

Format for ANSWERING REVIEWERS

December 2, 2015

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: 22707-review.doc).

Title: Isotretinoin was not associated with depression or anxiety: a 12-week study

Author: Bella Suarez, Ana Serrano, Yves Cova, Trino Baptista

Name of Journal: *World Journal of Psychiatry*

ESPS Manuscript NO: 22707

The manuscript has been improved according to the suggestions of reviewers:

- 1) Format has been updated: Yes
- 2) Revision has been made according to the suggestions of the reviewer

Reviewer 1: General comments:

In the study, 60 patients who diagnosed with acne divided into two groups according to the isotretinoin (ITT) treatment and non ITT , and treatment results were evaluated by using the standard tests of depression and anxiety . At the end of this evaluation has been found that the frequency of depression, as defined by the Zung scale cut-off points was similar in the ITT and in the non-ITT. Authors asserted that the ITT treatment was reliable regarding psychological side effects in regular dermatological patients.

- a) However, the corrections which stated below must be made by the authors How many patients excluded and why?

Response: No patient was excluded. This is now stated in the first paragraph, Result section, page 8.

- b) If there are ethical approval number and date, they must be specified.

Response: In the first paragraph of the "Method" section, page 6, we now state that there is no formal trial registration system in our country, however, our study was approved by the ethic committee and by the institutional review board of the department of psychiatry of our institution.

- c) Who has made spanish validity and reliability of the tests which used in study. It must be specified.

Response: Three references concerning his important comment were added and were numbered 9, 10 and 11. This issue is now addressed in page 7, Evaluation subsection, second paragraph.

Reviewer 2. General comments:

Well written manuscript: A few questions and comments:

- a) What is the severity level of the acne before commencement of treatment for both groups? isotretinoin is indicated for moderate to severe acne whereas antibiotics is indicated only for mild to moderate acne. Is the acne severity almost similar in both groups? Severe acne might contribute to depression and anxiety.

Response: This is a very important point; even though we addressed it in the original version, now we added the data and emphasized the lack of clinical and statistical significance in the outcome.

In fact, the acne severity was higher in the isotretinoin group. Now we present the statistics in page 8, Result section, second paragraph. However, the frequency of clinically-significant depression or anxiety and the scale scores did not change over time. More importantly, we state that "No significant correlations were observed between the clinical severity assessment of acne at baseline and the depression and anxiety scores at any time-point in the ITT group", page 11, last paragraph (page 9, Correlation analysis, second paragraph)..

In any case, we now state that it was an important study limitation, because treatment assignment could not be randomly conducted due to ethical reasons (page 12, Discussion section, second paragraph).

- b) Do the authors evaluate the patients after 12 weeks? It is good to have data until 6 months as depression and anxiety might develop later on. 3. Is the authors also considering other side effects of isotretinoin i.e. dry lips and skin; liver dysfunction contributing to the anxiety and depression due to isotretinoin?

Response: We did not. These limitations are now stated in the last paragraph of the Discussion section (page 12).

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3) References and typesetting were corrected: Yes

Thank you again for publishing our manuscript in the *World Journal of Psychiatry*.

Sincerely yours,

Trino Baptista

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