Title: Do phosphodiesterase 5 inhibitors improve exercise capacity in patients with COPD associated pulmonary hypertension? (3P study)

Body: Background PH complicates COPD, negatively influencing mortality, exercise tolerance and QOL. It is unknown whether pulmonary vasodilation through PDE5-inhibition has beneficial effects in COPD associated PH. Aims To determine if PDE5-Is improve exercise capacity, QOL and cardiac function in COPD-PH. Methods A randomised, double-blind, parallel group, placebo controlled study was conducted (60 patients per arm). The active arm received 10 mg daily tadalafil for 12 weeks. Primary endpoint: 6MWD. Secondary endpoints: SGRQ, SF-36 and Minnesota questionnaires (QOL); BNP; DLCO and echo parameters. Inclusion: moderate-severe COPD and PH [RVSP >30mmHg and/or a pulmonary acceleration time (PAT) <120ms]. Exclusion: LVSD, aortic stenosis or use of nitrates. Results (n=120) Mean FEV1 1.06±0.41 L (41% pred.), mPAP 30±7 mmHg (PAT derived), RVSP 42±10 mmHg. At 12 weeks the mean placebo corrected ∆6MWD=0.5m. Clinically significant divergence of QOL scores favoured the active group with between group differences of -4.41 95%CI(-9.20-0.38), p=0.071 for SGRQ activity levels and 4.08 95%CI(-1.35-9.52), p=0.139 for SF-36 physical function, although not statistically significant. No significant changes were noted in BNP, DLCO, or RV function (TAPSE). A significant between group ∆PAT occurred, 9.5ms 95% CI (3.24 to 12.56), p= 0.001. Conclusions Tadalafil did not increase 6MWD. Clinically significant QOL score divergence of >4 points occurred in domains of activity and physical function, favouring the active group. This warrants further exploration. An expected pulmonary vasodilatory effect as determined by PAT was found in the active group without significant change in RV function.