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Novartis study of real-world data concludes Jakavi is associated with a reduction in risk of death and dangerous blood clots for patients with rare blood cancer

- *Comparison of Jakavi® (ruxolitinib) vs. best available therapy presented at EHA suggests reduced risk of death in patients with inadequately controlled polycythemia vera (PV)¹*
- *Additional data at EHA suggests earlier treatment with Jakavi may lead to improved outcomes for patients with myelofibrosis (MF)^{2,3}*
- *Data underscores Novartis commitment to people with MF and PV through a robust ongoing research program in these rare blood cancers*

Basel, June 15, 2018 — Novartis announced today results from a new comparison study showing that Jakavi® (ruxolitinib)-treated patients with polycythemia vera (PV), who were resistant or intolerant to hydroxyurea (HU), had a significantly reduced risk of thrombosis (blood clots) and death compared to PV patients who received best available therapy¹. The study findings are based on a comparison of patients in the Phase III RESPONSE Jakavi clinical trial and the real-world Spanish GEMFINI patient registry. PV is a rare and incurable blood cancer associated with an overproduction of blood cells that can cause serious cardiovascular complications, such as blood clots, stroke and heart attack⁴.

The new findings were presented at the 23rd Congress of the European Hematology Association (EHA) in Stockholm, Sweden.

“When you can complement clinical trial data with real-world experiences, it can provide valuable insight into how treatments affect patients in their day-to-day lives,” said lead study investigator, Alberto Alvarez-Larran, MD, Hematology Department, Hospital Clinic, Barcelona, Spain. “This latest research supports the use of Jakavi to help people with polycythemia vera gain better control of their disease when hydroxyurea is not an option.”

Additional Jakavi data presented at the EHA Annual Congress includes efficacy and safety analyses of the largest expanded access trial of myelofibrosis (MF) patients treated with Jakavi to date (JUMP). An efficacy analysis showed that patients with lower-risk MF achieved spleen size reductions when treated with Jakavi, with most patients (82.1%) achieving a ≥50% reduction at any time^{2,3}. A separate analysis identified factors that may lead to a greater spleen response in patients with MF treated with Jakavi, including treating earlier in the course of the disease and at a higher dose (≥10 mg BID)⁵.

“With limited treatment options, patients with myeloproliferative neoplasms (MPNs) often struggle to keep their disease under control,” said Samit Hirawat, MD, Head, Novartis Oncology Global Drug Development. “The research conducted by Novartis teams and our physician partners in both PV and MF is helping to clarify how Jakavi can help relieve disease burden for patients.”

Additionally, 48-week data from the EXPAND study support Jakavi 10 mg BID as a starting dose in patients with MF with low platelet counts, providing important information in a patient

population at an increased risk of bleeding and serious complications⁵. Nearly one-third of patients in the study treated with Jakavi achieved a $\geq 50\%$ reduction in spleen size at week 48 (31.8% of patients [7/22] with a platelet count of 75 to 99 $\times 10^9/L$ and 35.7% [5/14] of patients with a platelet count of 50 to 74 $\times 10^9/L$)⁵.

About the PV Real-World Comparison Study

The new data presented at EHA compares overall survival and thrombosis (blood clots) rates using data from patients treated in the Jakavi arm of the RESPONSE trial and patients treated in a real-world setting with best available therapy (BAT) from the Grupo Español de Enfermedades Mieloproliferativas Crónicas Filadelfia Negativas (GEMFIN) registry¹.

In the previously reported Phase III RESPONSE trial, the high rate of crossover from BAT to Jakavi precluded the comparison of overall survival and thrombosis rates. RESPONSE was a global, open-label study that included patients with PV resistant to or intolerant of hydroxyurea, who were randomized 1:1 to receive either Jakavi (starting dose of 10 mg twice daily) or BAT, which was defined as investigator-selected monotherapy or observation only. The GEMFIN registry patients in the real-world BAT group had resistance or intolerance to hydroxyurea according to the modified European Leukemia Net criteria and received hydroxyurea (44%), busulfan (10%), radioactive phosphorus (2%), interferon (6%), anagrelide (12%), other therapy (11%) or no cytoreductive therapy (26%). Some patients were also treated with multiple therapies¹.

In the GEMFIN study, patients treated with Jakavi had a significantly prolonged overall survival (HR=0.28 [0.11–0.72]) and a lower risk of blood clots (HR=0.21 [0.06–0.76]) when compared to real-world patients treated with BAT¹.

About the JUMP Study

JUMP is an expanded access Phase IIIb study designed to further evaluate the safety and efficacy of Jakavi in MF. It includes the largest cohort of patients with MF treated with Jakavi, 2,233, to date. The study provided access to Jakavi for patients who had no access to the treatment outside of a clinical trial and included 60 patients who were determined to have DIPSS low-risk disease^{2,3}.

About the EXPAND Study

EXPAND is an open-label, Phase Ib, dose-finding study in patients with MF with baseline platelet counts of 50 to 99 $\times 10^9/L$. Results presented at EHA are from the 48-week follow-period⁵.

The study evaluated 10 mg BID as a safe starting dose of Jakavi. The key secondary endpoints are safety and efficacy, including proportion of patients achieving $\geq 50\%$ of reduction in spleen size. Safety findings were also consistent with previous studies of Jakavi⁵.

About Myelofibrosis and Polycythemia Vera

Myelofibrosis (MF) and polycythemia vera (PV) are part of a group of related and rare blood cancers called myeloproliferative neoplasms (MPNs) in which bone marrow cells responsible for the body's blood cells develop and function abnormally^{4,6}.

In patients with MF, the bone marrow can no longer produce enough normal blood cells, causing the spleen to enlarge. MF affects approximately one in every 100,000 people⁶.

PV is associated with an overproduction of blood cells that can cause serious cardiovascular complications if left inadequately controlled, such as blood clots, stroke and heart attack. PV affects up to three per 100,000 people globally each year⁴.

About Jakavi

Jakavi (ruxolitinib) is an oral inhibitor of the JAK 1 and JAK 2 tyrosine kinases. Jakavi is approved by the European Commission for the treatment of adult patients with polycythemia vera (PV) who are resistant to or intolerant of hydroxyurea and for the treatment of disease-related splenomegaly or symptoms in adult patients with primary myelofibrosis (MF) (also known as chronic idiopathic MF), post-polycythemia vera MF or post-essential thrombocythemia MF. Jakavi is approved in 101 countries for patients with MF, including EU countries, Switzerland, Canada, Japan and in more than 75 countries for patients with PV, including EU countries, Switzerland, Japan and Canada. The exact indication for Jakavi varies by country. Additional worldwide regulatory filings are underway in MF and PV.

Novartis licensed ruxolitinib from Incyte Corporation for development and commercialization outside the United States. Jakavi is marketed in the United States by Incyte Corporation as Jakafi® for the treatment of patients with PV who have had an inadequate response to or are intolerant of hydroxyurea and for the treatment of patients with intermediate or high-risk MF.

The recommended starting dose of Jakavi in PV is 10 mg given orally twice daily. The recommended starting dose of Jakavi in MF is 15 mg given orally twice daily for patients with a platelet count between 100,000 cubic millimeters (mm^3) and 200,000 mm^3 , and 20 mg twice daily for patients with a platelet count of $>200,000 \text{ mm}^3$. Doses may be titrated based on safety and efficacy. There is limited information to recommend a starting dose for MF and PV patients with platelet counts between 50,000/ mm^3 and $<100,000/\text{mm}^3$. The maximum recommended starting dose in these patients is 5 mg twice daily, and patients should be titrated cautiously⁷.

Jakavi is a registered trademark of Novartis AG in countries outside the United States. Jakafi is a registered trademark of Incyte Corporation. The safety and efficacy profile of Jakavi has not yet been established outside the approved indications.

Jakavi Important Safety Information for Treatment of Myelofibrosis (MF) and Polycythemia Vera (PV)

Jakavi can cause serious side effects, including a decrease in blood cell count and infections. Complete blood count monitoring is recommended. Dose reduction or interruption may be required in patients with any hepatic impairment or severe renal impairment or in patients developing hematologic adverse reactions such as thrombocytopenia, anemia and neutropenia. Dose reductions are also recommended when Jakavi is co-administered with strong CYP3A4 inhibitors or fluconazole. Use of Jakavi during pregnancy is not recommended, and women should avoid becoming pregnant during Jakavi therapy. Women taking Jakavi should not breast feed. Progressive multifocal leukoencephalopathy (PML) has been reported. Physicians should be alert for neuropsychiatric symptoms suggestive of PML. Hepatitis B viral load (HBV-DNA titer) increases have been reported in patients with chronic HBV infections. Patients with chronic HBV infection should be treated and monitored according to clinical guidelines. Non-melanoma skin cancer (NMSC) has been reported in Jakavi treated patients. Periodic skin examination is recommended. Very common adverse reactions in MF ($>10\%$) include urinary tract infections, anemia, thrombocytopenia, neutropenia, hypercholesterolemia, dizziness, headache, alanine aminotransferase increased, aspartate aminotransferase increased, bruising and weight gain. Common adverse reactions in MF (1 to 10%) include herpes zoster and flatulence. Uncommon adverse reactions in MF include tuberculosis. Very common adverse reactions in PV ($>10\%$) include anemia, thrombocytopenia, hypercholesterolemia, hypertriglyceridemia, dizziness, alanine aminotransferase increased and aspartate aminotransferase increased. Common adverse reactions in PV (1 to 10%) include urinary tract infections, herpes zoster, weight gain, constipation and hypertension.

Please see full Prescribing Information available at www.jakavi.com.

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About Novartis

Novartis provides innovative healthcare solutions that address the evolving needs of patients and societies. Headquartered in Basel, Switzerland, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, cost-saving generic and biosimilar pharmaceuticals and eye care. Novartis has leading positions globally in each of these areas. In 2017, the Group achieved net sales of USD 49.1 billion, while R&D throughout the Group amounted to approximately USD 9.0 billion. Novartis Group companies employ approximately 124,000 full-time-equivalent associates. Novartis products are sold in approximately 155 countries around the world. For more information, please visit <http://www.novartis.com>.

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Novartis Media Relations

Central media line: +41 61 324 2200

E-mail: media.relations@novartis.com

Eric Althoff

Novartis Global Media Relations

+41 61 324 7999 (direct)

+41 79 593 4202 (mobile)

eric.althoff@novartis.com

Mary Curtin Creaser

Novartis Oncology Communications

+1 862 778-2550 (direct)

+1 862 345-4102 (mobile)

mary.curtin_creaser@novartis.com

Novartis Investor Relations

Central investor relations line: +41 61 324 7944

E-mail: investor.relations@novartis.com

Central

Samir Shah

+41 61 324 7944

Pierre-Michel Bringer

+41 61 324 1065

Thomas Hungerbuehler

+41 61 324 8425

Isabella Zinck

+41 61 324 7188

North America

Richard Pulik

+1 212 830 2448

Cory Twining

+1 212 830 2417