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Letter to the Editor

Reply: Comparative Clinical Outcomes of Nintedanib and Pirfenidone in Idiopathic Pulmonary Fibrosis: A Five-Year Real-Life Study

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DEAR EDITOR,

We sincerely thank the authors for their thoughtful comments and their interest in our article entitled "Comparative Long-term Effects of Nintedanib and Pirfenidone in Idiopathic Pulmonary Fibrosis: A Real-life Study with Five-year Follow-up."[1] We appreciate their constructive remarks[2] and the opportunity to further clarify several methodological aspects of our study.

We fully agree that baseline disease severity should be carefully considered when interpreting survival outcomes in idiopathic pulmonary fibrosis (IPF). As noted by the authors, patients in the pirfenidone group had significantly higher Gender–Age–Physiology scores and more extensive radiological involvement at baseline. These findings were explicitly reported in the Results section and further discussed in both the Discussion and Limitations sections of our manuscript. Accordingly, we acknowledged that these baseline differences may have contributed to the observed mortality differences and that our findings should be interpreted with caution, rather than considered definitive evidence of treatment superiority.

We also appreciate the authors' comments regarding treatment switching during follow-up. Treatment switching is an inherent feature of real-world clinical practice and commonly occurs because of adverse events, disease progression, or individual patient characteristics. In our study, treatment-switching rates were transparently reported. To avoid attributing outcomes that occurred after treatment crossover to the initial antifibrotic therapy, patients who switched treatments were excluded from subsequent treatment-specific longitudinal analyses, including the overall mortality comparison presented in Table 5 of our original article.[1] We agree that future studies using time-dependent survival models may further strengthen the evaluation of long-term treatment effects in real-world cohorts.

We are also grateful for the authors' suggestions regarding more advanced survival analyses. Kaplan-Meier survival curves, log-rank testing, multivariable Cox proportional hazards regression models, and propensity score-based approaches are valuable statistical methods for evaluating survival outcomes in observational studies. Our primary objective was to describe long-term real-world clinical outcomes associated with antifibrotic therapy in a retrospective cohort. Considering the retrospective design of our study, baseline heterogeneity between treatment groups, treatment switching during follow-up, and incomplete longitudinal follow-up for some secondary outcomes, we presented direct comparative analyses and

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explicitly acknowledged these methodological limitations in our manuscript. We agree that prospective studies that include larger, more homogeneous patient populations and incorporate advanced survival analyses will provide further insight into the comparative effectiveness of antifibrotic therapies.

Finally, we appreciate the authors' recognition of our study's contribution to the limited body of long-term real-world evidence in IPF. We share their view that future multicenter prospective studies with balanced baseline characteristics and robust survival methodologies will further clarify the comparative effectiveness of nintedanib and pirfenidone.

We thank again the authors for their valuable comments and the editor for providing us with the opportunity to respond.

Footnotes

Authorship Contributions

Concept: A.Y., O.Y., Design: A.Y., O.Y., Data Collection or Processing: A.Y., O.Y., Analysis or Interpretation: O.Y., Literature Search: A.Y., O.Y., Writing: A.Y., O.Y.

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2. Mammadova A. Comparative clinical outcomes of nintedanib and pirfenidone in idiopathic pulmonary fibrosis: a five-year real-life study. *Thorac Res Pract.* 2026;27(5):337-338. **[Crossref]**