COST-EFFECTIVENESS OF LENOGRASTIM ON NEUTROPENIA DURATION IN ADULTS RECEIVING CHEMOTHERAPY FOR SOLID TUMORS OR LYMPHOMAS

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

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

Introduction

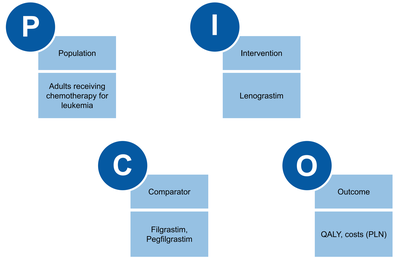
Neutropenia is defined as a situation, in which the absolute neutrophil count (ANC) falls below 1500/mm^3. Several grades of neutropenia are defined: in grade 3 neutropenia the ANC is below 1,000/mm^3, but over 500/mm^3 and in grade 4 neutropenia the ANC falls below 500/mm^3. Neutropenia is considered 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/mm^3. [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 solid tumors and lymphomas.

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 hospitalzation 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/mm^3;
- 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.

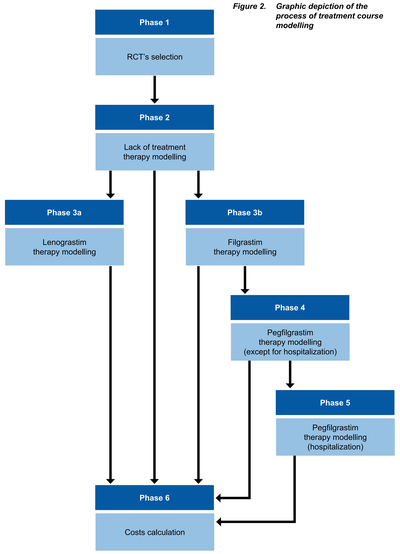
These parameters were estimated and analyzed in the following phases:

1. Trials in which adult patients receiving chemotherapy for solid tumors and lymphomas 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/mm^3, 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	13.69	0.385	0.385	0.385
Number of days with fever	4.00	0.522	0.522	0.522
Duration of hospitalization	7.89	0.599	0.599	0.599
Duration of antibiotic therapy	6.63	0.558	0.558	0.558

Figure 2. Graphic depiction of the process of treatment course modelling



Cost analysis

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).

Table 3. Prices of G-CSF products

Name	Price in inpatient treatment	Price in outpatient treatment
Lenograstim - 1 MIU	7.89 PLN	7.50 PLN
Filgrastim - 1 MIU	8.00 PLN	8.40 PLN
Pegfilgrastim - 1 mg	633.33 PLN	-

Table 4. Prices per patient day of hospitalization.

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

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/m^2 body surface area was -200 PLN (CI$_{95\%}$[-400; -100]) and compared to pegfilgrastim -1,900 PLN (CI$_{95\%}$ [-2,200; -1,600]). If lenograstim dosage were 0.64 MIU/kg body weight, estimated cost difference between lenograstim and filgrastim would be 500 PLN (CI$_{95\%}$ [300; 600]) and compared to pegfilgrastim -1,200 PLN (CI$_{95\%}$ [-1,600; -800]). 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/m^2 body surface area is less expensive than filgrastim and pegfilgrastim. Lenograstim dosed 0.64 MIU/kg body weight is more expensive than filgrastim and less expensive than pegfilgrastim.

Figure 3. Economic results (PLN). Lenograstim dosage 19.2 MIU/m^2 body surface area

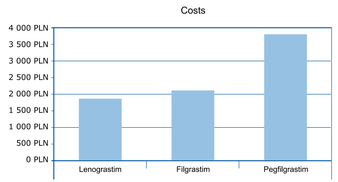
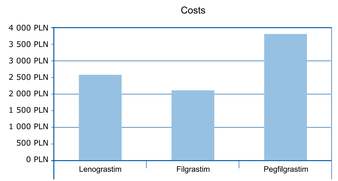


Figure 4. Economic results (PLN). Lenograstim dosage 0.64 MIU/m^2 body surface area



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	Costs			Incremental costs – Lenograstim vs	
	Lenograstim	Filgrastim	Pegfilgrastim	Filgrastim	Pegfilgrastim
Lenograstim dosage: 19.2 MIU/m^2 body surface area					
Base-case	1,900 PLN	2,100 PLN	3,800 PLN	200 PLN	1,900 PLN
Hospitalization costs included	4,500 PLN	4,800 PLN	6,400 PLN	200 PLN	1,900 PLN
RCT with mixed (adults + children or solid tumors, lymphomas + other cancers) population included	2,000 PLN	2,200 PLN	3,800 PLN	300 PLN	1,800 PLN
Lenograstim dosage: 0.64 MIU/kg body weight					
Base-case	2,600 PLN	2,100 PLN	3,800 PLN	500 PLN	1,200 PLN
Hospitalization costs included	5,200 PLN	4,800 PLN	6,400 PLN	500 PLN	1,200 PLN
RCT with mixed (adults + children or solid tumors, lymphomas + other cancers) population included	2,800 PLN	2,200 PLN	3,800 PLN	500 PLN	1,000 PLN
Minimum body weight	2,600 PLN	2,100 PLN	3,800 PLN	500 PLN	1,200 PLN
Maximum body weight	2,600 PLN	2,100 PLN	3,800 PLN	500 PLN	1,200 PLN

Conclusions:

From the perspective of the Polish public payer the use of lenograstim dosage of 19.2 MIU/m^2 body surface area in treatment of neutropenia in adult patients receiving chemotherapy for solid tumors and lymphomas is less expensive than use of filgrastim and pegfilgrastim. Lenograstim dosed 0.64 MIU/kg body weight is more expensive than filgrastim and less expensive than pegfilgrastim.

Abstract

Objectives

A number of studies have demonstrated beneficial effects of granulocyte colony-stimulating factors (G-CSF) on duration of neutropenia in adults receiving chemotherapy for solid tumors and lymphomas. 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 chemotherapy for solid tumors or lymphomas.

Methods

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

Results

Under the assumption of lenograstim dosage 19.2 MIU/m^2 body surface area, the total cost difference between lenograstim and filgrastim was -200 PLN (CI$_{95\%}$[-400; -100]) and compared to pegfilgrastim -1,900 PLN (CI$_{95\%}$ [-2,200; -1,600]).

If lenograstim dosage were 0.64 MIU/kg body weight, estimated cost difference between lenograstim and filgrastim would be 500 PLN (CI$_{95\%}$ [300; 600]) and compared to pegfilgrastim -1,200 PLN (CI$_{95\%}$ [-1,600; -800]).

Conclusions

Lenograstim dosed 19.2 MIU/m^2 body surface area is less expensive than filgrastim and pegfilgrastim. Lenograstim dosed 0.64 MIU/kg body weight is more expensive than filgrastim and less expensive than pegfilgrastim.

Acknowledgements

This analysis was supported by Sanofi-Aventis.

Acknowledgements

The analysis was commissioned and financed by Sanofi-Aventis.

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