

9-13-2016

Dear *World Journal of Hepatology*,

Attached please find a manuscript entitled, "Phase 3 Trial of First Generation Protease Inhibitor Therapy For HCV/HIV Coinfection" which we are submitting for publication as a Clinical Trials Study Original Article.

This manuscript reports on a multicenter phase 3 HCV treatment trial to evaluate the efficacy and safety of a regimen using a first generation HCV protease inhibitor (boceprevir) in combination with pegylated interferon alfa and ribavirin. Both HCV treatment-naïve and treatment-experienced HCV/HIV coinfecting participants were enrolled. Though the results were positive, we are well aware that boceprevir, the first generation HCV protease inhibitor that was studied, has been withdrawn from the commercial marketplace. However, the study illustrates several important principles that are relevant to development of newer agents, and we feel it is important to have this information available in the research community.

This manuscript has undergone review at the *World Journal of Gastroenterology* (ESPS Manuscript NO: 28585) who indicated that it can be accepted at no charge for publication in the *World Journal of Hepatology*. (see attached email from Dr. Jin-Lei Wang). We have addressed the reviewers' comments as listed below.

All authors have seen and approved the manuscript, have significantly contributed to the work, and the work in the manuscript has never been published nor is being considered for publication elsewhere.

We hope the editors consider this submission favorably for publication in *World Journal of Hepatology*.

Please feel free to call with any questions.

Sincerely,

Kenneth E. Sherman, MD, PhD

Gould Professor of Medicine

Director, Division of Digestive Diseases

University of Cincinnati College of Medicine

Cincinnati, OH 45267-0595

Dear Dr. Wang,

Thank you for your interest in sending a revised version of our manuscript "Phase 3 Trial of First Generation Protease Inhibitor Therapy for HCV/HIV Coinfection" to the World Journal of Hepatology. We have modified the manuscript as documented below in response to the comments raised by the reviewers. We hope that this now will be acceptable for publication.

Sincerely,

Kenneth E. Sherman, MD, PhD

Director, Division of Digestive Diseases

University of Cincinnati College of Medicine

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WJG Reviewers' Comments to the Authors:

REVIEWER COMMENTS:

Reviewer: 1 Comments to the Author

In the section I don't see a description of genotype 1 subtype (1a,1b), have the authors these data?

The breakdown of HCV subtypes is not available nor was it considered important at the time this study was conceived.

Could the authors make a table describing the results? A table showing the SVR rates has been added.

Could the authors describe if all the other non-viral causes of liver disease have been excluded? A sentence describing these exclusions has been added.

Could the authors confirm that cirrhotics had stage A Child-Pugh disease? A sentence describing this has been added.

Reviewer: 2 Comments to the Author

Reviewer comments do not request any revision.

Reviewer: 3 Comments to the Author

The topic is outdated since triple combination should not be used any more.

Although the trial results were positive, we are well aware that boceprevir, the first generation HCV protease inhibitor that was studied, has since been withdrawn from commercial use. However, we feel that the study illustrates several important principles that are relevant in the development of newer agents, and we feel that it is important to have this information available to the research community.

WJH Editor's' Comments to the Authors:

You need to provide the grant application form(s) or certificate of funding agency for every grant, or we will delete the part of "Supported by...". These grants were awarded to the AIDS Clinical Trial Group so the certificates of

award are not available to us. The award numbers are correct and need to be acknowledged as NIH research support.

No more than 100 words in the core tip. The word count is now 100.

List all abbreviations used in the table and explain them below please. A list of abbreviations used in the tables has been added.

Should not cite references here. References have been removed from the Comments Background section.

We request that the author make an audio file describing your final core tip, it is necessary for final acceptance.

Please check that there are no repeated references! This has been done.

At last, sign (handwrite) your name in the end of file. This has been added to the end of the last page.