Reviewer’s report

Title: Serum HE4 as a Biomarker to Detect Recurrent Endometrial Cancer in Patients Undergoing Routine Clinical Surveillance

Version: 2
Date: 17 December 2014
Reviewer: Michael Frumovitz

Reviewer’s report:

Thank you for the opportunity to read your manuscript entitled “Serum HE4 Detects Recurrent Endometrial Cancer in Patients Undergoing Routine Clinical Surveillance.” This manuscript retrospectively analyzed 98 patients with endometrial cancer of which 26 (27%) recurred. The authors found HE4 to be a better biomarker for recurrence than CA125 although the sensitivity was still only 84%. The authors conclude that HE4 may be a useful marker for following patients with uterine cancer, particularly endometrioid histologies.

Prior to consideration for publication, the following concerns should be addressed:

1. Page 3, lines 89-90. The authors state “With more than 300,000 cases occurring annually worldwide, endometrial adenocarcinoma (EAC) is the most common gynecological cancer.” This is not true. Cervical cancer, with almost 500,000 annual cases worldwide, is the most common gynecological cancer.


3. Page 4, line 128: Please remove extra period.

4. Page 8, line 192: Please change “diagnostic” to “diagnosis”.

5. Page 8, lines 203-205: The authors write: “While increased HE4 levels at diagnosis have been shown to be prognostic by many groups, this study focuses on HE4 and CA125 levels at the interval and recurrence/final time points.” This statement does not belong in the Results but rather in the Introduction just prior to the objectives of the study.

6. Page 8, line 209: Please capitalize the “T” in “table”.

7. Page 10-11, final paragraph: The authors are quick to give full sets of numbers for sensitivity, specificity and NPV for all patients and the subset with endometrioid histology. For CA125, they only give the full percentages for all cancers and ask us to assume that there was no “significant” change for those with endometrioid. Please provide all the numbers and let the reader decide.
8. Page 14, line 336: The authors state that HE4 is elevated in 88% of patients with recurrent endometrioid endometrial cancer. I believe this should be 84%.

9. Do the authors have any comparator group of recurrent patients who did not get HE4? In other words, did following HE4 make a difference in survival? They write in the Conclusion that their numbers approach those for CA125 in ovarian cancer yet we know that following CA125 in ovarian cancer patients does not change survival so why should we follow HE4 in women with endometrial cancer especially when only 20% or so will recur?

**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