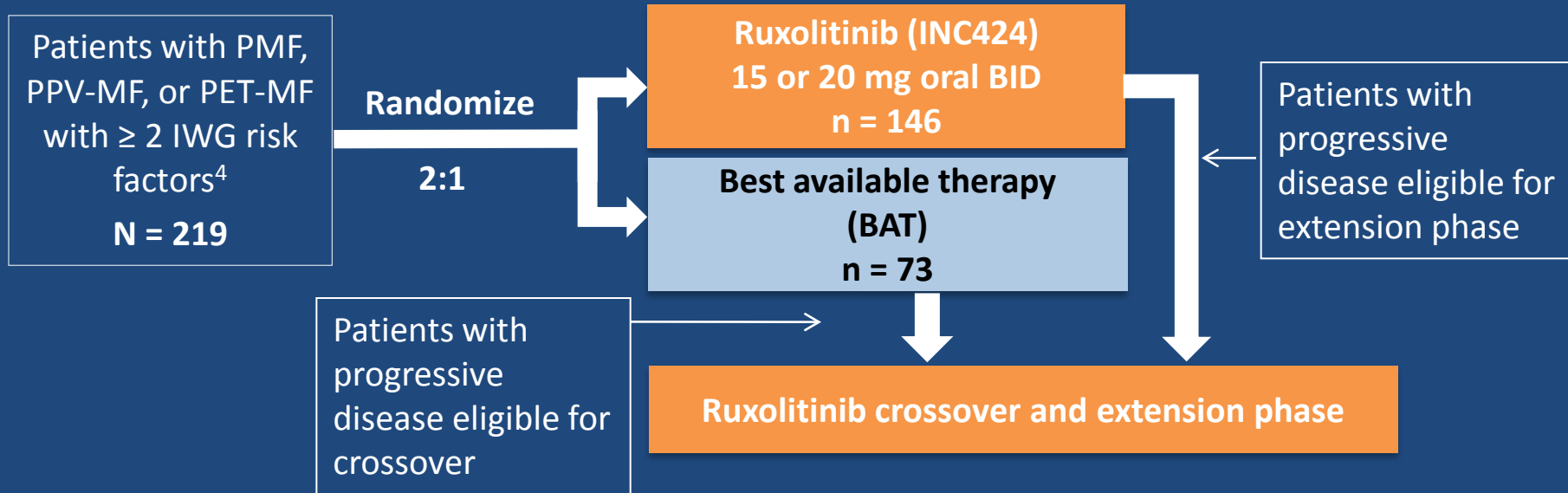


Ruxolitinib Provides Reductions in Splenomegaly Across Subgroups: An Analysis of Spleen Response in the COMFORT-II Study

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COMFORT-II Study Design

- Ruxolitinib is a potent and selective oral JAK1/2 inhibitor that has demonstrated rapid and durable reductions in splenomegaly, improved disease-related symptoms and QoL, and prolonged overall survival for patients with MF¹⁻³
- COMFORT-II is a randomized, open-label, multicenter phase 3 trial



- Patients were stratified based on baseline IWG prognostic risk category⁴

1. Verstovsek S, et al. Oral presentation at ASCO Annual Meeting; June 3-7, 2011; Chicago, IL. Abstract 6500.

2. Harrison C, et al. Oral presentation at 16th Congress of EHA; June 9-12, 2011; London, UK. Abstract 1020.

3. Verstovsek S, et al. Oral presentation at 53rd ASH Annual Meeting; December 10-13, 2011; San Diego, CA. Abstract 278.

4. Cervantes F, et al. *Blood*. 2009;113(13):2895-2901.

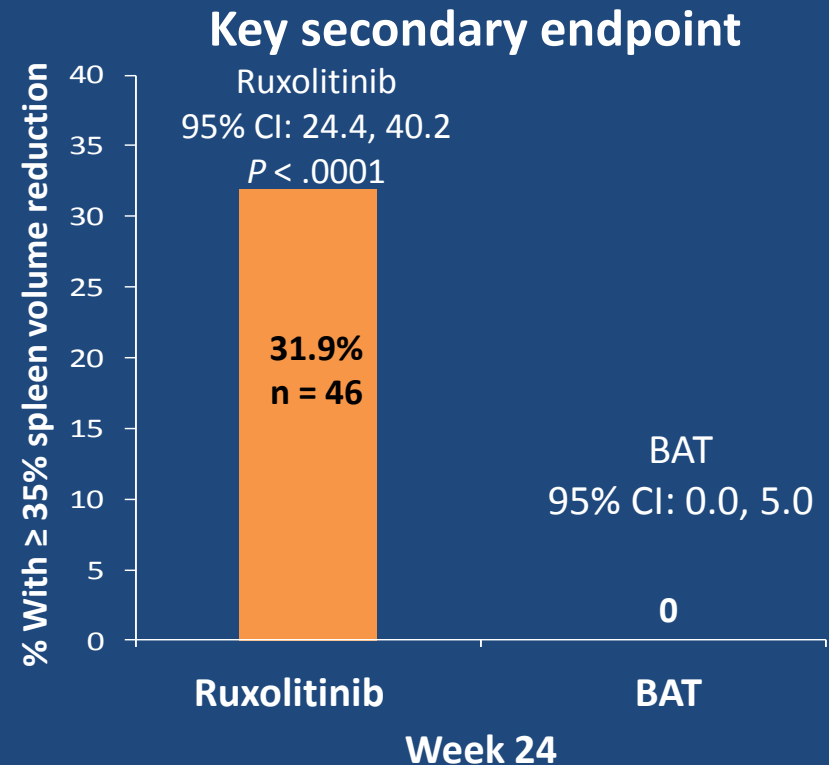
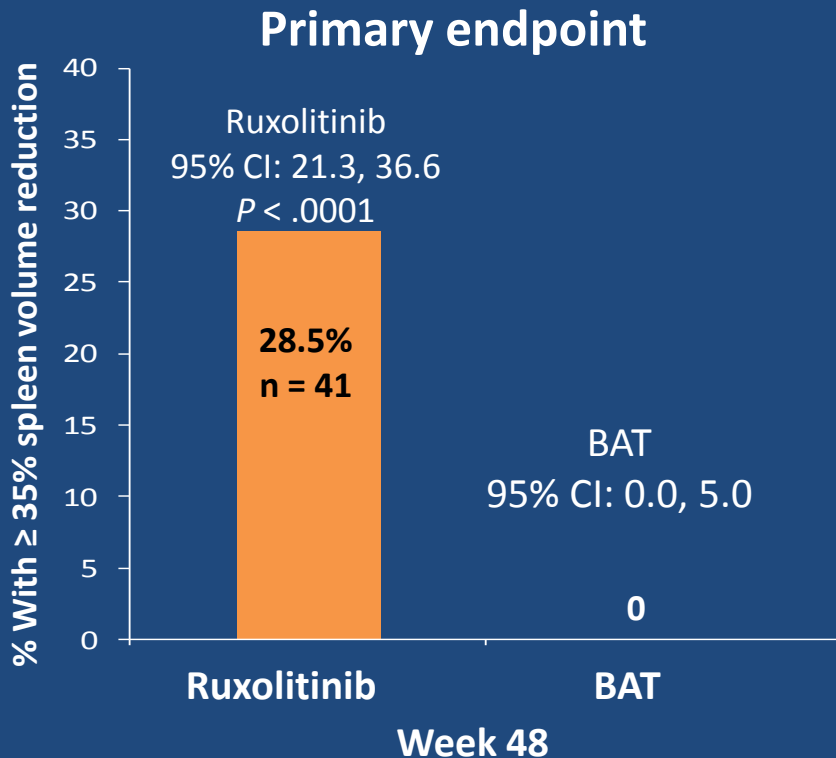
Demographics and Baseline Patient Characteristics (ITT)

| | Ruxolitinib (n = 146) | BAT (n = 73) |
|--|--------------------------|-----------------|
| Age, median, y | 67 | 66 |
| ≤ 65 years, n (%) | 69 (47) | 36 (49) |
| Male, n (%) | 83 (57) | 42 (58) |
| Myelofibrosis type, n (%) | | |
| PMF | 77 (53) | 39 (53) |
| PPV-MF | 48 (33) | 20 (27) |
| PET-MF | 21 (14) | 14 (19) |
| Platelet count > 200,000/μL, n (%) ^a | 88 (61) | 47 (65) |
| High/intermediate-2 IWG risk | 49%/51% | 49%/51% |
| <i>JAK2V617F</i> positive, n (%) | 110 (75) | 49 (67) |
| Palpable spleen size below costal margin, median, cm | 14 | 15 |
| Spleen volume, ^b median, cm ³ | 2408 | 2318 |
| Prior hydroxyurea, n (%) | 110 (75) | 50 (68) |

^a Full analysis set: ruxolitinib, n = 144; BAT, n = 72; ^b Normal spleen volume is 150 to 200 cm³.

Primary and Key Secondary Endpoints

Proportion of patients achieving $\geq 35\%$ reduction in spleen volume from baseline at weeks 48 and 24 as measured by MRI/CT^a



- Median time to response, 12.3 weeks
- Of the 69 patients who achieved $\geq 35\%$ reduction in spleen volume at any time during the study, 44 (64%) did so at the first assessment

^a CT for patients unable to undergo MRI.

Adverse Events Regardless of Study Drug Relationship ($\geq 10\%$ in Any Group)

| Adverse Event, ^a n (%) | Ruxolitinib (n = 146) | | BAT (n = 73) | |
|-------------------------------------|-----------------------|------------|--------------|------------|
| | All Grades | Grades 3/4 | All Grades | Grades 3/4 |
| Diarrhea | 34 (23) | 2 (1) | 8 (11) | 0 |
| Peripheral edema | 32 (22) | 0 | 19 (26) | 0 |
| Asthenia | 24 (16) | 2 (1) | 7 (10) | 1 (1) |
| Dyspnea | 23 (16) | 1 (1) | 13 (18) | 3 (4) |
| Nasopharyngitis | 22 (15) | 0 | 10 (14) | 0 |
| Pyrexia | 20 (14) | 3 (2) | 7 (10) | 0 |
| Nausea | 19 (13) | 1 (1) | 5 (7) | 0 |
| Arthralgia | 18 (12) | 1 (1) | 5 (7) | 0 |
| Cough | 19 (13) | 0 | 11 (15) | 1 (1) |
| Fatigue | 17 (12) | 1 (1) | 6 (8) | 0 |
| Pain in extremity | 17 (12) | 1 (1) | 3 (4) | 0 |
| Abdominal pain | 15 (10) | 5 (3) | 10 (14) | 2 (3) |
| Headache | 15 (10) | 2 (1) | 3 (4) | 0 |
| Back pain | 13 (9) | 3 (2) | 8 (11) | 0 |
| Pruritus | 7 (5) | 0 | 9 (12) | 0 |
| Worst Lab Value, [*] n (%) | Grades 1/2 | Grades 3/4 | Grades 1/2 | Grades 3/4 |
| Hemoglobin ^b | 79 (54) | 62 (42) | 44 (63) | 22 (31) |
| Platelet count ^c | 89 (61) | 12 (8) | 15 (22) | 5 (7) |

^a Occurring on the randomized treatment phase only; ^b BAT, n = 70; ^c BAT, n = 69.

Patient Disposition

| Patients ^a | Ruxolitinib | BAT |
|---------------------------------------|----------------------|-------------------|
| | (n = 146) n (%) | (n = 73) n (%) |
| Ongoing in randomized treatment phase | 91 (62) ^b | 31 (42) |
| Discontinued | 26 (18) | 24 (33) |
| Discontinued for adverse event(s) | 12 (8) | 4 (5) |

^a Median follow-up, 52.4 weeks.

^b An additional 29 patients (20%) continued ruxolitinib therapy in the extension phase of COMFORT-II

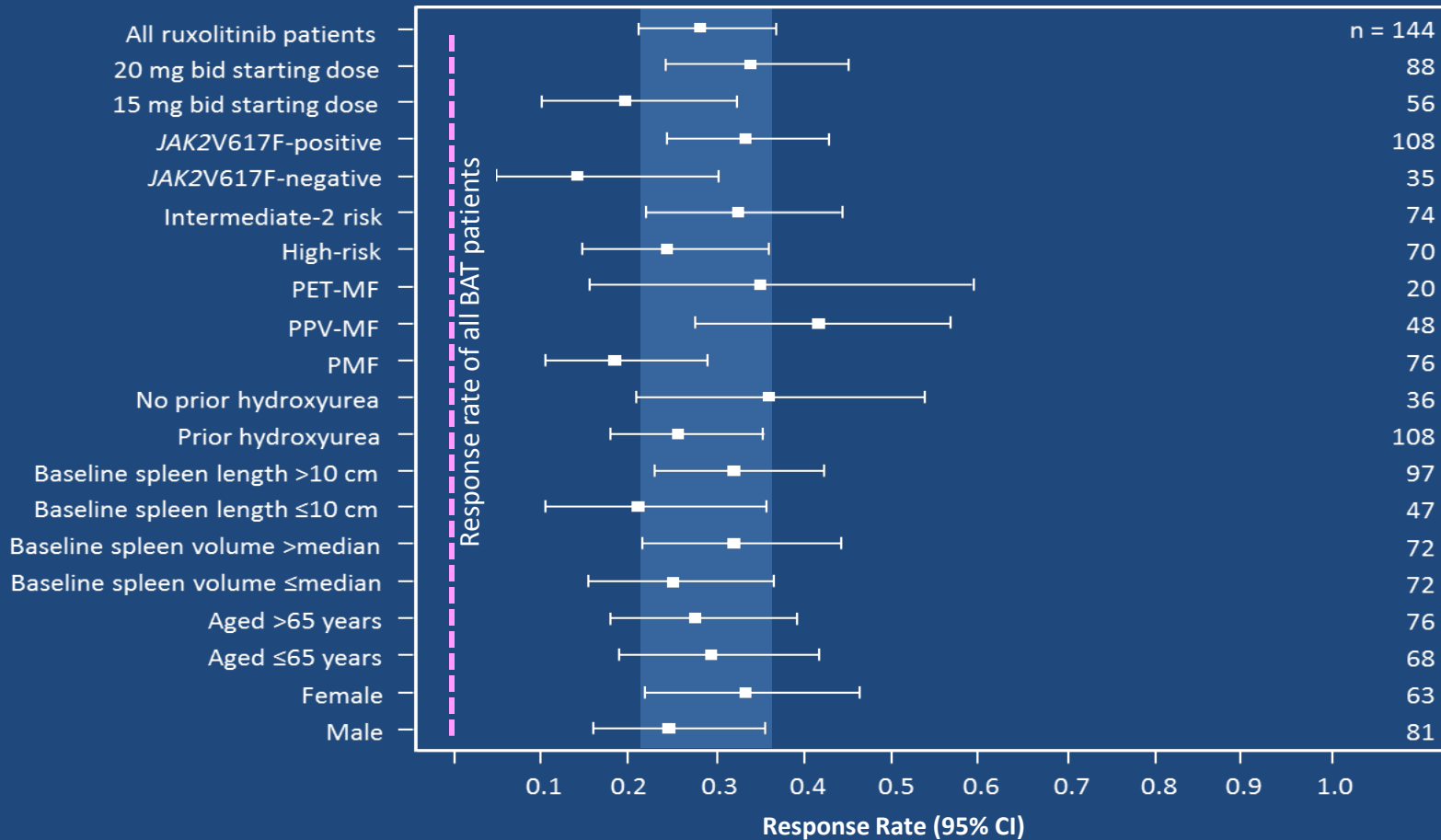
- After a median follow-up of 61.1 weeks, 19 patients reported AEs \leq 2 weeks following discontinuation
 - 3 events were reported as CTCAE grade 3: general physical health deterioration, pyrexia, and fatigue
 - 6 patients had \geq 1 symptoms referable to MF, and there was no pattern of event type or severity observed for the remaining patients

Methods

- The proportions of ruxolitinib-treated patients achieving the primary and key secondary endpoints were analyzed by subgroup for:
 - Gender (male or female)
 - Age (≤ 65 or > 65 years)
 - Starting dose (15 or 20 mg BID)
 - Baseline MF type (PMF, PPV-MF, or PET-MF)
 - Previous hydroxyurea (hydroxycarbamide) use (yes or no)
 - Baseline palpable spleen length (≤ 10 or > 10 cm)
 - Baseline spleen volume ($>$ median or \leq median)
 - *JAK2V617F* mutation (positive or negative)
 - IWG risk category (intermediate risk-2 or high risk)
- In addition, the relationships between these factors and spleen volume reduction were investigated by multivariate logistic regression

COMFORT-II Efficacy by Subgroup

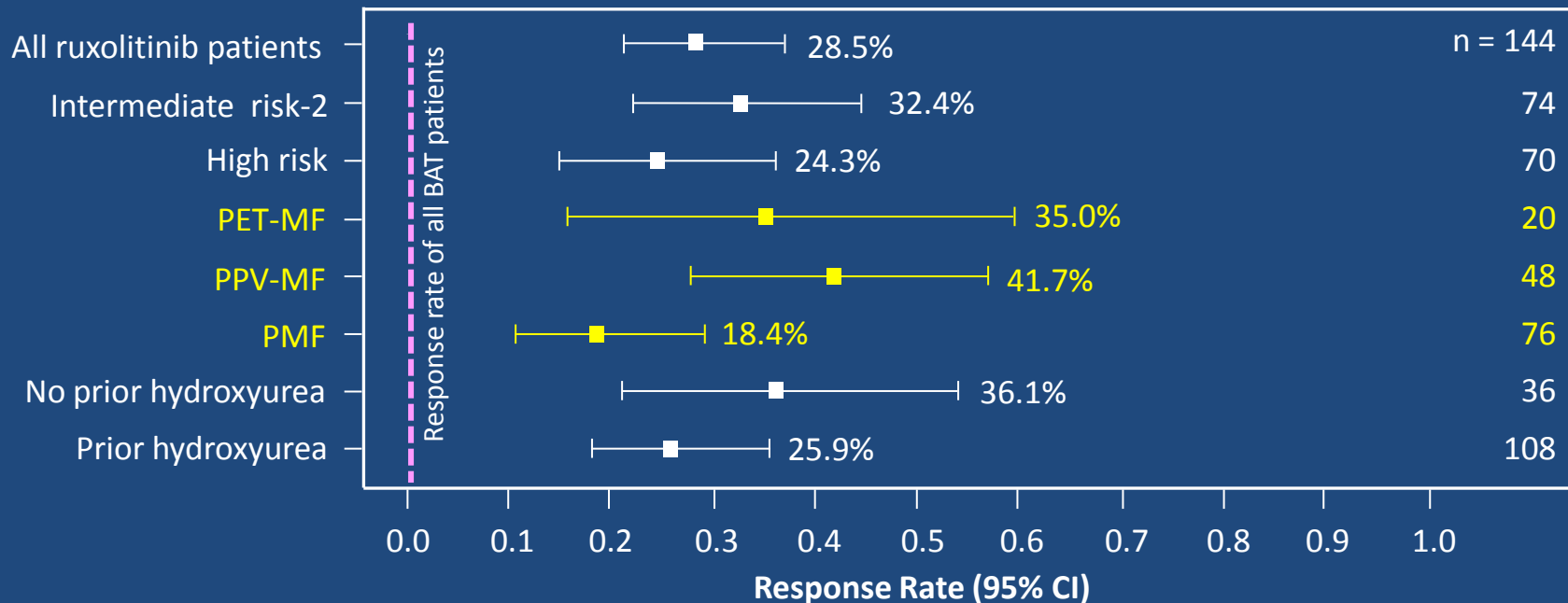
Proportion of Patients in Each Subgroup With $\geq 35\%$ Reduction in Spleen Volume From Baseline at Week 48



- Response rates were observed for ruxolitinib-treated patients in all subgroups and were higher than patients receiving BAT

COMFORT-II Efficacy by Subgroup

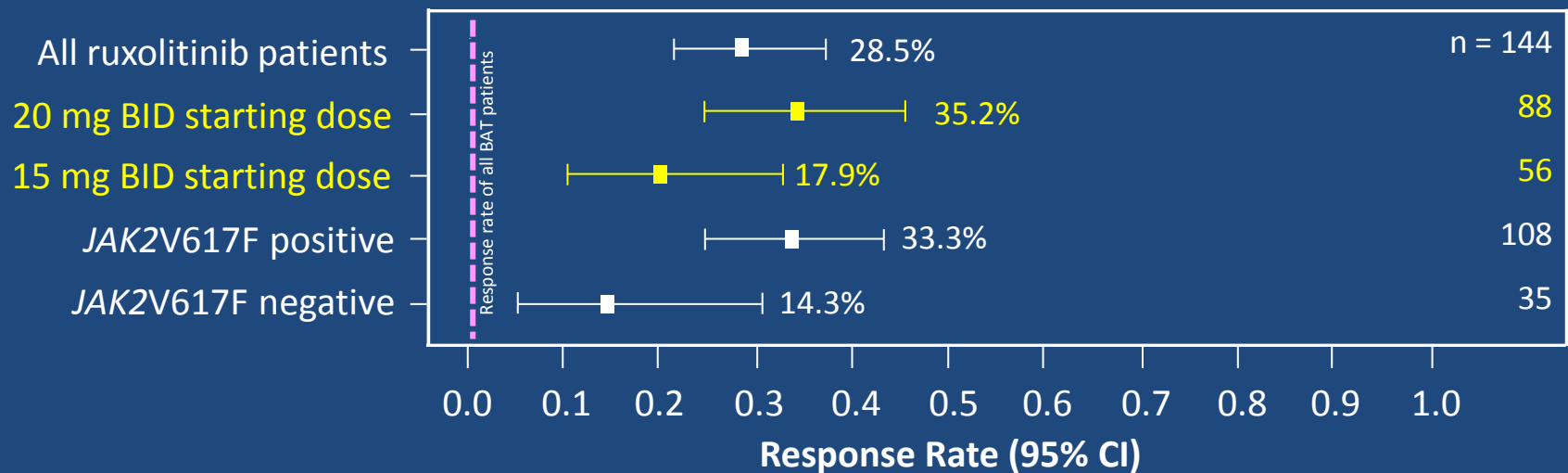
Proportion of Patients in Each Subgroup With $\geq 35\%$ Reduction in Spleen Volume From Baseline at Week 48



- At week 48, there were no significant differences in response rates among patients with intermediate risk-2 or high-risk MF, by MF subtype, or by prior exposure to hydroxyurea

COMFORT-II Efficacy by Subgroup

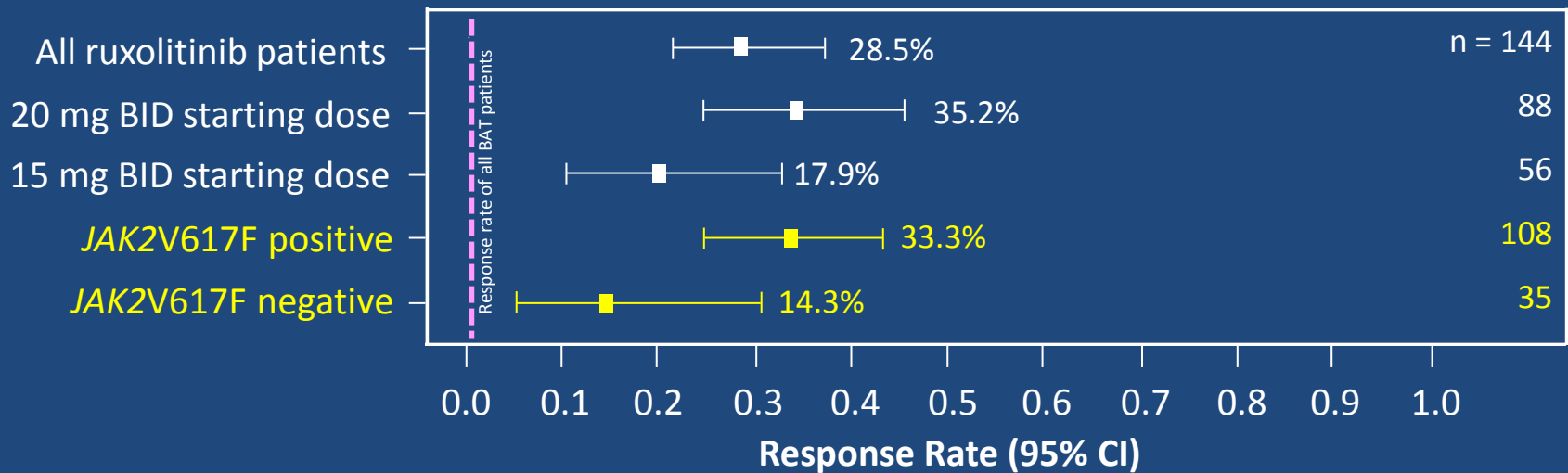
Proportion of Patients in Each Subgroup With $\geq 35\%$ Reduction in Spleen Volume From Baseline at Week 48



- At week 48, the response rates among patients who received starting doses of 15 mg BID or 20 mg BID were not statistically different
 - At week 24, there was a trend toward a higher response rate among patients who received a starting dose of 20 mg BID compared with those who received 15 mg BID

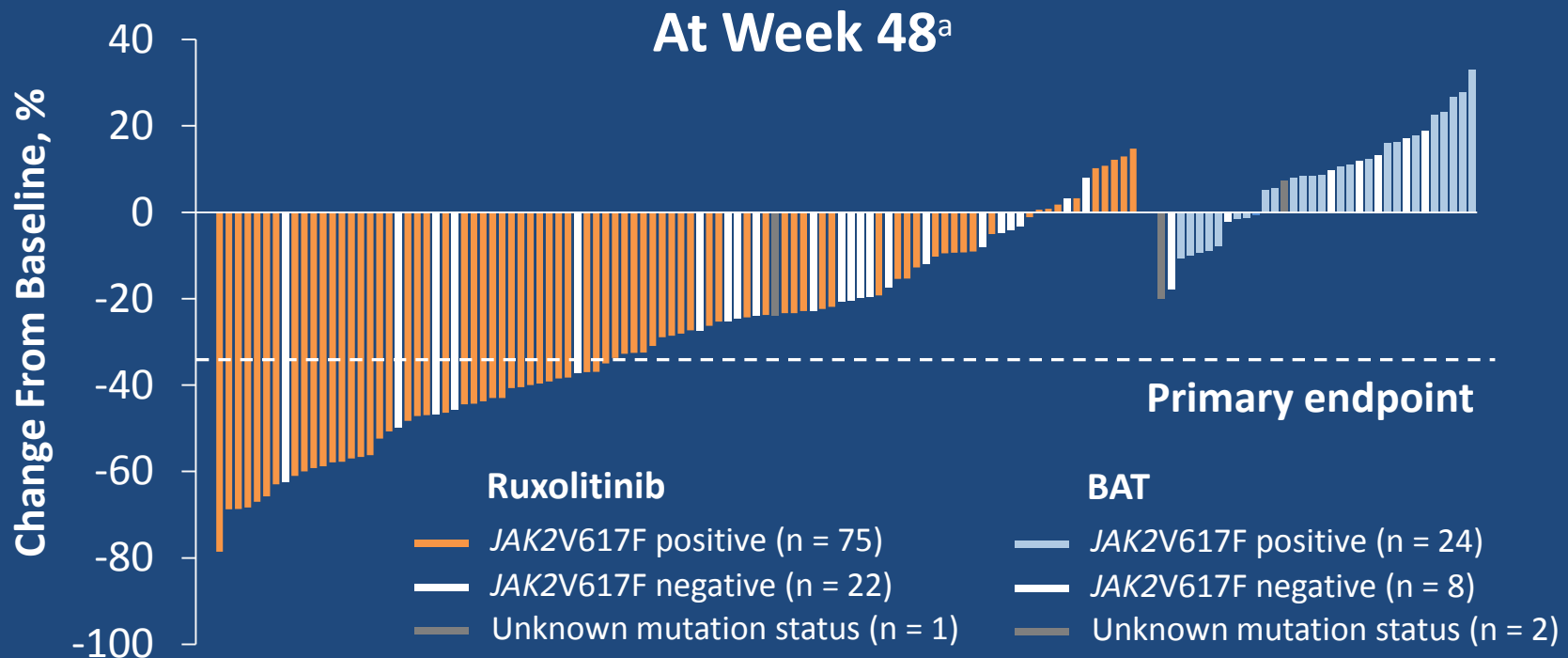
COMFORT-II Efficacy by Subgroup

Proportion of Patients in Each Subgroup With $\geq 35\%$ Reduction in Spleen Volume From Baseline at Week 48



- Although not statistically significant, some differences were observed in response rates among patients based on the starting dose of ruxolitinib and *JAK2V617F* mutation status

Percent Change From Baseline in Spleen Volume by *JAK2V617F* Mutation Status



- At week 48, the vast majority of patients receiving ruxolitinib experienced spleen volume reductions, including *JAK2V617F*-positive (88% [66/75]) and *JAK2V617F*-negative (91% [20/22]) patients

^a For patients with spleen volume assessments by MRI/CT at both baseline and week 48.

Multivariate Logistic Regression Model

Predictive Factors for Response at Week 48

| | Odds Ratio ^a | 95% CI |
|---|-------------------------|----------------|
| Starting dose (15 vs 20 mg BID) | 0.441 | (0.184; 1.055) |
| Gender (female vs male) | 1.646 | (0.726; 3.732) |
| Age (≤ 65 vs > 65 years) | 0.911 | (0.389; 2.135) |
| Baseline MF type | | |
| PMF vs PET-MF | 0.237 | (0.063; 0.891) |
| PPV-MF vs PET-MF | 0.738 | (0.192; 2.833) |
| Previous hydroxyurea use (no vs yes) | 2.521 | (0.964; 6.595) |
| Baseline palpable spleen length (≤ 10 vs > 10 cm) | 0.419 | (0.166; 1.058) |
| <i>JAK2V617F</i> mutation (negative vs positive) | 0.383 | (0.112; 1.310) |
| IWG risk category (high vs intermediate-2 risk) | 0.640 | (0.268; 1.531) |

^a An odds ratio < 1 indicates a lower chance for response and > 1 indicates a higher chance for response compared with reference.

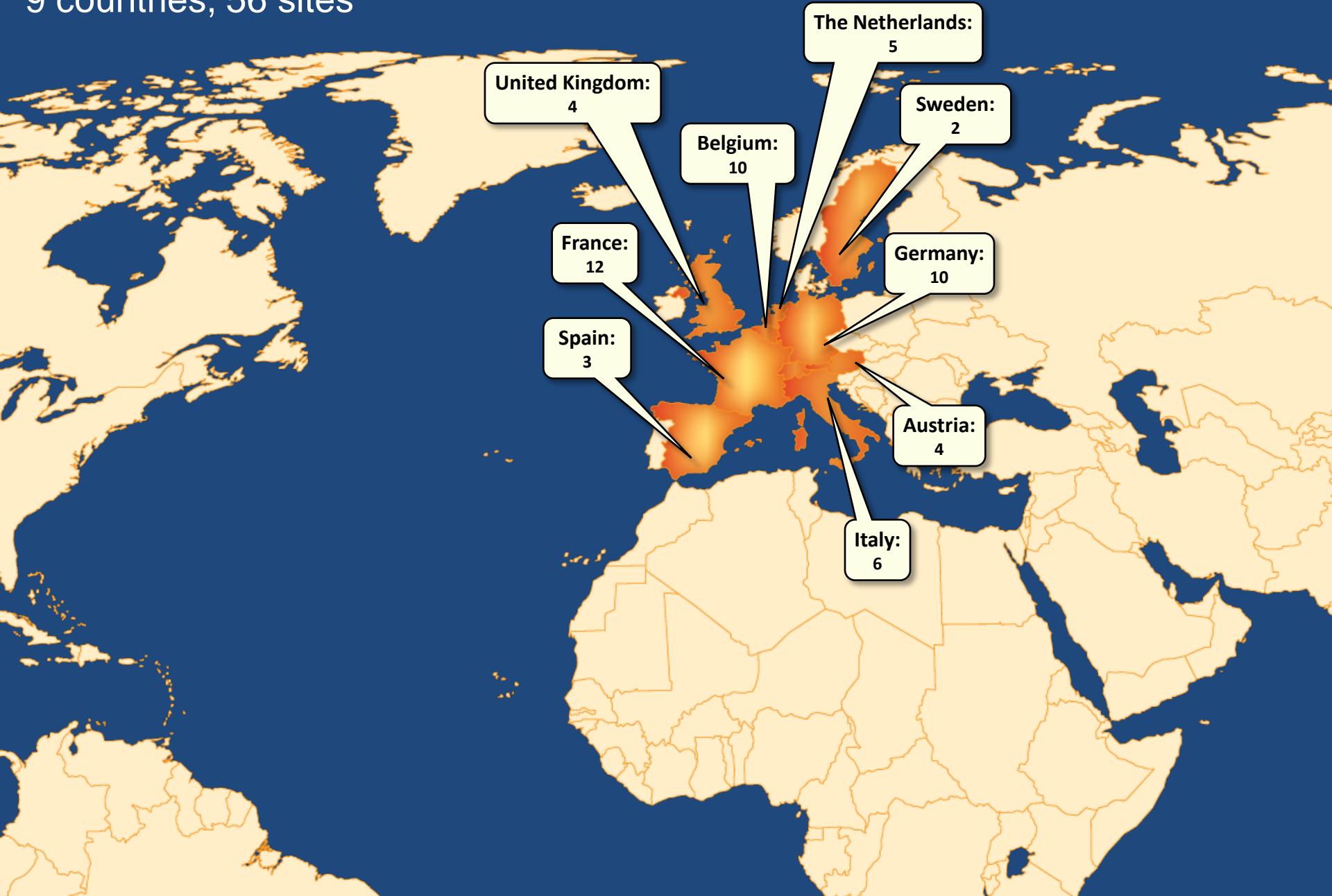


Conclusions

- In COMFORT-II, 28.5% of patients who received ruxolitinib achieved a $\geq 35\%$ reduction in spleen volume from baseline compared with 0% of BAT-treated patients ($P < .0001$)
- The univariate analysis demonstrated that ruxolitinib was more effective than BAT at reducing spleen volume regardless of gender, age, mutation status, IWG risk category, baseline spleen size, MF subtype, or ruxolitinib starting dose
- Multivariate analysis suggests a higher response rate among patients with PET-MF compared with PMF; trends were noted for starting dose, palpable spleen length and *JAK2V617F* mutation status

COMFORT-II

9 countries, 56 sites



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