

A double blind placebo controlled study to assess the effect of Roflumilast in addition to LABA/LAMA/ICS treatment in COPD patients using novel biomarkers

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Rationale

Recently Roflumilast (PDE4 inhibitor, Daxas®, Takeda) has been added as therapeutic option for severe COPD patients. The current study aims to 1) assess the mode of action 2) identify responder type of Roflumilast as add-on to LABA/LAMA/ICS therapy in severe COPD patients.

Methods

41 patients were randomized to Roflumilast or placebo. At baseline and after 6m of treatment PFT, exercise tolerance tests (ETT) and functional respiratory imaging (FRI) were performed and patient reported outcomes (PRO) were measured.

Results

FEV1 did improve by 66 ± 120 ml ($p=0.01$) after Roflumilast as compared to baseline. Response was driven by a subset ($n=8$) of patients with a change in FEV1 >120 ml (= measurement error of FEV1). Responders experienced worse dynamic hyperinflation during exercise at baseline compared to non-responders. FRI indicated regional changes in hyperinflation after Roflumilast leading to an improvement in PFT, PRO and ETT.

Conclusions

Roflumilast seems to reduce inflammation in the smaller airways resulting in reduced hyperinflation and changing internal airflow distribution (IAD). Changed IAD enhances deposition of LABA/LAMA/ICS leading to clinical improvements. Patients with dynamic hyperinflation tend to benefit from Roflumilast. These findings are relevant because 1) this is the first study to report effects of PDE4 inhibitor on top of ICS/LABA/LAMA; 2) sensitive, image-based endpoints provide insights in the mode of action of anti-inflammatory compounds and a basis for responder phenotyping. The current study provides hypotheses that need to be confirmed in larger clinical trials.

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