Objective

The purpose of the study was to compare efficacy and safety of allelo- 
phic peripheral blood stem cell transplantation after mobilization with ei-
ther lenograstim or filgrastim.

Introduction

Peripheral blood stem cell transplantation is an alternative to bone 
marrow transplantation in patients with various malignancies and 
bone or bone marrow disorders. Collecting hematopoietic stem cells 
(HSC) from peripheral blood, rather than from bone marrow, provides 
a larger quantity of cells and does not require general anesthesia to 
collect the graft from the donor. Moreover, time to engraftment seems to 
be shorter in case of PBSC.

In normal, physiologic conditions only a small amount of HSC circula-
tes in peripheral blood. Release of HSC from bone marrow occurs in 
response to a cytokine stimulus, such as the mobilization of HSC in order to 
support hematopoiesis. Administration of recombinant human granulocyte 
colonystimulating factor, termed matured mobilization, results in HSC release 
from bone marrow into peripheral blood and allows harvesting them for 
transplantation.

Two forms of recombinant human granulocyte colony stimulating factor 
are available for clinical use in Europe and are associated with PBSCT: leno-
grastim and filgrastim.

Comparison of efficacy and safety of the analysed drugs was based on 
randomized controlled trials (RCTs) identified by means of a systematic 
review, carried out in the framework of the European Network 
for Health Technology Assessment (HTA) on Stem Cell Transplantation 
and Related Interventions and Polish HTA Guidelines. The most 
important drug characteristics were derived (EBMbase, MEDLINE, CE-
TRAL). Two reviewers independently selected trials, assessed their 
quality and extracted data. No head-to-head trials were identified, the 
refined inclusion criteria using Bucher’s method was performed.

Methods

Characteristics of clinical trials

The search in medical databases resulted in a total number of 9144 
identified publications (including repeated titles). 290 positions were 
qualified for full text analysis. Finally 9 trials met predefined inclusion 
criteria and were suitable for further analysis:

- 2 RCTs comparing PBSCT after mobilization with lenograstim with 
  bone marrow transplantation.
- 7 RCTs comparing PBSCT after mobilization with filgrastim with 
  bone marrow transplantation.

All studies had parallel design. Methodological credibility of the trials 
included in the analysis was medium in most cases.

In all patients in the included studies were diagnosed with haematological 
disorders (bone marrow transplantation, vital-conditioning regimen – 
dose-intensive chemotherapy) with or without transplantation. Followed by transplan-
tation of hematopoietic stem cells. HSC (either peripheral blood stem cells 
or bone marrow stem cells) were obtained from a stooling donor. In all but two studies no posttransplant G-CSF was used. GvHD preven-
tion regimens usually included methotrexate and Cyclosporin-A.

In one study 1:1 callibration of PBSCT was used.

In total, 280 positions qualified for further full text analysis.

Results

No significant differences between lenograstim and filgrastim were fo-
rmed with respect to mortality rate, either overall or treatment-related 
mortality (RR = 0.81 [0.59;1.12]; 95% CI: [0.60;1.19], respectiv-
ely). For non-treatment-related mortality the results were inconsistent 
(RR=0.79 [0.59;1.07], 95% CI: [0.58;1.35]). While no difference was 
detected in the risk of overall or treatment-related mortality, acute 
coronary disease, or chronic graft versus host disease, or relapse. The only 
difference was associated with higher risk of acute GvHD than BMT (RR=1.19 
[0.96;1.47], 95% CI: [0.80;1.76]). Use of lenograstim or filgrastim was asso-
ciated with higher risk of acute GvHD than BMT (RR=1.33 [0.84;2.11], 95% CI: 
[0.58;2.97]). There was also no difference in the risk of chronic 
GvHD-related mortality (RR = 0.84 [0.49; 1.42], RR= 1.11 [0.60; 2.04], respective-
ly). However, the risk of secondary malignancy was doubled in the group 
of patients mobilized with filgrastim (RR=2.03 [1.06; 3.88], 95% CI: [1.05; 
[1.99]).

Table 4. Results of indirect comparison between PBSCT after mobilization with lenograstim or filgrastim

<table>
<thead>
<tr>
<th>Outcome</th>
<th>PBSCT (LEN) vs PBSCT (FIL)</th>
<th>PBSCT (LEN) vs PBSCT (FIL)</th>
<th>PBSCT (LEN) vs PBSCT (FIL)</th>
<th>PBSCT (LEN) vs PBSCT (FIL)</th>
<th>PBSCT (LEN) vs PBSCT (FIL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>0.28</td>
<td>0.05</td>
<td>-0.20</td>
<td>0.11</td>
<td>0.02</td>
</tr>
<tr>
<td>PMF</td>
<td>0.09</td>
<td>0.03</td>
<td>-0.06</td>
<td>0.11</td>
<td>0.02</td>
</tr>
<tr>
<td>TRM</td>
<td>0.38</td>
<td>0.09</td>
<td>-0.29</td>
<td>0.15</td>
<td>0.07</td>
</tr>
<tr>
<td>aGVHD</td>
<td>0.45</td>
<td>0.10</td>
<td>-0.35</td>
<td>0.19</td>
<td>0.06</td>
</tr>
<tr>
<td>cGVHD</td>
<td>0.45</td>
<td>0.10</td>
<td>-0.35</td>
<td>0.19</td>
<td>0.06</td>
</tr>
</tbody>
</table>

Conclusions

Indirect comparisons indicate similar efficacy and safety of PBSCT 
after mobilization with lenograstim and PBSCT after 
mobilization with filgrastim. No differences were 
detected in the risk of overall or treatment-related mortality, acute 
coronary disease, or chronic graft versus host disease, or relapse. The only 
difference was associated with higher risk of acute GvHD than BMT (RR=1.19 
[0.96;1.47], 95% CI: [0.80;1.76]). Use of lenograstim or filgrastim was asso-
ciated with higher risk of acute GvHD than BMT (RR=1.33 [0.84;2.11], 95% CI: 
[0.58;2.97]). There was also no difference in the risk of chronic 
GvHD-related mortality (RR = 0.84 [0.49; 1.42], RR= 1.11 [0.60; 2.04], respective-
ly). However, the risk of secondary malignancy was doubled in the group 
of patients mobilized with filgrastim (RR=2.03 [1.06; 3.88], 95% CI: [1.05; 
[1.99]).

Regarding PBSCT donors, both interventions seem to be 
associated with comparable incidence of hospitalization.

Limitations

The limitations of the analysis are due to lack of clinical trials with head-
to-head comparison of peripheral blood stem cell transplantation after 
mobilization with PBSC and PBSCT. Conclusions are based on indirect comparison and thus is a major weakness of this study. How-
never, because of lack of evidences in direct comparison, indirect 
comparison is the best available source of information about relative effi-
cacy and safety of both recombinant G-CSFs in peripheral blood stem 
cell transplantation.

Table 1. Indicators for the analysis

<table>
<thead>
<tr>
<th>Measure</th>
<th>Score</th>
<th>Score</th>
<th>Score</th>
<th>Score</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>nTRM</td>
<td>0.14</td>
<td>0.11</td>
<td>0.35</td>
<td>0.24</td>
<td>0.32</td>
</tr>
<tr>
<td>TRM</td>
<td>0.24</td>
<td>0.24</td>
<td>0.26</td>
<td>0.26</td>
<td>0.26</td>
</tr>
<tr>
<td>aGVHD</td>
<td>0.45</td>
<td>0.10</td>
<td>-0.35</td>
<td>0.19</td>
<td>0.06</td>
</tr>
<tr>
<td>cGVHD</td>
<td>0.45</td>
<td>0.10</td>
<td>-0.35</td>
<td>0.19</td>
<td>0.06</td>
</tr>
</tbody>
</table>

Table 2. Indicators for the analysis

<table>
<thead>
<tr>
<th>Measure</th>
<th>Score</th>
<th>Score</th>
<th>Score</th>
<th>Score</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>nTRM</td>
<td>0.14</td>
<td>0.11</td>
<td>0.35</td>
<td>0.24</td>
<td>0.32</td>
</tr>
<tr>
<td>TRM</td>
<td>0.24</td>
<td>0.24</td>
<td>0.26</td>
<td>0.26</td>
<td>0.26</td>
</tr>
<tr>
<td>aGVHD</td>
<td>0.45</td>
<td>0.10</td>
<td>-0.35</td>
<td>0.19</td>
<td>0.06</td>
</tr>
<tr>
<td>cGVHD</td>
<td>0.45</td>
<td>0.10</td>
<td>-0.35</td>
<td>0.19</td>
<td>0.06</td>
</tr>
</tbody>
</table>