Design and rationale for a phase 3 trial of admilparant (BMS-986278), an oral lysophosphatidic acid receptor 1 antagonist, in patients with idiopathic pulmonary fibrosis: ALOFT-IPF

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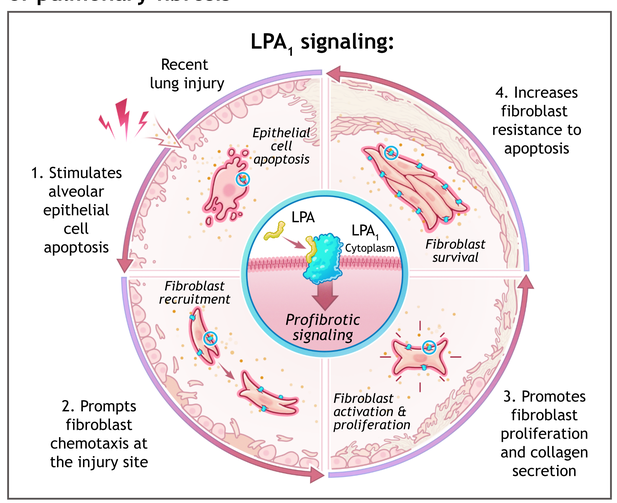
*At the time study was conducted

Rationale

- Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive fibrosing form of interstitial lung disease with no identifiable cause and poor prognosis[1]
- Approved antifibrotics slow lung function decline but do not halt disease progression, and patients often do not tolerate treatment[2-5]
- Lysophosphatidic acid receptor 1 (LPA_1) signaling plays a central role in the pathogenesis of fibrotic lung diseases (**Figure 1**)[6]
  - In a phase 2 trial, 60 mg twice daily (BID) admilparant (BMS-986278), an oral LPA_1 antagonist, slowed lung function decline and was well tolerated in patients with IPF over 26 weeks[7]

Figure 1. The role of LPA_1 signaling in the pathogenesis of pulmonary fibrosis

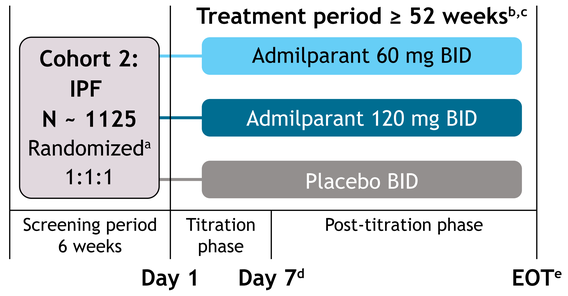


Aim

- The ALOFT-IPF phase 3 trial aims to further evaluate admilparant as a treatment option for patients with IPF

Methods

Figure 2. ALOFT-IPF trial design



Primary endpoint

- Absolute change in FVC (mL) from baseline at week 52

Key secondary endpoints

- Time to first disease progression event in ≥ 1 of the following (from baseline through the primary endpoint visit[f]):
  - Absolute ppFVC decline of ≥ 10% from baseline
  - Acute exacerbation of pulmonary fibrosis
  - Respiratory-related hospitalization
  - All-cause mortality
- Change in L-PF cough domain score (from baseline at week 52)
- Change in walking distance measured in 6MWT (from baseline at week 52)
- Change in L-PF dyspnea domain score (from baseline at week 52)

[a]Stratified by concomitant use of approved antifibrotic therapy (pirfenidone vs nintedanib vs none) and sex (male vs female). [b]Treatment period is a minimum of 52 weeks and up to approximately 3 years, except for patients in European Economic Area countries, who will participate for a maximum of 2 years. [c]Schedule for the treatment period for both cohorts includes an approximate 7 to 16 days dose titration period from day 1 followed by the assigned treatment arm dose, with visits Q6W up to week 52 and Q12W from week 52 to EOT. [d]Titration period is intended to be completed in 7 to 16 days with a minimum of 2 consecutive days of dosing required between titration visits. [e]EOT is defined as when each patient completes their last scheduled treatment visit. [f]Defined as the date when the last patient completes their 52-week treatment visit. This visit date marks the completion of the primary endpoint for the study and is crucial for data collection and analysis.
6MWT, 6-minute walk test; EOT, end of treatment; FVC, forced vital capacity; L-PF, Living with Pulmonary Fibrosis questionnaire; ppFVC, percent of predicted forced vital capacity; Q×W, every × weeks.

- ALOFT-IPF (NCT06003426) is a global, phase 3, multicenter, randomized, double-blind, placebo-controlled clinical trial currently randomizing adults with IPF to receive admilparant 60 or 120 mg or placebo (1:1:1) orally, BID for ≥ 52 weeks (**Figure 2**)
- The trial enrolls patients in > 400 sites across > 30 countries. Trial completion is estimated to be October 2026
- ALOFT-IPF is a trial with a 2-cohort design
- Cohort 1 (N ~ 60) has a single-blind design and enrolls patients with IPF to evaluate the safety and tolerability of admilparant (not shown)
  - Cohort 1 primary endpoint: number of patients experiencing spontaneous syncopal episodes (admilparant 120 mg BID vs placebo) from day 7 to day 29 post-treatment
- Cohort 2 design is shown in **Figure 2**
- Key patient eligibility criteria are presented in **Table 1**

Table 1. Key patient eligibility criteria

Main inclusion criteria

1. ≥ 40 years of age
2. Diagnosis of IPF within 7 years supported by centrally read chest high-resolution computed tomography during screening, and verification of usual interstitial pneumonia
3. ppFVC ≥ 40%
4. Forced expiratory volume in 1 second (FEV_1)/FVC ≥ 0.7
5. Single-breath, hemoglobin-corrected percent of predicted diffusing capacity of the lung for carbon monoxide ($ppDL_{CO}$) ≥ 25%
6. Stable-dose (≥ 90 days before screening) background antifibrotic treatment (nintedanib or pirfenidone) is permitted; if not currently on treatment, patients must not have received either medication within 28 days before screening

Main exclusion criteria

1. History of stroke or transient ischemic attack within 3 months before screening
2. Symptoms of heart failure at rest
3. Patients who have a current malignancy or a previous malignancy with < 2 years free of recurrence

Conclusions

- Admilparant (BMS-986278) is a potent, selective, second-generation, oral, small-molecule LPA_1 antagonist in development for the treatment of patients with IPF
- The ALOFT-IPF trial is evaluating the effect of admilparant on absolute change in FVC, disease progression, safety, and quality of life over 52 weeks in patients with IPF

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