



# Real-world Comparative Effectiveness of Pegfilgrastim Biosimilars versus Originator

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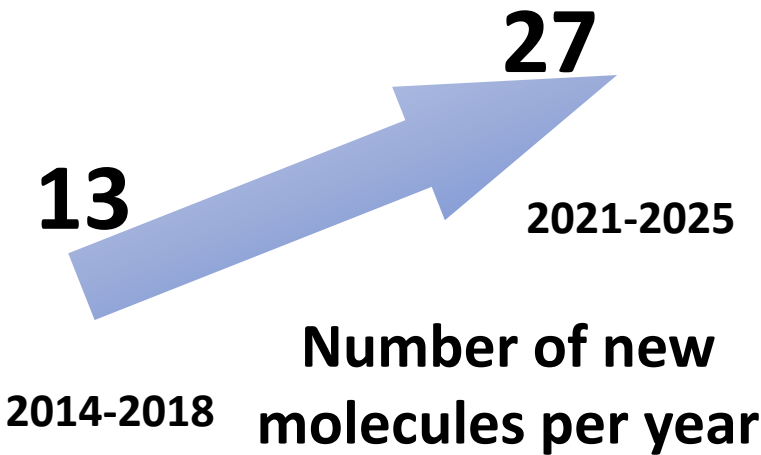
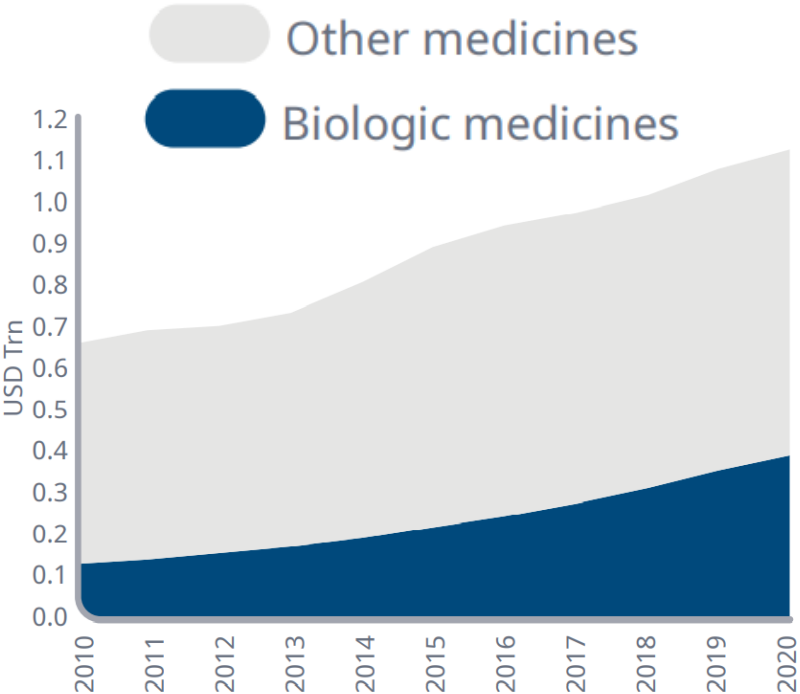
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# Background

# Era of biologics

**\$320 billion**

**Global biologic medicines market in 2020**



- Anti-infectives
- Heart failure
- Migraine
- Pain
- Respiratory

**Expand into traditional primary care conditions**

# Potential

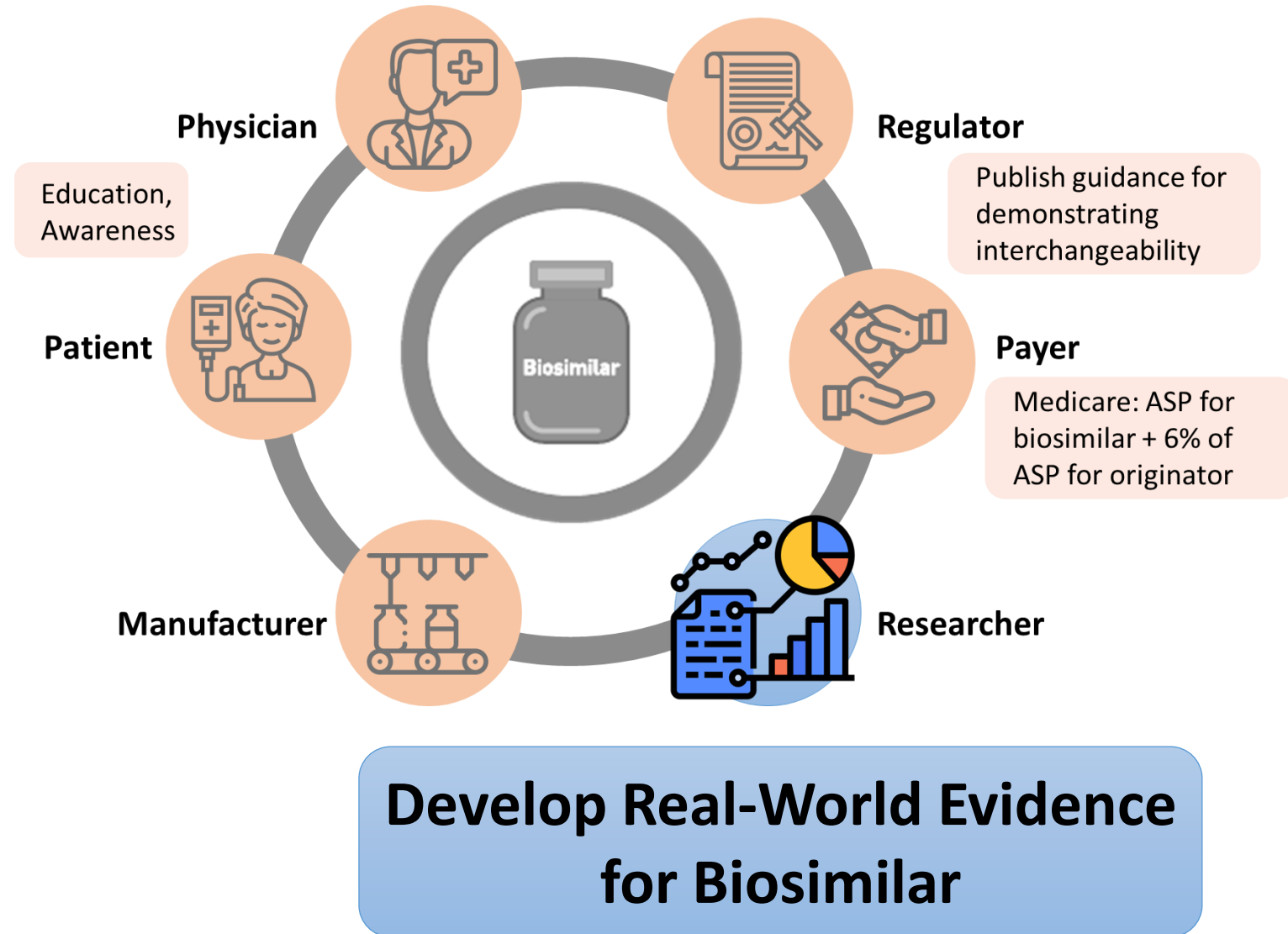
- RAND estimated **\$54 billions** saving between 2017-2026

| Biosimilar Price<br>Relative to<br>Reference Biologic | Biosimilar Market Share Assumption |           |                  |            |            |            |                   |
|-------------------------------------------------------|------------------------------------|-----------|------------------|------------|------------|------------|-------------------|
|                                                       | 20%                                | 25%       | 30%              | 35%        | 40%        | 45%        | 50%               |
| 50%                                                   | \$60 Bill                          | \$75 Bill | \$90 Bill        | \$105 Bill | \$120 Bill | \$135 Bill | <b>\$150 Bill</b> |
| 55%                                                   | \$54 Bill                          | \$67 Bill | \$81 Bill        | \$94 Bill  | \$108 Bill | \$121 Bill | \$135 Bill        |
| 60%                                                   | \$48 Bill                          | \$60 Bill | \$72 Bill        | \$84 Bill  | \$96 Bill  | \$108 Bill | \$120 Bill        |
| 65%                                                   | \$42 Bill                          | \$52 Bill | \$63 Bill        | \$73 Bill  | \$84 Bill  | \$94 Bill  | \$105 Bill        |
| <b>70%</b>                                            | \$36 Bill                          | \$45 Bill | <b>\$54 Bill</b> | \$63 Bill  | \$72 Bill  | \$81 Bill  | \$90 Bill         |
| 75%                                                   | \$30 Bill                          | \$37 Bill | \$45 Bill        | \$52 Bill  | \$60 Bill  | \$67 Bill  | \$75 Bill         |
| 80%                                                   | <b>\$24 Bill</b>                   | \$30 Bill | \$36 Bill        | \$42 Bill  | \$48 Bill  | \$54 Bill  | \$60 Bill         |

**Access Expansion: bring lower-cost options to more patient**

# Obstacles & Solution

- Delayed market entry: patent litigation
- Interchangeability designation
- Reimbursement policy: Medicare ASP<sup>a</sup>+6%
- Price: discount not as great as generic drug
- PBM<sup>b</sup>: Rebate trap
- Physician attitude: clinical consideration



<sup>a</sup>ASP=average sale price; <sup>b</sup>PBM=pharmacy benefit manager

# Granulocyte colony-stimulating factors (G-CSFs)

One of earliest drug classes with biosimilars available

Reduce the risk of febrile neutropenia (FN) in patients with cancer receiving chemotherapy

Filgrastim (short-acting)  
Pegfilgrastim (long-acting)

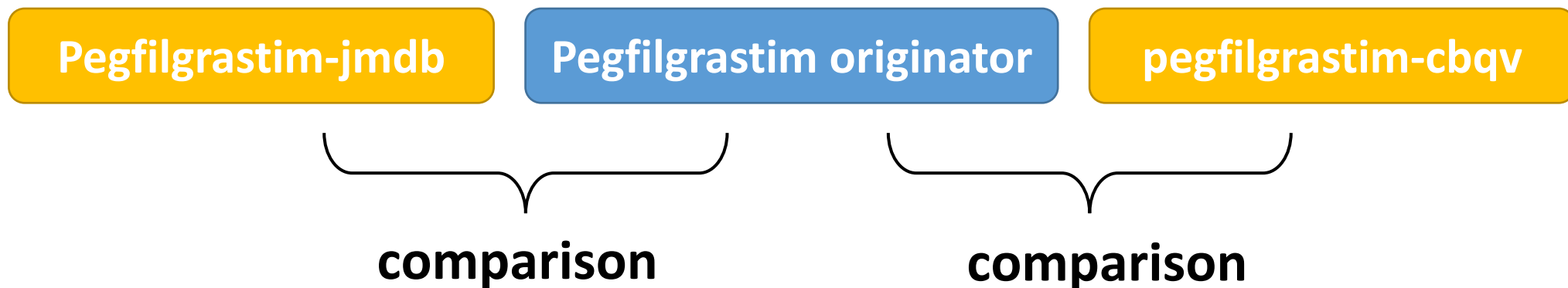
Trials for G-CSFs biosimilars are based on indirect comparison or PK/PD data

Current RWE focuses on filgrastim

Pegfilgrastim accounts for 97% of G-CSFs use

# RWE needs for pegfilgrastim biosimilars

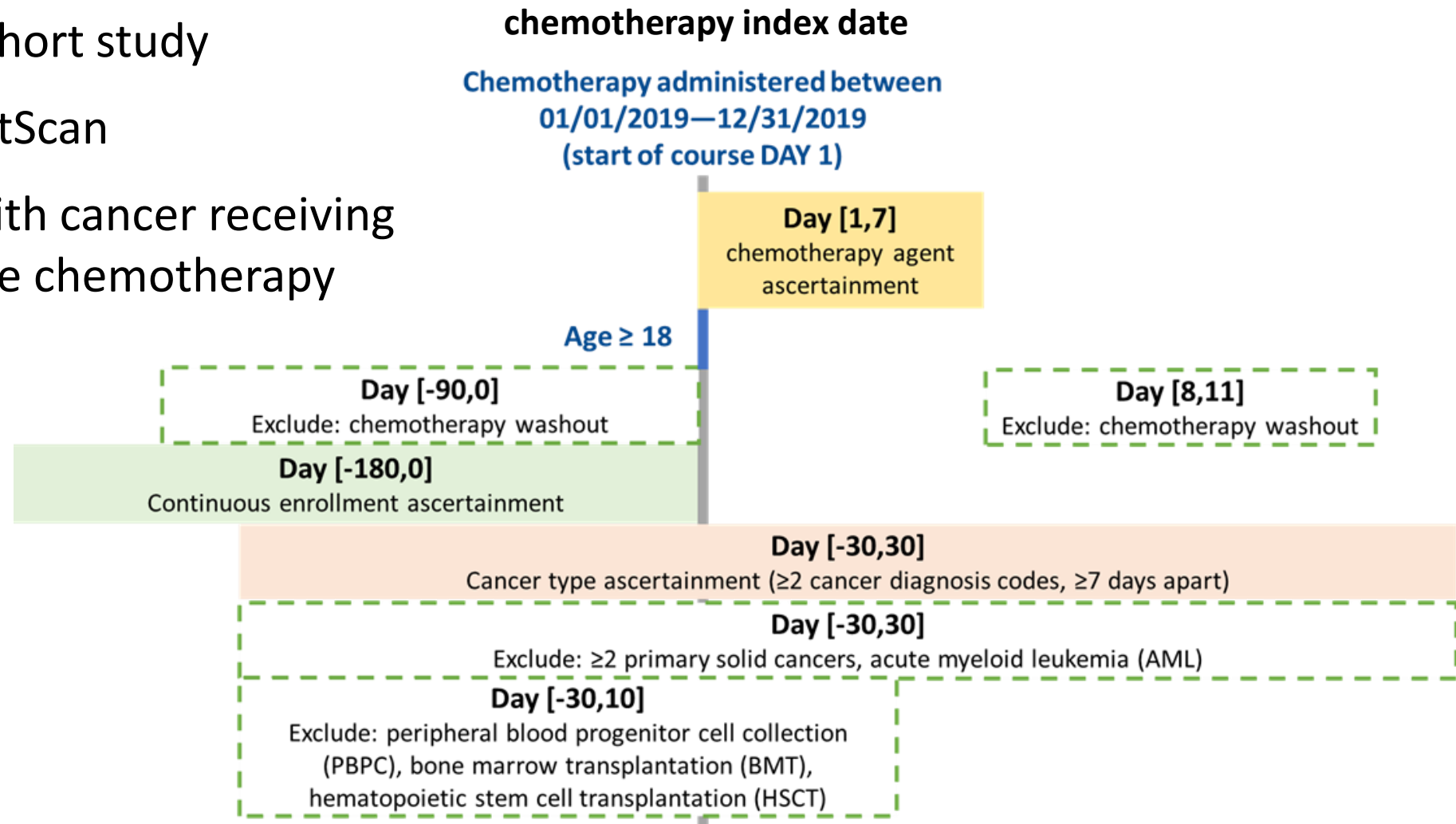
- Series of RWE studies for pegfilgrastim biosimilars
- Comparative effectiveness of pegfilgrastim biosimilars
- **Are there any meaningful differences in effectiveness between pegfilgrastim originator and biosimilars for the prevention of febrile neutropenia in patients receiving myelosuppressive chemotherapy?**



# Methods

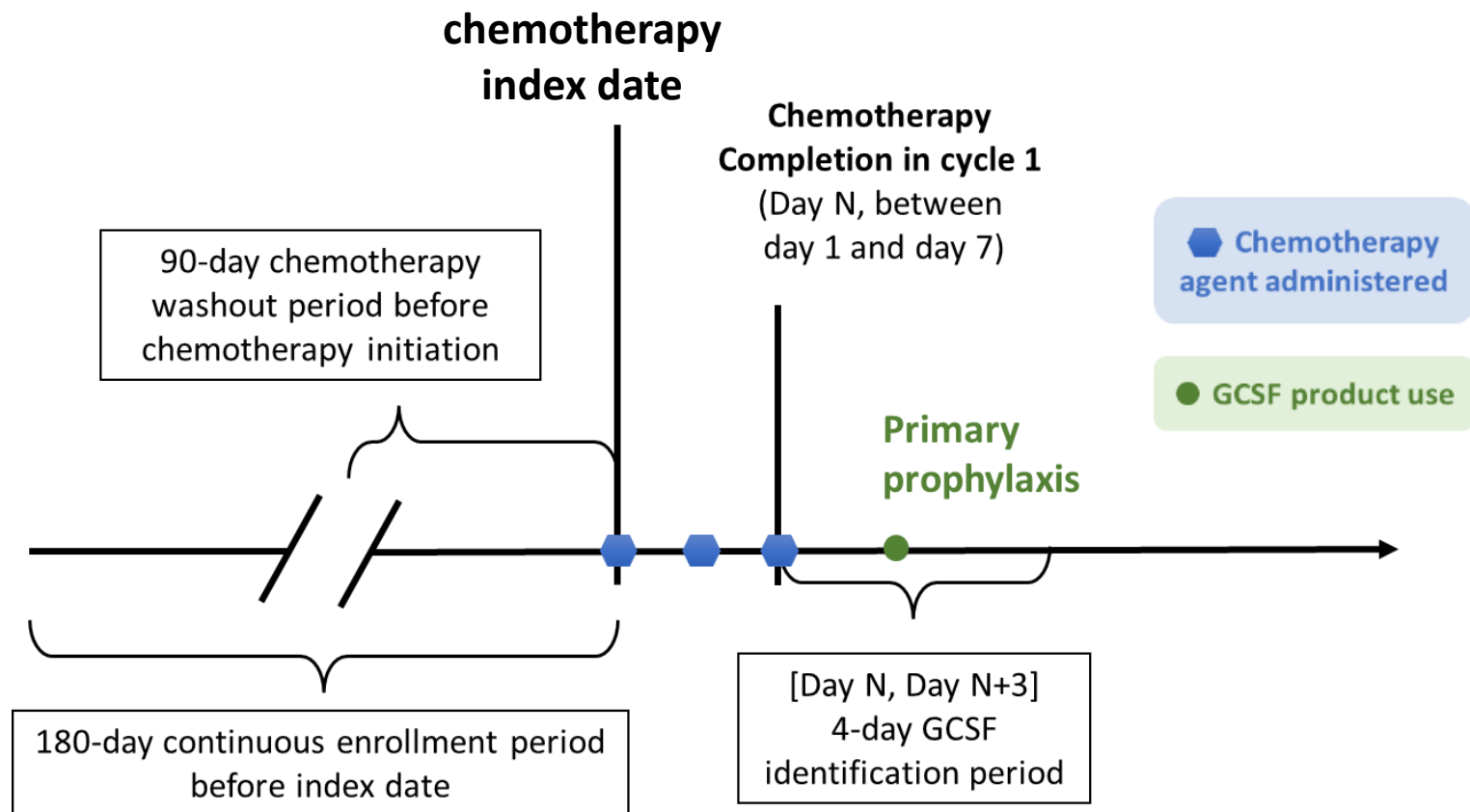
# Data source & Study population

- Retrospective cohort study
- 2019 IBM MarketScan
- Adult patients with cancer receiving myelosuppressive chemotherapy



# Pegfilgrastim identification

- Identify all G-CSF product, including both filgrastim & pegfilgrastim
- NDC & HCPCS
- From chemotherapy completion to up to 3 days afterward
- Include patients received pegfilgrastim originator, pegfilgrastim-jmdb, or pegfilgrastim-cbqv
- Exclude patients with multiple G-CSF products

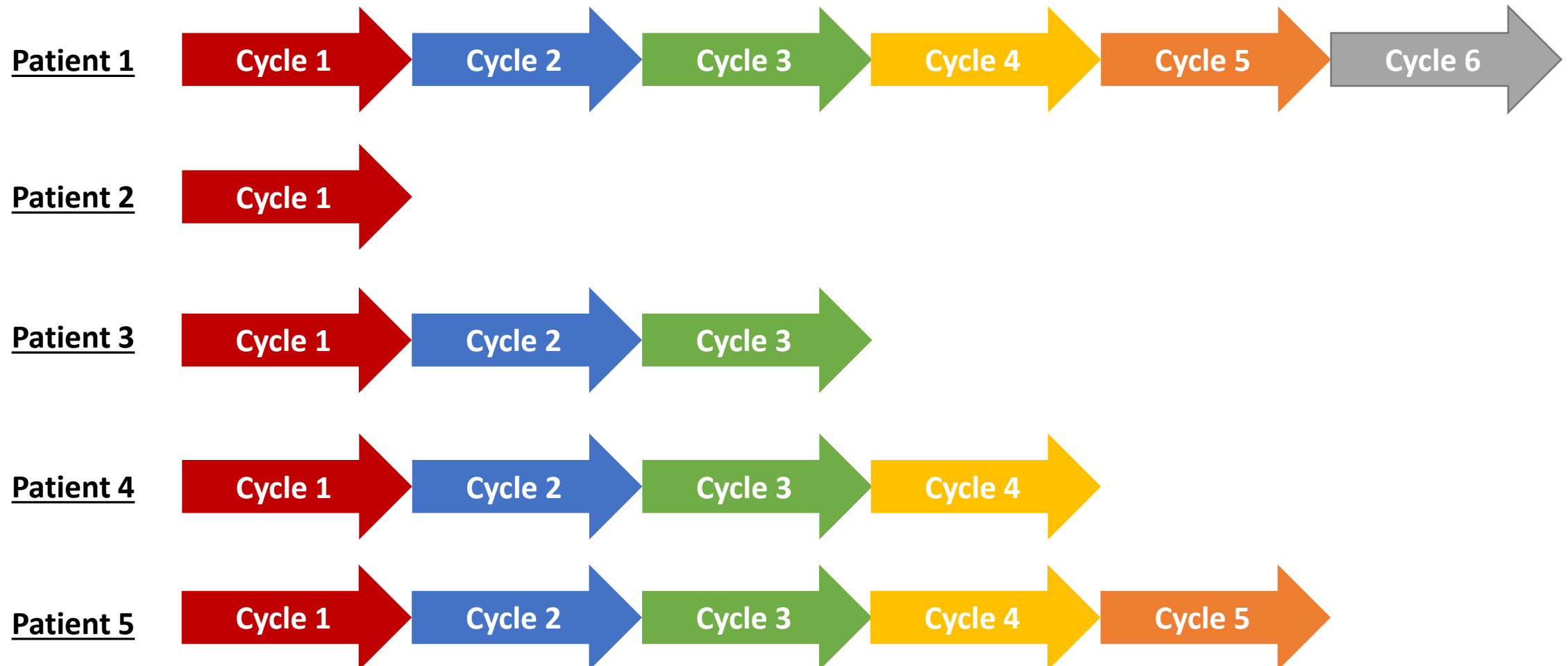


# Cycle identification algorithm

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- Up to 8 cycles (consecutively qualified cycles)
- The first cycle began on the index date and ended on the day prior to the next chemotherapy administered between day 12 and day 60
- The second cycle followed immediately beginning on the day of the next chemotherapy administration. If no chemotherapy was administered between day 12 and day 60, the cycle and follow up were considered completed on day 35, disenrollment, or end of study period, whichever came first
- To be a qualified cycle, there needed to be no change in chemotherapy agents administered compared to the first cycle and patients needed to be using the same pegfilgrastim product as the first cycle
- Only qualified and complete cycles were included in the analysis

# Cycle identification algorithm



# Outcome measures

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- FN associated hospitalization was measured from the date pegfilgrastim was administered to the end of the cycle
- Using ICD-10-CM diagnosis codes
- Two definitions:
  - 1) Neutropenia, fever, or infection ICD-10-CM diagnosis code in any position (“broad definition”);
  - 2) Neutropenia ICD-10-CM diagnosis code in any position (“narrow definition”)
- These two definitions for FN were validated in administrative claims databases<sup>1</sup> and widely used by previous studies<sup>2,3</sup>

<sup>1</sup>Weycker D, Sofrygin O, Seefeld K, Deeter RG, Legg J, Edelsberg J. Technical evaluation of methods for identifying chemotherapy-induced febrile neutropenia in healthcare claims databases. *BMC Health Serv Res*. Feb 13 2013;13:60.

<sup>2</sup>Weycker D, Li X, Tzivelekis S, et al. Burden of Chemotherapy-Induced Febrile Neutropenia Hospitalizations in US Clinical Practice, by Use and Patterns of Prophylaxis with Colony-Stimulating Factor. *Support Care Cancer*. Feb 2017;25(2):439-447.

<sup>3</sup>Weycker D, Doroff R, Hanau A, et al. Use and effectiveness of pegfilgrastim prophylaxis in US clinical practice:a retrospective observational study. *BMC Cancer*. Aug 9 2019;19(1):792.

# Statistical methods

## Main Analyses

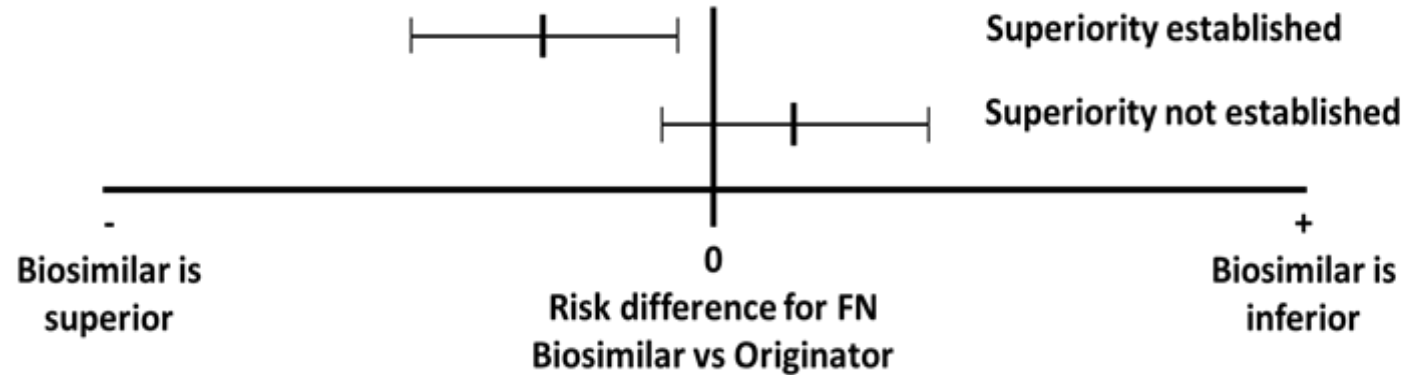
- Cumulative Incidence of febrile neutropenia (both broad and narrow definition) were compared in the **first cycle** and **across all cycles** between pegfilgrastim-PFS and pegfilgrastim-jmdb as well as between pegfilgrastim-PFS and pegfilgrastim-cbqv
- **Propensity score (PS) matching** to balance baseline characteristics

## Secondary Analyses

- Cumulative Incidence of febrile neutropenia (both broad and narrow definition) were compared **within each cycle** between pegfilgrastim-PFS and pegfilgrastim-jmdb as well as between pegfilgrastim-PFS and pegfilgrastim-cbqv
- **Propensity score (PS) matching** to balance baseline characteristics

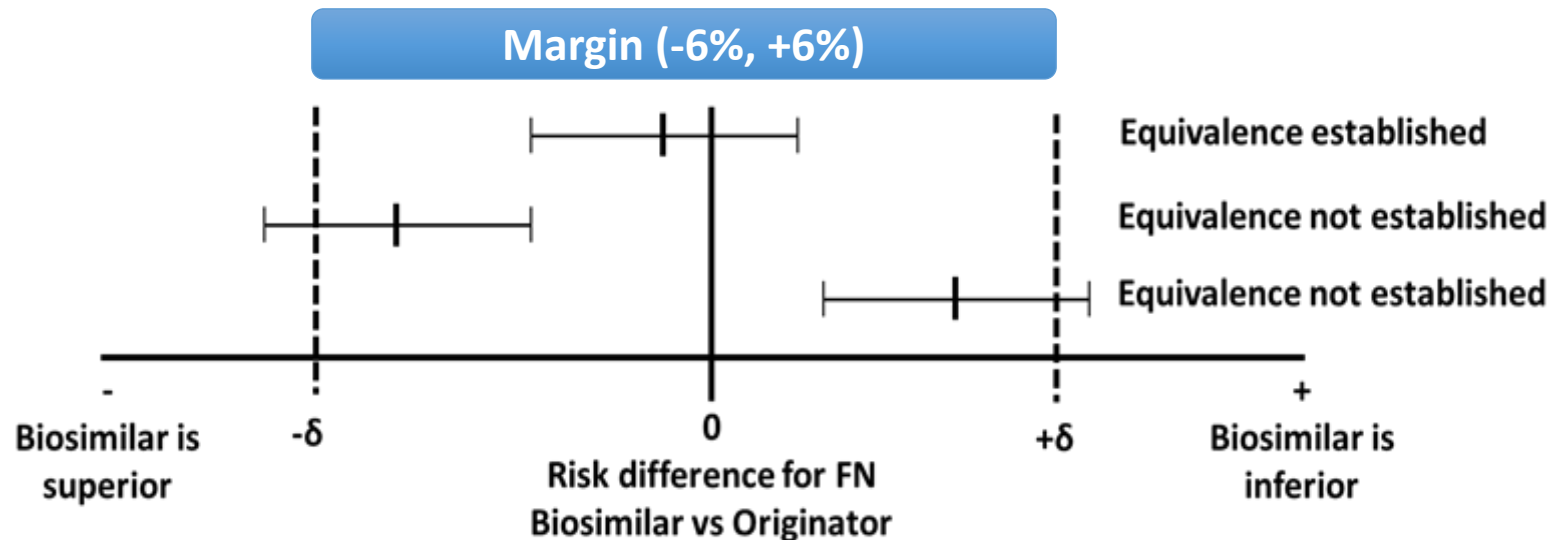
# Statistical methods

**95%  
Confidence  
interval**



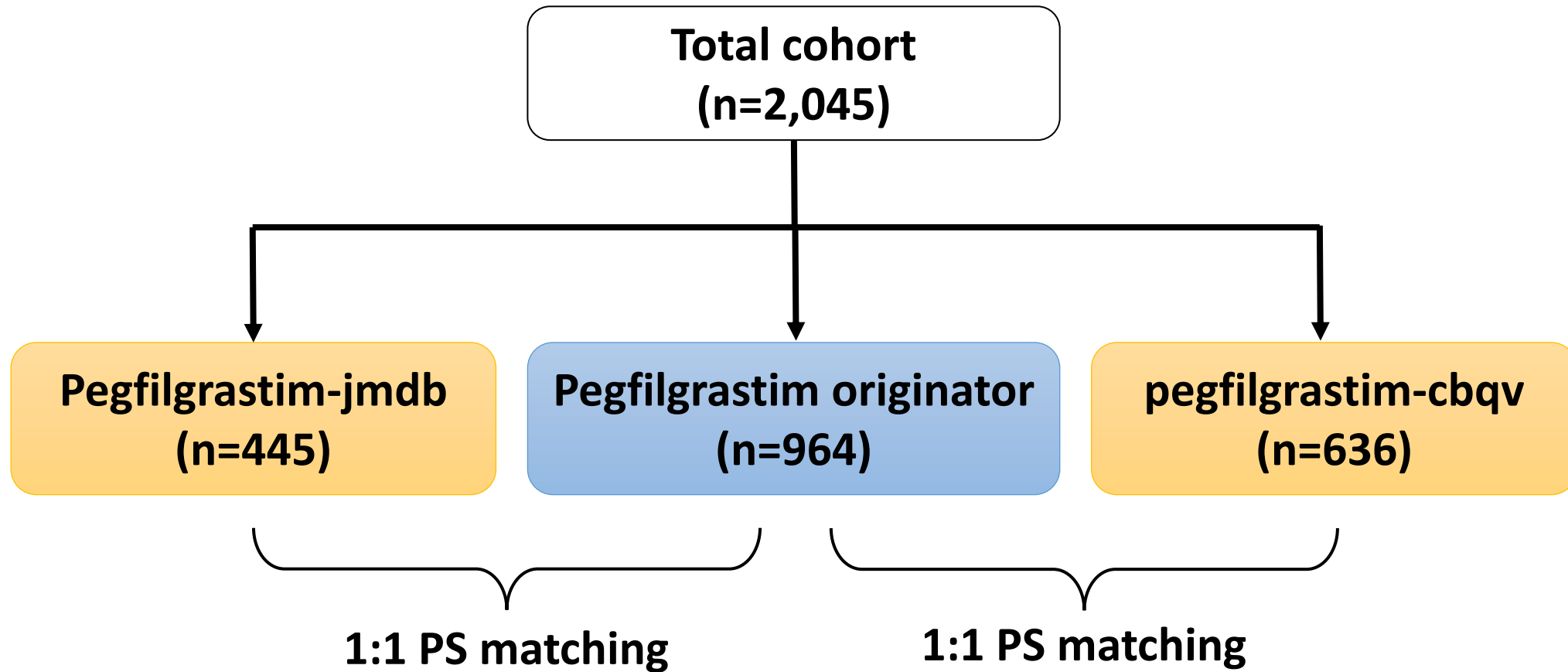
**Two one-  
side test  
(TOST)**

**90%  
Confidence  
interval**



## Results & Implications

# Study population



# After PS matching, covariates were all balanced

| Covariates            | Standardized difference between pegfilgrastim originator (n=445) and pegfilgrastim-jmdb (n=445) |
|-----------------------|-------------------------------------------------------------------------------------------------|
| Age                   | 1.7%                                                                                            |
| Female                | 3.6%                                                                                            |
| Region                | 9.6%                                                                                            |
| Plan type             | 0%                                                                                              |
| Provider type         | 5.1%                                                                                            |
| Place of service      | 2.1%                                                                                            |
| Cancer type           | 3.6%                                                                                            |
| Regimen FN risk level | 4.1%                                                                                            |
| Other FN risk factors | 0%-6.1%                                                                                         |

| Covariates            | Standardized difference between pegfilgrastim originator (n=633) and pegfilgrastim-cbqv (n=633) |
|-----------------------|-------------------------------------------------------------------------------------------------|
| Age                   | 1.5%                                                                                            |
| Female                | 0.9%                                                                                            |
| Region                | 7.3%                                                                                            |
| Plan type             | 8.1%                                                                                            |
| Provider type         | 7.5%                                                                                            |
| Place of service      | 6.2%                                                                                            |
| Cancer type           | 7.7%                                                                                            |
| Regimen FN risk level | 4.0%                                                                                            |
| Other FN risk factors | 0-5.6%                                                                                          |

# FN incidence in cycle 1— pegfilgrastim-PFS vs pegfilgrastim-jmdb

- Risk difference is 0.9% for broad definition and 0% for the narrow definition

| Cohort and FN definition |           | pegfilgrastim originator |                       |                            | pegfilgrastim-jmdb |                       |                            | Risk difference (90% CI) (95% CI)         | p-value for equivalence test† |
|--------------------------|-----------|--------------------------|-----------------------|----------------------------|--------------------|-----------------------|----------------------------|-------------------------------------------|-------------------------------|
|                          |           | # of patients            | # of patients with FN | Cumulative incidence of FN | # of patients      | # of patients with FN | Cumulative incidence of FN |                                           | superiority test‡             |
|                          |           |                          |                       |                            |                    |                       |                            |                                           |                               |
| Matched cohort           | Broad FN  | 445                      | 13                    | 2.92                       | 445                | 17                    | 3.82                       | <b>0.90</b><br>(1.54–3.34)<br>(1.47–3.27) | <0.0001†                      |
|                          |           |                          |                       |                            |                    |                       |                            |                                           | 0.4575‡                       |
|                          | Narrow FN |                          | 8                     | 1.80                       |                    | 8                     | 1.80                       | <b>0</b><br>(2.14–2.14)<br>(1.75–1.75)    | <0.0001†                      |
|                          |           |                          |                       |                            |                    |                       |                            |                                           |                               |

# FN incidence in cycle 1— pegfilgrastim-PFS vs pegfilgrastim-jmdb

- Risk difference is 0.9% for broad definition and 0% for the narrow definition
- **Equivalence test** → FN incidence was **statistically equivalent** between pegfilgrastim-PFS and pegfilgrastim-jmdb users

| Cohort and FN definition |           | pegfilgrastim originator |                       |                            | pegfilgrastim-jmdb |                       |                            | Risk difference (90% CI) (95% CI) | p-value for equivalence test† |
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|                          |           |                          |                       |                            |                    |                       |                            |                                   | 1.0000‡                       |

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- **Equivalence test** → FN incidence was **statistically equivalent** between pegfilgrastim-PFS and pegfilgrastim-jmdb users
- **Superiority test** → There is **no statistically significant difference** in FN incidence between pegfilgrastim-PFS and pegfilgrastim-jmdb users

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|                          |           |                          |                       |                            |                    |                       |                            |                                   | 1.0000‡                       |

# FN incidence in cycle 1— pegfilgrastim-PFS vs pegfilgrastim-cbqv

- Risk difference is 0.32% for both broad and narrow definition

| Cohort and FN definition |           | pegfilgrastim originator |                       |                            | pegfilgrastim-cbqv |                       |                            | Risk difference (90% CI) (95% CI)            | p-value for equivalence test† |
|--------------------------|-----------|--------------------------|-----------------------|----------------------------|--------------------|-----------------------|----------------------------|----------------------------------------------|-------------------------------|
|                          |           | # of patients            | # of patients with FN | Cumulative incidence of FN | # of patients      | # of patients with FN | Cumulative incidence of FN |                                              | superiority test‡             |
|                          |           |                          |                       |                            |                    |                       |                            |                                              |                               |
| Matched cohort           | Broad FN  | 633                      | 14                    | 2.21                       | 633                | 16                    | 2.53                       | <b>0.32</b><br>(-1.57–2.20)<br>(-1.36–1.99)  | <0.0001†                      |
|                          |           |                          |                       |                            |                    |                       |                            |                                              | 0.7117‡                       |
|                          | Narrow FN |                          | 9                     | 1.42                       |                    | 7                     | 1.11                       | <b>-0.32</b><br>(-2.05–1.42)<br>(-1.99–1.36) | <0.0001†                      |
|                          |           |                          |                       |                            |                    |                       |                            |                                              | 0.6148‡                       |

# FN incidence in cycle 1— pegfilgrastim-PFS vs pegfilgrastim-cbqv

- Risk difference is 0.32% for both broad and narrow definition
- **Equivalence test** → FN incidence was **statistically equivalent** between pegfilgrastim-PFS and pegfilgrastim-cbqv users

| Cohort and FN definition |           | pegfilgrastim originator |                       |                            | pegfilgrastim-cbqv |                       |                            | Risk difference (90% CI) (95% CI) | p-value for equivalence test† |
|--------------------------|-----------|--------------------------|-----------------------|----------------------------|--------------------|-----------------------|----------------------------|-----------------------------------|-------------------------------|
|                          |           | # of patients            | # of patients with FN | Cumulative incidence of FN | # of patients      | # of patients with FN | Cumulative incidence of FN |                                   | superiority test‡             |
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|                          |           | # of patients            | # of patients with FN | Cumulative incidence of FN | # of patients      | # of patients with FN | Cumulative incidence of FN |                                   | superiority test‡             |
|                          |           |                          |                       |                            |                    |                       |                            |                                   |                               |
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|                          |           |                          |                       |                            |                    |                       |                            | <0.0001†                          |                               |
|                          |           |                          |                       |                            |                    |                       |                            | 0.6148‡                           |                               |

# Implication

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- The incidence of FN associated hospitalizations among patients with cancer undergoing chemotherapy was statistically equivalent between those received pegfilgrastim-jmdb and pegfilgrastim originator as well as between pegfilgrastim-cbqv and pegfilgrastim originator in the first cycle and across all cycles
- The first study in the United States confirming the clinical equivalence by evaluating occurrence of febrile neutropenia between pegfilgrastim biosimilars and originator using real-world data
- With appropriate dissemination, the results from the study will strengthen payers, physicians and patients confidence in adopting pegfilgrastim biosimilars



# CoDES

CENTER FOR DRUG EVALUATION & SAFETY

# Thank you for your attention

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