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Utilization Patterns of the First US Biosimilar, Filgrastim-Sndz, Observed Between 2015 and 2017 in a Medical Transcription Database

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Objectives

- To identify utilization of short-acting granulocyte colony-stimulating factor (G-CSF) as documented by physicians during patients' healthcare encounters, with a focus on filgrastim-sndz
- To compare annual utilization between 2015 and 2017 of filgrastim-sndz relative to other G-CSFs available in the United States (US)

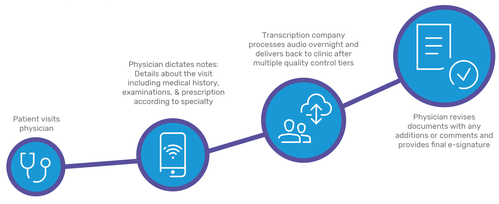
Background

- Filgrastim-sndz, the first biosimilar approved in the US, has been available since September 2015[1]
- Like all G-CSFs, filgrastim-sndz is typically administered by a healthcare provider[1]
- US expenditures on biologic drugs have continued to grow, from an estimated $106.7 billion (Bn) in 2016 to $120.1 Bn in 2017; however, competition from the handful of biosimilars available in the US represents less than 1% of the annual biologic spend[2,3]
- Research has shown slow US biosimilar uptake to date despite over 2 years on the market; in the case of filgrastim-sndz, this may be due in part to relatively modest price discounting (~15%-20%) compared with its reference agent, filgrastim[4,5]
- Filgrastim-sndz, a short-acting G-CSF, has been approved for 5 of the 6 licensed indications for filgrastim, including prophylaxis for and treatment of febrile neutropenia in patients with cancer receiving myelosuppressive chemotherapy[6]
- Another short-acting G-CSF, tbo-filgrastim, is approved for only 1 of the 6 filgrastim indications[7]
  - Tbo-filgrastim is not approved as a biosimilar in the US, as the Food and Drug Administration (FDA) biosimilars regulatory pathway was not yet available at the time of its regulatory submission[8]
- The American Society of Clinical Oncology includes filgrastim-sndz among the G-CSFs recommended for prevention of treatment-related febrile neutropenia in patients with a solid tumor or lymphoma undergoing chemotherapy[9]
- This study provides an update of previous research[10] to assess whether filgrastim-sndz utilization has increased as of 2017

Methods

- Mentions of a G-CSF were identified in physician records of patient consultations in RealHealthData (RHD), a US nationwide medical transcription database, for the period January 1, 2015 through December 31, 2017 (Figure 1)

Figure 1. Data capture process



- The Amplity database consists of unstructured data, reflecting clinicians' transcribed notes (ie, the patient record) of patients' outpatient, emergency department (ED), or inpatient healthcare encounters
- G-CSF utilization was identified from patient records, queried for mention of the following:
  - Short-acting G-CSFs: "filgrastim" or "Neupogen"; "tbo-filgrastim", "Granix", or "Neutroval"; "filgrastim-sndz", "Zarxio", or "Zarzio"
  - Long-acting G-CSFs: "pegfilgrastim" or "Neulasta"
- Data included either the physicians' intention-to-treat with a G-CSF at the time of consultation or upon discharge, G-CSF treatment history, or both
- Abbreviated examples of the unstructured data are shown in (Figure 2)
- Structured data were generated from patient records to provide the annual percentage share of G-CSFs received by unique patients, which was compared annually over the study period

Figure 2. Abbreviated examples of unstructured data from patient records

Patient 1: 67-year-old woman presenting to the Emergency Department and seen by an Urgent Care Provider for acute respiratory failure; had received Granix (tbo-filgrastim) prophylaxis after chemotherapy

PRESENTATION:
The patient is a 57-year-old woman with a history of chronic congestive heart failure… Emergency Department with acute respiratory failure… She underwent a pericardiocentesis… pericardial fluid was **positive for…species**…patient was started on **micafungin**…Pathology confirmed neuroendocrine tumor consistent with **small cell lung cancer**… I discussed the side effects of the regimen of **carboplatin and etoposide**, and the patient agreed to proceed with **chemotherapy**. She received her first dose of **chemotherapy** on **/**/2017… she had 3 fractions of radiation therapy… Following her **chemotherapy**, she was started on **Granix to stimulator her bone marrow**. She **developed a leukocytosis from this**. After several days of **Granix**, the **Granix was discontinued**… She demonstrated dramatic **improvement with the chemotherapy** and radiation therapy… Her platelets remain low at 62,000 per microliter. She then became **neutropenic** after discontinuation of the **Granix**, and thus the **Granix** was restarted. Prior to discharge, her **ANC had increased** to 1.4 taper microliter. She had no fevers and otherwise felt well.
ASSESSMENT AND MEDICAL DECISION MAKING:
1. Acute respiratory failure – resolved…
2. …glabrata pericardial fluid. The patient will remain on **fluconazole** 600 mg daily…for 6 weeks…patient should have a 1, 3 beta-D-glucan evaluation at the **end of an antifungal** treatment.
3. **Small cell lung cancer**. The patient has started **chemotherapy**.
4. Thrombocytopenia…
5. **Leukopenia**. The patient will **resume her Granix daily. This will continue as an outpatient for 7 days**. She should have her blood counts checked at least twice weekly to evaluate…
DISPOSITION:
Discharge home. We will need home care…as well as **Granix** and Lovenox.
MEDICATIONS:
1-9…
10. **Fluconazole** 600 mg p.o. daily.
11-17…
18. **Granix** 480 mcg subcutaneous daily x7 days.

Patient 2: 62-year-old woman newly started on chemotherapy and Neupogen (filgrastim), presenting to the Emergency Department, seen by a Multispecialty Physician, and hospitalized

HISTORY OF PRESENT ILLNESS:
The patient is a 62-year-old female with history of **metastatic breast cancer**, apparently metastatic to not only the liver, but also spine, who presents with complaint of generalized malaise. She went out today to get A Bite To Eat a sandwich and fell in the parking lot… She said she fell because she was just severely weak… She recently **started on a new chemotherapy** yesterday, Monday was her **second dose**… as well as **Neupogen**. She currently had a **Neupogen pump on her right arm**… In the ED, the patient was found to have an elevated lactic acid, **leukocytosis**, generalized malaise, and evidence of suspected **urinary tract infection**. She is being prompted for admission to the hospitalist service.
HOME MEDICATIONS:
1-8…
9. She recently was started on a **new Doxil medication for chemo last month**. Yesterday was her **second dose** and also is on **Neupogen**.
LABORATORY DATA:
…White count of 20, hemoglobin 11, hematocrit 35, platelet count 261… chronically elevated due to her liver metastasis…
ASSESSMENT AND PLAN:
A 62-year-old female with a history of **metastatic breast cancer post-chemo** yesterday with a **Neupogen** ____ **in place**, who presents with complaints of generalized malaise and fall.
1. Severe **sepsis** with **leukocytosis**, lactic acidosis; and a heart rate of 92 on my exam puts her at the **severe sepsis** criteria… **abnormal urinalysis**… she is **afebrile**. It is common in this patient population to have no febrile response.
2-7…
8. **Metastatic breast cancer:** We will consult with her NYOH team in regard to the **Neupogen**. She is supposed to have this **Neupogen pump on her arm until Thursday**. I will consult with them **whether or not she should keep this in place** in the setting of **infection**.

Key: G-CSF | Treatment with a G-CSF | Infection or anti-infective medication | Cancer or cancer treatment

Results

- A total of 38,253 mentions were identified for all G-CSFs, which were attributable to 21,479 patients visiting 9096 different providers (Table 1)

Table 1. Counts of G-CSF mentions and patients, January 1, 2015–December 31, 2017

G-CSF, n (%)	Mentions*	Patients*	Providers*
All G-CSFs	38,253 (100.0)	21,479 (100.0)	9,096 (100.0)
Pegfilgrastim	20,555 (54.0)	10,859 (51.0)	3,530 (39.0)
Filgrastim	14,231 (37.0)	8,539 (40.0)	4,372 (48.0)
Tbo-filgrastim	3,172 (8.0)	1,867 (9.0)	1,030 (11.0)
Filgrastim-sndz	295 (1.0)	214 (1.0)	164 (2.0)

*More than 1 G-CSF may have been mentioned during a healthcare encounter, patients may have received more than 1 G-CSF, and providers may have mentioned more than 1 G-CSF for the same patient as well as for different patients under their care

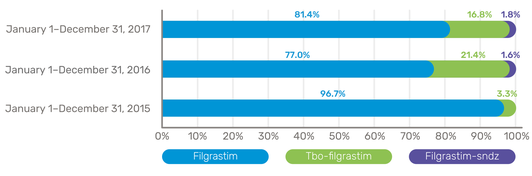
- Annual trends for 2015–2017 show the long-acting G-CSF, pegfilgrastim, dominating utilization, along with a modest uptake of filgrastim-sndz over the study period (Table 2)
- In 2015, a total of 2,847 G-CSF mentions were identified, comprising the following:
  - Pegfilgrastim: 71.0%; filgrastim: 28.1%; tbo-filgrastim: 0.9%; filgrastim-sndz: 0%
- In 2016, counts increased to 14,382 G-CSF mentions, reflecting growth in the number of participating providers in the RHD database and also a reduction in the share of pegfilgrastim mentions
  - Pegfilgrastim: 53.3%; filgrastim: 36.0%; tbo-filgrastim: 10.0%; filgrastim-sndz: 0.8%
- In 2017, despite a further increase to 21,022 G-CSF mentions as new providers were added to the database, the distribution of agents did not materially differ compared with 2016
  - Pegfilgrastim: 51.7%; filgrastim: 39.3%, tbo-filgrastim: 8.1%; filgrastim-sndz: 0.9%

Table 2. Annual counts (percentages) of G-CSF mentions, patients, and providers, January 1, 2015–December 31, 2017

G-CSF, n (%)	Mentions*	Patients*	Providers*
January 1, 2015–December 31, 2015			
All G-CSFs	2,849 (100.0)	1,378 (100.0)	186 (100.0)
Pegfilgrastim	2,022 (71.0)	905 (65.7)	95 (51.1)
Filgrastim	800 (28.1)	457 (33.1)	83 (44.6)
Tbo-filgrastim	27 (0.9)	16 (1.2)	8 (4.3)
Filgrastim-sndz	0 (0.0)	0 (0.0)	0 (0.0)
January 1, 2016–December 31, 2016			
All G-CSFs	14,382 (100.0)	9,546 (100.0)	3,784 (100.0)
Pegfilgrastim	7,662 (53.3)	4,924 (51.6)	1,658 (43.8)
Filgrastim	5,172 (36.0)	3,568 (37.4)	1,719 (45.4)
Tbo-filgrastim	1,439 (10.0)	956 (10.0)	351 (9.3)
Filgrastim-sndz	109 (0.8)	98 (1.0)	56 (1.5)
January 1, 2017–December 31, 2017			
All G-CSFs	21,022 (100.0)	11,282 (100.0)	5,126 (100.0)
Pegfilgrastim	10,871 (51.7)	5,572 (49.4)	1,777 (34.7)
Filgrastim	8,259 (39.3)	4,671 (41.4)	2,570 (50.1)
Tbo-filgrastim	1,706 (8.1)	920 (8.1)	671 (13.1)
Filgrastim-sndz	186 (0.9)	119 (1.1)	108 (2.1)

- Analysis of the short-acting G-CSFs confirms growth in use of filgrastim alternatives after 2015, led by tbo-filgrastim (Figure 3)
  - Between 2016 and 2017, filgrastim-sndz mentions increased slightly while those for tbo-filgrastim decreased by 21%
  - Approximately 97% of all short-acting G-CSF mentions in 2015 were attributable to filgrastim
  - The percentage of filgrastim mentions decreased to 77% during 2016, while the percentage increased for tbo-filgrastim (21.4%) and filgrastim-sndz (1.6%)
  - In 2017, the percentage of filgrastim mentions increased slightly (81.4%), mainly at the expense of tbo-filgrastim (16.8%), with a very minor increase of filgrastim-sndz (1.8%) mentions

Figure 3. Annual mentions of short-acting G-CSFs: percentages by type of agent, 2015–2017



Limitations

- This study provides only a proxy for utilization of G-CSF agents, over 3 distinct time periods, as identified in a medical transcription database
  - Provider notes may have been repeated in cases of multi-day hospitalizations, resulting in potential duplicated G-CSF mentions; however, counts of unique patients were reported to address this
- The data presented here may not be representative of US treatment patterns and clinical practice
  - It is not clear why the share of mentions of pegfilgrastim decreased and the percentage of short-acting G-CSFs increased over time, particularly between 2015 and 2016
  - Despite coverage from all 50 states in the RHD database, patient records meeting study inclusion were not representative of all states
  - Results were based on mentions of G-CSFs in provider records, including G-CSF history such as noted during an ED visit or hospitalization, and therefore may not be reflective of prescribing patterns in clinical practice
  - A 2015–2016 administrative claims study of filgrastim-sndz versus filgrastim utilization in commercial or Medicare Advantage health plans identified 4.9% filgrastim-sndz and 95.1%filgrastim utilization among 3,542 patients,[11] indicating higher utilization of filgrastim-sndz than that observed in the current study
- These limitations are not unique to the Amplity database; all observational databases, including those from administrative claims or electronic health records, are limited in their representation of clinical treatment patterns, characteristic of the type of data

Conclusions

- Among 38,253 records reporting a G-CSF in the RHD medical transcription database, only 295 mentions (0.8%) of filgrastim-sndz among 214 patients (1.0%) were documented in the more than 2 years since its entry into the US marketplace, with almost no observable increase in mentions between 2016 and 2017
- Greater utilization of long-acting pegfilgrastim compared with short-acting G-CSFs may be a factor in the low uptake of filgrastim-sndz, as may be minimal pricing discounts compared with reference agent filgrastim and limited incentives for provider use
- Further research is needed to understand the factors driving US biosimilars uptake
- Raising awareness and understanding of biosimilars among US clinicians and payers, as well as availability of additional approved biosimilars to provide greater competition and pricing pressure, is likely required for greater utilization in clinical practice

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