

NADIR: A Non-Interventional Study on the Prophylaxis of Chemotherapy-Induced Neutropenia Using Lipegfilgrastim – First Interim Analysis

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Keywords

Lipegfilgrastim · Granulocyte-colony stimulating factor · Chemotherapy-induced neutropenia · Febrile neutropenia · Severe neutropenia

Summary

Background: The non-interventional study (NIS) NADIR was designed to assess the effectiveness and safety of lipegfilgrastim, a novel glycopegylated granulocyte-colony stimulating factor, in reducing the risk of both febrile and severe neutropenia. **Methods:** Here, the interim analysis of NIS Nadir performed under real-world conditions at 80 oncology practices across Germany is reported. For a patient to be included, lipegfilgrastim at a subcutaneous single dose of 6 mg had to be administered during at least 1 cycle of the chemotherapy under consideration. **Results:** The interim analysis included 224 patients. Median patient age was 61.1 years (interquartile range 51.2–70.2 years). Main tumor type was breast cancer followed by lung cancer, and non-Hodgkin's lymphoma (46.0, 13.4, and 10.7%, respectively). When lipegfilgrastim was given as primary prophylaxis, no patient developed febrile neutropenia (FN). 1.3% of patients developed FN when pri-

mary prophylaxis was withheld. Only 68.6% of patients undergoing chemotherapy and at high risk (> 20%) of developing FN were treated with lipegfilgrastim during the first cycle, exposing disparity between real-world practices and current treatment guidelines. Lipegfilgrastim was well tolerated. The only grade 3/4 treatment-related adverse event was anemia in 1 patient. **Conclusion:** Lipegfilgrastim was effective and safe when administered for the prevention of chemotherapy-induced neutropenia under real-world conditions.

Introduction

Chemotherapy-induced neutropenia is characterized by a marked decrease in the peripheral blood neutrophil count. Since neutrophils are an integral part of the innate immune system, this may result in severe complications such as life-threatening infections [1–3]. As a result, neutropenia is considered to be the most serious chemotherapy-related hematological adverse event, frequently leading to dose delays or reductions which may compro-

mise treatment outcomes [4, 5]. Neutropenia dampens most of the signs and symptoms of infection, and patients typically present with only fever, which is why this neutropenia-associated complication is referred to as febrile neutropenia (FN) [6]. Depending on the number of comorbidities, chemotherapy-induced FN is thought to be responsible for the deaths of up to 50% of affected patients [7]. Therefore, prevention of FN is considered a primary goal of supportive care in cancer patients at high risk undergoing cytotoxic chemotherapy [8].

Apart from chemotherapy-related factors, neutropenic risk assessment includes disease characteristics such as presence of metastases, as well as individual patient risk factors such as reduced performance status, comorbidities, presence of elevated lactate dehydrogenase levels, or age older than 65 years [8]. Preventing neutropenia in elderly patients is especially important as they often receive lower doses of chemotherapy, and further dose reduction can substantially compromise treatment success [8–10].

Besides significant morbidity and mortality, FN also has a substantial negative economic impact. One of the main drivers of costs related to antineoplastic chemotherapy is hospitalization which often includes other direct and indirect medical costs such as antibacterial treatment and inability to work [11, 12].

Recently, lipegfilgrastim (Lonquex[®], TEVA Ltd., Petach Tikva, Israel), a novel long-acting glycopegylated granulocyte-colony stimulating factor (G-CSF), obtained EMA (European Medicines Agency) regulatory approval to reduce both the duration of neutropenia and the incidence of chemotherapy-induced FN. The pharmacodynamic properties of lipegfilgrastim are similar to those of conventional pegylated G-CSF albeit with greater structural homogeneity achieved by choosing the endogenous but unused natural O-glycosylation site in the G-CSF molecule for enzyme-mediated site-specific glycopegylation at threonine 134 [13, 14].

Current guidelines of the European Organisation for Research and Treatment of Cancer (EORTC) recommend use of G-CSFs in adult patients at high risk of FN as primary prophylaxis when undergoing cytotoxic chemotherapy for solid tumors or lymphoproliferative disorders [8].

According to a recently presented retrospective survey performed in hospitals and practices in Germany, the adherence to national and international guidelines on the use of G-CSF may not be sufficient for patients at intermediate or high risk of FN [15]. The question was raised whether the data of the prospective non-interventional study (NIS) NADIR currently running in Germany reflects this notion. The hereby presented interim analysis of this study documents data showing whether adherence to guidelines for the prevention of FN is appropriate or not.

Patients and Methods

NADIR (Non-interventional study on the treatment of chemotherapy-induced neutropenia with Lipegfilgrastim) is a prospective NIS performed under real-world conditions at 80 oncology practices across Germany. The protocol identifier is TV44689-ONC-4004. Patients were treated according to daily clinical practice. All patients provided written informed consent prior to study ini-

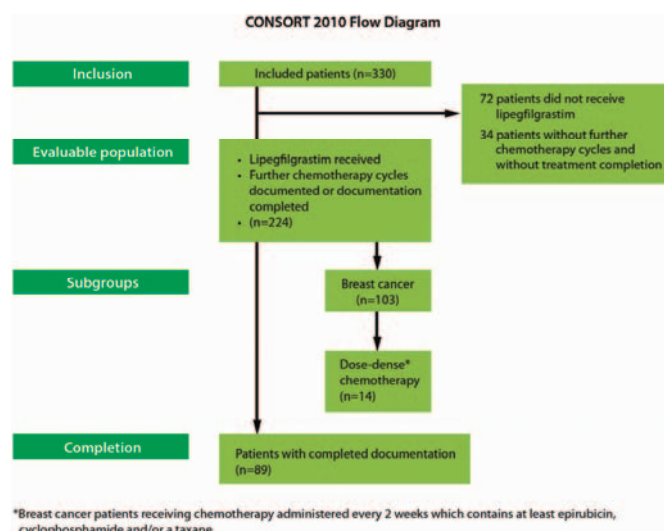


Fig. 1. CONSORT flow diagram.

Table 1. Characteristics of the interim analysis population (n = 224)

| Characteristics | | | |
|-----------------------------------|------|-------------|--|
| Median age, years (range) | 61.1 | (51.2–70.2) | |
| | n | % | |
| Sex | | | |
| Female | 155 | 69.2 | |
| Male | 69 | 30.8 | |
| ECOG score | | | |
| 0 | 111 | 49.6 | |
| 1 | 87 | 38.8 | |
| 2 | 14 | 6.3 | |
| 3 | 1 | 0.4 | |
| 4 | 1 | 0.4 | |
| Comorbidity | | | |
| Overall (at least 1) | 150 | 67.0 | |
| Arterial hypertension | 84 | 37.5 | |
| Thyroid disease | 25 | 11.2 | |
| Diabetes mellitus ^a | 23 | 10.3 | |
| Type of chemotherapy ^b | | | |
| Taxane-based | 86 | 38.4 | |
| Non-taxane-based | 138 | 61.6 | |

^aWithout end-stage organ damage.

^bUp to and including the first lipegfilgrastim-supported cycle.

tiation. The study was reviewed by the Ethics Committee of the Medical Association of Baden-Württemberg. 20% of all data in electronic case report forms of each patient were checked against all source documents with respect to accuracy at each site. All serious adverse event report entries were checked for consistency against source data at all sites.

For a patient to be included, lipegfilgrastim at a subcutaneous dose of 6 mg had to be administered during at least 1 cycle of the chemotherapy under consideration.

The primary objective was a systematic assessment of the incidence of severe chemotherapy-induced neutropenia and FN during lipegfilgrastim-supported cytotoxic chemotherapy. Secondary objectives included the timing of lipegfilgrastim administration according to the first day of a chemotherapy cycle,

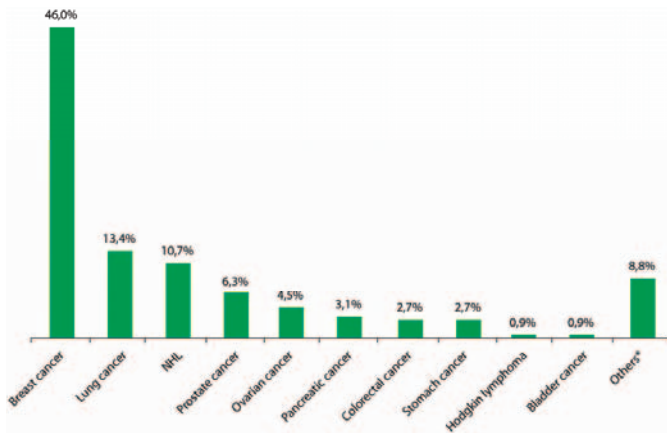


Fig. 2. Distribution of tumor entities. *B-cell chronic lymphocytic leukemia (4); cholangiocarcinoma (3); esophageal cancer (3); multiple myeloma (2); chronic lymphocytic leukemia, carcinoma of unknown primary origin, cervical cancer, glioblastoma multiforme, hemangioblastoma, plasmacytoma, tube cancer, uterine cancer (1 each).

the use of antibiotics/antimycotics as prophylactic and/or therapeutic treatment, total leukocyte and absolute neutrophil counts as measured in daily clinical practice, the patient's experience with lipegfilgrastim prophylaxis, and the oncologist's assessment of lipegfilgrastim feasibility and effectiveness.

Neutropenia was graded according to National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) v4.03 [16].

According to the German Society of Hematology and Oncology (Deutsche Gesellschaft für Hämatologie und Onkologie, DGHO) guidelines, FN is defined as a single increase in temperature to above 38.2 °C or higher for any length of time or a temperature of above 38 °C for more than 1 h. Additionally, a leukocyte count of below $1 \times 10^9/l$ (neutrophil count of below $0.5 \times 10^9/l$) should be present [17]. In our study, existence of FN was determined by the oncologist. The first day of chemotherapy administration was defined as day 0. Injection of lipegfilgrastim up to day 4 (i.e. 96 h) after the start of chemotherapy was considered to be primary prophylaxis, and administration beyond day 4 was considered to be a therapeutic intervention. If neutropenia/FN occurred in a patient who did not receive primary lipegfilgrastim prophylaxis, lipegfilgrastim was applied in the following cycle as secondary prophylaxis.

Adverse events were recorded for up to 30 days post administration, and adverse event intensity was assessed using NCI CTCAE v4.03 [18].

Eligible patients were at least 18 years of age, male or female, and undergoing antineoplastic treatment for non-myeloid malignancies. Exclusion criteria comprised the use of another G-CSF formulation during the current line of chemotherapy, females who were pregnant or breastfeeding, planned myelosuppressive or myeloablative therapy with stem cell support, existing or newly diagnosed myelodysplastic syndrome, chronic myeloid leukemia or acute myeloid leukemia, human immunodeficiency virus (HIV)-positive status, severe chronic neutropenia, and congenital, idiopathic or cyclic neutropenia. There was no upper age limit. Patients were to receive a single subcutaneous dose of 6 mg lipegfilgrastim administered according to the oncologist's choice after chemotherapy administration. A maximum of 6 chemotherapy cycles was documented (fig. 1). Patients who had chosen to self-inject lipegfilgrastim were asked to fill in a questionnaire about their experience.

Results

Clinical Use of Lipegfilgrastim

This interim analysis included 224 patients who were enrolled and treated between December 2013 and July 2014; the analysis

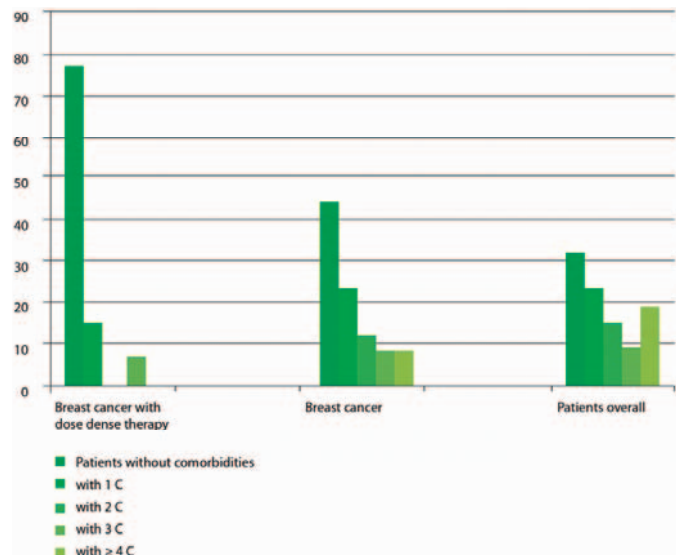


Fig. 3. Incidence of comorbidities in %.

Table 2. Lipegfilgrastim administration in patients stratified according to febrile neutropenia risk (n = 224)

| Outcomes, n (%) | Risk < 10% | Risk 10–20% | Risk > 20% | Risk overall |
|-----------------------|------------|-------------|------------|--------------|
| Overall | 7 | 113 | 102 | 224 |
| Primary prophylaxis | 1 (14.3) | 78 (69.0) | 70 (68.6) | 150 (67.0) |
| Secondary prophylaxis | 4 (57.1) | 11 (9.7) | 19 (18.6) | 34 (15.2) |
| Therapeutic intent | 2 (28.6) | 23 (20.4) | 13 (12.7) | 39 (17.4) |
| Missing data | 0 (0) | 1 (0.9) | 0 (0) | 1 (0.4) |

Table 3. Efficacy outcomes during the first cycle of lipegfilgrastim-supported chemotherapy (n = 224)

| Febrile neutropenia outcomes | n | % (95% confidence interval) |
|------------------------------|-----|-----------------------------|
| Febrile neutropenia | 3 | 1.3 (0.3–4.2) |
| No febrile neutropenia | 210 | 93.8 (89.5–96.4) |
| Missing data | 11 | 4.9 |

population was restricted to patients having completed at least 1 cycle of chemotherapy with lipegfilgrastim support (fig. 1). The median patient age was 61.1 years (interquartile range 51.2–70.2 years). Most of the patients had an ECOG score of 0 or 1 (49.6 and 38.8% of patients, respectively) (table 1).

The main tumor type was breast cancer followed by lung cancer (both non-small cell and small cell), and non-Hodgkin's lymphoma with 46.0, 13.4, and 10.7%, respectively (fig. 2).

Overall, 67.0% of patients suffered from 1 or more comorbidities, with 24.1% having 1, 14.7% having 2, 9.4% having 3, and

Table 4. Incidence of febrile neutropenia in the first cycle according to intention of lipegfilgrastim treatment

| | Primary prophylaxis | | Secondary prophylaxis | | Therapeutic intent | |
|-------------------------------------|---------------------|------------------|-----------------------|------------------|--------------------|------------------|
| | n | % (95% CI) | n | % (95% CI) | n | % (95% CI) |
| <i>Patients overall^a</i> | 150 | 100.0 | 34 | 100.0 | 39 | 100.0 |
| Febrile neutropenia | 0 | 0.0 (0.0–3.1) | 1 | 2.9 (0.2–17.1) | 2 | 5.1 (0.9–18.6) |
| No febrile neutropenia | 143 | 95.3 (90.3–97.9) | 31 | 91.2 (75.2–97.7) | 35 | 89.7 (74.8–96.7) |
| Missing | 7 | 4.7 | 2 | 5.9 | 2 | 5.1 |
| <i>Breast cancer</i> | 76 | 100.0 | 14 | 100.0 | 13 | 100.0 |
| Febrile neutropenia | 0 | 0.0 (0.0–6.0) | 1 | 7.1 (0.4–35.8) | 0 | 0.0 (0.0–28.3) |
| No febrile neutropenia | 71 | 93.4 (84.7–97.6) | 13 | 92.9 (64.2–99.6) | 12 | 92.3 (62.1–99.6) |
| Missing | 5 | 6.6 | 0 | 0.0 | 1 | 7.7 |

^aFor 1 patient intention of lipegfilgrastim application could not be evaluated due to missing data.
CI = Confidence interval.

Table 5. Patients with severe (grade 3/4) neutropenia in the first lipegfilgrastim-supported cycle (n = 224a)

| | Lipegfilgrastim as primary prophylaxis (n = 150) | Lipegfilgrastim as secondary prophylaxis (n = 34) | Therapeutic lipegfilgrastim (n = 39) |
|---------------------------|--|---|--------------------------------------|
| Severe neutropenia, n (%) | 2 (1.3) | 1 (2.9) | 5 (12.8) |

^aFor 1 patient intention of lipegfilgrastim application could not be evaluated due to missing data.

18.8% having 4 or more intercurrent medical disorders (fig. 3). 45.5% of patients were in the FN high-risk group (FN risk > 20%, as assessed by investigator), 50.4% were in the medium-risk group (FN risk between 10 and 20%), and 3.1% were in the low-risk group (FN risk < 10%). In the subgroup of breast cancer patients undergoing dose-dense chemotherapy (i.e. chemotherapy protocols with an intercycle interval of less than 3 weeks), 78.6% had no comorbidities, 14.3% had 1, and 7.1% had 3 (fig. 3). Lipegfilgrastim was applied as primary prophylaxis in 67.0% of patients, as secondary prophylaxis in 15.2%, and with therapeutic intent in 17.4%. Data were missing for 0.4% of patients (table 2). In the subgroup of patients with breast cancer, lipegfilgrastim was administered as primary prophylaxis in 73.8% of patients, as secondary prophylaxis in 13.6%, and therapeutically in 12.6% (data not shown). In patients with an FN risk of more than 20%, lipegfilgrastim was administered as primary prophylaxis in 68.6%, as secondary prophylaxis in 18.6%, and with therapeutic intent in 12.7% (table 2). Among patients subjected to a chemotherapy regimen with an intrinsic risk of 10–20%, lipegfilgrastim was used as primary prophylaxis in 69.0%, as secondary prophylaxis in 9.7%, and therapeutically in 20.4% (table 2). It should be noted, however, that only 1 patient undergoing a chemotherapy regimen with an estimated intrinsic FN risk of less than 10% received lipegfilgrastim as primary prophylaxis. 17 (7.6%) patients had previously experienced an FN episode during an earlier line of chemotherapy, whereas 203 (90.6%) patients had no history of prior FN.

Neutropenic episode data were missing for a total of 4 (1.8%) patients (data not shown).

Effectiveness

During the first cycle of lipegfilgrastim-supported chemotherapy, 1.3% (95% confidence interval (CI) 0.3–4.2) of patients developed FN compared with 93.8% (95% CI 89.5–96.4) without FN; for 4.9% data are missing (table 3). Lipegfilgrastim was effective regardless of whether administered as primary or secondary prophylaxis or with curative intent. When lipegfilgrastim was given as primary prophylaxis, no FN episodes were observed during the first course of chemotherapy (0%; 95% CI 0.0–3.1). When lipegfilgrastim was given as secondary prophylaxis, 1 out of 34 patients had FN in the first lipegfilgrastim-supported cycle (2.9%; 95% CI 0.2–17.1). 2 patients out of 39 who received lipegfilgrastim with therapeutic intent developed FN (5.1%; 95% CI 0.9–18.6) (table 4). In the subgroup of patients with breast cancer, as in the overall patient population, no FN was observed during the first course of chemotherapy when lipegfilgrastim was used as primary prophylaxis (0%; 95% CI 0.0–6.0) whereas 1 out of 14 patients experienced FN when lipegfilgrastim was administered as secondary prophylaxis (7.1%; 95% CI 0.4–35.8) (table 4).

Severe neutropenia (i.e. grade 3 or 4) during cycle 1 was observed in 2 patients receiving lipegfilgrastim as primary prophylaxis and in 1 patient receiving secondary prophylaxis (table 5). In 5 patients in whom lipegfilgrastim was withheld, severe neutropenia grade 3/4 developed, and lipegfilgrastim was given therapeutically (table 5).

Safety

Lipegfilgrastim was generally well tolerated. Overall, 10.3% of patients experienced at least 1 treatment-related adverse event (TRAE). However, the only severe TRAE was anemia in 1 (0.4%) patient, which could also have been related to the chemotherapy. No serious TRAEs, including therapy-related death, were reported. Reported grade 1/2 TRAEs included bone pain, musculoskeletal/connective tissue disorders, myalgia, and arthralgia in 2.7, 1.3, 0.4, and 0.4% of patients, respectively (table 6).

Table 6. Adverse events in the interim analysis population (n = 224)

| Adverse event | All grades | | Grade 3/4 | | Grade 5 | | Serious | |
|-----------------|------------|------|----------------|------|---------|------|---------|------|
| | n | % | n | % | n | % | n | % |
| At least 1 TEAE | 88 | 39.3 | 25 | 11.2 | 0.00 | 0.00 | 9 | 4 |
| At least 1 TRAE | 23 | 10.3 | 1 ^a | 0.4 | 0.00 | 0.00 | 0.00 | 0.00 |
| TRAE in detail | | | | | | | | |
| Overall | 23 | 10.3 | 1 ^a | 0.4 | 0.00 | 0.00 | 0.00 | 0.00 |
| Bone pain | 6 | 2.7 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| M/CTD | 3 | 1.3 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Myalgia | 1 | 0.4 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Arthralgia | 1 | 0.4 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |

^aAnemia.

TEAE = Treatment-emergent adverse event; TRAE = treatment-related adverse event; M/CTD = musculoskeletal/connective tissue disorder.

Discussion

The aim of NADIR is to assess the effectiveness of lipegfilgrastim for the prevention of chemotherapy-induced FN and severe neutropenia in clinical practice. In recent years, pragmatic studies focusing on real-world populations of patients as reported here have attracted increasing recognition in the context of evidence-based medicine. Although randomized controlled phase III trials are considered to provide essential scientific evidence with respect to therapeutic outcomes, their results cannot always be easily applied to the real-world setting. This is partly due to strict patient inclusion criteria that do not necessarily reflect typical patient populations, alongside with other requirements such as standardized treatment and delivery protocols as well as good patient compliance. Therefore, there is a need to validate clinical trial data in real-world settings. As well as being able to recruit a broad range of patients including those that would never be accepted to participate in a phase III trial, another benefit of many non-interventional studies is the fact that they take into account the reality of how oncologists practice medicine [19].

In this hereby reported study, oncologists were free to decide which patients they treated with lipegfilgrastim, at what time it was to be administered, and which supplemental drugs they prescribed. Lipegfilgrastim was effective when administered as primary or secondary prophylaxis and also therapeutically for chemotherapy-induced FN. A patient's FN risk assessment was done by the individual oncologist. In our study, roughly half of the patients were in the FN risk category of 10–20% according to the physician's evaluation, with 69.0% of them receiving lipegfilgrastim as primary prophylaxis (table 2). This meant a large extent because a high number of patients in the intermediate chemotherapy risk group bare comorbidities or other risk factors such as age that required the administration of lipegfilgrastim [8]. This was reflected by the 67% of patients who had at least 1 comorbidity (table 1).

In the subgroup of patients with a chemotherapy-induced FN risk of above 20%, only approximately two thirds of patients (68.6%) received lipegfilgrastim as primary prophylaxis according to guidelines (table 2). 18.6% of patients in the high-risk group re-

ceived lipegfilgrastim as secondary prophylaxis. 12.7% of patients received lipegfilgrastim therapeutically. These numbers are comparable to the observational study PROTECT in which 94% of patients received pegfilgrastim as primary or secondary prophylaxis and 6% of patients received pegfilgrastim as a therapeutic intervention [20]. Pegfilgrastim was administered as primary prophylaxis during the first chemotherapy cycle in 77% of patients in the group with the highest risk of FN [20].

Interestingly, in our study, only 68.6% of patients in the high-risk group received primary prophylaxis with lipegfilgrastim, exposing a disparity between treatment guidelines and oncologists' real-world prescribing behavior. This percentage of patients could be even smaller due to the fact that for the documentation of a patient the administration of lipegfilgrastim was necessary. International EORTC guidelines published in 2006 recommend all patients with a 20% FN risk and more to be treated with a G-CSF in primary prophylaxis [21], a recommendation that is upheld in the updated 2010 EORTC guidelines [8].

Similar results were seen in an integrated analysis combining observational, randomized, and retrospective trials of breast cancer patients receiving chemotherapy with an at least 15% risk of inducing FN [22]. In this analysis, current practice (no G-CSF or any cycle G-CSF with pegfilgrastim) was compared with primary pegfilgrastim prophylaxis. All patients in the primary prophylaxis arm received pegfilgrastim for the first cycle, and almost all patients received pegfilgrastim for the remaining cycles. However, 75% of patients in the current practice arm did not receive G-CSF during the first cycle, and most patients without primary prophylaxis remained without G-CSF support up to cycle 4. By cycle 6, 49% of patients had received some form of G-CSF [22]. As was observed in our study, administration of G-CSFs under routine practice conditions did not appear to be in line with current treatment guidelines. As a result, the current practice group in this integrated interim analysis experienced significantly higher incidences of FN, chemotherapy dose reductions, and FN-associated hospitalizations, compared with the primary pegfilgrastim prophylaxis group. Of the patients in the current practice treatment group who did receive treatment, most received daily G-CSFs,

and administration was delayed in most cases and of short duration [22].

This inappropriate use of daily G-CSFs instead of single-dose pegfilgrastim may be due to the common misconception that pegfilgrastim is associated with increased bone pain compared with daily G-CSF. Bone pain is the most frequently reported adverse event associated with G-CSF use [23, 24]. In a systematic analysis of clinical trials assessing G-CSFs, bone pain was reported in 23% of pharmaceutical company-sponsored trials, 11% of trials with other types of sponsors, and 7% of trials with no reported funding source [25].

However, in clinical trials, rates of bone pain have been found to be similar across different G-CSF formulations. Fortunately, most patients can be successfully treated with nonsteroidal analgesics for their G-CSF-induced bone pain [26].

The 2 long-acting G-CSF preparations lipegfilgrastim and pegfilgrastim have a similar safety profile, including the incidence of bone pain [23, 27]. In our study, the occurrence of bone pain was rare, with only 2.7% of patients experiencing grade 1/2 and no incidences of severe bone pain. Similarly, in a large community-based study of pegfilgrastim by Ozer et al. [28], the incidence of bone pain was low, with serious bone pain reported by only 0.1% of patients. Moreover, when directly compared in an analysis of clinical trials, the safety profiles of lipegfilgrastim and pegfilgrastim were also found to be generally comparable [29].

In our study, 5 (12.8%) out of 39 patients in whom lipegfilgrastim had been withheld developed severe neutropenia, in comparison with 2 (1.3%) out of 150 patients receiving lipegfilgrastim primary prophylaxis and 1 (2.9%) out of 34 patients receiving secondary prophylaxis (table 5).

It should be noted, however, that underuse of G-CSFs in patients at high risk of FN can well be accompanied by overuse in low-risk patients in routine clinical practice. A recent survey found that 40% of pegfilgrastim requests in oncology practices in the US during a 10-month period were made for patients with an FN risk of less than 10%, resulting in a waste of resources of approximately 2.1 million dollars [24]. In contrast to these findings, prescription behavior seem to be far more disciplined in oncology practices in Germany. Of the 224 individuals included in this interim analysis, only 1 with a low FN risk received lipegfilgrastim as primary prophylaxis (table 2).

FN rates were also similar in our study to those observed in the pegfilgrastim study by Ozer et al. [28]. In our study, 1.3% of lipegfilgrastim recipients experienced FN during the first chemotherapy cycle, compared with 3.6% of patients in the first cycle of the pegfilgrastim study [28]. Interestingly, in our study, FN was not observed in patients who received lipegfilgrastim as primary prophylaxis (table 4). Although the overall FN incidence in our interim analysis was low, these findings argue in favor of administering li-

pegfilgrastim as primary prophylaxis due to a clinically meaningful reduction in the risk of developing FN, compared to withholding lipegfilgrastim administration. A phase III multicenter non-inferiority trial directly compared the use of lipegfilgrastim and pegfilgrastim in breast cancer patients undergoing doxorubicin/docetaxel chemotherapy. Compared with pegfilgrastim, lipegfilgrastim resulted in a similar mean duration of severe neutropenia during cycle 1 (primary endpoint) (0.7 vs. 0.8 days). In this direct comparative trial, no FN episodes were reported in the lipegfilgrastim arm whereas 3% of patients developed FN in the pegfilgrastim arm. Moreover, an analysis of secondary endpoints from this study showed that lipegfilgrastim significantly reduced the mean time to absolute neutrophil count recovery during cycle 1 compared with pegfilgrastim (5.9 vs. 7.4 days; $p = 0.0026$) as well as during cycles 2 (3.6 vs. 5.3 days; $p = 0.0082$) and 3 (3.9 vs. 5.1 days; $p = 0.0332$) [30]. Consequently, lipegfilgrastim should be considered to be at least as effective as pegfilgrastim in its ability to prevent chemotherapy-induced neutropenia.

Lipegfilgrastim was effective regardless of whether G-CSF prophylaxis was given as primary or secondary prophylaxis during a maximum of 6 monitored cycles. Furthermore, it has to be considered that FN was not observed in patients who received lipegfilgrastim as primary prophylaxis.

Conclusion

To date, mostly breast cancer, lung cancer, and non-Hodgkin's lymphoma patients have been included in NADIR. Only two thirds of the high-risk patients in our study received lipegfilgrastim as primary prophylaxis as recommended in the corresponding guidelines. FN did not occur when lipegfilgrastim was applied as primary prophylaxis. Lipegfilgrastim seems safe and effective when administered under real-world conditions for the prevention of chemotherapy-induced FN.

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Disclosure Statement

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