Community Pharmacy Respiratory Update April 2016

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Qvar

- beclomethasone dipropionate
- Ultrafine particle (<1.5µm) solution (not suspension) (only one currently available in NZ)
- Radio-labelled deposition studies show more deposition in the lungs (>55% dose ex actuator) and less in the oropharnx (< 35% dose actuator)
- Lower dose equivalents:
 - 100mcg Qvar
 - 125 mcg Flixotide
 - 200mcg Budesonide
 - 250mcg CFC Beclomethasone (eg Beclazone)
- Evidence:
 - 2 papers for HFC BDP showing improved asthma control, n = 2-300





Journal of Allergy and Clinical Immunology 2000 106, 1209-1226DOI: (10.1067/mai.2000.111582) Copyright © 2000 Mosby, Inc. <u>Terms and Conditions</u>





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Clinical Pearl

- Using an inhaler correctly is a skill must be learned and maintained.
- Up to 70-80% of patients cannot use their inhalers correctly
- Many healthcare providers are unable to demonstrate the correct technique for the inhalers they prescribe
- Most people with incorrect techniques are unaware that they have a problem
- There is no "perfect inhaler" patients can have difficulties with any inhaler device

This happens more often than you think.....



Pick up your pens!

¤	Relieve [.] symptoms¤	Improve exercise tol & QoL ¤	Improve·lung· function¤	Reduce- exacerbation:/- hospitalisation¤	Reduce [.] mortality¤	α
SABA¤	α	α	α	α	α	α
Theophylline¤	α	α	α	α	α	α
LAMAs¤	α	α	α	α	α	α
ICS¤	α	α	α	α	α	¤
ICS/LABA¤	α	α	α	α	α	¤
LAMA/LABA¤	α	α	α	α	α	¤
Oral·steroids¤	α	α	α	¤	α	α
Smoking- cessation¤	α	α	α	α	α	¤
Pulmonary· rehabilitation¤	α	¤	¤	α	α	¤
Prophylactic- antibiotics¤	α	¤	¤	α	α	α
LTOT¤	α	α	ß	n	α	α
α	α	α	α	¤	α	α

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Short acting Beta2-Agonists

- Reduce symptoms
 - Relieve symptoms
 - Improve exercise tolerance/daily function

Reduce risk

- Prevent disease progression/improve lung function
- Prevent exacerbations/hospitalisations
- Reduce mortality





Methylxanthines

- Reduce symptoms
 - Relieve symptoms
 - Improve exercise tolerance/daily function

Reduce risk

- Prevent disease progression/improve lung function
- *

- Prevent exacerbations/hospitalisations
- Reduce mortality



Ram et al. Cochrane DSR 2003; CD00003902 Zhou et al. Respirology 2006:11:603 ZuWallack et al. Chest 2001; 119:1661

Theophylline S.R.

Theophylline Anhydrous

Bronchodilator

20 tablets



Anticholinergics

- Reduce symptoms
 - Relieve symptoms
 - Improve exercise tolerance/daily function



Reduce risk

Prevent disease progression/improve lung function



- - Prevent exacerbations/hospitalisations
 - Reduce mortality

?? Increase cardiovascular risk?

Barr et al. Cochrane DSR 2005; CD00002876 Kestin etl al. Int J COPD 2008; 3:127 Tashkin et al. NEJM 2008; 359:1543 Vogelmeier et al. NEJM 2011; 364(12): 1093 Wise et al. NEJM 2013; 369:1491

New LAMAs

- Tiotropium via soft mist inhaler (Respimat)
 - Less inspiratory effort with good delivery
 - But stiff cartridge loading
 - Same SA criteria as existing Spiriva
 - ?? Increased cardiovascular risk concerns

• Glycopyrronium (Seebri Breezehaler)

- 50mcg OD LAMA
- Improvements similar to tiotropium
 - Dyspnoea, SGRQ, rescue inhaler use
- One year data only
- Endorsement on script only (not SA)





New LAMAs

• Umeclidinium (Incruse Ellipta)

- Fast onset LAMA (within 15min)
- 62mcg OD
- No SA, endorsed on script
- Similar efficacy to other existing LAMAs
 - improved FEV1
 - Symptoms scores
 - Caution in high CVS risk group
- Aclidinium (Bretaris Genuair)
 - Selective LAMA (for the M3 receptor)
 - 322mcg x 1 inh BD
 - Not pharmac subsidized

Decramer et al. Lancet RM 2014; 2: 472-86 Donohue JF et al. J Clin Pharamacol. 2014 Nov;54(11):1214-20 Church A et al. BMC Pulm Med. 2014 Jan 6;14:2. Feldman G et al. Pulm Pharmacol Ther. 2012 Dec;25(6):465-71





Cat's Bottomline

- All LAMAs on the market are equal in terms of evidence based benefits
- Spiriva has the longest follow up time
- Respimat Increased CVS mortality has been largely addressed but not my first choice in someone with CVS risk factors
- Device based differences in terms of handling – the Breezehaler seemed easiest to me



• Further reading:

• 2015 systematic review + meta-analysis Ismaila AS et al, Comparative efficacy of long acting muscarinic antagonist monotherapies in COPDInt J Chron Obstruct Pulmon Dis. 2015 Nov 16;10:2495-517)



Inhaled corticosteroids

- Reduce symptoms
 - Relieve symptoms
 - Improve exercise tolerance/daily function





Reduce risk

Prevent disease progression/improve lung function



- Prevent exacerbations/hospitalisations If FEV1<60%
- Reduce mortality

Increase risk of pneumonia! Esp fluticasone!

Drummond et al. JAMA 2008; 300: 2407 Singh et al. Arch Int Med 2009I 169: 219 Calverley et al. Chest 2011; 139: 505

New ICS

• Fluticasone furoate –

- Different ligand binding domain of fluticasone with better affinity to the glucocorticoid receptor
- Increased affinity → increased potency → increased lung occupancy (in theory) reduced systemic side effects.
- Dose equivalent: FF 100mcg OD = FP 250mcg BD
- Only available in NZ as combination inhaler (FF/VI Breo Ellpita)
- Series of studies (funded by GSK) showing not inferior to Seretide
- Qvar ultra-fine particles of beclomethasone for better deposition but all the studies are done in patients with asthma



The issue of colour...

- What is wrong with this ICS/LABA "preventer"?
- In January 2015, GSK in Europe changed the colour of Relvar inhaler from blue to yellow after feedbacks concerning blue inhalers can be confused as "as required reliever" inhaler.



gsk gsk) RELVAR RELVAR 2/22 mcg 184/22 mcg 184/22 µ nhalation powdedPulver zur Inhalation/ inhalation powder/Pulver zur Inhalation halatiepoeder nhalatiepoeder luticasone furoate/vilanterol uticasone furoate/vilanterol Fluticasonfuroat/Vilanterol Fluticasonfuroat/Vilanterol fluticasonfuroaat futicasonfurosat/ 30 30 30 doses Dosen Dosen



Combination ICS/LABA



- Relieve symptoms
- Improve exercise tolerance/daily function



Reduce risk

- Prevent disease progression/improve lung function
- Prevent exacerbations/hospitalisations
- Reduce mortality

Increase risk of pneumonia! Esp fluticasone!

Calverley et al. NEJM 2007; 356:775 Calverly et al. ERJ 2009; 34:641-7

The new ICS/LABA

Fluticasone furoate/vilanterol (Breo Ellipta)

- Ultra-long acting
- OD 100/25mcg (equivalent to FP/salm 250/50 BD)
- Fully funded for COPD & adult asthma with no SA
- No difference in terms of QoL or lung function benefits
- All studies are short (most < 12 weeks, x1 24 weeks)
- Limited shelf life:

Once foil is opened and desiccant removed, the shelf life is only 6 weeks. Potential problem of keeping one inhaler in different locations....



Bottomline: I would only consider switching from existing ICS/LABA combination if patient is known to have poor compliance ?more likely to take OD drug.

> O'Byrne PM et al. ERJ 2014;43:773-82 Woodcock A et al. Chest 2013; 144:1222-9 Bateman ED et al. Thorax 2014;69:312-9 Dransfield et al. Lancet Respir Med. 2013; 1:210-23

Indication: COPD at low risk of exacerbations NOT ASTHMA

- Reduce symptoms
 - Relieve symptoms
 - Improve exercise tolerance/daily function

Reduce risk

- Prevent disease progression/improve lung function
- Prevent exacerbations/hospitalisations
- Reduce mortality



Bateman ED et al. ERJ 2013; 42: 1484-94, Celli B et al. Chest 2014; 145:981-91 Singh D et al BMC Pulm Med 2014; 14; 178

Umeclidinium/vilanterol (Anoro Ellipta)

- 62.5/25mcg OD
- No SA
- Easy to use inhaler
- Same issue with limited shelf life as other Ellepta devices
- Potential confusion with Symbicort
- Improved lung function, SGRQ, rescue medication use compared to single bronchodilator.
- Longest study so far 24 weeks

EEP OUT OF REACH OF CHILDREN NORO® FLUETA® r for inhalation, pre-dispensed eclidinium (as bron S mre and lanterol (at rifenatate 25 mce 30 AUST R 207529 30 Doses 012655

Maleki-Yazdi (Toronto) et al Respiratory Medicine 2014;108:1752-1760

- Glycopyrronium/indacaterol (Ultibro breezhaler)
 - 50/110mcg OD
 - No SA
 - Improved lung function, SGRQ, rescue medication use compared to single bronchodilator.
 - SPARK small reduction in exacerbations in GOLD III-IV patients
 - Overall 12 to 10% p.a.
 - i.e. NNT = 50
 - No difference in death & SAEs



Eric D. Bateman et al. Eur Respir J 2013;42:1484-1494 Vogelmeier et al. LRM 2013

Tiotropium/olodaterol (Spiolto Respimat)

- 2.5/2.5mcg 2 puffs OD
- LABA component 5 min onset of action
- Same SA criteria as tiotropium
- Improved lung function, SGRQ, rescue medication use compared to single bronchodilator.
- Small reduction in exacerbations
- No change to hospitalisation or mortality
- Longest study so far 52 weeks



Cat's Bottomline

- All LAMA/LABAs on the market are equal in terms of evidence based benefits
- Indicated in COPD with low risk of exacerbations. NOT ASTHMA
- Device based differences in terms of handling. The Respimat device is stiff but makes a nice mist (? For patients who like nebulisers?)
- Spiolto still requires SA (FEV1 <60% predicted)
- Further reading:

• 2015 cochrane review LABA + tiotropium available via the Cochrane website



