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Letter to the Editor

Comparative Clinical Outcomes of Nintedanib and Pirfenidone in Idiopathic Pulmonary Fibrosis: A Five-year Real-life Study

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DEAR EDITOR,

We read with great interest the article by Yanalak and Yazıcı[1] entitled "Comparative Long-term Effects of Nintedanib and Pirfenidone in Idiopathic Pulmonary Fibrosis: A Real-life Study with Five-year Follow-up." The authors should be congratulated for providing valuable five-year real-world data comparing the long-term outcomes of the two currently approved antifibrotic therapies in idiopathic pulmonary fibrosis (IPF). The availability of long-term real-world follow-up remains relatively limited in the literature; therefore, studies such as this provide important evidence that complements randomized clinical trials.[1]

The aim of this letter is to highlight selected methodological considerations that may influence the interpretation of survival outcomes in real-world comparative studies. We would like to emphasize that baseline disease severity should be carefully considered when interpreting survival differences. In the present study, patients receiving pirfenidone had higher gender-age-physiology (GAP) scores and more extensive radiological involvement at baseline, both of which are well-established predictors of mortality in IPF.[2] Therefore, the observed differences in mortality may partially reflect baseline disease severity rather than treatment effect alone. Another important issue is treatment switching during follow-up. A considerable proportion of patients crossed over between antifibrotic therapies, which reflects routine clinical practice and increases the real-world relevance of the study. However, such treatment changes may introduce bias in long-term outcome assessment. Future studies incorporating time-dependent survival models may provide additional insight into the independent effects of antifibrotic therapies.[3]

In addition, because survival was a primary outcome, we believe that more robust survival analysis methods would further strengthen the interpretation of the findings. Kaplan and Meier[4] survival curves with log-rank testing would improve visualization of time-to-event differences between groups. Furthermore, multivariable Cox[5] proportional hazards regression models could help adjust for key baseline confounders such as GAP score and radiological extent. Alternatively, propensity score-based approaches (matching or weighting) may reduce selection bias inherent in observational cohort studies.[6,7]

Overall, this study provides valuable long-term real-world evidence supporting individualized antifibrotic treatment strategies in IPF. Future prospective multicenter studies with more homogeneous baseline characteristics and advanced survival methodologies will further clarify the comparative effectiveness of nintedanib and pirfenidone.

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Footnotes

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