

Incyte Announces Publication of Phase III RESPONSE Trial in Patients with Polycythemia Vera in New England Journal of Medicine

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- *Data show Jakafi® (ruxolitinib) was superior to standard therapy; resulting in durable hematocrit control, spleen volume reduction and complete hematological remission in patients with uncontrolled polycythemia vera (PV)¹*
- *PV is a rare blood cancer associated with overproduction of blood cells that can cause serious cardiovascular complications, such as stroke and heart attack²*
- *Jakafi® was recently approved by the FDA as the first treatment for patients with PV who have had an inadequate response to or are intolerant of hydroxyurea*

WILMINGTON, Del.--(BUSINESS WIRE)--Jan. 28, 2015-- Incyte Corporation (Nasdaq: INCY) today announced that *The New England Journal of Medicine (NEJM)* published results from the pivotal Phase III RESPONSE clinical trial demonstrating that, compared to standard therapy, Jakafi® (ruxolitinib) significantly improved hematocrit control and reduced spleen volume in patients with polycythemia vera (PV) who had an inadequate response to or had unacceptable side effects from hydroxyurea¹.

PV is a myeloproliferative neoplasm (MPN) and is typically characterized by elevated hematocrit, the volume percentage of red blood cells in whole blood, which can lead to a thickening of the blood and an increased risk of blood clots, as well as an elevated white blood cell and platelet count². PV may occur at any age but often presents later in life, with a median age at diagnosis of 60 years^{2,3}.

Approximately 100,000 patients in the U.S. are living with PV⁴. Current standard treatment for PV is phlebotomy (the removal of blood from the body) plus aspirin. When phlebotomy can no longer control PV, chemotherapy such as hydroxyurea, or interferon, is utilized^{5,6}. Approximately one in four (~25,000) patients with PV are considered uncontrolled^{7,8} because they had an inadequate response to or had unacceptable side effects from hydroxyurea, the most commonly used chemotherapeutic agent for the treatment of PV.

"A key challenge in treating patients with PV is the development of resistance or intolerance to currently available therapies such as hydroxyurea, which leaves us with no effective treatment options to manage the disease," said Dr. Alessandro M. Vannucchi, Department of Hematology, University of Florence, Italy and lead study author. "This study indicates that ruxolitinib may represent an important advance for patients with uncontrolled PV."

In the RESPONSE trial, a significantly greater proportion of patients achieved the composite primary endpoint of hematocrit control without use of phlebotomy and at least a 35% spleen volume reduction when treated with ruxolitinib compared to standard therapy (21% compared to 1%, respectively; $p < 0.001$) as measured at week 32, and 91% of these patients treated with ruxolitinib maintained their response at week 48¹. Assessing the components of the composite primary endpoint separately, 60% of patients randomized to ruxolitinib achieved hematocrit control without use of phlebotomy in comparison with 20% of patients randomized to standard therapy; 38% of patients randomized to ruxolitinib achieved at least a 35% spleen volume reduction in comparison with 1% of patients randomized to standard therapy¹. 77% of patients randomized to ruxolitinib achieved one or both components of the composite primary endpoint, in comparison with 20% of patients randomized to standard therapy¹. Additionally, 84.5% of patients randomized to ruxolitinib were still receiving treatment at a median follow-up of 81 weeks¹.

A greater proportion of patients on the ruxolitinib treatment arm achieved complete hematologic remission, a key secondary endpoint, when compared to the standard therapy arm (24% compared to 9%, respectively; $p = 0.003$)¹. Complete hematologic remission was defined⁹ as achieving hematocrit control without the use of phlebotomy, platelet count $\leq 400 \times 10^9/L$ and white blood cell count $\leq 10 \times 10^9/L$, which are all important markers of disease control in PV.

"The publication of the data from our pivotal RESPONSE Phase III study demonstrates the importance of Jakafi as the first FDA-approved treatment for patients with uncontrolled polycythemia vera," stated Rich Levy, M.D., Incyte's EVP, Chief Drug Development and Medical Officer. "These data, together with those seen with Jakafi therapy in myelofibrosis, add further to our confidence in the potential therapeutic value of JAK inhibition in the treatment of patients with myeloproliferative neoplasms."

Overall, non-hematologic adverse events (AEs) were consistent with those previously seen in ruxolitinib studies in PV and myelofibrosis^{1,10,11}. Within the first 32 weeks of treatment, the most common non-hematologic AEs in the ruxolitinib arm were headache (16.4%), diarrhea (14.5%) and fatigue (14.5%), which were mainly Grade 1 or 2¹. During the first 32 weeks, grade 3/4 anemia or thrombocytopenia occurred in 2% and 5% of ruxolitinib patients, respectively, vs 0% and 4% of standard therapy patients¹.

Study Design

RESPONSE is a global, randomized, open-label Phase III study conducted at more than 90 sites. 222 patients with PV resistant to or intolerant of hydroxyurea were randomized 1:1 to receive either ruxolitinib (starting dose of 10 mg twice daily) or standard therapy (best available therapy), which was defined as investigator-selected monotherapy or observation only¹. Ruxolitinib dose could be adjusted as needed throughout the study¹.

The primary endpoint of the study was the proportion of patients whose hematocrit was controlled without phlebotomy eligibility from week 8 through 32 (with no more than one phlebotomy eligibility between randomization and week 8) and whose spleen volume was reduced by 35% or more from

baseline as assessed by imaging at week 32¹. Phlebotomy eligibility was defined as hematocrit (volume percentage of red blood cells in whole blood) greater than 45% and that was ≥ 3 percentage points higher than baseline, or hematocrit greater than 48%, whichever was lower. In addition, efficacy was further assessed using two key secondary endpoints: durable primary response and complete hematological remission¹. Other endpoints included safety, symptom improvement (as measured by the MPN-SAF 14-item total symptom score) and quality of life¹.

About Polycythemia Vera

Polycythemia vera (PV) is a myeloproliferative neoplasm (MPN) and is typically characterized by elevated hematocrit, the volume percentage of red blood cells in whole blood, which can lead to a thickening of the blood and an increased risk of blood clots, as well as an elevated white blood cell and platelet count². Patients with PV who fail to consistently maintain appropriate blood count levels, including appropriate hematocrit levels, have an approximately four times higher risk of major thrombosis (blood clots) or cardiovascular death¹². Patients with PV can also suffer from an enlarged spleen and a significant symptom burden which may be attributed to thickening of the blood and lack of oxygen to parts of the body¹³. These symptoms commonly include fatigue, itching, night sweats, bone pain, fever, and weight loss⁶.

Approximately 100,000 patients in the U.S. are living with PV⁴. Current standard treatment for PV is phlebotomy (the removal of blood from the body) plus aspirin. When phlebotomy can no longer control PV, chemotherapy such as hydroxyurea, or interferon, is utilized^{5,6}. Approximately one in four patients with PV are considered uncontrolled^{7,8} because they have an inadequate response to or are intolerant of hydroxyurea, the most commonly used chemotherapeutic agent for the treatment of PV.

About Incyte

Incyte Corporation is a Wilmington, Delaware-based biopharmaceutical company focused on the discovery, development and commercialization of proprietary therapeutics, primarily for oncology. For additional information on Incyte, please visit the Company's website at www.incyte.com.

About Jakafi® (ruxolitinib)

Jakafi is a first-in-class JAK1/JAK2 inhibitor approved by the U.S. Food and Drug Administration for treatment of people with polycythemia vera (PV) who have had an inadequate response to or are intolerant of hydroxyurea.

Jakafi is also indicated for treatment of people with intermediate or high-risk myelofibrosis (MF), including primary MF, post-polycythemia vera MF, and post-essential thrombocythemia MF.

Jakafi is marketed by Incyte in the United States and by Novartis as Jakavi® (ruxolitinib) outside the United States.

Important Safety Information

Jakafi can cause serious side effects, including:

Low blood counts: Jakafi may cause your platelet, red blood cell, or white blood cell counts to be lowered. If you develop bleeding, stop taking Jakafi and call your healthcare provider. Your healthcare provider will perform blood tests to check your blood counts before you start Jakafi and regularly during your treatment. Your healthcare provider may change your dose of Jakafi or stop your treatment based on the results of your blood tests. Tell your healthcare provider right away if you experience unusual bleeding, bruising, fatigue, shortness of breath, or a fever.

Infection: You may be at risk for developing a serious infection during treatment with Jakafi. Tell your healthcare provider if you develop any of the following symptoms of infection: chills, nausea, vomiting, aches, weakness, fever, painful skin rash or blisters.

Skin cancers: Some people who take Jakafi have developed certain types of non-melanoma skin cancers. Tell your healthcare provider if you develop any new or changing skin lesions.

The most common side effects of Jakafi include: anemia, low platelet count, bruising, dizziness, headache.

These are not all the possible side effects of Jakafi. Ask your pharmacist or healthcare provider for more information. Tell your healthcare provider about any side effect that bothers you or that does not go away.

Before taking Jakafi, tell your healthcare provider about all the medications, vitamins, and herbal supplements you are taking and all your medical conditions, including if you have an infection, have or had tuberculosis (TB), or have been in close contact with someone who has TB, have or had liver or kidney problems, are on dialysis, had skin cancer or have any other medical condition. Take Jakafi exactly as your healthcare provider tells you. Do not change or stop taking Jakafi without first talking to your healthcare provider. Do not drink grapefruit juice while on Jakafi.

Women should not take Jakafi while pregnant or planning to become pregnant, or if breast-feeding.

Please see the Full Prescribing Information available at www.jakafi.com, which includes a more complete discussion of the risks associated with Jakafi.

Forward-Looking Statements

Except for the historical information set forth herein, the matters set forth in this press release, including without limitation statements with respect to the potential efficacy, safety and therapeutic value of Jakafi® (ruxolitinib) in uncontrolled polycythemia vera, and the potential therapeutic value of JAK inhibition in myeloproliferative neoplasms, contain predictions and estimates and are forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. These forward-looking statements are based on Incyte's current expectations and subject to risks and uncertainties that may cause actual results to differ materially, including unanticipated developments in and risks related to the efficacy or safety of Jakafi, the results of further research and development, other market or economic factors, competitive and technological advances, and other risks detailed from time to time in Incyte's filings with the Securities and Exchange Commission, including its Quarterly Report on Form 10-Q for the quarter ended September 30, 2014. Incyte disclaims any intent or obligation to update these forward-looking statements.

References

- ¹ Vannucchi A, et al. Ruxolitinib versus Standard Therapy for the Treatment of Polycythemia Vera. The New England Journal of Medicine. 2015 372;5.
- ² Leukemia & Lymphoma Society . Polycythemia Vera Facts 2012. Available [here](#).
- ³ Tefferi A, Rumi E, Finazzi G, et al. Leukemia. 2013;27:1874-81.
- ⁴ Data on file. Incyte Corporation
- ⁵ Vannucchi AM. Blood 2014; 124(22):3212-20.
- ⁶ Passamonti F. Blood 2012; 120(2):275-84.
- ⁷ Barosi G, Birgegard G, Finazzi G, et al. Br J Haematol. 2010; 149:961-3.
- ⁸ Alvarez-Larrán A, Pereira A, Cervantes F, et al. Blood. 2012; 119:1363-9
- ⁹ Modified 2009 European LeukemiaNet (ELN) criteria.
- ¹⁰ Vannucchi, A, et al. Long-Term Outcomes from a Phase 3 Study Comparing Ruxolitinib with Best Available Therapy (BAT) for the Treatment of Myelofibrosis (MF): A 3 Year Update of Comfort II. Abstract # S1111.18th Congress of European Hematology Association (EHA), 2013. Stockholm, Sweden.
- ¹¹ Verstovsek S, Ruben M, Gotlib J, et al. Long-Term Outcome of Ruxolitinib Therapy in Patients with Myelofibrosis: 3-Year Update from COMFORT-I. Abstract #396. 55th American Society of Hematology (ASH) Annual Meeting and Exposition, 2013. New Orleans, LA.
- ¹² Marchioli R, et al. N Engl J Med. 2013;368:22-33.
- ¹³ National Institutes of Health <http://www.nhlbi.nih.gov/health/health-topics/topics/poly/signs>.

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