Reviewer’s report

Title: Study protocol of the RAND-study: a multicenter, prospective cohort study investigating response and adherence to first-line nilotinib treatment in chronic myeloid leukemia

Version: 1 Date: 28 January 2014

Reviewer: Lucien Noens

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2.1 Major Compulsory Revisions
The precise definition of non-adherence, according to predefined criteria including persistence and execution is lacking. The criterium of 90% compliance is not evidence-based and will not allow delineating the margin of non-adherence (‘forgiveness’), that actually needs to be determined: this is a major drawback (reference 1).

The patient reported outcomes will be assessed by a number of validated questionnaires but first a specific questionnaire assessing health related quality of life in CML patients (EORTC QLQ-CML24) is not used, and secondly the study protocol does not mention how these different questionnaires will be weighted. There will be considerable overlap and also contradictions. It is not clear whether the questionnaires will be used comparably. Therefore the study carries the risk of not being able to make an evidence-based selection between these questionnaires (reference 2).

2.2 Minor Essential Revisions
The reasons for lack of response should be divided in BCR-related and BCR-unrelated.

The current guideline, evaluating the TKI-therapy at three months should be included.

The acronym MEMS also stands for: Medication Event Monitoring System.

The pill count methodology includes unannounced interviews by phone: it is not mentioned at what time point and how frequent these will be planned. The fact that these interviews by phone will be unannounced should be mentioned in the informed consent (not included in the manuscript).

Statistical review
In view of the need for better definition of non-adherence, as a continuous variable, the statistics need to be reassessed, including an expert statistician.

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Needs some language corrections before being published.

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I disclose being a member of advisory reports of Novartis, and Bristol-Myers Squibb. I have no other disclosures to declare.