A pooled analysis of mortality in patients with COPD receiving triple therapy versus dual bronchodilation

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Introduction: A possible mortality benefit of long-acting muscarinic antagonist (LAMA)/long-acting β2-agonist (LABA)/inhaled corticosteroid (ICS) versus LAMA+LABA combination treatment is reported in patients with highly symptomatic chronic obstructive pulmonary disease (COPD) with a history of exacerbations (≥1 moderate/severe exacerbation in previous year). We compared the time to all-cause mortality with LAMA+LABA+ICS versus LAMA+LABA in patients with moderate-to-severe COPD and predominantly lower exacerbation risk.

Methods: Patients who received either LAMA+LABA+ICS (n=11,891) or LAMA+LABA (n=3,156) were pooled from phase 3/4 randomized controlled trials (TONADO 1/2, DYNAGITO, WISDOM, UPLIFT and TIOSPIR). Analysis was on-treatment and censored at 52 weeks. Propensity score (PS)-matched cohorts (covariates: age, sex, geographical region, smoking status, postbronchodilator forced expiratory volume in 1 second (FEV1) percent predicted, exacerbation history, body mass index and time since diagnosis) were used to ensure well-balanced treatment groups. Time to all-cause mortality was assessed using Cox proportional-hazards regression models adjusted for covariates.

Results: Each PS-matched treatment group had 3,133 patients with well-balanced baseline characteristics and comorbidities (LAMA+LABA+ICS vs. LAMA+LABA: male: 72.0% vs. 71.7%; age, mean±SD: 65.5±8.7 vs. 65.5±8.8 years; postbronchodilator FEV1% predicted, mean±SD: 48.4±13.3% vs. 48.6±13.2%; patients with ≥2 COPD exacerbations in prior year: 19.0% vs. 19.1%). No statistically significant difference in time to all-cause mortality was observed between treatment groups (hazard ratio [95% CI]: 1.06 [0.68–1.64]; P=0.806). There were 41 (1.3%) deaths in the LAMA+LABA+ICS group and 41 (1.3%) in the LAMA+LABA group.
Conclusions: This pooled analysis showed no differences in mortality between LAMA+LABA and LAMA+LABA+ICS in patients with moderate-to-severe COPD and predominantly lower exacerbation risk.