Research Developments in COPD

OVERVIEW

The latest research related to the treatment of patients with COPD is often first made public at the annual CHEST meeting. In this CME activity, Barbara Yawn, MD, provides an introduction related to the role of triple inhaled therapy in selected patients with COPD to treat symptoms and prevent exacerbations. She discusses 3 posters presented at the 2021 CHEST meeting related to triple therapy. Dr. Yawn first summarizes the methods and results of each of these posters, then provides her own thoughts as to the importance of the research findings and implications for clinical practice in the treatment of patients with COPD.

CONTENT AREAS

- Post hoc analysis of ETHOS
- Dual vs triple inhaled therapy
- Timing of therapy after an exacerbation

FACULTY

Barbara P. Yawn, MD
Adjunct Professor
University of Minnesota
Department of Family and Community Health
Minneapolis, Minnesota

TARGET AUDIENCE

This activity is intended for pulmonologists, allergists, critical care specialists, primary care physicians, and other clinicians involved in the management of patients with COPD.

LEARNING OBJECTIVES

At the conclusion of this activity, participants should be better able to:

- Describe how new data and recommendations can impact clinical practices to improve care
- Incorporate evidence-based research into clinical practice

ACCREDITATION AND CERTIFICATION

The Annenberg Center for Health Sciences at Eisenhower is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

The Annenberg Center for Health Sciences at Eisenhower designates this enduring material for a maximum of .75 *AMA PRA Category 1 Credits*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

DISCLOSURE STATEMENT

It is the policy of the Annenberg Center for Health Sciences to ensure fair balance, independence, objectivity, and scientific rigor in all programming. All faculty and planners participating in accredited education activities are expected to identify and reference off-label product use and disclose any relationship with those supporting the activity or any others with products or services available within the scope of the topic being discussed in the educational presentation.

The Annenberg Center for Health Sciences assesses conflict of interest with its instructors, planners, managers, and other individuals who are in a position to control the content of CE/CME activities. All relevant conflicts of interest that are identified are thoroughly vetted by the Annenberg Center for fair balance, scientific objectivity of studies utilized in this activity, and patient care recommendations. The Annenberg Center is committed to providing its learners with high-quality CE/CME activities and related materials that promote improvements or quality in healthcare and not a specific proprietary business interest of an ineligible company.

In accordance with the Accreditation Council for Continuing Medical Education Standards, parallel documents from other accrediting bodies, and Annenberg Center for Health Sciences policy, the following disclosures have been made:

Faculty
Barbara P. Yawn, MD, MSc, MPH

Advisory Board:	AstraZeneca, Boehringer Ingelheim, GSK, Novartis, TEVA
Consultant:	TEVA
Research Support:	GSK

The faculty for this activity has disclosed that there will be no discussion about the use of products for non-FDA approved applications.

Additional content planners
The following have no significant relationship to disclose:
Tim Drake, PharmD (medical writer)
Eugene Cullen, MD (peer reviewer)

Annenberg Center for Health Sciences
Staff at the Annenberg Center for Health Sciences at Eisenhower have no relevant commercial relationships to disclose.

The ideas and opinions presented in this educational activity are those of the faculty and do not necessarily reflect the views of the Annenberg Center and/or its agents. As in all educational activities, we encourage practitioners to use their own judgment in treating and addressing the needs of each individual patient, taking into account that patient's unique clinical situation. The Annenberg Center disclaims all liability and cannot be held responsible for any problems that may arise from participating in this activity or following treatment recommendations presented.

This educational activity is supported by an independent educational grant from AstraZeneca.

This activity is an online enduring material. Successful completion is achieved by reading and/or viewing the materials, reflecting on its implications in your practice, and completing the assessment component.

The estimated time to complete the activity is .75 hour.

This activity was released on November 12, 2021 and is eligible for credit through November 12, 2022.

OUR POLICY ON PRIVACY

Annenberg Center for Health Sciences respects your privacy. We don't share information you give us, or have the need to share this information in the normal course of providing the services and information you may request. If there should be a need or request to share this information, we will do so only with your explicit permission. See Privacy Statement and other information at https://annenberg.net/pages/privacyPolicy.php

CONTACT INFORMATION

For help or questions about this activity please contact Continuing Education:
ce@annenberg.net

INTRODUCTION

Barbara Yawn, MD: I want to highlight some of the things that you are going to see from the CHEST abstracts, important information that was shared during the meeting. First of all, they reiterated the importance of the goals of therapy in COPD, improving quality of life and functional abilities by not only treating symptoms, but also preventing or reducing exacerbations. The highlights that were of particular importance were really around preventing exacerbations in patients with severe or frequent exacerbations. By preventing those exacerbations, we know we can slow or prevent the accelerated decline in lung function, decreased health status, quality of life, and mortality, that is associated with exacerbations, especially the severe exacerbations. One of the points that was important was the triple therapy. That's therapy with a LAMA, a LABA and an ICS and it's recommended for patients with significant persistent symptoms on dual therapy and those at high risk of exacerbations, namely those that have had frequent exacerbations, 2 or more moderate in the past year or a severe exacerbation with hospitalization. And those are the gold recommendations.

The advent of triple therapy with LABA, LAMA and ICS in a single inhaler has really been very helpful in simplifying treatment and exacerbation prevention. The impact of the single inhaler continues to be studied because we need to know exactly how much it's going to reduce the disease burden, the roles of patient self-management, the importance of improving adherence by a single inhaler vs multiple, and reducing total steroid doses. That means the oral steroid or systemic steroid, as well as the inhaled steroids. In this activity, we're going to give you key studies that were presented as posters at the American College of Chest Physicians annual meeting in October of 2021. I want to close by just telling you about some new information that was shared. We haven't had many new COPD therapies for quite a while, but there was information coming out about new targeted COPD therapies, specifically information on PDE III, IV inhibitors and the use of IL-5 inhibitors, which are currently used for eosinophilic asthma. I hope you enjoy this information.

Research Developments in COPD

TRIPLE THERAPY REDUCES COPD EXACERBATIONS REQUIRING SYSTEMIC CORTICOSTEROIDS: A POST-HOC ANALYSIS OF THE ETHOS STUDY

Lead author: Celli B

Abstract: Click Here

Study Conclusion:

This analysis of the ETHOS trial showed that patients with moderate-to-very-severe chronic obstructive pulmonary disease (COPD) who used triple inhaled therapy compared to dual inhaled therapy had fewer exacerbations that required systemic corticosteroids (SCS) and fewer days of oral corticosteroid use for moderate exacerbations.

Study Details:

The study is a post-hoc analysis of the ETHOS trial that compared exacerbation rates requiring SCS and the duration of oral corticosteroids (OCS) between different treatment groups. The parent ETHOS trial was a 52-week, phase 3, randomized trial that compared the annual rate of moderate or severe exacerbations in patients with moderate-to-very-severe COPD assigned twice-daily treatment. The groups included in this post-hoc analysis were:

- Triple therapy with inhaled corticosteroid, long-acting beta agonist, and long-acting muscarinic agent--ICS/LABA/LAMA (320 mcg budesonide, 9.6mcg formoterol, 18 mcg glycopyrrolate)
- Dual bronchodilator (LAMA/LABA) (18 mcg glycopyrrolate, 9.6 mcg formoterol) or
- Dual therapy with ICS/LABA (320 mcg budesonide, 9.6 mcg formoterol).

Using a negative binomial regression, the post-hoc analysis compared the actual number and adjusted annual rate of moderate-to-severe exacerbations requiring SCS and summary statistics to the number of days per year of OCS among the groups.

Study Results:

2137 patients received triple therapy ICS/LABA/LAMA, 2120 received LAMA/LABA, and 2131 received ICS/LABA. There were 1539 exacerbations treated with SCS in the ICS/LABA/LAMA group compared with 1837 and 1729 in the LAMA/LABA and ICS/LABA groups, respectively. This corresponds to an adjusted rate ratio (95% CI) for moderate to severe exacerbations for ICS/LABA/LAMA of 0.71 (0.64-0.78) compared to LAMA/LABA and 0.84 (0.76-0.93) compared to ICS/LABA. The mean number of days OCS use/year (with or without antibiotics) for moderate exacerbations was 20.9, 30.0, and 23.2 for ICS/LABA/LAMA, LAMA/LABA, and ICS/LABA, respectively.

Discussion and Clinical Implications:

In patients with moderate-to-very-severe COPD, exacerbation rates requiring SCS can be decreased as can the number of days of OCS use with use of combined ICS/LABA/LAMA. For patients at high risk of repeated exacerbations—those with frequent prior exacerbations and those with low lung function, ICS/LABA/LAMA therapy should be considered as suggested in the ATS guidelines and GOLD recommendations. A limitation of this post-hoc analysis is that it does not assess the impact of blood eosinophil levels that may be important in better targeting patients most responsive to ICS as part of triple therapy.

Research Developments in COPD

EFFECTIVENESS OF COPD MAINTENANCE THERAPY WITH LAMA/LABA VS LAMA/LABA/ICS IN A UNITED STATES CLAIMS DATABASE

Lead author: Quint J

Abstract: Click Here

Study Conclusion:

Among patients with no recent COPD exacerbations, there was no significant difference in time to first exacerbation between patients who were treatment naïve or newly starting maintenance therapy and treated with dual inhaled bronchodilator therapy (LAMA/LABA) vs triple inhaled (LAMA/LABA/ICS) therapy.

Study Details:

The study used retrospective administrative data from the US HealthCore Integrated Research Database. Inclusion criteria were patients with COPD age ≥40 years initiating treatment with ≥1 prescriptions of dual bronchodilator (tiotropium/olodaterol) or triple therapy. Patients were excluded if they had an exacerbation within 30 days of study initiation and in subanalyses if they had prior use of maintenance therapy. The purpose of the study was to compare the time to a hospitalization for community-acquired pneumonia or first COPD exacerbation. A Cox proportional hazard regression model was used to determine outcomes. Reweighting and stratification were used to balance the covariates between the groups including prior exacerbation history.

Study Results:

After reweighting, the study included 2785 patients with dual bronchodilator therapy compared to 15,465 patients with triple therapy. The adjusted hazard ratio for pneumonia for dual vs triple therapy was 0.83 (95% CI: 0.64-1.07). The adjusted hazard ratio for time to first COPD exacerbation for dual vs triple therapy was 1.04 (95% CI: 0.91-1.19). Results were similar when restricting to treatment-naïve patients.

Discussion and Clinical Implications:

When initiating maintenance therapy, both dual bronchodilator therapy and triple therapy can be considered. In this cohort of patients, the risks of pneumonia and COPD exacerbations did not differ between the 2 choices even when the group included only treatment-naïve patients. The study required extensive adjustments to the populations and results to account for differences in the groups—especially the higher baseline rate of severe exacerbations in the triple therapy group.

In practice, treatment choice might be further guided by blood eosinophil count, smoking status, and prior medication use. The study highlights the need to consider initiation of dual bronchodilator therapy as highlighted in ATS guidelines and GOLD recommendations.

Research Developments in COPD

PROMPT INITIATION OF MAINTENANCE THERAPY IN THE UNITED STATES (PRIMUS): AN ANALYSIS OF TRIPLE THERAPY FOLLOWING A DISEASE EXACERBATION AMONG PATIENTS WITH COPD

Lead author: Tkazc J

Abstract: Click Here

Study Conclusion:

Prompt initiation of triple inhaled maintenance therapy (TT) following an exacerbation resulted in a lower risk of future exacerbations in patients with Gold C or D COPD.

Study Details:

The study goal is to compare the risk of future COPD exacerbations between patients receiving early vs delayed initiation of TT following either a severe (hospital treated) exacerbation or ≥2 moderate (outpatient steroid treated) exacerbations. Patients were identified from the IBM MarketScan databases between 2010 and 2019. Patients were categorized based on the timing of the initiation of TT following COPD exacerbation: prompt (<30 days), delayed (31-180 days), and very delayed (>180 days). Chi-square and ANOVA were used to compare the number and severity of exacerbations during the 12 months after initiation of TT.

Study Results:

The analysis included 7577 patients with prompt initiation, 9676 delayed, and 7517 very delayed. The mean (SD) number of severe exacerbations for the 3 groups was 1.3 (1.6), 2.1 (1.8), and 2.8 (2.2), respectively. The proportion of patients with ≥4 exacerbations was 9.6%, 19.3%, and 32.6%, respectively. The proportion of patients with a severe exacerbation was 9.4%, 14.7%, and 21.7%, respectively. All results in the delayed and very delayed groups were statistically different when compared to the prompt initiation group.

Discussion and Clinical Implications:

A delay initiating triple therapy in this group of severe or frequent exacerbators resulted in greater morbidity, higher hospital admission rates, and more frequent exacerbations. The results highlight the importance of follow-up visits after exacerbations to review medications and start appropriate therapy. Smoking status and blood eosinophil levels were not considered which might further help to identify the group with the best response to TT. Additionally, a study of barriers to early treatment (eg, lack of follow-up, cost of therapy, patient reluctance or clinician reticence) would be helpful.