Author’s response to reviews

Title: Can hybrid hyaluronic acid represent a valid approach to treat rizoarthrosis? A retrospective comparative study

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Author’s response to reviews:

Siena, 06 September 2017

Dear Editor,

We thank editors and reviewers for your careful reviews and thoughtful comments on our manuscript. According to your perfect comments, we have revised the manuscript. As you perfectly suggest, we have completed the response to reviewers.

Thank you very much.

Your sincerely,

Tenti Sara

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Rewiever 1

“….. the study design is retrospective, not controlled and notably without placebo arm. End points are VAS and functional scores. There is no radiographic assessment. I'm afraid that based on this purely observational and retrospective study, the statement that HA is superior to triamcinolone should be made more carefully.”

Response: Thank you very much for your perfect suggestion. we provided some modifications in the Conclusions of the Abstract (line 58, page 3) and in the Section “Conclusions” of the manuscript (line 330-331, page 14).

“There further limitations of this study: 55 patients in the HA and 45 in the triamcinolone arm seem to be underpowered. There is no power analysis in the methods section. Kellgren & Lawrence grade II and III as an inclusion criterion is very heterogenic so the groups might differ in OA severity.”

Response: Thank you very much. As you properly suggested, we discussed these limitations (Discussion section, line 317-320, page 13,14).

“To this end, cholesterol levels (which are associated with hand OA) are significantly higher in the HA arm which also point out a potential difference of the groups.”

Response: Thank you for your careful checking. We specified that the difference in the cholesterol serum levels can represent a source of bias (Discussion section, line 321-323, page 14; reference 35).

“Another limitation is the lack of ultrasound-guided infiltration. Joint infiltration by palpation as performed in this study has significant rates of extra-articular drug application which might bias the study.”

Response: We reported a previous study that demonstrated the accuracy of not ultrasound-guided infiltrations and we added the corresponding reference (Discussion section, line 275-277, page 12; reference 29). We updated the limitations of the study with the lack of ultrasound guidance (Discussion section, line 325-326, page 14).

“As a minor point, 6 smokers are found in the Triamcinolone group whereas there is only 1 smoker in the HA group. Smoking is a potential negative confounder of treatment in OA. This should be discussed. Also, the SF36-mental component summary is significantly lower in the triamcinolone group. Taken together, this relatively small and uncontrolled retrospective survey potentially is biased by a heterogenic patient cohort. The conclusion made by the authors in their abstract is completely supported by the data and should be drawn more carefully.”

Response: According to you useful suggestion, we discussed the potential confounding role of smoking in the treatment of OA (Discussion section, line 321-323, page 14; reference 34). We, also, added a sentence indicating more caution in the interpretation of our results (Discussion section, line 332, page 14).
Reviewer 2

Thank you for your kind appreciation.

“Please use either kDa or Da, instead of as now, using both”

Response: We adapted the manuscript according to your correct suggestion (Background section, line 108-109, page 5).

“From the method section: "After palpating the TMC joint space, laterally to the abductor pollicis longus tendon,...” Please make a clearer definition of where is "lateral of" this tendon.”.

Response: Thank you very much for your important question. We specified that the injections were performed within the anatomic snuffbox (Methods section, line 167, page 7).

“The limitations of this being a retrospective study are discussed.

However, it should be included whether there were any reasons for why a patient was treated with the one or the other medication. Doctor's preference? Clinical experience by the doctor? Patient characteristics?

Was is systematically some doctors choosing one type? If so, what was the clinical experience performing i.a. injections? It is of major importance to know whether there were some reasons for the choice of either of the medications, since this may influence the result”.

Response: As you requested, we discussed that the main reason for not always using the most suitable product for treatment is its cost. Then, the choice is influenced by possible allergy or intolerance to different formulations (Methods section, line 155-157, page 7).