Long-term Safety Data of Inhaled Pirfenidone (AP01) in Idiopathic Pulmonary Fibrosis (IPF) and Non-IPF Interstitial Lung Disease (ILD) Patients

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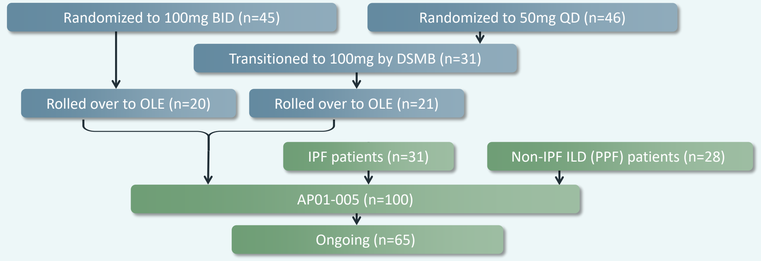
OBJECTIVES

Oral pirfenidone reduces FVC decline compared to placebo in Idiopathic Pulmonary Fibrosis (IPF), albeit with side effects[1]. AP01 is an aqueous pirfenidone formulation optimized for nebulization and inhaled administration. A 100mg of AP01 delivers pulmonary pirfenidone concentrations 35 times higher than that following an 801mg oral dose with 1/15 the systemic exposure[2]. AP01-002 was a two-part, 72 week open-label study in IPF patients comparing 50 mg once daily with 100 mg twice daily[3]. AP01-005 is a follow-on open-label extension study of 100mg AP01 twice daily in interstitial lung disease (ILD) patients who were in AP01-002 (IPF patients only), and patients that were antifibrotic medication intolerant, ineligible for antifibrotics due to national guidelines, diagnosed with chronic progressive fibrosing ILD, or with other types of primary or secondary ILD. Here we report long-term safety results in AP01-naïve patients from AP01-005. This study is the first use of inhaled AP01 in a cohort not exclusively including IPF.

METHODS

A total of 59 AP01- naive patients were enrolled into the study. The interim results from June 11, 2021 (enrollment) to March 8, 2023, are presented.

AP01-005 OPEN LABEL EXTENSION STUDY DESIGN



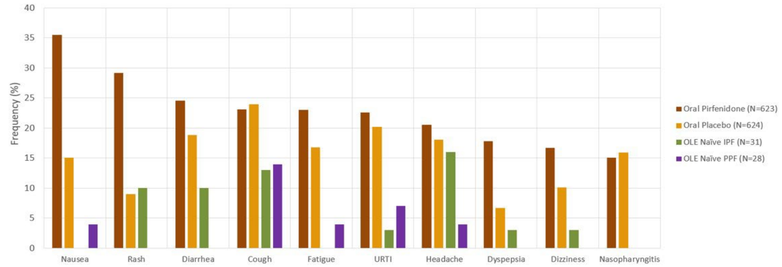
RESULTS

Of 100 patients enrolled (41 rollover, 31 naïve IPF, and 28 naïve PPF), 71 patients completed at least 48 weeks and 8 rollover patients completed more than 3 years on AP01. The 100 mg BID initial clinic doses were safe and well-tolerated. No adverse effects on respiratory rate, spirometry or oxygenation were observed during or following drug administration. The top three treatment emergent adverse events were LRTI, Cough and COVID-19. Some rollover subjects have taken AP01 for over 3 years.

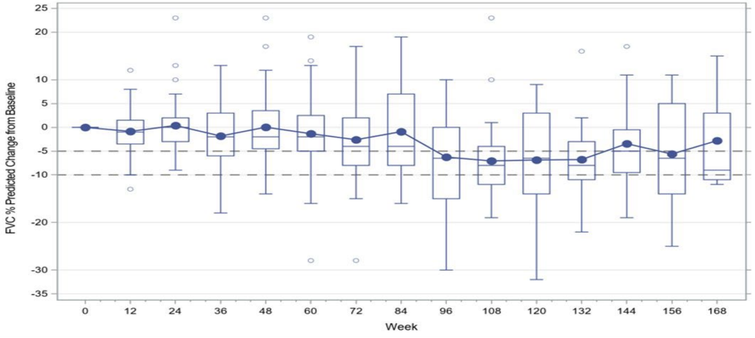
AP01-005 BASELINE CHARACTERISTICS

Variable	AP01 Naïve: -005 IPF (N=31)	AP01 Naïve: -005 PPF (N=28)	AP01-005 Rollover (N=41)	AP01-002 100 mg BID (N=45)
Europe Region, n(%)	18 (58)	14 (50)	22 (54)	24 (53)
Age, mean (SD)	71.2 (9.47)	63.8 (11.59)	74.0 (7.82)	71.3 (8.08)
Male Sex, n(%)	17 (55)	12 (43)	28 (68)	32 (71)
Duration of Diagnosis, mean (SD)/median (range)	2.4 (2.00) 2.3 (0.0 – 6.2)	3.1 (2.95) 2.4 (0.2 – 13.2)	002 entry: 2.1 (1.46) 2.0 (0.1 – 5.0) 005 entry: 3.7 (1.48) 3.8 (1.7 – 6.7)	2.1 (1.44) 2.3 (0.1 -4.9)
Disease Severity at Baseline, n (%)				
≤ 65 % predicted	5 (16)	11 (39)	002: 11 (27) 005: 12 (31)	14 (31)
>65 and <80	8 (26)	8 (29)	002: 18 (44) 005: 18 (46)	21 (47)
≥80	18 (58)	9 (32)	002: 12 (29) 005: 9 (23)	10 (22)
FVC % Predicted at Baseline, mean (SD)	84.6 (18.00)	75.3 (20.46)	002: 73.5 (10.46) 005: 71.8 (13.46)	72.1 (9.81)

AP01 SAFETY PROFILE



AP01 ROLLOVER IPF FVC % PRED CHANGE FROM BASELINE



CONCLUSIONS

Based on the interim long-term safety data analyzed in AP01- 005, findings demonstrate that AP01 continues to be well-tolerated in patients with ILD, including IPF. Serious safety indicators were not observed, and the observed tolerability has been better than tolerability published on oral antifibrotics.

REFERENCES:

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2. Khoo, J. K. et al. A Randomized, Double-Blinded, Placebo-Controlled, Dose-Escalation Phase 1 Study of Aerosolized Pirfenidone Delivered via the PARI Investigational eFlow Nebulizer in Volunteers and Patients with Idiopathic Pulmonary Fibrosis. Journal of Aerosol Medicine and Pulmonary Drug Delivery 33, 15–20 (2020).
3. West, A. et al. Inhaled pirfenidone solution (AP01) for IPF: a randomised, open-label, dose–response trial. Thorax (2023) doi:10.1136/thorax-2022-219391.

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