

## **The rush to novelty and high expectations in surgery: the case of ALPPS**

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Handling editor:

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Ref.: Ms. No. JCTRes-D-16-00024

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Journal of Clinical and Translational Research

Dear Mr. Olthof,

Reviewers have submitted their critical appraisal of your paper. The reviewers' comments are appended below. Based on their comments and evaluation by the editorial board, your work was **FOUND SUITABLE FOR PUBLICATION AFTER MINOR REVISION.**

If you decide to revise the work, please itemize the reviewers' comments and provide a point-by-point response to every comment. An exemplary rebuttal letter can be found on at <http://www.jctres.com/en/author-guidelines/> under "Manuscript preparation." Also, please use the track changes function in the original document so that the reviewers can easily verify your responses.

Your revision is due by Sep 29, 2016.

To submit a revision, go to <http://jctres.edmgr.com/> and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely

Michal Heger  
Editor-in-Chief  
Journal of Clinical and Translational Research

Dear Dr. Olthof and Dr. Schadde,

In addition to the off-system comments provided by me, your work was reviewed by one of the greatest HPB experts in the world and by a reviewer whose expertise was more remote. The latter reviewer was recruited because I wanted to make sure that the message was also understood by somebody outside of the field. The HPB expert, reviewer 1, thought your work was commendable and provided an accept verdict. Consequently, your work will be published after you implement the minor revisions of reviewer 2. A re-review will not be necessary.

Congratulations and thank you very much for your contribution.

Kindest regards,

Michal.

Reviewers' comments:

Reviewer #1: None

Reviewer #2: 1) In paragraph 1, sentence revising 'The key element of the procedure is the induction of...'

2) Perhaps some more details on 'the FLR is cleaned of tumor' would be helpful to readers.

3) Sentence revising in paragraph 3 'The main controversy is on ...'

4) The author should clarify his opinion on what is an unacceptable outcome as mentioned in paragraph 3. 'The outcomes specifically for hepatocellular carcinoma (HCC) and cholangiocarcinoma were unacceptable.'

5) 'All conclusions...' in paragraph 4 seems to be a rather sweeping statement. Is the author referring to editorials on the subject or research manuscripts or clinical databases.

6) '..led to the manifestation of single-center mini-series that were often too small to evaluate anything at all.' Does the author mean multiple small trials at the same centre? Were the data from these studies statistically insignificant mainly due to small sample size?

7) Paragraph 7, needs a comma after 'Additionally..'

8) Paragraph 7, typo de should be the

9) 'However, from the beginning numerous experienced groups doubted the (argumentative) validity of this low drop-out rate, and rightfully so.' The author clearly is not in favor of the ALPPS procedure and makes good points to support his case but it would be helpful to avoid phrases like 'and rightfully so'. Also, references of other work from noted groups can be cited here to strengthen this claim.

10) Paragraph 9, calls in to question the advantage conferred by low drop out rate on clinical benefit of ALPPS however the previous sentence suggests that such an analysis has not been done yet.

11) Please elaborate on the use for ALPPS procedure in preclinical studies. Since this procedure is already in the clinic, what are the preclinical animal researchers hoping to study with it. The author makes a very valid point that it is quite alarming that these surgical procedures unlike therapeutic drugs are tested in humans without prior validation in animal models.

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2<sup>nd</sup> editorial decision:

Date: 7-Sep-2016

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Dear Mr. Olthof,

I am pleased to inform you that your manuscript has been accepted for publication in the Journal of Clinical and Translational Research.

Comments from the editor and reviewers can be found below.

Thank you for submitting your work to JCTR.

Kindest regards,

Michal Heger  
Editor-in-Chief  
Journal of Clinical and Translational Research