

Peer Review File

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Reviewer #1

The topic covered in this paper is of great interest in the gynaecologic oncology.

Statistics are well set up and calculated. The article is easy to understand and the message is direct.

I believe that the article is suitable for publication, however I believe that a revision of the language and the correction of some verbal and syntactic forms in the text are necessary.

In particular, here are the most important:

Comment 1: Page 6. “Average temperature” please change the phrase with “mean temperature”

Reply 1: the sentence was corrected (page 6 line 141-142)

Comment 2: “Recurrent ovarian cancer” was shortened in “ROC” in Background. Please use the shortened version it in the following phrases.

Reply 2: the sentence was corrected (page 6 line 149)

Comment 3: “Overall survivor” was shortened in “OS” in Methods. Please use the shortened version it in the following phrases.

Reply 3: the sentence was corrected (page 6 line 150)

Comment 4: The verb “to furnish” was used starting from Background section to the end of the article; in order to pursue a more correct meaning please use another verb: e.g. to provide, to give etc...

Reply 4: the sentence was corrected (page 3 line 75)

Comment 5: Page 7. The verbal form “depicted” is not the more correct for the meaning of the sentence, please use “reported” or “noticed”.

Reply 5: the sentence was corrected (page 7 line 167)

Comment 6: Page 7. Please remove the word “rate” after the percentage 53%.

Reply 6: the sentence was corrected (page 7 line 167)

Comment 7: Page 7. The sentence “No complications were not reported” contains a double negation, please use the sentence “no complications were reported”.

Reply 7: the sentence was corrected (page 7 line 171)

Comment 8: Page 7. Please correct the adjective “controversials” with the noun “controversies”. Moreover, I think the whole sentence is too long and contains too much repetitions. I suggest to rewrite it.

Reply 8: the sentence was rewrite (page 7 lines 183-184)

Comment 9: page 8. Please rewrite the sentence: “However, the study was focused on a different subset of patients the ROC and no concrete randomized studies are actually available for recurrent ovarian cancer treatment with HIPEC.”

Reply 9: the sentence was rewrite (page 8 lines 188-190)

Comment 10: Page 8. Please rewrite the sentence: “However even, even acknowledging such limitations, the fact that the results of the meta-analysis were statistically significant in favour of HIPEC, especially for the two years follow-up ($P < 0.0001$), is a crucial strength of our study”.

Reply 10: the sentence was rewrite (page 8 lines 205-207)

Comment 11: Page 9. Please rewrite the sentence with correct punctuation and/or conjunctions: “Considering that even if the HIPEC treatment seems to be safe in terms of intra-operative and

post-operative complications; however, it represents an additional risk, often related to the number of surgical procedures performed”.

Reply 11: the sentence was rewrite (page 9 lines 217-221)

Reviewer #2

Comment 1: English Language should be corrected throughout the manuscript and particularly in the Background chapter.

Reply 1: According with reviewer suggestion we revised and corrected the languages. (pages 2,3,6,8,9,10)

Just some examples in the Background:

Comment 2: “The most part of patients” should be “the majority”

Reply 2: the sentence was corrected (page 3 line 56)

Comment 3: However, the results obtained are still partial and not completely effective. Please define percentage moreover the hyperthermia addiction allowed to enhance the tissue absorption and consequently” into “The effect of the hyperthermia enhances..”

Reply 3: the sentence was corrected (page 3 line 64-66)

Comment 4: “For ovarian cancer treatment, this technique was for a long time debated ...” and subsequently “The role of HIPEC remains controversial” is a not necessary repetition. Please correct and rephrase

Reply 4: the sentence was corrected (page 3 line 71-72)

Comment 5: "did not allow to furnish definitive conclusions" should be “did not allow to draw” or “to provide”. Please do not use the term “furnish” in medical English because it is mainly used as a synonym of “decorate”.

Reply 5: the sentence was corrected (page 3 line 75)

Minor points

Background:

Comment 6: “target therapies, monoclonal antibodies and biological therapy” Not target but targeted. Maybe could be important to mention in brackets some of the drugs approved for the treatment of OC amongst monoclonal (Bevacizumab), targeted (parp inhibitors).

Reply 6: according with reviewer the sentence was corrected and specified.

Comment 7: primary ovarian cancer (POV) should be (POC) as recurrent ovarian cancer (ROC).

Reply 7: the sentence was corrected (page 3 line 71)

Comment 8: "The present study is focused on ROC subset, with the aim to evaluate the available literature and the results obtained to furnish indication about the role of HIPEC for ROC treatment" should indicate the aim of the study and the methods “The present study aims to explore whether the addition of HIPEC in recurrent ovarian cancer patients could improve clinical outcome. A systematic review of the literature and meta-analysis was performed.

Reply 8: the sentence was corrected (page 3-4 lines 76-79)

Methods:

Comment 9: It should be stated if were assessed studies with only ROC at first line or second line. In the first line whether platinum-sensitive or resistant or all the patients with ROC.

Reply 9: the sentence was specified according with reviewer (Page 4 lines 97-98)

Comment 10: Basically, it would be correct to insert if any inclusion or exclusion criteria were applied

Reply 10: the inclusion/exclusion criteria sentences were specified according with reviewer (page 4 line 100 – Page 5 lines 113)

Comment 11: It should be mentioned in the figure the reasons for not having included the 28 studies. In fact 35 studies were selected but only 7 included. Please add a box in the Figure

Reply 11: The figure was modified according with reviewer suggestion (figure 1)

Results

Comment 12: At least a Table summarizing the clinical data of the studies should be presented. such as the Age of the patients, the number of previous cycles, if R0 was achieved, type of the study, HIPEC regimen etc.. Most of the data have been presented in the text. However a Table would be easier to read.

This would be important for the clinicians as similar to what demonstrated by the Dutch study, the selection of the patients is a key determinant for the efficacy of the use of HIPEC but also the main bias for its widespread use.

Reply 12: New table was added according with reviewer suggestion (page 18)

Conclusions

Comment 13: Please be consistent with acronyms. Often it is used ROC other times recurrent ovarian cancer.

Reply 13: All sentences were corrected (page 6 line 149 – Page 9 line 222)

Comment 14: A couple of lines of new ongoing (ClinicalTrials.gov) such as the multicentre French HIPOVA-01 should be mentioned.

Reply 14: The study was added in background according with reviewer (page 4 line 74)

Comment 15: “the HIPEC addition during surgery for ROC could be the best time to perform it “. I cannot understand the phrase as it seems that the choice of HIPEC in the primary versus the recurrent setting should be based on the difficulty of the surgical resection. Maybe the point is that often surgery for oligometastatic ROC can be easier than PDS or IDS, thus the addition of HIPEC does not add additional morbidity.

Reply 15: The sentence was modified and clarified according with reviewer (page 9 line 217 -221)

Comment 16: The Risk of anastomotic leakage and bowel-related problems should be mentioned as it is one of the main criticism for HIPEC after surgery also in the context

Reply 16: the leakage risk was commented in the text according with reviewer (9 line 216)