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Calverly P, Rabe K, Goehring UM, Kristiansen S, Fabbri LM, Martinez FJ; M2-124 and M2-125 study groups. Roflumilast in symptomatic chronic obstructive pulmonary disease: two randomised clinical trials. *Lancet* 2009;374:685-94.

The use of phosphodiesterase inhibitors in COPD is not a nouveau concept. Since their introduction in the early 1970's its role in COPD has been tangential. Nonselective phosphodiesterase inhibitors such as aminophylline and theophylline showed efficacy as bronchodilators and anti-inflammatories. The nonselective PDE inhibitors fell out of favor due to its side effect profile and narrow therapeutic index. With the approval of roflumilast by the Federal Drug Administration, we reviewed the study by Calverly et al. which reviewed two trials of roflumilast as a selective PDE4 inhibitor and its capacity to improve lung function and reduce COPD exacerbations. The two studies were large multicenter double blinded placebo controlled trials which followed patients over 52 weeks. Patients with severe COPD were divided into two subsets; a placebo group and a roflumilast treatment group. Primary endpoints were a change in FEV1 and number of COPD exacerbations. The results showed patients on roflumilast had a slight statistically significant improvement in lung function with an increase in prebronchodilator FEV1 of 40ml. The study also showed a reduction in COPD exacerbations by 17% in the treatment arm. Main side effects were severe nausea, vomiting, diarrhea and an average weight loss of 4.2 kg when compared to placebo. The main limitation of this study is that it failed to show that medication related improvements were anything more than a bronchodilator effect. A cost analysis would also have been helpful.

Overall, Roflumilast as a new selective PDE4 inhibitor does show some mild improvement in lung function and reduction in COPD exacerbations. However, the benefits are small and cost may be a factor. Its main role may be limited to very severe COPD patients with cardiac disease and a BMI greater than 30.

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