Buloxibutid's Efficacy in the Phase 2a AIR IPF Trial: Comparative Analysis of Baseline Characteristics of Indian Versus World Cohorts

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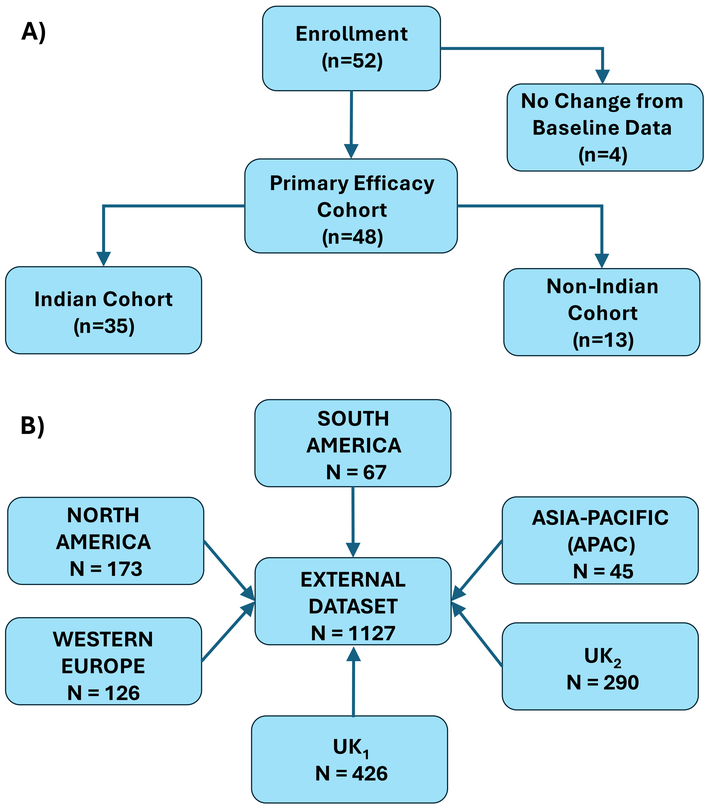
Introduction

Buloxibutid is a first-in-class angiotensin II type 2 (AT2) receptor agonist in clinical development for idiopathic pulmonary fibrosis (IPF). The AIR trial (ClinicalTrials.gov ID NCT04533022) was a multicentre, open-label, single-arm phase 2a trial which investigated the safety and efficacy of Buloxibutid in patients with IPF. In patients treated with Buloxibutid, stabilization and improvement in FVC was observed [1]. Since many of the enrolled patients were from India, this analysis compared their baseline characteristics to those of a global external dataset of treatment-naive IPF patients.

Methods

The AIR trial enrolled 52 patients at 21 sites in India, Russia, Ukraine, and the UK. Four patients with no change from baseline FVC data were excluded from the efficacy analysis. Of the remaining 48 patients 35 were from India (Figure 1.a). An external IPF cohort was drawn from the OSIC and two UK datasets (Figure 1.b). Comparison of the external cohort with AIR patients was performed on seven clinical and two high-resolution computed tomography (HRCT) baseline features. The similarity between cohorts was assessed using univariable χ^2, *t*, and Mann-Whitney tests and a multivariable maximum mean discrepancy (MMD) test [2]. Dimensionality reduction to two dimensions was performed using the Isomap algorithm [3].



Clinical Features: Sex, Age, Forced vital capacity (FVC, L), Forced Expiratory Volume in 1s (FEV_1, L) , FEV_1/FVC, FVC (% predicted), FEV_1 (%predicted);
HRCT Features: Lung Volume (L); Fibrosis Volume (%);

Figure 1. Schematic of cohort comparison experiments. **A)** Overview of the AIR trial population; **B)** Overview of the external data and baseline features.

Baseline Characteristics of AIR and External Cohorts

Quantitative comparison on baseline characteristics between the AIR patients in the primary efficacy cohort and the external dataset showed similarity on sex, age, FEV_1/FVC, FVC (% predicted), and FEV_1 (% predicted). Statistically significant differences were observed on FVC (L), FEV_1 (L), Lung Volume (L), and Fibrosis Volume (%). The overall multivariate distributions were found not to be statistically significantly different (p_{MMD} = 0.057). Due to smaller lung function volume and HRCT lung volume, and higher fibrosis percentage, the baseline distribution of the Indian patients in AIR was statistically different from that of the external dataset (p_{MMD} = 0.013).

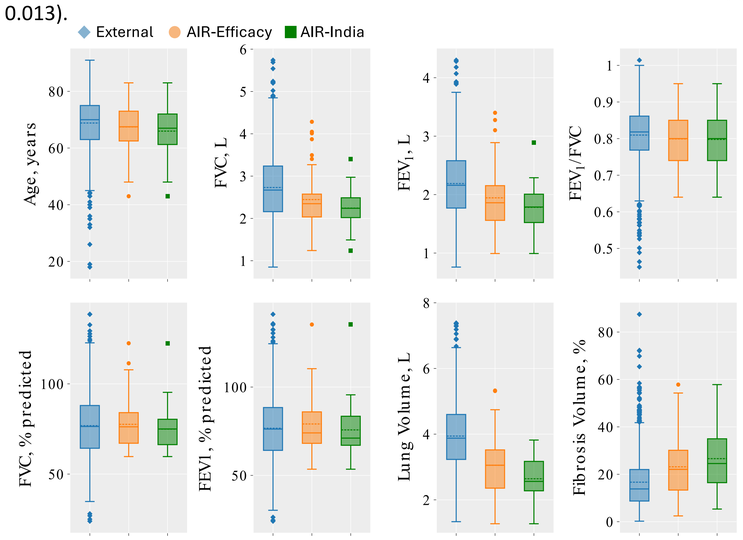


Figure 2. Baseline characteristics of the AIR cohort and the external dataset. Mean values are represented with a dashed line.

Dimensionality Reduction

Isomap-based dimensionality reduction from nine to two dimensions was used to visualise baseline characteristics. AIR–India (green) and AIR–Other (orange) patients are shown relative to the external cohort (blue). The combined AIR primary efficacy cohort occupies a similar region of the embedded space as the external dataset, consistent with comparable baseline profiles.

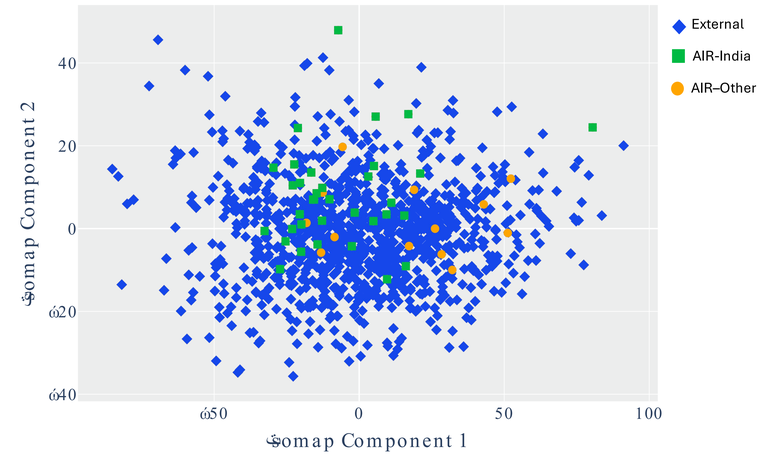


Figure 4. Visualisation of the study distributions using dimensionality reduction to two dimensions based on the Isomap algorithm.

Distance between the Baseline Distributions

Except for Lung Volume (L), the Hedge's g distances between the primary efficacy cohort and the external dataset are small to medium. The increased distance between the external cohort and the subset of patients from India on absolute lung function and HRCT features is in part due to the smaller average height of the latter: 1.74m (SD=0.10m, N=825) versus 1.59m (SD=0.08m, N=35), respectively.

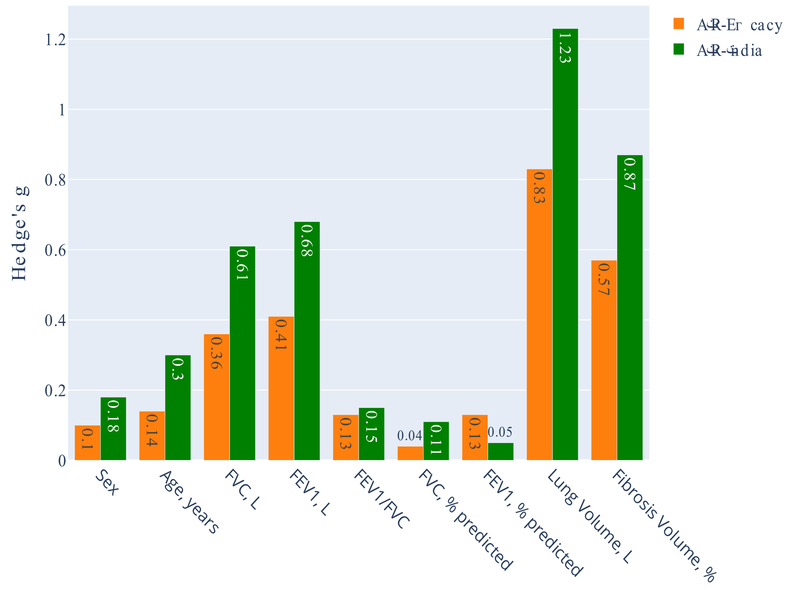


Figure 3. Univariate distances between the AIR cohort and the external set of IPF patients. Hedge's g – standardized mean difference.

Conclusions

- ❑ While % predicted features were similar, absolute lung volumes were smaller in Indian patients probably due to their small height and higher fibrosis content.
- ❑ Overall, the Indian subgroup of AIR patients falls within the global distribution of clinical and HRCT features.
- ❑ These findings support the overall generalizability of the AIR trial results.
- ❑ Buloxibutid is currently being investigated in a global 52-week Phase 2b study (ASPIRE).

References

1. Ganslandt C, Maher TM, Molyneaux, PL, et al. American Journal of Respiratory and Critical Care Medicine 2025;211(suppl 1):A7747..
2. Gretton A, Borgwardt KM, Rasch MJ, et al. Journal of Machine Learning Research 2012;13:723-773.
3. Tenenbaum JB, Silva V, Langford JC, Science 290;5500:2319-2323.

Conflicts of Interest

Kirov, Thillai and Walsh are employees of Qureight Ltd. Van den Blink, Mousa, Santermans and Lindmark are employees of Vicore Pharma AB. This work is funded by Vicore Pharma AB and Qureight Ltd.

ATS 2026