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

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INTRODUCTION

Active and systematic post-marketing evidence generation for biologics, including biosimilars, is a critical public health need.

The Biologics and Biosimilars Collective Intelligence Consortium (BBCIC) is a non-profit initiative convened in 2015 under 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, patient organizations, and public representatives including a liaison from the US Food and Drug Administration (FDA). The Consortium uses a distributed research network (DRN) approach that includes medical and pharmacy claims data on up to approximately 95 million patient-lives from up to 6 Research Partners to perform ongoing analyses of biologics, including biosimilars.[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]

In this analysis, the BBCIC DRN was used to study 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 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 88 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 March 31, 2020. Data were incomplete in 2018, with complete data available through 3/31/2018 and up to 3/31/2019 depending on current availability of Partner data
- Patients receiving chemotherapy for breast- or lung-cancer treatment were included to provide a broad picture of real-world G-CSFs use patterns
- Patients were required to have medical and pharmacy coverage and be enrolled for a minimum 183 days before an exposure
- An enrollment gap of 45 days was permitted

Medications Included:

- filgrastim (Neupogen®)
- filgrastim-sndz (Zarxio®)
- tbo-filgrastim (Granix®)
- pegfilgrastim (Neulasta®)
- pegfilgrastim-jmdb (Fulphila®)

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

Data were analyzed for incident (new) users of in this analysis, defined as no G-CSF dispensing in the 183 days before the index episode. Due to this relatively short lookback period, the same patient could contribute more than one episode as long as the second dispensing was >183 days since the last exposure. Clinical characteristics were assessed in the 183 days before index exposure.

RESULTS

Over 38 million eligible health plan members representing over 88 million person-years of data were evaluated; 31,023 filgrastim, 5,325 tbo-filgrastim, 6,305 filgrastim-sndz, 82,671 pegfilgrastim, and 192 pegfilgrastim-jmdb incident users were identified. Patients were similar across groups in age and sex (**Table 1**). This analysis focused primarily on filgrastim products as pegfilgrastim-jmdb utilization was still low in available 2018 data

Table 1. Episode and Patient Characteristics

G-CSF Exposure Episodes	filgrastim	filgrastim-sndz	tbo-filgrastim	pegfilgrastim	pegfilgrastim-jmdb
No. patients*	31,023	6,305	5,325	82,671	192
G-CSF episodes*, n	33,118	6,525	5,561	87,180	192
Patient Characteristics					
Mean age, yr (SD)	59.8 (13.6)	59.8 (13.2)	60.5 (13.1)	59.6 (12.8)	62.7 (11.7)
Female, %	58.2	61.1	58.5	67.4	62.0
Age groups**, %					
18-49 years	20.4	21.6	18.4	21.3	14.6
50-64 years	44.5	44.0	45.4	45.3	41.7
65-79 years	29.3	29.1	30.7	28.5	37.5
80+ years	5.8	5.4	5.5	4.9	6.3

* 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

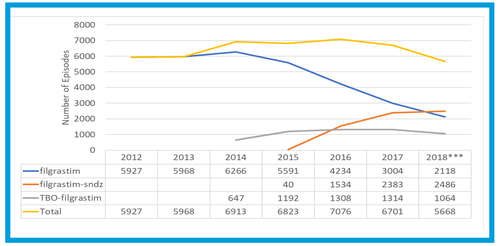

Figure 1. Longitudinal Utilization Trends Across Filgrastim Products by Incident Exposure

Total use of all filgrastim products remained consistent at about 6,900 users annually (**Figure 1**); 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 1, Figure 2).**

*** 2018 data incomplete due to differing Research data update cycles

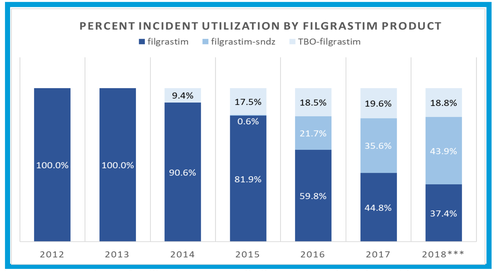

Figure 2. Comparison of Utilization Across All Filgrastim Products by Incident Exposure

*** 2018 data incomplete due to differing Partner data update cycles

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.

Of incident filgrastim-sndz users, 9.5% had a recorded history of filgrastim use and 17.1% had a history of pegfilgrastim use. Of filgrastim users, 1.0% had prior use of filgrastim-sndz, and 20.4% had prior use of pegfilgrastim. 6.8% of current pegfilgrastim users had a history of filgrastim use, and 1.1% had a history of filgrastim-sndz use. **(Table 2).** This suggests some switching between products occurred. Clinical characteristics of patients evaluated during 183 days prior to the index exposure, by product, are shown in **Table 3**.

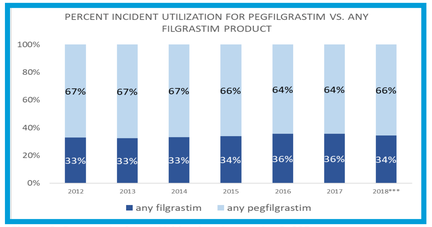

Figure 3. Percent Incident Utilization Across All G-CSF

The proportion of patients treated with any filgrastim product compared to any pegfilgrastim product remained constant over time at approximately 34% **(Figure 3).**

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

		Current Treatment, n (%)				
		filgrastim	filgrastim-sndz	tbo-filgrastim	pegfilgrastim	pegfilgrastim-jmdb
Prior Treatment	filgrastim	0 (0.0)	620 (9.5)	909 (16.3)	5,904 (6.8)	<10 (NC)
	filgrastim-sndz	322 (1.0)	0 (0.0)	220 (4.0)	944 (1.1)	<10 (NC)
	tbo-filgrastim	434 (1.3)	242 (3.7)	0 (0.0)	813 (0.9)	<10 (NC)
	pegfilgrastim	6,765 (20.4)	1,117 (17.1)	1,025 (18.4)	0 (0.0)	75 (39.1)
	pegfilgrastim-jmdb	<10 (NC)	<10 (NC)	<10 (NC)	10 (0.0)	0 (0.0)

NC = Not calculated due to small counts

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

Clinical Characteristics by Exposure Episode*, n (%)	filgrastim	filgrastim-sndz	tbo-filgrastim	pegfilgrastim	pegfilgrastim-jmdb
CCI**, mean (SD)	5.4 (3.3)	6.0 (3.5)	6.1 (3.5)	5.3 (3.3)	6.3 (3.4)
Breast Cancer	7,038 (21.3)	1,669 (25.6)	1,153 (20.7)	33,777 (38.7)	60 (31.3)
Lung Cancer	4,343 (13.1)	692 (10.6)	769 (13.8)	14,001 (16.1)	34 (17.7)
Breast Chemo – GCSF Prophylaxis	4,052 (12.2)	891 (13.7)	740 (13.3)	46,243 (53.0)	92 (47.9)
Lung Chemo – GCSF Prophylaxis	88 (0.3)	18 (0.3)	26 (0.5)	297 (0.3)	0 (0.0)
Breast Chemo – GCSF Treatment	6,608 (20.0)	1,374 (21.1)	1,168 (21.0)	6,962 (8.0)	20 (10.4)
Lung Chemo – GCSF Treatment	134 (0.4)	26 (0.4)	33 (0.6)	377 (0.4)	<10 (NC)
Other Chemotherapy	21,613 (65.3)	4,248 (65.1)	3,673 (66.0)	60,521 (69.4)	162 (84.4)
Cancer radiation	5,845 (17.6)	1,115 (17.1)	1,051 (18.9)	11,500 (13.2)	22 (11.5)
Neutropenia	11,368 (34.3)	2,513 (38.5)	2,397 (43.1)	18,937 (21.7)	75 (39.1)
Anaphylaxis	3,515 (10.6)	1,656 (25.4)	1,204 (21.7)	8,100 (9.3)	34 (17.7)
Anemia	17,295 (52.2)	3,319 (50.9)	3,106 (55.9)	29,110 (33.4)	87 (45.3)
Bone pain	6,642 (20.1)	1,401 (21.5)	1,179 (21.2)	14,340 (16.4)	34 (17.7)
Hyperleukocytosis	3,223 (9.7)	676 (10.4)	560 (10.1)	6,032 (6.9)	24 (12.5)
Antibiotics	19,727 (59.6)	3,724 (57.1)	3,271 (58.8)	46,280 (53.1)	99 (51.6)

NC = Not calculated due to small counts
* Counts based on the number of episodes in which a characteristic of interest was observed in the 183-day lookback period prior to the index date
** CCI = Charlson/Elixhauser Combined Comorbidity Index calculated based on comorbidities observed in the 183 days prior to the index date

CONCLUSIONS

- New users of biosimilars continues to increase 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.

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