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NEW STUDY DEMONSTRATES ROPEGINTERFERON ALFA-2B-NJFT IS A COST-EFFECTIVE TREATMENT OPTION FOR A BROAD RANGE OF PATIENTS WITH POLYCYTHEMIA VERA

Analysis published in the Journal of Comparative Effectiveness Research shows ropeginterferon alfa-2b-njft provided a cost-effective benefit in quality-adjusted life years compared to a commonly used treatment pathway

August 4, 2023, Burlington, MA – PharmaEssentia USA Corporation, a subsidiary of PharmaEssentia Corporation (TPEx:6446), a global biopharmaceutical innovator based in Taiwan leveraging deep expertise and proven scientific principles to deliver new biologics in hematology and oncology, today announced the publication of a cost-effectiveness analysis of ropeginterferon alfa-2b-njft (marketed as BESREMi®) in the *Journal of Comparative Effectiveness Research.* The analysis, titled *"*Cost-Effectiveness of Ropeginterferon Alfa-2b-njft for the Treatment of Polycythemia Vera*,"* showed that ropeginterferon alfa-2b-njft provided a cost-effective benefit for a broad range of patients with polycythemia vera (PV) versus first-line hydroxyurea followed by ruxolitinib. Cost effectiveness was demonstrated in a modeled population including both low- and high-risk patients receiving first- or second-line treatment with ropeginterferon alfa-2b-njft.

"PV is a chronic blood cancer that requires lifelong therapy, which can prevent or delay negative clinical outcomes, but is also associated with additional costs to patients and payers. These new data demonstrate ropeginterferon alfa-2b-njft's value not only to people living with PV, but also to the healthcare system at large," said Dr. Aaron Gerds, MD, MS, Medical Director at Case Comprehensive Cancer Center and lead study author. "This study shows ropeginterferon alfa-2b-njft is a cost-effective treatment option over the modeled lifetime and that earlier initiation of treatment of PV with effective therapy can translate to more favorable cost to benefit ratios."

PV is the most common myeloproliferative neoplasm (MPN) and a long-term, potentially life-threatening disease with limited approved treatment options. Patients with PV are at risk for disease progression to myelofibrosis (post-PV MF) or transformation to blast phase (MPN-BP) which is akin to acute myeloid leukemia[1-3]. Patients are also at an increased risk for arterial and venous thromboembolic events (TEs) which are associated with higher mortality, lower quality of life, and higher healthcare costs[4-7].

This new study used an economic model developed from the United States healthcare system perspective. Inputs were informed by the data from randomized clinical trials, including the PROUD-PV and CONTINUATION-PV studies, and from real-world sources. The model compared ropeginterferon alfa-2b-njft used either as first- or second-line therapy versus an alternative treatment pathway of first-line hydroxyurea followed by ruxolitinib. To reflect the long-term consequences of treating PV, results were presented over a lifetime horizon.

Findings from the study conclude ropeginterferon alfa-2b-njft is a cost-effective treatment option for a broad range of patients with PV, including both low- and high-risk patients and patients with and without prior cytoreductive treatment with hydroxyurea. Of note:

- These data show that over the modeled lifetime, patients who receive ropeginterferon alfa-2b-njft have more years alive (0.4), higher quality-adjusted life years (QALYs) (0.4),

and higher cost ($60,175) as compared to the alternative treatment pathway. Weighing the additional costs versus the additional QALY gains results in a cost per QALY of $141,783.

- This cost per QALY is less than a standard willingness to pay threshold of $150,000 per QALY[8].
- In this study, treating patients at a younger age or those with low-risk disease led to more cost-effective results, suggesting that earlier initiation of treatment of PV with effective therapy can translate to more favorable cost to benefit ratios.
- The model was sensitive to treatment costs, the percentage of patients who discontinue hydroxyurea, the percentage of ropeginterferon alfa-2b-njft users who switch to monthly dosing, the percentage of ropeginterferon alfa-2b-njft users as 2nd line treatment, and the treatment response rates.

“Ropeginterferon alfa-2b-njft has demonstrated safety and efficacy in studies including both low- and high-risk patients and patients with and without prior cytoreductive treatment with HU. Recently, the National Comprehensive Cancer Network (NCCN) updated their treatment guidelines to include ropeginterferon as a preferred treatment regimen for both low- and high-risk PV patients[9]. As ropeginterferon continues to be more widely used in clinical practice, this study was imperative to demonstrate the cost-effectiveness of ropeginterferon alfa-2b-njft for a broad range of patients with PV,” said Raymond Urbanski, M.D., Ph.D., Senior Vice President and U.S. Head of Clinical Development and Medical Affairs at PharmaEssentia. “This analysis also underscores the importance of treating low-risk patients and patients early in their disease journey to help minimize more severe events and their corresponding costs to the healthcare system.”

The full benefits of ropeginterferon alfa-2b-njft may not be fully captured in the model, and in particular, data on disutility of phlebotomy are lacking. Although some patients may tolerate regular phlebotomies, others can experience iron deficiency which can negatively impact quality of life. While the results from a scenario analysis incorporating a small decrement in utility had minimal impact on the cost-effectiveness results, due to the lack of data in this area, this estimate remains conservative. This study took a U.S. healthcare perspective, and the results may not generalize to other countries given the differences in healthcare resource use, costs and cost-effectiveness thresholds.

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About Polycythemia Vera (PV)

Polycythemia vera (PV) is a cancer originating from a disease-initiating stem cell in the bone marrow resulting in a chronic increase of red blood cells, white blood cells, and platelets. PV may result in cardiovascular complications such as thrombosis and embolism, and often transforms to secondary myelofibrosis or leukemia. While the molecular mechanism underlying PV is still subject of intense research, current results point to a set of acquired mutations, the most important being a mutant form of JAK2.[10]

About BESREMi® (ropeginterferon alfa-2b-njft)

BESREMi is an innovative monopegylated, long-acting interferon. With its unique pegylation technology, BESREMi has a long duration of activity in the body and is aimed to be

administered once every two weeks (or every four weeks with hematological stability for at least one year), allowing flexible dosing that helps meet the individual needs of patients.

BESREMi has orphan drug designation for the treatment of polycythemia vera (PV) in adults in the United States. The product was approved by the European Medicines Agency (EMA) in 2019, in the United States in 2021, and has recently received approval in Taiwan and South Korea. The drug candidate was invented by PharmaEssentia and is manufactured in the company's Taichung plant, which was cGMP certified by TFDA in 2017 and by EMA in January 2018. PharmaEssentia retains full global intellectual property rights for the product in all indications.

Indication

BESREMi is indicated for the treatment of adults with polycythemia vera.

Important Safety Information

WARNING: RISK OF SERIOUS DISORDERS

Interferon alfa products may cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders. Patients should be monitored closely with periodic clinical and laboratory evaluations. Therapy should be withdrawn in patients with persistently severe or worsening signs or symptoms of these conditions. In many, but not all cases, these disorders resolve after stopping therapy.

CONTRAINDICATIONS

- Existence of, or history of severe psychiatric disorders, particularly severe depression, suicidal ideation, or suicide attempt
- Hypersensitivity to interferons including interferon alfa-2b or any of the inactive ingredients of BESREMi.
- Moderate (Child-Pugh B) or severe (Child-Pugh C) hepatic impairment
- History or presence of active serious or untreated autoimmune disease
- Immunosuppressed transplant recipients

WARNINGS AND PRECAUTIONS

- Depression and Suicide: Life-threatening or fatal neuropsychiatric reactions have occurred in patients receiving interferon alfa-2b products, including BESREMi. These reactions may occur in patients with and without previous psychiatric illness.

  Other central nervous system effects, including suicidal ideation, attempted suicide, aggression, bipolar disorder, mania and confusion have been observed with other interferon alfa products.

  Closely monitor patients for any symptoms of psychiatric disorders and consider psychiatric consultation and treatment if such symptoms emerge. If psychiatric symptoms worsen, it is recommended to discontinue BESREMi therapy.

- Endocrine Toxicity: These toxicities may include worsening hypothyroidism and hyperthyroidism. Do not use BESREMi in patients with active serious or untreated endocrine

disorders associated with autoimmune disease. Evaluate thyroid function in patients who develop symptoms suggestive of thyroid disease during BESREMi therapy. Discontinue BESREMi in patients who develop endocrine disorders that cannot be adequately managed during treatment with BESREMi.

- Cardiovascular Toxicity: Toxicities may include cardiomyopathy, myocardial infarction, atrial fibrillation and coronary artery ischemia. Patients with a history of cardiovascular disorders should be closely monitored for cardiovascular toxicity during BESREMi therapy. Avoid use of BESREMi in patients with severe or unstable cardiovascular disease, (e.g., uncontrolled hypertension, congestive heart failure (≥ NYHA class 2), serious cardiac arrhythmia, significant coronary artery stenosis, unstable angina) or recent stroke or myocardial infarction.
- Decreased Peripheral Blood Counts: These toxicities may include thrombocytopenia (increasing the risk of bleeding), anemia, and leukopenia (increasing the risk of infection). Monitor complete blood counts at baseline, during titration and every 3-6 months during the maintenance phase. Monitor patients for signs and symptoms of infection or bleeding.
- Hypersensitivity Reactions: Toxicities may include serious, acute hypersensitivity reactions (e.g., urticaria, angioedema, bronchoconstriction, anaphylaxis). If such reactions occur, discontinue BESREMi and institute appropriate medical therapy immediately. Transient rashes may not necessitate interruption of treatment.
- Pancreatitis: Pancreatitis has occurred in 2.2% of patients receiving BESREMi. Symptoms may include nausea, vomiting, upper abdominal pain, bloating, and fever. Patients may experience elevated lipase, amylase, white blood cell count, or altered renal/hepatic function. Interrupt BESREMi treatment in patients with possible pancreatitis and evaluate promptly. Consider discontinuation of BESREMi in patients with confirmed pancreatitis.
- Colitis: Fatal and serious ulcerative or hemorrhagic/ischemic colitis have occurred in patients receiving interferon alfa products, some cases starting as early as 12 weeks after start of treatment. Symptoms may include abdominal pain, bloody diarrhea, and fever. Discontinue BESREMi in patients who develop these signs or symptoms. Colitis may resolve within 1 to 3 weeks of stopping treatment.
- Pulmonary Toxicity: Pulmonary toxicity may manifest as dyspnea, pulmonary infiltrates, pneumonia, bronchiolitis obliterans, interstitial pneumonitis, pulmonary hypertension, and sarcoidosis. Some events have resulted in respiratory failure or death. Discontinue BESREMi in patients who develop pulmonary infiltrates or pulmonary function impairment.
- Ophthalmologic Toxicity: These toxicities may include severe eye disorders such as retinopathy, retinal hemorrhage, retinal exudates, retinal detachment and retinal artery or vein occlusion which may result in blindness. During BESREMi therapy, 23% of patients were identified with an eye disorder. Eyes disorders ≥5% included cataract (6%) and dry eye (5%). Advise patients to have eye examinations before and during BESREMi therapy, specifically in those patients with a retinopathy-associated disease such as diabetes mellitus or hypertension. Evaluate eye symptoms promptly. Discontinue BESREMi in patients who develop new or worsening eye disorders.
- Hyperlipidemia: Elevated triglycerides may result in pancreatitis. Monitor serum triglycerides before BESREMi treatment and intermittently during therapy and manage when elevated. Consider discontinuation of BESREMi in patients with persistently, markedly elevated triglycerides.

- Hepatotoxicity: These toxicities may include increases in serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT) and bilirubin. Liver enzyme elevations have also been reported in patients after long-term BESREMi therapy. Monitor liver enzymes and hepatic function at baseline and during BESREMi treatment. Discontinue BESREMi in patients who develop evidence of hepatic decompensation (characterized by jaundice, ascites, hepatic encephalopathy, hepatorenal syndrome or variceal hemorrhage) during treatment.
- Renal Toxicity: Monitor serum creatinine at baseline and during therapy. Avoid use of BESREMi in patients with eGFR <30 mL/min. Discontinue BESREMi if severe renal impairment develops during treatment.
- Dental and Periodontal Toxicity: These toxicities may include dental and periodontal disorders, which may lead to loss of teeth. In addition, dry mouth could have a damaging effect on teeth and mucous membranes of the mouth during long-term treatment with BESREMi. Patients should have good oral hygiene and regular dental examinations.
- Dermatologic Toxicity: These toxicities have included skin rash, pruritus, alopecia, erythema, psoriasis, xeroderma, dermatitis acneiform, hyperkeratosis, and hyperhidrosis. Consider discontinuation of BESREMi if clinically significant dermatologic toxicity occurs.
- Driving and Operating Machinery: BESREMi may impact the ability to drive and use machinery. Patients should not drive or use heavy machinery until they know how BESREMi affects their abilities. Patients who experience dizziness, somnolence or hallucination during BESREMi therapy should avoid driving or using machinery.
- Embryo-Fetal Toxicity: Based on the mechanism of action, BESREMi can cause fetal harm when administered to a pregnant woman. Pregnancy testing is recommended in females of reproductive potential prior to treatment with BESREMi. Advise females of reproductive potential to use an effective method of contraception during treatment with BESREMi and for at least 8 weeks after the final dose.

ADVERSE REACTIONS

The most common adverse reactions reported in > 40% of patients in the PEGINVERA study (n=51) were influenza-like illness, arthralgia, fatigue, pruritis, nasopharyngitis, and musculoskeletal pain. In the pooled safety population (n=178), the most common adverse reactions greater than 10%, were liver enzyme elevations (20%), leukopenia (20%), thrombocytopenia (19%), arthralgia (13%), fatigue (12%), myalgia (11%), and influenza-like illness (11%).

DRUG INTERACTIONS

Patients on BESREMi who are receiving concomitant drugs which are CYP450 substrates with a narrow therapeutic index should be monitored to inform the need for dosage modification for these concomitant drugs. Avoid use with myelosuppressive agents and monitor patients receiving the combination for effects of excessive myelosuppression. Avoid use with narcotics, hypnotics or sedatives and monitor patients receiving the combination for effects of excessive CNS toxicity.

USE IN SPECIFIC POPULATIONS

- Pregnancy: Based on mechanism of action and the role of interferon alfa in pregnancy and fetal development, BESREMi may cause fetal harm and should be assumed to have abortifacient potential when administered to a pregnant woman. There are adverse effects on maternal and fetal outcomes associated with polycythemia vera in pregnancy. Advise pregnant women of the potential risk to a fetus.
- Lactation: There are no data on the presence of BESREMi in human or animal milk, the effects on the breastfed child, or the effects on milk production. Because of the potential for serious adverse reactions in breastfed children from BESREMi, advise women not to breastfeed during treatment and for 8 weeks after the final dose.
- Females of Reproductive Potential: BESREMi may cause embryo-fetal harm when administered to a pregnant woman. Pregnancy testing prior to BESREMi treatment is recommended for females of reproductive potential. Advise female patients of reproductive potential to use effective contraception during treatment with BESREMi and for at least 8 weeks after the final dose.
- Pediatric Use: Safety and effectiveness in pediatric patients have not been established.
- Geriatric Use: In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function and of concomitant disease or other therapy.

Please see accompanying full Prescribing Information, including Boxed Warning.

About PharmaEssentia

PharmaEssentia (TPEx: 6446), headquartered in Taipei, Taiwan, is a global and rapidly growing biopharmaceutical innovator. Leveraging deep expertise and proven scientific principles, PharmaEssentia aims to deliver effective new biologics for challenging diseases in the areas of hematology and oncology, with one approved product and a diversifying pipeline. Founded in 2003 by a team of Taiwanese-American executives and renowned scientists from U.S. biotechnology and pharmaceutical companies, today PharmaEssentia is expanding its global presence with operations in the U.S., Japan, China, and Korea, along with a world-class biologics production facility in Taichung, Taiwan.

For more information about PharmaEssentia USA, visit the website, LinkedIn or Twitter.

Forward Looking Statement

This press release may contain forward-looking statements, including statements about a cost-effectiveness analysis involving BESREMi and the expected impact of BESREMi on healthcare outcomes. For those statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995 and similar legislation and regulations under Taiwanese law. These forward-looking statements are based on management expectations and assumptions as of the date of this press release, and actual results may differ materially from those in these forward-looking statements as a result of various factors. These factors include changes in healthcare policies and regulations, the availability and acceptance of BESREMi in the market, changes in reimbursement that may impact the acceptance and adoption of BESREMi, and competition from other products. We do

not undertake to update any of these forward-looking statements to reflect events or circumstances that occur after the date hereof.

Media Contact:

Rachel Lipsitz, rachel_lipsitz@pharmaessentia.com

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