

ESPS Peer-review Report

Name of Journal: World Journal of Gastrointestinal Pathophysiology

ESPS Manuscript NO: 9019

Title: 'Mucosal Healing' in Ulcerative Colitis: between clinical evidence and market suggestion

Reviewer code: 02530755

Science editor: Zhai, Huan-Huan

Date sent for review: 2014-01-16 19:24

Date reviewed: 2014-01-18 19:02

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input checked="" type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input checked="" type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

This paper addresses an extremely important topic, and the title itself is very intriguing.

However, the authors acknowledge that a thorough revision of the literature has not been performed: as a result, the paper appears to be a “narrative” one and the conclusions based on “common sense” rather than on the evidence (although I personally fully agree with them).

Therefore, I believe that a more exhaustive (although not necessarily systematic) review of the literature should be provided, and that the following issues need to be more in depth addressed:

- it is not correct that mucosal healing concept has been first introduced for Crohn’s disease. On the contrary, for a long time international guidelines and experts have recommended that the treatment of UC flares should be continued until achievement of endoscopic remission (see for instance Kornbluth A, Sachar DB *Ulcerative colitis practice guidelines in adults. American College of Gastroenterology, Practice Parameters Committee. Am J Gastroenterol* 1997 Feb;92(2):204-11). On the other hand, only after the advent of biologic therapies the concept of endoscopic-guided therapy has been proposed for Crohn’s disease
- as far the reliability of endoscopic remission assessment is concerned, it would be desirable to mention the fact that, in most recent clinical trials, the rate of endoscopic remission was even higher than the rate of clinical remission and to discuss the possible causes, including disparities between definition (in particular discrepancies between Mayo 0, Mayo 0-1 and Mayo modified according to friability) and the recently reported usefulness of centralized assessment of endoscopic activity

- evidence in favour of the importance of histologic remission needs to be more accurately reported, and some mention should also be made on the recently reported evidence of the possible prognostic role of advanced imaging techniques
- regarding, biologics, some mention should be made on the somewhat disappointing data presently exiting on the prognostic role of mucosal healing. In a subsequent analysis of data from the ACT trial (*Colombel et al, Gastroenterology 2011*) mucosal healing appeared to be a strong predictor of subsequent relapse in the whole cohort of patients: however, when only patients achieving clinical remission were considered, no correlation at all emerged (data presented only in the online supplementary material). Similarly , in the analysis of the Leuven cohort (*Ferrante et al, IBD 2008*), short term mucosal healing was associated with risk of colectomy only in the univariate analysis
- regarding corticosteroids, the efficacy of topical and systemic formulations need to be addressed separately: more evidence of the discrepancy between rates of clinical and endoscopic remission (besides the landmark study by *Ardizzone et al*) should be provided
- regarding mesalazine: although it is correctly stated that rates of endoscopic remission vary widely across clinical trials, several lines of evidence suggest, in patients treated with mesalazine regimens of adequate dose and duration, the discrepancies between clinical and endoscopic remission are minimal (see for instance: *Vecchi et al. Aliment Pharm Ther. 2001;15:251–256; Lewis et al. Inflamm Bowel Dis. 2008;14:1660–1666; Lichtenstein GR et al Clin Gastroenterol Hepatol. 2007;5:95–102; Hanauer SB. Et al Inflamm Bowel Dis. 1998;4:79–83; Pokrotnieks et al Aliment Pharmacol Ther. 2000;14:1191–1198 ; Higgins PD et al Am J Gastroenterol 2005;100:355–361*). Nonetheless, some recent evidence indicate a highly increased risk of flare in the small group of patients not achieving endoscopic remission (see for instance *Meucci et al, IBD 2012*). Also these issues need to be properly addressed
- in my opinion, a critical point is that current evidence indicates, at best, that patients achieving mucosal healing have a better outcome than patients achieving only symptom disappearance. However, it is presently far from clear if an endoscopic-oriented therapeutic approach will be beneficial in the latter group of patients. Indeed, no evidence presently exists that treatment escalation in asymptomatic patients with endoscopic evidence of inflammation will indeed improve the prognosis of such patients. On the other hand, the evidence that in patients with mucosal healing biologic treatment can be safely discontinued is presently very scanty, and mainly limited to CD patients. I believe that also this issue needs to be discussed
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ESPS Peer-review Report

Name of Journal: World Journal of Gastrointestinal Pathophysiology

ESPS Manuscript NO: 9019

Title: 'Mucosal Healing' in Ulcerative Colitis: between clinical evidence and market suggestion

Reviewer code: 02462725

Science editor: Zhai, Huan-Huan

Date sent for review: 2014-01-16 19:24

Date reviewed: 2014-01-18 20:06

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input checked="" type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

This is a review article regarding MH of UC. The authors have been aware of the true problems involved in MH, that is, whether MH is truly the best goal for UC patients and whether MH should be obtained by any means with enthusiastic endoscopic inspections. The awareness of the true problems is applaudable and this reviewer is completely sympathetic to the author's concern. Unfortunately, however, the materials for the debate are still lacking and the future perspective on advance in this field would not be unambiguous, because achievement of the optimization of therapy tailored for each UC patient is an ultimate goal of UC treatment in either symptomatic or endoscopic meaning. In this regard, the aim of this article is substantive but the written matter does not contain much. At this time, however, it should be accepted as the inevitable.



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ESPS Peer-review Report

Name of Journal: World Journal of Gastrointestinal Pathophysiology

ESPS Manuscript NO: 9019

Title: 'Mucosal Healing' in Ulcerative Colitis: between clinical evidence and market suggestion

Reviewer code: 02548913

Science editor: Zhai, Huan-Huan

Date sent for review: 2014-01-16 19:24

Date reviewed: 2014-02-07 22:43

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input checked="" type="checkbox"/> Minor revision
		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

In this article, the authors discussed the problem of the term 'Mucosal Healing'. The concept of MH was not therapeutic end-point, or rather one of clinical assessment items. Although this was a matter of course, it was also a fact that this term was still going out of control. The authors should be praised for their challenges to raise the issue. I have some minor concerns about this paper:

1. There are some grammar errors. Please make a modification. (ex. In abstract, there's a typo of "jet" in the 9th line from the top.)
2. While the authors referred to demands of the "biologic agent" market, they admit the utility. When you make opinions about biologic agents, you should point the problem that maintenance therapy costs too much as well as induction therapy. You should add the issue, and consider when to stop the agents.



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ESPS Peer-review Report

Name of Journal: World Journal of Gastrointestinal Pathophysiology

ESPS Manuscript NO: 9019

Title: 'Mucosal Healing' in Ulcerative Colitis: between clinical evidence and market suggestion

Reviewer code: 02548692

Science editor: Zhai, Huan-Huan

Date sent for review: 2014-01-16 19:24

Date reviewed: 2014-02-08 13:29

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input checked="" type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input checked="" type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

Too many grammatical errors. Introduction should be precise. MH concept should be explained "to the point"

ESPS Peer-review Report

Name of Journal: World Journal of Gastrointestinal Pathophysiology

ESPS Manuscript NO: 9019

Title: 'Mucosal Healing' in Ulcerative Colitis: between clinical evidence and market suggestion

Reviewer code: 02548786

Science editor: Zhai, Huan-Huan

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Date reviewed: 2014-02-11 19:47

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input checked="" type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

In the present manuscript, the authors have discussed the role of 'Mucosal Healing' in Ulcerative Colitis. ? The significance of mucosal healing in ulcerative colitis (UC) is well-described. ? However, the authors should elaborate on how to increase mucosal healing in UC patients. Are there the agents, which can do so? If yes, then what are their mechanisms, dose and duration? ? The authors should emphasize on the novel concept in the manuscript. ? The authors should elaborate on the term "between clinical evidence and market suggestion". The term has been mentioned in the title, but not explained thoroughly in the manuscript. ? There are grammatical errors at some instances. Hence, the manuscript requires critical proof reading by an expert. ? Many of the important and latest references are missing.