**ACTIVATE: the effect of aclidinium/formoterol on hyperinflation, exercise capacity, and physical activity in COPD patients.**

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**Background**
- COPD patients often suffer from breathlessness that affects their ability to exercise and go about their daily activities. Being less physically active can lead to an increase in COPD symptoms and a worsening of the patient’s COPD, which in turn can result in further reductions of physical activity.
- Therefore, a key part of COPD management is helping patients to increase their activity levels and to stay active.

**Methods**
- **ACTIVATE** is a phase IV, multi-center, 8-week, multiple-dose, randomized, double-blind, placebo-controlled, parallel-group study. Patients were aged ≥ 40 years, current or former cigarette smokers with a clinical diagnosis of moderate/severe COPD.
- Patients were randomized to receive AB/FF (aclidinium/formoterol) or placebo. During the first 4 weeks of the study, patients received pharmacotherapy alone and, during the second 4 weeks, behavioural intervention (BI; daily messages providing step goals) was added to both treatment arms.
- Study objectives were the effect of AB/FF versus placebo on lung hyperinflation, exercise endurance time and physical activity with/without BI.

**Results**

**Lung Function**
- Patients receiving AB/FF demonstrated a greater reduction in adjusted mean change from baseline vs placebo in **trough FRC** (functional residual capacity) at week 4, but this did not reach statistical significance. However, once outliers were excluded a statistically significant reduction of 0.196L (p=0.0010) was demonstrated.
- **Post-dose lung hyperinflation** measurements showed significant improvements in change from baseline in FRC, RV (residual volume), IC (inspiratory capacity), and sGaw (specific airway conductance) at week 4 with AB/FF vs placebo (0.366L, 0.465L, 0.293L, and 0.341s⁻¹ kPa⁻¹; all p<0.0001). Furthermore, a significant improvement in adjusted mean change from baseline in **pre-dose (tough) FEV₁** was found for AB/FF vs placebo at week 4 (0.205L; p<0.0001).

**Exercise Capacity**
- Patients treated with AB/FF had greater improvements in exercise capacity compared with placebo as demonstrated in change from baseline in **EET (exercise endurance time)** at week 4 (58.9s; p=0.0089) and week 8 (55.2s; p=0.0292).
- Additionally, improvements in IC (inspiratory capacity) during exercise were observed at week 4 and 8 (treatment difference in IC at isotime of 0.246L and 0.226L, and at the end of exercise 0.218L and 0.194L; all p<0.0001).

**Physical Activity**
- After 4 weeks, the percentage of **inactive patients** on AB/FF was significantly reduced with 13.8% compared with placebo (OR 0.27; p<0.0001).
- Patients receiving AB/FF showed significant improvements in the **number of steps per day** (+621) compared with a decrease (-110) in placebo (treatment difference of 731 steps per day; p=0.0016). During the last 4 weeks, BI maintained improvements achieved in the number of steps per day after 4 weeks of AB/FF treatment.
Conclusion

- AB/FF demonstrated improvements in hyperinflation, exercise tolerance, and physical activity versus placebo. In short term, BI did not further augment the improvements observed with AB/FF.
- The results suggest that an increase in physical activity due to bronchodilation does not result in an unpleasant, burdensome experience for patients when increasing their activity levels. This is potentially highly relevant for health care providers trying to motivate patients to adopt and maintain a more active lifestyle.

Reference: