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Inhalation innovation: phase 2 study design of inhaled nintedanib in the treatment of idiopathic pulmonary fibrosis

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BACKGROUND

- Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive form of fibrotic interstitial lung disease (ILD) characterized by cough and dyspnea[1]. The prognosis of patients with IPF is poor, with median life expectancy of 3 to 4 years after diagnosis if left untreated[2].
- Clinical trials with oral nintedanib demonstrated a reduction in the annual rate of decline in FVC, however its use is often limited by tolerability due to the side effects such as diarrhea and elevated liver enzymes[3-4].
- AP02 is a novel solution for inhalation of nintedanib being investigated with the intent to increase delivery to the lungs while reducing systemic exposure. Data from the phase 1 dose ranging study of inhaled nintedanib in healthy volunteers and IPF patients demonstrated acceptable safety.[5]

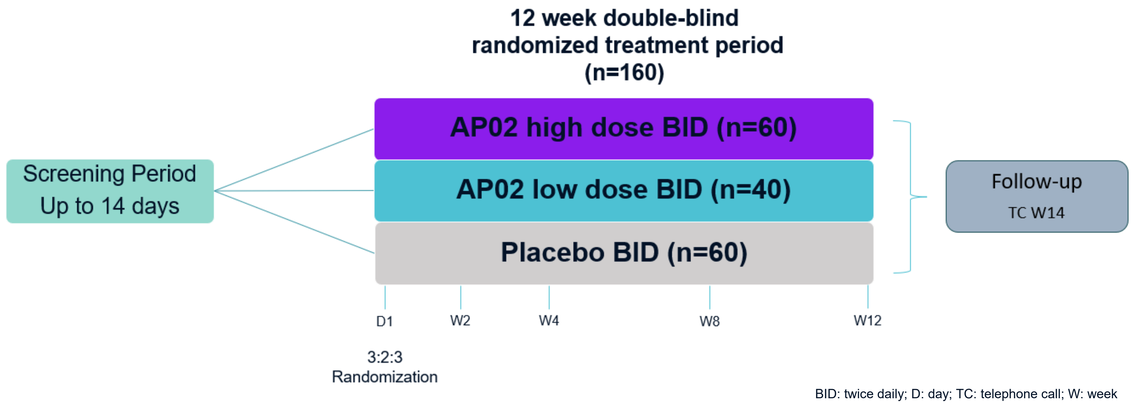
AIMS

- AURA-IPF[6] (NCT07194382) is a phase 2 proof of concept study to evaluate the safety, tolerability, and efficacy of 2 doses of AP02 compared to placebo in patients with IPF over 12 weeks to further guide clinical development and dose selection of AP02 as a potential new treatment option for IPF[6].

METHODS

- Target number of participants: 160
- Patients will be randomized 3:2:3 to 1 of 3 treatment arms: AP02 high dose BID, AP02 low dose BID, or placebo BID.
- Both AP02 and placebo will be administered by oral inhalation using the PARI eFlow Nebulizer System.
- Cough will be analyzed through assessment of reported adverse events of cough and the use of cough questionnaires, which should allow differentiation of cough related to IPF vs. the nebulization procedure.

STUDY DESIGN



BID: twice daily; D: day; TC: telephone call; W: week

KEY INCLUSION CRITERIA

- Age ≥40 years
- A diagnosis of IPF according to international guidelines[1] within 5 years of visit 1
- Combination of HRCT pattern, and if available, surgical lung biopsy pattern consistent with a diagnosis of IPF
- FVC ≥45% predicted normal
- DLCO >30% to <80% predicted of normal

KEY EXCLUSION CRITERIA

- Current treatment with oral nintedanib or oral pirfenidone, or previous treatment with oral nintedanib or pirfenidone within at least 3 months prior to screening. Participants who previously received combination modality therapy with oral nintedanib and pirfenidone will be excluded.
- Any other investigational therapy received within the 30 days prior to screening
- FEV_1/FVC ratio < 0.7 as per Global Lung Function Initiative LLN

PATIENT POPULATION

- IPF treatment-naïve patients
- IPF patients previously treated with oral nintedanib or pirfenidone who discontinued 3 months prior to screening

RESTRICTED MEDICATIONS

- Oral pirfenidone, or any other drug indicated for the treatment of IPF
- Azathioprine, cyclophosphamide, cyclosporine A within 8 weeks prior to screening
- Prednisone >15 mg/day within 2 weeks prior to screening
- Vaccines for influenza, respiratory syncytial virus, pneumonia, or COVID-19 received within 2 weeks prior to screening

DLCO: diffusing capacity of the lungs for carbon monoxide, FEV: forced expiratory volume, FVC: forced vital capacity, HRCT: high-resolution computed tomography, LLN: lower limit of normal, LCQ: Leicester cough questionnaire, L-PF: living with pulmonary fibrosis questionnaire

ENDPOINTS

PRIMARY ENDPOINT

- Change from baseline in FVC (mL) at week 12

SECONDARY ENDPOINTS

- Time to disease progression
- Quantitative change from baseline in lung fibrosis on HRCT at week 12

EXPLORATORY ENDPOINTS

- Change in Cough Severity Numerical Rating Scale from baseline to week 12
- Absolute change from baseline in LCQ total score at week 12
- Absolute change from baseline in L-PF total score, dyspnea and impact domain scores at week 12

SAFETY ASSESSMENTS

- 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 in electrocardiogram pattern

CONCLUSION

- AURA-IPF will evaluate the safety and efficacy of AP02 (nintedanib solution for inhalation) in patients with IPF.
- In addition to the safety and efficacy endpoints, AURA-IPF will carefully examine cough in this population of patients.

REFERENCES:
1. Raghu et al. Am J Respir Crit Care Med. 2022;205(9): e18-e47
2. Maher et al. Respir Res (2021) 22:197
3. EPAR OFEV: https://www.ema.europa.eu/en/medicines/human/EPAR/ofev (last access Aug 14, 2025)
4. Chaudhuri N et al. Adv Ther. 2024 Dec;41(12):4581-4590
5. Palacios et al. Am J Respir Crit Care Med 2025;211:A2088.
6. https://clinicaltrials.gov/study/NCT07194382 (last access Sep 29, 2025)

AUTHOR DISCLOSURES:
Michael Kreuter has received renumeration for counseling with Boehringer Ingelheim and Avalyn;

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