

ANSWERING REVIEWERS



June 14, 2013

Dear Editor,

3436-review.doc

Title: Eviendep® reduces number and size of duodenal polyps in FAP patients with IPAA

Author: Carlo Calabrese, Chiara Praticò, Andrea Calafiore, Giulia Straforini, Maurizio Coscia, Lorenzo Gentilini, Gilberto Poggioli, Paolo Gionchetti, Massimo Campieri, Fernando Rizzello.

Name of Journal: *World Journal of Gastroenterology*

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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) Review 1

The paper of Calabrese et al. is well structured and explores an innovative area in intestinal carcinogenesis chemoprevention, i. e. the role of beta estrogen receptor agonists in the control of cell proliferation and apoptosis. Nevertheless some points need to be marked:

1) Table 2 reports at T1 the number and size of polyps with Spigelman score in all patients after the polypectomy performed before starting Eviendep. It is surprising the high number of removed polyps in patient number 8 (12), number 9 (11), number 10 (46) and number 11 (18) in a single endoscopic session. More details could be useful.

RE: The referee is right. We are sorry; we badly reported three values in the table. Table II has now been corrected.

2) Considering the possibility of small bowel involvement in the course of FAP, features of this aspect need to be reported in the manuscript. It is interesting to know whether the patients had been investigated by video capsule endoscopy or balloon assisted enteroscopy and checked before and after the therapeutic effect of Eviendep in this area.

RE: The observation is right. Yamada A et al performed a study with capsule endoscopy and found that patients with duodenal polyps had a larger number of polyps in the small intestine than those without duodenal polyps. However, in our study population, only 8 of the 11 patients had performed a CE before treatment and there was no evidence of polyps after the Treitz. The CE was then not repeated. We have included this comment in the text.

3) As far as the section of "RESULTS", we invite the authors to check the numerical values reported and, consequently, statistical analysis. We have observed some discrepancies in the mean number of duodenal polyps at T1 and in the Spigelman score in T2.

RE: The referee is right. We corrected the table as you can see in the first answer. Now there are no discrepancies in the reported means.

(2) Review 2

The authors investigated the effects of short-term (90 days) supplementation with Eviendep on the reduction of the number and size of duodenal polyps in FAP patients who had undergone IPAA. Although this report is interesting and may be acceptable for publication, the authors should make the following modifications:

1) The authors should show the germline mutation profiles of the APC gene in all 11 patients.

RE: The suggestion is interesting; however, we performed a genetic analysis only to evaluate the deletion of APC gene and not the germline mutations. This suggestion could be interestingly evaluate in further studies.

2) The authors should examine the expression levels of mRNA and/or protein of ER in biopsied specimens from duodenal polyps.

RE: The aim of this study was to evaluate the efficacy of the oral supplementation from an endoscopic and histological point of view. A further molecular evaluation will be performed in subsequent patients.

3) Review 3

This study is a good beginning study. I look forward to more of the study. Thank you.

RE: Thank you.

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

Sincerely yours,



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