Assessment of Device Failures and Medication Errors With the Pegfilgrastim On-body Injector in the US and EU

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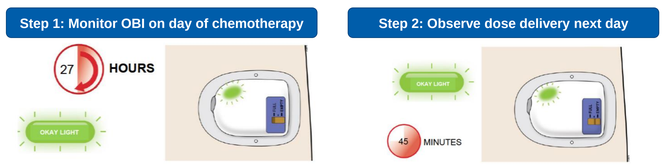
BACKGROUND

- Pegfilgrastim is a pegylated, long-acting granulocyte colony-stimulating factor (G-CSF), which is highly effective at reducing febrile neutropenia (FN) risk when administered the day after myelosuppressive chemotherapy for each cycle in patients receiving treatment for nonmyeloid malignancies, as recommended by clinical guidelines[1-5]
- However, the return to clinic the next day after chemotherapy is a significant burden for patients and their caregivers
- Despite longstanding interest in same-day pegfilgrastim administration to minimize outpatient visits, same-day administration is not as effective as next-day administration[6-8]
  - No prospective randomized clinical trial has definitively shown that deviating from the Food and Drug Administration (FDA)- and guideline-recommended dosing schedule is an acceptable alternative
- The pegfilgrastim on-body injector (OBI), which is applied the same day of chemotherapy and administers pegfilgrastim approximately 27 hours later, was approved by the United States (US) FDA in 2015, the European Medicines Agency in 2018, and facilitates the time-released administration of pegfilgrastim resulting in improved patient-centered care[9] **(Figure 1)**
  - With the true purpose to improve the patients' OBI experience, there have been two device updates in the US (2016 and 2021) and one in the EU (2019)

Figure 1A. Common Challenges After Myelosuppressive Chemotherapy Addressed by the Pegfilgrastim OBI

Figure adapted from https://www.neulasta.com/stay-at-home-with-neulasta-onpro

Figure 1B. Instructions on Pegfilgrastim OBI Use



Source: Pegfilgrastim on-body injector; Patients Instructions for Use (IFU) v9; November 2020. Amgen Inc.

The healthcare provider applies the OBI to the patient's skin immediately after completion of their chemotherapy cycle. The OBI is designed to automatically deliver the prescribed pegfilgrastim dose over 45 minutes, approximately 27 hours after application. Flashing green light indicates the OBI is working properly. During dose delivery, the OBI flashes a fast, green light. Once the dose is complete, a long beep sound occurs, and the status light turns solid green. The patient then removes the OBI and disposes of according to the Patients Instructions for Use.

BACKGROUND (continued)

- Past studies reported OBI failure rates between 1.3% and 6.9% **(Table 1)**[10-12]
  - However, these studies were single-institution reports, thus highlighting the need for an accurate, real-world assessment of the device failure rate to inform clinical decision making and aid in economic assessments
- An overestimation of failure rates can negatively influence physicians' perception of the OBI and consequently, physicians may be deterred from administering the OBI
- As patients undergo multiple chemotherapy cycles and receive a new OBI device each cycle, estimation of device failure rates should be normalized to the number of devices used
- Therefore, we aimed to determine the real-world reliability of the pegfilgrastim OBI
- This analysis is the first multi-country, multi-institution, real-world assessment of the OBI and represents the experience with over 30,000 devices used in clinical practice

Table 1. Previously Reported Failure Rates of the Pegfilgrastim OBI

Study	Number of patients	Number of cycles OBI device was used	Number of patients with device failures	Failure rate
Maahs LG, et al. *J Oncol Pharm Pract* 2020	182	395	5	1.26%
Patel J, et al. *Hosp Pharm* 2021	28	104	2	1.92%
Townley C, et al. *J Hematol Oncol Pharm* 2018	58	Not reported	4[a]	6.9%

[a]The authors concluded that only two of the four observed failures were attributed to device malfunction.

OBJECTIVE

- As over 1 million patients have received the OBI, we evaluated OBI device failures reported in the postmarketing setting and in a large prospective observational study

METHODS

- We report medication errors and device failures with OBI use in patients receiving chemotherapy from two sources: postmarket surveillance data from the European Union (EU) and a prospective observational study conducted in the US (Rifkin et al. *manuscript in review*) **(Figure 2)**

Figure 2. Data Sources for Medication Errors and Device Failures Reported With Pegfilgrastim OBI Use

Postmarketing commitment

Definition of medication error
- Missed or incomplete dose, dose delay or dose interruption of pegfilgrastim due to user error or device malfunction

Reporting period
- May 15, 2018 to May 15, 2021

Methodology
- To capture all cases relevant to the topic of medication errors with the use of the pegfilgrastim OBI, a search of the Amgen Global Safety Database (AGSD) retrieved all cases from the postmarketing setting
- All retrieved cases of medication errors were summarized, assessed, and evaluated to determine if any harm occurred to the patient
- Harm was defined as an adverse reaction resulting from the reported medication error, specifically events occurring because of a missed or incomplete dose

Eligible cases/data
- ≥ 1 event from the Medication Errors Standardised MedDRA Query (Broad) was reported; and
- The pegfilgrastim OBI was used; and
- Were within the reporting period; and
- Were reported in the EU region

N = 27,666 distributed devices

Prospective observational study

Definition of device failure
- Physician-reported failure of the OBI cited on the G-CSF administration form as the reason for a zero or partial dose, dose delay, or dose interruption

Enrollment period
- November 07, 2018 to April 09, 2020

Methodology
- Patients were classified into two groups, curative or palliative treatment intent, and then categorized by FN prophylaxis (treating physicians had the discretion to select pegfilgrastim or biosimilar pegfilgrastim prefilled syringe, daily filgrastim, or no G-CSF) for up to four planned chemotherapy cycles

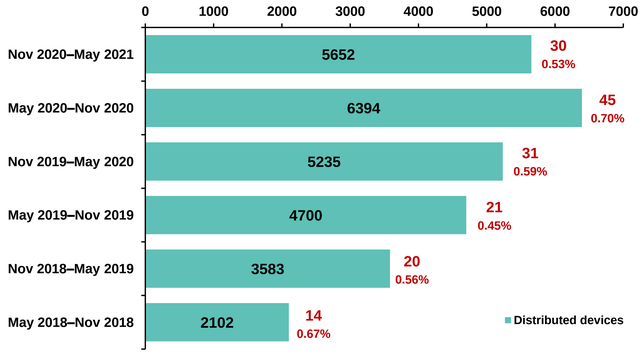
Eligible patients
- Adult patients diagnosed with non-Hodgkin lymphoma, breast, lung, or prostate cancer
- Up to four anticipated chemotherapy cycles
- Life expectancy > 6 months
- Starting myelosuppressive chemotherapy regimens administered every 3 to 4 weeks with a high FN risk or an intermediate FN risk plus ≥ 1 patient risk factor

Patients were administered the OBI in 6,087 chemotherapy cycles

RESULTS

- The postmarketing surveillance data revealed that the reporting rate of medication errors of pegfilgrastim with the OBI within the EU was 0.58% (161 events in 27,666 distributed devices) over 3 years
- Overall, medication errors with the OBI in the EU remained stable over the 3-year period of monitoring, with no new safety concerns identified **(Figure 3)**
- In the prospective observational study (n = 1,624), six failures were reported in 6,087 chemotherapy cycles (0.1%) during which the OBI was administered **(Table 2)**

Figure 3. Reporting Rate of Medication Errors, Error Events, and Distributed Devices of Pegfilgrastim OBI Within the EU by Reporting Period



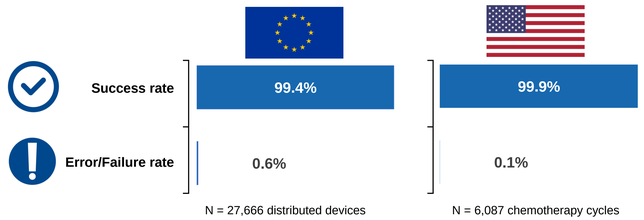
Numbers in dark red denote the number of error events and the reporting rate of medication errors for the reporting period.

Table 2. Device Failure Rate in the Prospective Observational Study

	All Patients (N = 2,575)[a]
Number of pegfilgrastim OBI administrations	6,087
Device failure rate, n (%)	6 (0.1)[b]

[a]A total of 1,624 patients received the OBI device.
[b]Percentage is based on the number of pegfilgrastim OBI administrations.
Device failure is defined as number of responses given for "Reason for None or Partial Dose" or "Reason for Dose Delay" or "Reason for Dose Interruption" as "Device failure" with device name as "On Body Injector" in the G-CSF administration form.

Figure 4. Summary of Key Findings



LIMITATIONS

- Postmarketing surveillance
  - Several limitations of postmarketing surveillance data, mainly related to reporting bias (underreporting as well as overreporting) and data quality, must be considered[13]
    - Spontaneous reports from patients and physicians are voluntary; therefore, reporters are neither a random sample nor a census of the population using medical products
  - Despite its limitations, the spontaneous reporting system is an extremely valuable mechanism for safety monitoring[13]
- Prospective observational study
  - Device failures in the prospective study were physician-reported and were not actively monitored
  - Device failure was not a prespecified endpoint in the prospective study, which was designed to assess the effectiveness of the OBI with respect to FN incidence

CONCLUSIONS

- **Experience with > 30,000 OBIs in the EU and US suggest medication errors (0.58%) and reported failures (0.1%) are lower than those previously reported**
- **The benefit-risk profile of the pegfilgrastim OBI remains favorable**

DISCLOSURES

- All authors are employees and stockholders of Amgen Inc.

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