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World Journal of Gastroenterology

Re: Manuscript #5771 – Response to reviewers

Dear Professor Ma:

I have here responded to the critique of the three reviewers and appreciate their comments.

I hope you will approve of my changes and additions and will now find our manuscript acceptable for publication in the World Journal of Gastroenterology.

With warm regards,

Sincerely,

Burton I. Korelitz, M.D.

BIK:js

Title: Histological Healing Favors Lower Risk of Colon Carcinoma in Extensive Ulcerative Colitis

Authors: Burton I. Korelitz, MD; Keith Sultan, MD; Megha Kothari, MD; Leo Arapos, MD; Judy Schneider, Georgia Panagopoulos, PhD

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript #5771 – Response to reviewers

RESPONSE TO REVIEWER #1. The issues to which I am able to respond are #2 and #4 concerning medical therapy and have extended Table 1 to include 1B to show those who received 6-Mercaptopurine or Infliximab at some time during their course of therapy or prior to any diagnosis of HGD/CRC.

In regard to number 2, Table 1, I have added the percentage of patients who had received 6MP ± Remicade during the decades when these drugs were available. Clearly in Group 1 treatment with 6-MP coincided with the decades 1970-1979 and 1980-1989 in 55% but in Group 2 this figures increased to 79%. Regarding Remicade (Infliximab) no patient in Group 1 received the drug which was not then available, but 27% did receive it in Group 2. Therefore either 6-MP alone or in combination with Remicade contributed to the favorable outcome regarding neoplasia in contrast to Group 1. This is now also found in the discussion.

In regards to calculating Odds Ratios, my statistician states that the data is far too variable to create these figures.

In regard to number 3, it is true that the criteria for inclusion was at least 20 years unless HGD/CC developed earlier than that time. The heading of the table had to do with decades of surveillance and indeed patients who had less than 20 years were excluded.

In regard to number 5, there were no instances of HGD/CC within the first 10 years from diagnosis and we present no data on left-sided disease or proctitis since patients with that limited distribution were excluded from the study.

I understand and appreciate the comments of this reviewer since, I too, always have new questions that are raised by the observed outcomes.

RESPONSE TO REVIEWER #2

1. The definition of gross endoscopic disease is active ulcerative colitis as identified by the endoscopist which was consistent in interpretation since one colonoscopist was common to all procedures. This is described in the text.

2. Similarly the definition of microscopic inflammation was the interpretation of the Lenox Hill Pathologists all of whom were experienced in surveillance biopsies for ulcerative colitis and reviewed by other pathologists when high grade dysplasia or carcinoma was found. This is described in the text.

3. We now present the number of patients with and without treatment with immunosuppressives and infliximab and the subject is discussed and referenced.

RESPONSE TO REVIEWER #3:

We are not equipped to deal with genetically defective cells though I appreciate the comment of the reviewer. The issues of a scoring system for inflammation and the influence of medical treatment in the development of malignancies have been dealt with in the original manuscript and supplemented in response to Reviewers 1 and 2.

Thank you for your comments.

Sincerely,

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