Disclosures

Consultant/Independent Contractor:
AstraZeneca; Boehringer-Ingelheim Pharmaceuticals; Monaghan Medical Corporation; Nonin Medical; Sunovion Pharmaceuticals, Philips

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Philips Respironics

Speakers Bureaus:
Boehringer Ingelheim Pharmaceuticals; GlaxoSmithKline; Sunovion Pharmaceuticals
Pharmacologic Treatment Options
Treatment Options for COPD

ICS, inhaled corticosteroid; SABA, short-acting beta$_2$-adrenoceptor agonist; SAMA, short-acting muscarinic antagonist; mMRC = mMRC Breathlessness Scale; CAT = COPD Assessment Test

# Pharmacologic Options

<table>
<thead>
<tr>
<th>Bronchodilators</th>
<th>Anti-Inflammatory</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Short-Acting</strong></td>
<td><strong>Long-Acting</strong></td>
</tr>
<tr>
<td><strong>Anticholinergic (SAMA)</strong>&lt;br&gt;Ipratropium</td>
<td><strong>Anticholinergic (LAMA)</strong>&lt;br&gt;Tiotropium, or aclidinium, or umeclidinium, or glycopyrrolate</td>
</tr>
<tr>
<td><strong>$\beta_2$-Agonists (SABA)</strong>&lt;br&gt;Albuterol&lt;br&gt;Levalbuterol&lt;br&gt;Metaproterenol&lt;br&gt;Pirbuterol</td>
<td><strong>$\beta_2$-Agonists (LABA)</strong>&lt;br&gt;Salmeterol, or formoterol, or arformoterol, or indacaterol (ultra), or olodaterol</td>
</tr>
<tr>
<td><strong>SAMA + SABA</strong>&lt;br&gt;Ipratropium + albuterol</td>
<td><strong>LAMA + LABA</strong>&lt;br&gt;Tiotropium + olodaterol&lt;br&gt;Umeclidinium + vilanterol&lt;br&gt;Indacaterol + glycopyrrolate</td>
</tr>
</tbody>
</table>

**Oral Steroids**<br>Prednisone<br>Methylprednisolone

**Xanthine Derivative:** Theophylline
### Newer Therapies *(continued)*

<table>
<thead>
<tr>
<th>Medication/Formulation</th>
<th>Class</th>
<th>Approved</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vilanterol/umeclidinium bromide inhalation powder&lt;sup&gt;1&lt;/sup&gt;</td>
<td>LABA + LAMA</td>
<td>Dec 2013</td>
<td>Long-term, once-daily maintenance treatment, COPD-related airflow obstruction, including chronic bronchitis/emphysema</td>
</tr>
<tr>
<td>Fluticasone furoate/vilanterol inhalation powder&lt;sup&gt;2&lt;/sup&gt;</td>
<td>ICS + LABA</td>
<td>May 2013</td>
<td>Once-daily alternative to fluticasone/salmeterol, budesonide/formoterol</td>
</tr>
<tr>
<td>Aclidinium bromide inhalation powder&lt;sup&gt;3&lt;/sup&gt;</td>
<td>LAMA</td>
<td>July 2012</td>
<td>Long-term, twice-daily maintenance treatment, COPD-related bronchospasm</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Medication/Formulation</th>
<th>Class</th>
<th>Approved</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olodaterol inhalation spray(^1)</td>
<td>LABA</td>
<td>Aug 2014</td>
<td>Long-term, once-daily maintenance treatment, COPD-related airflow obstruction, including chronic bronchitis/emphysema</td>
</tr>
<tr>
<td>Umeclidinium bromide inhalation powder(^2)</td>
<td>LAMA</td>
<td>April 2014</td>
<td>Long-term, once-daily maintenance treatment, COPD-related airflow obstruction, including chronic bronchitis/emphysema</td>
</tr>
</tbody>
</table>

## Newer Therapies

<table>
<thead>
<tr>
<th>Medication/Formulation</th>
<th>Class</th>
<th>Approved</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indacaterol + glycopyrrolate inhalation powder&lt;sup&gt;1&lt;/sup&gt;</td>
<td>LAMA + LABA</td>
<td>Oct 2015</td>
<td>Long-term maintenance treatment of airflow obstruction in patients with COPD</td>
</tr>
<tr>
<td>Glycopyrrolate inhalation powder&lt;sup&gt;2&lt;/sup&gt;</td>
<td>LAMA</td>
<td>Oct 2015</td>
<td>Stand-alone, long-term maintenance treatment of airflow obstruction in patients with COPD</td>
</tr>
<tr>
<td>Tiotropium/olodaterol inhalation spray&lt;sup&gt;3,4&lt;/sup&gt;</td>
<td>LAMA + LABA</td>
<td>April 2015</td>
<td>Long-term, once-daily from start of maintenance treatment, COPD-related airflow obstruction, including chronic bronchitis/emphysema</td>
</tr>
</tbody>
</table>

Adverse Effects of Therapy

- Anticholinergics
  - Dry mouth, urinary retention, glaucoma

- Beta$_2$-agonists
  - Tachycardia, palpitations, premature ventricular contractions, tremors, hypokalemia

- Inhaled corticosteroids
  - Dysphonia, thrush, systemic effects (bruising, bone density, cataract), pneumonia, local irritation

Most COPD Patients Do Not Receive Recommended Treatment

Patients not receiving recommended maintenance therapy

Retrospective Review of Medical Records
>50,000 COPD Cases

LAAC, long-acting anticholinergic; SAAC, short-acting anticholinergic; Ach, inhaled anticholinergic

INHALED DRUG DEPOSITION

- Patient inhalational flow
- Aerosol velocity
- Inhaled drug particle size
Delivery Devices
### Table 2. Typical Operation of a Valved Holding Chamber With a Pressurized Metered-Dose Inhaler

<table>
<thead>
<tr>
<th>Step</th>
</tr>
</thead>
<tbody>
<tr>
<td>Take cap off the pMDI boot and insert into chamber</td>
</tr>
<tr>
<td>Shake pMDI with Chamber</td>
</tr>
<tr>
<td>Actuate 1 dose into chamber</td>
</tr>
<tr>
<td>Inhale from the chamber for several breaths</td>
</tr>
<tr>
<td>Adults: 1–3 inhalations</td>
</tr>
<tr>
<td>Slow deep breath with breath hold if possible, or tidal breathing</td>
</tr>
<tr>
<td>Infants: ( \leq 10 ) breaths or 30 seconds tidal breathing</td>
</tr>
<tr>
<td>Remove pMDI from chamber</td>
</tr>
<tr>
<td>Replace cap on pMDI and chamber</td>
</tr>
<tr>
<td>Store both chamber and pMDI properly</td>
</tr>
<tr>
<td>Chamber maintenance: Periodically wash chamber in warm soapy water, rinse, and air dry</td>
</tr>
</tbody>
</table>

*pMDI = pressurized metered-dose inhaler*
Table 6. Errors in MDI Use*

<table>
<thead>
<tr>
<th>Error</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hand-breath discoordination</td>
<td>27</td>
</tr>
<tr>
<td>Breath-hold too short</td>
<td>26</td>
</tr>
<tr>
<td>Inspiratory flow too rapid</td>
<td>19</td>
</tr>
<tr>
<td>Inadequate shaking of inhaler</td>
<td>13</td>
</tr>
<tr>
<td>Abrupt stop of inhalation (&quot;cold-Freon effect&quot;)</td>
<td>6</td>
</tr>
<tr>
<td>MDI actuation at total lung capacity</td>
<td>4</td>
</tr>
<tr>
<td>Multiple actuations with a single breath</td>
<td>3</td>
</tr>
<tr>
<td>Firing MDI in mouth, inhaling through nose</td>
<td>2</td>
</tr>
<tr>
<td>Exhaled during actuation</td>
<td>1</td>
</tr>
<tr>
<td>Wrong end of inhaler in mouth</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Cap left on MDI boot</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Inspiration without actuation</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Actuation without inspiration</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>
Table 10. Problems in Patient Education

<table>
<thead>
<tr>
<th>Problem</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low literacy</td>
</tr>
<tr>
<td>Poor attention span, especially when sick</td>
</tr>
<tr>
<td>Inadequate time to learn</td>
</tr>
<tr>
<td>Inadequate information</td>
</tr>
<tr>
<td>Inadequate follow-up</td>
</tr>
<tr>
<td>Patient hesitant to ask questions</td>
</tr>
<tr>
<td>Limited financial incentives for education</td>
</tr>
</tbody>
</table>
Table 11. Problems in Clinician Teaching

<table>
<thead>
<tr>
<th>Problem</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lack of familiarity with use of specific devices</td>
</tr>
<tr>
<td>Inadequate time to teach</td>
</tr>
<tr>
<td>Poor training techniques</td>
</tr>
<tr>
<td>Poor training materials</td>
</tr>
<tr>
<td>Lack of follow-up</td>
</tr>
</tbody>
</table>
Table 5. What Clinicians Need to Know About Each Inhaler

<table>
<thead>
<tr>
<th>How to select an inhaler</th>
<th>Advantages</th>
<th>Limitations</th>
<th>Performance</th>
<th>Ease of use</th>
<th>Cost</th>
<th>How to use</th>
<th>How to maintain</th>
</tr>
</thead>
</table>

Factors That Determine Selection of Delivery System

- Clinical efficacy
- Disease severity
- Need for combination therapy
- Cost
- Ease of use
- Portability
- Lifestyle/preference
- Cognitive/dexterity issues

Photo credit: www.humana.com
Inhaler Devices Available
United States

MDI
Handihaler®
Aerolizer™
Twisthaler®
Diskus®
Pressair®
Flexhaler®
Ellipta®
Respimat®
Spacer Devices
Inhaler Devices Available
United States

Small-Volume Nebulizer

- Select a medication delivery system/regimen that is aligned with treatment goals, patient abilities and preferences; consider costs
- Train patients on proper device technique; reinforce training at each visit
pMDI

- HFA driven, breath-actuated

**Advantages**
- Portable, compact

**Disadvantages**
- Requires coordination
- Shaken prior to use
- Oropharyngeal deposition
DPI

- Single, multidose

Advantages
- Portable, compact
- No spacer required

Disadvantages
- Inspiratory flow dependent
- Poor dose reproducibility
Soft mist

- Single, multidose

**Advantages**
- Portable, compact
- No spacer required

**Disadvantages**
- Newer model of use
Nebulizers

- Jet, vibrating mesh, ultrasonic

**Advantages**
- Propellant free
- Slow velocity aerosol

**Disadvantages**
- Bulky
- Power sources
- Frequent cleaning
Individualizing Inhaled Therapy$^{1,2}$

- Good hand-breath coordination required for MDIs
  - May not be suitable for elderly, confused, those with hand conditions (e.g., arthritis)

- Dry-powder inhalers (DPIs) do not require coordination of actuation, inhalation; easier to use than MDIs
  - Breath actuation may be difficult in patients with poor inspiratory effort

- Avoid changing inhaler types for individual patients

Types of Inhaler Errors

1. Device care and preparation
2. Exhalation before use
3. Timing
4. Coordination with device
5. Flow rate errors
6. Completing inhalation/breath hold
7. After care (ie, rinsing/gargling)

- Extremely high rate of device technique errors with use of chronic inhaled medications
- Incorrect technique poorly perceived by patient; must be assessed by HCPs
Increasing Patient Adherence to COPD Treatment
Adherence to Medications: Poor

- 167 patients with COPD
  - LABA: 54% adherence\(^a\)
  - ICS: 40% adherence

- Patients more adherent when they perceive clinician as a lung disease expert

\(^a\)Adherence measured by electronic pharmacy records to assess adherence, defined as medication possession ratio $\geq 0.80$

Barriers to Treatment Adherence

- Inadequate education about COPD, therapy\(^1\)
- Perceived burden of medication regimen\(^1,2\)
- Device difficult to use\(^3\)
- Depressed mood\(^3\)
- Medication-related cost\(^3\)
- Adverse effects\(^3\)

Features of Devices

- pMDIs (pressurized metered-dose inhalers)
- DPIs (dry powder inhalers)
- Soft-mist inhaler
- Nebulizers
Systematic Review of Errors in Inhaler Use
Sanchis, CHEST 2016 (in press)
144 articles (n = 54354 patients)

MDI errors
- Co-ordination (45%)
- Speed and/or depth of inspiration (44%)
- No post-inhalation breath-hold (46%)

DPI errors
- Incorrect preparation (28%)
- No full expiration before inhalation (46%)
- No post-inhalation breath hold (37%)
Prevalence (technique)

- Correct: 31% (33-40%)
- Acceptable: 41% (36-47%)
- Poor: 31% (27-36%)
EFFECTIVENESS OF INTERVENTIONS
Press et al, Annals ATS 2016

- Evaluate the relative effects of two educational strategies in adults hospitalized with asthma/COPD
  - Teach to goal
  - Brief verbal instruction
- Randomized trial
- Inhaler technique
  - Standardize checklists
  - Misuse (<75% steps or less correct)
  - Primary outcome – use at 30 days post discharge
EFFECTIVENESS OF INTERVENTIONS
Press et al, Annals ATS 2016

![Graph showing the effectiveness of interventions.](image)

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>BI</th>
<th>TTG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-Education</td>
<td>84% (49/58)</td>
<td>92% (57/62)</td>
</tr>
<tr>
<td>Post-Education</td>
<td>60% (35/58)</td>
<td>11% (7/62)</td>
</tr>
<tr>
<td>30d Follow-up</td>
<td>70% (37/53)</td>
<td>54% (29/54)</td>
</tr>
<tr>
<td>90d Follow-up</td>
<td>76% (39/51)</td>
<td>48% (25/52)</td>
</tr>
</tbody>
</table>
EFFECTIVENESS OF INTERVENTIONS

Press et al, Annals ATS 2016

Diskus Inhaler Subset (N=38)

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>BI</th>
<th>TTG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-Education</td>
<td>89% (16/18)</td>
<td>75% (15/20)</td>
</tr>
<tr>
<td>Post-Education</td>
<td>61% (11/18)</td>
<td>5% (1/20)</td>
</tr>
<tr>
<td>30d Follow-up</td>
<td>59% (10/17)</td>
<td>53% (9/17)</td>
</tr>
<tr>
<td>90d Follow-up</td>
<td>63% (10/16)</td>
<td>38% (6/16)</td>
</tr>
</tbody>
</table>
Results

- **N = 120**
- **Women 73%, African-Americans 90%**
- **Pre-education**
  - TTG 92%
  - Brief intervention 84%
- **Post-education (immediate)**
  - TTG 11%
  - Brief instruction 60%
- **Post-education (30 day)**
  - TTG 54%
  - Brief instruction 70%
- Teach to goal instruction in inhaler technique
  - Did not reduce inhaler misuse at 30 days
  - Associated with fewer acute care events at 30 days
Pittsburgh Regional Health Initiative

- CMS innovation award grant
- Readmission reduction program
- Seven community hospitals
- Provider educational sessions
  - COPD
  - Spirometry
  - Inhaled device use
Standardized Inhaler Training Across a COPD Care Management Program

- Nurses, RTs, pharmacists
- 3 hour program
- Pre-test, Post-test
  - Written, simulation (checklists)
- Didactic session
- Training session
  - “Instructor”
  - “Patient”
  - “Assessor(s)”
  - Checklists, actual device placebos
Standardized Inhaler Training Across a COPD Care Management Program
Standardized Inhaler Training Across a COPD Care Management Program

- Written tests
  - 10 single best answer, multiple choice
  - Similar domain content (not same questions)
  - Results (number correct)
    - Pre 7.66
    - Post 9.24
## ADHERENCE TO INHALER “BEST PRACTICES” CHECKLIST
(N=28 TRAINEES)

<table>
<thead>
<tr>
<th>INHALER</th>
<th>ITEMS IN CHECKLIST</th>
<th>AVERAGE SCORE AT TRAINING</th>
<th>AVERAGE SCORE AT 30 DAY FOLLOW-UP</th>
<th>% CHANGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>ELLIPTA</td>
<td>5</td>
<td>4.72</td>
<td>5</td>
<td>+5.93%</td>
</tr>
<tr>
<td>DISKUS</td>
<td>9</td>
<td>7.71</td>
<td>8.88</td>
<td>+15.18%</td>
</tr>
<tr>
<td>MDI</td>
<td>12</td>
<td>8.65</td>
<td>11.69</td>
<td>+35.14%</td>
</tr>
<tr>
<td>HANDIHALER</td>
<td>9</td>
<td>8.26</td>
<td>9</td>
<td>+8.96%</td>
</tr>
<tr>
<td>RESPIMAT</td>
<td>12</td>
<td>8.94</td>
<td>11.61</td>
<td>+29.87%</td>
</tr>
<tr>
<td>AVERAGE</td>
<td>n/a</td>
<td>7.66</td>
<td>9.24</td>
<td>+19.02%</td>
</tr>
</tbody>
</table>
Table 3. Mean ± SD Scores by Profession

<table>
<thead>
<tr>
<th></th>
<th>RTs (n = 20)</th>
<th>Pharmacists (n = 8)</th>
<th>RNs (n = 21)</th>
<th>Physicians (n = 14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before</td>
<td>70.0 ± 11.4*</td>
<td>78.3 ± 18.9</td>
<td>60.5 ± 14.0</td>
<td>54.2 ± 11.1</td>
</tr>
<tr>
<td>After</td>
<td>71.9 ± 7.9</td>
<td>81.7 ± 20.2</td>
<td>63.5 ± 12.7</td>
<td>55.8 ± 12.4</td>
</tr>
<tr>
<td>Practical</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before</td>
<td>77.3 ± 12.2*</td>
<td>77.2 ± 8.0</td>
<td>67.4 ± 15.8</td>
<td>56.1 ± 8.6</td>
</tr>
<tr>
<td>After</td>
<td>83.6 ± 10.6†</td>
<td>82.5 ± 1.5</td>
<td>71.6 ± 12.2</td>
<td>64.0 ± 16.3</td>
</tr>
</tbody>
</table>

N = 63.
* Significant difference from registered nurses and physicians.
† Significant difference between before and after.
Inhaler Use
Alismail et al, Respir Care 2016
Common Myths About Inhaler Use

- Inhalers are so simple they need no instruction
- DPIs are easier to use than pMDIs
- Nebulizers are easier to use than inhalers
- Someone else will teach the patient if I don’t
Common Myths About Inhaler Use

- I know and follow the current guidelines
- Once inhaled medications are prescribed, the patient will conscientiously take them
- I teach the patient correctly, but they don’t use the inhalers right
Pulmonologist Survey
Braman et al, ATS 2016

- Survey regarding attitudes and practices
- Inhalational devices
- Knowledge
  - 98% somewhat knowledgeable
  - 54% extremely knowledgeable
  - 70% teach patient on first visit
Pulmonologist Survey
Braman et al, ATS 2016

- Discuss clean and store 9%
- Which patients should use a hand-held nebulizer (very knowledgeable) 31%
- Small volume nebulizers essential for some patients 56%
- Hand held nebulizers more effective than DPI/MDI (MMRC grade of 4) 63%
How Do I Use These Devices?
Summary
Tailoring Therapy

- **Individual Presentation, Underlying Mechanisms**
  - Mortality
  - Disease progression
  - Lung function
  - Symptoms
  - Exercise tolerance
  - Exacerbations
  - Disability
  - Health status, QOL

- **Individual Risk Factors**
  - Skin bruising
  - Nutritional impairment
  - Neuropsychological effects
  - GI symptoms

- **Comorbidities**
  - Pneumonia
  - Tuberculosis
  - Osteoporosis, fractures
  - Muscle dysfunction
  - Cataract
  - Diabetes
  - Tremor
  - Cardiovascular events

**Current Pharmacological Options**

- LABA
- LAMA
- LABA + LAMA
- LABA + ICS
- LABA + LAMA + ICS
- LABA + PDE-4
- LAMA + PDE-4

Steps to Improving Adherence

- Select best medication delivery system for patient
- Provide education about COPD
- Provide training on use of delivery system
- Develop a rapid action plan to prevent, manage exacerbations
REFERENCES

- Braman SS, Carlin BW, Dhand R, Hanania NA, Mahler DA, et al. Results of a pulmonologist survey regarding attitudes and practices with inhalation devices for COPD. Am J Respir Crit Care Med 193;2016,A7816A


REFERENCES


- Video courtesy of Paradigm Medical Communications. Monograph available at https://ce.paradigmmc.com/attendee/view_program.jsp?programCode=20117P3chNGf

- Paradigm Medical Communications: paradigmmmc.com
Thank You !!

bwcmd@yahoo.com