COPD: Treatment Update

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Disclosures

- Advisory board, consultant, multi-center trial, research funding, Data Safety Monitoring Board (DSMB), or speaker for topics related to COPD:
  - National Heart, Lung, and Blood Institute
  - Aerocrine
  - Baxalta
  - CSL Bering
  - GlaxoSmithKline
  - Spiration
  - Theravance
  - AstraZeneca
  - Boehringer-Ingelheim
  - Forest
  - Novartis
  - Sunovion
  - Verona
Learning objectives

• Review the modified COPD definition
• Outline the recent changes in available inhaled medications for COPD
  – Discuss the possible reduction in FEV1 decline in mild / moderate COPD with LAMA
  – Discuss the role of dual bronchodilators for COPD
• Review effective communication strategies to improve COPD patient care
  – Understand how to use inhaled medications
What is GOLD?

Global Strategy For The Diagnosis, Management And Prevention of COPD

- Evidence-based consensus of international experts
- Bring COPD to the attention of governments, public health officials, healthcare workers and general public
- Raise awareness of the burden of COPD
- Develop programs for early detection, prevention and management approaches

Global Initiative for Chronic Obstructive Lung Disease, 2018, goldcopd.org
Definition of COPD

COPD is a common preventable and treatable disease, characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles and gases.

GOLD 2018 Report  www.goldcopd.org
Definition of COPD

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GOLD 2018 Report  www.goldcopd.org
Definition of COPD

*Implies* the need for both symptoms and airflow limitation

- US Preventive Services Task Force report: Do not “screen” asymptomatic patients because of lack of evidence of benefit
- COPD is under diagnosed due to
  - Underappreciated importance by providers
  - Absence of symptoms / assessment
  - Underuse of spirometry
  - Lack of awareness by the public

GOLD 2018 Report  [www.goldcopd.org](http://www.goldcopd.org)
Smokers Without Airflow Limitation

Original Investigation

Clinical and Radiologic Disease in Smokers With Normal Spirometry

Elizabeth A. Regan, MD; David A. Lynch, MD; Douglas Curran-Everett, PhD; Jeffrey L. Curtis, MD; John H. M. Austin, MD; Philippe A. Grenier, MD; Hans-Ulrich Kauczor, MD; William C. Bailey, MD; Dawn L. DeMeo, MD; Richard H. Casaburi, PhD, MD; Paul Friedman, MD; Edwin J. R. Van Beek, MD; John E. Hokanson, PhD; Russell P. Bowler, MD; Terri H. Beaty, PhD; George R. Washko, MD; MeiLan K. Han, MD; Victor Kim, MD; Song Soo Kim, MD; Kunihiro Yagihashi, MD; Lacey Washington, MD; Charlene E. McEvoy, MD; Clint Tanner, MD; David M. Mannino, MD; Barry J. Make, MD; Edwin K. Silverman, MD; James D. Crapo, MD; for the Genetic Epidemiology of COPD (COPDGene) Investigators

Published online June 22, 2015.
Smoking History
With Normal Airflow

55% are impaired
Frequently have:
  Respiratory symptoms: 25%
  Impaired health status: 25%
  Severe acute respiratory events (AECOPD): > 4%
  Functional impairment: 15%
  Have radiologic evidence of lung disease: 20%
  Are receiving respiratory medications: 20%
Goals of Therapy for Stable COPD

- Relieve symptoms
- Improve exercise tolerance
- Improve health status

- Prevent disease progression
- Prevent and treat exacerbations
- Reduce mortality

REDUCE SYMPTOMS

REDUCE RISK
GOLD Symptom & Exacerbation Risk Categories

Exacerbation History

≥ 2 Exacerbations/yr
or
≥ 1 Exacerbation leading to hospitalization

≤ 1 Exacerbation/yr (not leading to hospitalization)

Symptoms

mMRC: modified Medical Research Council Dyspnea Scale. CAT: COPD Assessment Test.
Pharmacotherapy by GOLD Group A or B

<table>
<thead>
<tr>
<th>Group A</th>
<th>Group B</th>
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</thead>
<tbody>
<tr>
<td>Continue, stop, or try alternative class of bronchodilator</td>
<td>LAMA + LABA</td>
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<tr>
<td>Evaluate effect</td>
<td>Persistent symptoms</td>
</tr>
<tr>
<td>Bronchodilator (short-acting or long-acting)</td>
<td>Long-acting bronchodilator (LABA or LAMA)</td>
</tr>
</tbody>
</table>

Green arrows indicate preferred treatments.
LAMA = long-acting muscarinic antagonist; LABA = long-acting β₂ agonist.
COPD Maintenance Treatment: FDA-Approved Inhaled Bronchodilators

**Long-acting beta agonists (LABA)**
- Indacaterol (Arcapta®)
- Olodaterol (Striverdi®)
- Salmeterol (Serevent®)

**Long-acting muscarinic antagonists (LAMA)**
- Aclidinium (Tudorza®)
- Glycopyrronium (Seebri®)
- Tiotropium (Spiriva®)
- Umeclidinium (Incruse®)

**Nebulized**
- Arformoterol (Brovana®)
- Formoterol (Perforomist®)

**Nebulized**
- Glycopyrrolate (Magnair®)
COPD Maintenance Treatment: FDA-Approved Inhaled Anti-Inflammatories

Long-acting beta agonists / Inhaled Steroids (LABA / ICS)
• Fluticasone / salmeterol (Advair®)
• Fluticasone / vilanterol (Breo®)
• Budesonide / formoterol (Symbicort®)

Triple therapy (LABA / LAMA / ICS)
• Fluticasone / umeclidinium / vilanterol (Trelegy®)
COPD Maintenance Treatment: FDA-Approved Dual Bronchodilators

LABA + LAMA combinations
- Glycopyrronium + Formoterol (Bevespi®)
- Indacaterol and Glycopyrronium (Utibron®)
- Olodaterol + Tiotropium (Stiolto®)
- Vilanterol + Umeclidinium (Anoro®)
Pharmacotherapy by GOLD Group A or B

Group A

- Continue, stop, or try alternative class of bronchodilator
- Evaluate effect
- Bronchodilator (short-acting or long-acting)

Group B

- LAMA + LABA
- Persistent symptoms
- Long-acting bronchodilator (LABA or LAMA)

Green arrows indicate preferred treatments.
LAMA = long-acting muscarinic antagonist; LABA = long-acting $\beta_2$ agonist.
General Medication Options

- **Option 1:**
  Start with a single agent that may be effective
  How do you determine which agent to use?
  Assess effectiveness
  Determine need for change or added medication
General Medication Options

• **Option 1:**
  Start with a single agent that may be effective
  How do you determine which agent to use?
  Assess effectiveness
  Determine need for change or additional medication

• **Option 2:**
  Start with a two agents - more likely to provide the desired benefit
  Assess effectiveness
  Residual question: Which agent provided benefit or did the combination of both provide benefit
Effects of LABA and LAMA

- **LABA**
  - Improve lung function, dyspnea, health status.
  - Reduce exacerbation rate, hospitalizations
  - No effect on mortality, decline in lung function

- **LAMA**
  - Improve lung function, dyspnea, health status.
  - Reduce exacerbation rate (better than LABA), hospitalizations
  - No effect on mortality
  - May reduce decline in lung function in mild COPD
LAMA in Early COPD

• Randomized trial of tiotropium or placebo in mild / moderate COPD
  FEV1 ≥ 50% predicted
  N = 841
  2 year study
• Improved lung function with tiotropium
• Reduced FEV1 post-bronchodilator decline, but not decline pre-bronchodilator

LAMA in Early COPD

LAMA in Early COPD

Less frequent exacerbations:
  Risk ratio: 0.53 with tiotropium
  \( p = 0.0001 \)

Less frequent hospitalizations:
  Tio: 0.03 pt/yr
  Placebo: 0.07 pt/yr
  \( p = 0.0009 \)

Which of the following is correct about dual bronchodilators?

1. Reduce exacerbations more than inhaled steroid/LABA
2. Demonstrate consistently greater improvements compared to monotherapy
3. Both 1 and 2
4. None of the above
FLIGHT 1 and 2: Lung Function, LABA/LAMA compared to Monotherapies

Health Status (SGRQ), LABA/LAMA

n = 1,757   P < 0.001

LABA/LAMA compared to LABA/ICS

- Randomized non-inferiority 1-year trial
- Indacaterol / glycopyrronium (LABA/LAMA) vs. fluticasone / salmeterol 500/50 (LABA/ICS)
- 3,362 COPD patients
  - History of one exacerbation in the last year

COPD Exacerbations: LABA/LAMA compared to LABA/ICS

LABA Boxed Warning

• Previous LABA and LABA/ICS boxed warning: LABA increase the risk of asthma-related death
• Boxed warning removed December, 2017

Recent Safety Article

• Inpatient and ER cardiovascular disease cases in Japan
  – 37,719 with CVD matched to 146,139 controls w/o CVD
• 1.5 fold increased CVD risk within 30 days of initiation of LABA and LAMA
  – Irrespective of prior CVD status and exacerbation history
  – CVD risk absent or reduced with prevalent use of LABA, LAMA
  • Hypothesis: Depletion of susceptibles effect

LABA and LAMA Safety

Adjusted odds ratio of cardiovascular risk (inpatient or ER for coronary heart disease, arrhythmia, ischemic stroke) as a function of duration of new medications

Pneumonia With Inhaled Steroids

- Some studies show a 50% - 100% increase in pneumonia with inhaled steroids \(^1,^2\)
- Not shown in Salford study (community based primary care effectiveness trial of fluticasone furoate + vilanterol compared to usual care) \(^3\)
- May not occur with budesonide / formoterol \(^4\)
- Not shown in moderate COPD subjects in the SUMMIT study (n=23,835) \(^5\)
- May be associated with more severe COPD

\(^1\) Wedzicha. AJRCCM 2008. \(^2\) Crim 2009. Torch study. ERJ
\(^4\) Cochrane review, 2017
\(^5\) Crim. Resp Med 2017
Inhaled Steroids For COPD

- Reserved for patients with a history of exacerbations
- Role in patients with asthma features
- Role in patients with eosinophilia

GOLD 2018.
Treatment Adherence Improves Patient Outcomes

Higher Rates Of Mortality And Exacerbations Observed in Patients Non-adherent to COPD Maintenance Therapy