Cough is prevalent in higher proportion of the effect of naltrexone, an opioid receptor antagonist, on capsaicin evoked cough, in healthy male subjects

**Introduction**
Cough is a major symptom of idiopathic pulmonary fibrosis (IPF), a progressive, fatal lung disease with median survival of 3 years. The first study to suggest cough as an independent predictor of disease progression, reported it in 84% of the population. 1 The only study to quantify cough in 19 IPF patients, reported strong correlation between objective cough counts and cough related quality of life. 2 There is a lack of studies investigating the prevalence, pathogenesis or treatment of cough in IPF. We set up a study to evaluate the prevalence of cough in an incident IPF and non specific interstitial pneumonitis (NSIP) population.

**Methods**
A prospective, multi-centre, observational, cohort study, PROFILE-Central England (September 2009 to June 2014) was set up. Patients had a diagnosis of definite or probable IPF or NSIP based on the ATS consensus. Leicester cough questionnaire (LCQ) was used to assess presence or absence of cough at baseline. Furthermore, the cohort was divided into 3 groups to assess severity of cough: Mild (17–20), Moderate (11–16.9) and Severe (<11).

**Results**
312 incident patients with IPF or NSIP were enrolled. 261/312 (83.6%) patients had incident IPF whilst 51/312 (16.4%) had NSIP. The mean age of the cohort was 73.5 years (35–90 years). 235/312 (76%) were males with mean age 73.7 years (47–90 years); 74/312 (24%) were females with mean age of 72.9 years (35.8–88.8 years).

261/312 (83.6%) reported cough compared with 51/312 (16.4%) who reported no cough. Of the patients who reported cough, 45/261 (17.2%) had severe cough, 112/261 (42.9%) had moderate cough and 104/261 (39.8%) had mild cough. There was no effect of gender, however, older cohort reported more cough (age >55 years; p = 0.014). Smoking may be a confounder, however the number of current smokers in the cohort is too small (p = 0.05).

Interestingly both NSIP and IPF cohort reported cough; however, proportionally NSIP patients have less cough (14/51, 27.4%) compared with IPF (37/261, 14%).

**Conclusions**
Cough occurs in a huge majority of patients with both IPF and NSIP. Cough appears to be a greater problem in older patients.

**REFERENCES**
2. Key AL et al. Objective cough frequency in idiopathic pulmonary fibrosis. Cough, 2010;6:4
Conclusion This small pilot study suggest that opiate sensitive inhibitory mechanisms may have a role in controlling the cough reflex even in healthy subjects.

REFERENCES

Background Chronic cough represents an important unmet clinical need. Gamma-aminobutyric acid is a major inhibitory neurotransmitter in the central nervous system (CNS). GABAB receptors have been identified peripherally, as well as centrally. Studies in guinea-pigs, have suggested that the activation of GABAB receptors in the CNS and PNS can inhibit cough. The only clinically available GABAB agonist is Baclofen, and although it has been shown to suppress cough in animals and humans, it causes drowsiness as it is centrally acting. Lesogaberan, is a novel, predominantly peripherally acting GABAB agonist. Objective To determine whether both peripherally acting (Lesogaberan) and centrally acting (Baclofen) GABAB agonists modulate cough responses to inhaled capsaicin compared with placebo in healthy volunteers.

Methods Single centre, double-blind, double-dummy, three-way crossover trial in healthy controls of Lesogaberan (120 mg MR), Baclofen (40 mg) and placebo. Subjects were treated with single crossover trial in healthy controls of Lesogaberan (120 mg MR), Baclofen (40 mg) and placebo. Subjects were treated with single doses of each study medication with a washout period of ≥7 days between doses. Cough responses to inhaled capsaicin were assessed using a novel challenge protocol (1) measured at screening and 2 hrs post dosing (tmax) on each study day. The primary end point was the concentration of capsaicin (Emax). The secondary end point was the concentration of capsaicin evoking 50% of the maximal response (ED50). Results There were 15 patients enrolled onto the study with a median age of 29 years old (IQR25–44); 7 female; mean BMI was 24.6 (±3.0). Lesogaberan treatment was associated with a small, statistically significant increase in Emax (mean 13.4 coughs, 95% CI 10.1–17.9) compared with placebo (11.8, 95% CI 8.8–15.9) (p = 0.04), but had no effect on ED50 (geometric mean 47.4 μM 95% CI 24.4–91.7 vs Placebo 37.6 95% CI 19.2–73.5 p = 0.37), see Figure 1.

In contrast, Baclofen had no significant effect on Emax (11.1, CI8.1–15.4) (p = 0.23), but, ED50 was significantly increased compared with placebo (geometric mean 75.2 μM 95% CI 37.2–151.8 p = 0.002).

Conclusion This data suggests the anti-tussive actions of GABAB agonists, against capsaicin-induced cough in healthy volunteers, occurs in the central rather than the peripheral nervous system.

REFERENCES