Up in FLAMES: Stable Chronic Obstructive Pulmonary Disease (COPD) Management
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Disclosures

- I have no actual or potential conflicts of interest
Objectives

- Summarize the findings of the FLAME study
- Identify proper pharmacologic therapy for patients with stable COPD
- Describe various products and formulations available for treatment of COPD
Abbreviations

- Chronic Obstructive Pulmonary Disease (COPD)
- Long acting beta agonist (LABA)
- Long acting anti-muscarinic agent (LAMA)
- Sturdy pack animal with extraneous “l’s” (LLAMA)
- Inhaled corticosteroid (ICS)
- Global Initiative for Chronic Obstructive Lung Disease (GOLD)
COPD Overview

- COPD is characterized as persistent respiratory symptoms and airflow limitation that is due to airway and or alveolar abnormalities usually caused by significant exposure to noxious particles or gases.

- Disease pathway consists of impaired lung growth, accelerated lung decline and chronic lung and systemic inflammation.

- Symptoms include:
  - Dyspnea
  - Chronic cough
  - Sputum production

COPD can be a real snooze-fest
Indacaterol-Glycopyrronium versus Salmeterol-Fluticasone for COPD

- Objectives: Evaluate the role of a LABA-LAMA regimen in COPD patients
- 52 week, randomized, double-blind, double-dummy, noninferiority trial (Secondary objective to look for superiority)
- Inclusion: patients with COPD who had a history of at least 1 exacerbation during the previous year

Indacaterol-Glycopyrronium versus Salmeterol-Fluticasone for COPD

- Primary outcome: Annual rate of all COPD exacerbations
- Secondary endpoints: Lung function, quality of life, rate of moderate/severe exacerbations, adverse drug reactions

A Rate Ratio for All Exacerbations

Per-Protocol Population

Modified Intention-to-Treat Population

Superiority margin

Noninferiority margin

Indacaterol-Glycopyrronium Better
Salmeterol-Fluticasone Better

B Time to First Exacerbation

Salmeterol-fluticasone group
Indacaterol-glycopyrronium group

Any
Hazard ratio, 0.84 (95% CI, 0.78-0.91)
P<0.001

Moderate or Severe
Hazard ratio, 0.78 (95% CI, 0.70-0.86)
P<0.001

Severe
Hazard ratio, 0.81 (95% CI, 0.66-1.00)
P=0.046

Outcomes

- Primary Endpoint: Indacaterol/glycopyrronium was superior to salmeterol/fluticaonse in reducing the rate of all COPD exacerbations (11% reduction).
- Secondary Endpoints also favored indacaterol/glycopyrronium.
  - Rate of moderate or severe exacerbation
  - FEV1 (Forced expiratory volume) change
  - SGRQ-C (St George Respiratory Questionnaire) score change

Which of the following is the take home point of the FLAME trial?

- A) LAMA + LABA was shown to improve mortality among COPD patients compared to LABA + ICS
- B) LAMA + LABA was shown to reduce the rate of COPD exacerbations compared to LABA + ICS
- C) LAMA + LABA was shown to be inferior to LABA + ICS regarding improving FEV1 and FVC on spirometry
- D) LAMA + LABA was shown to have less side effects than LABA + ICS
2017 GOLD Guideline Updates

- Change in classification of patients
- Change in pharmacotherapy
- Increased focus on inhaler technique
- Emphasis on smoking cessation and pulmonary rehab

Diagnosis

- Spirometry is required to make the diagnosis
- Post bronchodilator FEV1/FVC <0.7

Classification of Severity of Airflow Limitations

- Once COPD is diagnosed, it can be classified based on the FEV1.
- However, lung function is no longer used to stratify patients into ABCD categories.

Table 2.4. Classification of airflow limitation severity in COPD (Based on post-bronchodilator FEV1)

<table>
<thead>
<tr>
<th>In patients with FEV1/FVC &lt; 0.70:</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>GOLD 1:</td>
<td>Mild</td>
<td>FEV1 ≥ 80% predicted</td>
</tr>
<tr>
<td>GOLD 2:</td>
<td>Moderate</td>
<td>50% ≤ FEV1 &lt; 80% predicted</td>
</tr>
<tr>
<td>GOLD 3:</td>
<td>Severe</td>
<td>30% ≤ FEV1 &lt; 50% predicted</td>
</tr>
<tr>
<td>GOLD 4:</td>
<td>Very Severe</td>
<td>FEV1 &lt; 30% predicted</td>
</tr>
</tbody>
</table>

Which of the following medications have been shown to improve mortality in COPD patients?

- A) Prednisone
- B) Long acting beta agonists
- C) Short acting beta agonists
- D) Long acting anti-muscarinics
- E) None of the above
Pharmacologic Therapy

- Pharmacologic therapy in COPD can:
  - Reduce COPD symptoms
  - Reduce frequency and severity of exacerbations
  - Improve health status and exercise tolerance
  - No conclusive evidence that any existing medications can modify long term decline in lung function

Management of Stable COPD

- The main treatment goals are reduction of symptoms and future risk of exacerbations.
- All individuals who smoke should be strongly encouraged and supported to quit.
- Management strategies are not limited to pharmacologic treatments, and should be complemented by appropriate non-pharmacologic interventions.
ABCD Assessment Tool

Figure 2.4. The refined ABCD assessment tool

Exacerbation history

≥ 2
or
≥ 1 leading to hospital admission

0 or 1
(not leading to hospital admission)

C

D

A

B

Symptoms

mMRC 0–1
CAT < 10

mMRC ≥ 2
CAT ≥ 10

Assessment of Exacerbation Risk

- COPD exacerbations are defined as an acute worsening of respiratory symptoms that result in additional therapy.

- Classified as:
  - **Mild** (treated with short acting bronchodilators only)
  - **Moderate** (treated with short acting bronchodilators plus antibiotics and/or oral corticosteroids)
  - **Severe** (patient requires hospitalization or visits the emergency room)

Symptom Assessment Scores

<table>
<thead>
<tr>
<th>Table 2.5. Modified MRC dyspnea scale&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLEASE TICK IN THE BOX THAT APPLIES TO YOU</td>
</tr>
<tr>
<td>(ONE BOX ONLY) (Grades 0–4)</td>
</tr>
<tr>
<td>mMRC Grade 0. I only get breathless with strenuous exercise.</td>
</tr>
<tr>
<td>mMRC Grade 1. I get short of breath when hurrying on the level or walking up a slight hill.</td>
</tr>
<tr>
<td>mMRC Grade 2. I walk slower than people of the same age on the level because of breathlessness, or I have to stop for breath when walking on my own pace on the level.</td>
</tr>
<tr>
<td>mMRC Grade 3. I stop for breath after walking about 100 meters or after a few minutes on the level.</td>
</tr>
<tr>
<td>mMRC Grade 4. I am too breathless to leave the house or I am breathless when dressing or undressing.</td>
</tr>
</tbody>
</table>

<sup>a</sup> Fletcher CM. BMJ 1960; 2: 1662.
COPD Assessment Test (CAT):

Example: I am very happy 0 2 3 4 5 I am sad

I never cough 0 1 2 3 4 5 I cough all the time

I have no phlegm (mucus) in my chest at all 0 1 2 3 4 5 My chest is full of phlegm (mucus)

My chest does not feel tight at all 0 1 2 3 4 5 My chest feels very tight

When I walk up a hill or one flight of stairs I am not breathless 0 1 2 3 4 5 When I walk up a hill or one flight of stairs I am very breathless

I am not limited doing any activities at home 0 1 2 3 4 5 I am very limited doing activities at home

Jones et al. ERJ 2009; 34(3); 648
Figure 4.1. Pharmacologic treatment algorithms by GOLD Grade [highlighted boxes and arrows indicate preferred treatment pathways]

In patients with a major discrepancy between the perceived level of symptoms and severity of airflow limitation, further evaluation is warranted.
A: 0 – 1 exacerbations, less symptomatic

- Group A
  - Bronchodilator
    - Can be short acting or long acting
    - Should be continued if symptomatic benefit is documented

B: 0 – 1 exacerbations, more symptoms

- Group B
- Initial therapy should consist of a long acting bronchodilator
- Persistent breathlessness on monotherapy?
  - Two bronchodilators are recommended
- Severe breathlessness?
  - Initial dual therapy may be considered

C: 2 or more exacerbations, less symptoms

- Group C
- Initial Therapy
  - LAMA
- Persistent exacerbations?
  - Switch to LABA/LAMA
  - Combo LABA/ICS

D: 2 or more exacerbations, more symptoms

- **Group D**
- Start therapy with a LABA/LAMA
- Further exacerbations?
  - LABA/LAMA/ICS
  - Or switch to ICS/LABA

Patient Case

- DB is a 56 year old male with a history of smoking and COPD. He is admitted to the hospitalist service for shortness of breath.
- The hospitalist diagnoses him with a COPD exacerbation and asks you to look at his home regimen and recommend any changes that need to happen. You read his H&P which states he is normally active at home and only gets short of breath when climbing stairs.
- His home COPD regimen is albuterol HFA PRN, salmeterol-fluticasone (Advair) 250/50 BID.
- What would you recommend?
### Patient Case

<table>
<thead>
<tr>
<th>2 or more exacerbation or any hospitalization</th>
<th>0-1 exacerbation</th>
</tr>
</thead>
<tbody>
<tr>
<td>mMRC 0-1</td>
<td>mMRC ≥ 2</td>
</tr>
</tbody>
</table>
DB is a has class C COPD

A) Switch his salmeterol-fluticasone (Advair) to a LAMA
B) Switch his salmeterol-fluticasone (Advair) to a LAMA + LABA
C) Assess his inhaler technique and ability to afford salmeterol-fluticasone (Advair)
D) Continue his salmeterol-fluticasone (Advair) and counsel him on smoking cessation
Inhaler Use

- The best inhaler is the one your patient can obtain and use properly
- Choice of inhaler will depend on access, cost, prescriber and patient preference
- It is essential to provide instructions and demonstrate technique when prescribing a device
- Device technique should be assessed frequently
Patient Case

- You switched DB to a LAMA + LABA. You sent a test script down to pharmacy and find that his insurance prefers the tiotropium-olodaterol (Stiloto) Respimat. What should you do prior to DB’s discharge?

- A) Do nothing because it is 3:30pm and you want to leave
- B) Assume that a Respimat is similar to a Diskus so DB probably already knows how to use it
- C) Assume the respiratory therapist reviews the EDI and will come do Respimat teaching
- D) Google “how to use a Respimat” and go to DB’s room and do inhaler technique education
Short Acting Bronchodilators

- Short Acting Beta Agonists (SABA)
  - Levalbuterol (Xopenex)
  - Albuero (ProAir, Ventolin, Proventil)

- Short Acting Anticholinergics (SAMA)
  - Ipratropium (Atrovent)
Long Acting Bronchodilators

- Long Acting Beta Agonists (LABA)
  - Formoterol (Foradil)
  - Arformoterol (Brovana)
  - Salmeterol (Serevent)
  - Olodaterol (Striverdi)
  - Indacaterol (Arcapta)

- Long Acting Anticholinergics (LAMA)
  - Tiotripium (Spiriva)
  - Aclidinium (Tudorza)
  - Glycopyrronium bromide (Seebri)
  - Umeclidinium (Incruse)
Combination Products

- Combination LABA + ICS
  - Formoterol + budesonide (Symbicort)
  - Formoterol + mometasone (Dulera)
  - Salmeterol + fluticasone (Advair)
  - Vilanterol + fluticasone (Breo)

- Combination LABA + LAMA
  - Albuterol + Ipratropium (Combivent, Duoneb)
  - Formoterol + glycopyrronium (Bevespi)
  - Indacaterol + glycopyrronium (Utibron)
  - Vilanterol + umeclidinium (Anoro)
  - Olodaterol + tiotripium (Stiolto)
Anoro, Breo, Incruse, Trilogy Ellipta

- Vilanterol + fluticasone (Breo)
- Vilanterol + umeclidinium (Anoro)
- Umeclidinium (Incruse)
- Vilanterol + umeclidinium + fluticasone (Trilogy)
Bevespi Aerosphere

- Formoterol + glycopyrronium (Bevespi)
Arcapta, Seebri, Utibron Neohaler

- Indacaterol (Arcapta)
- Glycopyrronium bromide (Seebri)
- Indacaterol + glycopyrronium (Utibron)
Spiriva, Stiolto Respimat

- Tiotripium (Spiriva)
- Olodaterol + tiotripium (Stiolto)
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