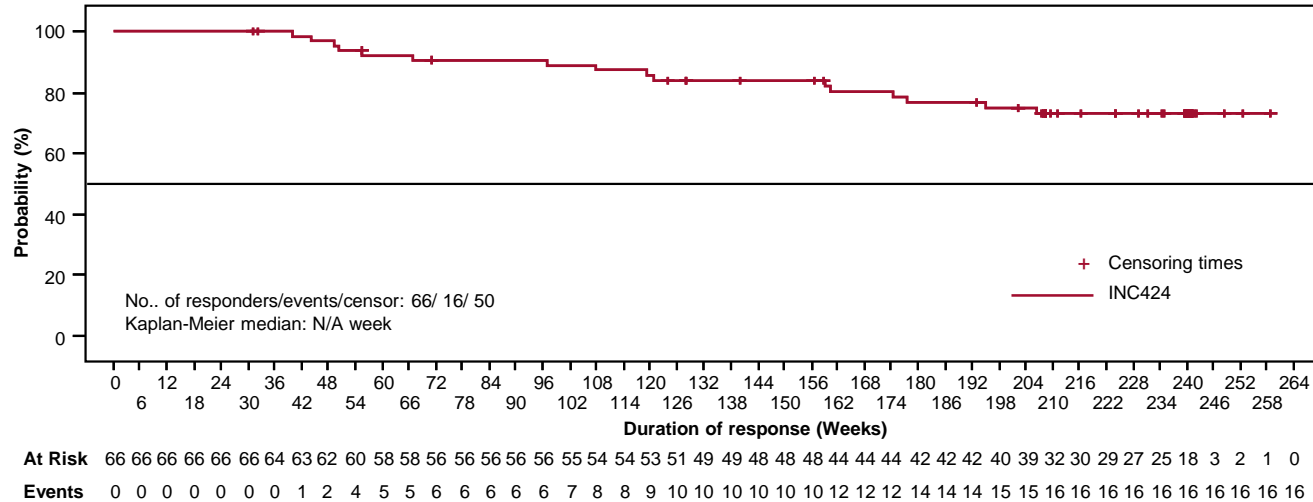
- Thanks to Mary Laughlin and Monika Wroclawska of Novartis for contribution to the study.
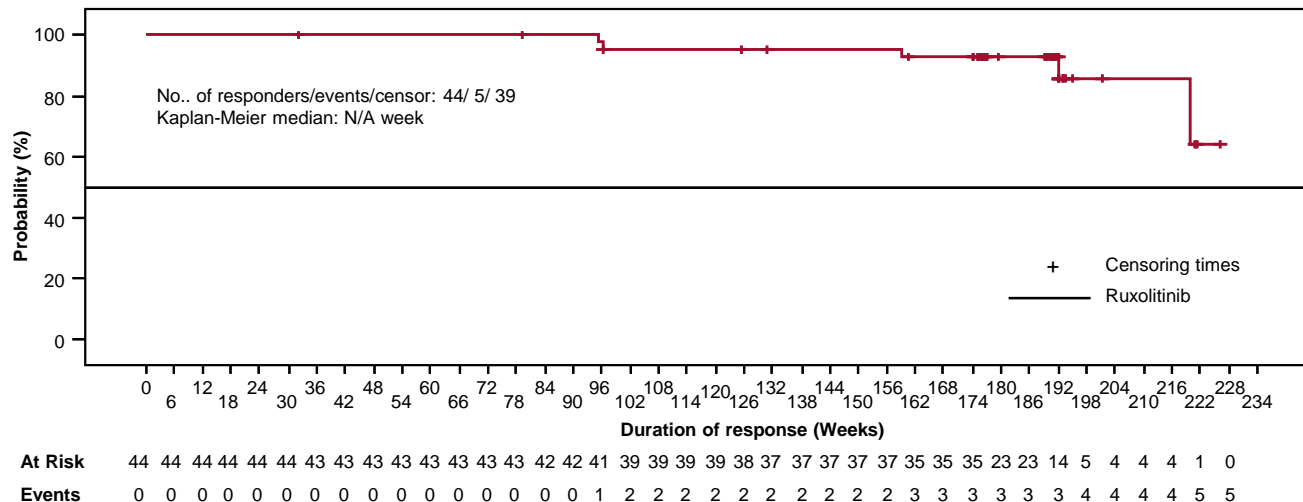
Back-up Slides

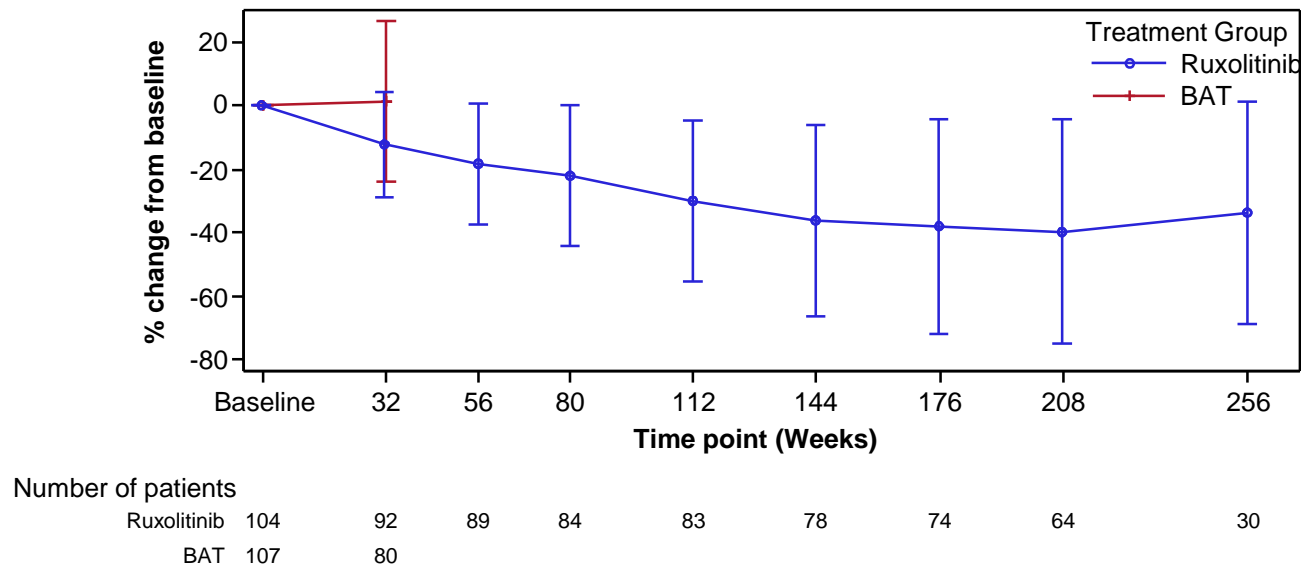# Duration of Absence of Phlebotomy Eligibility With Ruxolitinib

- The K-M estimates of duration of absence of phlebotomy eligibility for 208 weeks was 0.73 (95% CI: 0.60, 0.83).

Duration of Spleen Volume Reduction with Ruxolitinib

- The K-M estimates of duration of at least 35% reduction in the spleen volume for 208 weeks was 0.86 (95% CI: 0.61, 0.95).

American Society *of* Hematology

Percentage change from baseline in *JAK2*V617F allele burden

Number of patients

Ruxolitinib 104	92	89	84	83	78	74	64	30
BAT 107	80							

- The mean JAK2 V617F allele burden decreased consistently over time, similar to that observed at Week 80 and Week 48 analysis.
    - In the ruxolitinib arm, the median percent change from baseline in allele burden was −35.99% (range: −100 to 15.6, n = 64) at week 208 vs −18.35% (range: −94 to 30.0, n = 84) at week 80.
    - In the crossover population, the median percent change from baseline in allele burden was −11.83% (range: −97.4 to 114.3, n = 26) at week 224 vs −7.99% (range: −94.9 to 166.7, n = 78) at week 80.

American Society *of* Hematology