



May 25, 2014

Dear Editor,

Please find as enclosed the edited manuscript in Word format (file name: [7252-review.doc](#)).

Title: Double balloon enteroscopy evaluation of “top-down” treatment of early Crohn’s disease

Author: Rong FAN, Jie ZHONG, Zhengting WANG, Shuyi LI, Jie ZHOU, Yonghua TANG

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 7252

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

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

(1) As described by reviewer, the unique component is utilization of DBE for assessment of mucosal healing. The title has been changed to ‘Top-down treatment for deep remission in early Crohn’s disease: evaluation with DBE’ according to the suggestions of the reviewer. We have demonstrated that DBE may identify lesions in the small bowel beyond the reach of conventional ileocolonoscopy at baseline and at the end of trial, thus allow for a more comprehensive and objective measurement of MH, which was different from previous trial (e.g. EXTEND trial)

(2) In order to evaluate the long-term deep remission rate, we extend the follow-up time to 102 weeks and found the optimal time point for the first follow-up by DBE was between 30 and 54 weeks after treatment in group I and at least 54 weeks treatment in Group II, which conformed to our previous study. The 30-week evaluation showed a significantly higher MH rate in Group I than in Group II. Although there were no significant between-group differences, there have been a higher proportion of patients in deep remission in Weeks 54 and 102 in Group I. There has been a strong trend of earlier deep remission with infliximab as induction therapy.

(3) The benefits of early mucosal healing were recognized before approval of biologic therapies for inflammatory bowel disease. A population-based cohort study has confirmed that mucosal healing has a significant impact on disease outcome in patients with ulcerative colitis. In patients with ulcerative colitis, 3 of 178 patients (2%) with mucosal healing at 1 year underwent colectomy by 5 years as compared with 13 of 176 patients (7%) without mucosal healing at 1 year ($P=0.002$). Colombel et al. indicated that achievement of early mucosal healing (ie, endoscopy subscores of 0 or 1 at week 8) after

treatment with infliximab may lead to better long-term clinical outcomes for patients with moderately to severely active ulcerative colitis. The study of long-term outcome with regard to early mucosal healing of Crohn's disease is still warranted.

(4) We have mentioned that the author who performed endoscopy was unaware of the patient's clinical status and treatment category at baseline (Week 0), in Weeks 30, 54 and at the end of the study (Week 102) and the open-label study introduces bias in terms of evaluating subjective symptom scores.

3 References and typesetting have been corrected

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

Sincerely yours,

A handwritten signature in black ink, appearing to read 'Fan Rong', with a stylized, cursive script.

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