Inhalation innovation: phase 2b study design of inhaled pirfenidone in the treatment of progressive pulmonary fibrosis

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INTRODUCTION

- Progressive pulmonary fibrosis (PPF) is an increasingly recognized condition, defined in 2022 to address the progression of pulmonary fibrosis in patients with interstitial lung diseases (ILDs) other than idiopathic pulmonary fibrosis (IPF).[1]
- Oral pirfenidone has been studied in non-IPF ILDs but never achieved a statistically significant change in a primary endpoint. In those studies, primary endpoints were not focused on FVC change. Trends seen in forced vital capacity (FVC) change (a secondary endpoint in those studies) support efficacy in PPF.[2-4]
- Data from the AP01-002 (ATLAS) Study of inhaled pirfenidone in IPF demonstrated efficacy and improved safety compared to that historically seen with oral pirfenidone.[5]

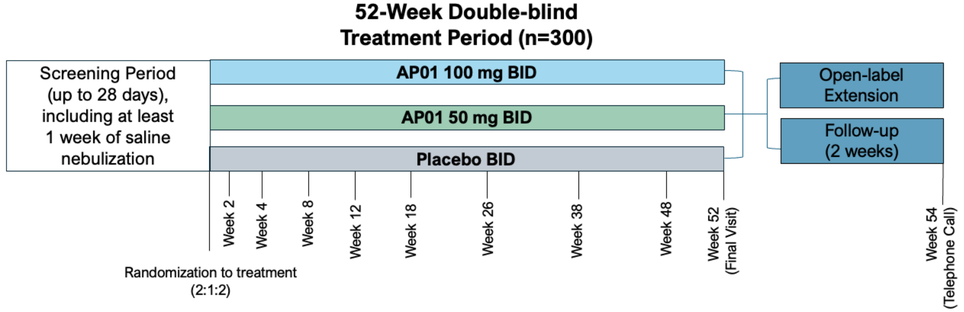
AIMS

- The AP01-007 (MIST Study) is designed to evaluate the efficacy and safety of AP01 (aerosolized pirfenidone) in patients with PPF.

METHODS

- In this Phase 2b study, patients will be randomized 2:1:2 to 1of 3 treatment arms: AP01 100 mg BID, AP01 50 mg BID, or placebo BID by oral inhalation using the investigational PARI eFlow® Nebulizer System.
- Patients can remain on background immunosuppression, and up to 30% of patients can remain on background oral nintedanib therapy.
- Cough will be analyzed through assessment of reported adverse events of cough and cough questionnaires, which should allow differentiation of cough related to PPF vs. the nebulization procedure.

STUDY DESIGN



KEY INCLUSION CRITERIA

PPF Diagnosis*

Physiologic evidence of progression within at least 1 of the following criteria:

- Relative decline in FVC ≥ 10% predicted within the previous 24 months compared to Screening visit 1
- Relative decline in FVC ≥ 5% to < 10% predicted within the previous 24 months compared to Screening visit 1 with at least 1 of the 2 following criteria:
  - Worsening respiratory symptoms **OR**
  - Radiological (high-resolution computed tomography [HRCT]) evidence of disease progression
- Worsening of respiratory symptoms **AND** radiological (HRCT) evidence of disease progression per a local or central radiologist

*At the time of poster submission, the trial application was under review via EU CTR

PFT Criteria at Screening Visit

- FVC ≥ 45% of predicted normal at Screening visit 1
- Forced expiratory volume (FEV_1)/FVC ≥ 0.7 or ≥ age-adjusted lower limit of normal (LLN) at Screening visit 1
- DLCO ≥ 30% of predicted, corrected for hemoglobin at Screening visit 1

Prior Therapy

- Patients on background oral nintedanib must have been on treatment for at least 6 months
- Patients on standard of care background immunosuppression must have been on therapy for at least 12 weeks prior to screening and 6 months for rituximab

KEY EXCLUSION CRITERIA

- Diagnosis of IPF
- Significant clinical worsening of PPF between Screening visits 1 and 3
- Previous or current treatment with oral pirfenidone within 3 months prior to Screening
- Extent of emphysema is greater than the extent of fibrosis on HRCT

ENDPOINTS

Primary Endpoint

- Change from baseline in FVC (mL) at Week 52

Secondary Endpoints

- Absolute change from Baseline in QoL measurements as assessed by Living with Pulmonary Fibrosis Symptoms and Impact Questionnaire total score at Week 52
- Time to disease progression. Disease progression is defined as absolute FVC percent predicted decline of ≥10% prior to Week 52
- Change in lung fibrosis score based on HRCT from Baseline to 52 weeks

SAFETY

- Incidence of adverse events and serious adverse events
- Incidence of treatment-emergent deaths
- Changes from Baseline in vital signs, physical examination, and body weight
- Changes from Baseline in clinical laboratory tests (hematology, serum chemistry, urinalysis, and urinary creatinine clearance)
- Changes from Baseline in electrocardiogram pattern

CONCLUSIONS

- MIST will study the safety and efficacy of AP01 (aerosolized pirfenidone) in patients with PPF.
- In addition to the safety and efficacy endpoints, MIST will carefully examine the presence of cough in this population of patients.

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PRESENTING AUTHOR DISCLOSURE
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