Reviewer's report

**Title:** Human Papillomavirus-associated oropharyngeal cancer: an observational study of diagnosis, prevalence and prognosis in a UK population

**Version:** 1 **Date:** 17 February 2013

**Reviewer:** Tsung-Lin Yang

**Reviewer's report:**

Major Compulsory Revisions

This study aims to study the significant impact of HPV infection on OPC. The authors states that HPV positivity alters the clinical behaviour of OPC, and is associated with significantly better clinical outcomes. Several different methods have been used to confirm the HPV positivity in the enrolled cases, and the correlation between HPV and clinical survival has also been clarified.

1. The analysis of HPV infection is mainly based on the FFPE which is retrieved from the pathological archive. Since the cases were enrolled from 2001 to 2006, many blocks were unable to be retrieved because of the quality of paraffin block. It may lead to a bias in the recruitment because the old blocks may be more difficult to be kept in good quality. 50% loss seems to be higher and may not be adequate for being presented as the whole population. A detail list and the clinical data of enrolled and excluded cases should be listed and compared to reveal the potential bias of block retrieval.

2. This study claims that the impact of HPV status on outcome is revealed in a ‘real-world’ population of patients with OPC without systematically excluding any patients. However, the selection bias may be encountered. The author needs to address in the discussion paragraph. Most palliative patients were noted in the true-negative group, which may change the analytic results of survival.

3. In the true negative group, not all patients receive radical treatment. Similarly, not all patients receive radical management. No cases are noted in the true positive cases. This leads to a worse outcome in this group, and results in the analysis unconvincing.

4. Since the quality of DNA is the most important factor for PCR analysis, how about the classification of 78 cases confirmed by HMBS positivity? how about the survival analysis based on the HMBS positive cases? It is also suggested to show the K-M plots based on these cases just like figure 1.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable
**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

Nothing to declare