Longitudinal evaluation of characteristics, treatment patterns, and general outcomes among patients using granulocyte colony stimulating factors: a study by the Biologics and Biosimilars Collective Intelligence Consortium.

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INTRODUCTION

Active and systematic post-marketing evidence generation for biologics, including their corresponding biosimilar products, is a critical public health need.

The Biologics and Biosimilars Collective Intelligence Consortium (BBCIC) is a non-profit initiative created in 2015 under the auspices of the Academy of Managed Care Pharmacy (AMCP). The BBCIC is a collaboration between product manufacturers, payers, managed care organizations, integrated delivery networks, other non-profit organizations, and public representatives. The Consortium uses a distributed research network (DRN) approach that includes medical and pharmacy claims data on approximately 95 million patient-lives to perform ongoing analyses of biosimilars and their innovator products.[1,2]

BBCIC leverages the FDA Sentinel System data and analytic infrastructure, including the Sentinel Common Data Model for data standardization and Sentinel-based analytic tools for distributed analyses and examining medical product risk and benefit. [3]

The BBCIC DRN is used to monitor utilization of medications of interest and capture basic patient characteristics to inform BBCIC research priorities and future research projects.

In 2015, a granulocyte colony stimulating factor (G-CSF) became the first biologic product to have an FDA-approved biosimilar introduced in the US. Since then, two filgrastim and two pegfilgrastim biosimilars have been approved. G-CSFs are used for prophylaxis and treatment of febrile neutropenia in patients receiving cytotoxic chemotherapy with a high risk of neutropenia. Here we present the results of the first BBCIC Monitoring Query in G-CSFs.

METHODS

This retrospective, observational, descriptive study evaluated utilization patterns and patient characteristics using data from five BBCIC DRN Research Partners that contributed over 80 million patient-years of data for individuals currently covered by Commercial or Medicare-Advantage health insurance.

Study Population:

- Adults who received G-CSF treatment for any indication between January 1, 2012 and June 30, 2018
- Patients receiving chemotherapy regimens or treatments other than high-neutropenic risk breast- or lung-cancer therapy were included to get a broader picture of the patients receiving G-CSFs in real clinical settings
- Patients were required to have medical and pharmacy coverage and be enrolled for a minimum 183 days before an exposure episode
- An enrollment gap of 45 days was permitted

Medications Included:

- filgrastim (Neupogen®)
- filgrastim-sndz (Zarxio®)
- TBO-filgrastim (Granix®)
- pegfilgrastim (Neulasta®)

Note: The biosimilars filgrastim-aafi (Nivestym®), pegfilgrastim-jmdb (Fulphila®), and pegfilgrastim-cbqv (Udenyca®) were approved too recently to appear in these results, but will be captured in future queries.

Data were analyzed for both incident (new) and prevalent (existing) users of G-CSF. An incident user was defined as no G-CSF dispensing in the 183 days before the episode of use. Due to the relatively short (183-day) lookback period, the same patient could contribute more than one episode as long as the second dispensing was >183 days since the last exposure.

RESULTS

A total of 29,992 filgrastim, 4,743 filgrastim-sndz , and 4,686 tbo-filgrastim incident users were identified **(Table 1)**. Patients were similar across groups in age and sex.

Table 1. Episode and Patient Characteristics

G-CSF Exposure Episodes			
Total number of episodes			
Incident	N = 41,718		
Prevalent	N = 319,624		
	filgrastim	**filgrastim-sndz**	**TBO-filgrastim**
Patients contributing to cohort*, n			
Incident	29,992	4,743	4,686
Prevalent	32,116	4,867	4,814
G-CSF episodes*, n			
Incident	31,984	4,856	4,878
Prevalent	250,742	34,318	34,564
Patient Characteristics			
Mean age, yr	59.9	59.8	60.4
Female, %	58.3	61.3	58.6
Age groups**,n (%)			
18-49 years	6,507 (20.3)	1,038 (21.4)	907 (18.6)
50-64 years	14,255 (44.6)	2,155 (44.4)	2,211 (45.3)
65-79 years	9,341 (29.2)	1,400 (28.8)	1,494 (30.6)
80+ years	1,881 (5.9)	263 (5.4)	266 (5.5)

* Patients could contribute more than one incident episode if the second episode met all incident criteria.
**Number of episodes observed for patients in each age category contributing time to the exposure category

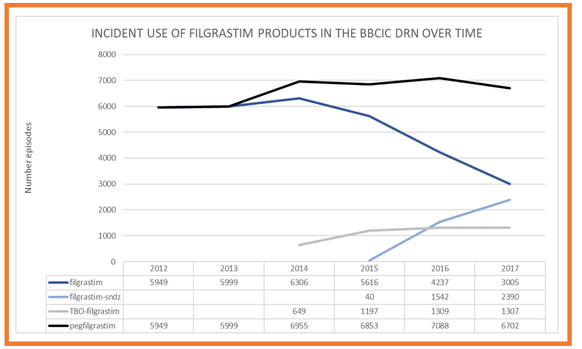

Figure 3. Longitudinal Utilization Trends Across Filgrastim Products

The proportion of patients treated with filgrastim products has varied over time, with declining relative utilization of filgrastim and increasing utilization of filgrastim-sndz **(Figure 2).** Utilization of TBO-filgrastim has remained constant since 2015.

The proportion of patients treated with any filgrastim product compared to pegfilgrastim remained constant over time. **(Figure 1)**

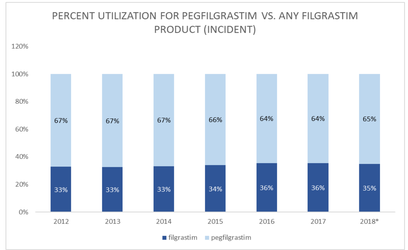

Figure 1. Percent Utilization of All G-CSF Products

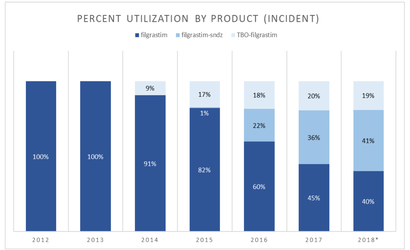

Figure 2. Comparison of Utilization Across All Filgrastim Products

* 2018 data through June 30 only

Total use of all filgrastim products remained consistent at about 6,900 users annually **(Figure 3)**; however, use of filgrastim decreased in 2017 in favor of increased use of filgrastim-sndz and tbo-filgrastim. Utilization of filgrastim decreased while utilization of tbo-filgrastim and filgrastim-sndz increased from 2014 to 2017 **(Figure 2, Figure 3).**

Table 2. Number of Patients with Prior Exposure to a Different G-CSF Product

		Current Treatment		
		filgrastim	**filgrastim-sndz**	**tbo-filgrastim**
Prior Treatment	**filgrastim**	0 (0)	556 (11.4)	855 (17.5)
	filgrastim-sndz	254 (0.8)	0 (0)	175 (3.6)
	tbo-filgrastim	399 (1.2)	191 (3.9)	0 (0)
	pegfilgrastim	6,562 (20.5)	846 (17.4)	923 (18.9)

Of filgrastim-sndz incident users, 11.4% had a recorded history of filgrastim use, and 0.85% of incident filgrastim users had a history of filgrastim-sndz use **(Table 3).** This suggests some switching between products occurred.

Table 3. Clinical Characteristics of Patients Receiving G-CSF Treatment

G-CSF Exposure Episodes			
Total number of episodes	N = 41,718		
	filgrastim	**filgrastim-sndz**	**TBO-filgrastim**
Clinical Characteristics by Exposure Episode*, n (%)			
Combined Comorbidity Index, mean (SD)	5.4 (3.3)	5.9 (3.5)	6 (3.5)
Breast Cancer	6,837 (21.4)	1,244 (25.6)	1,016 (20.8)
Lung Cancer	4,256 (13.3)	510 (10.5)	684 (14.0)
Breast Chemotherapy – GCSF Prophylaxis	3,965 (12.4)	689 (14.2)	657 (13.5)
Breast Chemotherapy – GCSF Treatment	6,392 (20.0)	1,065 (21.9)	1,049 (21.5)
Lung Chemotherapy – GCSF Prophylaxis	85 (0.3)	17 (0.4)	23 (0.5)
Lung Chemotherapy – GCSF Treatment	129 (0.4)	26 (0.5)	29 (0.6)
Other Chemotherapy	20,917 (65.4)	3,197 (65.8)	3,221 (66.0)
Bone/stem cell transplant	323 (1.0)	48 (1.0)	90 (1.8)
Cancer radiation	5,666 (17.7)	837 (17.2)	920 (18.9)
Neutropenia	10,888 (34.0)	1,883 (38.8)	2,105 (43.2)
Anaphylaxis	3,181 (9.9)	1,221 (25.1)	986 (20.2)
Anemia	16,659 (52.1)	2,467 (50.8)	2,737 (56.1)
Bone pain	6,371 (19.9)	1,028 (21.2)	1,000 (20.5)
Chronic obstructive pulmonary disease	6,508 (20.3)	923 (19.0)	1,056 (21.6)
Hyperleukocytosis	3,077 (9.6)	489 (10.1)	490 (10.0)
Kidney disorder	1,470 (4.6)	287 (5.9)	338 (6.9)
Lumpectomy/mastectomy	2,451 (7.7)	447 (9.2)	308 (6.3)
Metastatic disease	10,813 (33.8)	2,024 (41.7)	1,895 (38.8)
Any cancer diagnosis	22,548 (70.5)	3,307 (68.1)	3,437 (70.5)
Antibiotics	19,089 (59.7)	2,812 (57.9)	2,877 (59.0)

* Counts are based on the number of episodes in which a clinical characteristic of interest was observed in the 183-day lookback period prior to the episode index date

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CONCLUSIONS

- This systematic, longitudinal surveillance on GCSF utilization patterns in the US showed that new users of biosimilars increased over time while the overall number of new users remained flat.
- Switching to a biosimilar from the reference product was observed in some patients, though the reason for switching is not available.
- This analysis suggests sufficient utilization of biosimilar GCSFs to conduct a comparative safety and effectiveness study using the BBCIC DRN.