A Placebo-Controlled Trial of Aprepitant for Cough in Lung Cancer

Amelie Sylvia Mary Harle[1,2], Jaclyn A Smith[3,4], Alex Molassiotis[5], Kimberley Lofthouse[3], Rachel Dockry[3], Philip Russell[2], Katy Burns[2], Fiona Helen Blackhall [2,6]

[1] *Dorset Cancer Centre, Poole NHS Foundation Trust, UK*

[2] *Department of Medical Oncology, The Christie NHS Foundation Trust, UK*

[3] *Division of Infection, Immunity and Respiratory Medicine, University of Manchester, Manchester, UK*

[4] *Manchester University NHS Foundation Trust, Manchester, UK*

[5] *School of Nursing, The Hong Kong Polytechnic University, Hong Kong*

[6] *Division of Cancer Sciences, University of Manchester, Manchester, UK*

Background: There are no evidence-based therapies for cough in lung cancer (LC).The neurokinin-1 (NK-1) pathway is implicated in cough. Aprepitant is an NK-1 antagonist used as an antiemetic. We assess aprepitant as an antitussive, using objective daytime ambulatory cough monitoring (ACM) as the primary endpoint.

Methods: LC patients with a "bothersome" cough were enrolled on an exploratory single-arm randomised double-blind crossover trial and received 125mg aprepitant on day 1 and 80mg on days 2 and 3 or matched placebo capsules. After a 3 day wash out, patients crossed over to placebo or aprepitant for 3 days (days 7-9). They completed ACM and validated subjective cough tools.

Results: 20 LC patients were enrolled between 7th Oct 2013-3rd Nov 2014; mean age 66 yrs (SD 7.69); 60% (n=12) female; 70% (n=14) ex, 25% (n=5) current and 5% (n=1) never smokers respectively. 20% (n=4), 55% (n=11) and 25% (n=5) had a performance status of 0, 1 and 2 respectively. The majority (80% n=16) had non-small cell LC; half (n=10) had advanced stage; 20% (n=4) were on anticancer therapy. Daytime cough frequency was 15.9 (95%CI 10.1-28.3 n=19), 12.8 (95% CI 8.7-18.8 n=18) and 16.2 (11.3-23.0 n=19) coughs/hr at baseline, on aprepitant and on placebo respectively: p=0.03. Visual analogue scale scores (range 0-100, high score=worse severity) were 57.0mm (95% CI 47.4-67.2 n=19), 40.8mm, (95%CI 34.3-47.3 n=18), and 49.8mm (95%CI 44.2-55.4 n=19) at baseline, on aprepitant and on placebo respectively: p=0.008. The Manchester Cough in Lung Cancer Scale score (range 1-50, high score = worse cough impact) was 25.2 (95%CI 23.0-28.0 n=19), 19.5 (95%CI 17.8-21.2 n=18) and 21.7 (20.3-23.1 n=18) at baseline, on aprepitant and on placebo respectively: p<0.001.There were no serious adverse events.

Conclusions: This is the first trial to assess the efficacy of a novel antitussive using validated subjective and objective cough tools in LC and the first to investigate a centrally acting NK-1 antagonist in humans. Aprepitant treatment was associated with statistically significant improvements in objective and subjective scores. The NK-1 receptors may be key mediators in cough in LC. It is possible to run a robust trial using validated measures with clinically meaningful endpoints in a LC population