

July 12th, 2013

Dear Editor

Please find enclosed the edited manuscript in Word format (file name: 3395-Edited AB1)

Title: Refining Pathological evaluation of Neoadjuvant Therapy for Adenocarcinoma of the Esophagus

Authors: F Noble, L Nolan, AC Bateman, JP Byrne, JJ Kelly, IS Bailey, DM Sharland, CN Rees, TJ Iveson, TJ Underwood, AR Bateman, on behalf of the South Coast Cancer Collaboration – Oesophago-Gastric (SC³-OG).

Name of journal: World Journal of Gastroenterology

ESPS Manuscript NO: 3395

Columns: ORIGINAL ARTICLES

The manuscript has been improved according to the suggestions of the reviewers as detailed below:

Reviewer 00227592

In this manuscript, Noble et al. evaluated neoadjuvant chemotherapy (NAC) in esophageal and gastroesophageal adenocarcinoma and found that nodal down-staging conferred a significant disease free survival advantage for those patients with a poor primary tumor response to NAC. The study is well-designed. The paper is well written and the data are of interest. I have some minor issues that I would like to see addressed.

Methods: 1) What is TNM-7? Please explain in detail. [International Union Against Cancer \(UICC\) TNM Classification 7th Edition](#) added to the text.

2) In the Factors analyzed, please add “see Table 1” after “TRG 1-5,”. [Added](#)

Results: 1) In the Study patients, please move “Detailed patient characteristic and clinical and pathological outcomes are summarized in Table 2, grouped by treatment” to the end of the 1st Paragraph. [Moved](#)

2) In The relationship of TRG and clinicopathological characteristics, second paragraph, please delete “lymphatic (p=0.338)”, which is not statistically significant. [Removed](#)

Please add (p=0.04) after “Complete resection (R0) was achieved.....” [Added](#)

3) In the Univariate and multivariate analysis, please define "OAC" [Added](#)

4) Please define ASA and O-POSSUM in the tables. [Added](#)

Reviewer 00186496

In the retrospective study, the authors sought to evaluate tumor regression and lymph node downstaging to help define patients who benefit from neoadjuvant chemotherapy (NAC). They have found that response to NAC was associated with significantly increased DFS, and nodal down-staging conferred a significant DFS advantage for those patients with a poor primary tumour response to NAC. They conclude that attention needs to be given to both response in the primary tumour and in the lymph nodes, as a previously unidentified group of patients who appear to have a poor tumoural response to NAC benefit from combination therapy by nodal downstaging. The topic is interesting and the paper is well written. I have a minor point need to be commented by the authors prior to the publication: How can we select the "RIGHT" patient to undergo NAC before the operation? Are there any pathological or clinical features of the cases? Is there any robust molecular biomarker? [Added in Core tip and expanded in the "Comment" section.](#)

Reviewer 00068809

This study is an excellent clinical research as it confirms the association between regression grade and prognosis in a large and histologically homogenous group of patients treated with platinum based triplet chemotherapy and staged uniformly. It contains novel findings that are clinically relevant to physicians treating oesophageal cancer and assessment of both T and N responses to neoadjuvant therapy may be of relevance and interest to specialists treating other solid tumours. The study is well designed and carried out, the study results are very convincing, the discussion part is reasonable, and all the paper is clearly written. I'd strongly recommend it be accepted for publication in WJG. [Included in the "Comment" section.](#)

In addition format has been amended with regard to abstract content/arrangement as suggested in the editorial process.

Thank you again for publishing our manuscript in World Journal of Gastroenterology

Yours sincerely



Andrew Bateman

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