CME/CPE

The Fundamental Role of the Pharmacist in the Comprehensive Management of Patients With COPD

Course Director

David M. Mannino, MD

Faculty

Roy A. Pleasants, II, PharmD

Full faculty details inside

PeerView inReview

Message From the Course Director

Dear Colleague,

The treatment armamentarium for COPD is continuously expanding. Advances in technology have resulted in the development of novel devices and formulations. Pharmacists are in a unique position to improve outcomes in patients with COPD because of their access to the community and extensive clinical knowledge. They can play an important role in the multifactorial management of this disease, which includes components such as education about inhaler technique, immunization against respiratory diseases, and smoking-cessation counseling.

In this two-part CME/CPE activity, we review available and investigational agents used to treat COPD in terms of their mechanism of action, efficacy, and safety. We also discuss current and emerging delivery devices for COPD treatments, as well as factors that influence the selection of a particular drug delivery system. We explore strategies to effectively communicate with COPD patients regarding their disease, avoidance of risk factors, and proper inhaler technique. In addition, we examine approaches to monitor patients with COPD for treatment response, immunization status, success in smoking cessation, and appropriate delivery device use. I hope you find this educational activity useful in your daily practice.

Sincerely,

David M. Mannino, MD

MLI
Medical Learning Institute, Inc.

This CME/CPE activity is jointly provided by Medical Learning Institute, Inc. and PVI, PeerView Institute for Medical Education.

Activity Information

Activity Description and Educational Objectives
In this activity, experts in chronic obstructive pulmonary disease (COPD) discuss available as well as emerging treatments and delivery devices for COPD and explore the pharmacists' role in the comprehensive management of patients with this disease.

Upon completion of this activity, participants will be able to:
- Evaluate currently available as well as emerging agents used to treat COPD in terms of their mechanism of action, efficacy, and safety
- Describe available and emerging delivery devices for COPD treatments as well as factors that influence the selection of a particular drug delivery system
- Apply strategies to effectively communicate with COPD patients regarding their disease, avoidance of risk factors, treatment goals, proper inhaler technique, pulmonary rehabilitation, and the importance of medication adherence
- Employ approaches to monitor patients with COPD for treatment response, immunization status, success in smoking cessation, proper inhaler use, and medication adherence

Target Audience
This activity has been designed to meet the educational needs of pharmacists and other clinicians involved in the care of patients with COPD.

Requirements for Successful Completion
In order to receive credit, participants must view the activity and complete the post-test and evaluation form. A score of 70% or higher is needed to obtain CME/CPE credit. There are no pre-requisites and there is no fee to participate in this activity or to receive CME/CPE credit. Statements of Credit are awarded upon successful completion of the post-test and evaluation form.

Media: Enduring Material
Release and Expiration Dates: June 10, 2016 - June 09, 2017
Time to Complete: 30 minutes

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Course Director
David M. Mannino, MD
Professor of Medicine
Division of Pulmonary, Critical Care and Sleep Medicine
University of Kentucky Medical Center, College of Public Health
Lexington, Kentucky

David M. Mannino, MD, has a financial interest/relationship or affiliation in the form of:
Speakers Bureau participant with Sunovion Pharmaceuticals Inc.
Advisory Board for Amgen Inc.; Boehringer Ingelheim GmbH; GlaxoSmithKline; Novartis Pharmaceuticals Corporation; and Sunovion Pharmaceuticals Inc.
David M. Mannino, MD does intend to discuss either non–FDA-approved or investigational use for the following products/devices: Treatments used off-label in COPD, as well as drugs being investigated for this disease.

Faculty
Roy A. Pleasants, II, PharmD
Clinical and Investigational Pharmacist
Duke Asthma, Allergy, and Airways Center
Division of Pulmonary, Allergy, and Critical Care Medicine
Duke University School of Medicine
Research Associate in Pulmonary Medicine
Department of Pulmonary Medicine
Durham Veterans Administration Medical Center
CoChair, NC COPD Taskforce
Durham, North Carolina

Roy A. Pleasants, II, PharmD, has a financial interest/relationship or affiliation in the form of:
Consultant for Boehringer Ingelheim and Teva Pharmaceuticals.
Roy A. Pleasants, II, PharmD, does intend to discuss either non-FDA approved or investigational use for the following products/devices: Delivery devices being investigated for COPD treatments.

CME Reviewer
Joseph G. Crocetti, DO
Abington Jefferson Health
Abington, Pennsylvania

Joseph G. Crocetti, DO, has no financial interests/relationships or affiliations in relation to this activity.

CPE Reviewer
Nancy Nesser, JD, PharmD
Oklahoma Health Care Authority
Oklahoma City, OK

Nancy Nesser, JD, PharmD, has no financial interests/relationships or affiliations in relation to this activity.

Medical Director
Kate Nelson, PhD
PVI, PeerView Institute for Medical Education

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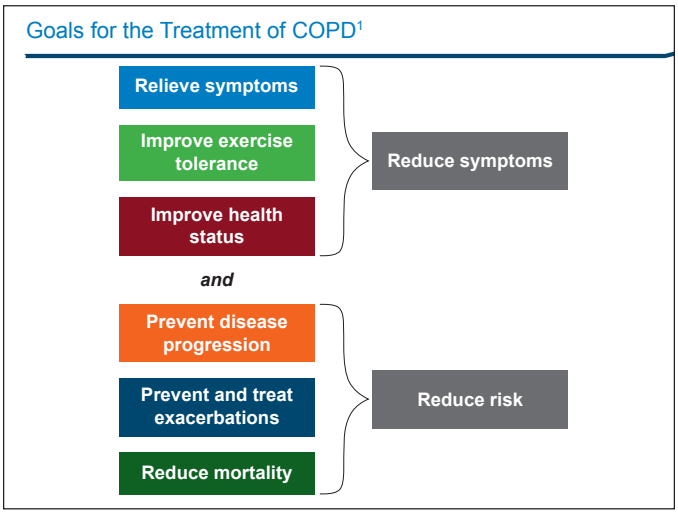
Comprehensive Care in COPD: Pharmacologic and Nonpharmacologic Approaches

David M. Mannino, MD
University of Kentucky Medical Center, College of Public Health
Lexington, Kentucky

Dr. Mannino: Hello, this is Dr. David Mannino from the University of Kentucky in Lexington, Kentucky. Welcome to this educational activity focused on the role of the pharmacist in the treatment of COPD. Joining me in this discussion is Dr. Roy Pleasants from Duke University School of Medicine in Durham, North Carolina. After completing the activity, access the post-test and evaluation form by clicking the red "Get certificate" button. I encourage you to download the slides, Practice Aids, and any other activity features that may interest you.



COPD: chronic obstructive pulmonary disease.
1. http://goldcopd.org/gold-reports/. Accessed May 23, 2016.

Dr. Mannino: Now this slide describes our goals for the treatment of COPD, and as you can see there are two basic goals that we target our therapy towards. The first is the reduction of symptoms that patients report, and the second one is to reduce the risk of future events, mostly exacerbations and hospitalizations that really are the drivers of the major morbidities in COPD.

COPD Management: Avoidance of Risk Factors[1]

Tobacco Smoke

- Smoking cessation is the key intervention for all patients with COPD who continue to smoke
- At each visit, determine current smoking status and smoke exposure

Occupational Exposures

- Although studies have not yet investigated whether interventions to reduce occupational exposures also reduce the burden of COPD, patients should be advised to avoid continued exposures to potential aggravants, if possible

Indoor and Outdoor Air Pollution

- Reducing risk requires a combination of public policy, local and national resources, cultural changes, and protective steps taken by individual patients
- Reduction of exposure to smoke from biomass fuel, particularly among women and children, is a crucial goal to reduce the prevalence of COPD worldwide
- Efficient ventilation, non-polluting cooking stoves, use of flues, and similar interventions are feasible and should be recommended

1. http://goldcopd.org/gold-reports/. Accessed May 23, 2016.

Dr. Mannino: The cornerstone of all COPD management is the avoidance of key risk factors. Of course, smoking is the main risk factor for patients who are currently smoking, and this is something that you speak on over with patients at each visit.

Of course, patients don't need to be smoking their own cigarettes to be adversely affected by tobacco smoke. So we also encourage the elimination of exposure to environmental tobacco smoke, in addition to other forms of air pollution, both in indoor and outdoor environments. And in addition, if patients are in workplaces where they are exposed to dust, vapors, gases, or fumes, this also needs to be modified, as these can contribute to COPD exacerbations.

COPD Management: Pulmonary Rehabilitation[a]

Components include exercise training, nutritional and psychological counseling, and patient education[1]

All COPD patients benefit from rehabilitation and maintenance of physical activity programs, with improvements in exercise tolerance and symptoms of dyspnea and fatigue[2]

Although an effective pulmonary rehabilitation program is ≥6 weeks, the longer the program continues, the more effective[2]

- **If patients are unable to participate in a structured program, they can be advised to exercise on their own (eg, walking 20 minutes daily)[2]**

If exercise training is maintained at home, the patient's health status remains above pre-rehabilitation levels[2]

[a] Physical activity is recommended at all stages of COPD; pulmonary rehabilitation is recommended for patient groups B-D.

1. Butts JF et al. *Phys Sportsmed*. 2013;49-57.
2. http://goldcopd.org/gold-reports/. Accessed May 23, 2016.

Dr. Mannino: Another cornerstone of COPD management that involves all patients is some type of either exercise or pulmonary rehabilitation program. And depending on what state you are in, there are different criteria for pulmonary rehabilitation programs that are also somewhat influenced by a variety of different insurers and payers. But certainly every COPD patient should be in some type of exercise program, and if they qualify for a formal pulmonary rehabilitation program, they should be involved in this. I found that in my COPD patients, this has probably been the intervention that is often the most helpful in really improving the well-being of patients.

COPD Management: Vaccinations[1,2]

Influenza Vaccination	• Recommended that patients with COPD receive a yearly influenza vaccine • Can reduce serious illness (such as LRTIs requiring hospitalization) and death in COPD patients **(Evidence A)** • Vaccines containing killed or live, inactivated viruses are recommended, as they are more effective in elderly patients with COPD • Patients with COPD should not get the nasal spray vaccine (LAIV)[3]
Pneumococcal Vaccination	• Has been shown to reduce the incidence of community-acquired pneumonia in COPD patients younger than age 65 with FEV_1 <40% predicted **(Evidence B)** • PPSV23 should be administered to adults aged 19 to 64 years with COPD • At age ≥65 years, administer PCV13 at least 1 year after PPSV23, followed by another dose of PPSV23 at least 1 year after PCV13 and at least 5 years after the last dose of PPSV23

FEV_1: forced expiratory volume in 1 second; LAIV: live attenuated influenza vaccine; LRTI: lower respiratory tract infection; PCV: pneumococcal conjugate vaccine; PPSV: pneumococcal polysaccharide vaccine.

1. http://goldcopd.org/gold-reports/. Accessed May 23, 2016.
2. http://www.cdc.gov/vaccines/schedules/downloads/adult/adult-combined-schedule.pdf. Accessed April 19, 2016.
3. http://www.cdc.gov/h1n1flu/guidance/copd.htm#b. Accessed May 4, 2016.

Dr. Mannino: Another important component of treatment for all COPD patients is vaccinations. Every patient should be vaccinated against influenza. This is because patients who get an influenza infection are much more likely to go on to develop exacerbations and hospitalizations, and this is something that we try to avoid at all times. In addition, patients should be treated with pneumococcal vaccination, including both the conjugate vaccine and the polysaccharide vaccine to prevent the development of pneumonia.

Pharmacotherapy in COPD: Short-Acting Bronchodilators[1-6]

SABAs	**Albuterol (salbutamol), levalbuterol, terbutaline, fenoterol[a]** • Onset of effect achieved in 3-5 minutes, duration is only 4-6 hours • Typically prescribed "as needed" to allow for urgent relief • AEs associated with increased doses (eg, cardiac arrhythmias, hypokalemia) can create dose limitations • Escalating doses have not shown clinical benefit
SAMAs	**Ipratropium bromide, oxitropium bromide[a]** • Rapid onset, last for ~8 hours • Ipratropium as effective as albuterol in improvement of FEV_1 • Main AE is dry mouth; some pts using ipratropium report a bitter, metallic taste • Urinary retention and precipitation or worsening of narrow angle glaucoma may occur • Unexpected small increase in CVEs in COPD pts regularly treated with ipratropium has been reported, which requires further investigation
SAMA/SABA Combination	**Ipratropium/albuterol, ipratropium/fenoterol[a]** • Produce greater and more sustained improvements in FEV_1 than either drug alone • Do not produce evidence of tachyphylaxis over 90 days of treatment • AEs include URTI, nasopharyngitis, cough, bronchitis, headache, and dyspnea

[a] Not available in United States.

CVE: cardiovascular event; SABAs: short-acting β2-agonists; SAMAs: short-acting muscarinic antagonists; URTI: upper respiratory tract infection.

1. http://goldcopd.org/gold-reports/. Accessed May 23, 2016.
2. Patel HJ. *Curr Opin Pulm Med*. 2016;22:119-124.
3. Friedman M et al. *Chest*. 1999;115:635-641.
4. Buttaro T et al. *Primary Care: A Collaborative Practice*. 4th Ed. St Louis, Missouri: Mosby.
5. Atrovent HFA (ipratropium bromide HFA). http://docs.boehringer-ingelheim.com/Prescribing%20Information/PIs/Atrovent%20HFA/10003001_US_1.pdf. Accessed April 25, 2015.
6. Combivent Respimat (ipratropium/albuterol inhalation spray). http://docs.boehringer-ingelheim.com/Prescribing%20Information/PIs/Combivent%20Respimat/CMVTRSPT.pdf. Accessed April 25, 2016.

Dr. Mannino: There are a number of different pharmacotherapy interventions for patients with COPD. For patients in all stages of COPD, we treat symptomatic worsenings with short-acting agents, and these are listed on this slide, including the freestanding short-acting beta agonists, short-acting muscarinic agents, and combinations.

Long-Acting Bronchodilators: β_2-Agonists

Several studies show long-acting medications are more beneficial than repetitive use of short-acting agents[1]

LABAs

Formoterol, arformoterol, indacaterol, olodaterol, salmeterol, tulobuterol[a], vilanterol[b,2]

- Arformoterol improved lung function vs placebo & demonstrated an approximately 40% lower risk of respiratory death or COPD exacerbation-related hospitalization over 1 year vs placebo[3]
  - Can potentially benefit pts w/ hyperinflation & low inspiratory flow rates[4]
- Formoterol & salmeterol significantly improve FEV_1 & lung volumes, dyspnea, health-related QOL, & exacerbation rate, but have no effect on mortality & rate of decline of lung function[2]
- Salmeterol reduces rate of hospitalization[2]
- Indacaterol, olodaterol, & vilanterol are newest options[5]
  - Longer durations of action[6]
  - Lung function effects of indacaterol significantly greater than that of formoterol, salmeterol, & arformoterol; similar to tiotropium[5]
  - Long-term efficacy & safety of QD olodaterol 5 µg & 10 µg in pts w/ moderate to very severe COPD, continuing w/ usual care maintenance therapy, demonstrated in two replicate, randomized, double-blind, placebo-controlled, parallel group phase 3 trials[7]
- Black box warning for asthma-related death
- Common class effects include palpitations, headache, & tremor; may limit dose[8]

[a] Not available in the United States. [b] Currently available in combination treatment.

LABAs: long-acting β_2-adrenoceptor agonists; QD: once daily.

1. Biller J. *The Interface of Neurology & Internal Medicine*. Philadelphia, Pennsylvania: Lippincott Williams & Wilkins; 2008.
2. http://goldcopd.org/gold-reports/. Accessed May 23, 2016.
3. Donohue JF et al. *Chest*. 2014;146:1531-1542.
4. Loh CH et al. *Expert Opin Drug Saf*. 2015;14:463-472.
5. Patel HJ. *Curr Opin Pulm Med*. 2016;22:119-124.
6. Montuschi P, Ciabattoni G. *J Med Chem*. 2015;58:4131-4164.
7. Ferguson GT et al. *Int J Chron Obstruct Pulmon Dis*. 2014;9:629-645.
8. Tashkin DP, Fabbri LM. *Respir Res*. 2010;11:149.

Dr. Mannino: Another key component of the treatment of COPD patients are long-acting bronchodilators. These include long-acting beta agonists that can either be taken twice a day, or now we have new therapies that can be used once a day. And in general, we prefer to have our patients on these rather than them taking multiple doses of short-acting agents. Of course, all long-acting beta agonists have a black box warning for asthma-related death.

Long-Acting Bronchodilators: Muscarinic Antagonists

Tiotropium
- Hallmark of COPD treatment; only LAMA available until recently[1]
- **UPLIFT:** At 4 years and 30 days, associated with reduced risk of exacerbations, related hospitalizations, and respiratory failure[2,a]

Aclidinium
- **ACCLAIM studies:** Improved FEV_1 (both studies) and delayed time to first exacerbation (1 study)[3,b]
- **ATTAIN:** Clinically significant increase in trough and peak FEV_1 and improvement in SGRQ and TDI focal scores[4,b]
- **Meta-analysis of seven studies (7,001 pts):** Reduced incidence of exacerbation-related hospitalizations and improved QOL, COPD symptoms, and lung function[5,b]

Umeclidinium
- A pooled analysis of phase 3 and comparative studies of umeclidinium showed significant improvement in lung function, as well as in acute exacerbations of COPD, dyspnea, and quality of life[6,a]

Glycopyrrolate
- **GEM 1 and 2:** Significant improvements in lung function and health status vs placebo[7,b]
- Improvements in COPD symptoms, QOL, and rescue medication use in pts w/ moderate to severe airflow limitation[8,9,b]

AEs include nasopharyngitis and URTI
Worsening of narrow angle glaucoma or urinary retention may occur[10-13]

[a] Conducted in pts w/ moderate to very severe COPD. [b] Conducted in pts w/ moderate to severe COPD.

LAMA: long-acting muscarinic antagonists; SGRQ: St. George Respiratory Questionnaire; TDI: Transition Dyspnea Index.

1. Patel HJ. *Curr Opin Pulm Med*. 2016;22:119-124.
2. Tashkin DP et al. *N Engl J Med*. 2008;359:1543-1554.
3. Jones PW et al. *Respir Res*. 2011;12:55.
4. Jones PW et al. *Eur Respir J*. 2012;40:830-836.
5. Zou Y et al. *COPD*. February 4, 2016. [Epub ahead of print].
6. Pleasants RA et al. *Drugs*. January 11, 2016. [Epub ahead of print].
7. Mahler D et al. American Thoracic Society 2016 International Conference (ATS 2016). Abstract 6774.
8. LaForce C et al. American Thoracic Society 2015 International Conference (ATS 2015). Abstract 62680.
9. Kerwin EM et al. ATS 2015. Abstract 63673.
10. Spiriva Handihaler (tiotropium bromide inhalation powder). http://docs.boehringer-ingelheim.com/Prescribing%20Information/PIs/Spiriva/Spiriva.pdf. Accessed April 21, 2016.
11. Tudorza Pressair (aclidinium bromide inhalation powder). http://www.azpicentral.com/tudorza/tudorza_pi.pdf. Accessed March 18, 2016.
12. Incruse Ellipta (umeclidinium inhalation powder). https://www.gsksource.com/pharma/content/dam/GlaxoSmithKline/US/en/Prescribing_Information/Incruse_Ellipta/pdf/INCRUSE-ELLIPTA-PI-PIL.PDF. Accessed March 18, 2016.
13. Seebri Neohaler (glycopyrrolate) inhalation powder. http://pharma.us.novartis.com/product/pi/pdf/seebri.pdf. Accessed March 18, 2016.

Dr. Mannino: Another class of long-acting bronchodilators are the muscarinic antagonists, and these are listed on this slide. They do not have a black box warning, although they do have sometimes significant adverse effects, including nasopharyngitis. Patients will frequently complain of other symptoms with these, as are noted on this slide.

LAMA/LABA Combinations: Umeclidinium/Vilanterol Inhalation Powder

- FDA approved in 2013 as a long-term maintenance treatment in COPD[1]

Systematic Review of Efficacy and Safety of UMEC/VIL: 11 Trials From 10 Studies (9,609 Patients)[2]

Clinical Parameter	Results/Conclusions
Mean trough FEV_1, mL	• Improvements vs UMEC, VIL, TIO, and fluticasone/salmeterol (mean trough FEV_1: 60 mL, 110 mL, 90 mL, and 90 mL, respectively; $P < .0001$)
Likelihood of MCID on Transition Dyspnea Index	• Greater likelihood vs UMEC (NNTB = 14) • Greater likelihood vs VIL (NNTB = 10) • No significant difference vs tiotropium
Risk of exacerbations	• Significantly reduced vs UMEC (NNTB = 42) • Significantly reduced vs VIL (NNTB = 41) • No significant difference vs tiotropium
Incidence of AEs, SAEs, SCVEs, mortality on Tx	• Similar across treatments

Most common AEs (incidence ≥1% and more common than placebo): pharyngitis, sinusitis, LRTI, constipation, diarrhea, pain in extremity, muscle spasms, neck pain, and chest pain[3]

MCID: minimal clinically important difference; NNTB: number needed to treat for benefit; SAEs: severe adverse events; SCVEs: serious cardiovascular events; TIO: tiotropium; UMEC: umeclidinium; VIL: vilanterol.

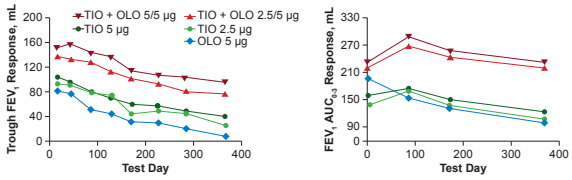
1. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm379057.htm. Accessed January 14, 2016.
2. Rodrigo GJ, Neffen H. *Chest*. 2015;148:397-407.
3. Anoro Ellipta (umeclidinium and vilanterol inhalation powder). https://www.gsksource.com/pharma/content/dam/GlaxoSmithKline/US/en/Prescribing_Information/Anoro_Ellipta/pdf/ANORO-ELLIPTA-PI-MG.PDF. Accessed April 21, 2016.

Dr. Mannino: Some recently approved therapies are a combination of long-acting bronchodilators, including those from the LABA class and those from the LAMA class. The first of this class of therapies is the combination of umeclidinium and vilanterol, which has shown dramatic improvements in patients in its clinical trials.

LAMA/LABA Combinations: Tiotropium/Olodaterol in Soft Mist Inhaler

- FDA approved in 2015 as a long-term maintenance treatment in COPD[1]

TONADO 1 & 2:
Lung Function Endpoints (Combined Data Set) Over 52 Weeks: Full Analysis Set



- **TONADO 1 & 2[a]:** Significant improvements in lung function at 2.5/5-µg & 5/5-µg doses compared with monocomponents[2]
  - Significant improvements in SGRQ scores vs monocomponents observed with 5/5 µg[2]
- **OTEMTO 1 & 2[b]:** TIO + OLO improved lung function & QOL compared with placebo & TIO 5 µg[3]
- **ENERGITO:** Improvements in lung function vs fluticasone/salmeterol[4]

Most common AEs (>3% incidence and more than an active control): nasopharyngitis, cough, and back pain[5]

[a] Replicate, randomized, double-blind, parallel group, multicenter phase 3 trials in pts with moderate to very severe COPD (GOLD 2-4). [b] Replicate, double-blind, parallel group, phase 3b placebo-controlled trials in pts with moderate to severe COPD.

GOLD: Global Initiative for Chronic Obstructive Lung Disease; OLO: olodaterol.

1. http://www.prnewswire.com/news-releases/fda-approves-boehringer-ingelheims-stiolto-respimat-inhalation-spray-as-once-daily-maintenance-treatment-for-copd-300088485.html. Accessed April 25, 2016.
2. Buhl R et al. *Eur Respir J.* 2015;45:969-979.
3. Singh D et al. *Respir Med.* 2015;109:1312-1319.
4. Beeh KM et al. *Int J Chron Obstruct Pulmon Dis.* 2016;11:193-205.
5. Stiolto Respimat (tiotropium bromide and olodaterol). http://docs.boehringer-ingelheim.com/Prescribing%20Information/PIs/Stiolto%20Respimat/stiolto.pdf. Accessed April 25, 2016.

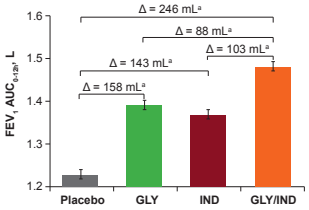
Dr. Mannino: Another newly approved therapy in this class of combination therapy is the combination of tiotropium and olodaterol, which is available in a device called a soft mist inhaler. One of the advantages of this device is that patients have a slightly longer time to get the medication in, as opposed to other types of inhaled therapies.

LAMA/LABA Combinations: QVA149 (GLY/IND Inhalation Powder)

- FDA approved in 2015 as long-term maintenance treatment in COPD, along with monocomponent GLY in an inhalation powder[1]

Data From FLIGHT Studies: Pooled Analysis (2,038 Patients)

In patients with moderate to severe COPD, treatment with GLY/IND resulted in[2]
- ✓ Significant improvements in lung function vs placebo and monocomponents
- ✓ Significant improvements in SGRQ scores, dyspnea, and daily symptoms vs placebo and monocomponents
- ✓ Significant reductions in rescue medication use vs placebo
- ✓ Rapid onset



- **LANTERN and FLAME studies:** GLY/IND was superior to fluticasone/salmeterol in improving lung function and reducing exacerbation rates[3,4]

Most common AEs (≥2% incidence and higher than placebo): nasopharyngitis and hypertension[5]

[a] $P < .001$.

GLY: glycopyrrolate; IND: indacaterol.

1. http://www.businesswire.com/news/home/20151029006934/en/Sosei-Confirms-FDA-Approvals-Dual-Combination-Bronchodilator. Accessed April 25, 2016.
2. Mahler DA et al. *Am J Resp Crit Care Med.* 2015;192:1068-1079.
3. Wedzicha J et al. *N Engl J Med.* May 15, 2016 [Epub ahead of print].
4. Zhong N et al. *Int J Chron Obstruct Pulmon Dis.* 2015;10:1015-1026.
5. Utibron Neohaler (indacaterol and glycopyrrolate inhalation powder). http://www.pharma.us.novartis.com/product/pi/pdf/utibron.pdf. Accessed April 25, 2016.

Dr. Mannino: A third type of combination therapy that is newly available is the combination of glycopyrrolate and indacaterol. As is similar to the other two types of combination LABA/LAMA therapies, patients on this therapy have this improvement in their lung function following administration of the medication, in addition to reductions in their symptoms.

Corticosteroids for the Treatment of COPD

Inhaled

Beclomethasone, budesonide, fluticasone
- Recommended for late-stage COPD or patients with frequent exacerbations[1,2]
- Not recommended as long-term monotherapy because of lower efficacy than when combined with LABA, increased risk of pneumonia, and possible increased risk of fractures[1,2]
- Associated with higher prevalence of oral candidiasis, hoarse voice, and skin bruising[1]
- WISDOM trial evaluated effects of withdrawing ICS from triple therapy[3,4]
  - ICSs had no additional benefit when added to LABA + LAMA in 80% of patients
  - Moderate or severe exacerbation rate was higher in the ICS-withdrawal group versus the ICS-continuation group in patients with eosinophil counts (out of total white blood cell count) of ≥2%, ≥4%, and ≥5%
  - The increase in exacerbation rate became more pronounced as the eosinophil cutoff level rose

Systemic

Prednisone, methylprednisolone[a]
- Used for exacerbations[1]
- Chronic treatment with systemic corticosteroids should be avoided because of unfavorable benefit-to-risk ratio[1]

[a] Off label.

ICS: inhaled corticosteroids.

1. http://goldcopd.org/gold-reports/. Accessed May 23, 2016.
2. Patel HJ. *Curr Opin Pulm Med.* 2016;22:119-124.
3. Magnussen H et al. *Respir Med.* 2014;108:593-599.
4. Watz H et al. *Lancet Respir Med.* April 7, 2016. [Epub ahead of print].

Dr. Mannino: Corticosteroids are also an important part of treatment of COPD. Systemic steroids are used when patients are having exacerbations or acute worsening of their COPD. Chronic steroids are typically used in an inhaled form for patients who have had particular problems either with exacerbations, or they are also used in patients who may have some asthmatic overlap to their COPD.

LABA/ICS Combinations[1]

Medication	Inhaler	Nebulizer	Oral	Injection
Formoterol/beclomethasone[a]	✓			
Formoterol/budesonide	✓			
Formoterol/mometasone[b]	✓			
Salmeterol/fluticasone	✓			
Vilanterol/fluticasone	✓			

Comments

- More effective than the individual components in improving lung function and health status and reducing exacerbations in patients with moderate to very severe COPD

AEs

- Combination therapy is associated with increased risk of pneumonia

[a] Not available in the United States. [b] Off label.

1. http://goldcopd.org/gold-reports/. Accessed May 23, 2016.

Dr. Mannino: There are a number of different combinations of long-acting beta agonists and inhaled steroids that are used. This slide lists all current forms that are available in inhaled form. Not all these are actually available in United States, and one, while it is available, does not have an indication for COPD, so that would be considered off label.

Methylxanthines[1]

Medication	Inhaler	Nebulizer	Oral	Injection
Aminophylline			✓	✓
Theophylline			✓	

Comments

- Controversy about exact effects of xanthine derivatives
- Theophylline is less effective and less well tolerated than inhaled long-acting bronchodilators and is not recommended if those treatments are available and affordable

AEs

- Toxicity is dose-related; problem because therapeutic ratio is small and most benefit occurs when near-toxic doses are given
- Arrhythmias, grand mal convulsions, headaches, insomnia, nausea, and heartburn
- May involve risk of overdose

1. http://goldcopd.org/gold-reports/. Accessed May 23, 2016.

Dr. Mannino: Another class of medication that has been traditionally used in COPD, and is still used in some patients, are methylxanthines. These include aminophylline and theophylline. These have been used less frequently in recent years because of toxicity issues, although they are still used in some patients at lower doses than would have been used previously, in the belief that it may enhance some of the other medications that are being used in the treatment of COPD.

Other Treatments for COPD Exacerbations

PDE4 Inhibitors (eg, roflumilast)[1-3]

- Reduces inflammation by inhibiting breakdown of intracellular cAMP
- Studies suggest that benefits of roflumilast are most applicable to patients at high risk of exacerbations[2,3]
  - Also targets patients with chronic bronchitis and FEV_1 <50%
- Most common SAEs: COPD exacerbations and pneumonia
- Conflicting data about potential benefit-to-risk balance because of significant GI and neurologic AEs[1]

Macrolides (eg, azithromycin)[4,5a]

- When added to usual treatment, azithromycin 250 mg taken daily for 1 year (n = 570) reduced the frequency of exacerbations and improved QOL compared with placebo (n = 572)
- Hearing decrements were more common in the azithromycin group than in the placebo group (25% vs 20%, *P* = .04)
- Concerns with CV effects

[a] Off label.

PDE4: phosphodiesterase 4.

1. Patel HJ. *Curr Opin Pulm Med.* 2016;22:119-124.
2. Yu T et al. *Thorax.* 2014;69:616-622.
3. Martinez FJ et al. *Lancet.* 2015;385:857-866.
4. Albert RK et al. *N Engl J Med.* 2011;365:689-698.
5. Ray W et al. *N Engl J Med.* 2012;366:1881-1890.

Dr. Mannino: Other treatments that are used to either treat or prevent COPD exacerbations are PDE4 inhibitors. One that is currently available in the United States is roflumilast, and this can be used to prevent exacerbations when being taken daily.

Although they are not approved for the treatment of COPD or prevention of exacerbations, clinicians are now using based on some clinical trials macrolides. One of the most commonly used is azithromycin, that is used typically 2 to 3 days a week for the prevention of exacerbations. Of course, with the use of any chronic antibiotics, one has to be concerned about potential side effects, including development of resistance of organisms, and with macrolides in particular, one has to be concerned about cardiovascular effects in addition to hearing issues.

Emerging Treatments for COPD: Phase 3 of Development

Treatment	Class	Mode of Delivery
Glycopyrrolate/formoterol[1,a]	LAMA/LABA	Co-suspension MDI
Aclidinium/formoterol[2,3,b]	LAMA/LABA	Inhalation powder
Fluticasone/vilanterol/umeclidinium[4]	ICS/LABA/LAMA triple combo	Inhalation powder
PT010 (budesonide/formoterol/glycopyrrolate)[5]	ICS/LABA/LAMA triple combo	Co-suspension MDI
SUN-101 (glycopyrrolate)[6-8]	LAMA	Nebulizer
TD-4208 (revefenacin)[9-11]	LAMA	Nebulizer
Mepolizumab[12]	Anti–IL-5 Ab	SC injection
Benralizumab[13,14]	Anti–IL-5 Ab	SC injection

[a] FDA approved in April 2016. [b] Approved in EU.[3]

Ab: antibody; IL: interleukin; MDI: metered dose inhaler.
1. Rabe K et al. *Eur Respir J.* 2015;46(suppl 59):PA4363.
2. Bateman ED et al. *Respir Res.* 2015;16:92.
3. http://www.firstwordpharma.com/node/1247765?tsid=17#axzz3x88zhV4R. Accessed April 25, 2016.
4. https://www.clinicaltrials.gov/ct2/show/NCT02164513. Accessed April 25, 2016.
5. https://www.clinicaltrials.gov/ct2/show/NCT02465567. Accessed April 25, 2016.
6. https://clinicaltrials.gov/ct2/show/NCT02347774?term=SUN-101&rank=3. Accessed April 25, 2016.
7. https://clinicaltrials.gov/ct2/show/NCT02347761?term=SUN-101&rank=4. Accessed April 25, 2016.
8. https://clinicaltrials.gov/ct2/show/NCT02276222?term=SUN-101&rank=1. Accessed April 25, 2016.
9. https://clinicaltrials.gov/ct2/show/NCT02512510?term=td4208&rank=5. Accessed April 25, 2016.
10. https://clinicaltrials.gov/ct2/show/NCT02459080?term=td4208&rank=6. Accessed April 25, 2016.
11. https://clinicaltrials.gov/ct2/show/NCT02518139?term=td4208&rank=8. Accessed April 25, 2016.
12. https://www.clinicaltrials.gov/ct2/show/NCT02105961. Accessed April 25, 2016.
13. https://www.clinicaltrials.gov/ct2/show/NCT02138916. Accessed April 25, 2016.
14. https://www.clinicaltrials.gov/ct2/show/NCT02155660. Accessed April 25, 2016.

Dr. Mannino: There are a number of potential emerging treatments for the development of COPD, and many of these are in various stages of clinical development. What we'll be seeing in the future are listed here, including some combination therapy that includes steroid, LABAs, and LAMAs all in one device. In addition to new LAMAs and LAMA/LABA combinations, there are some biologic therapies that will target certain interleukins.

Factors Influencing Treatment Selection: Disease Severity[1,a]

Patient Group	Recommended First Choice	Alternative Choice	Other Possible Treatments[b]
A Low risk, fewer symptoms	• SAMA PRN • SABA PRN	• LAMA • LABA • SABA and SAMA	• Theophylline
B Low risk, more symptoms	• LAMA • LABA	• LAMA and LABA	• SABA and/or SAMA • Theophylline
C High risk, fewer symptoms	• ICS + LABA • LAMA	• LAMA and LABA • LAMA and PDE4i • LABA and PDE4i	• SABA and/or SAMA • Theophylline
D High risk, more symptoms	• ICS + LABA and/or LAMA	• ICS + LABA and LAMA • ICS + LABA and PDE4i • LAMA and LABA • LAMA and PDE4i	• Carbocysteine • N-acetylcysteine • SABA and/or SAMA • Theophylline

[a] Medications in each box are mentioned in alphabetical order, not necessarily in order of preference. [b] Medications in this column can be used alone or in combination with other options in first and alternative choice columns.

PDE4i: phosphodiesterase 4 inhibitor; PRN: as needed.
1. http://goldcopd.org/gold-reports/. Accessed May 23, 2016.

Dr. Mannino: The GOLD guidelines for the treatment of COPD use various levels of disease severity to target therapy. This is listed in this slide, and I think the key take-home message, rather than memorizing this slide, is to realize that at the extremes—so people with, you know, a little impairment and few symptoms—you can treat symptomatically (so these would be under group A), with short-acting agents.

At the very other extreme, people who have advanced disease and a great deal of symptomatology, you need to treat with pretty much all therapies that we have available. So this would be for group D. And then in groups B and C, you have a lot more options. You can either treat with monotherapy, such as one long-acting agent, or dual therapy. You may or may not use inhaled steroids in this group, depending on the degree of symptomatology that patients have.

Monitoring Patients With COPD for Treatment Effectiveness[1]

- Spirometry performed at least once a year to identify patients whose lung function is declining quickly
- Questionnaires such as the COPD Assessment Test can be performed every 2-3 months; trends and changes are more valuable than single measurements

Questions that may help to determine effectiveness of treatment regimen
- Are you less breathless?
- Can you do more?
- Can you sleep better?
- Describe what difference the treatment has made for you. Is the change worthwhile?

Frequency, severity, and likely causes of any exacerbations should be evaluated
- Increased sputum volume, acutely worsening dyspnea, and the presence of purulent sputum should be noted
- Specific inquiry into unscheduled visits to providers, telephone calls for assistance, and use of urgent or emergency care facilities is important
- Severity can be estimated by the increased need for bronchodilator medication or corticosteroids and by the need for antibiotic treatment
- Hospitalizations should be documented, including the facility, duration of stay, and any use of critical care or mechanical ventilatory support

1. http://goldcopd.org/gold-reports/. Accessed May 23, 2016.

Dr. Mannino: How do we monitor our patients with COPD? Certainly, it's important at each visit to assess the degree of symptomatology that they have and to see whether or not they have either had or are at risk for having exacerbations. In addition, it is worthwhile checking spirometry at intervals. In my clinical population, I check this once every year to 2 years to see what is happening to their lung function. In addition, I will administer an assessment, such as the COPD assessment tool, to see how they are doing at that visit.

Delivery Devices, Patient Education, and Monitoring in COPD: The Pharmacist's Perspective

Roy A. Pleasants, II, PharmD
Duke Asthma, Allergy, and Airways Center
Duke University School of Medicine
Durham Veterans Administration Medical Center
NC COPD Taskforce
Durham, North Carolina

Top Three Roles for Pharmacists in COPD Management[1-3]

- ☑ **Improving adherence and compliance with medication regimens**
  - **Including proper use of delivery devices**
- ☑ **Incorporation of pharmacists into support groups, education programs, and smoking-cessation programs**
  - **Education and counseling of COPD patients by pharmacists has been associated with improvements in COPD knowledge, medication adherence, medication beliefs, HRQOL, and reductions in hospitalization**
- ☑ **Providing medication regimen reviews**

COPD: chronic obstructive pulmonary disease. HRQOL: health-related quality of life.

1. American Pharmacists Association Foundation. *J Am Pharm Assoc.* 2011;51:e20–e28.
2. Jarab AS et al. *Int J Clin Pharm*. 2012;34:53-62.
3. Wei L et al. *J Thorac Dis*. 2014;6:656-662.

Dr. Pleasants: : There are a number of a roles for the pharmacist in managing COPD patients, but here are some of the perhaps most important roles, not necessarily in order of importance. The first one is pharmacists working with patients to improve their adherence and compliance to medication regimens. One particularly important role is the pharmacist teaching patients how to properly use their inhalational devices.

Pharmacists can also, obviously, function in multidisciplinary sort of settings. These include patient support groups. Pharmacists can also be involved in individual or group educational programs for the COPD patient population. And then of course, pharmacists could have a particularly important role in helping facilitate smoking cessation on a one-to-one basis, or perhaps even in a group education sort of model. And then, of course, pharmacists' increasing role in medication regimen reviews, medication histories, and sort of working with a patient, working with the physicians on trying to optimize the drug therapy.

Delivery Devices in the Management of COPD: Dry Powder Inhalers[1,2]

Dry Powder Inhalers	Advantages	Disadvantages
• Pressair (aclidinium) • Diskus (fluticasone/salmeterol, salmeterol) • Aerolizer (formoterol)[a] • Neohaler (indacaterol, glycopyrronium, indacaterol/glycopyrronium FDC) • HandiHaler (tiotropium) • Ellipta (fluticasone/vilanterol FDC, umeclidinium, umeclidinium/vilanterol FDC)	• Compact, convenient, no hand–breath coordination required • Portable, rapid medication delivery • Individually packaged dose or dose counter makes it easy to know how many doses remain	• Dependent on peak inspiratory flow • Dose loading and activation are necessary for single-dose devices • Single-dose devices require dexterity • Do not have option to decrease oropharyngeal ADRs with use of a spacer

[a] Discontinued.

ADRs: adverse drug reactions; FDC: fixed-dose combination

1. Ray S et al. *Am Fam Physician*. 2013;8:651-652.
2. Godara N et al. *Lung India*. 2011; 28:272-275.

Dr. Pleasants: So now let's turn our attention to delivery devices commonly used in the COPD population. We'll start with dry powder inhalers. Some of the advantages—of course, they're small and compact. Dry powder inhalers are breath-actuated or breath-activated, and consequently don't require as much coordination in order to inhale the drug. And, you have a way of counting the doses.

Disadvantages—a particularly important one in the COPD population is patients have to have a very strong inspiratory rate, and therefore, the drug delivery into the lungs is highly dependent on having an adequate peak inspiratory flow rate. All of them do require some sort of dose loading or activation. Some of them require more coordination than others. Some of the additional disadvantages is, if you get, for example, oral thrush with an inhaled steroid, and it's a dry powder, you don't have a lot of options with the dry powder inhaler in order to solve that problem.

Delivery Devices in the Management of COPD: Pressurized Metered-Dose Inhalers[1-3]

Pressurized Metered-Dose Inhalers	Advantages	Disadvantages
• Albuterol • Beclomethasone • Budesonide/formoterol • Ciclesonide • Fluticasone • Fluticasone/salmeterol • Ipratropium • Levalbuterol • Mometasone/formoterol • Glycopyrrolate/formoterol	• Compact, convenient, may be used with a spacer or valved holding chamber • Not dependent on peak inspiratory flow • Portable, rapid medication delivery • Can add a spacer to decrease oropharyngeal ADRs • Can choose a product with small particle size to improve delivery to small airways	• Inconsistent dosing; variable delivery to airways • Difficult for patients with low cognition • Difficult to determine remaining doses if there is no dose counter • Inconvenient if spacer/chamber is required • Patient must actuate device; requires coordination of device actuation and inhalation, unless the patient consistently uses a spacer/chamber

1. Ray S et al. *Am Fam Physician*. 2013;8:651-652.
2. Godara N et al. *Lung India*. 2011;28:272-275.
3. Rubin BK, Fink JB. *Respir Care*. 2005;50:1191-1197.

Dr. Pleasants: So let's talk a little bit about metered dose inhalers. Some of the advantages, of course, it's compact and convenient. We can use a spacer or a holding chamber with it in order to improve the lung delivery or decrease oropharyngeal side effects.

Unlike the dry powder inhalers, the peak inspiratory flow is really not an issue. Another advantage of the metered dose inhalers is some of the formulations—you can get better delivery to the small airways with those smaller particle sizes, and I would say beclomethasone and ciclesonide would fit the definition of small particle–size inhaled steroids that give better delivery to the small airways.

Some of the disadvantages—there is a little more inconsistency in drug coming out of the device. That's particularly true if the inhaler's been sitting around a while. Some patients are very challenged to learn how to use these devices, particularly patients with low cognition or physical impairments. If there's no dose counter on the metered dose inhaler—which there are quite few of them anymore—there's no way of knowing how many doses are in there unless you have the dose counter.

You could argue that it's inconvenient if a spacer or holding chamber is required. The patient has to be more coordinated with the metered dose inhaler. Of course, if you put a spacer on there, they don't have to be quite as coordinated.

Delivery Devices in the Management of COPD: Nebulizers[1]

Nebulized Medications	Advantages	Disadvantages
• Albuterol • Arformoterol • Budesonide • Formoterol • Ipratropium • Ipratropium/albuterol	• Minimal cognition required, no hand–breath coordination required • Not dependent on peak inspiratory flow • Reimbursed by Medicare Part B • Strength and dexterity not required	• Device cleaning and maintenance needed • Long medication delivery time • Not portable, less convenient • Power source usually needed

1. Ray S et al. *Am Fam Physician*. 2013;8:651-652.

Dr. Pleasants: Nebulizers are used a fair amount in the COPD population. Some of the advantages—basically patients just have to be able to breathe in normally. And if necessary, we could use a mask rather than just a traditional nebulizer with a mouthpiece, in patients who may be a little more challenged in order to get the drug into their lungs. Inspiratory flow rate is not an issue with a nebulizer. Medicare Part B does cover 80% of the cost of these nebulized drugs.

Some of the disadvantages—have got to clean their nebulizer. I cannot stress that enough. Obviously, they're not quite as portable, although more and more of them are somewhat portable.

Delivery Devices in the Management of COPD: Soft Mist Inhalers[1-3]

Soft Mist Inhalers	Advantages	Disadvantages
• Respimat (ipratropium/albuterol, tiotropium, olodaterol, tiotropium/olodaterol FDC)	• Compact, convenient • Dose indicator and auto lock when cartridge is empty • More time to coordinate breath to actuation • Portable • Rapid medication delivery	• Expires 3 months after cartridge is inserted • Strength and dexterity required to prepare inhaler • Loss of dose if patient turns inhaler base past the “click” • Mist may be “too strong for some patients,” making them cough

1. Ray S et al. *Am Fam Physician*. 2013;8:651-652.
2. Asakura Y et al. *J Aerosol Med Pulm Drug Deliv*. 2013;26:41-45.
3. Stiolto respimat (tiotropium bromide and olodaterol). http://docs.boehringer-ingelheim.com/Prescribing%20Information/PIs/Stiolto%20Respimat/stiolto.pdf. Accessed April 25, 2016.

Dr. Pleasants: The last type of inhaler is called a soft mist inhaler. Some of the advantages—of course, it's small and convenient. It does have a dose counter on it. And then one thing that's different, when you reach zero, the patient can't try to squeeze doses out of there.

There are a few more steps required to make this device deliver compared to a metered dose inhaler. But once most patients get used to it, it's generally not a problem. When you insert the drug into the inhaler, it has an expiration period of 3 months. It is tough for some older patients to initially use or put the soft mist inhaler together.

Please note that when you instruct the patient to load a dose, you turn the base until it clicks. But if you turn that base past a click, it's going to administer a dose, and that oftentimes goes into the room. The mist makes some patients cough. It's a little bit challenging.

Emerging Devices: New High-Efficiency Nebulizers Such as eFlow (SUN-101 Studies)

- Glycopyrrolate delivered via eFlow nebulizer system (currently no nebulized LAMA is available)[1]
  - Portable, handheld electronic nebulizer

Phase 2 RCT in Patients With Moderate to Severe COPD[2]

Treatment Group	Improvements in Trough FEV_1 after 28 days Tx, mL (95% CI)[a,b]	FEV_1 AUC_{0-12}, Mean Change From BL (95% CI)[b]
12.5 mcg (n = 55)	116.8 (36.9, 196.6)	135.7 (70.9, 200.5)
25 mcg (n = 54)	128.4 (47.9, 208.9)	163.2 (98.2, 228.3)
50 mcg (n = 57)	146.2 (66.7, 225.7)	105.4 (41.5, 169.4)
100 mcg (n = 59)	177.0 (99.2, 254.8)	183.1 (119.9, 246.2)

- Most common AEs: COPD exacerbation (3.2%), headache (2.8%)[2]
- **GOLDEN-3 and GOLDEN-4 phase 3 trials:** Both 25 mcg and 50 mcg resulted in significant improvements in FEV_1 versus placebo from baseline to week 12 in patients with moderate to very severe COPD[3]

[a] Placebo-adjusted LS. [b] $P < .05$ vs. placebo.

FEV_1: forced expiratory volume in 1 second; LAMA: long-acting muscarinic antagonists.

1. http://lungdiseasenews.com/2015/03/05/sunovion-launches-phase-3-clinical-trial-for-first-nebulizer-delivered-lama-for-copd/. Accessed April 4, 2016.
2. Kerwin E et al. *Chest*. 2014;146(4_MeetingAbstracts):68A.
3. http://copdnewstoday.com/2016/05/03/sunovion-reports-positive-data-phase-3-trials-potential-copd-treatment/. Accessed May 4, 2016.

Dr. Pleasants: There are new devices that are in development for new drugs. For example, some new high-efficiency nebulizers. One of them is called the eFlow nebulizer, and this is one where glycopyrrolate, which is a long-acting antimuscarinic agent, is being developed as a nebulized form.

And this is a phase 2 study in COPD patients with moderate to severe disease. This just sort of gives you a basic idea of what sort of doses are used for this drug administered through the nebulizer.

Emerging Forms of Nebulized Bronchodilators: Revefenacin (TD-4208)

Drug and Delivery[1]	• Revefenacin (TD-4208) is a LAMA in development • Delivered via PARI LC Sprint jet nebulizer – Breath-enhanced
Phase 2 Trial Results[1]	• Once daily at 44 mcg, 88 mcg, 175 mcg, or 350 mcg for 28 days vs placebo; N = 355 • Doses of >88 mcg – Improved trough FEV_1 from baseline vs placebo ($P < .001$) – Improved 0-24–hr weighted mean FEV_1 ($P < .001$) – Reduced the use of rescue medication ($P < .001$) • Most common AEs: headache (3.1%), shortness of breath (2.8%), cough (2.0%)
Phase 3 Trials[2-4]	• 12-week efficacy study (two replicate studies): 88 mcg or 175 mcg vs placebo • 1-year safety study: 88 mcg or 175 mcg vs tiotropium

1. Haumann BK et al. *Am J Resp Crit Care Med.* 2015;191:A5750.
2. https://clinicaltrials.gov/ct2/show/NCT02512510?term=td4208&rank=5. Accessed April 4, 2016.
3. https://clinicaltrials.gov/ct2/show/NCT02459080?term=td4208&rank=6. Accessed April 4, 2016.
4. https://clinicaltrials.gov/ct2/show/NCT02518139?term=td4208&rank=8. Accessed April 4, 2016.

Dr. Pleasants: Here's another type of drug that's being developed in nebulized form, another LAMA. It's going to be given through an existing nebulizer called the PARI LC Sprint, which is a breath-enhanced nebulizer.

This is some data from the phase 2 trials. So we've got at least two nebulized LAMAs that are in development. And this is a need in the COPD population, because it's basically the only inhaled drug class that we don't have in nebulized forms.

Emerging Devices: Pressurized MDIs With Different Formulations

Co-Suspension MDI Technology[1]

- Uses lipid-based porous particles to create stable co-suspensions with drug crystals in HFA propellants, and high-performance aerosols upon actuation
  - May overcome some pharmaceutical challenges encountered with different combinations of drugs in inhalers

PINNACLE Phase 3 Trials[2]

- Four study arms: glycopyrronium/formoterol combination[a]; glycopyrronium; formoterol; placebo
  - BID for 24 weeks
- All treatment groups improved lung function vs placebo; combination was superior to monocomponents
- Most common AEs across all treatment groups (including placebo): nasopharyngitis, URTI, and dyspnea (similar incidence across treatment groups)

Other Formulations in Development[3-7]

- Phase 3: budesonide/glycopyrronium/formoterol FDC (PT010)
- Phase 3: budesonide/formoterol FDC (PT009)
- Phase 2: budesonide (PT008)

[a] FDA approved in April 2016.

BID: twice daily; fcn: function; HFA: hydrofluoroalkane; MDI: metered dose inhalers; URTI: upper respiratory tract infection.

1. Rennard S et al. *BMC Pulm Med.* 2014;14:118.
2. Rabe K et al. *Eur Respir J.* 2015;46(suppl 59):PA4363.
3. https://clinicaltrials.gov/ct2/show/NCT02536508?term=PT010&rank=3. Accessed April 4, 2016.
4. https://clinicaltrials.gov/ct2/show/NCT02497001?term=PT010&rank=5. Accessed April 4, 2016.
5. https://clinicaltrials.gov/ct2/show/NCT02536508?term=PT010&rank=3. Accessed April 4, 2016.
6. https://clinicaltrials.gov/ct2/show/NCT02105012?term=pt008&rank=1. Accessed April 4, 2016.
7. https://clinicaltrials.gov/ct2/show/NCT02196077?term=pt008&rank=2. Accessed April 4, 2016.

Dr. Pleasants: There are some emerging products coming out, some new formulations. One of them is called a co-suspension technology. This co-suspension technology gives some greater options for mixing multiple drugs together. This particular company is developing several different products.

Electronic Monitoring Devices in COPD[1-8]

Doser	• Monitors MDI use • Records actuations; shows daily use & number of doses remaining • Battery lasts 13 months • 30-day data storage
Propeller	• Cleared for use with MDIs, as well as some SMIs and DPIs • Records time, date, and location of use, along with weather & air quality • Stores up to 3,900 events • 18-month battery (not rechargeable) • Smartphone app • Patient's healthcare provider receives the collected data in dashboards • Patient feedback with weekly email reports and smartphone app; provides reminders/alerts • Wireless, remote server, and online support
Smartinhaler	• Records date & time of medication usage • Connects to a range of inhalers • Provides reminders
Qualcomm (in development)	• Pre-attaches to Breezhaler device • Patients can access their data in real time to track inhaler usage & quality of their inhalation (data upload automatically to the patient's smartphone, as well as to a cloud)

DPIs: dry powder inhaler; SMIs: soft mist inhaler.

1. Chan AHY et al. *J Allergy Clin Immunol Pract*. 2015;3:335-349.e335.
2. http://www.rtmagazine.com/2015/10/smart-inhalers-future-respiratory-health-management/. Accessed April 4, 2016.
3. Burgess SW et al. *Respir Med.* 2006;100:841-845.
4. Patel M et al. J Allergy Clin Immunol Pract. 2013;1:83-91.
5. Merchant RK et al. *J Allergy Clin Immunol Pract*. 2016;4:455-463.
6. http://www.meddeviceonline.com/doc/novartis-next-gen-copd-device-gets-connected-with-qualcomm-0001. Accessed April 4, 2016.
7. http://www.firstwordpharma.com/node/1368323#axzz44rXQxzZq. Accessed April 4, 2016.
8. Simmons MS et al. *J Allergy Clin Immunol*. 1998;102:409-413.

Dr. Pleasants: One of the real exciting areas in, really, the asthma and COPD world is that now we've got electronic monitoring devices for the inhalers. Of course, we've had one on the market for a number of years called the Doser. But the next generation of electronic monitoring devices—for example, the Propeller system—very sophisticated. It's been developed for use on dry powder inhalers, the soft mist inhaler, and metered dose inhalers. But it does a lot of things. And there's a lot of data suggesting that this improves patient outcomes for COPD, as well as the asthma population.

There's other electronic monitoring devices. I think you're going to see more and more. I think it's a very exciting area for COPD and monitoring compliance, as well as identifying people who might be developing exacerbations.

Importance of Appropriate Device Selection and Proper Use

Misuse of inhaler devices (because of inadequate training for patients or nonconsenting switch of inhaled medications) can be associated with a decrease in disease control and an increase in healthcare resource consumption and costs[1]

Patients who report low confidence in inhaler use (at least one in three, regardless of device used) also exhibit poorer COPD-related health outcomes and treatment satisfaction vs those who are confident in their inhaler use[2]

1. Roggeri A et al. *Int J COPD*. 2016;11:597-602.
2. Amin A et al. *J Hosp Med*. 2016;11(suppl 1). http://www.shmabstracts.com/abstract/confidence-in-correct-inhaler-device-technique-and-its-association-with-health-status-and-patient-satisfaction-an-analysis-of-real-world-us-chronic-obstructive-pulmonary-disease-copd-patients/. Accessed May 23, 2016.

Dr. Pleasants: Some of the importance in appropriately choosing devices—misuse of inhalers is common. So it really is important to make sure that patients know how to use their devices.

Factors Influencing Device Selection[1-4]

Factors	• Age (many COPD patients are older) • Cognition • Strength and dexterity • Inspiratory flow – A PIFR ≥60 L/min with a particular DPI is considered optimal to achieve bronchodilation – However, 70% of patients with PIFR <60 L/min receive treatment through a DPI • Convenience • Solving ADRs (such as DPI change to MDI + spacer because of oral thrush) • Patient preference, lifestyle • Need for multiple medications – May have different delivery mechanisms • Availability of medicine formats • Cost (Medicare)

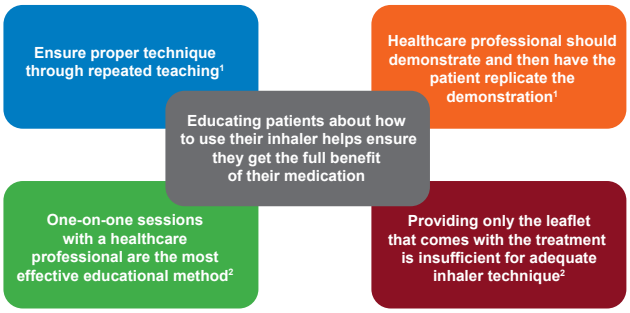
PIFR: peak inspiratory flow rate.

1. Ray S et al. *Am Fam Physician*. 2013;8:651-652.
2. Bonini M, Usmani OS. *COPD Res Pract*. 2015;1:1-9.
3. Sharma G et al. *J Hosp Med*. 2016;11(suppl 1). http://www.shmabstracts.com/abstract/analyses-of-real-world-treatment-patterns-among-hospitalized-chronic-obstructive-pulmonary-disease-copd-patients-with-low-peak-inspiratory-flow-interim-findings-from-a-prospective-observational-stu/. Accessed May 23, 2016.
4. Godara N et al. *Lung India*. 2011; 28:272-275.

Dr. Pleasants: Some of the factors influencing device selection: age, some of the older patients might be challenged to use some of the more complicated inhalers. Obviously, cognition in the elderly person is important.

The COPD patients with more advanced airway obstruction, we need to be really careful about choosing a device, particularly dry powder inhalers. If in solving ADRs—for example, if a patient gets oral thrush with a DPI—a good way to solve that is switch to a comparable product with an MDI and a spacer. Of course, patients have their preferences. We have now multiple medications, and that may influence which device that we choose, and of course cost is a very important issue in the COPD population.

Patient Education: Proper Inhaler Technique



1. Press VG et al. *J Gen Intern Med*. 2012;27:1317-1325.
2. Lavorini F. *J Aerosol Med Pulm Drug Deliv*. 2014;27:414-418.

Dr. Pleasants: Somebody needs to be taking responsibility for teaching proper inhaler technique, and I would suggest pharmacists should take the responsibility to ensure that through not only one-time teaching, but really it's been well documented that patients need to be taught more than once.

Ideally, you should demonstrate to the patient how to use the device, and then have the patient replicate the demonstration. It's actually been studied that one-on-one with that patient inhaler teaching does really work. And you should not just provide a leaflet, although I think a leaflet should be given with the verbal instruction.

COPD Management: Smoking Cessation[1-4]

- The GOLD report names pharmacists as one of the key healthcare professionals for delivering smoking-cessation messages and interventions
- Pharmacists should assess the smoking status of their patients
- All patients who smoke should be encouraged to quit, even when patients visit for reasons unrelated to COPD or breathing problems

Brief Strategies to Help the Patient Willing to Quit
ASK. Systematically identify all tobacco users at every visit.
ADVISE. In a clear, strong, and personalized manner, urge every tobacco user to quit.
ASSESS. Ask every tobacco user if he or she is willing to make a quit attempt at this time (eg, within the next 30 days).
REFER. Refer patients for treatment for smoking cessation (eg, state tobacco quit lines).

GOLD: Global Initiative for Chronic Obstructive Lung Disease.
1. http://goldcopd.org/gold-reports/. Accessed May 23, 2016.
2. http://www.pharmacytimes.com/publications/issue/2013/november2013/chronic-obstructive-pulmonary-disease-seven-specifics-to-remember. Accessed March 24, 2016.
3. American Pharmacists Association Foundation. *J Am Pharm Assoc*. 2011;51:e20-e28.
4. Patwardhan PD et al. *Int J Pharm Pract*. 2009;17:221-229.

Dr. Pleasants: I think a great area for pharmacists to get involved in is smoking cessation. I would suggest that, just like physicians do, when that patient comes to you, you need to assess their smoking status, their current smoking status. Every visit, if you know them to be a smoker, they should be encouraged to quit. And then I would suggest to you that we should recommend drug therapies, because that's going to double their quit rates.

And I strongly recommend that you do fax referrals to your state tobacco quit line. Basically, I think the role of the pharmacist is ask, advise, assess, and refer, that refer would be the state tobacco quit line.

COPD Management: Immunization[1,2]

- **All pharmacists need to promote annual immunizations with influenza and pneumococcal vaccines**
- **Immunizing COPD patients in the pharmacy creates an opportunity to discuss the patient's medications, control of the disease, and concerns**
- **Patients can be reminded about immunizations and monitored for smoking status when visiting the pharmacy for COPD treatments**

1. http://www.pharmacytimes.com/publications/issue/2013/november2013/chronic-obstructive-pulmonary-disease-seven-specifics-to-remember. Accessed April 25, 2016.
2. http://goldcopd.org/gold-reports/. Accessed May 23, 2016.

Dr. Pleasants: Of course, immunizations are a giant area that pharmacists have gotten involved with. That's a great opportunity to engage them in their medicines and compliance and so forth. And of course, it's also an opportunity for you as a pharmacist to aid with smoking cessation.

Conclusions

- A variety of treatments and delivery devices are available for patients with COPD
- Treatment and device selection is dependent upon a variety of factors
- In addition to pharmacotherapy, the management of COPD also includes avoidance of risk factors (eg, tobacco smoke), influenza and pneumococcal immunizations, as well as patient education and monitoring
- Pharmacists play an important role in the management of patients with COPD by improving adherence and compliance to medication regimens (including inhaler use), educating patients, and monitoring them to ensure that they are undergoing comprehensive care

Dr. Pleasants: So in conclusion, there's lots of different treatments for COPD today and delivery devices. Choosing the drugs and the devices is a very patient-specific issue.

In addition to dealing with the drug therapy in those patients, we really need to talk to them about preventative therapy—avoiding smoking or secondhand smoke, and of course vaccinations. So pharmacists can play an important role in management of patients with COPD by improving adherence, inhaler teaching, teaching them about their disease and drugs, and then monitoring them.

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