# Evaluation of granulocyte colony-stimulating factor use following inpatient administration of chemotherapy at a large academic medical center

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## BACKGROUND

- Certain high-risk chemotherapy regimens for treatment of hematologic malignancies necessitate inpatient administration during a new cancer diagnosis or due to frequent monitoring requirements.
- Granulocyte colony-stimulating factor (G-CSF) is a blood growth factor that stimulates the bone marrow to produce more neutrophils[1].
  - It is administered 24 to 72 hours after such chemotherapy regimens as primary prophylaxis to reduce the incidence of febrile neutropenia.
- There are two G-CSF formulations available:

| Filgrastim | Pegfilgrastim |
|---|---|
| • Weight-based dose, rounded to 300 mcg or 480 mcg vial size<br>• Subcutaneous injection<br>• Given once daily post chemotherapy until neutrophil recovery<br>• Current inpatient G-CSF formulation | • Flat 6 mg dose<br>• Subcutaneous injection<br>• Given once post chemotherapy<br>  ○ Pegylated formulation<br>  ○ One injection ≈ 10 days of filgrastim<br>• Restricted to outpatient setting due to cost and reimbursement |

- With the introduction of biosimilars, both formulations of G-CSF are more affordable and easily accessible.
  - Due to recent cost changes, it may be beneficial for The University of Kansas Health System (TUKHS) to expand pegfilgrastim use in the inpatient setting.

## OBJECTIVE

- Evaluate the inpatient use of filgrastim, or its FDA-approved biosimilars, and determine the potential cost-saving opportunity to substituting pegfilgrastim biosimilars.

## METHODS

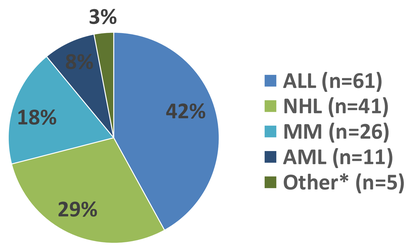
- Single-center, retrospective medication use evaluation
- Time frame: February 2013 to October 2020
- A total of 144 patients hospitalized at TUKHS with leukemia, lymphoma, or multiple myeloma met inclusion criteria.
- A total of 190 cycles of chemotherapy requiring G-CSF were analyzed.

| Inclusion Criteria | Exclusion Criteria |
|---|---|
| • Adult patients (≥ 18 years old)<br>• Received at least one cycle of myelosuppressive chemotherapy during the hospital admission<br>• Received 5 or more doses of filgrastim post chemotherapy | • G-CSF received post hematopoietic stem-cell transplant<br>• Received filgrastim for less than 5 days or for reasons unrelated to a cycle of chemotherapy |

- Formulary biosimilar products used in analysis:
  - Filgrastim-aafi (Nivestym®)
  - Pegfilgrastim-cbqv (Udenyca®)
- Costs were based on whole acquisition costs (WAC) pricing specific to TUKHS on 11/5/2020.

## RESULTS

**Figure 1. Hematologic malignancy types included in analysis**




*CML-blast crisis (n=4), CLL (n=1)

ALL = acute lymphoblastic leukemia; NHL = Non-Hodgkin lymphoma; MM = multiple myeloma; AML = acute myelogenous leukemia; CML = chronic myelogenous leukemia; CLL = chronic lymphocytic leukemia

| Table 1: Baseline Characteristics | |
|---|---|
| **Characteristic** | **(n=144)** |
| Males, n (%) | 89 (62) |
| Median age, years (range) | 56 (24-48) |
| Dose received, n (%)<br>300 mcg<br>480 mcg | <br>56 (39)<br>88 (61) |
| ANC < 500 cells/uL upon hospital discharge ±, n (%) | 27 (19) |

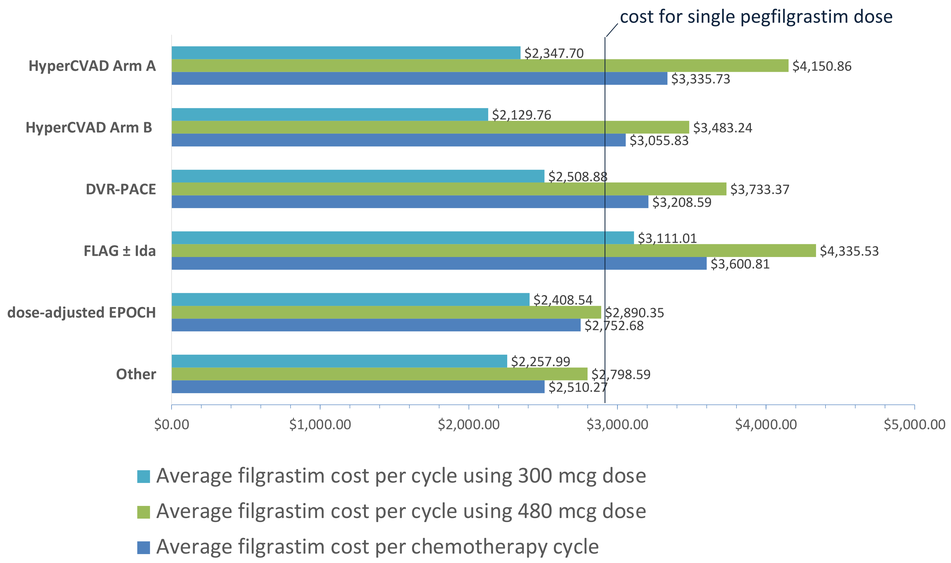
±Reasons for discharge prior to ANC recovery: continued daily G-CSF as an outpatient (n = 19), expired during hospital admission (n = 4), discharged home with hospice (n = 4).

**Table 2. Days of Filgrastim Use and Length of Hospital Stay based on Chemotherapy Regimen Received**

| Chemotherapy Regimen * (number of cycles) | Average Days of Filgrastim Use (range) | Average Length of Hospital Stay , days |
|---|---|---|
| HyperCVAD Arm A (73) | 12.4 (5-28) | 28.1 |
| HyperCVAD Arm B (57) | 10.8 (5-25) | 38.6 |
| DVR-PACE (28) | 12 (5-24) | 20.8 |
| FLAG-Ida (10) | 14.7 (7-34) | 26.5 |
| dose-adjusted EPOCH (7) | 9.9 (6-14) | 20.8 |
| Other¥ (15) | 10.1 (5-19) | 26.1 |

HyperCVAD Arm A = cyclophosphamide, dexamethasone, doxorubicin, vincristine; HyperCVAD Arm B = methotrexate, cytarabine; DVR-PACE = dexamethasone, bortezomib, lenalidomide, cisplatin, doxorubicin, cyclophosphamide, etoposide; FLAG-Ida = fludarabine, cytarabine, G-CSF, idarubicin; EPOCH = etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin.
* Regimens may have also contained a monoclonal antibody or a tyrosine kinase inhibitor
¥ Included various ALL (n=5) and NHL regimens (n=10)

**Figure 2. Average Filgrastim Cost per Chemotherapy Cycle Based on Regimen or Dose Received**




## DISCUSSION

- Baseline characteristics are reflective of the patient type, malignancy, and chemotherapy that is expected to require inpatient administration.
- A greater number of patients were male or required the 480 mcg dose; it is unknown if gender had an impact on the results but the more frequent need for the 480mcg dose appears to impact cost per cycle.
- Nineteen percent of patients included were sent home neutropenic; this may have negatively impacted findings related to hospital length of stay and average number of filgrastim days.
- The use of filgrastim-aafi exceeded the cost of a single pegfilgrastim-cbqv dose for several inpatient regimens, including both arms of HyperCVAD, VDR-PACE, and FLAG-Ida.
  - Difference in cost was more prominent in regimens requiring 12 or more filgrastim doses or in patients who require the 480 mcg dose.
- Substitution of pegfilgrastim biosimilars also has potential to:
  - Reduce hospital length of stay as providers may feel comfortable discharging stable patients prior to ANC recovery given its reliable kinetics.
  - Improve patient satisfaction due to decrease in required injections.

Limitations

- Retrospective review, limited to accuracy of medical record and by search criteria which may not have captured all eligible patients.
- Availability of multiple G-CSF biosimilars and changing hospital-contract prices limits the generalizability of described cost per cycle.
- Prospectively predicting patients who are eligible for pegfilgrastim but who are unable to receive on an outpatient basis is difficult to consistently determine.

## CONCLUSIONS & FUTURE DIRECTIONS

- There may be financial benefit to utilizing pegfilgrastim biosimilars on an inpatient basis for patients who receive certain high-risk chemotherapy regimens and meet predetermined criteria.
- Follow up studies to better quantify cost-savings or to evaluate for decreases in hospital length of stay would be beneficial in confirming the true value of pegfilgrastim biosimilars in an inpatient setting.
- These results encourage periodic evaluation of filgrastim and pegfilgrastim biosimilars as additional products come to market or as contract prices change.

## REFERENCES

1. Brender E, Lynm C, Glass RM. Granulocyte-Colony Stimulating Factor. *JAMA*. 2006;295(9):1088.
2. Fox E, Widemann BC, Hawkins DS, et al. Randomized trial and pharmacokinetic study of pegfilgrastim versus filgrastim after dose-intensive chemotherapy in young adults and children with sarcomas. *Clin Cancer Res*. 2009;15(23):7361-7367. doi:10.1158/1078-0432.CCR-09-0761

## CONTACT INFORMATION

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