Triple Therapy Superior to Long-acting Muscarinic Antagonist for COPD

Moderate to severe exacerbations were significantly reduced in the fixed triple therapy group compared with tiotropium monotherapy.

Extrafine triple therapy consisting of a corticosteroid, a long-acting β2-agonist, and a long-acting muscarinic antagonist taken in a single inhaler significantly reduced the rate of chronic obstructive pulmonary disease (COPD) exacerbations compared with m3monotherapy, while also improving lung function and a range of other clinically relevant measures of COPD in high-risk patients. These results from the multinational TRINITY study were reported in the*Lancet*.

The TRINITY study was a double-blind, parallel-group, randomized controlled trial (ClinicalTrials.gov Identifier: [**NCT01911364**](https://clinicaltrials.gov/ct2/show/NCT01911364?term=NCT01911364&rank=1)) assessing 52 weeks of treatment at 224 sites located in 15 countries in Europe and South America, plus Mexico. From January 2014 to March 2016, enrolled patients were randomized (stratified by country and severity of airflow restriction) to receive 1 of 3 treatments in a 2:2:1 ratio: fixed triple therapy with extrafine beclomethasone dipropionate, formoterol fumarate, and glycopyrronium bromide (n=1078); the muscarinic antagonist tiotropium 18 μg (n=1075); or open triple therapy (beclomethasone dipropionate/formoterol fumarate plus tiotropium n=538). The patients in the study were all older than 40 years, with some history of smoking, and had [**diagnosed COPD**](http://beta.pulmonologyadvisor.com/copd/common-smoke-related-pulmonary-disease-gets-new-definition/article/655102/) with at least 1 moderate to severe exacerbation in the last 12 months. All participants used some single or combination inhaled therapy at baseline and had a postbronchodilator forced expiratory volume in 1 second of less than 50%.

Current triple therapy for COPD requires the use of at least 2 inhalers, often produced by different manufacturers, which may in turn hamper proper administration and lessen adherence. The rate of moderate to severe exacerbations in the TRINITY trial was significantly reduced in the fixed triple therapy group compared with tiotropium monotherapy (0.46 vs 0.57 per patient, respectively, with an adjusted rate ratio of 0.80; 95% CI, 0.69-0.92; *P* =.0025), and was similar to the open-triple therapy group.

Subgroup analysis in patients with higher eosinophil concentrations of >2% showed a greater reduction of exacerbations with fixed triple therapy (rate ratio, 0.70; 95% CI, 0.58-0.85) and open triple therapy (rate ratio, 0.69; 95% CI, 0.55-0.87) compared with tiotropiummonotherapy.

Median exposure to all therapies was 365 days, with high treatment compliance in all 3 groups anda median of 94.6% (interquartile range, 87.2%-98.4%) doses in the fixed triple group, 94.3% (interquartile range, 85.7%-98.3%) in the tiotropium group, and 94.9% (interquartile range, 88.7%-98.5%) in the open triple group.

These results showed clear clinical benefit to extrafine fixed triple therapy compared with tiotropium alone in this base of patients with COPD.

**Reference**

Vestbo J, Papi A, Corradi M, et al. [**Single inhaler extrafine triple therapy versus long-acting muscarinic antagonist therapy for chronic obstructive pulmonary disease (TRINITY): a double-blind, parallel group, randomised controlled trial**](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2817%2930188-5/fulltext) [published online April 3, 2017]. *Lancet.* doi: 10.1016/S0140-6736(17)30188-5