Author's response to reviews

Title: Safety and hemostatic efficacy of fibrin pad in partial nephrectomy: Results of an open label Phase I and a randomized, standard-of-care-controlled Phase I/II study

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Author's response to reviews: see over
To
Dr Henderson
BMC Nephrology
BioMed Central
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Subject: Re-submission of manuscript (MS: 4135873367507093) entitled “Safety and hemostatic efficacy of fibrin pad in partial nephrectomy: Results of an open-label Phase I and a randomized, standard-of-care-controlled Phase I/II study”

Dear Dr Henderson:

Thank you for your accepting our manuscript (MS: 4135873367507093) entitled “Safety and hemostatic efficacy of fibrin pad in partial nephrectomy: Results of an open-label Phase I and a randomized, standard-of-care-controlled Phase I/II study”. We have made the changes suggested by the reviewers and are submitting 2 versions of the revised manuscript, i.e. the clean version and the version with changes tracked. Detailed responses to all the reviewer comments are attached at the end of this letter. We hope that our revised manuscript will be judged suitable for publication in BMC Nephrology. We look forward to your feedback and are willing to make any further changes to the manuscript, if necessary.

We hope to hear from you soon.

Sincerely,
Dr James C. Hart

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Response to reviewer comments:

Reviewer 1

Comment 1: To improve the quality and understandability of the manuscript, however, they should indicate what techniques were used as SOC during the phase II trial.

Response: The techniques that were used as SOC included electrosurgery, suture, absorbable hemostat, and SURGICEL®. This information has been included in the Phase III study design section of Methods (page 7, paragraph 1).

Comment 2: It is not entirely clear whether both arms had arterial clamping prior to tumor excision in this trial, and whether suture ligature was used for TBS in either arm.

Response: Arterial clamping was employed in Phase I study but not during active hemostat application in Phase II. This information has been included in the Phase I/II study design section of Methods (page 7, paragraph 2).

Comment 3: In addition, this article seems more suited to BMC Urology then BMC Nephrology. Why has it not been submitted/published there?

Response: Since the study included patients undergoing nephron-sparing surgery, we felt the article would be of interest to the readership of BMC nephrology.

Reviewer 2

No comments

Reviewer 3

Comment 1: The size of the pad is given; but how much fibrin is used per cm2 area is not clear from the manuscript.

Response: Thank you for your query. Fibrin pad contains 4.7-12.4 mg/cm2 fibrinogen and 15-45 IU/cm2 thrombin. This information has been added in the Fibrin pad section of the Methods (page 5, paragraph 2).

Comment 2: Is the size of the pad used dependent on the size of the wound or the intensity of bleeding.

Response: Although fibrin pad is supplied in 10 × 10 cm2 units, it could be cut to fit the target bleeding site such that a margin of 1-2 cm is available beyond the wound. This information has been included in the Fibrin pad section of the Methods (page 5, paragraph 2).

Comment 3: It would have been nice if images of the application site was also provided, so that the readers will see if pad is fully soaked with blood or partially soaked.

Response: We do not have images of the application site in patients as it was not a part of the informed consent. We do, however, have images of the application site during a porcine
partial nephrectomy procedure conducted in a preclinical laboratory setting. We have included this as Figure 1C and described it in the *Fibrin pad* section of the Methods (pages 5-6, paragraph 2).