

Characteristics of Participants with Refractory Chronic Cough Enrolled in A Phase 2b Trial of BLU-5937

Morice A.H¹, Smith J², Birring S.S³, McGarvey L⁴, Dicipinigaitis P⁵, Sher M⁶, Lanouette S⁷, Yang R⁸, Garin M⁸, Bonuccelli C⁸

1.Hull York Medical School, Cottingham, UK 2.University of Manchester, Manchester, UK 3.King's College London, London, UK 4.Queen's University Belfast, Belfast, UK 5.Albert Einstein Hosp, Bronx, NY, USA 6.Center for Cough, Largo, USA 7.Bellus Health Inc., Laval, Canada 8.Bellus Health Inc., Wilmington, DE, USA

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 exaggerated cough in response to innocuous or absent stimuli demonstrated by RCC patients results in significant physical, psychological and social burden².

Results

- Overall, the RCC populations randomized in SOOTHE (Tab. 1) had characteristics representative of those reported for RCC elsewhere³⁻⁶. Arms were overall balanced within each population.
- The main population (n=249) included 82% women, presented a mean age of 60.9 ±10.6 years and mean BMI of 28.2 ±6.0 kg/m². Overall, the exploratory population (n=61) presented similar demographics, except for a slightly lower proportion of women (61%) and a trend toward a higher BMI (30.1 ±5.3 kg/m²).

TABLE 1. Participants Demographics And Characteristics at Baseline

	Main population (≥25 awake coughs/h)				Total	Exploratory population (10-25 awake coughs/h)			
	Placebo	12.5 mg	50 mg	200 mg		Placebo	BLU-5937 (BID) 200 mg	Total	
Number of participants, n	63	62	62	62	249	30	31	61	
Female, n (%)	49 (78%)	48 (77%)	52 (84%)	55 (89%)	204 (82%)	19 (63%)	18 (58%)	37 (61%)	
Age, mean (SD)	61.4 (11.3)	60.7 (10.1)	61.6 (9.6)	59.7 (11.4)	60.9 (10.6)	60.8 (8.1)	61.7 (10.6)	61.3 (9.4)	
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)	29.9 (5.2)	30.4 (5.5)	30.1 (5.3)	
FEV₁/FVC, mean (SD)*	0.77 (0.07)	0.77 (0.07)	0.76 (0.07)	0.77 (0.08)	0.77 (0.07)	0.77 (0.06)	0.77 (0.08)	0.77 (0.07)	
Race, n (%)	White	62 (98%)	58 (94%)	60 (97%)	60 (97%)	240 (96%)	29 (97%)	28 (90%)	57 (93%)
	Black	0	0	1 (2%)	2 (3%)	3 (1%)	1 (3%)	2 (7%)	3 (5%)
	Asian	1 (2%)	3 (5%)	0	0	4 (2%)	0	1 (3%)	1 (2%)
	American Indian/ Alaska Native	0	1 (2%)	1 (2%)	0	2 (1%)	0	0	0
	USA	25 (40%)	29 (47%)	34 (55%)	34 (55%)	122 (49%)	21 (70%)	18 (58%)	39 (64%)
Region, n (%)	Canada	7 (11%)	4 (7%)	7 (11%)	2 (3%)	20 (8%)	2 (7%)	3 (10%)	5 (8%)
	Europe	31 (49%)	29 (47%)	21 (42%)	26 (42%)	107 (43%)	7 (23%)	10 (32%)	17 (28%)

* Measured at Day -16 (screening) or within 2 years prior to screening and after the onset of cough

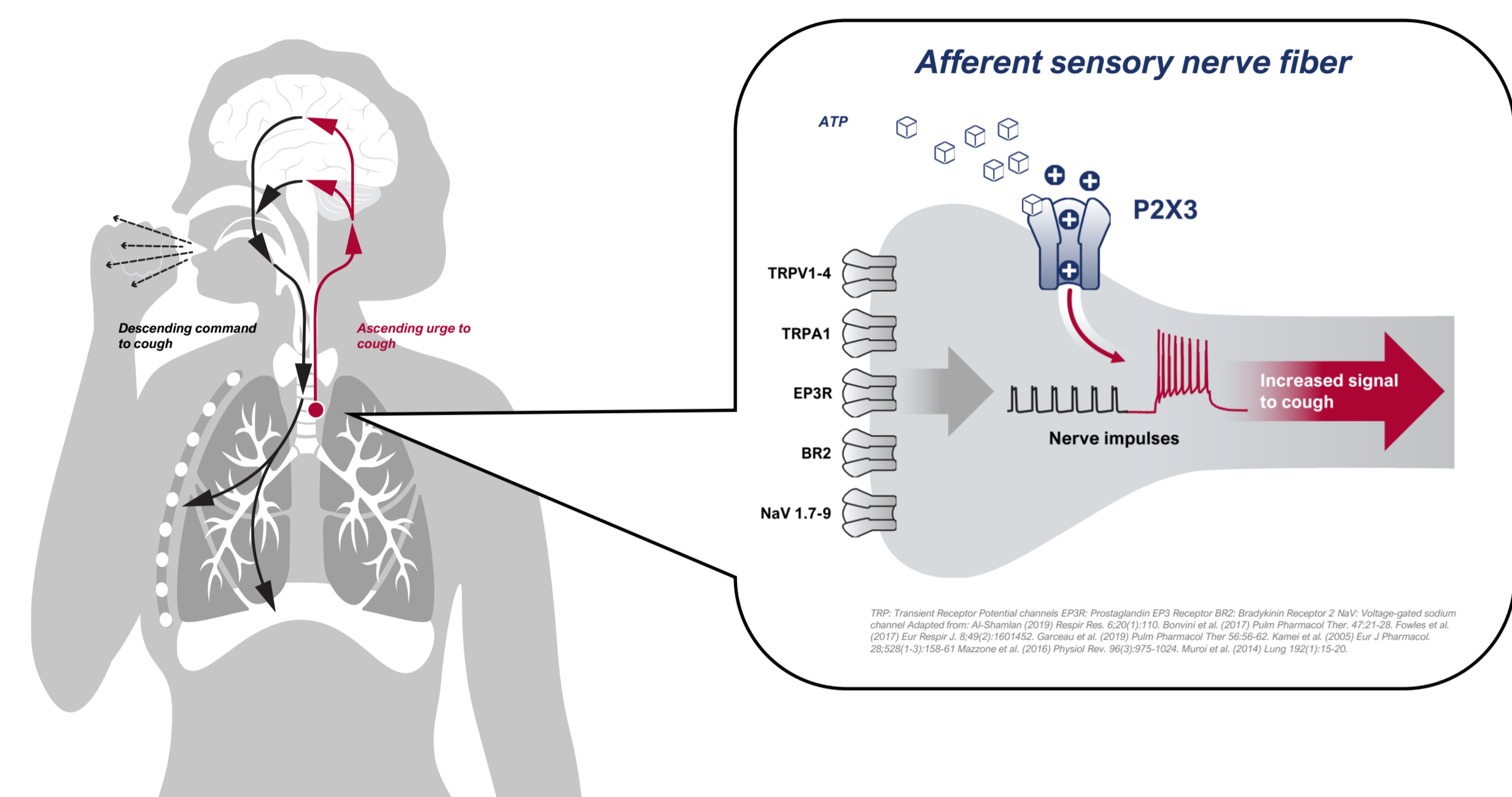


Figure 1. Model of the Role of P2X3 in Refractory Chronic Cough

- The ATP-gated ion channel P2X3 is suggested to play a role in the pathophysiology of RCC (Fig 1.).
- There are currently no approved medications outside of Japan and Switzerland for RCC. P2X3 antagonists have been validated in clinical trials as a potential option for the management of RCC³⁻⁵.

Methods

- 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.

- In addition to cough frequency and duration of cough, cough severity and cough-related burden on quality of life were assessed at baseline
- Patient-reported cough severity was assessed using a Visual Analogue Scale (CS-VAS) ranging from 0 to 100mm, 0 mm representing no cough and 100 mm the worst imaginable cough.
- Burden on quality of life was assessed using the Leicester Cough Questionnaire (LCQ), which reflects the impact of cough on quality of life on a scale from 3 to 21, with higher scores indicating a better quality of life.
- As expected from the inclusion criteria, the main and exploratory populations differed in baseline cough frequency with (mean_{geo}) 24H cough frequency of 38.9 coughs/h and 11.2 coughs/h, respectively.
- Both populations showed reported similar mean cough duration of 11.7 ±9.9 (main) and 11.8 ±11.8 (exploratory) years.
- The main and exploratory populations had similar baseline CS-VAS (72.9 ±14.8 vs 69.5 ±16.0 mm, respectively), with a minimal difference in cough-related quality of life as reported by the LCQ (10.6 ±3.1 vs 11.8 ±3.0).

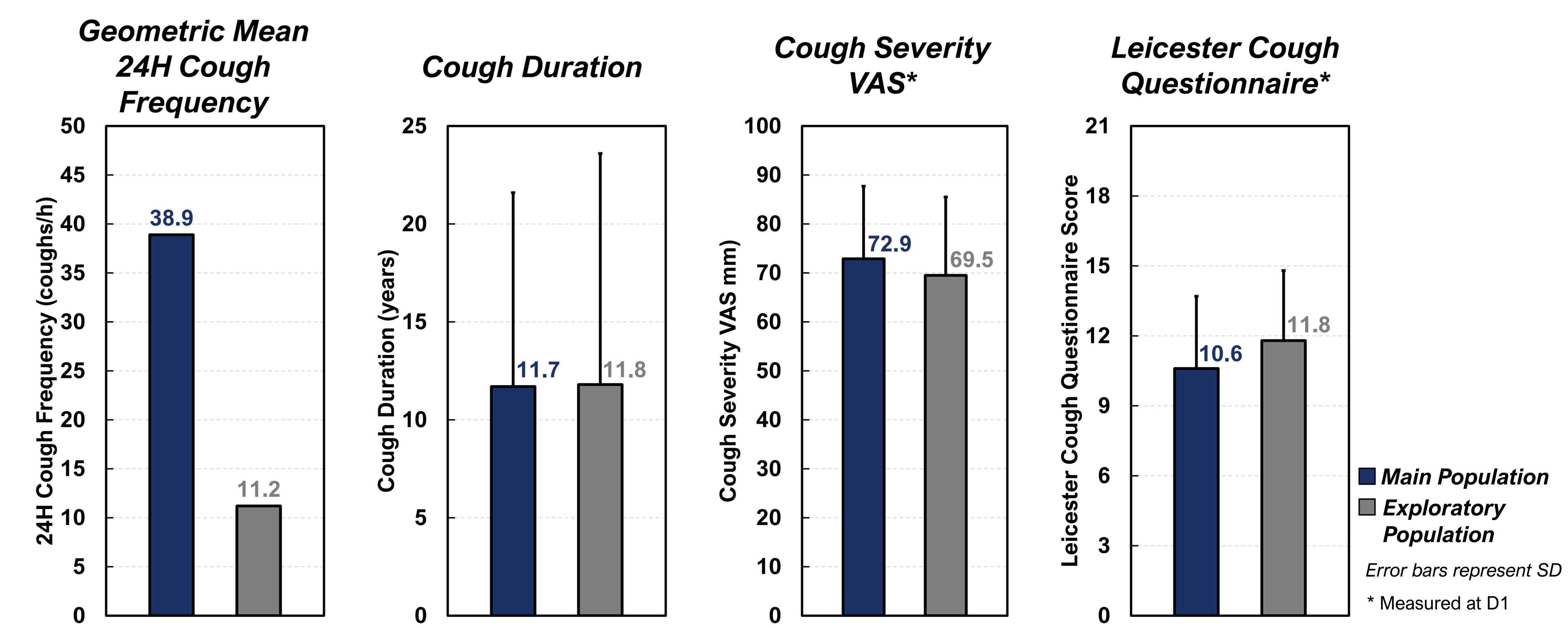


Figure 3. Cough Characteristics At Baseline in SOOTHE Populations

Conclusions

- The main populations of SOOTHE, enriched for higher baseline cough frequency, had a demographic profile consistent with other non-enriched studies in RCC.³⁻⁶
- Partition by cough frequency between the main and exploratory populations resulted in broadly similar cough characteristics at baseline, apart from a difference in mean cough frequency at baseline. The exploratory population of SOOTHE, with lower baseline cough frequency, had a higher proportion of men than is typical in RCC studies, but this may be due to the small numbers in this group. The small difference in LCQ score underscore the similarity of the burden of cough, regardless of cough frequency.

References

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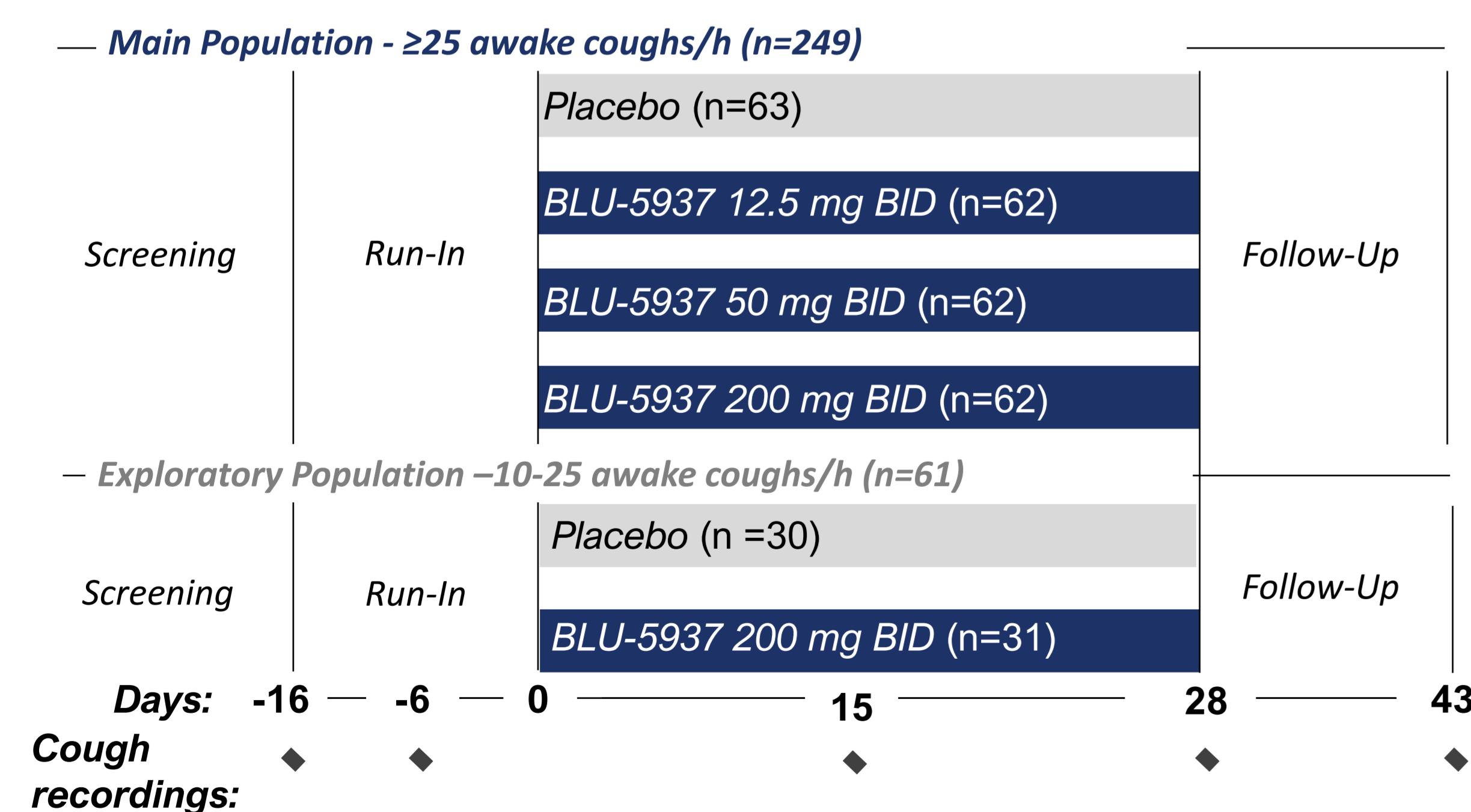


Figure 2. SOOTHE Study Design

- Following a run-in period, participants who maintained an awake cough frequency ≥25 or ≥10 to <25 coughs/h were randomized respectively to a main (n=249) or exploratory (n=61) population for a double-blind treatment period.