Reviewer 2 v.1

Comments to the Author

This is a retrospective single center review of patients with IPF treated with pirfenidone between 2011-2019. 91 patients are presented looking at the safety and efficacy of pirfenidone.

The objectives of the study are clear. In that to explore long term efficacy and safety in a real world setting. Compared to other studies that have been published over the years on the real world safety of pirfenidone in IPF this study has a longer duration of follow up.

91 patients collected over a 8 year period spanning clinical trial, compassionate use and post authorisation (june 2013). This is a relatively small number of 11 patients per year.

This study is not novel as there are other similar studies published of retrospective real world data n=12.

I enclose a number of comments that need addressing:

1. Abstract - Conclusion. Last sentence. I disagree with authors re further long term data required re pirfenidone. There are now numerous real world and post authorisation studies that confirm the safety and effectiveness of pirfenidone. So as a final sentence I would add that this study adds to the growing real world evidence to the safety and efficacy of pirfenidone in IPF.

2. Introduction line 12. References 6-8 are real world studies so I'd make it clear in this sentence that your statement is regarding real world studies. It makes logical sense to reference and discuss the clinical trial data before the open label extension studies and then the real world studies after these. This would make more chronological sense than the order at present which is ref 6-8 real world studies ref 9-10 clinical trials. 11-12 post authorisation studies and 13-14 real world data.

3. Methods: clear. How often were lung function measurements taken?

4. Results. Table 1 : I presume by Typical UIP you mean Definite UIP pattern. I would change this term to definite to be in line with ATS/ERS IPF guidelines

5, I would suggest a small paragraph summarising table 1 and 2 rather that just presenting the tables. Particularly with respect to your lung function findings

6. Page 5 line 50. 10 patients switched from pirfenidone due to disease progression. How did you define progression. Please elaborate

7.Table 2. the mean FVC at pre treatment and baseline look similar yet the percentage FVC change at pretreatment is +6.6%. How is this the case. This is similar with the absolute values.

Similarly the FVC% looks similar at every time point post baseline yet the change in FVC% is very different. Please can this be explained

This is similar with DLCO results.

8. Discussion paragraph 2: May be worth describing the ml decline pre and post treatment.

9. discussion Page 8 Line 5. Term progressive increase in reduction is confusing please clarify/make clear

10. discussion page 8 Line 22. Cant say that pirfenidone prolonged life as no control. I would compare your survival to other published data

11. General comments regarding discussion. Needs rewriting. No limitations discussed. Comment on the fact that HTN and GOR higher than registry data.

84% definite UIP high. Who looked at scans.. ?blinded

PFTs on 40 pre starting treatment limited numbers pre and post PFT data

Please explain drop out rates of patients at 12, 24, 36, 48 months. Not all due to deaths. Were patients lost to follow up. how does this affect your results

Side effects much lower than trials and other real world studies. needs discussion

AE-IPF 26% higher than trials discuss

Limitations not discussed; missing data ; retrospective nature potential bias.

12. Figure 1. Please put statistical results on graph figure and improve legend by explaining the stats

13. Figure 3 . Not sure if it adds anything to the text. consider removing

I am happy to re review once these comments are addressed