A-046 A Study of Granulocyte-Colony Stimulating Factor (G-CSF) Reference and Biosimilar Products Using Real World Data to Emulate a Target Trial for Switching A Biologics and Biosimilars Collective Intelligence Consortium Experience

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CONCLUSIONS

- Three independent real-world data (RWD) sources successfully emulated a target trial.
- Strengths and limitations of different RWD sources led to variations in analytic approaches that should be considered when designing real-world studies.

BACKGROUND

- US biosimilar interchangeability requires no increased safety risk or loss of efficacy when switching between a reference biologic and biosimilar.
- Sufficiently powered clinical trials to examine switching are often infeasible.
- The 20th Century Cures Act requires the US FDA to identify how real-world data (RWD) could be used in regulatory decision-making.
- A promising application is interchangeability. However, understanding RWD quality and relevance is necessary.

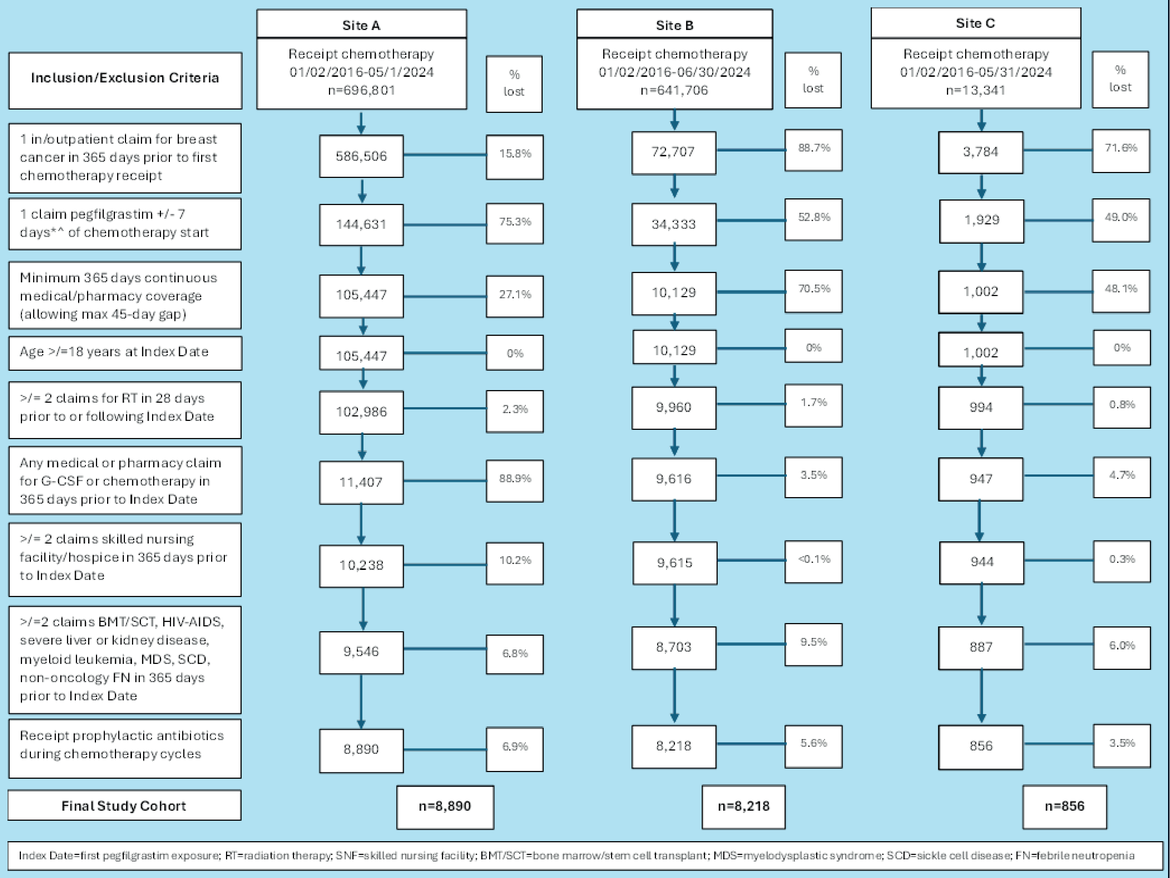
OBJECTIVE

- To assess the extent RWD from electronic health records and administrative claims are suitable to emulate clinical trials targeting biosimilar interchangeability.

METHODS

- A target trial emulation of pegfilgrastim use in breast cancer was used to assess RWD availability and completeness to assess interchangeability across three research partners: a large, national multi-payer claims database, a national insurer, and an integrated healthcare system.
- A hypothetical trial based on a switching study to evaluate filgrastim products was modified to assess pegfilgrastim products for febrile neutropenia (FN) prophylaxis and adverse events in the first 6 chemotherapy cycles.
- Chemotherapy regimen and discontinuation, pegfilgrastim utilization, switching, and discontinuation, adverse events, and laboratory results were assessed.
- Sites independently examined outcomes among switchers between reference pegfilgrastim and biosimilars compared with non-switchers. Inverse probability of treatment weighting at the national insurer and the integrated health care system sites was used.

Figure 1. The Attrition of Study Participants by Site based on Inclusion and Exclusion Criteria



RESULTS

Table 1. Demographic characteristics of the patient cohort

Characteristic	Site A n=8,890	Site B n=8,218	Site C n=856
Age at Index Date (years), mean (SD)	58.14 (12.33)	56.27 (12.46)	53.78 (10.83)
Female Sex, n (%)	8,805 (99.0)	8,119 (98.8)	848 (99.1)
Combined Comorbidity Score, mean (SD)	1.1 (1.49)	0.29 (0.41)	0.07 (0.20)
Metastatic Disease Diagnosis Code	1,735 (19.5)	2,978 (36.2)	261 (30.5)
Receipt of bone-targeting agent before Index Date	165 (1.9)	307 (3.7)	<11
Most Common Chemotherapy Regimens (Cycle 1), n (%)			
AC (cyclophosphamide, doxorubicin)	311 (3.5)	3,537 (43.0)	419 (49.0)
TC (docetaxel, cyclophosphamide)	50 (0.6)	2,095 (25.5)	207 (24.2)
TCH (docetaxel, carboplatin, trastuzumab)	326 (3.7)	19 (0.2)	28 (3.3)
TCHP (docetaxel, carboplatin, trastuzumab, pertuzumab)	1,594 (17.9)	<11	170 (19.9)
CMF (cyclophosphamide, methotrexate, fluorouracil)	<11	65 (0.79)	0 (0.0)
Docetaxel	3,362 (37.8)	2,059 (25.1)	<11
Paclitaxel	3,220 (36.2)	127 (1.6)	<11
G-CSF Initial Product Receipt, n (%)			
Pegfilgrastim reference	7695 (86.6)	6,263 (76.2)	685 (80.0)
Pegfilgrastim-jmdb	312 (3.5)	761 (9.3)	16 (1.9)
Pegfilgrastim-cbqv	542 (6.1)	971 (11.8)	128 (15.0)
Pegfilgrastim-bmez	293 (3.3)	189 (2.3)	21 (2.5)
Pegfilgrastim-apgf	48 (0.5)	15 (0.2)	<11
Pegfilgrastim-pbbk	0 (0.0)	<11	0 (0.0)
Pegfilgrastim-fpgk	0 (0.0)	<11	0 (0.0)
Combination reference and biosimilar	0 (0.0)	16 (0.2)	<11
G-CSF=Granulocyte-colony stimulating factor			

Table 2. Characteristics of Pegfilgrastim Switchers across Study Sites

Characteristic	Site A n=8,880*	Site B n=8,184*	Site C n=850*
Number Switched After Cycle 1 Chemotherapy, n (%)	**220 (2.48)**	**311 (3.80)**	**24 (2.82)**
Age (years), n (%)			
<65	169 (76.8)	229 (73.6)	>11
>/=65	51 (23.2)	82 (26.4)	<11
Female Sex, n (%)	218 (99.1)	308 (99.0%)	24 (100%)
Combined Comorbidity Score, mean (SD**)	1.21 (1.36)	0.27 (0.43)	0.05 (0.17)
Metastatic Disease Diagnosis Code	116 (52.7)	141 (45.3)	<11
Receipt of bone-targeting agent before Index Date	24 (10.9)	<11	<11
Follow-up Time (days) to G-CSF Switch or Censor, mean (SD)	51.3 (180.4)	69.9 (159.4)	38.9 (19.4)
Chemotherapy Regimens (Cycle 1), n (%)			
AC (cyclophosphamide, doxorubicin)	12 (5.5)	115 (37.0)	11 (45.8)
TC (docetaxel, cyclophosphamide)	0 (0.0)	90 (28.9)	<11
TCH (docetaxel, carboplatin, trastuzumab)	<11	0 (0.0)	<11
TCHP (docetaxel, carboplatin, trastuzumab, pertuzumab)	41 (18.6)	<11	<11
CMF (cyclophosphamide, methotrexate, fluorouracil)	0 (0.0)	0 (0.0)	0 (0.0)
Docetaxel	61 (27.7)	92 (29.6)	0 (0.0)
Paclitaxel	99 (45.0)	<11	0 (0.0)
Follow-up Time to Switch (days), mean (SD)	51.3 (180.4)	69.9 (159.4)	38.9 (19.4)
Chemotherapy Cycle at G-CSF Switch, n (%)			
Cycle 2	N/A^	174 (55.9)	9 (37.5)
Cycle 3	N/A	61 (19.6)	13 (54.2)
Cycle 4	N/A	40 (12.9)	1 (4.2)
Cycle 5	N/A	22 (7.1)	1 (4.2)
Cycle 6	N/A	14 (4.5)	0

* People who received combination or unknown G-CSF products were excluded; G-CSF=Granulocyte-colony stimulating factor; **SD = Standard Deviation; ^N/A=Not Available

Table 3. Incidence of Febrile Neutropenia Events

Characteristic	Site A n=8,890	Site B n=8,218	Site C n=856
FN* Events, n (%)	143 (1.6)	247 (3.0)	30 (3.5)
Cycle 1 chemotherapy	113 (1.3)	96 (1.2)	<11
Cycle 2 chemotherapy	77 (0.9)	95 (1.2)	14 (1.6)
Cycle 3 chemotherapy	37 (0.4)	47 (0.6)	<11
Cycle 4 chemotherapy	<11	32 (0.4)	<11
Cycle 5 chemotherapy	<11	13 (0.2)	<11
Cycle 6 chemotherapy	0 (0.0)	12 (0.1)	0 (0.0)
Hospitalizations due to SN** or FN	N/A	N/A^	40 (4.7)

*FN=Febrile Neutropenia; **SN=Severe Neutropenia; SD=Standard Deviation; N/A=Not Available

Table 4. Safety Events After Pegfilgrastim Use

Characteristic	Site A n=8,890	Site B n=8,218	Site C n=856
Safety Events Associated with G-CSF, n (%)			
Acute Respiratory Distress Syndrome	<11	15 (0.2)	<11
Capillary Leak Syndrome	<11	<11	<11
Cutaneous Vasculitis	<11	<11	<11
Glomerulonephritis	0 (0.0)	0 (0.0)	<11
Leukocytosis	237 (2.7)	753 (9.2)	79 (9.2)
Serious Allergic Reaction	1,106 (12.4)	2,968 (36.1)	347 (40.5)
Splenic Rupture	0 (0.0)	<11	<11
Thrombocytopenia	159 (1.8)	457 (5.6)	77 (9.0)
G-CSF=Granulocyte-colon stimulating factor			

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