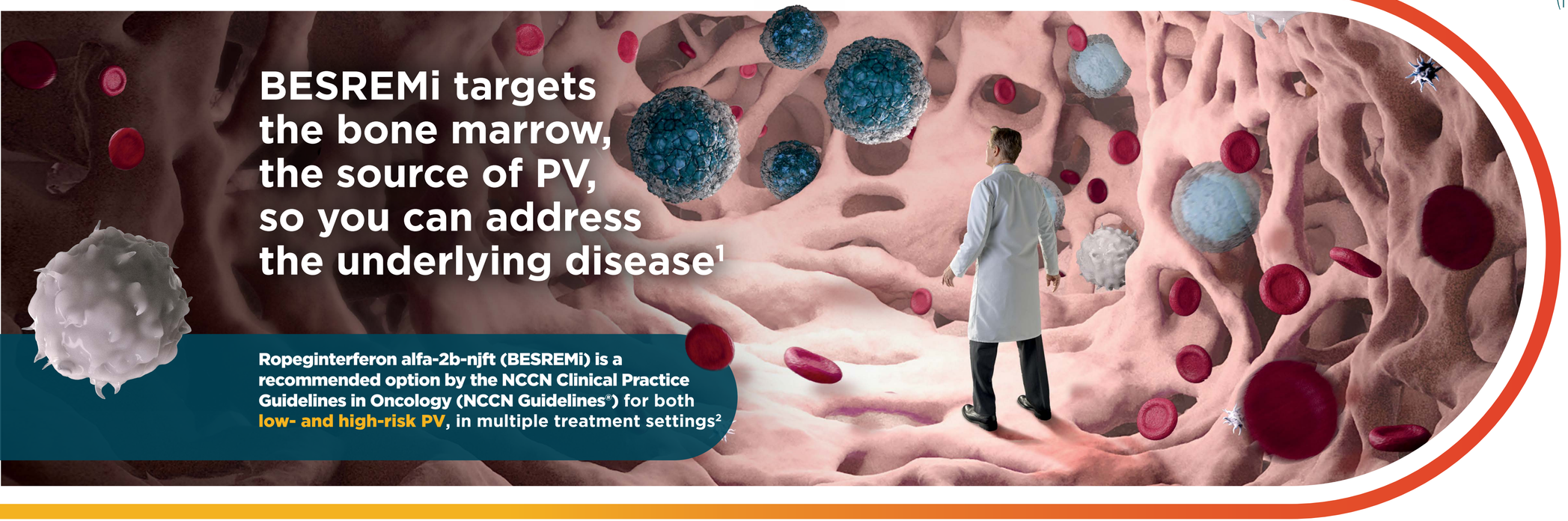
BESREMi®
(ropeginterferon alfa-2b-njft)
INJECTION



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See NCCN Guidelines for Myeloproliferative Neoplasms, V.2.2022, for complete recommendations.

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 Therapy should be withdrawn in patients with persistently severe or worsening signs or symptoms of these conditions.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.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including Boxed Warning.

In nearly all patients, the source of disease is a mutated hematopoietic stem cell (HSC) in the bone marrow[3,4]

A *JAK2* mutation drives pathogenesis in >95% of patients with PV[4]

- The mutation acquires a selective advantage over normal cells as the disease develops, which leads to the expansion of the malignant clone in the bone marrow[3-5]

Patients with PV face severe clinical consequences, including:

- Abnormal hematopoiesis, characterized by excessive levels of circulating erythrocytes, leukocytes, and platelets[6,7]
- The threat of thrombosis and other related cardiovascular events[7,8]
- The potential for progression to myelofibrosis (MF) or transformation to acute myeloid leukemia (AML)[9]

PV is characterized by heterogeneity in disease severity, which explains the variability in patient outcomes[5,7]

- There is no reliable way to predict who may experience the life-threatening consequences of the disease and when

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IMPORTANT SAFETY INFORMATION (continued)

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.

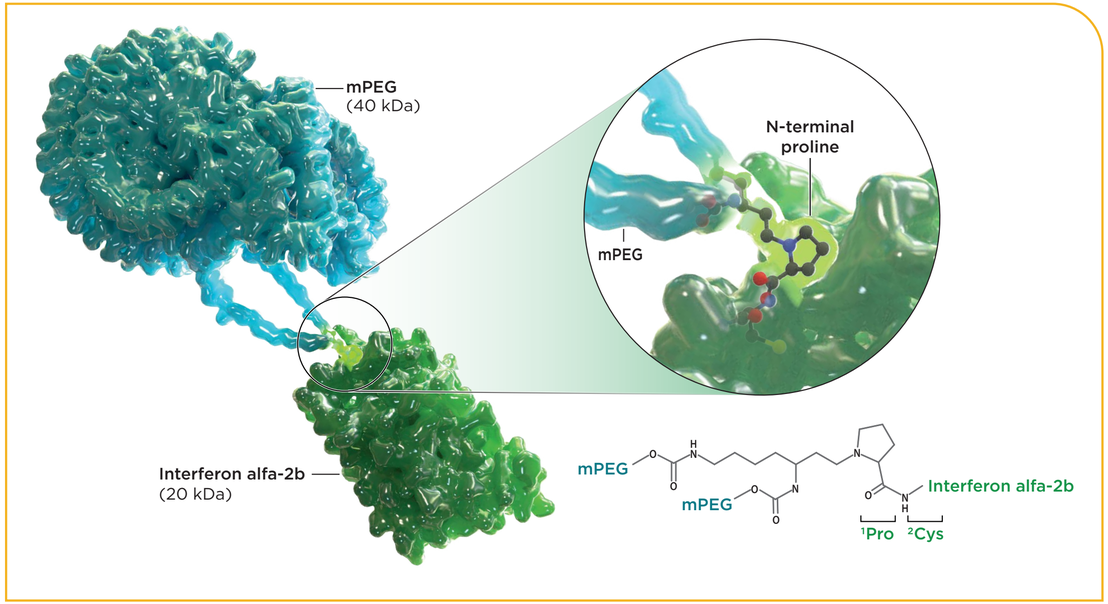
Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including Boxed Warning.

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

BESREMi: An innovative monopegylated long-acting interferon[1]

Site-specific monopegylation technology

- Provides prolonged release due to its unique pharmacokinetic properties
  - A half-life of 7 days extends the dosing interval
  - 1 subcutaneous dose every 2 weeks, which may be extended to 1 dose every 4 weeks after hematologic stability is achieved for at least 1 year
- In the bone marrow, interactions of type 1 interferons exhibit their cellular effects in PV



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IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

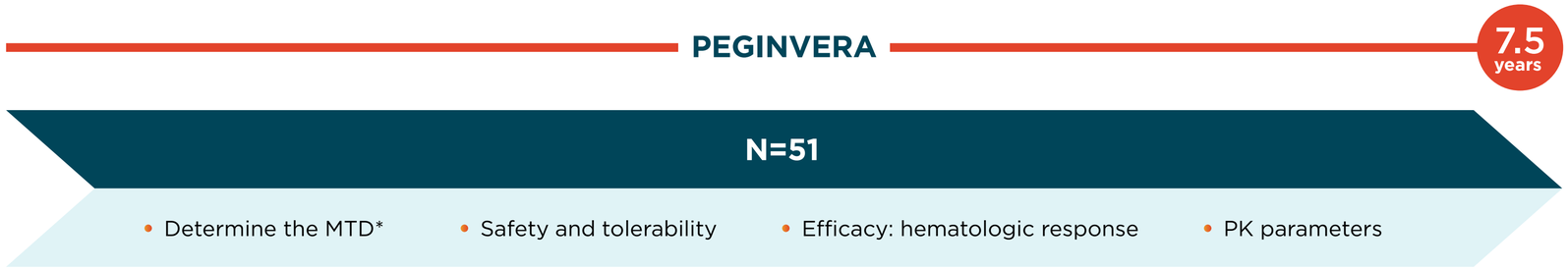
- Endocrine Toxicity: These toxicities may include worsening hypothyroidism and hyperthyroidism. Do not use BESREMi in patients with active serious or untreated endocrine disorders associated with autoimmune disease. Evaluate thyroid function in patients who develop symptoms suggestive of thyroid disease 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.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including Boxed Warning.

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

PEGINVERA evaluated the efficacy and safety of BESREMi over 7.5 years[1]

Prospective, multicenter, single-arm trial of 7.5 years' duration



Inclusion criteria

PV diagnosis with *JAK2* positivity

Broad range of patients with PV were included

- Newly diagnosed
- High- and low-risk patients
- HU treatment-naive
- Pretreated with HU/phlebotomy

*MTD, defined as highest administered dose without dose-limiting toxicities, was determined to be 540 mcg.

HU, hydroxyurea; MTD, maximum tolerated dose; PK, pharmacokinetic.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- 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.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including Boxed Warning.

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

BESREMi was initiated in a broad range of patients with PV[1]

Baseline patient characteristics

PARAMETER	BESREMi (N=51)
Age (mean), y (range)	**56** (35-82)
Sex	
Female, % (n)	**39%** (20)
Male, % (n)	**61%** (31)
Prior diagnosis of PV, % (n)	**84%** (43)
Duration of PV from diagnosis (median)	**2.2 years**
Previous treatment with HU, % (n)	**33%** (17)
Newly diagnosed, % (n)	**16%** (8)
History of major CV event, % (n)	**22%** (11)
Hematologic parameters (mean)	
Hematocrit, %	**45%±4.0**
Leukocytes, 10^9/L	**11.8±5.2**
Platelets, 10^9/L	**457±187**
Presence of splenomegaly*	
Yes, % (n)	**31%** (16)

*Defined as a longitudinal diameter of >12 cm for women and >13 cm for men.

CV, cardiovascular.

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IMPORTANT SAFETY INFORMATION (continued)

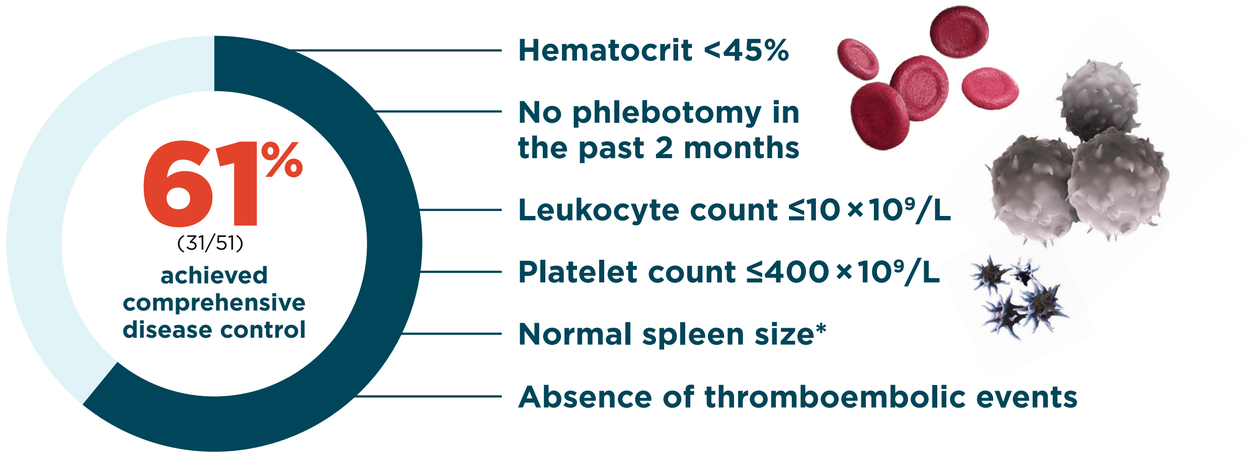
WARNINGS AND PRECAUTIONS (continued)

- 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.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including Boxed Warning.

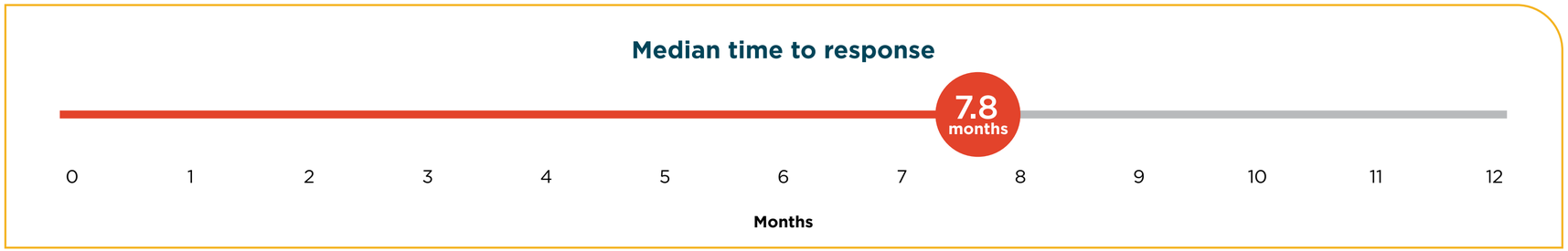
BESREMi® (ropeginterferon alfa-2b-njft) INJECTION

BESREMi: Comprehensive disease control over 7.5 years, with no thromboembolic events[1]



*Defined as longitudinal diameter ≤12 cm for females and ≤13 cm for males assessed by ultrasound.

Comprehensive disease control was achieved in the first year of treatment



IMPORTANT SAFETY INFORMATION (continued)

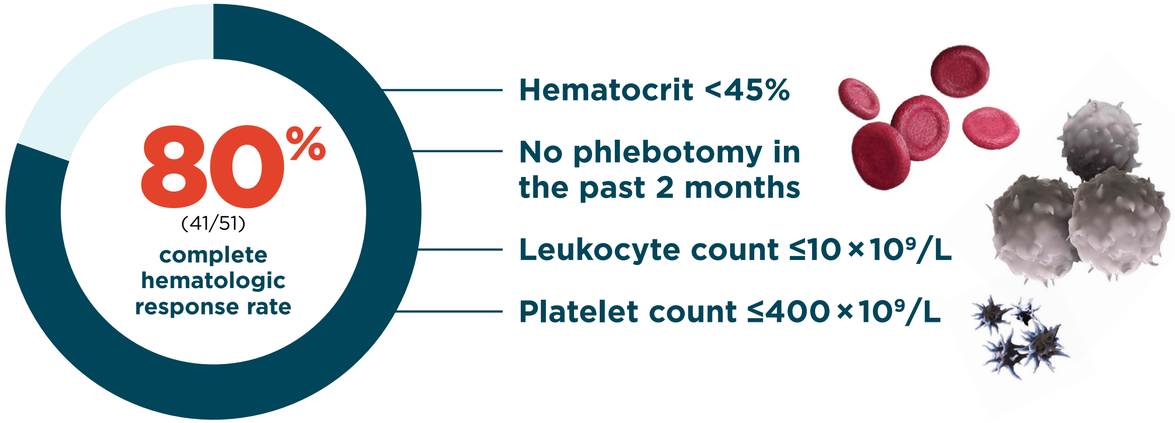
WARNINGS AND PRECAUTIONS (continued)

- 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.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including Boxed Warning.

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

High and durable rates of complete hematologic response over 7.5 years[1]



IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- 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.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including Boxed Warning.

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

BESREMi: A manageable long-term safety profile[1]

- The pooled safety population represents 178 patients with PV who were treated with BESREMi monotherapy in two open-label trials (PEGINVERA and PROUD/CONTINUATION-PV)

Most common adverse reactions (>10%) in the pooled safety population

ADVERSE REACTIONS	BESREMi (N=178)
Liver enzyme elevations	20%
Leukopenia	20%
Thrombocytopenia	19%
Arthralgia	13%
Fatigue	12%
Myalgia	11%
Influenza-like illness	11%

PEGINVERA: The majority of patients continued treatment for more than 5 years

- Among the 51 patients treated with BESREMi
  - 71% were exposed for 12 months or longer
  - 63% were exposed for 3 years or longer
  - 53% were exposed for >5 years

Most common serious adverse reactions (≥4%)

- Urinary tract infection (8%)
- Transient ischemic attack (6%)
- Depression (4%)

Treatment discontinuation

- Adverse reactions requiring permanent discontinuation in >2% of patients who received BESREMi included depression (8%), arthralgia (4%), fatigue (4%), and general physical health deterioration (4%)
  - Patients were not pre-screened for depression or anxiety disorders

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

PEGINVERA: Adverse reactions in >10% of patients with PV over 7.5 years[1]

ADVERSE REACTIONS (all treatment-emergent adverse events)	BESREMi (N=51)
Influenza-like illness[a]	59%
Arthralgia	47%
Fatigue[b]	47%
Pruritus	45%
Nasopharyngitis[c]	43%
Musculoskeletal pain[d]	41%
Headache[e]	39%
Diarrhea	33%
Hyperhidrosis[f]	29%
Nausea	28%
Upper respiratory tract infection[g]	27%
Local administration site reactions	26%
Dizziness	22%
Abdominal pain[h]	20%
Depression	20%
Sleep disorder[i]	20%
Leukopenia	18%
Decreased appetite	18%
Alopecia	16%
Edema[j]	16%
Hypertension[k]	16%
Muscle spasms	16%
Neutropenia	16%
Rash[l]	16%
Transaminase elevations[m]	16%
Urinary tract infection	16%
Thrombocytopenia	12%
Vertigo	12%

[a] Includes pyrexia, chills, and influenza-like illness.
[b] Includes asthenia, malaise, and fatigue.
[c] Includes pharyngitis and nasopharyngitis.
[d] Includes musculoskeletal pain, back pain, pain in extremity, bone pain, flank pain, and spinal pain.
[e] Includes headache, migraine, and head pain.
[f] Includes night sweats and hyperhidrosis.
[g] Includes upper respiratory tract infection, rhinitis, bronchitis, and respiratory tract infection.
[h] Includes abdominal pain upper, abdominal pain lower, and abdominal pain.
[i] Includes insomnia, sleep disorder, and abnormal dreams.
[j] Includes peripheral edema and generalized edema.
[k] Includes hypertension and hypertensive crisis.
[l] Includes rash, maculopapular rash, and pruritic rash.
[m] Includes transaminase increase, hepatic enzyme increase, GGT increase, AST increase, and ALT increase.

Additional observations[10]

- No cases of AML and 1 case of MF were observed over 7.5 years of BESREMi treatment

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

Low-PV study evaluated the efficacy and safety of BESREMi in low-risk patients[11]

Multicenter, open-label, two-arm, parallel-group, investigator-initiated, randomized trial (N=127)

Participants

- Adults aged 18-60 years
- Diagnosis of PV
- Hct <45% and in need of phlebotomy
- All patients met the definition of low risk: younger than 60 years of age with no history of arterial or venous thrombosis*

Treatment arms

Phlebotomy and low-dose aspirin (n=63)†

OR

BESREMi

on top of phlebotomy and low-dose aspirin (n=64)

Composite primary endpoint

- Maintenance of median Hct <45% over 12 months in the absence of disease progression‡

Key secondary endpoints

- Reduction in phlebotomy
- Reduction in leukocyte and platelet counts
- Reduction in spleen size

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Study limitations

- BESREMi was administered subcutaneously every 2 weeks at a fixed dose of 100 mcg, which differs from the approved dosing regimen[1,11]
  - For patients not already on HU, the recommended BESREMi starting dose is 100 mcg by subcutaneous injection every 2 weeks; the dose is increased by 50 mcg every 2 weeks (up to a maximum of 500 mcg) until hematologic parameters are stabilized[1]
- The absence of blinding was another limitation, which could potentially introduce some biases; however, the authors stated "these biases would be expected to have little effect on objectively measured endpoints, such as hematocrit measurements and disease progression"[11]

*The Low-PV study did not exclude patients with vascular risk factors, stable leukocytosis, or thrombocytosis.[11]

†Patients were treated with phlebotomy (300 mL for each phlebotomy to maintain Hct lower than 45%) and low-dose aspirin (100 mg daily), if not contraindicated.[11]

‡Definition of disease progression in low-risk patients with PV was in agreement with National Comprehensive Cancer Network Guidelines and included progressive symptomatic thrombocytosis and progressive leukocytosis, as well as the occurrence of any vascular or major bleeding complication.[11]

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

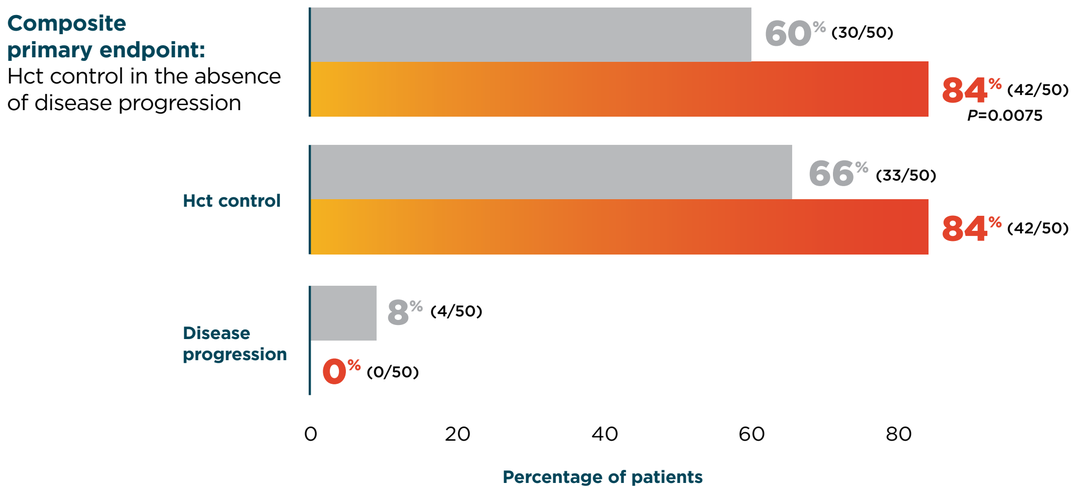
- Hepatotoxicity: These toxicities may include increases in serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT) and bilirubin. Liver enzyme elevations have also been reported in patients after long-term BESREMi therapy. Monitor liver enzymes and hepatic 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

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including Boxed Warning.

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

BESREMi: Comprehensive disease control in low-risk patients[11]

Significantly more patients achieved Hct control over 12 months in the absence of disease progression in the BESREMi group



Patients without disease progression had an absence of

- Progressive symptomatic thrombocytosis
- Progressive leukocytosis
- Any vascular or major bleeding complication

Phlebotomy and low-dose aspirin
BESREMi on top of phlebotomy and low-dose aspirin

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Adverse events by group and severity, regardless of causality

- In the phlebotomy and low-dose aspirin group (n=50), Grade 1-2 adverse events included asthenia (4%) and pruritus (2%); Grade 3 adverse events included skin symptom (4%), pain not otherwise specified (2%), knee impingement syndrome (2%), and thrombosis (2%)
- In the BESREMi group (n=50), Grade 1-2 adverse events included flu-like symptoms (16%), neutropenia (10%), asthenia (10%), pruritus (4%), hypertransaminasemia (4%), and skin symptom (2%); Grade 3 adverse events included neutropenia (8%), pruritus (2%), and hypertransaminasemia (2%)

Treatment reduction/discontinuation

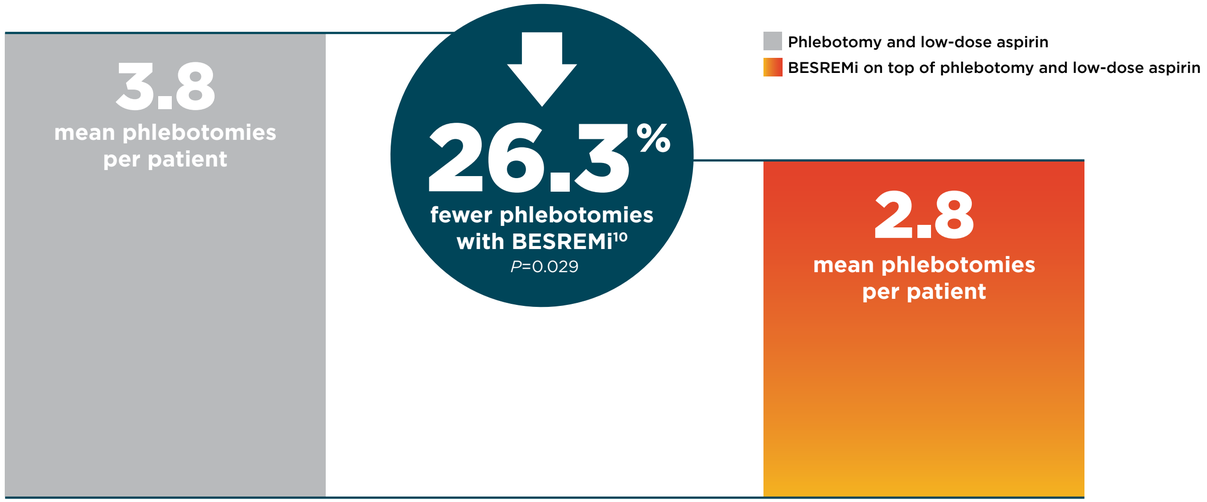
- Adverse events that caused treatment reduction occurred in one (2%) of 50 patients receiving phlebotomy and low-dose aspirin and three (6%) of 50 patients in the BESREMi group
- Three (6%) of 50 patients in the BESREMi group discontinued therapy
  - No treatment discontinuation occurred in patients receiving phlebotomy and low-dose aspirin

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including Boxed Warning.

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

BESREMi: Reduced need for phlebotomy in low-risk patients[11]

Number of phlebotomies per patient was significantly lower in the BESREMi group



8/50 (16%) of patients in the BESREMi group remained **phlebotomy-free** throughout the 12-month period

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

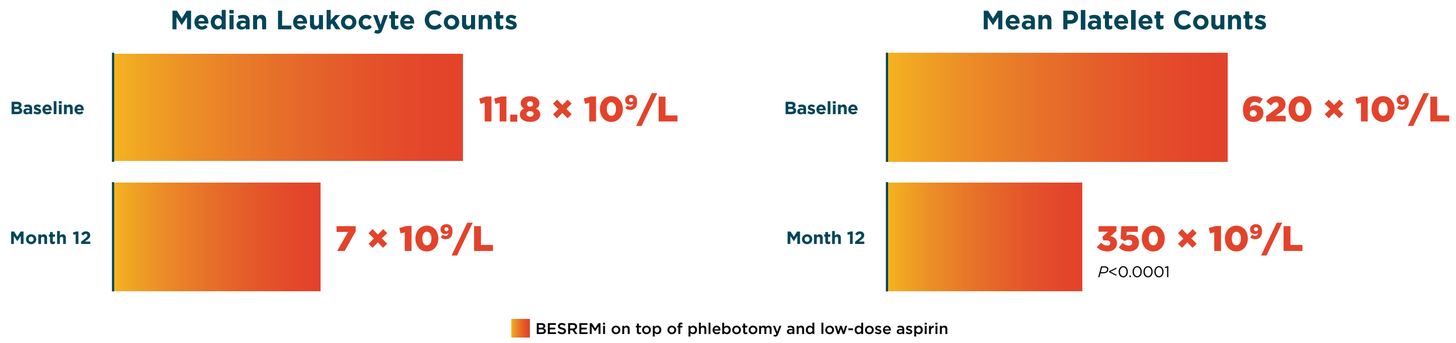
- Renal Toxicity: Monitor serum creatinine at baseline and during therapy. Avoid use of BESREMi in patients with eGFR <30 mL/min. Discontinue BESREMi if severe renal impairment develops during treatment.
- Dental and Periodontal Toxicity: These toxicities may include dental and periodontal disorders, 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.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including Boxed Warning.

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

Leukocyte and platelet normalization in low-risk patients[11]

Leukocytes and platelets decreased over time in the BESREMi group



Blood counts in the phlebotomy and low-dose aspirin group remained stable over 12 months at around 13.5 x 10^9/L (median leukocytes) and 700 x 10^9/L (mean platelets)

Patients with palpable splenomegaly

- BESREMi on top of phlebotomy and low-dose aspirin: **Significant reduction** from baseline (38% [19/50]) to Month 12 (23% [11/49]); *P*=0.045
- Phlebotomy and low-dose aspirin: **Relatively unchanged** from baseline (32% [16/50]) to Month 12 (28% [14/50])

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- 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.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including Boxed Warning.

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

An innovative monopegylated interferon that provides long-term chronic dosing[1]

1 subcutaneous dose every 2 weeks

Starting dose:	Increasing the dose:	Maximum dose:
• Patients not already on HU: **100 mcg** every 2 weeks • Patients transitioning from HU: **50 mcg** every 2 weeks	**50 mcg** every **2 weeks** (up to a maximum of 500 mcg), until hematologic parameters are stabilized	**500 mcg** every **2 weeks**

Hematologic stability defined

- **Hematocrit <45%**
- **Leukocytes <10 x 10^9/L**
- **Platelets <400 x 10^9/L**

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- 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.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including Boxed Warning.

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

Dose titration[1]

Patients not already on HU

- Increase the dose by 50 mcg every 2 weeks (up to a maximum of 500 mcg), until hematologic parameters are stabilized

Patients transitioning from HU

- Gradually taper off HU by reducing the total biweekly dose by 20% to 40% every 2 weeks during Weeks 3-12
- Increase the dose of BESREMi by 50 mcg every 2 weeks (up to a maximum of 500 mcg), until hematologic parameters are stabilized
- Discontinue HU by Week 13

Maintain the 2-week dosing interval of BESREMi at which hematologic stability is achieved for at least 1 year. After that time, the dosing interval may be expanded to 1 dose every 4 weeks.[1]

- All eligible patients in the PEGINVERA study (n=28) switched to 1 dose every 4 weeks as early as 1 year after starting BESREMi
- The mean dose of BESREMi was 237 mcg (±110) during the treatment period

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IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- 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.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including Boxed Warning.

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

Dose modifications[1]

- Monitor complete blood counts (CBC) every 2 weeks during the titration phase and dose modification phase, and every 3-6 months during the maintenance phase (after the patient's optimal dose is established). Monitor CBC more frequently if clinically indicated
- Phlebotomy as rescue treatment to normalize blood hyperviscosity may be necessary
- If dose interruption occurs, resume dosing at previously attained levels
- If drug-related toxicities arise, reduce the dose to the next lower level or interrupt in accordance with the table below
- If there is insufficient efficacy at the decreased dose following dose modification, a dose increase attempt to the next higher dose level should be considered after recovery to grade 1 toxicity

ADVERSE REACTION*	SEVERITY	DOSAGE MODIFICATION
Liver enzyme elevation with concomitant bilirubin elevation, or other evidence of hepatic decompensation	Any increase above baseline	Interrupt treatment until recovery, restart at dose 50 mcg lower than the interrupted dose. If the interrupted dose is 50 mcg, refrain from treatment until recovery. Consider permanent discontinuation if toxicity persists after four dose-modifications.
Liver enzyme elevation	>5 x the upper limit of normal (ULN) but ≤20 x ULN	Decrease dose by 50 mcg; if toxicity does not improve, continue decreasing at biweekly intervals until alanine aminotransferase (ALT) and aspartate aminotransferase (AST) recover <3 x ULN if baseline was normal; 3 x baseline if baseline was abnormal, and gamma-glutamyltransferase (GGT) recovers to <2.5 x ULN if baseline was normal; 2.5 x baseline if baseline was abnormal. If the interrupted dose is 50 mcg, refrain from treatment until recovery.
	>20 x ULN	Interrupt treatment until ALT and AST recover to <3 x ULN if baseline was normal; 1.5 x baseline if baseline was abnormal, and gamma-glutamyltransferase (GGT) recovers to <2.5 x ULN if baseline was normal; 2 x baseline if baseline was abnormal. Consider permanent discontinuation if toxicity persists after four dose-modifications.
Cytopenia	Anemia: hemoglobin (Hgb) <8 g/dL Thrombocytopenia: platelet count <50,000/mm^3 but ≥25,000/mm^3 Leukopenia: white blood cell count (WBC) <2,000/mm^3 but ≥1,000/mm^3	Decrease dose by 50 mcg; if toxicity does not improve, continue decreasing at biweekly intervals until recovery of Hgb >10.0 g/dL, platelets >75,000/mm^3, and WBC >3,000/mm^3. If the interrupted dose is 50 mcg, refrain from treatment until recovery.
	Anemia: hemoglobin levels are life threatening, or urgent intervention needed Thrombocytopenia: platelet count <25,000/mm^3 Leukopenia: WBC <1,000/mm^3	Interrupt treatment until recovery of Hgb >10.0 g/dL, platelets >75,000/mm^3, and WBC >3,000/mm^3. Consider permanent discontinuation if toxicity persists after four dose-modifications.
Depression	Mild, without suicidal ideation	Consider psychiatric consultation if persistent (>8 weeks).
	Moderate, without suicidal ideation	Consider dose reduction and psychiatric consultation.
	Severe, or any severity with suicidal ideation	Discontinue therapy, recommend psychiatric consultation.

*National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE), version 3.0.

IMPORTANT SAFETY INFORMATION (continued)

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 additional Important Safety Information throughout and accompanying full Prescribing Information, including Boxed Warning.

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

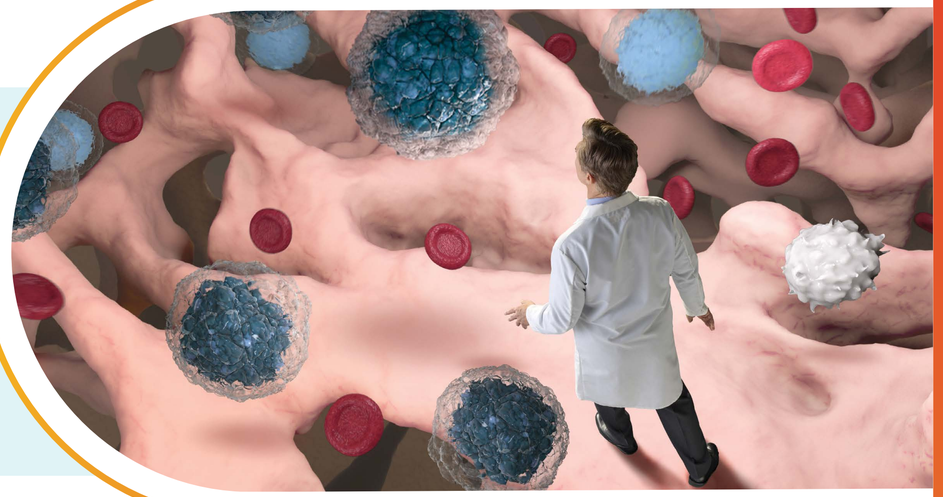
BESREMi targets the bone marrow, the source of PV, so you can address the underlying disease[1]

High and durable rates of complete hematologic response over 7.5 years, across a broad range of patients with PV[1]

A manageable long-term safety profile[1]

An innovative monopegylated interferon with PK properties that allow dosing once every 2 weeks[1]

- After hematologic stability is achieved for at least 1 year, the dosing interval may be expanded to 1 dose every 4 weeks



Ropeginterferon alfa-2b-njft (BESREMi) is a recommended option by the NCCN Guidelines
Discover more at BESREMiHCP.com

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.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including Boxed Warning.

References: 1. Besremi. Package insert. PharmaEssentia Corporation; 2021. **2.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Myeloproliferative Neoplasms V.2.2022. © National Comprehensive Cancer Network, Inc. 2022. All rights reserved. Accessed August 15, 2022. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **3.** Mead AJ, Mullally A. Myeloproliferative neoplasm stem cells. *Blood*. 2017;129(12):1607-1616. **4.** Tefferi A, Vannucchi AM, Barbui T. Polycythemia vera treatment algorithm 2018. *Blood Cancer J*. 2018;8(1):3. **5.** Palumbo GA, Stella S, Pennisi MS, et al. The role of new technologies in myeloproliferative neoplasms. *Front Oncol*. 2019;9:321. **6.** Shaikh SS, Stein BL. Polycythemia vera: contemporary updates in diagnosis, prognosis, and treatment. *Am J Hematol Oncol*. 2017;13(9):23-31. **7.** Raedler LA. Diagnosis and management of polycythemia vera: proceedings from a multidisciplinary roundtable. *Am Health Drug Benefits*. 2014;7(7 suppl 3):S36-S47. **8.** Finazzi G. A prospective analysis of thrombotic events in the European collaboration study on low-dose aspirin in polycythemia (ECLAP). *Pathol Biol (Paris)*. 2004;52(5):285-288. **9.** Stein BL, Oh ST, Berenzon D, et al. Polycythemia vera: an appraisal of the biology and management 10 years after the discovery of *JAK2 V617F*. *J Clin Oncol*. 2015;33(33):3953-3960. **10.** Data on file. PharmaEssentia Corporation. **11.** Barbui T, Vannucchi AM, De Stefano V, et al. Ropeginterferon alfa-2b versus phlebotomy in low-risk patients with polycythaemia vera (Low-PV study): a multicentre, randomised phase 2 trial. *Lancet Haematol*. 2021;8(3):e175-184.

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

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