The Effect of Oral Nalbuphine Extended Release on Patient-Reported Outcome Measures in Patients With Idiopathic-Pulmonary-Fibrosis-Related Chronic Cough

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BACKGROUND

- Cough is a common symptom for individuals with idiopathic pulmonary fibrosis (IPF), contributing to disease-associated morbidity and diminished quality of life (QoL) through effects on breathlessness, and an individual's ability to work and socialize[1]
- Several tools are available for determining the QoL impact from chronic cough:
  - The Exacerbations of Chronic Obstructive Pulmonary Disease Tool (EXACT) is a patient reported, 14-item questionnaire[1]
  - Cough Severity Numerical Rating Scale (CS-NRS) is an 11-point Likert scale
  - Clinical Global Impression of Change (CGI-C), a 1-item, clinician reported evaluation of disease state

OBJECTIVE

- Here we report QoL-related data from the phase 2 study of oral nalbuphine extended release (ER) for IPF-related chronic cough
  - κ-receptor agonist and μ-receptor antagonist **(Figure 1)**

METHODS

- Randomised, double-blind, placebo-controlled, crossover trial with two 22-day treatment periods separated by a 2-week washout period. Nalbuphine ER 27 mg once daily was titrated up to 162 mg twice daily at Day 16 (Figure 1)
- Adults diagnosed with definite/probable IPF using international criteria and chronic cough for > 8 weeks were enrolled
- Of the 56 screened patients, 38 comprised the 1-period full analysis set
- The **completers analysis set** was comprised of the 28 patients who completed both treatment periods
- Secondary endpoints for patient/clinically reported outcomes include EXACT2 mean cough frequency, Cough Severity Numerical Rating Scale (CS-NRS), EXACT7-11 mean breathlessness, and Clinical Global Impression of Change (CGI-C)

Figure 1. Nalbuphine extended release (ER) tablets mechanism of action.

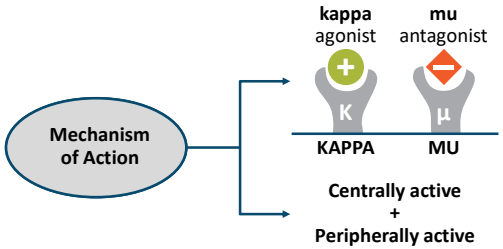


Figure 2. Study design

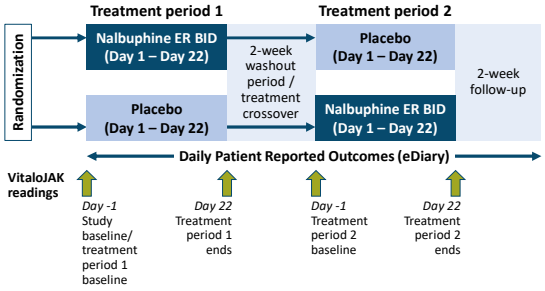
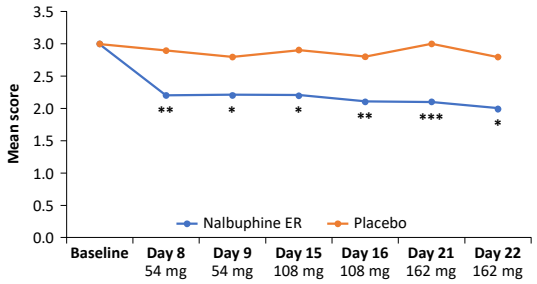
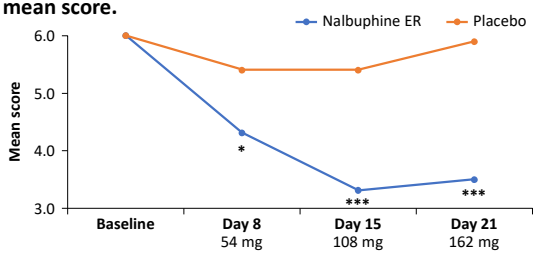


Figure 3. EXACT2 mean cough frequency score.



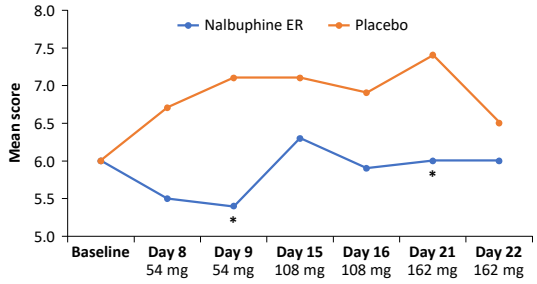
*p < 0.01; **p < 0.001; ***p < 0.0001.

Figure 4. Cough Severity Numerical Rating Scale mean score.



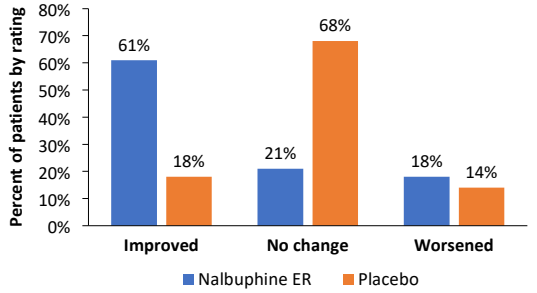
*p < 0.05; ***p < 0.0001.

Figure 5. EXACT7-11 mean breathlessness score.



*p < 0.05.

Figure 6. Clinical Global Impression of Change.



RESULTS

- Reduction in EXACT2 mean cough frequency was statistically significant between nalbuphine ER and placebo-treated patients at all timepoints **(Figure 2)**
- Mean cough severity (CS-NRS) was numerically lower and statistically significant at all timepoints measured, Day 8 ($p = 0.0382$), and at Days 15 and 21 ($p < 0.0001$) **(Figure 3)**
- EXACT7-11 mean breathlessness was numerically lower for nalbuphine ER at all timepoints and significantly different for Days 9 and 21 ($p \leq 0.05$) **(Figure 4)**
- CGI-C showed 61% of patients treated with nalbuphine ER improved, 21% had no change, and 18% worsened, compared with 18%, 68%, and 14%, respectively, of patients receiving placebo. **(Figure 5)**

CONCLUSIONS

- Nalbuphine ER demonstrated a significant improvement in patient reported quality of life in the phase 2 study
- Significant improvement in patient reported cough frequency (EXACT2) and severity (CS-NRS)
- Patient reported breathlessness (EXACT7-11) was lower than placebo
- 61% of patients had a significant improvement in physician determined assessment of clinical global impression of change (CGI-C)

References: 1. Lee J, et al. Chest 2022:S0012-3692(22)00545-1; 2. van Manen MJG, Wijsenbeek MS. Curr Opin Support Palliat Care. 2019;13(3):143-151. **Acknowledgments and funding sources**: This presentation was prepared by the authors with medical-writing assistance from Excerpta Medica, funded by Trevi therapeutics.
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