A POPULATION-BASED ANALYSIS OF PROPHYLACTIC G-CSF BIOSIMILAR AND ORIGINATOR ADMINISTRATION OVER TIME AMONG PATIENTS DIAGNOSED WITH BREAST CANCER

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BACKGROUND

- Since 2015, several filgrastim biosimilars have been introduced to the US market and pegfilgrastim biosimilars began entering the market in 2018
- Biosimilar availability can increase patient access to biologics and decrease the financial burden on patients and health care systems
- In 2015, the Biologics and Biosimilars Collective Intelligence Consortium (BBCIC) was established to fill a public health gap by monitoring biosimilar effectiveness and safety relative to the originator products
- The BBCIC's Distributed Research Network (DRN) is a uniquely positioned data resource designed to support pharmacoepidemiologic studies of biologics and biosimilars
- The BBCIC G-CSF study team has demonstrated febrile neutropenia (FN) and G-CSF originator product adverse event rates identified in the DRN are consistent with previously reported outcomes

OBJECTIVES

- To characterize G-CSF product use, including product switching, for the prevention of chemotherapy-induced neutropenia (CIN) among patients diagnosed with breast cancer in the DRN

METHODS

- Retrospective descriptive analysis of administrative claims to assess prophylactic G-CSF originator product and biosimilar administration
- BBCIC Data Partner DRN sites: CVS Health Clinical Trial Services, an Aetna affiliate, Harvard Pilgrim Health Care Institute (HPHCI), HealthCore Inc., (Elevance Health), HealthPartners Institute (HPI)
- Patients 20 years and older receiving any G-CSF product* for febrile neutropenia (FN) prophylaxis from 2015-2019 during first cycle chemotherapy for breast cancer were included
- CIN was determined using National Comprehensive Cancer Network (NCCN) guidelines
- Chemotherapy drug codes were identified from Healthcare Common Procedure Coding System (HCPCS) J-codes, National Drug Codes (NDC), and Current Procedural Terminology (CPT) Level II codes

*G-CSF product is not described by administration route

RESULTS

- 11,788 patients were included, 0.8% were male, 49% were age 50-64 years, and the Charlson/Elixhauser Combined Comorbidity Score was low as described in Table 1
- Table 2 describes the commonly administered intravenous chemotherapy drugs: carboplatin, cyclophosphamide, docetaxel, doxorubicin, fluorouracil, methotrexate, paclitaxel, pertuzumab, and trastuzumab
- 93% of patients received high FN risk chemotherapy (Table 2)
- Other risk factors associated with FN are described in Table 3 and those most commonly occurring include surgery n=371 (3.1%), open wounds n=372 (3.2%), and severe hepatic disease n=850 (7.2%)
- 218 patients (1.8%) developed FN during the first chemotherapy cycle, serious allergic reaction was identified in 786 (6.7%, range 1.9%-11.5%), and other adverse events occurred in total among 485 (4.1%) patients (Table 4)
- Filgrastim originator use decreased from 2016 to 2019 and in 2019, 76% of pegfilgrastim use was with the originator product as described in Table 5
- Overall, 374 (2.6%) did not receive cycle 2 G-CSF; of those receiving filgrastim in cycle 1, 26% received a pegfilgrastim product in cycle 2, and of those receiving pegfilgrastim in cycle 1, 96.5% received a pegfilgrastim product in cycle 2 as demonstrated in Table 6

Table 1. Cycle 1 G-CSF receipt by product type and patient characteristics among patients diagnosed with breast cancer

Characteristic	n	%
Cycle 1 G-CSF Use	11,788	100
Age (at Index Date)		
20-49	4,296	36
50-64	5,743	49
65+	1,749	15
Female Sex	11,699	99
Mean CC Score Range^ (SD)	0.1 (0.7)-0.8 (1.6)	
Secondary Cancer*	217	2
Other Cancer**	5,502	47

^Mean Combined Comorbidity Score; *Second Cancer=Diagnosis for brain, bone, liver, or lung cancer on/after Index date; **Other Cancer=Cancer other than inclusion diagnosis or brain, bone, liver, or lung diagnosis on/after Index Date

Table 2. Cycle 1 G-CSF receipt by chemotherapy drug administration* and febrile neutropenia risk

Characteristic	n	%
Cycle 1 G-CSF Use	11,788	100
Cyclophosphamide	85	<1
Cyclophosphamide Docetaxel	1,383	12
Cyclophosphamide Docetaxel Doxorubicin	147	1
Cyclophosphamide Docetaxel Trastuzumab	29	<1
Cyclophosphamide Doxorubicin	7,377	63
Cyclophosphamide Fluorouracil Methotrexate	59	<1
Docetaxel Pertuzumab Trastuzumab	128	1
Doxorubicin	28	<1
Paclitaxel	20	<1
Cycle 1 FN risk^		
High	10,953	93
Intermediate	815	7
Low	20	<1

*Most administered chemotherapy regimens (n≥25); ^FN risk based on chemotherapy regimen

Table 3. Patient characteristics associated with febrile neutropenia risk in 6 months prior to cycle 1 G-CSF initiation and antibiotic use during cycle 1 chemotherapy

Characteristic	n	%
Cycle 1 G-CSF Use	11,788	100
Surgery	371	3
Open wounds	373	3
Persistent neutropenia	<10	--
Hyperbilirubinemia	14	<1
Severe hepatic disease^	850	7
Chronic kidney disease	34	<1
Cycle 1 Antibiotic use	821	7

^defined as hepatitis, non-alcoholic steatohepatitis, cirrhosis, fibrosis

Table 4 . Febrile neutropenia and adverse events associated with cycle 1 chemotherapy

Characteristic	n	%
Cycle 1 G-CSF Use	11,788	100
Febrile neutropenia event	218	2
Serious allergic reaction	786	7
Splenic rupture	0	--
Acute respiratory distress syndrome	<10	--
Capillary leak syndrome	<10	--
Thrombocytopenia	112	1
Leukocytosis	181	2
Cutaneous vasculitis	0	--
Glomerulonephritis	0	--

Table 5. Cycle 1 G-CSF administration by product and year

Characteristic	Filgrastim Originator n (%)	tbo-filgrastim n (%)	Filgrastim-sndz n (%)	Pegfilgrastim Originator n (%)	Pegfilgrastim-cbqv n (%)	Pegfilgrastim-jmdb n (%)
Cycle 1 G-CSF Use	156	46	118	10,895	315	225
2015	55 (3)	<10		2,008 (97)		
2016	37 (2)	<10	12 (<1)	2,351 (98)		
2017	27 (1)	15 (<1)	37 (2)	2,437 (97)		
2018	25 (1)	13 (<1)	36 (2)	2,256 (96)		21 (<1)
2019	12 (<1)	<10	33 (1)	1,842 (76)	313 (13)	204 (8)

Table 6. Cycle 2 G-CSF receipt by product indicating treatment switching patterns

Characteristic	Filgrastim Originator n (%)	tbo-filgrastim n (%)	Filgrastim-sndz n (%)	Pegfilgrastim Originator n (%)	Pegfilgrastim-cbqv n (%)	Pegfilgrastim-jmdb n (%)
None	<10	<10	<10	311 (3)	31 (10)	15 (7%)
Filgrastim	105 (67)	<10	<10	36 (<1)	--	--
tbo-filgrastim	--	33 (72)	--	<10	--	<10
Filgrastim-sndz	<10	--	86 (73)	13 (<1)	<10	--
Filgrastim combination	--	--	--	<10	--	--
Pegfilgrastim combination	39 (25)	10 (22)	21 (18)	10,487 (96)	17 (5)	16 (7)
Pegfilgrastim-cbqv	<10	--	<10	11 (<1)	265 (84)	<10
Pegfilgrastim-jmdb	--	--	<10	11 (<1)	--	183 (81)
Pegfilgrastim/filgrastim combination	<10	--	<10	17 (<1)	<10	--

CONCLUSIONS

- Most G-CSF utilization for the treatment of breast cancer is with a pegfilgrastim product but the route of administration is not described
- Filgrastim and pegfilgrastim originator utilization decreased with the introduction of pegfilgrastim biosimilars
- FN events occurred at a low rate; however, G-CSF is administered to a small proportion of patients receiving chemotherapy associated with low FN risk and other adverse events occurred at a low rate
- Pegfilgrastim biosimilar uptake occurred following market availability
- Most patients received the same product type during the second cycle of chemotherapy

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