Review responses

Reviewer 1

1. The introduction is well written with clear rationale and logical description.
    a. We are grateful for this kind comment. There does not appear to be any need for article adjustment.
2. The major concern if this study is the recruit time. It ranged for 9 years and the prognosis of colorectal patients improved a lot due to improvement of general care and medical facilities. Dose the recruit time associated with prognosis? That is, do patients with similar condition and treatment survive well in those with later recruitment?
    a. This is a valid comment. The study does span over a long time period. We have added an analysis comparing time period and neutropenia in a two-variable Cox regression analysis. The time period was divided into early and late using the median date as cut-off. As it turns out, both time period and neutropenia were prognostic factors. So while it did matter if you were treated in the latter period with a better overall survival, postoperative neutropenia remained a significant prognostic factor. See statistics section and results section and discussion for article amendments relevant to this comment.

Reviewer 2

1- the title is long.
    a. We agree so we have shortened the article title
2- multiple abbreviations and acronyms are included in the study and need to be written in details.
    a. We agree that there is a lot of acronyms. We have decreased them now to less than five and they are all common within this field. I noticed like the review says that some were missing the detailed in writing so we have changed that as well. Also we have repeated the written details in order to be a clear in the communication as possible. See changes throughout the article.

3- 3 lines tables are recommended
    a. We were unaware of the preferred table format. But we have adjusted the format to three-line table as requested by the reviewer.
4- one of your references no 16, the whole paper is retracted according to the journal site.
    a. Thank you for bringing this to our attention. We were not aware that the article had been retracted. We have removed it and the reference to it in the discussion.
5- the number of neutropenic patients is too small.
    a. We do agree that the sample size of neutropenic patients is small. Nonetheless, this fact does not detract from the study results. In fact, it is quite unexpected that the prognostic effect is so pronounced. Thus, we believe these results are important to publish and disseminate. It is however, prudent to follow-up these results with a much larger study. We are hoping to start a national study in Sweden further investigating this issue more in-depth.
6- is their an explanation for the less mortality and morbidity in the neutropenic group.
    a. This is an interesting observation. The morbidity was 19% in the neutropenic group and 31% in the non-neutropenic group. However, it was not statistically significant with p-value 0.18. Similar for the reoperation variable. The neutropenia group was small as commented on previously which makes the cohort prone to a wider margin of morbidity. So we believe it is a random difference primarily and not suggestive of neutropenia being a protective factor. Importantly, this study shows that there is not an increase in surgical complications as defined by Clavien-Dindo morbidity guidelines.
7- it is a retrospective study, not a strong type of statistical studies.
    a. We agree. Retrospective studies have their limitations. However, evaluating potential prognostic factors is a suitable aim for such study methodology. Because postoperative neutropenia after HIPEC has never been studied with

this aim, we believe this is the best first step of determining its potential effect on other Clavien-Dindo morbidity and survival.

8- what is the limitations of your study.
    a. The limitations have not been clearly stated in the discussion. We have adjusted this in the discussion section. We now have a more thorough description of potential limitations to the study. The retrospective nature is discussed has well as the neoadjuvant treatment that can of course also play a role in neutropenia development postoperatively. See the extra paragraph in the discussion section.

9- is there any reduction in the dose of chemotherapy or all the patients received the same amount of therapy.
    a. Yes, there were dose reductions involved. However, difficulties in acquiring data on this leaves this variable with significant missing data. However, the details are included in Table 1 (see HIPEC dose reductions). There is a trend towards more dose reductions in the neutropenia group. However, this occurred in the neutropenia group not the non-neutropenia group (probably due to more patients receiving intensified HIPEC treatment in the neutropenia group). So dose reductions cannot explain the prognostic benefit of neutropenia as they affected the neutropenia group itself and not the non-neutropenia group. Likewise, the intensified treatment itself was not prognostic (see Table 2). Therefore, the prognostic benefit of neutropenia still remains.

10- why not the authors did not classify the patients according to the severity of neutropenia i.e mild moderate severe neutropenia.
    a. We agree that this is an important aspect. We have added this in the results section. 20% severe neutropenia, 13% moderate, and 67% mild. Thank you for bringing this to our attention.

11- some corrections in the uploaded file
    a. These corrects have been added to the manuscript.

Thank you for being given the opportunity to respond to these comments.