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
*P ≤ 0.003 vs placebo
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!

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<th>Relieve symptoms</th>
<th>Improve exercise tol. &amp; QoL</th>
<th>Improve lung function</th>
<th>Reduce exacerbation/hospitalisation</th>
<th>Reduce mortality</th>
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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 ❌

Sestini P et al. Cochrane DSR 2002; CD00001495
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
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
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
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 COPD
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
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 $\rightarrow$ increased potency $\rightarrow$ 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.
Combination ICS/LABA

- Reduce symptoms
  - 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
Combination LAMA/LABAs

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
Combination LAMA/LABAs

- **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

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

- **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

Vogelmeier et al. LRM 2013
Combination LAMA/LABAs

- **Tiotropium/olodaterol (Spioltto 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*