

Response In Patient-Reported Cough Severity in SOOTHE, A Phase 2b Trial of Camlipixant in Refractory Chronic Cough



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Introduction

- Refractory Chronic Cough (RCC) manifests as a cough lasting > 8 weeks that does not respond to treatment of other etiologies associated or without other discernable etiologies (unexplained)¹.
- Dysfunction of the neuro-respiratory pathways controlling cough contributes to the disease pathology².
- Current options targeting the neuro-respiratory pathways driving cough are not approved by the FDA and can suffer from serious side effects or the risk of addiction².
- CamliPIXANT (BLU-5937) selectively inhibits P2X3 receptors, which are expressed on sensory neurons considered important in the pathophysiology of RCC (fig. 1)³, and is in development 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.
- The primary endpoint was the log-transformed change from baseline in 24H cough frequency.
- Improvement in patient-reported cough severity was assessed by the Cough Severity VAS.
- Following a 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

Table 1. Baseline Demographics And Characteristics

| | Placebo (BID) | CamliPIXANT (BID) | | | Total |
|---|---------------|-------------------|-------------|-------------|-------------|
| | | 12.5 mg | 50 mg | 200 mg | |
| Number of subjects, n | 63 | 62 | 62 | 62 | 249 |
| Female, n (%) | 49 (78%) | 48 (77%) | 52 (84%) | 55 (89%) | 204 (82%) |
| Age (years), mean (SD) | 61.4 (11.3) | 60.7 (10.1) | 61.6 (9.6) | 59.7 (11.4) | 60.9 (10.6) |
| BMI (kg/m²), mean (SD) | 27.9 (5.6) | 28.1 (5.3) | 28.6 (7.3) | 27.9 (5.7) | 28.1 (6.0) |
| FEV₁/FVC, mean (SD) | 0.77 (0.07) | 0.77 (0.07) | 0.76 (0.07) | 0.77 (0.08) | 0.77 (0.07) |
| Cough Characteristics | | | | | |
| Duration of cough (years), mean (SD) | 11.1 (9.7) | 11.9 (9.1) | 13.5 (11.5) | 10.3 (9.1) | 11.7 (9.9) |
| 24H cough frequency** (coughs/h), mean_{geo} | 39.6 | 41.3 | 39.9 | 35.2 | 38.9 |
| Cough Severity VAS* (mm), mean (SD) | 73.9 (14.9) | 71.7 (14.5) | 74.0 (14.4) | 72.0 (15.6) | 72.9 (14.8) |
| Leicester Cough Questionnaire*, mean (SD) | 10.4 (3.1) | 10.7 (3.0) | 10.0 (3.1) | 11.4 (3.0) | 10.6 (3.1) |

* Measured at Day 1
** Measured at D-6

- Rapid and sustained concurrent improvements in cough frequency and patient-reported cough severity were observed in all camliPIXANT treatment groups over the randomized treatment period.
- All treatment groups demonstrated highly statistically significant improvements in CS-VAS over placebo (p ≤ 0.001).
- For all doses, a greater proportion of participants experienced meaningful improvements compared to placebo.
- At day 29 all doses show significant (p ≤ 0.05) odds ratio over placebo to achieve either a response of at least 20 or 30 mm.

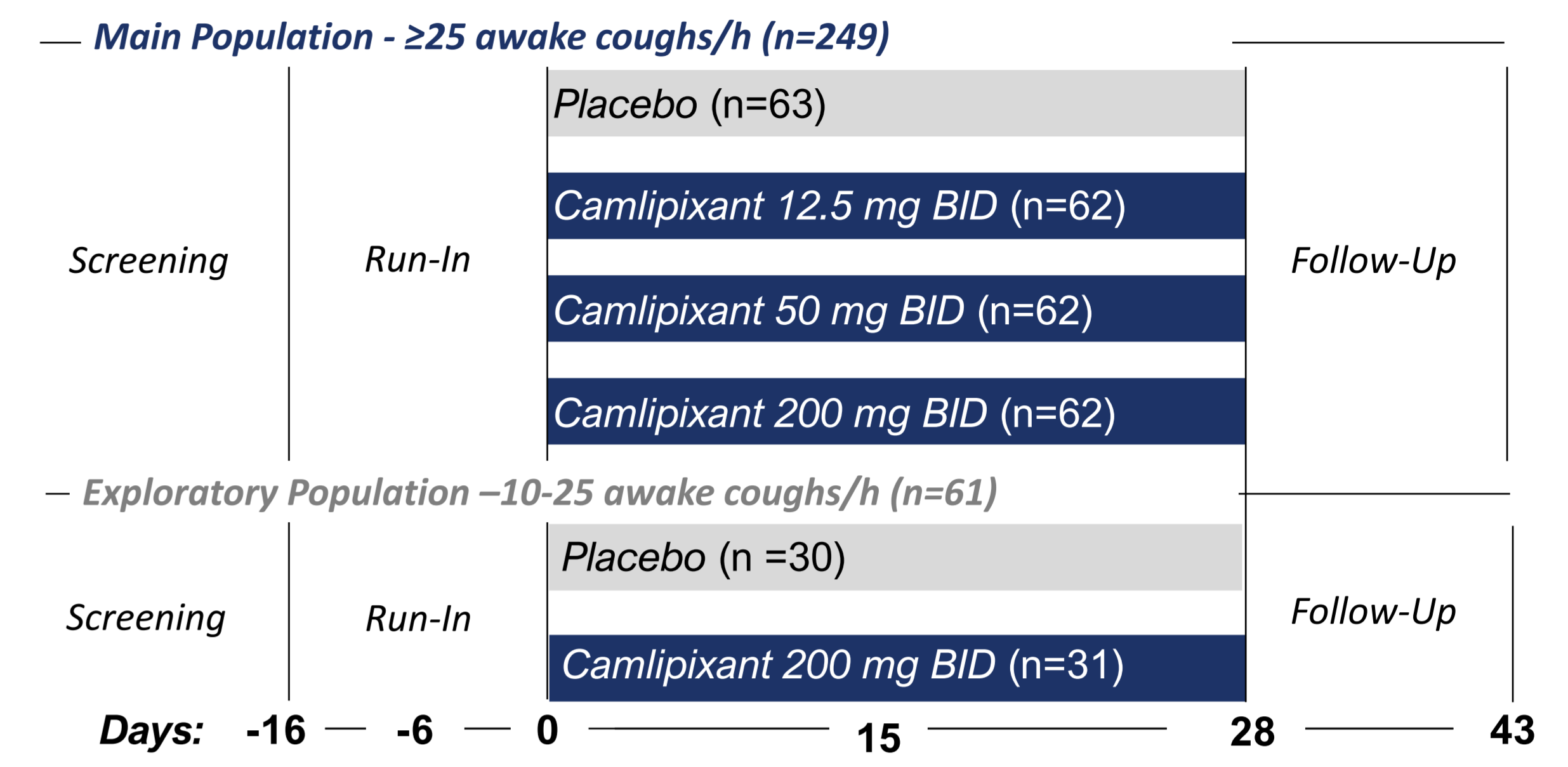


Figure 2. SOOTHE Study Design

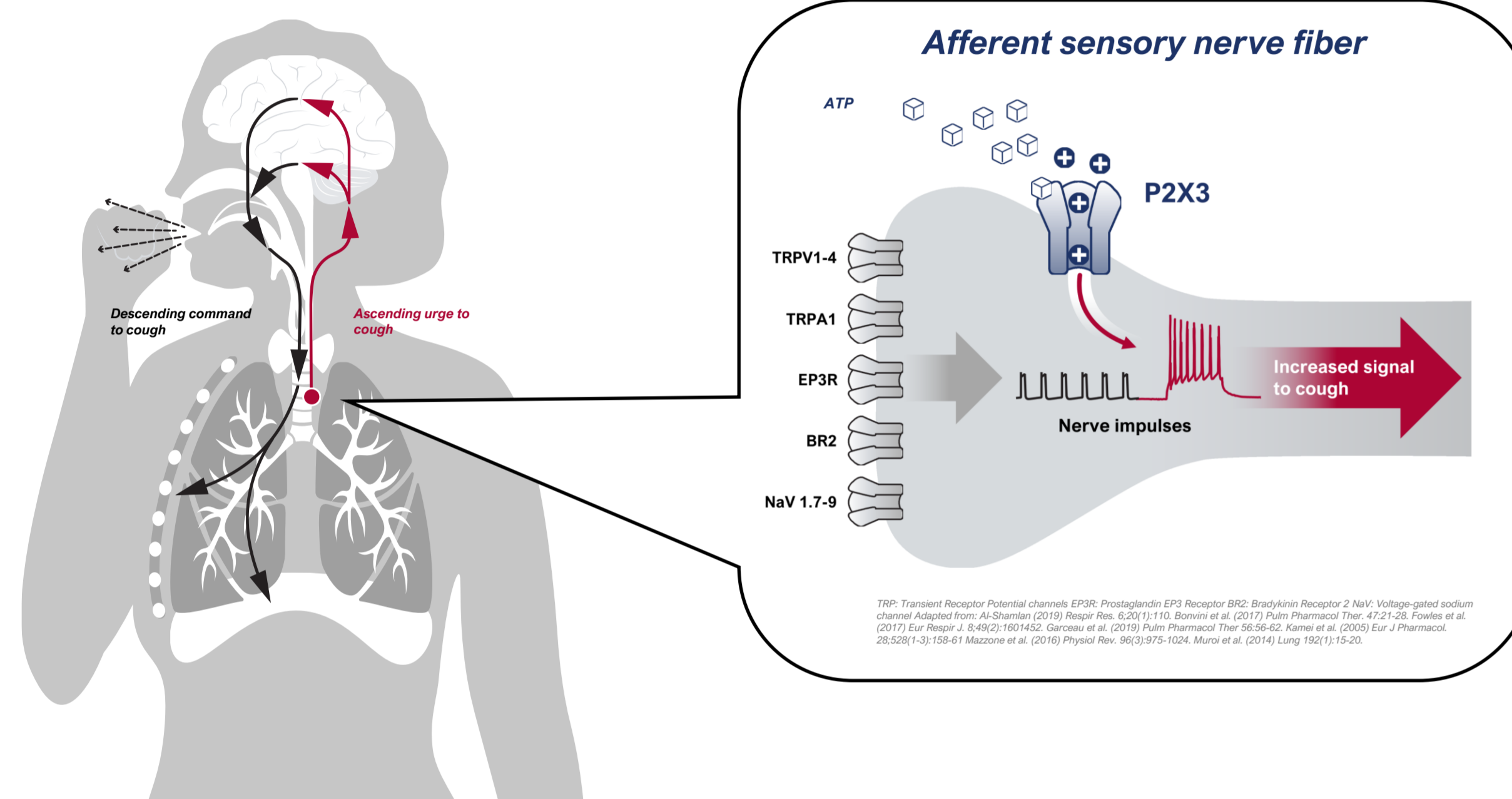
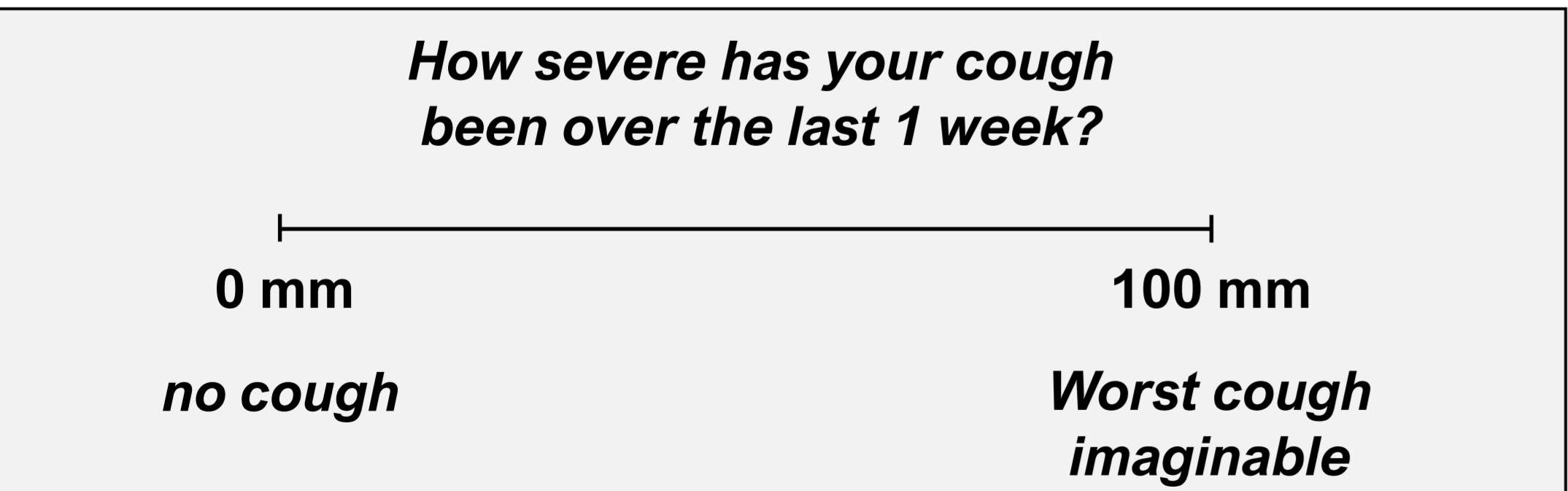


Figure 1. Model of P2X3 in Refractory Chronic Cough

Assessment of cough severity in RCC

- Impact on quality of life can be severe and heterogeneous, including social isolation, anxious state and depressive symptoms, cough-related incontinence, sleep disturbances and severe physical outcomes (fractures, syncope, etc.)⁴.
- Frequency and intensity of the cough also impact the overall severity of cough experienced by patients⁵.
- The Cough Severity Visual Analog Scale (VAS) is a measure of the patient-experienced severity of cough⁶.



- The Cough Severity VAS was recently validated in RCC⁷
 - A reduction of ≥20 mm was determined to be a minimal clinically important change.
 - A reduction of ≥30mm was suggested as a clinically meaningful change.

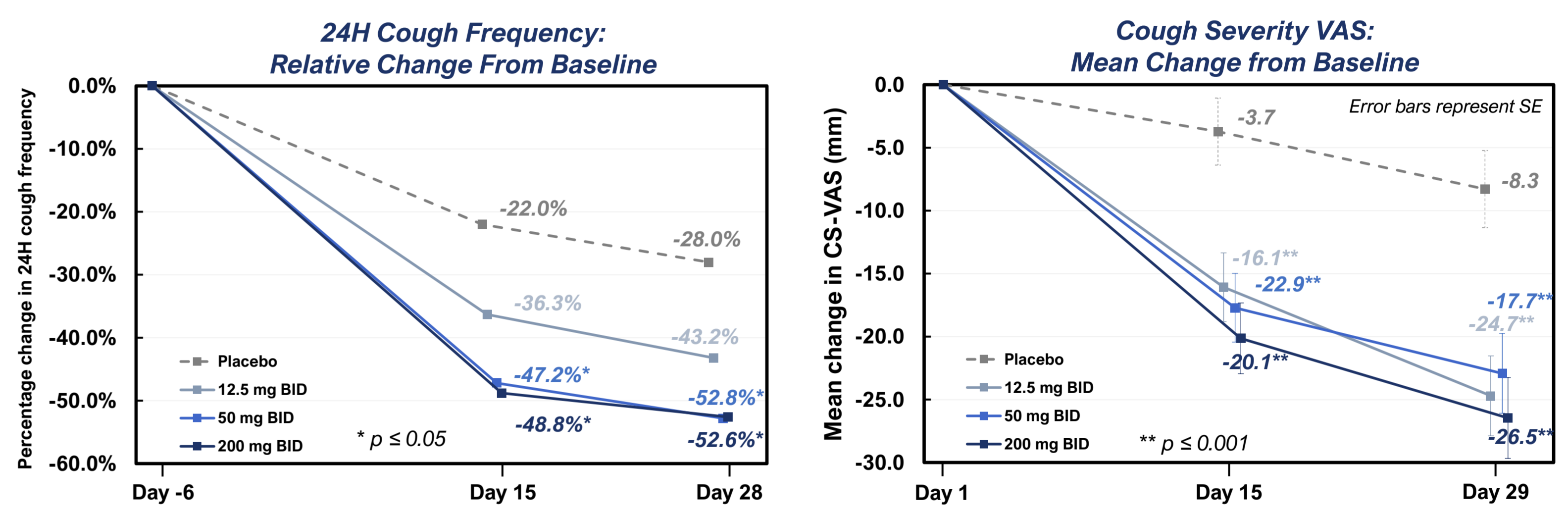


Figure 3. Changes in Objective Cough Frequency And Cough Severity VAS

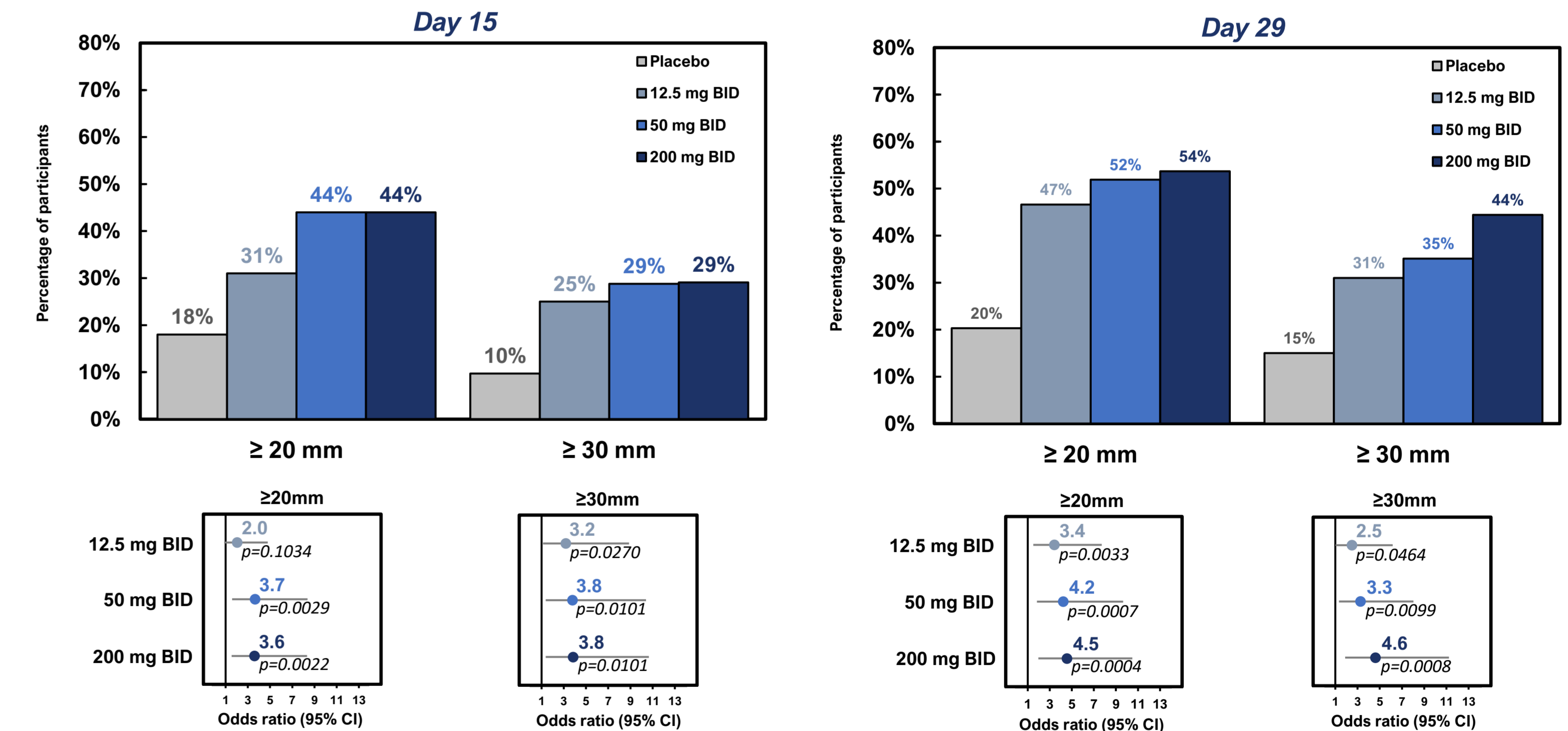


Figure 4. Responder rates in Cough Severity VAS

Conclusions

- SOOTHE demonstrated the potential for camliPIXANT to improve both objective cough frequency and patient-reported cough severity in a RCC population enriched for higher baseline cough frequency.
- More participants reported meaningful improvements in cough severity after 15 and 29 days of treatment with camliPIXANT than with placebo

References

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