

Reviewer 1 v.1

Comments to the Author

This is single center, retrospective study to evaluate the efficacy and safety of triple oral therapy for pulmonary arterial hypertension.

I read the manuscript with great interest, because it presented the unique population of PAH patients treated with uncommon combination of specific medications.

Although the study is innovative and the results are very promising, there are some important limitations as: retrospective nature of the study, small study sample and heterogenic population of PAH patients.

I have some major and minor remarks:

1. Please, explain in details how were the drugs up-titrated for treatment-naive patients. Was selexipag and riociguat up-titrated in the same time period? Was this direct up-front combination? Or was it sequential combination therapy in a short time period?

2. Was the thermodilution also used for cardiac output measurement? The authors described that indirect Fick was used to calculate it, which is imprecise method of analysis according to current standards.

3. Please explain the results of tables 2 and 3. Were the parameters analysed for the same equal number of subjects at the baseline and follow-up?

4. In my opinion the Authors can not present and title table 2 "Changes in clinical parameters among all enrolled patients" when the RHC data were collected only for 18 patients and ECHO parameters for 20 subjects (but the same equal ones?).

5. In my opinion, there should be presented the the results of paired analysis for specific clinical parameters, and that would reflect a real improvement (those who had not completed follow up in a single parameter should be excluded from the analysis).

6. Please explain the supplementary table 1 and one patient who reached maximum tolerated dose of 0.0 mg of macitentan? The doses for riociguat and selexipag are unclear in the table.

7. There is a mismatch between main text and supplementary table 2 regarding the number of treatment naive patients. What was the real number of treatment naive patients?

8. I suggest to remove supplementary figure 1.