

April 22, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 2884-review.doc).

Title: ACTH: A powerful but underappreciated therapeutic tool for acute crystal induced arthritis?

Author: Dimitrios Daoussis, M.D. and Andrew P. Andonopoulos, M.D., FACP

Name of Journal: *World Journal of Rheumatology*

ESPS Manuscript NO: 2884

We have improved the quality of the manuscript according to the suggestions of the reviewers.

To our major surprise, we have been asked to improve the quality of the language. I can only assume that this is some kind of error. I can reassure you that the quality of the language is more than adequate. Please check this yourself or send it to an alternative reviewer. I am a Canadian citizen and I have worked for a long time in UK whereas Prof Andonopoulos has received all his medical training in USA. I have published many articles in major scientific journals and this is the first time that I receive a comment about the quality of the language!!!

Reviewer 1: this is an interesting manuscript discussing the efficacy of using ACTH in patients with Gout. 1--There are many statements the need reference: "Gout is the most common form of inflammatory arthritis affecting 1% of the male population in Western countries . (need reference) "The prevalence of hyperuricemia and gout has been constantly rising during the last decades. Many causes have contributed to this increase: dietary changes, widespread use of medications associated with hyperuricemia, increase in life expectancy and most importantly, the metabolic syndrome "epidemic ".(Need a reference) . "Evidence suggests that it is safe and does not seem to associate with immunosuppression; moreover ACTH is a low cost drug at least in Europe". (Need reference) 2- The author should mention some detail about the studies that showed its equal efficacy to Indomethacin , the rapidity of ACTH efficacy and side effects and its benefit over Steroids use in acute in diabetic patient

Reply: we have added the references requested by the reviewer. Moreover, we have added more details regarding the clinical studies assessing the efficacy of ACTH in gout as requested

Reviewer 2: the reviewer requests more data on the anti-inflammatory properties of gout in other diseases. However, there are already many excellent reviews in the literature summarizing the anti-inflammatory properties of ACTH in multiple settings. We have included one detailed review (Ref 7) and interested readers can find more information there. Our goal was to focus on gout.

Many thanks for your time and consideration

Kind regards

Dr Dimitrios Daoussis