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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 12369
Title: Growth and bone health in paediatric patients with Crohn's disease receiving subcutaneous tumor necrosis factor antibody
Reviewer code: 02563370
Science editor: Su-Xin Gou
Date sent for review: 2014-07-05 19:14
Date reviewed: 2014-07-22 23:00

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A: Excellent	[Y] Grade A: Priority publishing	Google Search:	[Y] Accept
[Y] Grade B: Very good	[ ] Grade B: Minor language polishing	[ ] Existing	[ ] High priority for publication
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] No records	
[ ] Grade D: Fair		BPG Search:	[ ] Rejection
[ ] Grade E: Poor	[ ] Grade D: Rejected	[ ] Existing	[ ] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS

Pichler et al. describes the effect of Adalimumab on the growth and bone health in 18 pediatric Inflammatory Bowel Disease. Most of the children in the trial loss Infliximab (murine monoclonal antibody linked to the constant domains of human kappa and immunoglobulin) efficacy and once switched to Adalimumab (human recombinant IgG1 monoclonal antibody) showed improvement in Pediatric Crohn's Disease Activity Index with some children showing catch-up growth. The children also underwent bone densitometry measurements—it is these measurements that appear to be unique to this study. There are at least 13 published papers (2008-2014) on Crohn's disease and the use of Adalimumab and its effect on children's growth. The authors do attempt to compare their results to some of these previously published results with all eighteen pediatric patients receiving Adalimumab between 2007 and 2011. Thus, the timeline of treatment in this study correlates with the other publications. In all the study complements the other studies and supports the role for inflammation in Crohn's disease.

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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 12369
Title: Growth and bone health in paediatric patients with Crohn's disease receiving subcutaneous tumor necrosis factor antibody
Reviewer code: 02530792
Science editor: Su-Xin Gou
Date sent for review: 2014-07-05 19:14
Date reviewed: 2014-07-06 01:39

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] Existing	[ ] High priority for publication
[Y] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] No records	
[ ] Grade D: Fair	[ ] Grade D: Rejected	BPG Search:	[ ] Rejection
[ ] Grade E: Poor		[ ] Existing	[Y] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS

Overall a very nice presentation of the data. I agree with the authors that the small sample size is likely the main limiting factor. The authors nicely point out that there is an overall dearth of evidence for growth on adalimumab. Thus even small studies are valuable. A few suggestions 1. The section on "Predictors for improvement in growth and bone mineralisation" is confusing. I would recommend re-writing this section, with more information, to be more readable. 2. In the conclusion in both the abstract and the paper, the authors conclude that adalumumab induced and maintained remission in children with CD. However the design of the trial was a retrospective, observational study without a control group. The study was not designed nor powered to assess adalumumab for the induction and maintenance of remission. I would recommend removing this from the conclusions and focusing only on the growth catch up which the authors primarily evaluated. 3. It is odd steroid cessation was not associated with an improvement in anthropometry and bone health. This may be due to small sample size. Given the pathophysiology of steroids and bone disease, the authors should comment on this in the discussion briefly. Overall nicely done. This study is consistent with prior published literature and adds to the growing body of literature on anti-TNF use in children.

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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 12369
Title: Growth and bone health in paediatric patients with Crohn's disease receiving subcutaneous tumor necrosis factor antibody
Reviewer code: 02903629
Science editor: Su-Xin Gou
Date sent for review: 2014-07-05 19:14
Date reviewed: 2014-07-10 00:01

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[Y] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] Existing	[ ] High priority for publication
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] No records	
[ ] Grade D: Fair		BPG Search:	[Y] Rejection
[ ] Grade E: Poor	[ ] Grade D: Rejected	[ ] Existing	[ ] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS

This retrospective cohort study, is well planned and well executed. The most major problem is the statistical analysis method because of the smaller sample size although the author has pointed it out. 1. The sample size is just 18 that is too small to use the mean±SE, especially in Table 3 and Table 4, let alone these analysis methods(?2- test, paired t-test, t-test and ANOVA). Generally, more than 30 samples are treated as a large sample in statistical field. 2. Median and quartile should be used for statistical description. Non-parametric test should be used for hypothesis testing. Multivariate analyses includes too few variables, which makes the results unreliable. My suggestion is that qualitative analysis should be applied in this paper, and quantitative analysis has many limitations. 3. P7. What is 400IE cholecalciferol (vitamin D3)? You mean 400 IU? 4. P13, the author seemed to take more in explaining the reason affecting the results of the study. This may be put in the limitation part. 5. In 'Conclusion' section, the author stated that "A better nutritional status is positive predictor for improved growth and bone mineralisation". How does this point come from the present study?