Responders Analyses in Objective 24H Cough Frequency in SOOTHE, A Phase 2b Trial of a Selective P2x3 Antagonist in Refractory Chronic Cough

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Introduction

- Refractory Chronic Cough (RCC) is a cough that persists for 8 weeks or more despite adequate treatment of all identifiable associated diseases or without identifiable cause[1,2].
- The current lack of approved treatment exacerbates the significant physical, psychological, and social burdens RCC imposes on patients.

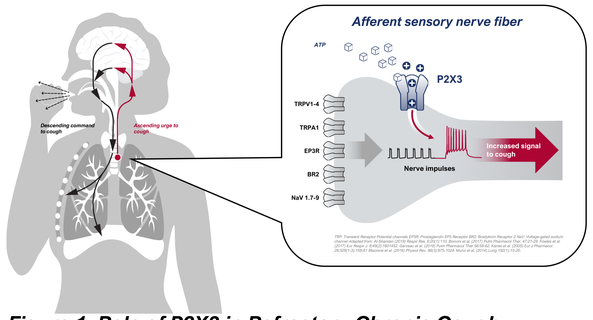

Figure 1. Role of P2X3 in Refractory Chronic Cough

- The ATP-gated ion channel P2X3 is suggested to play a role in the pathophysiology of RCC (Fig 1.), and P2X3 antagonists have shown promise as a treatment for RCC[3-5].
- We report the responder analyses from a Phase 2b study in RCC of BLU-5937, a highly selective P2X3 antagonist, for the treatment of RCC.

Methodology

- SOOTHE (NCT04678206) was a multi-center phase 2b, randomized, placebo-controlled, parallel arm, clinical dose-finding study in participants diagnosed with RCC for ≥1 year.

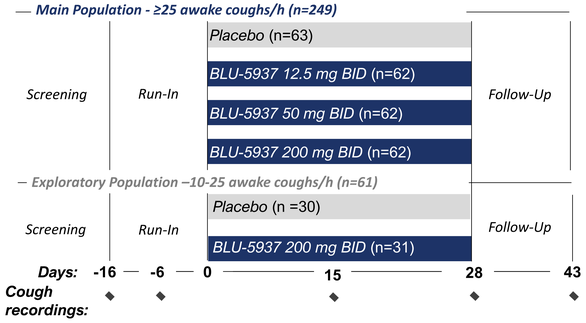

Figure 2. SOOTHE Study Design

- The primary endpoint was the change from baseline in 24H cough frequency.
- Following a single-blind run-in period, 249 participants who had maintained a baseline awake cough frequency ≥25 coughs/h were randomized 1:1:1:1 to the three active treatment arms of BLU-5937 (12.5, 50 and 200 mg BID) or placebo for 4 weeks of double-blind treatment.

Results

24H Cough Frequency

- In SOOTHE, statistically significant reductions in change in 24-hour cough frequency over placebo were observed at Days 15 and 28 with treatment with BLU-5937 50 and 200 md BID (Fig. 3).
- A dose response was observed between the 12.5 mg and 50 mg BID doses.

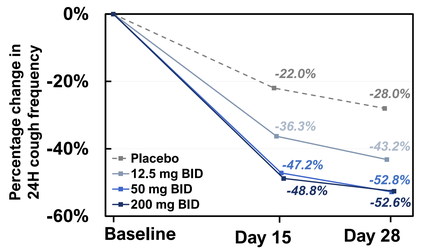

Figure 3. Change From Baseline In 24H Cough Frequency

Responder Analyses

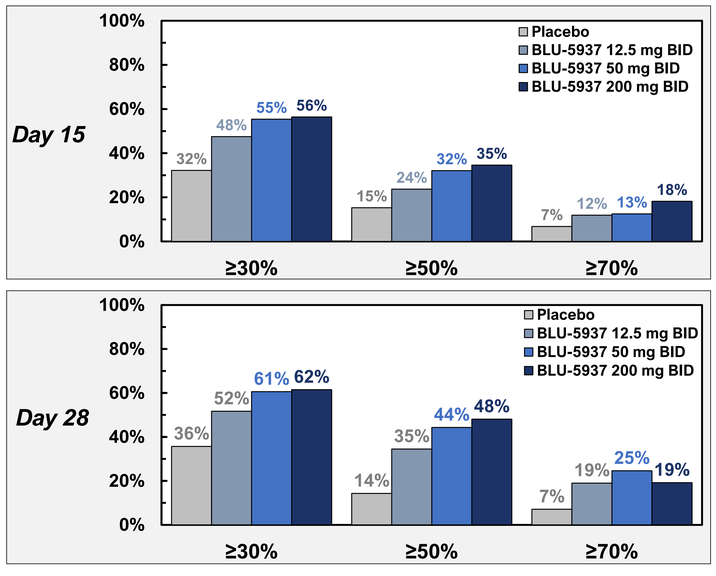

Figure 4. Responder rates in 24H Cough Frequency

- Cough frequency response was assessed by analyzing the percentage of patients achieving ≥30, 50 and 70% reduction in 24H cough frequency from baseline after 15 and 28 days of treatment.
- After 28 days of treatment, 52%, 61%, 62% and 36% experienced at least 30% improvement in 24H cough frequency for the 12.5, 50 and 200 mg BID doses and placebo, respectively (Fig. 4).
- Furthermore, 35%, 44%, 48,1% and 14% of participants experienced at least 50% improvement and 19%, 25%, 19%, and 7% experienced at least 70% improvement in 24H cough frequency at the 12.5, 50 and 200 mg BID doses and placebo, respectively (Fig. 4).

Odds Ratios of Response

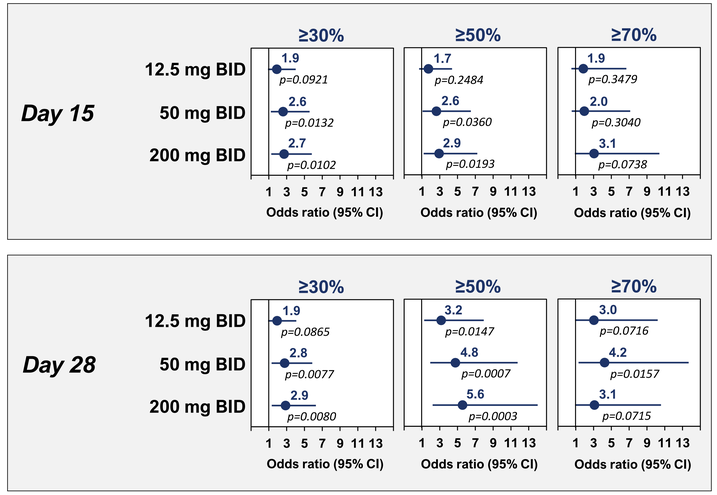

Figure 5. Odds Ratios Of ≥30, 50 and 70% Response in 24H Cough Frequency

- Odds ratios for achieving a clinically meaningful cough frequency reduction favored treatment at every dose of BLU-5937 over placebo at Day 28 (Fig 5).
- Higher proportions of responders on treatment versus on placebo were also noted at Day 15.(Fig. 5)
- Cumulative odds ratio across thresholds of response at Day 28 show that participants treated with BLU-5937 were consistently more likely to experience improvements over placebo (12.5 mg BID: OR=2.2, p=0.0276; 50 mg BID: OR=3.4, p=0.0008; 200 mg BID: OR=3.3, p=0.011).

Conclusions

- A greater proportion of participants experienced at least 30%, 50% or 70% reduction in 24H cough frequency when treated with BLU-5937 than with placebo.
- The results suggest that participants treated with BLU-5937 are more likely to experience not only a minimal clinically important change in cough frequency (30%), but are also more likely to experience more important reductions in cough (50, 70%).

References

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