Paris, March 31st

Dear Editors,

Please find enclosed a revised version of our manuscript"**Hepatic complications induced by immunosuppressants and biologics in inflammatory bowel disease"**

The relevant and insightful comments from the reviewers were carefully revised and supplementary data were provided accordingly.

We hope that our revised manuscript now meets the high standards for publication in World Journal of Hepatology

Looking forward to hearing from you.

Yours sincerely,

Dr My-Linh TRAN-MINH

General remark to the Editor

The corresponding author is Dr Gornet and not Dr Maillet

Reviewer: 1

Comments to the Author
This study by Maillet and colleagues is a multicenter study of patients undergoing early post-operative chemotherapy for colon cancer carcinomatosis.
It includes patients from several centers in France. This study was retrospective in nature. I have several questions and comments:

Methods: what are the specific surgical considerations for CS/HIPEC - open vs closed, what agents used, any exclusion based on PCI score? Was diagnostic laparoscopy before CS/HIPEC utilized?

The surgical procedure (open versus closed) was decided according to the routine practice of each center. One the center (Lyon Sud Hospital; 97 patients included; 42% of the cohort) used closed procedure only. This point was added in the text page 9 in the "HIPEC and adjuvant chemotherapy regimens" section.

The agents used during HIPEC procedure were already detailed in Table 1.

All the patients who underwent a CC0 procedure were enrolled in our cohort whatever the PCI score. This point was added in the text page 7 in the "inclusion criteria" section.

A laparoscopic approach before CRS and HIPEC was frequently done in one center (Lariboisière Hospital; 47 patients included; 20% of the cohort) and marginally in the others. However, we are unable to provide a valid pourcentage.

Results:
Page 8 - Leucovorin is spelled incorrectly.

Done

Page 9 - 54 % of patients had a HIPEC completed through an open abdominal procedure. This is unclear - does that mean some had laparoscopic HIPEC, or had a closed circuit HIPEC?

Page 10 - 151 patients received post-operative chemotherapy and 70 did not. 60 % was related to "medical decision". How was this decided? Was this related to physician practice, particular center, or any specific criteria (pathology report from HIPEC related to tumor features)? Although the groups are considered comparable based on Table 2 it is unclear how they were chosen (or not chosen) to receive systemic post operative chemotherapy.
Table 1: number of preoperative cure - does this mean complete response to neoadjuvant chemo?
Table 3: results are not surprising (that patients with PCI scores > 20 have high hazard ratio for recurrence/death).

Discussion:
Page 11 - second sentence - should be "While CRS with HIPEC is proven to increase survival..."
The authors mention a highly selected group of patients, but I am unsure if I understand how they were selected, for both HIPEC and for systemic chemo.
Please correct the spelling of oxaliplatin and mitomycin (no "e" at the end of each word)
For those patients that did not get post operative chemotherapy, and then had a relapse, what was the median time to this, and what agents did they receive?
Given the chemotherapy regimens provided, it would be interesting to know what grades of toxicity from systemic postoperative chemotherapy were experienced (as it appears that only 47 % of patients had no modification of protocol). A major concern of those clinicians that offer CS/HIPEC followed by systemic therapy is the toxicity that is experienced (and that patients can tolerate this better if given preoperatively). More information is needed here to be able to make any conclusions.

Reviewer: 2

Comments to the Author
This is an interesting manuscript on a topic that is difficult to study given the heterogenous cohorts involved. This is a retrospective review of outcomes in patients who underwent cytoreductive surgery and HIPEC with and without adjuvant chemotherapy. It is a highly specialised area in which clinical trials represent a considerable challenge. The authors acknowledge the limitations of this type of study, namely that inherent differences between the groups are extremely difficult to control for.

I think the use of the term 'arm' is misleading - to me this implies a prospective type of study. Terms such as 'cohort' or 'grouping' would be more appropriate.