Ruxolitinib versus best available therapy in patients with polycythemia vera: 80-week follow-up from the RESPONSE trial

Srdan Verstovsek,1 Alessandro M. Vannucchi,2 Martin Griesshammer,3 Tamas Masszi,4 Simon Durrant,5 Francesco Pas- samonti,6 Claire N. Harrison,7 Fabrizio Pane,8 Pierre Zachée,9 Keita Kirito,10 Carlos Besses,11 Masayuki Hino,12 Beatriz Moiraghi,13 Carole B. Miller,14 Mario Cazzola,15 Vittorio Rosti,16 Igor Blau,17 Ruben Mesa,18 Mark M. Jones,19 Huiling Zhen,19 Jingjin Li,20 Nathalie Francillard,21 Dany Habr,20 and Jean-Jacques Kiladjian22

1The University of Texas MD Anderson Cancer Center, Houston, TX, USA; 2Center for Research and Innovation of Myeloproliferative Neoplasms, AOU Careggi, University of Florence, Italy; 3Johannes Wesling Clinic, Minden, Germany; 4St. István and St. László Hospital, Semmelweis University 3rd Department of Internal Medicine, Budapest, Hungary; 5Royal Brisbane & Women’s Hospital, Brisbane, QLD, Australia; 6Department of Clinical and Experimental Medicine, University of Insubria, Varese, Italy; 7Guy’s and St. Thomas’ NHS Foundation Trust, London, UK; 8University of Naples Federico II, Italy; 9ZNA Stuivenberg, Antwerp, Belgium; 10Department of Hematology and Oncology, University of Yamanshi, Chuo-shi, Japan; 11Hematology Department, Hospital del Mar, Barcelona, Spain; 12Department of Clinical Hematology and Diagnostics, Osaka City University Graduate School of Medicine, Japan; 13Hospital Jose Maria Ramos Mejia, Buenos Aires, Argentina; 14Saint Agnes Cancer Institute, Baltimore, MD, USA; 15Department of Hematology, University of Pavia, Italy; 16Center for the Study of Myelofibrosis, IRCCS Policlinico San Matteo Foundation, Pavia, Italy; 17Medical Department, Division of Hematology, Oncology, and Tumor Immunology, Charité Universitätsmedizin Berlin, Germany; 18Department of Hematology/Oncology, Mayo Clinic Cancer Center, Scottsdale, AZ, USA; 19Incyte Corporation, Wilmington, DE, USA; 20Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA; 21Novartis Pharma S.A.S, Rueil Malmaison, France; and 22Centre d’Investigations Cliniques (INSERM CIC 1427), Hôpital Saint-Louis and Université Paris Diderot, Paris, France

©2016 Ferrata Storti Foundation. This is an open-access paper. doi:10.3324/haematol.2016.143644

Received: February 2, 2016.
Accepted: April 15, 2016.
Pre-published: April 21, 2016.
Correspondence: sverstov@mdanderson.org
Supplemental Material

Ruxolitinib Versus Best Available Therapy in Patients With Polycythemia Vera: 80-Week Follow-Up From the RESPONSE Trial

Srdan Verstovsek, Alessandro M. Vannucchi, Martin Griesshammer, Tamas Masszi, Simon Durrant, Francesco Passamonti, Claire N. Harrison, Fabrizio Pane, Pierre Zachee, Keita Kirito, Carlos Besses, Masayuki Hino, Beatriz Moiraghi, Carole B. Miller, Mario Cazzola, Vittorio Rosti, Igor Blau, Ruben Mesa, Mark M. Jones, Huiling Zhen, Jingjin Li, Nathalie Francillard, Dany Habr, Jean-Jacques Kiladjian

Supplemental Methods

Exploratory Analyses

The efficacy of ruxolitinib was evaluated among patients who crossed over to ruxolitinib from the best available therapy arm relative to the arm comprising patients originally randomized to ruxolitinib; these analyses included patients who completed the Week 48 visit or discontinued. The first phlebotomy that occurred in the first 8 weeks was not counted in the calculation of median time to first phlebotomy or exposure-adjusted phlebotomy rate in the ruxolitinib (randomized) arm. In patients receiving ruxolitinib after crossover, the first phlebotomy during the first 8 weeks after crossing over was not counted in calculating median time to first phlebotomy. Changes in spleen volume and blood counts after 32 weeks of study treatment were based on the original Baseline value for the randomized treatment arms and in the crossover treatment group.
*JAK2*V617F allele burden was assessed at Baseline and Weeks 32 and 80 in the ruxolitinib and best available therapy arms, as well as at the date of crossover to ruxolitinib and 48 weeks after crossover to ruxolitinib.

**Statistical Analyses**

The statistical methods used for primary study analyses were described previously. Analysis of change from Baseline in CHR at Week 32 was performed using the Cochran-Mantel-Haenszel test (1) adjusted for abnormal versus normal white blood cell and/or platelet status at Baseline (abnormal status defined as white blood cell count $>$15×10⁹/L and/or platelet count $>$600×10⁹/L) and (2) unadjusted. All new data in the current analysis were summarized using descriptive statistics.
Supplementary Table 1. Spleen volume change from original Baseline by percent reduction after 32 weeks on treatment

<table>
<thead>
<tr>
<th>Proportion of Patients, n (%)</th>
<th>Ruxolitinib (n=110)</th>
<th>Ruxolitinib Crossover (n=96)</th>
<th>Best Available Therapy (n=112)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increase in spleen volume</td>
<td>17 (15.5)</td>
<td>11 (11.5)</td>
<td>50 (44.6)</td>
</tr>
<tr>
<td>0 to &lt;10% reduction</td>
<td>4 (3.6)</td>
<td>9 (9.4)</td>
<td>16 (14.3)</td>
</tr>
<tr>
<td>10% to &lt;35% reduction</td>
<td>33 (30.0)</td>
<td>21 (21.9)</td>
<td>20 (17.9)</td>
</tr>
<tr>
<td>≥35% reduction</td>
<td>44 (40.0)</td>
<td>18 (18.8)</td>
<td>1 (0.9)</td>
</tr>
</tbody>
</table>
Supplementary Figures

Supplementary Figure 1. Mean daily dose of ruxolitinib over time.

Supplementary Figure 2. Distribution of ruxolitinib dosing at Week 32 and Week 80.

Supplementary Figure 3. Change in spleen volume from Baseline over time. *Data after crossover to ruxolitinib are excluded; only visits with data from >5 patients are included.

Supplementary Figure 4. Individual changes in spleen volume from original Baseline after 16 weeks on treatment.
Supplementary Figure 1. Mean daily dose of ruxolitinib over time

Mean Total Daily Dose of Ruxolitinib, mg

Patients, n
110 105 104 101 97 96 95 95 94 94 94
Supplementary Figure 2. Distribution of ruxolitinib dosing at Week 32 and Week 80

Week 32 (n=97) | Week 80 (n=94)
---|---
Total Daily Dose, mg | Patients, %
5 | 9.3 | 6.4
10 | 3.1 | 3.2
15 | 1.0 | 2.1
20 | 36.1 | 33.0
25 | 28.9 | 28.7
30 | 15.5 | 17.0
35 | 6.2 | 9.6
40 | 0 | 0
50 | 0 | 0

Patients, %
Supplementary Figure 3. Change in spleen volume from Baseline over time

<table>
<thead>
<tr>
<th></th>
<th>Ruxolitinib, n 110</th>
<th>Best Available Therapy, n 109</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>100</td>
<td>103</td>
</tr>
<tr>
<td>16</td>
<td>98</td>
<td>87</td>
</tr>
<tr>
<td>32</td>
<td>89</td>
<td></td>
</tr>
<tr>
<td>48</td>
<td>91</td>
<td></td>
</tr>
<tr>
<td>64</td>
<td></td>
<td></td>
</tr>
<tr>
<td>80</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Supplementary Figure 4. Individual changes in spleen volume from original Baseline after 16 weeks on treatment
References