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: 11 July 2012

Reviewer: Arnoud Templeton

Reviewers's report:

Major Compulsory Revisions

The author must respond to these before a decision on publication can be reached. For example, additional necessary experiments or controls, statistical mistakes, errors in interpretation.

1. Abstract: The authors should explain why they feel comfortable with the reported high adherence rates if the concordance between the assessment tools was so low.

2. Several points in the introduction should be addressed:
   a) It is not correct that AI’s have shown a „tremendous reduction in breast cancer recurrence and mortality“. E.g. the ATAC study (Ref 1) in did not show any OS advantage for anastrozole compared to tamoxifen.
   b) Ref 3. does not quite support the statement that patient are highly adherent as they have „too much to lose“, in fact the papers concludes the abstract with „Patients SRs and PCs likely overestimate the degree to which patients adhere to their tamoxifen regimen“.
   c) The study cited as ref 6 did not include any cancer patients.
   d) The editorial cited as ref 7 only mentions adherence rates between 20 and 100% as citation from Partridge et al. JNCI 2002
   e) What does „prevalence rates“ mean here?

3. The following points in the methods section should be addressed:
   a) How do the authors know that the questionnaire proved to be applicable in the specific patient population they studied (having mentioned the lack of questionnaires to specifically assess treatment adherence in early breast cancer)?
   b) Physician rating: How often did a physician rate adherence? The authors state that except for refills this was done cross-sectionally (implicating once) and further down „after each check-up“
   c) The authors write, „Medical expert ratings are an established method for assessing treatment-related side-effects.“ More relevant is whether they are
established for rating of adherence?

4. The following points in the result section should be addressed:
   a) It would be nice to see a distribution curve for the anastrozole serum levels and to know how many patients were below the 10th or 25th percentile (the rate of biochemical adherence of 98.2% only results from defining those as non-adherent where no anastrozole could be measured)
   b) Table 1: did patients with diagnosis “in situ” have invasive disease? The total number in diagnosis is not 242. For age and duration of treatment medians rather than means should be reported (if endocrine treatment was anastrozole only, this should be mentioned, else other endocrine treatment and time of switch reported)

5. In the very well written discussion section the following points should be addressed:
   a) Different rates of completion of the assessment tool (e.g. only 50% for prescription refill, 77% for self-reported adherence # did the good ones complete this form?)
   b) Reasons for non-concordance between the methods
   c) All patients identified as eligible form the charts seem to have participated what is quite a high rate

6. I suggest to modify the title as the paper does not answer the question raised.

Minor Essential Revisions

The author can be trusted to make these. For example, missing labels on figures, the wrong use of a term, spelling mistakes.

1. Title page:
   a) Affiliation of author Kemmler is missing.
   b) Initial of first name should be before the name, no superscript of comma after B. Holzner1
   c) Use same format for phone and fax number

2. The section procedures refers to a chapter assessment instruments which I cannot find (= assessment methods?)

3. Key words: “adherence” should be added

Discretionary Revisions

These are recommendations for improvement, which the author can choose to ignore. For example clarifications, data that would be useful but not essential.

1. Title page: Add Austria after address of corresponding author
2. Abstract: Methodological limitations are not necessarily due to validated
assessment tools # authors should think of re-wording this
3. Abstract: what is the difference between well-validated and validated?
4. Table 1 and Results: tumour grades are not really relevant for this study

**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 declare that I have no competing interests.