Reviewer’s report

Title: What is the key issue in adherence evaluation of endocrine treatment of early breast cancer? - Methodological aspects of the study 'Patient-reported outcomes in breast cancer patients undergoing endocrine therapy (PRO-BETH)

Version: 1 Date: 10 July 2012

Reviewer: Karin Ribi

Reviewer’s report:

The study compares four different approaches to assess adherence to endocrine (i.e. anastrozole) therapy in patients with early breast cancer: a patient-reported outcome scale, a physician rating, refill records, and determination of anastrozole serum concentration. It aims to compare adherence rates based on these different measurement methods and to evaluate the concordance between these methods in the same study population. This is a valid approach for a better understanding of the accuracy of each method. The data the authors present is sound and clearly presented and the limitations are addressed adequately. Therefore it is worth to be published. Although the manuscript in generally well-written, the methods section lacks some clarity, especially for a manuscript on measurement methods. In addition, the reader may be interested in some considerations how to weight these methods against each other for the assessment of adherence to endocrine therapy (see comments below).

Minor essential revisions

1. Title: The first part of the title (question) is not exactly reflecting the content of the manuscript, and the second part is misleading. Not the methodology of the PRO-BETH study is the topic of the manuscript, only the methodology referring to adherence. The running title is more adequate.

2. Assessment methods, self-report questionnaire: From the description it is not clear how the scale was composed. The SMAQ has six items and as I understand was supplemented with 3 items of the revised Morisky scale, still resulting in 6 items? Were three of the SMAQ items replaced by three of the items of the Morisky scale? It is also not clear what the original response format to the six final questions was, and how exactly the scoring was adapted to receive a score ranging from 2 to 12. Please clarify. Some more details on translation process would also be appreciated.

3. Please provide some argument for the decision on cutoffs defining a patient as adherent vs. non-adherent (i.e. in particular for the self-report and the prescription refill)

4. Results: There is no information on how many of the approached patients were not willing to participate in this study. Those who are less adherent to therapy may also more often decline to participate, which could introduce a
selection bias that affects the adherence rates found in this study.

General:
5. The expression ‘methodological consistency’ could be mistaken as ‘internal consistency’ of one specific method, and seems inadequate in this context. It should be ‘consistency of results from different methods’ or ‘concordance between methods’.

Discretionary Revisions

Introduction:
1. Although it is mentioned within the paragraph describing the aims, a few sentences introducing the methods that are commonly used to assess adherence in general and specifically in adjuvant breast cancer care would be helpful to see, why the four specific approaches were chosen for comparison.

Discussion:
2. In the discussion the reader may be interested not only in the limitations of each method, but also in some considerations how to weight these methods against each other for the assessment of adherence to endocrine therapy, and in some suggestions/recommendations with respect to the development of new methods.

Minor issues not for publication:
Discussion towards the end of second paragraph sentences with ref 7. This sentence is grammatically not correct.

**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:**
'I declare that I have no competing interests'