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

P552

Fernando J. Martinez,[1] Tamera J. Corte,[2,3] Vincent Cottin,[4] Aryeh Fischer,[5]* Sinae Kim,[5] Aditya Patel,[5] Mudiaga Sowho[5]

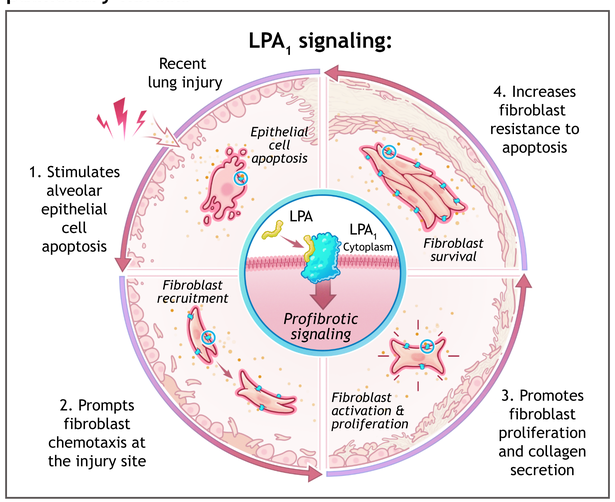
[1]University of Massachusetts Chan Medical School/UMass Memorial Health System, Worcester, MA; [2]Royal Prince Alfred Hospital, Camperdown, NSW, Australia; [3]University of Sydney, Sydney, NSW, Australia; [4]National French Reference Coordinating Center for Rare Pulmonary Diseases, Louis Pradel Hospital, Hospices Civils de Lyon, University Claude Bernard, Lyon, France; [5]Bristol Myers Squibb, Princeton, NJ

*At the time study was conducted

Rationale

- Progressive pulmonary fibrosis (PPF) encompasses a group of interstitial lung diseases (ILDs) characterized by a progressive fibrotic phenotype, and is associated with declining lung function, worsening of symptoms, deterioration in quality of life, and early death[1-3]
  - The antifibrotics pirfenidone and nintedanib, both approved for idiopathic pulmonary fibrosis (IPF) and the latter for PPF, slow the decline in lung function but are associated with adverse events, limiting treatment duration.[2,4-7] There remains a high unmet need for effective and tolerable treatments for patients with PPF
- Lysophosphatidic acid receptor 1 (LPA_1) activation drives progression of lung fibrosis through epithelial cell apoptosis and fibroblast recruitment (**Figure 1**)[8,9]
  - 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 PPF over 26 weeks[4]

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

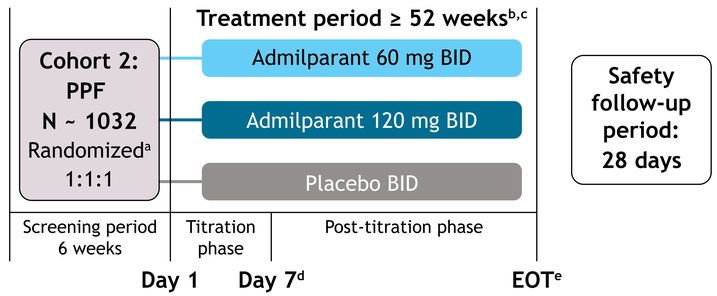


Aim

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

Methods

Figure 2. ALOFT-PPF 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 background therapy (antifibrotics and/or immunosuppression, or none) and usual interstitial pneumonia pattern (present or absent). [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. If a patient chooses not to continue in the study or terminates the treatment beyond week 52, the week 52 visit will be considered their EOT 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; QxW, every x weeks.

- ALOFT-PPF (NCT06025578) is a global, phase 3, multicenter, randomized, double-blind, placebo-controlled clinical trial currently randomizing adults with PPF to receive admilparant 60 or 120 mg or placebo (1:1:1) orally, BID for ≥ 52 weeks (**Figure 2**)
- The trial enrolls patients in > 500 sites across > 30 countries. Trial completion is estimated to be December 2027[10]
- ALOFT-PPF is a trial with a 2-cohort design
- Cohort 1 (N ~ 60) has a single-blind design to evaluate the short-term safety and tolerability of admilparant (not shown)
  - Cohort 1 primary endpoint: number of patients experiencing spontaneous syncopal episodes from day 7 to day 29 post-treatment (admilparant 120 mg BID vs placebo)
- 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. ≥ 21 years of age
2. Diagnosis of ILD and ≥ 10% parenchymal fibrosis supported by high-resolution computed tomography at screening, and features consistent with progressive ILD within 24 months before screening
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) or immunosuppressive therapies (mycophenolate mofetil, mycophenolic acid, azathioprine, tacrolimus; traditional [eg, methotrexate, leflunomide, sulfasalazine, or hydroxychloroquine] and biologic [eg, tumor necrosis factor and interleukin-1 inhibitors] disease-modifying antirheumatic drugs; and Janus kinase inhibitors); if not currently on treatment, patients must not have received medication within 28 days before screening
Main exclusion criteria
1. Diagnosis of IPF confirmed by usual interstitial pneumonia pattern
2. Emphysema ≥ 50%, or emphysema greater than the extent of fibrosis
3. Acute exacerbation of pulmonary fibrosis within 4 weeks before or during screening
4. Clinically significant non-parenchymal lung disease at screening or respiratory tract infection within 4 weeks before or during screening
5. History of stroke or transient ischemic attack within 3 months before screening
6. Symptoms of heart failure at rest
7. History of lung reduction surgery or lung transplant
8. Pulmonary arterial hypertension with multidrug therapy
9. Cigarette smoking (including e-cigarettes) within 3 months before day 1

Conclusions

- Admilparant (BMS-986278) is a potent, selective, second-generation, oral, small-molecule LPA_1 antagonist in development for the treatment of patients with PPF
- The ALOFT-PPF 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 PPF

References

1. Rajan SK, et al. *Eur Respir J* 2023;61:2103187.
2. Flaherty KR, et al. *N Engl J Med* 2019;381:1718-1727.
3. Kolb M, Vašáková M. *Respir Res* 2019;20:57. doi: 10.1186/s12931-019-1022-1.
4. Corte TJ, et al. *Am J Respir Crit Care Med* 2025;211:230-238.
5. Maher TM, et al. *Lancet Respir Med* 2020;8:147-157.
6. Behr J, et al. *Lancet Respir Med* 2021; 9:476-486.
7. Cottin V, et al. *Respir Res* 2022;23:85. doi: 10.1186/s12931-022-01974-2.
8. Tager AM, et al. *Nat Med* 2008;14:45-54.
9. Funke M, et al. *Am J Respir Cell Mol Biol* 2012;46:355-364.
10. ClinicalTrials.gov. Accessed March 2025. https://clinicaltrials.gov/study/NCT06025578

Acknowledgments

- The authors would like to thank the study staff and investigators as well as the patients and their families for their participation in this study
- All authors contributed to and approved the presentation; writing and editorial assistance were provided by Jo Fetterman, PhD, of Parexel, funded by Bristol Myers Squibb
- This study was funded by Bristol Myers Squibb

Scientific Content on Demand

To request a copy of this poster:

Scan QR code via a barcode reader application

QR codes are valid for 90 days after the congress presentation date.

Presented at the 2025 American Thoracic Society (ATS) International Conference; May 16–21; San Francisco, CA

Email: fernando.martinez1@umassmed.edu