

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

ASTHMA INHALED MEDICATIONS

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



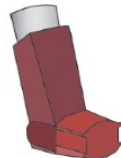
Flovent® Diskus®
(fluticasone propionate)
100; 250; 500 mcg/blister

Duration: 12h
Company: GSK



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

Duration: 24h
Company: GSK



Flovent® MDI
(fluticasone propionate)
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

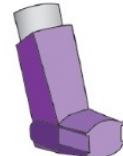
AZ - AstraZeneca Canada Inc.
Bausch - Bausch Health Canada Inc.
BI - Boehringer Ingelheim Canada Ltd.
Covis - Covis Pharma
GSK - GlaxoSmithKline Inc.
Novartis - Novartis Pharmaceuticals Canada Inc.
Organon - Organon Canada Inc.
Takeda - Takeda Canada Inc.
TEVA - TEVA Canada
Valeo - Valeo Pharma Inc.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

BL+
CS+
ML

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



Atecura®
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: Viartis



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

Duration: 12h
Company: Organon



Trimbow® pMDI
(beclomethasone dipropionate /
formoterol fumarate dihydrate /
glycopyrronium)
100/6/10 mcg per actuation

Duration: 12h
Company: Chiesi

BS

Bronchodilators

SABA (Short-Acting Beta2-Agonist) Reliever



Airomir™ MDI
(salbutamol sulphate)
100 mcg/actuation

Duration: 3-6h
Company: Bausch



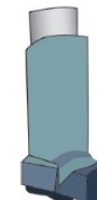
Bricanyl®
Turbuhaler®
(terbutaline sulphate)
0.5 mcg/actuation

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

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



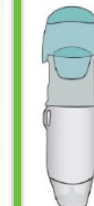
Serevent® Diskus®
(salmeterol xinafoate)
50 mcg/blister

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



Airomir™ MDI
(salbutamol sulphate)
100 mcg/actuation

Duration: 3-6h
Company: Bausch



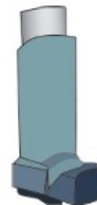
Bricanyl® Turbuhaler®
(terbutaline sulphate)
0.5 mcg/actuation

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.
Viatis – Viatis

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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



Trimbow® pMDI
(beclomethasone dipropionate /
formoterol fumarate dihydrate /
glycopyrronium)
100/6/10 mcg per actuation
Duration: 12h
Company: Chiesi



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

Duration: 12h
Company: AZ

BL+
CS

Combination Inhalers

BS+
MS

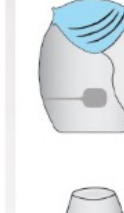
ICS/LABA

(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



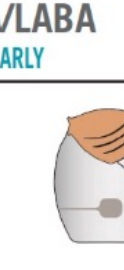
Symbicort® Turbuhaler®
(budesonide/formoterol fumarate)
200/6; 400/12 mcg/actuation

Duration: 12h
Company: AZ



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

Duration: 12h
Company: Viatis



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



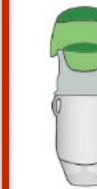
Anoro™ Ellipta®
(umeclidinium bromide/
vilanterol trifenate)
62.5/25 mcg/actuation

Duration: 24h
Company: GSK



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

Duration: 12h
Company: Covis



Inspiolto® 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



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)**

PLEASE GO TO THIS SITE

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http://wiki.ubc.ca/Evidence_Appraisal_Integrated_Activities

ACADEMIC YEAR 2 - FIRST TERM

7) RESPIROLOGY STUDIES [File:IA COPD info.pdf](#)

- [First inhaled steroid study](#) [↗](#) Groups 1,13,25
- [As-Needed Albuterol-Budesonide in Mild Asthma](#) [↗](#) Groups 2,14,26
- [Albuterol-Budesonide Fixed-Dose Combination Rescue Inhaler for Asthma](#) [↗](#) Groups 3,15,27
- [Combined Budesonide–Formoterol as Needed in Mild Asthma](#) [↗](#) Groups 4,16,28
- [Doubling dose of inhaled corticosteroid](#) [↗](#) Groups 5,17,29
- [As-Needed Budesonide–Formoterol versus Maintenance Budesonide in Mild Asthma](#) [↗](#) Groups 6,18,30
- [Triple Inhaled Therapy at Two Glucocorticoid Doses in Moderate-to-Very-Severe COPD](#) [↗](#) Groups 7,19,31
- [Tiotropium and olodaterol in the prevention of COPD](#) [↗](#) Groups 8,20,32
- [Short VS long steroids for COPD exacerbation](#) [↗](#) Groups 9,21,33
- [Stopping inhaled steroids in COPD](#) [↗](#) Groups 10,22,34
- [Once-Daily Single-Inhaler Triple versus Dual Therapy in Patients with COPD](#) [↗](#) Groups 11,23,35
- [Tezepelumab in Adults and Adolescents with Severe, Uncontrolled Asthma](#) [↗](#) Groups 12,24,36

ACCORD Study - NEJM 2008

N=10,251 - 3.5 years

Age 62, Female 38%, Diabetes 10 years, Previous CV event 35%, White 65%, Smoker 14%, BMI 32, BP 136/75, A1C 8.3, Total cholesterol 183

	Intensive therapy	Standard therapy	Hazard Ratio	Hazard Ratio 95% CI
Primary outcome (%)	6.9	7.2	0.90	0.78-1.04
Death (%)	5.0	4.0	1.22	1.01-1.46
Non-fatal MI (%)	3.6	4.6	0.76	0.62-0.92
Non-fatal stroke (%)	1.3	1.2	1.06	0.75-1.50
CHF (%)	3.0	2.4	1.18	0.93-1.49
Hypoglycemia (%)	10.5	3.5		
Serious adverse event	2.2	1.6		
Weight gain >10kg	27.8	14.1		

Does the child have asthma that is well-controlled with as needed salbutamol?

Yes

Review with patient:

- Optimizing technique
- Trigger avoidance
- Co-morbidities

No

Discuss using an inhaled corticosteroid (ICS) plus a beta agonist

Ongoing daily symptoms?

Yes

Consider daily ICS + PRN SABA

Choose ICS based on cost and device (pMDI or DPI)

EVIDENCE

Daily ICS + PRN SABA

vs

PRN ICS + SABA

Similar asthma outcomes – PRN ICS = less CS than daily*

or

PRN SABA

vs

PRN ICS + LABA

Fewer exacerbations with PRN ICS + LABA**

No

PRN ICS + LABA

1 inhaler

2 inhalers

Definition of Well-Controlled

Daytime symptoms	2 or fewer days per week
Nighttime symptoms	Fewer than 1 night per week and mild*
Physical activity	Normal
Exacerbations	None requiring steroids or ED visit
Absence from school due to asthma	None
Need for a reliever (SABA or bus/form)	2 or fewer doses per week
FEV1 or PEF	90% or better of personal best
PEF diurnal variation	Less than 10–15%

Symbicort Turbuhaler (DPI)***

budesonide 100 mcg / formoterol fumarate 6 mcg
1 puff PRN
120 doses = \$100 = \$0.83/dose



Side effects (SABA/LABA dose related)

SABA / LABA

- Tremor
- Nervousness
- Tachycardia

ICS

- Oral thrush
- Voice changes

~1/2 the price of combo inhaler

Qvar HFA (MDI)

beclomethasone 50 mcg
1 puff PRN
200 doses = \$63 = \$0.32/dose



Ventolin HFA (MDI)

salbutamol 100 mcg
1 puff PRN
200 doses = \$21 = \$0.10/dose



EVIDENCE

* Daily ICS vs PRN ICS + SABA – Similar asthma outcomes but in PRN group, less CS used, ~0.5 cm greater height increase and lower inhaler cost – TREXA

** PRN ICS + LABA vs PRN SABA – ages 5–15 – over 1 year – at least one asthma attack 32% (PRN SABA) vs 17% (PRN ICS + LABA) – CARE

OTHER

*** Not approved by Health Canada <12 y/o – use would be considered off-label

Higher doses not shown to be more effective