Correlation of early cough with disease activity measured by high-resolution CT in ATLAS: a phase 1b study of inhaled pirfenidone in idiopathic pulmonary fibrosis

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POSTER PA691
12.02
ILD/DPLD of known origin
Idiopathic pulmonary treatments
Diagnosis

INTRODUCTION

- Cough is a prevalent symptom of idiopathic pulmonary fibrosis (IPF).
- While the manifestation of early cough (EC) may relate to a response to the nebulization procedure, its correlation with structural characteristics may reveal another underexplored etiology.

AIMS

- This study aimed to explore the incidence and implications of EC in a cohort of 91 subjects with IPF enrolled in the phase 1b AP01-002 clinical trial (ATLAS[1]) of 50 mg once daily (qd) and 100 mg twice daily (bid) aerosolized pirfenidone.

METHODS

- This phase 1b, randomized, open-label, dose-response trial assessed the safety, tolerability, and efficacy of inhaled pirfenidone (AP01) in IPF.
- Patients with forced vital capacity (FVC) 40%–90% predicted, and intolerant, unwilling, or ineligible for oral pirfenidone or nintedanib were randomized to nebulized AP01 50 mg once per day or 100 mg two times per day for 24 weeks.
- Among 70 participants who underwent baseline and 24-week high-resolution computed tomography (HRCT) scans, 69 scans were deemed acceptable in image quality.
- Participants were categorized by the onset day of cough: EC (≤10 days), late cough (>10 days), and no cough.
- Quantitative assessments of ground glass (QGG) and lung fibrosis (QLF) were derived from HRCT.
- Multivariable linear regressions assessed the relationship between cough and HRCT changes.

RESULTS (1)

- The distribution of participants reporting EC, late cough, and no cough was 14.5% (N=10), 15.9% (N=11), and 69.6% (N=48), respectively.

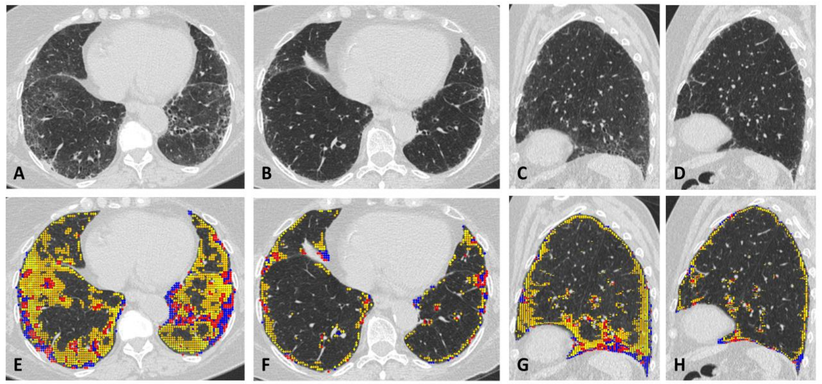

Figure 1 A, B, C, and D: axial and sagittal HRCT images; E, F, G, and H: overlaid quantitative results of the corresponding images of A, B, C, and D. Blue and red dots indicate the results of QLF classification; yellow dots indicate the ground glass. A and C: from the baseline CT. B and D: from the 6-month follow-up CT scans. QLF score in whole lung was 8.5% at baseline and 4.9% at 6-month follow-up. QLF volume in whole lung was 258.2 mL at baseline and 154.2 mL at 6-month follow-up. The QLF in the left lower lobe, especially, was reduced from 23.7% (90.6 mL) to 10.6% (45.2 mL).

	No Cough	Late Cough	Early Cough
QLF (%) Mean ± SD P50 ± IQR	15.87 ± 10.67 13.00 ± 15.80	15.64 ± 8.89 14.05 ± 9.10	12.15 ± 6.04 10.85 ± 9.30
QGG (%) Mean ± SD P50 ± IQR	18.93 ± 6.72 17.35 ± 12.00	16.49 ± 4.04 16.45 ± 5.60	17.91 ± 8.00 16.65 ± 9.60
QHC (%) Mean ± SD P50 ± IQR	0.57 ± 0.83 0.20 ± 0.70	0.35 ± 0.20 0.30 ± 0.30	0.33 ± 0.30 0.25 ± 0.40

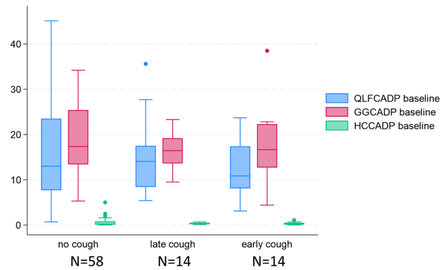

Figure 2: Figure 2 Baseline quantitative HRCT findings comparing EC group with non-EC.

RESULTS (2)

	No Cough	Late Cough	Early Cough
Δ QLF Mean ± SD P50 ± IQR	0.77 ± 5.67 0.30 ± 4.00	2.37 ± 3.18 2.00 ± 4.90	-1.17 ± 6.23 0.95 ± 6.50
Δ QGG Mean ± SD P50 ± IQR	-0.06 ± 4.09 -0.05 ± 3.90	1.15 ± 3.14 0.30 ± 5.10	-2.47 ± 5.96 -0.50 ± 8.30
Δ QHC Mean ± SD P50 ± IQR	-0.02 ± 0.88 0.00 ± 0.40	0.02 ± 0.36 0.00 ± 0.30	0.08 ± 0.30 0.10 ± 0.30

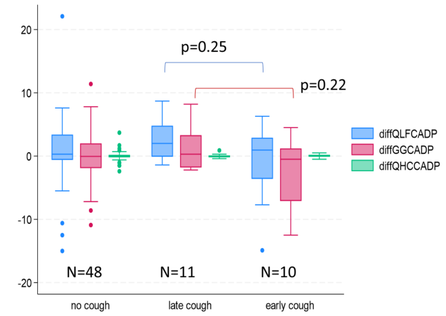

Figure 3 Delta (6 month – baseline) quantitative HRCT findings comparing EC group with non-EC.

- Mean (SD) HRCT changes in the EC, late, and no cough groups were - 2.5% (6.0), -0.1% (4.1), and 1.2% (3.1) for QGG, and -1.2% (6.2), 2.4% (3.2), and 0.8% (5.7) for QLF, respectively.
- Participants with EC were predominantly female, had less extensive interstitial lung disease at baseline HRCT, and showed significant reductions in QGG compared to those without cough (p=0.034, 95% confidence interval [-6.2, -0.3]).
- No significant changes in QLF were observed with EC.

CONCLUSIONS

- Early cough was associated with a reduction in ground glass opacities at week 24, thought to represent an inflammatory process.
- Early cough may serve as a useful surrogate marker of treatment response and warrants further exploration in future studies.

PRESENTING AUTHOR DISCLOSURES
Dr. Kim was issued patent 2016-635-1 and is a consultant for Voiant.

1. West A et al. *Thorax.* 2023 Sep; 78(9): 882-889.