**Topic:** Interstitial Lung Diseases

**Title: Patient-reported treatment satisfaction and tolerability of nerandomilast in IPF and PPF: a pilot real-world study**

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**Introduction:** Nerandomilast, a selective phosphodiesterase-4B inhibitor, has recently emerged as a treatment option for idiopathic pulmonary fibrosis (IPF) and progressive pulmonary fibrosis (PPF). However, real-world data on patient treatment experience remain limited. We aimed to evaluate patient-reported treatment satisfaction and tolerability in patients receiving nerandomilast through a compassionate use program, and to explore the relationship between symptom burden and treatment experience.

**Methods:** We conducted a pilot, observational, cross-sectional study in patients with IPF or PPF receiving nerandomilast. Treatment satisfaction was evaluated with the 9-item Treatment Satisfaction Questionnaire for Medication (TSQM-9), administered via telephone interview after a variable duration of nerandomilast treatment. The TSQM-9 assesses three domains: Effectiveness, Convenience, and Global Satisfaction (each scored from 0 to 100). Patient-reported tolerability was explored using a prespecified 17-item PRO-CTCAE subset covering eight treatment-relevant symptoms with a 7-day recall period (appetite loss, nausea, vomiting, diarrhea, abdominal pain, dizziness, headache, fatigue). Demographic, anthropometric, functional and treatment-related characteristics were also collected. Analyses were primarily descriptive and exploratory. TSQM-9 domain scores were compared across clinically relevant categorical subgroups (including diagnosis, sex, nerandomilast dose, add-on treatment, and presence of treatment-related symptoms) using the Mann-Whitney U test, while associations with continuous or ordinal variables were assessed using Spearman's rank correlation.

**Results and conclusions:** 18 patients were included (12 IPF, 6 PPF; 66.7% male), with a mean age of 76.1 ± 6.3 years and a median nerandomilast exposure of 99 days (IQR 60-123.5). Median pre-treatment FVC and DLCO were 60.5% (54.5-72.8) and 30.0% (26.0-43.0) predicted, respectively. Median TSQM-9 scores (IQR) were 77.8 (55.6-81.9) for Effectiveness, 100 (100-100) for Convenience and 78.6 (71.4-85.7) for Global Satisfaction; 16/18 patients (88.9%) achieved the maximum Convenience score. PRO-CTCAE was evaluable in 17 patients, as one patient had discontinued nerandomilast before the assessment. The most frequently reported symptomatic adverse events were fatigue (64.7%), diarrhea (35.3%) and decreased appetite (29.4%); vomiting was not reported, and 5/6 patients with diarrhea described it as occurring rarely. A higher number of reported symptoms was associated with lower Global Satisfaction ($\rho$=-0.751; $p<0.001$) and perceived Effectiveness ($\rho$=-0.644; $p=0.005$). Patients with gastrointestinal symptoms (n=9) had lower median Effectiveness and Global Satisfaction scores than those without gastrointestinal symptoms (n=8): 61.1 vs 80.6 ($p=0.022$) and 71.4 vs 85.7 ($p=0.041$), respectively.

In this early real-world pilot study, patients reported very high treatment convenience and generally favorable treatment satisfaction. Greater overall symptom burden and the presence of gastrointestinal symptoms were associated with a less favorable treatment experience. These exploratory findings require confirmation in larger cohorts.