ONCE VERSUS TWICE DAILY FORMOTEROL VIA NOVOLIZER® FOR PATIENTS WITH MODERATE TO SEVERE COPD – A DOUBLE-BLIND, RANDOMISED, CONTROLLED TRIAL


**Objective:** To evaluate in patients with moderate to severe COPD if a single morning dose of 24 μg formoterol (OD) from the Novolizer® is not inferior to 12 μg formoterol twice daily (BID) inhaled in the morning and evening.

**Design:** Randomised, double-blind, active-controlled, parallel-group, multi-centre study with a 2-week run-in phase and a 12-week treatment phase.

**Patients:** 321 symptomatic patients with moderate to severe COPD (mean age: 60.3 years, mean duration of COPD: 8.8 years) with an FEV₁ of 30-80 % predicted and requiring 3-12 actuations of salbutamol per day on ≥ 5 days during the run-in phase.

**Methods:** Following the run-in phase with salbutamol as active treatment, patients were randomised to therapy with 24 μg formoterol from the Novolizer® in the morning (once daily regimen) or 12 μg formoterol in the morning and evening (BID regimen). At the study visits, pulmonary function was measured before and after administration of the study medication. COPD symptoms graded by severity, morning/evening peak expiratory flow (PEF), and use of rescue medication (salbutamol) were recorded by the patients in a diary. Quality of life was assessed by St. George’s respiratory questionnaire (SGRQ).

**Primary efficacy endpoint:** Change of predose forced expiratory volume (FEV₁) between baseline and 12 weeks after treatment.

**Results:** Following treatment, FEV₁ had increased in both groups (OD: +104 ml; BID: +135 ml). The statistical hypothesis of non-inferiority of OD was not confirmed, because of too narrow margins set for the primary end point FEV₁. In contrast, no statistically significant differences were shown between groups for all secondary efficacy parameters (e.g. PEF, COPD symptoms, salbutamol usage). After 12 weeks of treatment, symptom-free days had increased by 10.4 % (OD) and 9.2 % (BID). Mean scores for COPD symptoms cough, sputum production, breathlessness and sleep disturbance and quality of life scores improved equivalently in both BID and OD treatment groups. A relevant difference between the groups in the incidence of adverse events was not observed.

**Conclusions:** Based on comparable efficacy and tolerability, formoterol inhaled via the Novolizer® once daily in the morning seems to be an alternative to treatment BID. Clinically the primary endpoint suggests the equivalence of both BID and OD treatment regimens. Thus, OD treatment may be an option for some COPD patients.

**Comment:** Due to the narrow margins chosen for the statistical evaluation of the primary endpoint FEV₁ (the 95% CI exceeded the predetermined margin of 100 ml by 2 ml), the statistical hypothesis of equivalence of both therapeutic regimens could not be confirmed by this study. As a consequence, only the BID treatment has been approved by the EU regulatory authorities. Clinically however, comparable and significant improvements in COPD symptoms, lung function, and quality of life were demonstrated with both BID and OD treatment regimes. Formoterol Novolizer provides flexible treatment depending on the patient’s adherence (once or bid) thereby relieving distressing COPD symptoms and improving quality of life.