Reviewer's report

Title: Efficacy and safety of lippegfilgrastim versus pegfilgrastim: a randomized, multi-center, active-control Phase 3 trial in patients with breast cancer receiving doxorubicin/docetaxel chemotherapy

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Reviewer: Jean Klastersky

Reviewer's report:

This is an interesting and potentially important study.

From the methodological point of view, the study is a prospective, randomized, blinded evaluation of 2 long acting G-CSF’s in a homogenous population (type of cancer and chemotherapy) for which the risk of febrile neutropenia (FN) is probably in the range of 20%, a clear indication according for primary G-CSF prophylaxis.

The statistical analysis looks adequate.

From the efficacy point of view, for the primary endpoint (mean duration of severe neutropenia) lippegfilgrastim was shown non inferior to pegfilgrastim.

More importantly for the clinician, there has been a spectacular reduction (in comparison to what is expected without G-CSF prophylaxis) of the incidence of FN: 3/101 in the pegfilgrastim arm and 1/101 in the lippegfilgrastim group (ITT population) with only 2 patients in the pegfilgrastim arm and one patient in the lippegfilgrastim arm requiring hospitalization for the management of FN.

No cost efficacy analysis has been done, and that would have been interesting, although there is no untreated group to be compared to and thus the estimation of the cost of a 20% incidence of FN (as expected) would be speculative.

As far as toxicity is concerned, there was a slight trend – although not statistically significant – for more bone pain, myalgia and arthralgia with lippegfilgrastim though none of these complications was severe enough to lead to discontinuation of the participation to the study.

Why might this study be important for clinical practice? Because the introduction of more affordable biosimilars might improve the cost efficacy of management of cancer patients receiving chemotherapy (a highly desirable issue) and might allow the extension for the indications of primary prophylaxis beyond the standards recommendations that are made today.

To conclude, I have no problems with recommending the publication of that paper.

Level of interest: An article of importance in its field

Quality of written English: Acceptable
**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

Prof. Klastersky received consulting fees from Amgen, Laroche, and Teva.