Reviewer’s report

Title: Pipelle Prospective ENDOmetrial carcinoma (PIPENDO) study, pre-operative recognition of high risk endometrial carcinoma: a multicentre prospective cohort study

Version: 3 Date: 25 January 2015

Reviewer: Alain G Zeimet

Reviewer’s report:

This contribution is not a classic original article with communication of scientific results but is a presentation of the study design of an ongoing trial.

The most critical issue of this study is that the authors don’t take into account that the one or the other of the evaluated IHC markers are not homogenously expressed in the tumors and staining may be focal. That is especially true when endometrial biopsies obtained by Pipelle are investigated. For some included markers these concerns were raised and confirmed with regard to false negative results when tissue arrays were used instead of full sections. This issue should be more carefully considered and measures should be included in the study design to avoid false negative evaluation for markers heterogeneously distributed in the tumor.

With regard to the included specimens authors don’t give clear insights into the real number of biopsies and curettage specimens included in the study. That should be done!

The possible difference in the predictive value between Pipelle biopsies and classical curettage is one critical study endpoint which is missing in my opinion.

I am not sure that the inclusion of co-morbidities into the calculations is really beneficial for the study and in the end may raise more questions than giving reliable answers. In this context the issue of selection bias is the most important and the most hindering. Authors refer to literature (25 and 28) which is not very conclusive. The work of Boll et al. is based on overall survival and not on EC-specific survival. Robbins’ work was unable to reveal an independent effect of comorbidity score on EC specific survival in multivariate analysis.

Furthermore, the relation between the IHC approach of the study and comorbidities as such is not very obvious.

At page 7 lines 141-142: I would recommend to write that all the mentioned biomarker (not only L1CAM) are lacking validation and are based on single studies!

I would highly suggest that authors should at least include a Table with all the patient characteristics, as patients are already included in the trial since Dec. 2013. This could be very informative for the reader.
Level of interest: An article whose findings are important to those with closely related research interests

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'