Reviewer's report

Title: Chemotherapy Followed by Surgery versus Surgery Alone in Patients with Oesophageal Squamous Cell Carcinoma: Long-term Results of a Randomized Controlled Trial

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Reviewer: Trevor Leong

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This paper is somewhat intriguing for several reasons. Firstly, I cannot understand why a study that completed recruitment in 1996 has taken so long to be reported. Secondly, this trial was conducted at approximately the same time period as the much larger US INT0113 and UK MRC OE2 trials, thereby allowing some comparisons to be made with these trials. The INT0113 trial showed no benefit for neoadjuvant chemotherapy while the OE2 trial demonstrated improved survival with neoadjuvant chemotherapy. I have some comments and questions.

Minor comments/questions/revisions

1) Did this trial include standardization of preoperative staging? ie. were all patients staged with CT scans. Was there standardization of surgical technique? One of the caveats of the OE2 trial is that there was no standardization of preoperative staging or surgical technique. In contrast, all patients in INT0113 underwent CT staging, and surgery was conducted according to protocol guidelines at experienced centres. This may partly explain the difference in results between the two trials.

2) It would be helpful to include the preoperative stage grouping of patients in Table 1. I note in Table 3 that 39% of patients in the surgery alone arm had nodal disease and 14% had celiac nodal disease. In other words, were these patients appropriately selected for surgery? The median survival in the surgery alone group was only 12mth, which is lower than in INT0113 (16.1mth) or OE2 (13.3mth).

3) The chemotherapy regimen of cisplatin and etoposide is unusual and would not be a commonly used regimen for oesophageal cancer. The INT0113, OE2 and RTOG 85-01 trials were all using cisplatin and 5-FU at the time this trial was being conducted.

4) RTOG 85-01 was a randomized trial comparing chemoradiation to radiotherapy alone (not chemotherapy alone as stated in the discussion).

5) The authors claim that the T-variant allele of the ABCB1 gene polymorphism may be a predictive marker for response to preoperative chemotherapy. However, the design of the study does not really allow differentiation between a predictive marker or a prognostic marker. Would patients harboring the variant allele have had better survival regardless of whether or not they received preoperative chemotherapy? This was not tested in the surgery alone group.
**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:**

I declare that I have no competing interests