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**ESPS Manuscript NO: 25574**

## **World Journal of Gastrointestinal Pharmacology and Therapeutics**

Dear Editor in Chief Prof. Wang/ Prof. Freeman

Thank you very much for giving us the opportunity to revise our paper and for the publication in the World Journal of Gastrointestinal Pharmacology and Therapeutics.

Below you find our revisions made according to the reviewer's comments. Changed text passages are marked red in the manuscript.

### **Comments to Reviewer No. 3553892**

No p value been written to show any statistic significance.

**In accordance with the "Instructions for authors" document only p-values with significant results were mentioned in the text.**

*("8 out of 10 patients with leukopenia were older than 50 years and was statistically significant ( $60 \pm 16$  vs.  $48,5 \pm 11$  years;  $p=0.01$ )") and*

*("Leukopenia occurred statistically more often in the MMC- than in the OX/5-FU-group ( $10/32$  vs.  $0/10$ ;  $p=0.042$ )")*

Have any of those patient been tested for any genetic mutation in association with leukopenia and chemotherapy ?

**Good question but as it was not the aim of our study, we did not evaluate any genetic mutation associated with leukopenia and chemotherapy.**

Have Epic early postoperative intra peritoneal chemotherapy been used in any of those patients ?

**No. All included patients were treated by intraoperative hyperthermic intraperitoneal chemotherapy.**

Have any of those patients develop Panc fistula and retroperitoneal sepsis or other source of sepsis induced leukopenia ?

**No. None of the 10 patients suffering from post-HIPEC leukopenia suffered one of the above mentioned postoperative complications.**

What is the rate of blood transfusion ?

**Of the 10 patients suffering from post-HIPEC leukopenia none required blood transfusions.**

Complications rate should be in Clavien-Dindo classification score

## Materials and Methods

“All complications were graded using the Clavien-Dindo classification of surgical complications [2]”

## Results

“No statistically significant differences were observed between the MMC- and the OX/5-FU-group regarding occurrence of hospital-acquired pneumonia (HAP) (two vs. zero patients), pleural effusion (PE) (two vs. two patients) surgical site infections (SSI) (one vs. one patient), intraabdominal abscess formations (IAA) (zero vs. one patient) and urinary tract infections (UTI) (one vs zero patient). Patients with HAP required antibiotic treatment (Clavien-Dindo grade II). Patients with SSI required bed-side wound treatment but no antibiotic treatment (Clavien-Dindo grade I). Two of four patients with PE needed pleural drainage (Clavien-Dindo grade IIIa). One patient with IAA required antibiotic treatment (Clavien-Dindo grade II) and one patient with a UTI also required antibiotic treatment (Clavien-Dindo grade II).”

## References

“2. Clavien PA, Barkun J, de Oliveira ML, Vauthey JN, Dindo D, Schulick RD, de Santibañes E, Pekolj J, Slankamenac K, Bassi C, Graf R, Vonlanthen R, Padbury R, Cameron JL, Makuuchi M . The Clavien-Dindo classification of surgical complications: five-year experience. Ann Surg. 2009; 250: 187-96 [PMID: 19638912 DOI: 10.1097/SLA.0b013e3181b13ca2]”

What was the wbc and other blood result prior to crs?

**The white-blood-cell count of the patients suffering from leukopenia was shown in Table 2 of our manuscript. We did not focus on other blood results.**

when blood result were taken prior to CRS?

**Blood samples were taken on the day of admission to our hospital, i.e. one day prior to CRS and HIPEC.**

What medical treatment used for leukopenia ?

was they treated by GSF or antibiotics and for how long ?

**For medical treatment filgastrim (neupogen® ) which is a G-CSF was used. No prophylactic antibiotic treatment was started. Treatment with G-CSF was continued till the white blood cell count reached normal levels.**

### **Results**

**“Three patients required medical treatment with filgastrim till leukocyte counts were in normal range”**

We're other blood result measures like platelet and RBC?

**No. We did only focus on the white blood cell count.**

### **Comments to Reviewer No. 02679607**

What was the absolute neutrophil counts on your patients. I know that you use a count of WBC < 4000 as your definition of leukopenia.

**Good question but in our hospital we do not routinely measure neutrophil counts, so that we cannot make statements about the neutrophil count of the included patients suffering from post-HIPEC leukopenia.**

### **Comments to Reviewer No. 03292914**

**No comments to be answered.**