Cost-effectiveness of granulocyte colony stimulating factors (G-CSFs) for the prevention of febrile neutropenia in breast cancer patients

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Background/objective

- International guidelines recommend primary prophylaxis of febrile neutropenia (FN) in patients with a high risk of FN (>20%). However, recommendations developed during COVID-19 pandemic in 2020 suggest to expand the threshold for granulocyte colony-stimulating factor (G-CSF) primary prophylaxis by including patients at intermediate (10-20%) risk of FN.
- **This study evaluates the cost-effectiveness of primary prophylaxis (PP) vs. secondary prophylaxis (SP) using a biosimilar filgrastim or pegfilgrastim, for the most common intermediate-risk chemotherapy regimen in patients with breast cancer in France, Germany and Austria.**

Methods

- A Markov model was constructed to evaluate the total costs and clinical outcomes of filgrastim or pegfilgrastim when used as PP vs. SP in patients with early-stage breast cancer[1].
- Patients had ≥1 FN risk factor (i.e., recent surgery) without the receipt of anti-HER2 therapy, representing a 16% baseline FN risk.
- Outcomes were cost per quality-adjusted life-year (QALY) gained. A one-way sensitivity analysis (OWSA) and a probabilistic sensitivity analysis (PSA) were also conducted.

Conclusions/Main Findings

- **At a WTP threshold of €50,000, primary prophylaxis with filgrastim and pegfilgrastim is cost-effective in patients with breast cancer with intermediate risk for FN receiving adjuvant docetaxel.**
- The model showed that expanding the use of colony-stimulating factors as primary prophylaxis is valuable in reducing unnecessary health care visits for patients with breast cancer and should continue to be considered for the indefinite future.

Model Inputs

- Model inputs (Table 1), including G-CSF efficacy, clinical utilities and mortality were estimated from publicly available data and literature.
- **Costs included in the model were treatment with filgrastim or pegfilgrastim and inpatient FN management. All cost and resource use data used in the model were country specific**.
- After 20 years, patients are assumed to be no longer at risk of dying from cancer.

Table 1. Model Parameters	Value
General Inputs	
Baseline FN risk (%, over all cycles)[1]	16%
# of cycles of adjuvant docetaxel	4
Probability & Effectiveness Inputs	
RR of FN in cycles 2+ with no history of FN (vs. cycle 1)[2,3]	0.21
RR of FN in cycles 2+ with history of FN (vs. no history)[2,3]	9.09
Probability of RDI <85% with no history of FN[4]	30.9%
Probability of RDI <85% with history of FN[4,5]	48.8%
RR of FN for filgrastim (vs. no G-CSF)[6]	0.42
Health Utility Inputs	
Utility – breast cancer, during chemotherapy[7]	0.55
Utility – breast cancer, during FN hospitalization[2,3]	0.33
Utility – breast cancer, after chemotherapy (year 1)[7]	0.66
Utility – breast cancer, after chemotherapy (year >1)[2]	0.86
Mortality Inputs	
% die with breast cancer over 1 year	3.0%
% die during FN event (inpatient)[8]	5.6%
Mortality hazard ratio for RDI <85% (vs RDI ≥85%)[4,9]	1.002

Table 2. Results	Total Cost	Incremental Cost	QALYs	ICER
Filgrastim – Austria				
Secondary prophylaxis	€994	-	10.932	-
Primary prophylaxis	€1,572	€788	10.997	€8,971
Filgrastim - France				
Secondary prophylaxis	€1,449	-	10.863	-
Primary prophylaxis	€1,888	€439	10.927	€6,851
Filgrastim - Germany				
Secondary prophylaxis	€532	-	11.606	-
Primary prophylaxis	€2,413	€1,881	11.674	€27,509
Pegfilgrastim - Austria				
Secondary prophylaxis	€972	-	10.983	-
Primary prophylaxis	€1,795	€823	11.062	€10,371
Pegfilgrastim - France				
Secondary prophylaxis	€1,435	-	10.910	-
Primary prophylaxis	€2,410	€975	10.989	€12,369
Pegfilgrastim - Germany				
Secondary prophylaxis	€654	-	11.657	-
Primary prophylaxis	€4,078	€3,424	11.742	€40,685

Results

- In France and Austria, filgrastim PP provided an additional 0.064 QALYs compared to SP, German gains were 0.068 QALYs. Incremental cost per QALY gains were €6,851 (France), €8,971 (Austria), and €27,509 (Germany) (Table 2).
- In France and Austria, pegfilgrastim PP provided an additional 0.079 QALYs compared to SP, German gains were 0.084 QALYs. This resulted in incremental cost per QALY gains of €12,369 (France), €10,371 (Austria), and €40,685 (Germany) (Table 2).

Results

- Probabilistic sensitivity analysis identified that for filgrastim, at a WTP threshold of €50,000 per QALY gained, **the probability of the cost-effectiveness of PP remained high (100% for France and Austria; 95.9% for Germany). The probabilities for pegfilgrastim were 99.8% (France), 100% (Austria), and 73.4% (Germany).**

Study Limitations

- Adverse events associated with G-CSFs were not included in the model, as associated costs and outcomes were assumed to be equivalent for biosimilar and reference products and therefore do not have an impact on incremental cost-effectiveness.
- Utility values in this model are based on data obtained from clinicians, as direct patient utility data for FN is not available.
- The model assumes that all FN events will require a hospital admission.

References

1. Li et al. JCO Oncology Practice 17(8).
2. Sparano JA et al. *N Engl J Med*. 2008 Apr 17;358(16):1663-71.
3. Whyte S et al. *Value Health*. 2011;14(4):465-74.
4. Fust K et al. *Pharmacoeconomics*. 2017;35(4):425-438.
5. Veitch Z, et al. *J Natl Compr Canc Netw*. 2019 Aug 1;17(8):957-967. (11):3.
6. Shayne M,et al. *Cancer*. 2007 Oct 1;110(7):1611-20.
7. Wang L et al. *Support Care Cancer*. 2015 Nov;23131-40.
8. Cámara RJA et al. *Breast Cancer Res Treat*. 2019 Jun;175(3):627-635.
9. Dulisse B et al. *J Med Econ*. 2013;16(6):720-35.
10. Cespedes Feliciano EM et al. *JAMA Oncol*. 2019 Dec 5.

Disclosures

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