

Name of Journal: *World Journal of Gastrointestinal Oncology*

ESPS Manuscript NO: 33308

Response to peer review:

We would like to thank the peer reviewers for their close reading of the manuscript and suggestions. Please find the replies below.

Reviewer 1:

In this study the authors have evaluated whether the response to first-line chemotherapy was different in patients with advanced oesophageal depending on whether the tumour histological subtype was adenocarcinoma and squamous cell carcinoma (SCC). The results revealed slightly worse outcome for SCC, although the authors have concluded that there is no significant difference between both subtypes. The study is interesting and relevant. I have some comments to improve the manuscript. 1. The title must be refined. Rather than "histology" the impact should refer to "the histological subtype of tumour".

2. In addition, the title is misleading. It should show that the conclusion is negative (for instance: "Absence of impact...") or leave the question open (for instance: "Is there an impact...?"), but as it is now, the title suggests the existence of such impact.

The title has been amended to: 'Impact of tumour histological subtype on chemotherapy outcome in advanced oesophageal cancer' to incorporate the above wording.

There was a statistically significant difference in response rates between the histological subtypes and a trend towards improved survival with adenocarcinoma. Thus we feel that the title as it stands is a fair reflection of the goals and outcomes of the study.

Furthermore given that the title must be restricted to 12 words further elaboration is difficult. We hope that this change to the wording of the title will be satisfactory.

Reviewer 2:

The study aimed to evaluate whether there was a differential treatment effect according to histology in three randomised phase III studies with advanced oesophageal SCC and adenocarcinoma. While there was no significant difference in survival between patients with adenocarcinoma and SCC, the overall response rate to chemotherapy was different. Thus, the authors conclude that SCC-specific trials in advanced oesophageal cancer are needed. In the Introduction section: ramucirumab is an antibody targeting VEGFR2 and not VEGF. This needs to be corrected.

This has been amended.

Further changes to the manuscript have been made in response to the comments made by the editorial team and are outlined below:

Title and running title amended

Authorship has been amended

Full address (including postcodes) of author institutions provided

Author contributions confirmed

Review board, registration, informed consent, biomedical statistics and conflict of interest statement provided, signed by first author

Abstract amended as per journal editorial guidelines

Core tip added

Audio core tip provided in separate file

References amended as per journal editorial guidelines

Comments added as per editorial guidelines

Of note a number of authors are practicing at different institutions across the United Kingdom and it was thus challenging to get a single copyright declaration signed. I have enclosed a single form signed by all authors affiliated to the Royal Marsden Hospital, and separate forms signed by those authors from other institutions. Two authors (MN and RH) did not respond to the request for copyright assignment in a timely manner so I have removed them from the authorship.

Kind Regards,

Michael Davidson