Analysis of Relief-of-Cough in Patients With Idiopathic Pulmonary Fibrosis Treated With Oral Nalbuphine Extended Release

Alyn H. Morice, MD, FRCP

Foundation Chair and
Professor of Respiratory Medicine
The University of Hull
Hull, United Kingdom

Co-authors: Kevin Carroll, PhD, and David Clark, MD

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Background

- Patients with idiopathic pulmonary fibrosis (IPF) have a high burden of disease, with significant impact on quality of life[1,2]
  - ~85% of patients with IPF experience chronic cough,[3] for which there are no approved therapies[4]
- Nalbuphine extended release (NAL ER) is a neuromodulator that acts centrally in the brain and peripherally in the lungs as a κ-opioid receptor agonist and μ-opioid receptor antagonist[5]
- Primary results from the randomized, double-blind, placebo-controlled, phase 2a crossover trial in patients with IPF (CANAL; NCT04030026) demonstrated that oral NAL ER:[6]
  - Reduced daytime cough frequency from baseline at day 22 by 75.1% versus 22.6% with placebo (primary end point; $P < 0.001$)
  - Reduced 24-hour cough frequency by 76.1% versus 25.3% with placebo

1. Key AL et al. *Cough*. 2010;6:4. 2. Swigris JJ et al. *Health Qual Life Outcomes*. 2005;3:61. 3. Ryerson CJ et al. *Respirology*. 2011;16:969-975. 4. Vigeland CL et al. *Respir Med*. 2017;123:98-104. 5. Mann J et al. *Front Rehabil Sci*. 2021;2:751798. 6. Maher TM et al. *NEJM Evid*. 2023;2(8):EVIDoa2300083.

Objectives

- Evaluate the effect of NAL ER on relief-of-cough duration in patients with IPF from the CANAL study
- To assess whether measuring cough severity, duration, and intensity could enhance communication between clinicians and patients

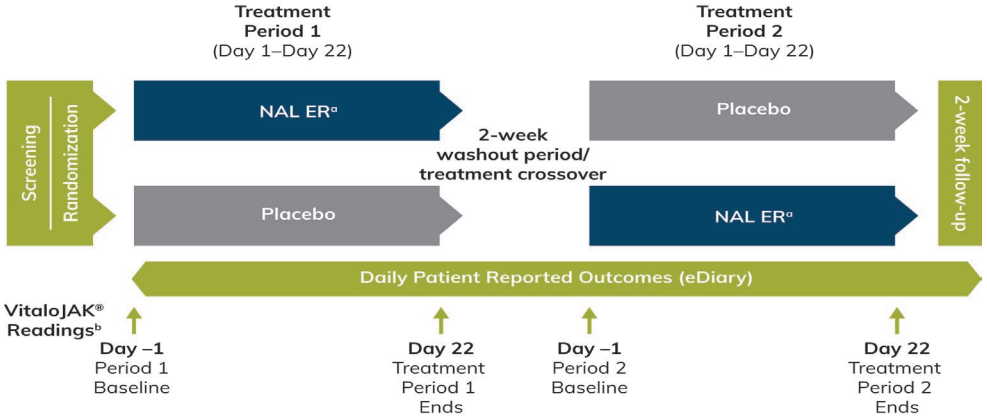
IPF, idiopathic pulmonary fibrosis; NAL ER, nalbuphine extended release.

Methods

Key Inclusion Criteria
- ≥18 years of age
- IPF diagnosis
- Self-reported chronic cough lasting ≥8 weeks
- Daytime CS-NRS ≥4

Key Exclusion Criteria
- ILD from environmental exposure, connective tissue disease, or drug toxicity
- Continuous oxygen therapy use ≥16 hours/day
- IPF-related treatment changes ≤8 weeks before screening

CANAL: Randomized, Double-Blind, Placebo-Controlled, Phase 2a Crossover Trial



Analyses

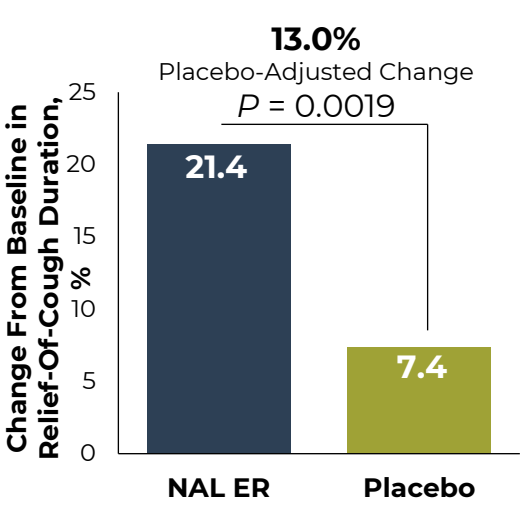
- Relief-of-cough duration = any ≥15-minute cough-free period (summed per patient)
- Cough time = (total observation time) – (relief time)
- Cough intensity = number of coughs during coughing time
- Data standardized to percentages for recordings <24 hours

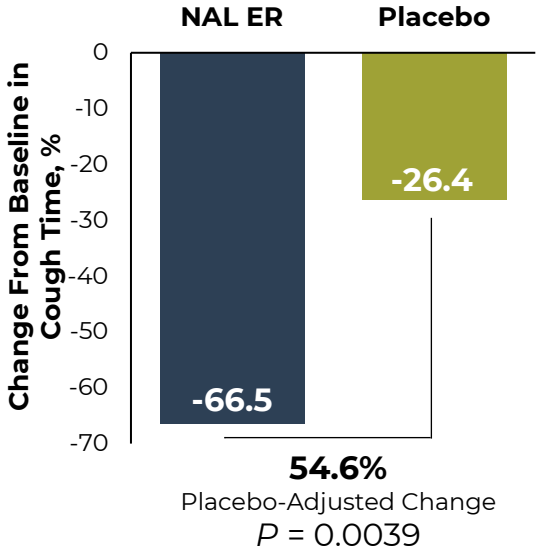
CS-NRS, cough severity numerical rating scale; ILD, intersitial lung disease; IPF, idiopathic pulmonary fibrosis; NAL ER; nalbuphine extended-release.
[a]Treatment was titrated to 162 mg twice daily over the active treatment period. [b]At the end of each recording session, the electronic cough monitor (VitaloJAK®; Vitalograph Ltd, Buckingham, United Kingdom), which was worn from a day prior to each study visit, was removed and returned to the clinical study center for processing.

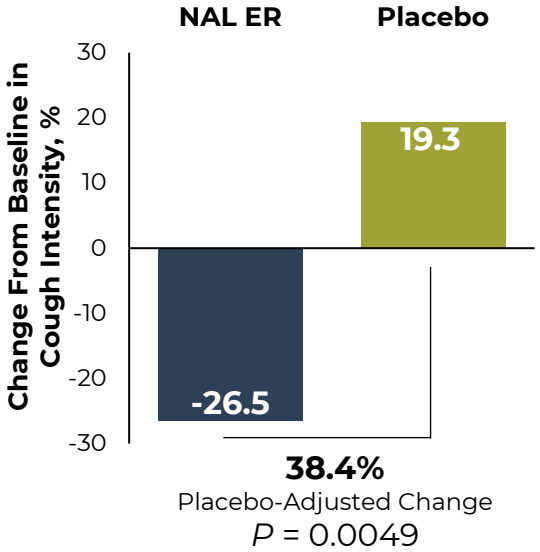
1. Maher TM et al. *NEJM Evid*. 2023;2(8):EVIDoa2300083.

Results

- NAL ER significantly increased relief-of-cough time, reduced cough time, and reduced cough intensity in patients with IPF compared with placebo







N = 38

IPF, idiopathic pulmonary fibrosis; NAL ER, nalbuphine extended-release.

Conclusions

- These post hoc analyses of end points relevant to patient quality of life extend the primary outcomes of the CANAL trial[1]
- In this study, treatment with **NAL ER produced significantly greater relief-of-cough duration, reduced cough time, and reduced cough intensity** compared with placebo, making it the first drug to achieve these outcomes in a study in patients with IPF
- Measuring the duration of freedom from coughing and cough intensity may be **more relevant to patient experience** than cough frequency due to the episodic nature of cough

IPF, idiopathic pulmonary fibrosis; NAL ER, nalbuphine extended-release.

1. Maher TM et al. *NEJM Evid*. 2023;2(8):EVIDoa2300083

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