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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 3986
Title: To Determine the Relationship Between Time of Infliximab Therapy Initiation and Infliximab Dose Escalation - A Retrospective Study
Reviewer code: 00004594
Science editor: Zhai, Huan-Huan
Date sent for review: 2013-06-07 18:55
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[Y] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[Y] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[ ]Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[ ] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[Y] Major revision
		[ ] No records	

COMMENTS TO AUTHORS
This is an interesting paper on the association of Infliximab with immunosuppressives in IBD patients. There are some points which need to be clarified for me: In the abstract : to state that "The etiology for this decrease in response is unclear...." is wrong since there are recent data on the role of trough level of infliximab and antibody to Infliximab (ATI) in IBD patients. In particular, patients with low trough level and/or ATI loose efficacy of Infliximab. Sometimes, in clinical practice we need both to increase the dose and reduce the interval between perfusions; this point should be added in the abstract and in the manuscript. In the methods of the abstract, it is stated that the study was performed from July 2009 to October 2010 while in the manuscript it is from July 2009 to July 2010. Globally, the authors included about 5 to 6 patients/month from 2 tertiary clinics. This is rather small i.e. 3 patients/clinic/month. Through levels and ATI were not performed. Were the patients on corticosteroids? It is not specified in the manuscript. There are no data regarding smoking in these patients and smoking is a factor of resistance to anti-TNF therapy. It seems that the authors did not look at mucosal healing as well as fecal calprotectin dosage. In the Extend study, performed in CD patients under adalimumab, patients with CD for less than 2 years were more in deep remission (clinical remission + mucosal healing).

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ESPS Manuscript NO: 3986
Title: To Determine the Relationship Between Time of Infliximab Therapy Initiation and Infliximab Dose Escalation - A Retrospective Study
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[Y] Grade C (Good)	[Y] Grade C: a great deal of language polishing	[ ] No records	[ ]Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[ ] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[Y] Major revision
		[ ] No records	

COMMENTS TO AUTHORS
English grammar should be corrected. In the abstract, it was less time consuming to do it myself. Conclusion: There are 2 terms to describe what I presume is 6 MP and Azathioprine, immunosuppressives, and immunosuppressants. I prefer the former - but also the immunosuppressives are not named. The conclusions as stated are not convincing. 4 groups are named earlier. What is needed is the length of time to start Infliximab (< 2 years), >2 years and each of the 2 groups with and without immunosuppressives. ?Format for bibliography? 3 authors followed by etal vs. all authors INTRODUCTION - LINE 1: We know that anti-TNF's have an important role in therapy but we don't know about its role in pathogenesis. 1st paragraph, last line - is, not was. 2nd paragraph, factors leading to dose escalation not influenced. They are not unknown; the ones serving to dose escalation are known. Indeed, there is a correlation of immunogenicity with clinical response. If the aim of the study is the time of IFX indication, either keep immunogenecity out of it or else include it in the goals. METHODS RESULTS: It would be helpful to define the 7 patients eliminated by the Harvey-Bradshaw scale as stated in Methods as well as the assessments by individual gastroenterologists. DISCUSSION: Paragraph 2, 3rd sentence - higher than what? Again it is not clear what groups are being compared. There are actually 8 groups: IFX Started < 2 years + 6MP or AZA IFX started > 2 years + 6MP or AZA IFX started < 2 years - 6MP or AZA IFX started > 2 years - 6MP or AZA + or Z dose escalation in all 4 above. Tables - too many factors are included such as gender, disease behavior (stricturing, penetrating, perianal) without their being utilized for the goal of the study. MY CONCLUSION: I like the idea of this paper and I dont' object to the study being retrospective or the

relatively small number of patients, but the paper is not well written and the conclusions as presented are not warranted by the data. It could be better divided into the pertinent variables before making conclusions about the note of early versus late introduction of Infliximab and the influence of immunogenecity. I don't feel that the management of IBD profits by accepting this paper as submitted.