Reviewer's report

Title: Phase II Study of Weekly Paclitaxel and Capecitabine in Patients with Metastatic or Recurrent Esophageal Cancer (PACE)

Version: 1 Date: 20 October 2010

Reviewer: Hugo Ford

Reviewer's report:

Overall this is a paper of interest to oncologists working in the field of oesophageal cancer. It describes a phase II study of a novel combination with apparent observed response rates apparently higher than other reported regimens. Despite the flaws in the paper, principally the change in the patient population partway through the study, I think it merits publication. My other criticism, which is impossible to rectify, is that it would have been very interesting to see molecular data from tissue samples included in this trial, and I would recommend that this should be included in future phase II protocols, as increasingly molecular data is essential for better interpretation of the clinical outcomes.

Major Revisions:

1. There needs to be a more detailed section in the discussion about the decision to change the patient population (from 2nd line to 1st and 2nd line) part way through the study, and particularly on the impact that this change has, if any, on the sample size calculation. The reasons for this change (seeing strong evidence of efficacy in the first 7 patients treated) do not make an especially good case for the change. I assume there may have been an element of slow recruitment as well, though this is not stated.

Discretionary Revisions:

1. It would be useful to have a wider review of existing data in the discussion, especially data from phase 3 trials to put the phase 2 data in perspective. For instance the authors cite reference 14 (a multicentre RCT), but then state in the text that response rate is 20-45% (and incidentally make no mention of the fact that this study was a study carried out in a largely adjuvant population in which response rates are meaningless, and in fact showed no benefit for chemotherapy over no chemotherapy). A fuller review of the (admittedly limited) phase III data for first line therapy would be helpful.

2. It might also be interesting to comment on the more recent data reported at ASCO using paclitaxel plus carboplatin and radiotherapy preoperatively and showing a survival benefit, reinforcing the evidence for paclitaxel in this disease.

3. The group comment that "this regimen deserves further evaluation as front-line treatment for oesophageal cancer" and "Ultimately randomized clinical trials are
needed to determine the efficacy and safety of paclitaxel and capecitabine for oesophageal cancer patients". They should state whether they feel this regimen is appropriate in first or second line therapy (or both) and whether they have plans to take it into phase III trials

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

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I have been consulted in a paid advisory capacity for Roche and Sanofi-Aventis.

I have received research funding from Sanofi-Aventis and Glaxo-SmithKline

I have no other competing financial interests