

21 Jan 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 6341-review.doc).

Title: Primary sclerosing cholangitis as an independent risk factor for colorectal cancer in the context of inflammatory bowel disease – a review of the literature.

Author: Ms Rosy Wang and Associate Professor Rupert W.L. Leong MBBS, FRACP, MD, AGAF

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 6341

We thank the reviewers for their expertise and have improved the manuscript accordingly.

Reviewer 1

This interesting review presents a good analysis about Primary sclerosing cholangitis (PSC) as an independent risk factor for colorectal cancer (CRC) in the context of inflammatory bowel disease (IBD). However, although the authors give a thorough review up to the year 2012, they miss the most recent developments, which are very important. Major comments: 1) The authors must add the most recent developments among which two recent meta-analyses concerning the use of ursodeoxycholic acid (UDCA) as a precaution to CRC patients suffering from PSC. Thus, they must add the following papers to their review: (a) Singh S, Khanna S, Pardi DS, Loftus EV Jr, Talwalkar JA. Effect of ursodeoxycholic acid use on the risk of colorectal neoplasia in patients with primary sclerosing cholangitis and inflammatory bowel disease: a systematic review and meta-analysis. *Inflamm Bowel Dis* 2013; 19:1631-1638. (b) Hansen JD, Kumar S, Lo WK, Poulsen DM, Halai UA, Tater KC. Ursodiol and colorectal cancer or dysplasia risk in primary sclerosing cholangitis and inflammatory bowel disease: a meta-analysis. *Dig Dis Sci* 2013; 58:3079-3087. 2) They must also comment on the Mayo Clinic meta-analysis which proposes Aggressive colonoscopic surveillance for CRC in patients with PSC-IBD after liver transplantation (Singh S, Varayil JE, Loftus EV Jr, Talwalkar JA. Incidence of colorectal cancer after liver transplantation for primary sclerosing cholangitis: A systematic review and meta-analysis. *Liver Transpl* 2013 In Press)

- We thank Reviewer 1 for updates on the literature and have modified the search terms to reflect inclusion of these important publications.

Reviewer 2.

This is a short and well performed review. The title reflects the content. For the readers this text gives a good overview. P. 7 line 12: Would it be better to write: "... has been widely debated.."? And: I suggest that the authors comment more on the topic surveillance in non-IBD PSC.

- We thank Reviewer 2 for their recommendation and have modified the text accordingly. The study of non-IBD PSC is the subject of a follow up review.

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

Sincerely yours,

A handwritten signature in black ink, appearing to be 'Rupert Leong', with a stylized, cursive script.

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