Title: Efficacy of Rifabutin-based Triple Teraphy as Second-line to Eradicate Helicobacter Pylori Infection

Authors:

Jose M Navarro-Jarabo (jnavarro@hcs.es)
Nuria Fernandez (jnavarro@hcs.es)
Francisca L Sousa (jarabo@tiscali.es)
Encarnacion Cabrera (jarabo@tiscali.es)
Manuel Castro (jarabo@tiscali.es)
Luz M Ramirez (lmramirez@yahoo.es)
Robin Rivera (robinriverai@yahoo.es)
Esther Ubina (estherillaua@hotmail.com)
Francisco Vera (jarabo@tiscali.es)
Isabel Mendez (chabeli_estepona@hotmail.com)
Francisco Rivas-Ruiz (frivasr@hcs.es)
Jose L Moreno (jlmharo@hcs.es)
Emilio Perea-Milla (eperea@hcs.es)

Version: 2 Date: 28 March 2007

Author’s response to reviews: see over
Dear Annabel Phillips: I would like to reply to your questions regarding my manuscript: “Efficacy of rifabutin-based triple therapy as second-line treatment to eradicate helicobacter pylori infection”.

1) Our control clinical trail is registered under EudraCT code by the Spanish Agency of Drug and European Drugs Agency under EudraCT code no. 2004-001320-20, written in the Abstract of the manuscript.

Unfortunately EudraCT code is not a publicly accessible registry.

At this moment we are registering our clinical trial ISRCTN scheme, our provisional code number is CCT-NAPN-16328. As soon as the trial would be register, I will email our code number.

We send for the meantime the answers to the referees to speed up the final decision, as you see below.

2) I will include in the methods the names of all the ethics committee that approved the study, and its compliance with the Helsinki declaration.

Please don’t hesitate to contact me if you have any questions regarding ISRCTN registering of my manuscript.

Yours sincerely,

Jose M Navarro-Jarabo
Dear Mr. Borody

1) QUESTION 1

In terms of possible selection bias in randomisation, we had analysed efficacy with respect to the endoscopic injury. As is showing in fourth paragraph of results section, similar efficacy was achieved (56% in ulcerous and 57% in non-ulcerous patients). Therefore, I think this is not the reason for our disappointing results.

2) QUESTION 2

In terms of the eradication rate in quadruple therapy (70.4% in ITT), it is not so high, in comparison with other rates reported in the literature (Ref. 24). Moreover, in unpublished data in our hospital, we achieved with eradicative regimen in clinical practice an eradication rate of 67%.

3) QUESTION 3

I quite agree with you that eradication rate with our rifabutin-based therapy is lower than we expected, and disappointing compared to other studies previously reported. Many thanks for calling my attention to your recently study published. I’m sorry about no being familiar with your outcomes, but our manuscript was written and sent previously to the publication of yours. I think that it is very interesting and therefore I’ll include your outcomes in the discussion section of the manuscript.

I think the most possible explanation for our poor outcome is the length of therapy and not the amoxicillin dose. It was similar to the dose used in previous studies that reached better eradication rates than ours. On the other hand, in your paper the difference between the two doses of amoxicillin (2 vs 3 grs. per day) was not statistically significant.

Recently, another study conducted in Spain by Gisbert achieved, similar to ours, negative findings by a third-line rifabutin-based regimen (added to amoxicillin). Thus, differences related to geographical areas cannot be excluded (this paper is referenced in the revised manuscript).

4) QUESTION 4

I am grateful for your comment regarding the length of my manuscript. I had tried to reduce it as much as possible and left out many phrases and graphics (figure 2) that would have been redundant.

Yours sincerely,

Jose M Navarro-Jarabo
Dear Mr. O’Morain:
I revised my manuscript based on your recommendations.

Question 1

As you can see in the Methods section, paragraph 3, the analysis of efficacy planned by ITT includes all the patients. In the case of loss of follow up, we considered positive value in the experimental group (rifabutin-based therapy), and negative in the quadruple therapy, following the Worse Case Method. Nevertheless, all the patients (6) in the control group who failed to complete the treatment due to adverse events, came back for UBT control. As you can see in table 2, one of these six patients achieved eradication, but not the other five

Question 2

I quite agree with you that figure 2 would be redundant and was left out in the revised manuscript.

Question 3

In our geographical area, “Test and Treat” is not a homogeneous schedule. Many patients are treated based on serological testing. As this was a multicentric study we designed it to avoid inadequate inclusion of patients.

Yours sincerely,

Jose M Navarro-Jarabo
Dear Mr. Giovanni Cammarota:

I have revised my manuscript “Efficacy of Rifabutin-based triple therapy as second-line eradicate Helicobacter pylori” based on your recommendations.

I have included in the discussion section a mention about the study recently conducted by Gisbert in Spain. This outcome agrees with ours as you noted in your review.

I regret that there was no reference to this paper, however, this study was published after our manuscript was written and sent.

I’m grateful for your last comment, and the English has been revised.

Yours sincerely,

Jose M Navarro-Jarabo