The way your patients receive G-CSF therapy makes a clinical difference

In the pivotal trial, next-day Neulasta® (pegfilgrastim) reduced the incidence of febrile neutropenia (FN) and FN-related hospitalizations when used **every cycle, at the right time.**[1,*]

REDUCED THE INCIDENCE OF FN BY

94%

Neulasta® 1% vs placebo 17%, $P < 0.001$

REDUCED FN-RELATED HOSPITALIZATION BY

93%

Neulasta® 1% vs placebo 14%, $P < 0.001$

Every cycle, right-time use is challenging in the real world

Only Onpro® is designed to automatically deliver pegfilgrastim ~27 hours after application†

*Do not administer Neulasta® between 14 days before and 24 hours after administration of cytotoxic chemotherapy.

Indication

Neulasta® is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.

Neulasta® is not indicated for the mobilization of peripheral blood progenitor cells for hematopoietic stem cell transplantation.

Important Safety Information

Contraindication

- Neulasta® is contraindicated in patients with a history of serious allergic reactions to pegfilgrastim or filgrastim
- Reactions have included anaphylaxis

Please see additional Important Safety Information throughout this piece, and Neulasta® full Prescribing Information.

Pivotal trial study design and results[1]

Phase 3, multicenter, multinational, double-blind, placebo-controlled trial of patients with breast cancer (Neulasta® [n = 463] or placebo [n = 465]) receiving 100 mg/m^2 docetaxel Q3W for up to 4 cycles. The key endpoint was the percentage of patients who developed FN (Neulasta® 1% versus placebo 17%, $P < 0.001$). Also, secondary endpoints were lower for Neulasta®-treated patients as compared to placebo-treated patients (the incidence of hospitalization [1% versus 14%] and IV anti-infective use [2% versus 10%]).

†Incomplete doses have been reported with Onpro® due to device not performing as intended. This may increase risk of neutropenia, FN, and/or infection.

FN = temperature ≥ 38.2°C and absolute neutrophil count < 0.5 x 10^9/L.

G-CSF = granulocyte colony-stimulating factor, FN = febrile neutropenia, Q3W = once every 3 weeks, IV = intravenous.

Returning to their doctor's office the day after chemotherapy is especially challenging for patients in today's environment, which can get in the way of receiving their G-CSF at the right time

Onpro® is the only G-CSF delivery method designed to:

Address patient barriers to receiving G-CSF protection, **every cycle**

- Barriers may include the need to avoid exposure to viruses, transportation struggles, day after chemo falling on weekend/holiday, scheduling conflicts, and weather delays

Automatically deliver Neulasta® **at the right time[2,*]**

*Incomplete doses have been reported with Neulasta® Onpro® due to device not performing as intended. This may increase risk of neutropenia, FN, and/or infection.

Important Safety Information (continued)

Splenic Rupture

- Splenic rupture, including fatal cases, can occur following the administration of Neulasta®
- Evaluate for an enlarged or ruptured spleen in patients who report left upper abdominal or shoulder pain

Acute Respiratory Distress Syndrome (ARDS)

- ARDS has occurred in patients receiving Neulasta®
- Evaluate patients who develop a fever and lung infiltrates or respiratory distress after receiving Neulasta®
- Discontinue Neulasta® in patients with ARDS

Please see additional Important Safety Information throughout this piece, and Neulasta® full Prescribing Information.

Neulasta® (pegfilgrastim) injection Onpro® kit

Prospective observational study of ~2600 cancer patients

Fewer patients experienced FN with Neulasta® Onpro®[3,4]

Patients who received Neulasta® Onpro® had a lower frequency of FN vs other FN-prophylaxis options

Patient Group	Relative decrease in FN for Onpro®*	% of patients with FN [95% CI]	N
Other FN-prophylaxis options	36%	9.4% [7.51% - 11.21%]	951
Neulasta® Onpro® (all cycles)		6.2% [4.95% - 7.42%]	1455
Other FN-prophylaxis options	33%	9.4% [7.51% - 11.21%]	951
Neulasta® Onpro® (1st cycle)		6.4% [5.21% - 7.59%]	1624

This was an observational study and no formal statistical testing was performed. Descriptive statistics are available.

*Adjusted for baseline clinical and demographic differences between the groups, eg, degree of FN risk of chemotherapy regimen.

The primary endpoint was the overall incidence of FN over four cycles of chemotherapy, measured as absolute neutrophil count (ANC) < 1,000 × 10^6/L and one of the following occurring within 24 hours of decreased ANC: Temperature > 38°C, use of specific oral antibiotics (eg, ciprofloxacin, levofloxacin, moxifloxacin, amoxicillin-clavulanate), or use of IV antibiotics.[4]

90% Of patients who received Neulasta® Onpro® in the first cycle, 90%† received Neulasta® Onpro® in all cycles.[4]

†1455/1624 = 90%.

Important Safety Information (continued)

Serious Allergic Reactions

- Serious allergic reactions, including anaphylaxis can occur in patients receiving Neulasta®
- Majority of events occurred upon initial exposure and can recur within days after discontinuation of initial anti-allergic treatment
- Permanently discontinue Neulasta® in patients with serious allergic reactions

Please see additional Important Safety Information throughout this piece, and Neulasta® full Prescribing Information.

Study Design[3,4]

Prospective, observational US study to describe frequency of FN, adherence, and compliance among patients receiving myelosuppressive chemotherapy for breast, lung, prostate, or NHL malignancies.

- The study enrolled patients from November 2018 to April 2020
- The primary analysis included 2575 patients who completed up to four chemotherapy cycles
- Investigators decided on the method of FN-prophylaxis. Patients were grouped into either the Neulasta® Onpro® group or other FN-prophylaxis group based on FN-prophylaxis method received in the first cycle. In both groups, physicians could change the type of G-CSF use in the following cycles (choice in first cycle was generally consistent across subsequent cycles)
  - » Other FN-prophylaxis options included Neulasta® PFS or pegfilgrastim biosimilar PFS (61.7%), daily short-acting filgrastim or filgrastim biosimilar (7.3%), or no G-CSF (30.9%)
- Secondary endpoints included: 1) Patients who received G-CSF support for all chemotherapy cycles regardless of timing of G-CSF administration (persistence) and 2) Patients who received pegfilgrastim on the day after chemotherapy in every cycle in which pegfilgrastim was administered (compliance)

Study Limitations[4]

- It was not possible to evaluate FN risk among patients lost to follow-up after study enrollment
- Although the analysis of FN incidence controlled for known baseline differences between the groups, the lack of randomization means that the groups may have differed in ways that were not measured or recorded. The impact of such differences on the study findings is unknown
- The study enrollment closed prematurely due to COVID-19 and did not achieve target sample sizes

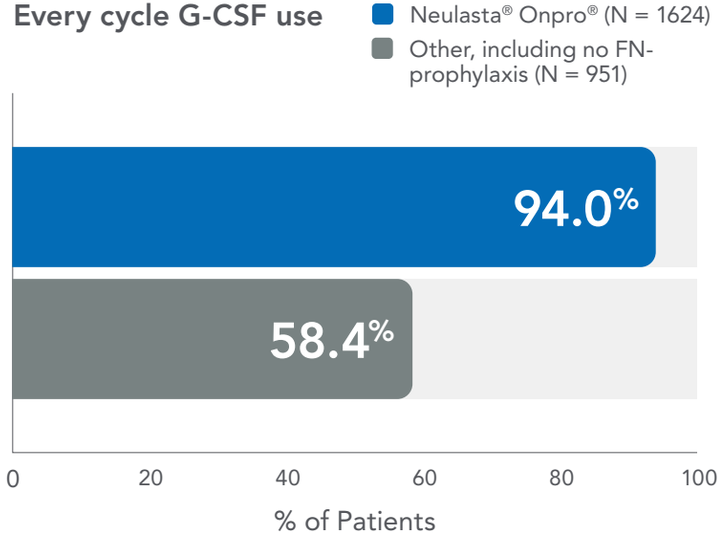
CI = confidence interval; PFS = prefilled syringe; NHL = non-Hodgkin's lymphoma; ANC = absolute neutrophil count.

Neulasta® (pegfilgrastim) injection Onpro® kit

A lower frequency of FN was shown by using Onpro® every cycle, at the right time

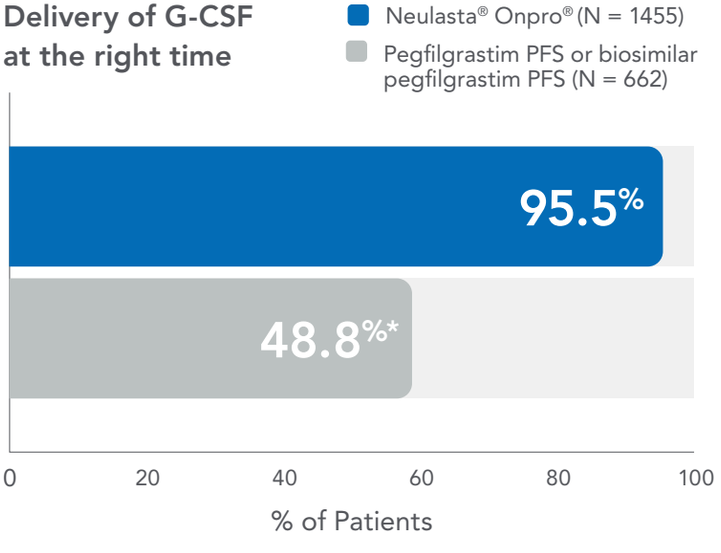
More patients received G-CSF support across every cycle with Neulasta® Onpro®[4]

94% of patients who received Neulasta® Onpro® in the **first cycle** received a G-CSF across **all cycles** of chemotherapy.



More patients received G-CSF support at the right time with Neulasta® Onpro®[4]

95.5% of patients receiving Neulasta® Onpro® **in every cycle** received it **on the day after** chemotherapy.



9 out of 10 patients who received Neulasta® Onpro® **in the first cycle received Onpro® in every cycle**

Important Safety Information (continued)

Allergies to Acrylics

- On-body injector (OBI) for Neulasta® uses acrylic adhesives
- Patients who are allergic to acrylic adhesives may have a significant reaction

Please see additional Important Safety Information throughout this piece, and Neulasta® full Prescribing Information.

*Percent of patients receiving pegfilgrastim PFS (innovator or biosimilar) on the day after chemotherapy, for all cycles in which pegfilgrastim PFS was administered.

Note: For any given patient, physicians generally chose the same FN-prevention therapy over time. However, a small percentage of patients received different therapies in different cycles. To facilitate comparison, the Onpro® group was comprised of patients who received Onpro® in every cycle. The comparator group was comprised of patients in the other physician-choice group who received pegfilgrastim PFS (innovator or biosimilar) at least once, and measured patient compliance for only those cycles in which pegfilgrastim PFS was administered.

Neulasta® (pegfilgrastim) injection Onpro® kit

The first prospective study of ~2600 cancer patients provides real-world evidence on the benefits of Neulasta® Onpro®

Neulasta® Onpro® had fewer cases of FN

- Patients who received Neulasta® Onpro® in the first and every cycle had a **lower frequency of FN** compared to other FN-prophylaxis options[3]
- With Neulasta® Onpro®, more patients received G-CSF support across **every cycle** compared to other FN-prophylaxis options[4]
- With Neulasta® Onpro®, more patients received G-CSF support **at the right time*** compared to pegfilgrastim PFS or biosimilar pegfilgrastim PFS[4]

*Do not administer Neulasta® between 14 days before and 24 hours after administration of cytotoxic chemotherapy.

Results are based on an observational study of 2575 patients and no formal statistical testing was performed. In the pivotal trial, Neulasta® significantly reduced the incidence of FN and FN-related hospitalization compared to placebo (see cover page).

Neulasta® (pegfilgrastim) injection Onpro® kit

G-CSF DELIVERY THAT MAKES A CLINICAL DIFFERENCE

Important Safety Information (continued)

Use in Patients With Sickle Cell Disorders
- In patients with sickle cell trait or disease, severe and sometimes fatal sickle cell crises can occur in patients receiving Neulasta®
- Discontinue Neulasta® if sickle cell crisis occurs

Please see additional Important Safety Information throughout this piece, and Neulasta® full Prescribing Information.

ONE MILLION PATIENTS

Neulasta® Onpro® is the #1 prescribed long-acting G-CSF and has been prescribed to **over 1 million patients**[5,6]

Important Safety Information (continued)

Glomerulonephritis

- Has occurred in patients receiving Neulasta®
- Diagnoses based on azotemia, hematuria, proteinuria, and renal biopsy
- Generally events resolved after dose reduction or discontinuation of Neulasta®
- If suspected, evaluate for cause and if cause is likely, consider dose-reduction or interruption of Neulasta®

Leukocytosis

- Increased white blood cell counts of 100 x 10^9/L have been observed
- Monitoring of complete blood count (CBC) during pegfilgrastim therapy is recommended

Thrombocytopenia

- Thrombocytopenia has been reported in patients receiving pegfilgrastim. Monitor platelet counts

Capillary Leak Syndrome (CLS)

- CLS has been reported after G-CSF administration, including Neulasta®
- Characterized by hypotension, hypoalbuminemia, edema, and hemoconcentration
- Episodes vary in frequency, severity, and may be life-threatening if treatment is delayed
- Patients with symptoms should be closely monitored and receive standard symptomatic treatment, which may include intensive care

Potential for Tumor Growth Stimulatory Effects on Malignant Cells

- G-CSF receptor has been found on tumor cell lines
- The possibility that pegfilgrastim acts as a growth factor for any tumor type, including myeloid malignancies and myelodysplasia, diseases for which Neulasta® is not approved, cannot be excluded

Myelodysplastic Syndrome (MDS) and Acute Myeloid Leukemia (AML) in Patients with Breast and Lung Cancer

- MDS and AML have been associated with the use of Neulasta® in conjunction with chemotherapy and/or radiotherapy in patients with breast and lung cancer. Monitor patients for signs and symptoms of MDS/AML in these settings

Potential Device Failures

- Missed or partial doses have been reported in patients receiving pegfilgrastim via the on-body injector (OBI) due to the device not performing as intended
- In the event of a missed or partial dose, patients may be at increased risk of events such as neutropenia, febrile neutropenia and/or infection than if the dose had been correctly delivered
- Instruct patients to notify their healthcare professional immediately in order to determine the need for a replacement dose if they suspect that the device may not have performed as intended

Aortitis

- Aortitis has been reported in patients receiving Neulasta®. It may occur as early as the first week after start of therapy
- Manifestations may include generalized signs and symptoms such as fever, abdominal pain, malaise, back pain, and increased inflammatory markers (e.g., c-reactive protein and white blood cell count)
- Consider aortitis in patients who develop these signs and symptoms without known etiology. Discontinue Neulasta® if aortitis is suspected

Nuclear Imaging

- Increased hematopoietic activity of the bone marrow in response to growth factor therapy has been associated with transient positive bone imaging changes. This should be considered when interpreting bone imaging results

Most common adverse reactions

- Bone pain
- Pain in extremity

Please see Neulasta® full Prescribing Information.

Neulasta® Injection: 6 mg/0.6 mL in a single-dose prefilled syringe for manual use only.

Neulasta® Injection: 6 mg/0.6 mL in a single-dose prefilled syringe co-packaged with the on-body injector (OBI) for Neulasta® (Neulasta® Onpro® kit).

Special Instructions for the On-body Injector (OBI) for Neulasta®

A healthcare provider must fill the on-body injector (OBI) with Neulasta® using the co-packaged prefilled syringe and then apply the OBI to the patient's skin (abdomen or back of arm). The back of the arm may only be used if there is a caregiver available to monitor the status of the OBI. Approximately 27 hours after the OBI is applied to the patient's skin, Neulasta® will be delivered over approximately 45 minutes. A healthcare provider may initiate administration with the OBI on the same day as the administration of cytotoxic chemotherapy, as long as the OBI delivers Neulasta® no less than 24 hours after the administration of cytotoxic chemotherapy.

The prefilled syringe co-packaged in the Neulasta® Onpro® kit contains additional solution to compensate for liquid loss during delivery through the OBI. If this syringe is used for manual subcutaneous injection, the patient will receive an overdose. If the prefilled syringe for manual use is used with the OBI, the patient may receive less than the recommended dose.

Do not use the OBI to deliver any other drug product except the Neulasta® prefilled syringe co-packaged with the OBI. Use of the OBI has not been studied in pediatric patients.

The OBI should be applied to intact, non-irritated skin on the arm or abdomen.

A missed dose could occur due to an OBI failure or leakage. Instruct patients using the OBI to notify their healthcare professional immediately in order to determine the need for a replacement dose of pegfilgrastim if they suspect that the device may not have performed as intended. If the patient misses a dose, a new dose should be administered by single prefilled syringe for manual use as soon as possible after detection.

Review the Patient Information and Patient Instructions for Use with the patient and provide the instructions to the patient.

Refer to the Healthcare Provider Instructions for Use for the OBI for full administration information.

For any OBI problems, call Amgen at 1-800-772-6436 or 1-844-MYNEULASTA (1-844-696-3852).

References

1. Vogel CL, et al. *J Clin Oncol.* 2005;23(6):1178-1184. **2.** Neulasta® (pegfilgrastim) Prescribing Information, Amgen. **3.** Data on file, Amgen; [1]; 2020. **4.** Mahtani RL, et al. A multicenter, prospective, observational study to determine the incidence of febrile neutropenia (FN), persistence and G-CSF utilization among cancer patients at high risk for FN receiving pegfilgrastim by an on-body injector (OBI) versus other FN-prophylaxis strategies. Poster presented at: San Antonio Breast Cancer Symposium®, Virtual. **5.** Data on file, Amgen; [2]; 2020. **6.** Data on file, Amgen; [3]; 2020.

Neulasta® Onpro® kit (pegfilgrastim) injection

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