**Reviewer's report**

**Title:** Diagnostic Accuracy of Cyst Fluid Amphiregulin in Pancreatic Cysts

**Version:** 1  **Date:** 18 September 2011

**Reviewer:** Christopher Halloran

**Reviewer's report:**

This is a retrospective, but small study of analysis of pancreatic cyst fluid using amphiregulin (AREG). The motivation was to use this novel biomarker to differentiate between non-mucinous, benign mucinous and malignant mucinous cysts. This is an important topic and the authors should be congratulated on their endeavours in this field.

**Major Revisions / Questions to be answered**

It is unclear whether AREG use was investigated as a biomarker for dysplasia/malignancy or for mucinous/non-mucinous lesions as suggested in the abstract.

It would be helpful to know whether the pre-operative diagnoses differed from the post operative histology and what the indications for surgery were.

This study attempts to differentiate between benign mucinous lesions and mucinous lesions, which have dysplastic or malignant cells. However the “benign” group contains 9 BD-IPMN, 3 MD-IPMN and 3 MCN. Practically MD-IPMN and MCD should be treated as pre-malignant cysts and should be resected regardless; therefore this use of tumour markers in these cases does help.

Furthermore 3 cases of high-grade dysplasia were found in the MD-IPMN, which were classified as “benign tumours”. Therefore was the analysis performed between the benign cysts and the malignant cyst groups? in which case there was bias or between those that were histologically benign with those of dysplasia/malignancy? Hence I am not sure what the authors point is exactly – clarification is required.

Looking at these data it is clear that MD-IPMN and MCD have a higher median AREG and should never have been included in the grouping. These data are summarized in table 3 that only have 9 patients not the 12 stated – where are the rest. Overall this is VERY confusing as it is unclear exactly which patients were compared.

As the data pertain to which patients were used in the accuracy testing and ROC curve are unclear I am hesitant to accept these findings without qualification.

Overall the use of AREG performs no better than CEA in those cases where both
results are included. Obviously the small numbers and retrospective approach hinder this study but it would be interesting to see how AREG performs along side CEA and CA 199.9 from cyst aspirates in a prospective group of patients presenting with non-inflammatory pancreatic cysts.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**
I declare that I have no competing interests