

Combination therapy for COPD associated with better outcomes

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Among older adults with chronic obstructive pulmonary disease (COPD), particularly those with asthma, newly prescribed long-acting beta-agonists (LABAs) and inhaled corticosteroid combination therapy, compared with newly prescribed LABAs alone, was associated with a lower risk of death or COPD hospitalization, according to a study in the September 17 issue of *JAMA*.

Chronic <u>obstructive pulmonary disease</u> is the third leading cause of death worldwide. Medications are a mainstay of COPD management, and knowing which are most effective in real-world practice is essential. Combination therapy consisting of LABAs and inhaled corticosteroids (ICSs) has been shown to decrease exacerbations and possibly decrease the risk of death compared with placebo. However, there are still gaps in what is known about its effectiveness compared with LABAs alone, according to background information in the article.

Andrea S. Gershon, M.D., M.Sc., of the Sunnybrook Health Sciences Centre and Institute for Clinical Evaluative Sciences, Toronto, and colleagues examined the outcomes of LABA-ICS combination therapy compared with LABAs alone in older COPD patients with other illnesses, including asthma. The study, which included data from 2003 to 2011 in Ontario, included individuals ages 66 years or older who met a validated case definition of COPD; there were 8,712 new users of LABA-inhaled corticosteroid combination therapy and 3,160 new users of LABAs alone who were followed up for a median of 2.7 years and 2.5 years, respectively.



The primary outcome (the composite of death and COPD hospitalizations) was observed among 2,129 new users of LABAs (1,179 deaths [37.3 percent]); 950 COPD hospitalizations [30.1 percent]) and 5,594 new users of LABAs and ICSs (3,174 deaths [36.4 percent]; 2,420 COPD hospitalizations [27.8 percent]). There was a modest but significantly lower risk of the composite outcome among new users of LABAs and ICSs compared with new users of LABAs alone.

The greatest difference was among COPD patients with a codiagnosis of asthma (difference in composite at 5 years, -6.5 percent) and those who were not receiving inhaled long-acting anticholinergic medication (a different class of COPD medication that works by inhibiting the transmission of certain nerve impulses to help reverse airway resistance; difference in composite at 5 years, -8.4 percent).

"Our finding of an association between LABAs and ICSs and outcomes helps clarify the management of patients with COPD and asthma, as many studies of COPD medications have excluded people with asthma and vice versa," the authors write. "In addition, practice guidelines for COPD recommend that LABAs be considered first-line treatment while asthma guidelines warn against use of LABAs without ICSs. Our findings also offer insight into the optimal treatment of COPD patients without asthma—those who would not be considered especially corticosteroid responsive."

The researchers add that these findings should be confirmed in randomized clinical trials.

Peter M. A. Calverley, M.B.Ch.B., D.Sc., of the University of Liverpool, England, comments on the findings of this study in an accompanying editorial.

"Perhaps the most noteworthy feature of the new data reported by



Gershon et al is the difference in the characteristics of the patients who use these treatments from those in whom therapy was validated in randomized clinical trials (RCTs). The outcomes of treatment in these 'real-world' patients were somewhat better than might have been expected from RCTs, but the patients were also much more diverse and often sicker. The study by Gershon et al shows that findings from appropriately conducted database analyses complement data from RCTs and should be considered when determining treatment algorithms."

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