Author's response to reviews

Title: Efficacy of inhibition of IL-1beta in patients affected by rheumatoid arthritis and type 2 diabetes mellitus: cases report and discussion of literature

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Author's response to reviews: see over
Dear Editor,

following the Reviewers’ comments, we revised the manuscript “Efficacy of inhibition of IL-1 in patients affected by rheumatoid arthritis and type 2 diabetes mellitus: cases report and discussion of literature” (MS: 3617136771565654), that is now ready for the new evaluation.

Hoping that in this version, it could be suitable for publication in your Journal, We remain

Sincerely yours

Piero Ruscitti and Co-authors

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Reviewer 1

The case report „Efficacy of inhibition of IL-1beta in patients affected by rheumatoid arthritis and type 2 diabetes mellitus: cases report and discussion of literature“ by P. Ruscitti et al. describes 2 cases where the treatment of patients with RA and type 2 diabetes not only improves RA but also the metabolic state of the patients. This is a very interesting and important observation with the potential to make a difference to the clinical practice of these patients with both diseases. The following points need to be addressed or clarified:

**We wish to thank the Reviewer for the interest in our paper and according to the suggestions we revised our manuscript.**

1. The patients are treated with Anakinra which is an IL-1 Receptor blocker, which blocks action of both IL-1 receptor agonists IL-1beta and IL-1alpha. Throughout the manuscript and even in the title the authors use the term „inhibition of IL-1beta“, this is not correct and should be changed in the whole manuscript to inhibition of IL-1. „IL-1beta inhibition“ should only used if a IL-1beta specific antibody is used for treatment (i.e. Ilaris).

*In according to Reviewer’ suggestion we changed “inhibition of IL-1β” in “inhibition of IL-1”.*

2. The improvement of metabolism is claimed to be due to the Anakinra treatment only. In case 2 the steroid dose was much higher before Anakinra and lower at the start of Anakinra. What was the dose of the steroids before and during Anakinra treatment and was it reduced under the Ankinra treatment? A reduction of steroids would also explain an improvement of the diabetes. Please clarify.

*We apologize for the lack of definite data about the treatment of patient 2. In this revised form, we better describe the therapy.*

3. Body weight has a major impact on metabolic parameters, this is only briefly mentioned, please add the body weight as a figure.

*We added the body weight of our patients in the figure (Panel f).*

4. The previously reported improvements of metabolism were reported to be mainly due to improved insulin secretion (Larsen CM et al. N Engl J Med 2007, 356:1517-1526). Did you measure C-peptide and insulin levels in these patients?

*We added the values of C-peptide and insulin levels.*

5. 2 of the authors of the present manuscript have previously published a similar observation in gout patients with type 2 diabetes, this should be included in the discussion.

*We added this reference in the discussion [Reference 7].*

6. Language revision of the whole manuscript is mandatory

*In according to the Reviewer’s suggestion, the language of our manuscript has been revised.*

Reviewer 2

The present manuscript presents two well described patients with rheumatoid arthritis and type 2 diabetes. Treatment with IL-1Ra improved both conditions. The patients are well described and the literature objectively discussed. The efficacy of the treatment are encouraging. The findings are novel and clinically relevant. I have no changes to propose.

**We wish to thank the Reviewer for the interest in our work and we greatly appreciated his kind comment.**