Psychometric properties of the Living with Pulmonary Fibrosis (L-PF) questionnaire in patients with idiopathic pulmonary fibrosis

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Objectives

To evaluate the psychometric properties (structural validity, reliability, construct validity and sensitivity to change) of the Living with Pulmonary Fibrosis (L-PF) questionnaire in an idiopathic pulmonary fibrosis (IPF) clinical trial population (FIBRONEER-IPF; NCT05321069).

Introduction

- IPF is characterized by progressive fibrosis, abnormal lung function, and burdensome symptoms that impair patients' quality of life.[1,2]
- The most common symptoms of IPF are dyspnea, cough and fatigue, all of which have been associated with decreased HRQoL in patients.[3]
- The L-PF questionnaire is a 44-item PROM for assessing symptoms (across three domains: dyspnea, cough and energy) and impacts of pulmonary fibrosis. Higher scores indicate greater severity of dyspnea and cough, less energy and greater impacts of the disease.
- L-PF is being used in ongoing trials for patients with IPF, including FIBRONEER-IPF, hence we investigated psychometric properties of this PROM.[3–5]

Methods

- Analyses are based on pooled and blinded data from the Phase 3 double-blind, randomized, placebo-controlled trial, FIBRONEER-IPF (n=1,177), evaluating the efficacy and safety of nerandomilast (BI 1015550) over at least 52 weeks in patients with IPF.[4] Follow-up information was available for 35% of participants at Week 52 (LPAS population).

Structural validity

- CFA was performed sequentially: on a calibration dataset (~50% of randomly selected baseline data), a validation dataset (remaining 50% of baseline data), and using the full available sample at Week 12. CFA using the baseline validation sample is presented here. Model fit indices (CFI, RMSEA, and SRMR) were used to evaluate appropriateness of the factor structure.
- Symptoms domain was represented as a second-order factor structure with two correlated factors: one factor including all 21 impacts items and another second-order factor including dyspnea, cough, and energy sub-domains. Psychometric properties of the domains as per this factor structure were assessed in reliability, construct validity and sensitivity to change analyses.

Reliability

- Internal consistency was assessed using Cronbach's α coefficient and McDonald's ω for each L-PF domain or sub-domain score at baseline and Week 12.
- Test-retest reliability from baseline to Week 12 was assessed using ICC for each domain and sub-domain score of L-PF on a population subset of stable patients as defined by the selected indicator measures.

Construct validity

- Correlations with convergent validity indicator measures were assessed at baseline and Week 12.
- Known-groups validity was assessed at baseline and Week 12; effect size was calculated as the mean difference in L-PF scores between groups divided by the pooled SD (i.e. Cohen's d).

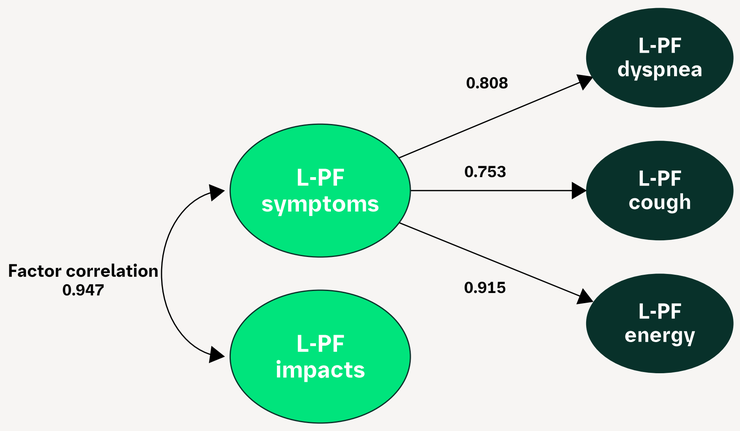
Sensitivity to change

- This was examined using correlations and separate analysis of covariance at baseline and Week 52. The analysis was performed on the LPAS population.

Structural validity

- The factor structure of L-PF showed adequate model fit for baseline validation analyses (CFI 0.897; RMSEA 0.102; SRMR 0.101). Results obtained at Week 12 were similar.
- High second-order factor loadings confirmed that symptoms sub-domains were consistent with each other.

Factor structure with second-order factor loadings in the validation sample at baseline



Reliability

- L-PF domain and sub-domain scores were shown to have acceptable-to-high Cronbach's α and McDonald's ω.
- Overall, test-retest reliability (as shown by ICC) was acceptable.

Internal consistency and test-retest reliability

Score	Cronbach's α[a]	McDonald's ω[a]	ICC[b]
Dyspnea	0.94–0.95	0.94–0.95	0.83
Cough	0.89	0.92	0.81
Energy[c]	0.72–0.76	0.76–0.77	0.69–0.71
Symptoms	0.94	0.94	0.80
Impacts	0.95	0.95–0.96	0.78–0.84

[a]Range is presented for values for baseline and Week 12. [b]Range is presented for L-PF-I20 and L-PF-I21 for energy, and EQ-5D-self-care and EQ-5D-usual activities for impacts. These indicator measures were used to define a stable population. [c]The lower reliability of L-PF energy may be due to the absence of an energy-specific indicator measure, as L-PF-I20 and L-PF-I21 measured overall health instead.

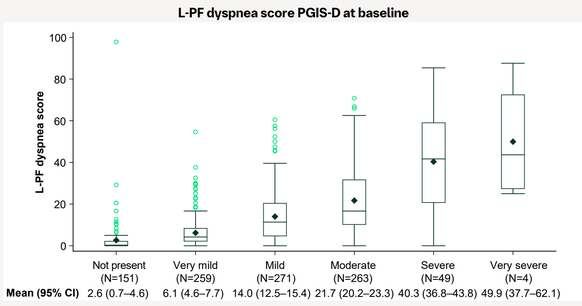
Construct validity

Correlation coefficients between L-PF scores and the selected indicator measures

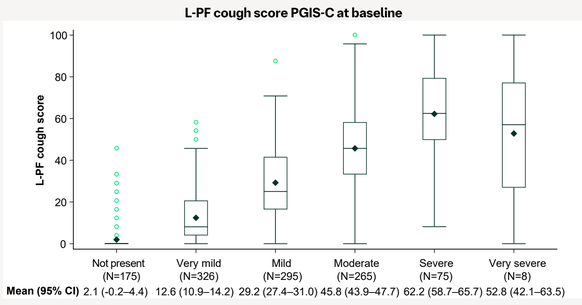
Time point/convergent validity measures	Dyspnea	Cough	Energy	Symptoms	Impacts
Baseline					
EQ-5D-self-care	0.559	0.391	0.520	0.584	0.642
EQ-5D-usual activities	0.615	0.419	0.602	0.620	0.714
EQ-5D-visual analog scale	-0.482	-0.342	-0.487	-0.473	-0.571
FVC (mL)	-0.281	-0.192	-0.245	-0.239	-0.289
FVC (% predicted)	-0.310	-0.238	-0.194	-0.235	-0.291
DLco (% predicted)	-0.348	-0.240	-0.198	-0.249	-0.306
Week 12					
EQ-5D-self-care	0.660	0.413	0.591	0.639	0.635
EQ-5D-usual activities	0.679	0.454	0.647	0.664	0.741
EQ-5D-visual analog scale	-0.556	-0.348	-0.549	-0.514	-0.586
FVC (mL)	-0.294	-0.188	-0.210	-0.214	-0.292
FVC (% predicted)	-0.329	-0.244	-0.177	-0.242	-0.306
DLco (% predicted)	-0.372	-0.288	-0.268	-0.314	-0.342

|r|<0.40 (weak); |r|≥0.40 and |r|<0.60 (moderate); |r|≥0.60 (strong)

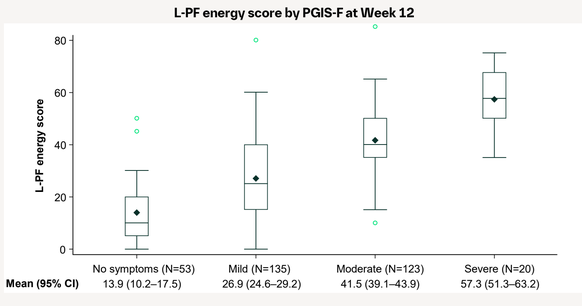
L-PF dyspnea score PGIS-D at baseline



L-PF cough score PGIS-C at baseline



L-PF energy score by PGIS-F at Week 12



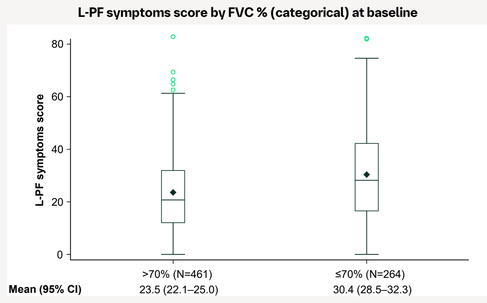
Convergent validity

- Generally, moderate-to-strong correlations were observed for EQ-5D-self-care, EQ-5D-usual activities and EQ-5D-visual analog scale.
- Correlations with clinical measures (FVC [mL], FVC [% predicted] and DLco [% predicted]) were observed in the expected direction, albeit weak.

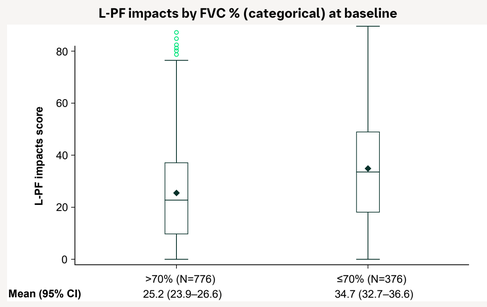
Known-groups validity analysis

- Results confirmed the expected differences in L-PF scores between groups as defined by the indicator measures, which included FVC % predicted and three PGIS scales for shortness of breath (PGIS-D), cough (PGIS-C) and energy (PGIS-F).

L-PF symptoms score by FVC % (categorical) at baseline

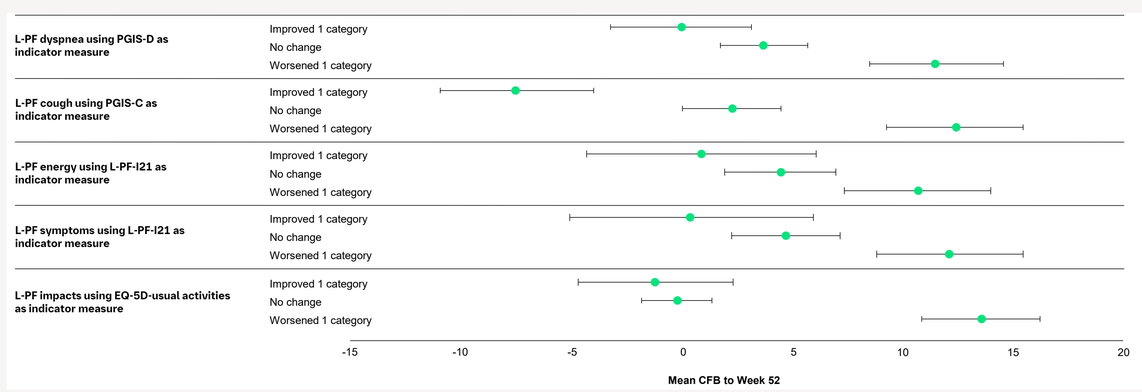


L-PF impacts by FVC % (categorical) at baseline



Sensitivity to change

- Statistically significant change (all p<0.001) was observed between groups defined by change in the indicator measures, providing supportive evidence for the sensitivity to change of all L-PF domain and sub-domain scores.



Conclusions

This study provided evidence for the structural validity, construct validity, reliability and sensitivity to change of the L-PF questionnaire in an IPF clinical trial population.

Overall, the L-PF questionnaire is a valid and reliable measure of patient-reported symptoms and severity of impacts in patients with IPF for potential use in clinical trials and clinical practice.

Abbreviations

CFA, confirmatory factor analysis; CFB, change from baseline; CFI, comparative fit index; CI, confidence interval; DLco, diffusing capacity of the lungs for carbon monoxide; EQ-5D, EuroQoL 5-dimension questionnaire; FVC, forced vital capacity; HRQoL, health-related quality of life; ICC, intraclass correlation coefficient; IPF, idiopathic pulmonary fibrosis; LPAS, longitudinal psychometric analysis set; L-PF, Living with Pulmonary Fibrosis scale; L-PF-I20, Living with Pulmonary Fibrosis scale Impacts item 20; L-PF-I21, Living with Pulmonary Fibrosis scale Impacts item 21; PGIS-C, patient's global impression of severity - cough; PGIS-D, patient's global impression of severity - dyspnea; PGIS-F, patient's global impression of severity - fatigue; PROM, patient-reported outcome measure; RMSEA, root mean square error of approximation; SD, standard deviation; SRMR, standardized root mean squared residual.

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Disclosures

AS-B and KS are employees of IQVIA, which received funding from Boehringer Ingelheim to conduct this study. KF, AL, PP and IJ are employees of Boehringer Ingelheim. JS is developer of L-PF and conducts paid consultancy work for Boehringer Ingelheim, AbbVie, Astra Zeneca, Avalyn, BMS, GSK, Liquidia, Pliant, Puretech, Quench and Tvardi.

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