

Format for ANSWERING REVIEWERS

January 9, 2015

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: 15176-review.doc).

Title: Recombinant Streptokinase versus Hydrocortisone Suppositories in Acute Hemorrhoids. Randomized, Controlled Trial (THERESA-4)

Author: Francisco Hernández-Bernal, Georgina Castellanos-Sierra, Carmen M. Valenzuela-Silva, Karem M. Catasús-Álvarez, Osmany Martínez-Serrano, Odalys C. Lazo-Diago, Cimara H. Bermúdez-Badell, José R. Causa-García, Juan E. Domínguez-Suárez, and Pedro A. López-Saura, for the THERESA-4 (Treatment of HEmorrhoids with REcombinant Streptokinase Application) Group of Investigators.

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 15176

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

1 We guarantee that the language of our manuscript has reached Grade A and therefore we choose not to have it edited by any English language editing company. Likewise, the text has been actively reviewed by the senior author of the paper (Dr. Pedro A. López Saura, MD, PhD), with wide experience in such writings, accepted by several English language journals (see enclosed letter). Besides it was reviewed by Dr. Yaima Doimeadiós, PhD, Full Professor of the University of Havana, who is English-certified by Cambridge University (certificate is enclosed)

2 Format has been updated

- Title was adjusted to 12 words
- Ethics approval declaration was added. Approval certificate by the NRA is enclosed.
- Clinical Trial registration declaration was added where requested.
- Informed consent declaration was added where requested. The consent and patient information forms in the local language: (Spanish) are enclosed.
- Biostatistics. The requested declaration was added. The final report of the trial was reviewed by the biostatistics experts of the Cuban NRA. A copy of the approval letter is enclosed in PDF format.
- Conflict of interest disclosure was added where requested.
- Data sharing statement was added.
- Some words in British English were changed to US English.
- Abstract was increased in details and number of words, according to the editor's suggestion.
- The Comments were written.

2 Revision has been made according to the suggestions of the reviewer 02979409

- (1) *Some language faults are need to be revised. For example: in the abstract, the aim of this study was written as " To compare the efficacy and safety of recombinant streptokinase (rSK) hydrocortisone acetate-based suppositories in acute haemorrhoidal disease", I think that is a tiny fault in expression. Do you mean that rSK versus hydrocortisone acetate-based suppositories ?*

Answer: The word vs. was added in the first sentence of the Abstract to make it have sense. It was a typing error.

(2) *Surgical approaches are usually the standard treatment for Grade III and IV hemorrhoid. In your study, acute hemorrhoids in Grade III and IV were also treated with medicines, although benefits were obtained in this study, how about the recurrences of these treatment? Do these patients need a further treatment?*

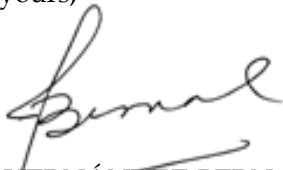
Answer: Although surgical approaches are usually the standard treatment for Grade III and IV hemorrhoid, but not always in the acute presentation. Therefore medical treatment was used, for the acute syndrome. This does not exclude surgery for a long term management. Recurrences were not an objective of this study so they cannot be reported. A long term follow-up of these patients is ongoing and will be reported in a further paper.

3 The second paragraph of the Results section was modified in order to provide more details on the course of the trial.

4 References were completed to 30 and typesetting were corrected

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

Sincerely yours,



Francisco HERNÁNDEZ-BERNAL, MD, MSc
Clinical Research Direction,
Center for Genetic Engineering and Biotechnology,
P.O. Box 6162, Havana, Cuba.
Telephone: +53-7-2087421; Fax: +53-7-2736008
Email: hernandez.bernal@cigb.edu.cu