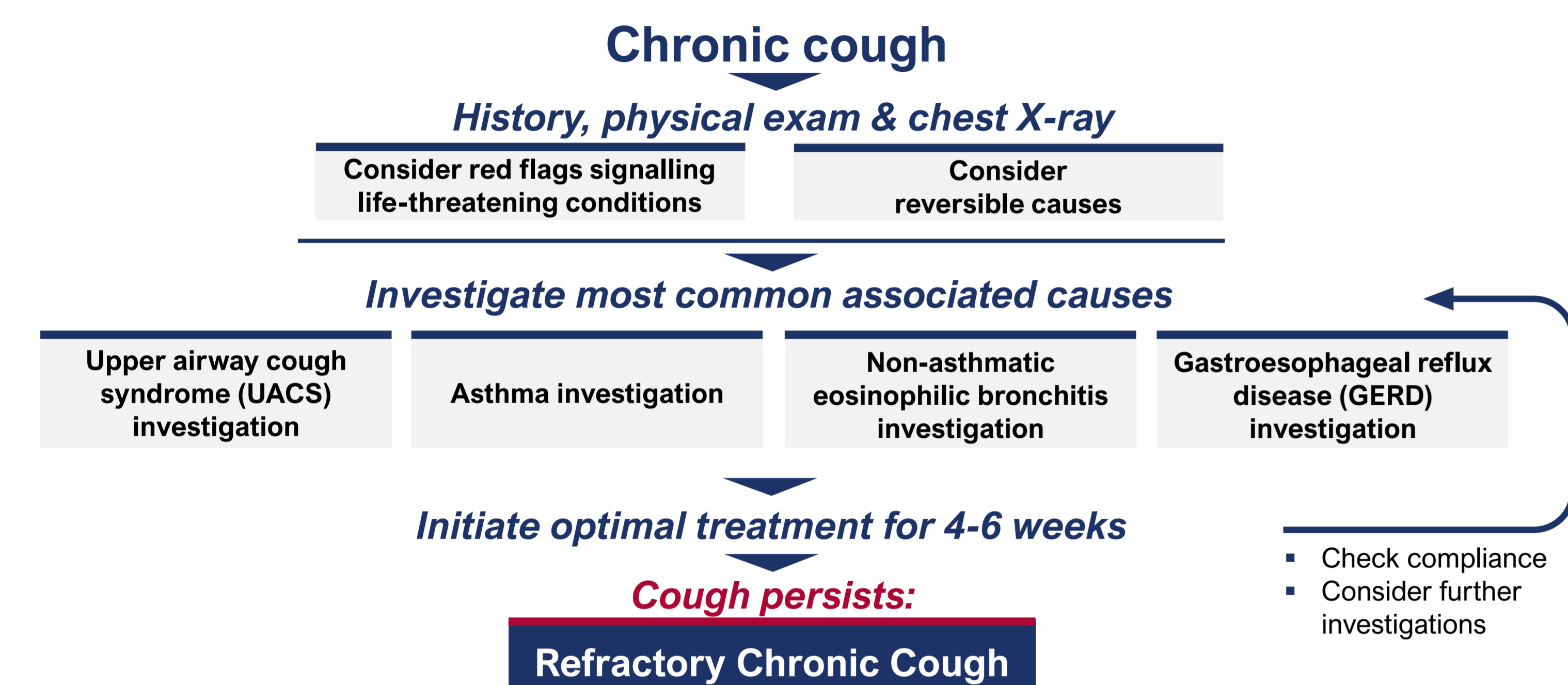


Introduction

- 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}. RCC can impose a significant physical, psychological and social burden on patients².
- Guided by patient history, the diagnostic journey of patients with chronic cough may involve multiple medical consultations, diagnostic investigations and trials of therapy to lead to a diagnosis of refractory chronic cough (Fig.1). These cycles of repeated consultations, tests and trials of ineffective treatments for RCC patients further add to the burden on patients.



Adapted from: Irwin RS et al. (2018) CHEST 153 (1): 196-209.

FIGURE 1. Diagnostic Algorithm of Refractory Chronic Cough²

- The development of P2X3 antagonists³⁻⁵ for the treatment of RCC and approvals in Japan and Switzerland have opened an avenue to alleviate the burden of RCC.
- To better understand the current experience of RCC patients, we report the prior specialty consultations, clinical tests and treatments in a RCC population enrolled in a Phase 2b study of BLU-5937, a selective P2X3 antagonist.

Methods

- SOOTHE (NCT04678206) was a multi-center Phase 2b, randomized, placebo-controlled, parallel arm clinical dose-finding study in participants with
 - Persistent Cough for ≥ 1 year
 - Cough severity of at least 40 mm on a 100 mm visual analog scale.
 - A FEV1/FVC score of at least 60%.
 - Patients with a diagnosis of COPD, bronchiectasis or IPF were excluded from the study.
 - Prohibited medications during the study included anti-tussive therapy, gabapentin, pregabalin, baclofen, tricyclic antidepressants, systemic corticosteroids and ACE inhibitors.
- Following a run-in period, participants who maintained a cough frequency ≥ 25 coughs/h (n=249) were randomized into the SOOTHE main population. Participants who maintained a cough frequency ≥ 10 coughs and < 25 coughs/h (n=61) were randomized into the SOOTHE exploratory population.

Results

- Overall, the RCC populations randomized in SOOTHE (Tab. 1) had characteristics representative of those reported for RCC elsewhere³⁻⁵ (Tab. 1).
- Similar proportions of participants in each the main vs exploratory populations had consulted at least one specialist for their cough (88 vs 87%;), undergone at least one medical test (88 vs 85%) or attempted at least one prior cough-related therapy (94 vs 92%) (Fig. 2).
- The proportion of participants that had consulted more specialists, undergone more medical tests or attempted more therapies showed a greater degree of difference between the main and exploratory populations (Fig. 2).

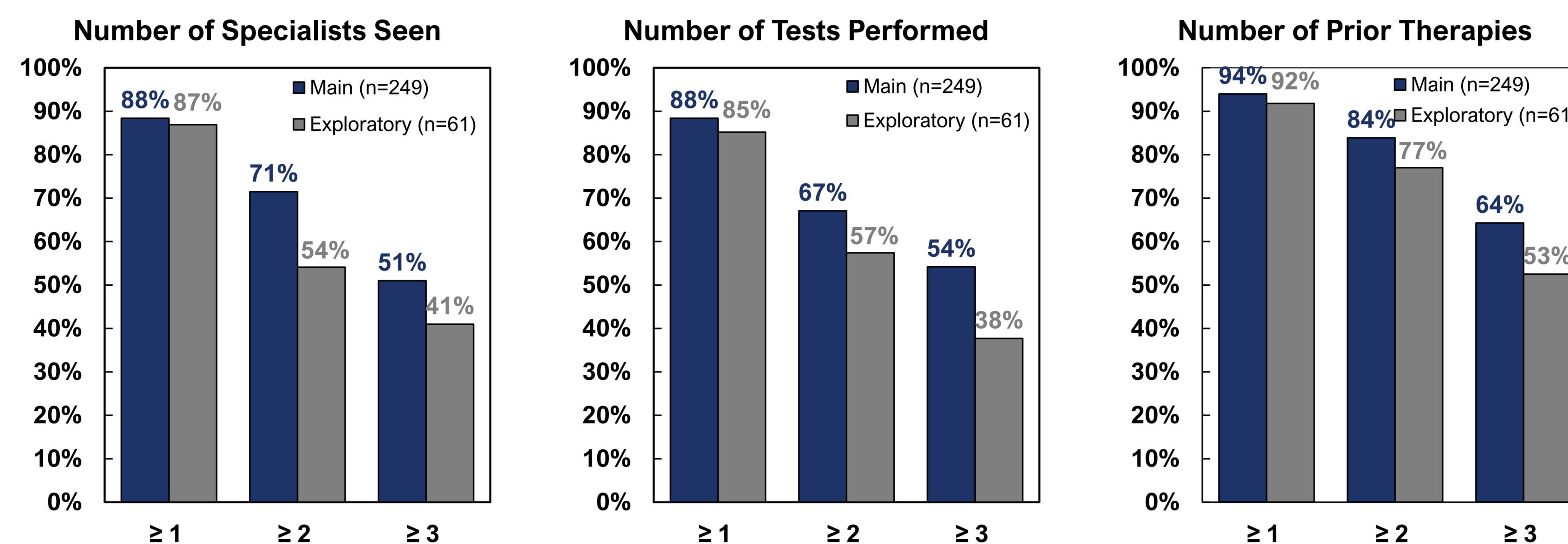


FIGURE 2. Number of cough-related specialists seen, tests performed and prior therapies

- In the main vs exploratory SOOTHE populations, 78 vs 62% of participants had consulted a pulmonologist, 59% vs 41% had consulted an otolaryngologist, 50 vs 44% had consulted an allergist/immunologist, 46% vs 44% had consulted a gastroenterologist, 16% vs 8% had consulted a speech pathologist (Fig. 3).
- Overall, tests performed, and prior cough therapies were similar between the main and exploratory populations. The most common prior cough therapies tried included acid reducers, inhaled bronchodilators and oral antihistamines (Fig. 3).

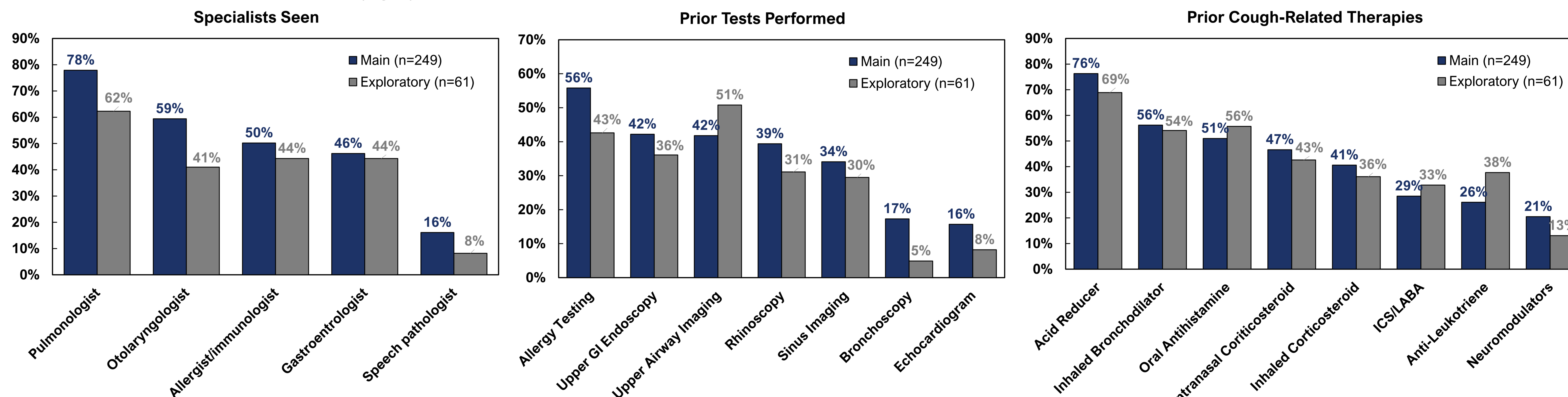


FIGURE 3. Types of cough-related specialists seen, tests performed and prior therapies

Conclusions

- The SOOTHE main population and exploratory population had similar demographic characteristics, cough duration and reported cough severity regardless of their average baseline cough frequency.
- Trends observed suggest that a higher proportion of participants in the SOOTHE main population had undergone a more extensive diagnostic process. This may imply that patients with more frequent cough may undergo more extensive assessment than those with less frequent cough.

TABLE 1. Baseline Demographics And Characteristics

	Main	Exploratory	
Participants, n	249	61	
Female, n (%)	204 (82%)	37 (61%)	
Age (years), mean (SD)	60.9 (10.6)	61.3 (9.4)	
BMI (kg/m ²), mean (SD)	28.1 (6.0)	30.1 (5.3)	
FEV ₁ /FVC, mean (SD)*	0.77 (0.07)	0.77 (0.07)	
Race, n (%)	White	240 (96%)	57 (93%)
	Black	3 (1%)	3 (5%)
	Asian	4 (2%)	1 (2%)
	American Indian/ Alaska Native	2 (1%)	0
	24H Cough Frequency** (coughs/h), mean _{geo}	38.9	11.2
LCQ, mean (SD)	10.6 (3.1)	11.8 (3.0)	
CS-VAS (mm), mean (SD)	72.9 (14.8)	69.5 (16.0)	
Cough Duration (years), mean (SD)	Asthma	76 (31%)	23 (38%)
	GERD	115 (46%)	33 (54%)
Cough-associated disease	UACS	64 (26%)	16 (26%)
	Unexplained	86 (35%)	16 (26%)

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

** Measured at baseline

References

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