

COST-EFFECTIVENESS OF LENOGRASTIM ON NEUTROPENIA DURATION IN ADULTS RECEIVING CHEMOTHERAPY FOR LEUKEMIA

ISPOR 15th Annual International Meeting May 15-19, 2010

Authors:

Jakub Rutkowski¹, Łukasz Deryło¹, Marta Fedyna¹, Joanna Lis², Robert Plisko¹, Magdalena Władysiuk¹

1 – HTA Consulting, Krakow, Poland, 2 – Sanofi-Aventis sp. z o.o, Warszawa, Poland



Incremental costs

A study conducted by HTA Consulting www.hta.pl Study supported by Sanofi-Aventis Poland

Introduction

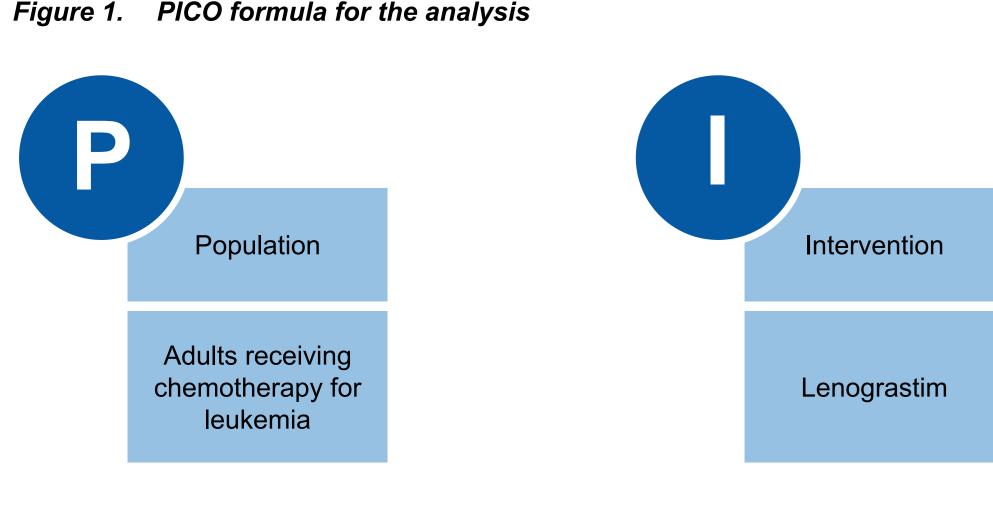
Neutropenia is defined as a situation, in which the absolute neutrophil count (ANC) falls below 1500/mm³. Several grades of neutropenia are defined: in grade 3 neutropenia the ANC is below 1,000/mm³, but over 500/mm³ and in grade 4 neutropenia the ANC falls below 500/mm³. Neutropenia is considered a major factor limiting applicability of anti-cancer treatment. Development of neutropenia may require chemotherapy dose reduction or discontinuation of treatment. Prevalence of neutropenia in patients with malignancies undergoing chemotherapy reaches 60-80%. A decrease of the neutrophil count results in impaired immunological response to pathogens. This manifests itself as decreased or absent inflammatory reaction to infectious factors as well as recurrent or severe infections. A drastic increase of susceptibility to infections is observed when the ANC falls below 1,000/mm³. [1-6]

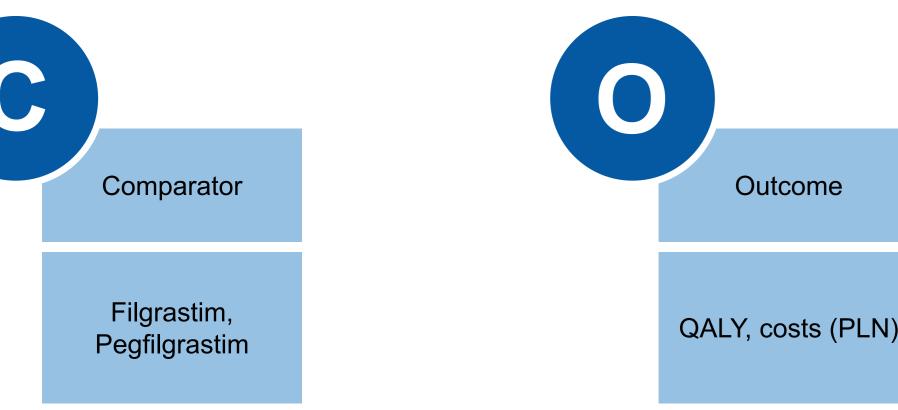
Objective

The objective of this economic analysis was to compare the costs of lenograstim therapy with those of other products containing granulocyte colony stimulating factor (G-CSF) available in Poland (i.e. filgrastim and pegfilgrastim) used in treatment of neutropenia in adult patients receiving chemotherapy for leukemia.

The analysis was performed according to the PICO formula:

Figure 1. PICO formula for the analysis





Methodology of the analysis

The time horizon of the analysis was one chemotherapy cycle. Data concerning recovery of the ANC to normal values, the number of days with fever, duration of hospitalization and antibiotic therapy were obtained from randomized controlled trials (RCTs) identified by means of a systematic review. These included both trials, in which products containing G-CSF were administered in prevention of neutropenia, and those in which the same products were used in immediate treatment of neutropenic episodes. Costs were analyzed from the Polish public payer's perspective. Costs of procedures and medications were obtained from the National Health Fund (NHF) catalogue. Dosage regimens for G-CSF products were determined based on the products' characteristics (SPC).

Table 1. Characteristics of intervention for G-CSF products.

Product	Dose	Dosage regimen	
Lenograstim	19.2 MIU/m ² body surface area or 0.64 MIU / kg of body weight	daily	
Filgrastim	0.5 MIU / kg of body weight	daily	
Pegfilgrastim	6 mg	single dose	

Modeling of the course of treatment

The course of treatment was described taking into account the following periods (in days):

- time to recovery of the ANC to 1,000/mm³;
- duration of fever;
- hospitalization;
- intravenous administration of antibiotics.

Due to no significant differences between comparators in efficacy and safety (adverse events) cost minimization analysis was conducted.

These parameters were estimated and analyzed in the following phases:

- 1. Trials in which adult patients receiving chemotherapy for leukemia took part were selected from the RCTs included in the systematic review.
- 2. Based on trials selected in Phase 1 mean values weighted with the number of patients were calculated for the time to recovery of the ANC to 1,000/mm³, duration of fever, hospitalization and antibiotic treatment (for no treatment).
- 3. The course of treatment with lenograstim and filgrastim was modeled based on the results for no treatment (Phase 2) and the RR values from RCTs selected in Phase 1.
- 4. Parameters of the course of treatment with pegfilgrastim were determined by the RR values calculated in relation to treatment with filgrastim and by the results for filgrastim obtained in Phase 3. The only exception was duration of hospitalization.
- 5. Due to the lack of data the same duration of hospitalization was assumed for pegfilgrastim as for filgrastim.
- 6. Based on the course of treatment costs were calculated for each G-CSF product. 7. In the base case analysis based on the results of the systematic review no differences
- between compared drugs were assumed.

Table 2. Modelling of the course of treatment – results

Parameter	No treatment (mean time, days)	Lenograstim (RR in relation to no treatment)	Filgrastim (RR in relation to no treatment)	Pegfilgrastim (RR in relation to no treatment)	
Recovery of the ANC to 1,000/mm ³	26.30	0.719	0.719	0.719	
Number of days with fever	9.47	0.823	0.823	0.823	
Duration of hospitalization	34.15	1.018	1.018	1.018	
Duration of anti- biotic therapy	18.58	0.861	0.861	0.861	

In a base-case analysis only G-CSF containing products costs were taken into account. In a sensitivity analysis also hospitalization costs were considered. Since costs of antibiotics administered intravenously are included in costs of hospitalization, these comprise no additional burden for the payer. Also the costs of adverse events were not included as they were not differential (no difference in safety between drugs). The prices of lenograstim, filgrastim (both per 1 MIU) and pegfilgrastim (per 1 mg) in inpatient treatment were obtained from the current NHF catalogue (June 2009). The price of 1 MIU of lenograstim and filgrastim in outpatient treatment was calculated as the mean price of specific products weighted with sales in 2008. Prices of specific products were obtained from the Ministry of Health. Costs of oncological and haematological hospitalization were obtained from the current NHF catalogue (June 2009).

Price in outpatient treatment

7.50 PLN

8.40 PLN

ace area is less expensive than fil- stim. Lenograstim dosed 0.64 MIU/kg	Name	Price in inpatient treatme
ilgrastim and pegfilgrastim.	Lenograstim - 1 MIU	7.89 PLN
entis.	Filgrastim - 1 MIU	8.00 PLN
	Pegfilgrastim - 1 mg	633.33 PLN

Cost analysis

Table 3. Prices of G-CSF products

Table 4. Prices per patient day of hospitalization.

able 4. Trices per patient day of nospitalization.	
Procedure	Price
Hematological hospitalization – adults (per patient day)	663 PLN
Oncological hospitalization – adults (per patient day)	561 PLN
Hematooncological hospitalization – children (per patient day)	765 PLN

Results

Figure 2. Graphic depiction of the

Phase 3b

Filgrastim

therapy modelling

Phase 4

Pegfilgrastim

therapy modelling

Phase 5

Pegfilgrastim

therapy modelling

Phase 1

RCT's selection

Phase 2

Lack of treatment

therapy modelling

Costs calculation

Phase 3a

Lenograstim

therapy modelling

In a time horizon of one chemotherapy cycle, the total cost difference between lenograstim and filgrastim calculated under the assumption of lenograstim dosage 19.2 MIU/m² body surface area was -500 PLN (Cl_{95%}[-600; -400]) and compared to pegfilgrastim 1,700 PLN (Cl_{95%} [600; 2,800]). If lenograstim dosage were 0.64 MIU/kg body weight, estimated cost difference between lenograstim and filgrastim would be 1,600 PLN (Cl₉₅% [1,300; 1,900]) and compared to pegfilgrastim – 3,800 PLN (Cl_{95%} [2,300; 5,200]). The differences in costs presented above are statistically significant (none of the confidence intervals includes zero).

These results indicated that lenograstim dosed 19.2 MIU/m² body surface area is less expensive than filgrastim and more expensive than pegfilgrastim. Lenograstim dosed 0.64 MIU/kg body weight is more expensive than both filgrastim and pegfilgrastim.

Figure 3. Economic results (PLN). Lenograstim dosage 19.2 MIU/m² body surface area

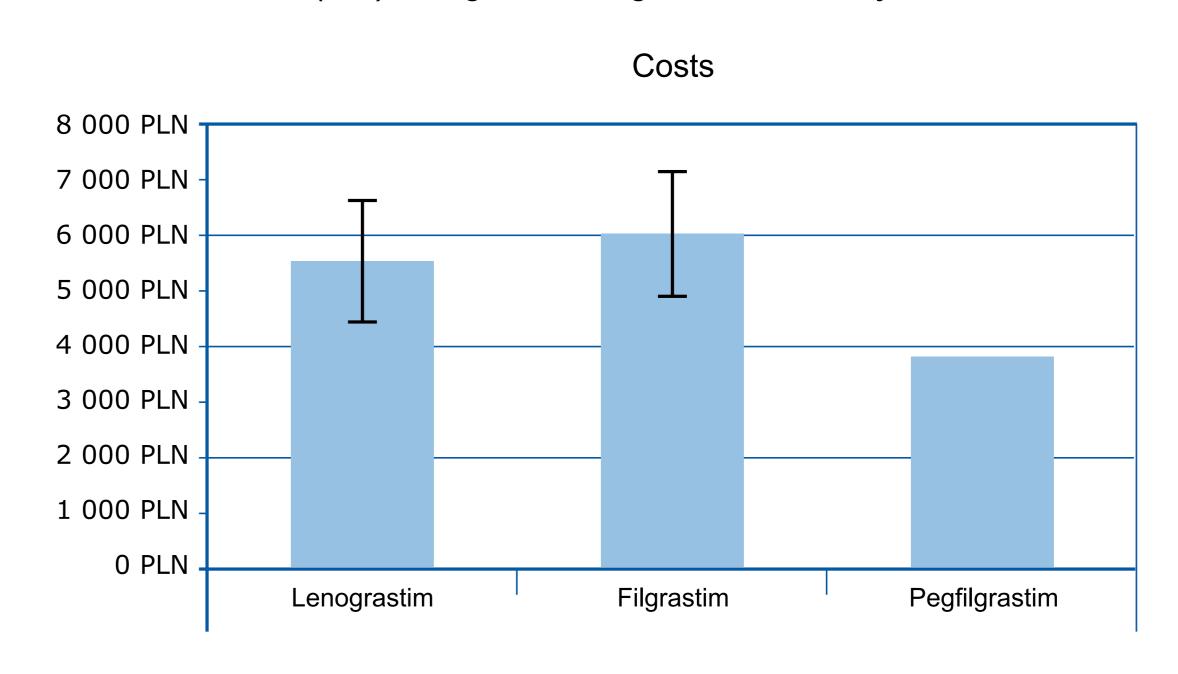
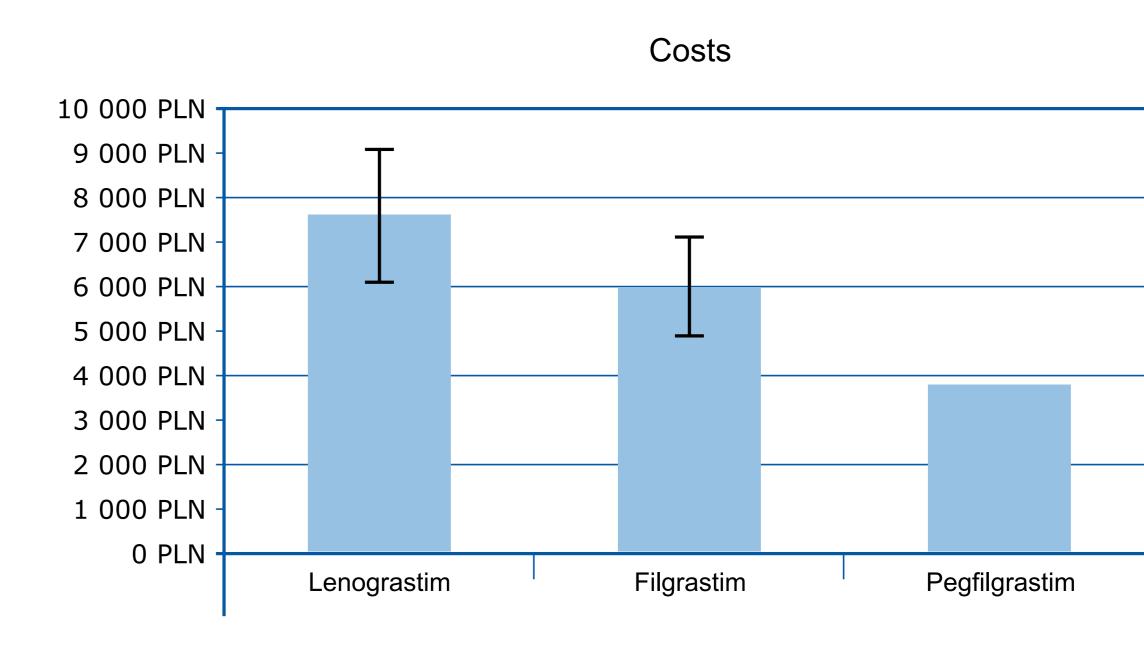


Figure 4. Economic results (PLN). Lenograstim dosage 0.64 MIU/m² body surface area



One-way sensitivity analysis

Inclusion of hospitalization costs results in much higher cost of therapy. However, none of the parameters included in the one-way sensitivity analysis affects incremental results.

Table 5. One-way sensitivity analysis.

Scenario				– Lenogi	rastim vs
	Lenograstim	Filgrastim	Pegfilgrastim	Filgrastim	Pegfilgrastim
Lenograstim dosage: 19.2 MIU/m ² body surface area					
Base-case	5,500 PLN	6,000 PLN	3,800 PLN	-500 PLN	1,700 PLN
Hospitalization costs included	28,500 PLN	29,100 PLN	26,900 PLN	-500 PLN	1,700 PLN
RCT with mi- xed (adults + children or leu- kemias + other cancers) popu- lation included	5,500 PLN	6,000 PLN	3,800 PLN	-500 PLN	1,700 PLN

Base-case	7,600 PLN	6,000 PLN	3,800 PLN	1,600 PLN	3,800 PLN
Hospitalization costs included	30,600 PLN	29,100 PLN	26,900 PLN	1,600 PLN	3,800 PLN
RCT with mi- xed (adults + children or leu- kemias + other cancers) popu- lation included	7,500 PLN	6,000 PLN	3,800 PLN	1,600 PLN	3,800 PLN
Minimum body weight	7,500 PLN	6,000 PLN	3,800 PLN	1,600 PLN	3,700 PLN
Maximum body weight	7,600 PLN	6,000 PLN	3,800 PLN	1,600 PLN	3,800 PLN

Lenograstim dosage: 0.64 MIU/kg body weight

Acknowledgements

The analysis was commissioned and financed by Sanofi-Aventis.

References

- 1. G. Herold, Medycyna wewnętrzna, repetytorium dla studentów medycyny i lekarzy, wydanie III, Wydawnictwo Lekarskie PZWL, Warszawa.
- 2. A. Szczeklik, Choroby wewnętrzne, Medycyna Praktyczna, Kraków 2006.
- 3. A. Fauci, E. Braunwald, K. Isselbacher, J. Wilson, J. Martin, D. Kasper, S. Hauser, D. Longo, Interna Harrisona, wydanie XIV, Wydawnictwo Czelej, Lublin 2000.
- 4. V. Lorusso, Clinical and economic benefit of G-CSF administration in the prevention of chemo-induced neutropenia. "Trends in Medicine" 2008; t. 8, nr. 1, s.1-18.
- 5. R. Ng, M. D. Green, Pegfilgrastim: evidence in support of its use with cytotoxic chemotherapy, "Expert Review of Anticancer Therapies". t. 5, nr. 4, s.585-590, 2005.
- 6. R. Kordek, Onkologia, Podręcznik dla studentów i lekarzy, Wydawnictwo Via Medica,

Conclusions

From the perspective of the Polish public payer the use of lenograstim dosage of 19.2 MIU/m² body surface area in treatment of neutropenia in adult patients receiving chemotherapy for leukemia is less expensive than use of filgrastim and more expensive than use of pegfilgrastim. Lenograstim dosed 0.64 MIU/kg body weight is more expensive than both filgrastim and pegfilgrastim.

Methods The analysis covered a time horizon of one chemotherapy cycle. The public payer's perspective

Abstract

Objectives

rapy for leukemia.

was adopted for cost-effectiveness analysis. The costs included were based on the Polish NHF reference costs list. Data concerning time to ANC recovery, the number of days with fever, length of hospital stay and use of antibiotics were obtained from randomized controlled trials (RCTs) identified in the conducted systematic review. These included trials on prophylactic G-CSF use as well as trials in which only patients with neutropenia were included. Based on the data from systematic review an assumption that no differences between analysed drugs exist was taken. Due to no significant differences between comparators in efficacy and safety (adverse events) cost minimization analysis was conducted. Equations for calculation of costs depending on the number of days with neutropenia and fever, hospital stay and antibiotic use were established.

A number of studies have demonstrated beneficial effects of granulocyte colony-stimulating fac-

tors (G-CSF) on duration of neutropenia in adults receiving chemotherapy for leukemia. The

aim of the present analysis was to assess the costs of lenograstim in comparison with other G-

CSF products, i.e. filgrastim and pegfilgrastim, in Polish settings in adults receiving chemothe-

Results

Under the assumption of lenograstim dosage 19.2 MIU/m² body surface area, the total cost difference between lenograstim and filgrastim was -500 PLN (Cl₉₅%[-600; -400]) and compared to pegfilgrastim 1,700 PLN (Cl₉₅% [600;

If lenograstim dosage were 0.64 MIU/kg body weight, estimated cost difference between lenograstim and filgrastim would be 1,600 PLN (Cl_{95%} [1,300; 1,900]) and compared to pegfilgrastim – 3,800 PLN (Cl_{95%} [2,300; 5,200]).

Conclusions

Lenograstim dosed 19.2 MIU/m² body surface grastim and more expensive than pegfilgrasti body weight is more expensive than both filgi

Acknowledgements

This analysis was supported by Sanofi-Aven