Inhaled pirfenidone (AP01) forced vital capacity (FVC) data from the ATLAS study vs placebo from 3 historical idiopathic pulmonary fibrosis (IPF) randomised controlled trials (RCTs)

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Introduction and Aims

The open-label Phase 1b ATLAS study compared the safety and tolerability of two doses of inhaled pirfenidone (AP01) 100 mg twice daily (bid) and 50 mg once daily (qd) in IPF. In light of the disease severity and availability of licensed treatments an active control was selected (ie 50mg once daily).

Progression of FVC over 48 weeks was modeled by a linear regression with random intercept and slope effects. The study demonstrated a statistically significant benefit of AP01 100mg BID compared to 50mg QD, based on the slopes of mean change in FVC % predicted over 48 weeks −0.4% [95% CI: −3.2, 2.3] vs −4.9% [−7.5, −2.3], respectively. The difference in slopes (100mg BID − 50mg QD) was 4.5% (95% CI: 0.7, 8.2; p=0.022, equating to 154 ml [95% CI: 25, 284]) at 48 weeks (1)

To evaluate the effectiveness of AP01 100 mg bid relative to placebo from previously-conducted pivotal ILD studies, meta-analysis was performed.

Methods

Placebo groups were collected from available data for 4 reference studies — INPULSIS-1 and INPULSIS-2 (2), INBUILD (3) and ASCEND (4)

To account for key population differences between ATLAS and reference studies, weights were assigned to ATLAS subject values to match the mean baseline characteristics of each reference study

The following baseline characteristics were used to normalize populations across studies

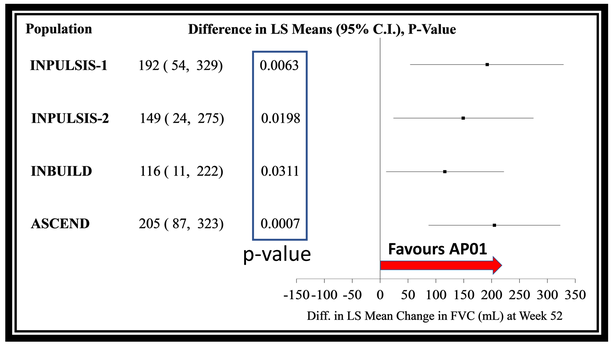
- Age
- Sex
- Baseline FVC percent predicted
- Baseline DLco percent predicted
- Time since diagnosis (excluded for INBUILD as data not available)

A random slopes model was used to estimate the mean annual rate of FVC decline in the AP01 100mg BID arm; estimates were compared by Z-test to the published RCT placebo rates (5). The same approach was used to compare 50 mg qd with placebo in each reference study.

Results

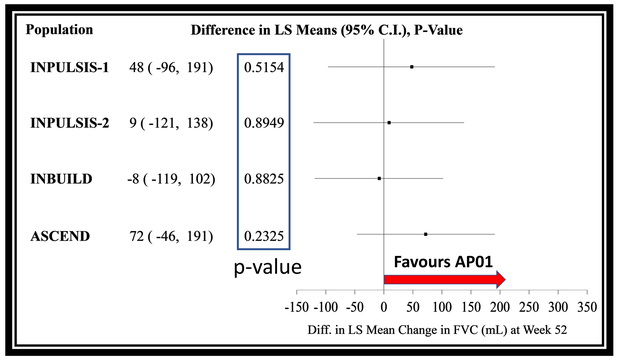
AP01 100 mg bid

Statistically-significant benefit (p<0.05) vs placebo from all studies



AP01 50 mg qd

Results comparable to placebo in all studies



Conclusion

This analysis suggests that 100mg bid of nebulised pirfenidone has superior efficacy compared to placebo

In contrast, the lower dose (50mg qd) was comparable to placebo, supporting 50mg qd as a non-effective dose.

These findings build on the existing data from the ATLAS study which showed the superiority of 100 mg bid to 50 mg qd

The results support the continued clinical development of nebulised AP01 in fibrotic lung diseases.

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