



## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Gastroenterology*

**Manuscript NO:** 81650

**Title:** Prolonged hyperthermic intraperitoneal chemotherapy duration with 90 minutes cisplatin might increase overall survival in gastric cancer patients with peritoneal metastases

**Provenance and peer review:** Invited manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 03260205

**Position:** Peer Reviewer

**Academic degree:** MD, PhD

**Professional title:** Academic Editor, Academic Research, Adjunct Professor, Associate Professor, Doctor, Surgical Oncologist

**Reviewer's Country/Territory:** Spain

**Author's Country/Territory:** Hungary

**Manuscript submission date:** 2022-11-18

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2022-12-30 07:30

**Reviewer performed review:** 2023-01-07 10:11

**Review time:** 8 Days and 2 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Novelty of this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty



<b>Creativity or innovation of this manuscript</b>	[ ] Grade A: Excellent [ ] Grade B: Good [ ] Grade C: Fair [ Y] Grade D: No creativity or innovation
<b>Scientific significance of the conclusion in this manuscript</b>	[ ] Grade A: Excellent [ Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No scientific significance
<b>Language quality</b>	[ ] Grade A: Priority publishing [ Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
<b>Conclusion</b>	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [ Y] Major revision [ ] Rejection
<b>Re-review</b>	[ ] Yes [ Y] No
<b>Peer-reviewer statements</b>	Peer-Review: [ Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [ Y] No

### SPECIFIC COMMENTS TO AUTHORS

Clinical data analysis of primary gastric cancer patients with peritoneal metastases, who underwent cytoreductive surgery with HIPEC \*General: The manuscript contains a retrospective study of 73 patients with peritoneal metastasis of gastric origin who underwent cytoreductive surgery and HIPEC. \*Title: The title could be improved as it does not give any clue about the findings of the study. I would recommend something like: "Prolonged HIPEC duration with 90 minutes cisplatin might increase overall survival in gastric cancer patients with peritoneal metastases" \*Abstract: Abstract is correct. Conclusion may not be adequate. As the study does not compare HIPEC with no HIPEC we could not conclude that. \*Background: Introduction is quite long. first paragraph should be shortened to less than a half. \*Material & Methods: The authors should explain better its protocol, especially regarding perioperative chemotherapy as later it is an important part of the study. It should stay



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clearly as well if they perform diagnostic laparoscopy in all patients and which is the management of positive cytology. How was laparoscopy preformed, was the current Sugarbaker's recommendations followed? Sugarbaker PH et al. Laparoscopy technique in the setting of peritoneal metastases to avoid port site relapse. Surg Oncol 2021; 37: 101543. There is no mention of thiosulfate, is it used to protect the kidney? It should be stated that 90-days complications by Clavien-Dindo Classification or NCI- CTCAE classification were recorded, mortality should be in 90 days too. \*Results: A flow chart will help to understand the inclusion and main outcomes of the study. The authors refer that "The need to remove any further organs than the ones detailed in Supplementary Table 1 during CRS (N = 9) was associated with a negative effect". Please explain which organs were resected that are not specified in the table. Sup Table 1 should be included in the main paper as it describes the population of study. There is a reduced number of patients who received trastuzumab (n=5) with such a sparse number is hazardous to establish a clear benefit. The authors "marginally better RFS was found in those patients who did not have to undergo peritonectomy of the pelvis (HR: 0.3382; 95% CI: 0.1099 - 1.0410; P = 0.0588)". Nevertheless, CI includes 1, so it should not be interpreted like that. \*Discussion: The authors state that "An important conclusion of the presented studies and our novel results is that patients with small tumor burden (PCI < 6, but maximally 9) benefit the most from this multimodal therapy". Nevertheless, the data given shows "DSS of patients were marginally affected by the duration of HIPEC [60 (ref.) vs. 90 min: HR: 0.5252; 95% CI: 0.2565 - 1.0750; P = 0.0781] and by PCI (HR: 1.0630; 95% CI: 0.9982 - 1.1310; P = 0.0569), and significantly by preoperative serum CEA levels (HR: 1.2220; 95% CI: 1.0880 - 1.3720; P = 0.0007)." So that affirmation is not supported by the data of this paper. It is stated that "Furthermore, an interesting observation emerged during the analysis of our data that in the course of time and an increasing number of cases, the duration of surgery to reach complete



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**E-mail:** [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
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cytoreduction has become shorter.". Please provide data effectively showing this progression towards lesser times in the theatre as it is an interesting learning curve point. It is stated right after talking about the learning curve that "In the current analysis, the median survival time was 27.30 mo in the 90-minute group, which was significantly longer than that of the 60-minutes group (12.86 mo)." It should be indicated that the learning curve could have affected this outcome. It is stated that "Moreover, we could make the observation that if the procedure of ovariectomy or peritonectomy of the pelvis during CRS is not necessary, the RFS of the patient improved". As mentioned before, this is not supported by the data. As mentioned before, I would recommend including learning curve and experience of the team as a potential bias in limitations. Discussion is quite long and have some parts that are too speculative. I would recommend the authors to focus on the main findings of the paper and reduce the review of the current state of the art in literature. Conclusions should be based on results of the study. So, I would recommend stripping the final paragraph of all recommendations that are not strictly produced by the study results (prehab, anemia, modern treatments...). Moreover, I would be more cautious pointing out benefit of 90 over 60 due to potential bias.



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**Provenance and peer review:** Invited manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 05088098

**Position:** Editorial Board

**Academic degree:** MD, PhD

**Professional title:** Professor

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** Hungary

**Manuscript submission date:** 2022-11-18

**Reviewer chosen by:** Dong-Mei Wang

**Reviewer accepted review:** 2023-01-31 11:37

**Reviewer performed review:** 2023-01-31 13:21

**Review time:** 1 Hour

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Novelty of this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty



<b>Creativity or innovation of this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation
<b>Scientific significance of the conclusion in this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input checked="" type="checkbox"/> Rejection
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

The authors have looked at a difficult topic, advanced gastric cancer patients with peritoneal metastasis where CRS and HIPEC was performed. They conducted a retrospective analysis of 73 patients with CRS followed by HIPEC, they confirmed applied over 90-minutes has a positive impact on disease-specific survival in comparison with CRS followed by 60-minutes of HIPEC and presented patients treated with neoadjuvant trastuzumab had significantly better DSS. Unfortunately, there are similar resent studies in the literature, Eur J Surg Oncol. 2019 Sep;45(9):1734-1739. The current study had a few limitations, including the small sample size, the a single-center retrospective nature of the study, and the heterogeneity of the data. During the time of evaluation, the protocols concerning the preoperative chemotherapy treatment did significantly change. Furthermore, in this small cohort of patients with GC and PM there was only very limited data on post-HIPEC treatment.



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**Peer-review model:** Single blind

**Reviewer's code:** 02732296

**Position:** Editorial Board

**Academic degree:** FEBS, MD

**Professional title:** Associate Professor

**Reviewer's Country/Territory:** Turkey

**Author's Country/Territory:** Hungary

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**Reviewer chosen by:** Dong-Mei Wang

**Reviewer accepted review:** 2023-02-02 11:03

**Reviewer performed review:** 2023-02-02 13:29

**Review time:** 2 Hours

<b>Scientific quality</b>	<input checked="" type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Novelty of this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty



<b>Creativity or innovation of this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation
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<b>Language quality</b>	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input checked="" type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

This is a very well organized manuscript with very objective evaluations about the shortcomings of the study such as heterogenous patient groups and low number of patients. However, even though not being substantial, it is promising to see HIPEC makes a difference to some extent for the patients with peritoneal carcinomatosis in the treatment of this difficult disease. The manuscript is worth publishing as it may guide possible future prospective studies.



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**Peer-review model:** Single blind

**Reviewer's code:** 05569322

**Position:** Peer Reviewer

**Academic degree:** MD, PhD

**Professional title:** Doctor, Surgeon, Surgical Oncologist

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** Hungary

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<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Novelty of this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty



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<b>Scientific significance of the conclusion in this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
<b>Language quality</b>	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

Good work! There are several questions: 1: What are the indications for this type of surgery? Is there a discussion of multidisciplinary treatment? How to determine the scope of surgery? 2: The probability of postoperative complications is high for this type of surgery, so how is it controlled? 3: Is preoperative PET-CT routinely performed?



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**Peer-review model:** Single blind

**Reviewer’s code:** 05497413

**Position:** Peer Reviewer

**Academic degree:** PhD

**Professional title:** Academic Research

**Reviewer’s Country/Territory:** New Zealand

**Author’s Country/Territory:** Hungary

**Manuscript submission date:** 2022-11-18

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**Reviewer accepted review:** 2023-01-29 20:57

**Reviewer performed review:** 2023-02-10 00:22

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<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Novelty of this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty



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<b>Creativity or innovation of this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation
<b>Scientific significance of the conclusion in this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## SPECIFIC COMMENTS TO AUTHORS

It is a very good paper



## RE-REVIEW REPORT OF REVISED MANUSCRIPT

**Name of journal:** *World Journal of Gastroenterology*

**Manuscript NO:** 81650

**Title:** Prolonged hyperthermic intraperitoneal chemotherapy duration with 90 minutes cisplatin might increase overall survival in gastric cancer patients with peritoneal metastases

**Provenance and peer review:** Invited manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 05569322

**Position:** Peer Reviewer

**Academic degree:** MD, PhD

**Professional title:** Doctor, Surgeon, Surgical Oncologist

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** Hungary

**Manuscript submission date:** 2022-11-18

**Reviewer chosen by:** Chen-Chen Gao

**Reviewer accepted review:** 2023-03-05 08:04

**Reviewer performed review:** 2023-03-05 08:11

**Review time:** 1 Hour

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection



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<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
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**SPECIFIC COMMENTS TO AUTHORS**

Good work!