

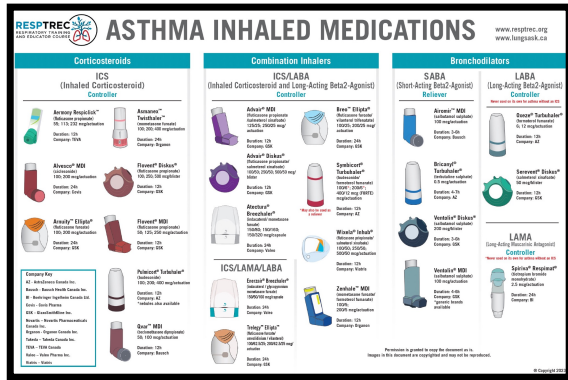
Suggested Hierarchy of Outcomes for Pulmonary Trials

CLINICAL OUTCOMES

- 1) Mortality
- 2) Quality of Life – typically a scale called the SGRQ is used – look at the minimally important clinical difference – also ACQ – how many people got a change that was at least past the MICD threshold – most trials don't give this
- 3) Symptom-free days, use of rescue meds
- 4) Improvement in exacerbation symptoms
- 5) Reduction in exacerbation rates (exacerbations/yr) – indicate if they are mild, moderate, severe and how are these terms are defined
- 6) Exacerbations/year – convert to how many less exacerbations/"x" number of years. For instance – a 0.2 exacerbation/yr difference means about 1 less exacerbation every 5 years
- 7) Look for rates of pneumonia in people getting a steroid inhaler
- 8) Thrush, voice changes
- 9) Feel free to add others if need be

FAR LESS IMPORTANT OUTCOMES

Pulmonary function tests



CS

Corticosteroids

ICS (Inhaled Corticosteroid) Controller



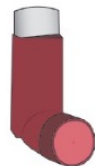
Aermony Resplick™
(fluticasone propionate)
55; 113; 232 mcg/actuation

Duration: 12h
Company: TEVA



Asmanex™
Twisthaler™
(mometasone furoate)
100; 200; 400 mcg/actuation

Duration: 24h
Company: Organon



Alvesco® MDI
(ciclesonide)
100; 200 mcg/actuation

Duration: 24h
Company: Covis



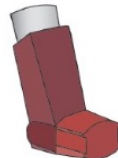
Flovent® Diskus®
(fluticasone propionate)
100; 250; 500 mcg/blister

Duration: 12h
Company: GSK



Arnuity™ Ellipta®
(fluticasone furoate)
100; 200 mcg/actuation

Duration: 24h
Company: GSK



Flovent® MDI
(fluticasone furoate)
50; 125; 250 mcg/actuation

Duration: 12h
Company: GSK



Pulmicort® Turbuhaler®
(budesonide)
100; 200; 400 mcg/actuation

Duration: 12h
Company: AZ
*nebulas also available



Qvar™ MDI
(beclomethasone dipropionate)
50; 100 mcg/actuation

Duration: 12h
Company: Bausch

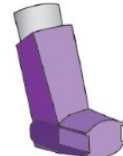
Company Key

AZ - AstraZeneca Canada Inc.
Bausch - Bausch Health Canada Inc.
BI - Boehringer Ingelheim Canada Ltd.
Covis - Covis Pharma
GSK - GlaxoSmithKline Inc.
Novartis - Novartis Pharmaceuticals Canada Inc.
Organon - Organon Canada Inc.
Takeda - Takeda Canada Inc.
TEVA - TEVA Canada
Valeo - Valeo Pharma Inc.
Viatriis - Viatriis

Combination Inhalers

**BL+
CS**

ICS/LABA (Inhaled Corticosteroid and Long-Acting Beta2-Agonist) Controller



Advair® MDI
(fluticasone propionate/
salmeterol xinafoate)
125/25; 250/25 mcg/
actuation

Duration: 12h
Company: GSK



Advair® Diskus®
(fluticasone propionate/
salmeterol xinafoate)
100/50; 250/50; 500/50 mcg/
blister

Duration: 12h
Company: GSK



Aectura®
Breezhaler®
(indacaterol/ mometasone
furoate)
150/80; 150/160;
150/320 mcg/capsule

Duration: 24h
Company: Valeo



Enerzair® Breezhaler®
(indacaterol / glycopyrronium
mometasone furoate)
150/50/160 mcg/capsule

Duration: 24h
Company: Valeo



Trelegy™ Ellipta™
(fluticasone furoate/
umeclidinium / vilanterol)
100/62.5/25; 200/62.5/25 mcg/
actuation

Duration: 24h
Company: GSK



Breo™ Ellipta®
(fluticasone furoate/
vilanterol trifenate)
100/25; 200/25 mcg/
actuation

Duration: 24h
Company: GSK



Symbicort®
Turbuhaler®
(budesonide/
formoterol fumarate)
100/6*; 200/6*;
400/12 mcg (FORTE)
mcg/actuation

Duration: 12h
Company: AZ
**May also be used as
a reliever*



Wixela® Inhub®
(fluticasone propionate/
salmeterol xinafoate)
100/50; 250/50;
500/50 mcg/actuation

Duration: 12h
Company: Viatriis



Zenhale™ MDI
(mometasone furoate/
formoterol fumarate)
100/5;
200/5 mcg/actuation

Duration: 12h
Company: Organon

**BL+
CS+
ML**

ICS/LAMA/LABA

BS

Bronchodilators

SABA (Short-Acting Beta2-Agonist) Reliever



Airmir™ MDI
(salbutamol sulphate)
100 mcg/actuation

Duration: 3-6h
Company: Bausch



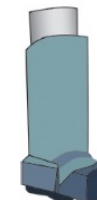
Bricanyl®
Turbuhaler®
(terbutaline sulphate)
0.5 mcg/actuation

Duration: 4-7h
Company: AZ



Ventolin® Diskus®
(salbutamol sulphate)
200 mcg/blister

Duration: 3-6h
Company: GSK



Ventolin® MDI
(salbutamol sulphate)
100 mcg/actuation

Duration: 4-6h
Company: GSK
*generic brands
available

BL

LABA (Long-Acting Beta2-Agonist) Controller

Never used on its own for asthma without an ICS



Oxeze® Turbuhaler®
(formoterol fumarate)
6; 12 mcg/actuation

Duration: 12h
Company: AZ



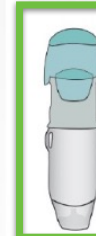
Serevent® Diskus®
(salmeterol xinafoate)
50 mcg/blister

Duration: 12h
Company: GSK

ML

LAMA (Long-Acting Muscarinic Antagonist) Controller

**Never used on its own for asthma without an ICS*



Spiriva® Respimat®
(tiotropium bromide
monohydrate)
2.5 mcg/actuation

Duration: 24h
Company: BI

Also used
for COPD

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MS

Short-Acting Bronchodilators

BS

SAMA

(Short-Acting Muscarinic Antagonist)
USE REGULARLY



Atrovent® MDI
(ipratropium bromide)
20 mcg/actuation

Duration: 4-6h
Company: BI

SABA

(Short-Acting Beta2-Agonist)
USE REGULARLY or PRN



Airomir™ MDI
(salbutamol sulphate)
100 mcg/actuation

Duration: 3-6h
Company: Bausch



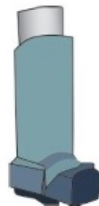
Bricanyl® Turbuhaler®
(terbutaline sulphate)
0.5 mcg/actuation

Duration: 4-7h
Company: AZ



Ventolin® Diskus®
(salbutamol sulphate)
200 mcg/blister

Duration: 3-6h
Company: GSK



Ventolin® MDI
(salbutamol sulphate)
100 mcg/actuation

Duration: 4-6h
Company: GSK
*generic brands available

Company Key

AZ – AstraZeneca Canada Inc.
Bausch – Bausch Health, Canada, Inc
BI – Boehringer Ingelheim Canada Ltd.
Covis – Covis Pharma Canada Ltd.
GSK – GlaxoSmithKline Inc.
Novartis – Novartis Pharmaceuticals Canada Inc.
Viatriis – Viatriis

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ML

Long-Acting Bronchodilators

BL

LAMA

(Long-Acting Muscarinic Antagonist)
USE REGULARLY



Incruse™ Ellipta®
(umeclidinium bromide)
62.5 mcg/actuation

Duration: 24h
Company: GSK



Seebri® Breezhaler®
(glycopyrronium bromide)
50 mcg/capsule

Duration: 24h
Company: Covis



Spiriva® Handihaler®
(tiotropium bromide monohydrate)
18 mcg/capsule

Duration: 24h
Company: BI
*generic brand available



Spiriva® Respimat®
(tiotropium bromide monohydrate)
2.5 mcg/dose

Duration: 24h
Company: BI



Tudorza® Genuair®
(aclidinium bromide)
400 mcg/capsule

Duration: 12h
Company: Covis

LABA

(Long-Acting Beta2-Agonist)
USE REGULARLY



Serevent® Diskus®
(salmeterol xinafoate)
50 mcg/blister

Duration: 12h
Company: GSK

**BL+
CS+
ML**



Breztri® Aerosphere®
(budesonide/glycopyrronium/formoterol fumarate)
160/7.2/5.0 mcg/actuation

Duration: 12h
Company: AZ

**BL+
CS**

Combination Inhalers

**BS+
MS**

ICS/LABA

(Inhaled Corticosteroid/Long-Acting Beta2-Agonist)
USE REGULARLY



Advair® Diskus®
(fluticasone propionate/salmeterol xinafoate)
250/50; 500/50 mcg/blister

Duration: 12h
Company: GSK



Breo™ Ellipta®
(fluticasone furoate/vilanterol trifenate)
100/25 mcg/actuation

Duration: 24h
Company: GSK



Symbicort® Turbuhaler®
(budesonide/formoterol fumarate)
200/6; 400/12 mcg/actuation

Duration: 12h
Company: AZ



Wixela® Inhub®
(fluticasone propionate/salmeterol xinafoate)
250/50; 500/50 mcg/actuation

Duration: 12h
Company: Viatriis

ICS/LAMA/LABA

USE REGULARLY

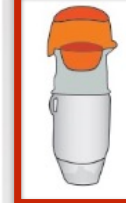


Trelegy™ Ellipta®
(fluticasone furoate/umeclidinium bromide/vilanterol trifenate)
100/62.5/25 mcg/dose

Duration: 24h
Company: GSK

SAMA and SABA

USE REGULARLY



Combivent® Respimat®
(ipratropium bromide/salbutamol sulphate)
20/100 mcg/actuation

Duration: 4-6h
Company: BI

LAMA and LABA

USE REGULARLY



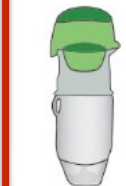
Anoro™ Ellipta®
(umeclidinium bromide/vilanterol trifenate)
62.5/25 mcg/actuation

Duration: 24h
Company: GSK



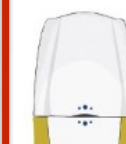
Duaklir® Genuair®
(aclidinium bromide/formoterol fumarate dehydrate)
400/12 mcg/actuation

Duration: 12h
Company: Covis



Inspilo® Respimat®
(tiotropium bromide monohydrate/olodaterol hydrochloride)
2.5/2.5 mcg/actuation

Duration: 24h
Company: BI



Ultibro® Breezhaler®
(glycopyrronium bromide/indacaterol maleate)
50/110 mcg/capsule

Duration: 24h
Company: Covis

**BL+
ML**



BL+
CS+
ML

Gold = \$60/gram



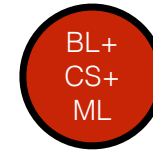
EACH PUFF = 190 mcg of medication/dose
30 doses = 5,700 mcg = 5.7mg = 0.0057grams
≅ 175 inhalers = 1 gram of medication

TRELEGY ELLIPTA
**(fluticasone furoate/
umeclidinium/
vilanterol)**

1 inhaler (30 days)
≅ \$140 or \$1700/year

BY WEIGHT TRELEGY IS

~400 times more expensive than gold
~200 times more expensive than the
most expensive metal in the world (Rhodium)



DYNAMIC DUO *vs.* TRIPLE THREAT

(LAMA+LABA) (LAMA+LABA+ICS)

3 meta-analyses:

- Reduction in **AECOPD** (Cazzola, *Eur Resp J* 2018)
NNT = **39** (for triple) 👍
- Increase in **PNEUMONIA** (Zheng, *BMJ* 2018; Zayed, *Clin Respir J* 2019)
NNH = **38-39** (against triple) 👎

But, did they at least **feel better** day-to-day?

Slide from Jamie Falk

NNTs... diminishing returns?

(ballpark)

any real net benefit?

≥ 1 mod-severe AECOPD
 ≥ 1 severe AECOPD
 MCID on dyspnea score
 MCID on QoL score

BL

ML

LAMA or LABA vs. SABD (scheduled or prn)
16-29
36
6
8-10

BL+
ML

LAMA+LABA vs. LAMA or LABA
42
NS
6-15
8-15

BL+
CS+
ML

LAMA+LABA+ICS vs. LAMA+LABA
38
NS - 0.05 less/pt/yr
NA
13-17

Adverse events: NO DIFFERENCE

Pneumonia:
39-59

Other AEs?
 • thrush
 • dysphonia

Thorax 2016;71:15-25

CDSR 2018, Issue 12. Art. No.: CD012620

Int J COPD 2017;12 907-922

Respir Res 2017;18:196

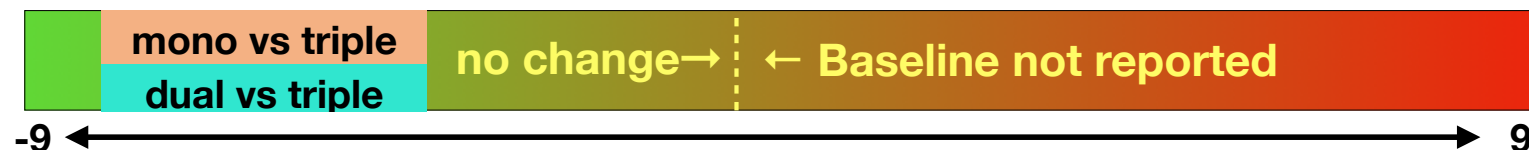
COPD: What to Do with all These New Inhalers? Dalhousie CPD Academic Detailing Service, 2017

Ballpark estimates of the benefits seen from inhalers on clinically important outcomes

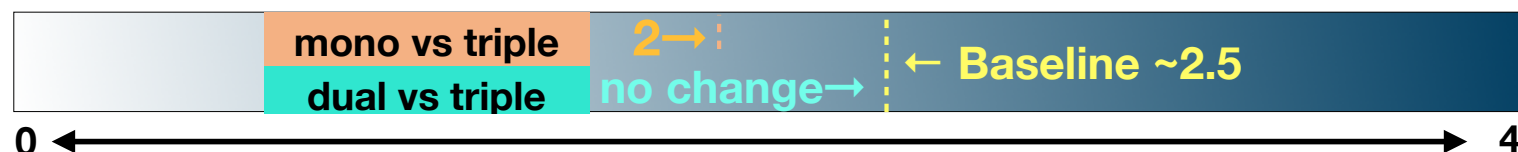
St George's Respiratory Questionnaire - MCID = - 4
(NNT to reach MCID)



Transition Dyspnea index - MCID = -1



Rescue inhaler puffs per day



Exacerbations/year (moderate/severe)
(NNT to prevent one exacerbation)



Exacerbations/year (severe)

