Shaping a Dynamic Future in Respiratory Practice

#DFResp

www.dynamicfuture.co.uk
Inhaled Therapy in COPD: Past, Present and Future

Richard Russell
Chest Physician
West Hampshire Integrated Respiratory Service

The views expressed in this presentation are those of the speaker and are not necessarily those of the meeting sponsors. This presentation may contain off-licence information. Please refer to the product SmPCs for the approved indication for use.
Disclosures:

Who
• Boehringer Ingelheim
• GlaxoSmithKline
• Teva UK Limited
• AstraZeneca
• Pfizer
• Napp
• British Lung Foundation
• Editor at Int J COPD

What
• Paid speaker
• Advisory boards
• Clinical trial investigator
• Travel support

I have no shares in pharmaceutical companies and do everything I can to hinder tobacco companies
Breathe
What you need to know about COPD, the lung disease that claims 30,000 lives in the UK each year
ICS therapies in COPD, the past...

• Numerous studies have looked at ICS therapies to improve outcomes in COPD
  - ISOLDE
  - TORCH
  - INSPIRE
  - FORWARD
  - BUD/FORM

5. Calverley PM, et al. ERJ 2003 (BUD/FORM vs BUD vs FORM vs Pla)
ICS monotherapy is more effective than placebo in stable COPD
(ICS monotherapy is NOT licenced in COPD)

### Conclusions from a Cochrane systematic review of 55 primary studies published up to and including 2011 (n=16,154)

<table>
<thead>
<tr>
<th>Lung function</th>
<th>Exacerbations</th>
<th>Mortality</th>
<th>Health status</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Significant improvement of lung function vs placebo</td>
<td>• Reduced exacerbation rates (mean difference of -0.26 exacerbations/patient/year, 95% CI: -0.37 to -0.14, n=2586)</td>
<td>• No significant effects on mortality (OR: 0.98, 95% CI: 0.83 to 1.16, n=8390)</td>
<td>• Slowing of the rate of decline in QoL (improvement in SGRQ of 1.22 units/year, 95% CI: -1.83 to -0.60, n=2507)</td>
</tr>
<tr>
<td>• Use of ICS for &gt; 6 months did not have a major effect on the rate of decline in FEV₁ (mean benefit of 5.80 mL/year with ICS over placebo, 95% CI: -0.28 to 11.88, n=2333)</td>
<td>• Increased risk of reported pneumonia</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ICS significantly reduces the rate of exacerbations needing medical intervention

Szafranski\textsuperscript{1}

<table>
<thead>
<tr>
<th></th>
<th>Budesonide</th>
<th>Formoterol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rate of exacerbations vs placebo (%)</td>
<td>-15%*</td>
<td>-2%</td>
</tr>
</tbody>
</table>

\textit{p}<0.05 vs placebo

Calverley\textsuperscript{2}

<table>
<thead>
<tr>
<th></th>
<th>Budesonide</th>
<th>Formoterol +3%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rate of exacerbations vs placebo (%)</td>
<td>-12% *</td>
<td></td>
</tr>
</tbody>
</table>

\textit{p}<0.05 vs placebo

Fewer future attacks

The risk of acute exacerbations in the TRISTAN study
There were no differences between the three active treatment groups.

- Mahler and Hanania studies – no significant differences between groups
The TORCH study: All-cause mortality at 3 years

The TORCH study: Rate of moderate and severe exacerbations over 3 years

Mean number of exacerbations/year

- Placebo: 1.13
- SALM: 0.97* (p<0.001 vs placebo)
- FP: 0.93*

Long-term inhaled steroids in COPD

<table>
<thead>
<tr>
<th>Trial</th>
<th>n</th>
<th>Duration</th>
<th>Severity</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Copenhagen City</td>
<td>290</td>
<td>3 years</td>
<td>Mild</td>
<td>No effect</td>
</tr>
<tr>
<td>EUROSCOP</td>
<td>1277</td>
<td>3 years</td>
<td>Mild</td>
<td>No effect</td>
</tr>
<tr>
<td>ISOLDE</td>
<td>751</td>
<td>3 years</td>
<td>Moderate</td>
<td>No effect</td>
</tr>
<tr>
<td>Lung Health 2</td>
<td>1116</td>
<td>3.5 years</td>
<td>Moderate</td>
<td>No effect</td>
</tr>
</tbody>
</table>

- 1º outcome = decline in FEV$_1$ over 3 years
- Cochrane Review: >16,000 COPD patients
  - No ↓ FEV$_1$ decline
  - No ↓ mortality
What are we doing now? The present...
COPD: What is on our wish list?

Unmet needs of patients with COPD
• More effective diagnosis and primary prevention
  Better symptom control
  Fewer exacerbations
  Slowing of disease progression
• Better life expectancy
• Less systemic disease secondary to COPD and fewer comorbidities

Unmet needs of the medical community
• Optimising disease prevention
  Improving symptom control
  Preventing exacerbations and decreasing their clinical impact
  Preventing disease progression
• Reducing disease-related mortality
• Identifying systemic effects and comorbidities

COPD, chronic obstructive pulmonary disease

FEV₁ decline: The traditional view

Modified version of the Fletcher and Peto graph showing the decline in FEV₁.
FEV₁, forced expiratory volume in 1 second.
More recent analyses concluded that, in contrast with earlier findings, 
FEV₁ decline was fastest in the early stages of COPD, particularly in 
GOLD 2 disease.
Affecting disease progression

- UPLIFT (subgroup)
- TORCH (subgroup)

- Real GOLD II FEV1 loss 61ml/year
- UPLIFT GOLD II loss 49ml/year
- UPLIFT GOLD III 38ml/year
TORCH study: FEV$_1$ loss

Jenkins et al, Respiratory Research 2009; 10:59
UPLIFT: GOLD II analysis

Decamer et al. Lancet 2009 374,9696;1171-1178
How do patients feel?

Decamer et al. Lancet 2009 374,9696;1171-1178
### UPLIFT: GOLD II exacerbations

<table>
<thead>
<tr>
<th>GOLD stage</th>
<th>Median time to first exacerbation (months [95% CI])</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>II</td>
<td>23.1 (21.0–26.3)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>III</td>
<td>13.2 (11.5–14.6)</td>
<td>0.002</td>
</tr>
<tr>
<td>IV</td>
<td>9.7 (8.2–12.0)</td>
<td>0.956</td>
</tr>
</tbody>
</table>

Decamer et al. Lancet 2009 374,9696;1171-1178
Paradigm of COPD management is shifting

Initial pharmacological COPD management according to symptoms / risk assessment

<table>
<thead>
<tr>
<th>Risk (GOLD classification of airflow limitation)</th>
<th>First Choice</th>
<th>Second Choice</th>
</tr>
</thead>
<tbody>
<tr>
<td>1, 2</td>
<td>A (SABA or SAMA prn)</td>
<td></td>
</tr>
<tr>
<td>3, 4</td>
<td>B (LABA or LAMA)</td>
<td>C (ICS/LABA or LAMA)</td>
</tr>
<tr>
<td>2, 4</td>
<td>D (ICS/LABA and/or LAMA)</td>
<td></td>
</tr>
</tbody>
</table>

MMRC = 2 or CAT = 10

High levels of off-guidelines ICS use worldwide*

Patients at GOLD Stage II with no history of exacerbations in the past year who were receiving ICS at baseline on enrolment

*Data from 11 studies in 44 countries with a total of 9482 patients

So what are we doing now?

It seems almost random:

• Population database study n=24,957
  - 17% no treatment
  - 24% ICS
  - 26% ICS/LABA
  - 23% ICS, LABA, LAMA
  - 2% LAMA alone

• Irrespective of GOLD stage or GOLD group (A-D)

When the 2010 guideline was being written, the available evidence for LABA plus LAMA combination therapy was relatively limited.

As the NICE guidelines are purely evidence-based, the recommendation for LABA plus LAMA therapy is restricted in the 2010 guideline.
Expiratory flow limitation has systemic effects in COPD

COPD

Expiratory flow limitations

Air trapping/hyperinflation

Breathlessness

Deconditioning

HRQoL

Inactivity

Reduced exercise capacity

Progression: decline in lung function

Disability

Mortality

COPD, chronic obstructive pulmonary disease; HRQoL, health-related quality of life

Bronchodilation and its consequences

- Relaxation of ASM
- Not the same as increased radius from reduction in oedema/cells
- Change in the degree/location of EFL
- Reduced static hyperinflation (EELV)
- Delays onset of dyspnoea when exercising
Beta-agonists and muscarinic antagonists
Anticholinergics

HENBANE

Deadly Nightshade
Duration of action of tiotropium

FEV$_1$ time profile (0-12 hours), test day 29

- Tiotropium Respimat® 5µg (n=187)
- Tiotropium Respimat® 10µg (n=179)
- Tiotropium HandiHaler® 18µg (n=186)
- Placebo (n=181)

Twice daily LAMA therapy

Change from baseline to Week 52 in trough and peak FEV₁ (Gelb et al)

- Trough FEV₁
- Peak FEV₁
Effects of aclidinium on FEV₁: ACCLAIM COPD trial results

Effects of aclidinium on FEV\textsubscript{1}:
ACCLAIM COPD trial results

Adapted from Jones PW, et al. Respir Res 2011;12:55

FEV\textsubscript{1}, forced expiratory volume in 1 second
Long-term impact on health status

LABA
Formoterol has a significantly faster onset of action *versus* salmeterol

(data presented after 28 days treatment)
Indacaterol provided significant sustained improvement in trough FEV$_1$ over 26 weeks versus placebo and salmeterol.

***p<0.001 vs placebo; †††p<0.001 vs salmeterol

Data are LSM

Olodaterol 5 and 10μg improve mean FEV₁ AUC₀⁻³h and trough FEV₁ responses over 48 weeks similarly.

Data on file. Studies 1222.11; 1222.12 1222.13; 1222.14

Common baseline mean (standard error): Studies 11/12: 1.145 (0.014); Studies 13/14: 1.208 (0.011). Analysis with imputation (full analysis set). AUC₀⁻³h, area under the plasma concentration time curve from 0 to 3 hours; FEV₁, forced expiratory volume in 1 second.
LAMA/LABA
Short-acting $\beta_2$-agonists versus anticholinergics

$\Delta \text{FEV}_1$ (%)

Day 1

Day 85

Hours after test dose

Combivent Study Group, Chest 1994; 105:1411
Dual bronchodilators for COPD

- **Anoro® Ellipta®▼**
  - VIL/UMEC
  - • 55µg umeclidinium
  - • 22µg vilanterol
  - • One inhalation
  - • Once daily

- **Duaklir® Genuair®▼**
  - ACL/FORM
  - • 340µg aclidinium
  - • 12µg formoterol
  - • One inhalation
  - • Twice daily

- **Spiolto® Respimat®**
  - • 2.5µg tiotropium
  - • 2.5µg olodaterol
  - • Two inhalations
  - • Once daily

- **Ultibro® Breezhaler®▼**
  - • 50µg glycopyrronium
  - • 110µg indacaterol
  - • One inhalation
  - • Once daily
24-hour FEV\(_1\) profile after six weeks of treatment – significant improvements in lung function versus monotherapy and placebo

![Graph showing FEV\(_1\) profile over time for different treatments](image-url)

*Difference between T+O FDC 5/5µg and placebo

- Tiotropium 2.5µg
- Tiotropium 5µg
- Placebo
- Olodaterol 5µg
- Tiotropium+olodaterol FDC 2.5/5µg
- Tiotropium+olodaterol FDC 5/5µg

Trough 207mL*

Change from baseline in pre-morning dose lung function (trough FEV₁) at Week 24: pooled data

- ACL/FORM significantly improved lung function pre-morning dose compared with aclidinium or formoterol
VIL/UMEC 55/22mcg improves lung function compared with TIO

- Primary endpoint: Trough FEV$_1$ at day 169

VIVACITO: Adjusted mean IC, TLC, FRC and RV response (L) at 2:30 post-dose after six weeks' treatment

FDC always superior over placebo.
*Indicates additional superiority over at least one of the monotherapies.
FDC, fixed-dose combination; FRC, functional residual capacity; IC, inspiratory capacity; L, litres; O/Olo, olodaterol; RV, residual volume; T/Tio, tiotropium; TLC, total lung capacity.

Rates of exacerbations at week 24: pooled data

- ACL/FORM was associated with a statistically significant reduction of 29% in the rate of moderate or severe exacerbations.
Exacerbations: Probability of moderate/severe exacerbations

### Numbers at risk

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Numbers at risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>T+O 5/5 µg</td>
<td>1029 963 909 862 811 775 735 706 686 646</td>
</tr>
<tr>
<td>T+O 2.5/5 µg</td>
<td>1030 979 937 884 839 791 753 720 696 668</td>
</tr>
<tr>
<td>Tiotropium 5 µg</td>
<td>1033 952 880 832 786 752 716 679 647 613</td>
</tr>
<tr>
<td>Tiotropium 2.5 µg</td>
<td>1032 937 895 832 787 736 691 665 648 615</td>
</tr>
<tr>
<td>Olodaterol 5 µg</td>
<td>1038 952 874 802 752 715 671 642 607 576</td>
</tr>
</tbody>
</table>

### Test day

- 0.00
- 0.05
- 0.10
- 0.15
- 0.20
- 0.25
- 0.30
- 0.35
- 0.40
- 0.45
- 0.50

- BI data on file. Studies 1237.5/.6 combined dataset.
Indacaterol– Glycopyrronium versus Salmeterol– Fluticasone for COPD

Jadwiga A. Wedzicha, M.D., Donald Banerji, M.D., Kenneth R. Chapman, M.D., Jørgen Vestbo, M.D., D.M.Sc., Nicolas Roche, M.D., R. Timothy Ayers, M.Sc., Chau Thach, Ph.D., Robert Fogel, M.D., Francesco Patalano, M.D., and Claus F. Vogelmeier, M.D., for the FLAME Investigators*
FLAME is the first study to demonstrate superiority of indacaterol/glycopyrronium (Ultibro® Breezhaler®) in exacerbation prevention versus SFC in COPD patients with ≥1 exacerbation in the preceding year.

Ultibro® Breezhaler® was non-inferior (primary endpoint) and superior to SFC for the rate of all (mild/moderate/severe) exacerbations over 52 weeks.

Updated treatment algorithm in GOLD 2017

Group C
- LAMA + LABA
- LABA + ICS
- Further exacerbation(s)
- LAMA

Group D
- Consider roflumilast if FEV₁ < 50% pred. and patient has chronic bronchitis
- Consider macrolide in former smokers
- Further exacerbation(s)
- LAMA + LABA + ICS
- Persistent symptoms
- Further exacerbation(s)
- LAMA → LAMA + LABA → LABA + ICS

Group A
- Continue, stop or try alternative class of bronchodilator
- evaluate effect
- A bronchodilator

Group B
- LAMA + LABA
- Persistent symptoms
- A long-acting bronchodilator (LABA or LAMA)
When should ICS be used in the management of COPD? – The Future...
When should we use ICS in COPD?

• My view...

• Disclaimer... the views represented are those of the speaker and his appraisal of current evidence; they are likely to be biased and may not be the TRUTH
GOLD recommendations for COPD treatment

In patients with a major discrepancy between the perceived level of symptoms and severity of airflow limitation, further evaluation is warranted.

- **Group A**: Continue, stop or try alternative class of bronchodilator. Evaluate effect.
  - A bronchodilator

- **Group B**: LAMA + LABA. Persistent symptoms.
  - A long-acting bronchodilator (LABA or LAMA)

- **Group C**: LAMA + LABA. LABA + ICS. Further exacerbation(s)
  - LAMA

- **Group D**: LAMA + LABA + ICS. Consider roflumilast if FEV₁ <50% pred. and patient has chronic bronchitis. Consider macrolide (in former smokers). Further exacerbation(s).

Additional clinics:

- **Group E**: Persistent symptoms / further exacerbation(s).
  - LABA + ICS

- **Group F**: LABA + ICS.

Prefered treatment

When should we use inhaled steroids in COPD?

• Consider use in GOLD groups C and D
• For patients with frequent exacerbations and poor lung function
• Do they help promote maximal bronchodilatation when added to LAMA/LABA?

• ICS can be withdrawn
• I make a positive decision to start ICS; it is NOT a default
Pneumonia risk with ICS

NNT and NNH for inhaled corticosteroids

Table 2: Comparison between the NNT to prevent a COPD exacerbation and the NNT to induce pneumonia properly computed from the corresponding cumulative incidences (CIs) for recent trials of the fluticasone-salmeterol combination inhaler (ICS) versus a long-acting bronchodilator.

<table>
<thead>
<tr>
<th>Study</th>
<th>Time span for NNT</th>
<th>COPD exacerbation</th>
<th>Pneumonia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>CI at end of study</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>ICS</td>
<td>No ICS</td>
</tr>
<tr>
<td>TORCH¹</td>
<td>3 years</td>
<td>0.922*</td>
<td>0.945*</td>
</tr>
<tr>
<td>INSPIRE⁴</td>
<td>2 years</td>
<td>0.578†</td>
<td>0.590†</td>
</tr>
<tr>
<td>Kardos³</td>
<td>44 weeks</td>
<td>0.47</td>
<td>0.55</td>
</tr>
<tr>
<td>Ferguson⁵</td>
<td>1 year</td>
<td>0.58</td>
<td>0.66</td>
</tr>
<tr>
<td>Anzuo⁶</td>
<td>1 year</td>
<td>0.60</td>
<td>0.67</td>
</tr>
</tbody>
</table>
Potential risks of ICS use

<table>
<thead>
<tr>
<th>Condition</th>
<th>Randomised controlled trial</th>
<th>Observational study</th>
<th>Systematic review</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonia</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Bone fracture</td>
<td>No effect on fracture risk</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Skin thinning/easy bruising</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cataract</td>
<td></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Oropharyngeal candidiasis</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>
New GOLD D: A treatable trait approach

• Several options are available if:
  – Patient on LAMA/LABA
  – Still exacerbating
  – Poor lung function (<50%)

1. ICS: with eosinophils
2. Roflumilast: if chronic bronchitis and emphysema and BMI >23
3. Macrolide therapy: if not smoking (bronchiectasis, check microbiology)
   – Role of therapeutic trial
   – Non-eosinophilic
   – Neutrophilic

Personal expert opinion Richard Russell
The blood eosinophil count: reducing risk and ICS in COPD
Blood eosinophils in COPD & ICS: reducing risk

- **INSPIRE**
  - Randomised, double-blind, parallel-group, double-dummy study with either salmeterol/fluticasone propionate 50/500µg twice daily (n=658) or tiotropium bromide 18µg once daily (n=665) for 2 years
  - Primary endpoint of health care utilisation exacerbation rate not different

Blood eosinophilia in COPD & ICS: reducing risk

- The effect of addition of fluticasone furoate (FF) to vilanterol (VI)
  - HZC102871 and HZC102970 studies; safety and efficacy study\(^1\)
  - To determine if the combination of FF and VI is more protective than VI alone against COPD exacerbations; more AE, however, reanalysis by eos\(^2\)...

---

Blood eosinophils in COPD & ICS: reducing risk

- FORWARD
  - Safety and efficacy of BDP/FORM vs FORM¹
  - Reduction in exacerbation rate in 3rd and 4th eosinophil quartile²

Blood eosinophils in COPD & ICS: reducing risk

- ISOLDE\(^1\)
  - Randomised, double-blind, parallel-group study with either fluticasone propionate 500µg twice daily (n=376) or placebo (n=375) for 3 years
  - No difference in primary outcome of rate of FEV1 decline (mL/year), until analysed by Eos\(^2\)

---

Withdrawal of Inhaled Glucocorticoids and Exacerbations of COPD

Helgo MagnusSEN, M.D., Bernd Disse, M.D., Ph.D., Roberto Rodriguez-RoIsin, M.D., Anne Kirsten, M.D., Henrik Watz, M.D., Kay Tetzlaff, M.D., Lesley Towse, B.Sc., Helen Finnigan, M.Sc., Ronald Dahl, M.D., Marc Decramer, M.D., Ph.D., Pascal Chanez, M.D., Ph.D., Emiel F.M. Wouters, M.D., Ph.D., and Peter M.A. Calverley, M.D., for the WISDOM Investigators®

<table>
<thead>
<tr>
<th></th>
<th>ICS (n=1243)</th>
<th>ICS withdrawal (n=1242)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, %</td>
<td>81.5</td>
<td>83.4</td>
</tr>
<tr>
<td>Mean (SD) age, years</td>
<td>63.6 (8.6)</td>
<td>64.0 (8.4)</td>
</tr>
<tr>
<td>Mean (SD) body mass index, kg/m²</td>
<td>25.3 (5.1)</td>
<td>25.2 (5.1)</td>
</tr>
<tr>
<td>Current smoker, %</td>
<td>34.8</td>
<td>32.1</td>
</tr>
<tr>
<td>Mean (SD) duration of COPD, years</td>
<td>7.8 (6.0)</td>
<td>8.0 (6.5)</td>
</tr>
<tr>
<td>Lung function</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD) post-dose screening FEV₁, L</td>
<td>0.93 (0.29)</td>
<td>0.94 (0.30)</td>
</tr>
<tr>
<td>FEV₁ 30–&lt;50% (GOLD 3), n (%)</td>
<td>760 (61.1)</td>
<td>761 (61.3)</td>
</tr>
<tr>
<td>FEV₁ &lt;30% (GOLD 4), n (%)</td>
<td>473 (38.1)</td>
<td>474 (38.2)</td>
</tr>
<tr>
<td>Mean (SD) baseline FEV₁, L*</td>
<td>0.97 (0.36)</td>
<td>0.98 (0.36)</td>
</tr>
</tbody>
</table>

*After 6-week run-in on triple therapy
Eosinophils and ICS

Is Blood Eosinophil Count A Predictor Of Disease Worsening After ICS Withdrawal?

H. Watz, H. Magnussen, K. Tetzlaff, L. Gronke, H. Finnigan, P.M. Calverley

*p<0.05; **p<0.01.
Watz et al., ATS 2016 Abstract 6944
WISDOM sub-analysis: ICS withdrawal only increased the exacerbation rate in patients with the combination of raised eosinophil counts and frequent exacerbations.
WISDOM sub-analysis: Only a small subset of clearly identifiable patients may benefit from adding ICS to LAMA/LABA

ICS may provide incremental benefit only in patients who meet 3 criteria:

1. Severe/very severe COPD
2. A history of ≥2 exacerbations/year
3. Blood eosinophil levels ≥300 cells/µL

This is only 7% of the entire WISDOM study population

2. Calverley PMA, et al. ERS 2016 oral presentation
Differential treatment effect by blood eosinophil counts: anti IL-5Rα in eosinophilic COPD

Using the blood eosinophil count to guide ICS treatment in COPD

• The blood eosinophil count as a biomarker in COPD:
  - Relevant and valid
    ▪ Easily accessible
    ▪ Repeatable
    ▪ Identifies risk
      o Type and frequency of exacerbations
      o Mortality
      o Infection
Using the blood eosinophil count to guide ICS treatment in COPD

The PBE:

• Predicts who can be taken off ICS (and who should not!)

• Predicts who should receive ICS
  - To reduce risk of exacerbation

• Predicts who will respond to new biological agents

PBE, Percentage blood eosinophils
Personal expert opinion Richard Russell
What about ACO?

• My view:
  - Truly try to diagnose asthma
  - Give steroids for a positive reason
  - Trial of treatment
  - Appropriate detailed testing

• Treatable trait approach will supersede labels
Choice

• Choice is good...
• 55-year-old man
• Ex-lorry driver
• Presented to GP with SOB
• Smoker 70 pack years
• GP worried by breathlessness and young age thus sent for specialist opinion
The CXR...What is abnormal?

A. Flat diaphragms
B. Hyperlucency
C. Consolidation
D. Cardiomegaly

Answers:
1. A,B,C,D
2. A,B
3. C
4. Normal CXR
What will his spirometry show?

1. Fixed airway obstruction
2. Extra-thoracic obstruction
3. Restriction
4. Reversible airway obstruction
Sex: male

Graph showing flow [l/s] against volume [l] with markers for F/V in and F/V ex.
<table>
<thead>
<tr>
<th></th>
<th>PredLL</th>
<th>PredUL</th>
<th>PRE</th>
<th>%Pred</th>
<th>POST</th>
<th>%Pred</th>
</tr>
</thead>
<tbody>
<tr>
<td>in</td>
<td>300</td>
<td>477</td>
<td>57</td>
<td>14.8</td>
<td>105</td>
<td>27.0</td>
</tr>
<tr>
<td>[1]</td>
<td>2.04</td>
<td>3.28</td>
<td>0.51</td>
<td>19.1</td>
<td>0.63</td>
<td>23.6</td>
</tr>
<tr>
<td>[1]</td>
<td>2.42</td>
<td>3.83</td>
<td>0.80</td>
<td>25.6</td>
<td>1.13</td>
<td>36.2</td>
</tr>
<tr>
<td>[%]</td>
<td>63.53</td>
<td>55.71</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>in</td>
<td>99</td>
<td>121</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>[1]</td>
<td>2.54</td>
<td>3.92</td>
<td>1.02</td>
<td>31.4</td>
<td>1.51</td>
<td>46.7</td>
</tr>
<tr>
<td>[1]</td>
<td>2.00</td>
<td>3.64</td>
<td>9.15</td>
<td>324.8</td>
<td>6.59</td>
<td>233.7</td>
</tr>
<tr>
<td>[1]</td>
<td>0.90</td>
<td>0.90</td>
<td>0.23</td>
<td>25.4</td>
<td>0.33</td>
<td>36.4</td>
</tr>
<tr>
<td>[1]</td>
<td>1.35</td>
<td>2.49</td>
<td>8.93</td>
<td>464.7</td>
<td>6.26</td>
<td>325.8</td>
</tr>
<tr>
<td>[1]</td>
<td>2.54</td>
<td>3.92</td>
<td>1.00</td>
<td>30.9</td>
<td>1.22</td>
<td>37.8</td>
</tr>
<tr>
<td>[1]</td>
<td>4.31</td>
<td>6.28</td>
<td>9.93</td>
<td>187.3</td>
<td>7.48</td>
<td>141.1</td>
</tr>
<tr>
<td>[%]</td>
<td>28.10</td>
<td>47.22</td>
<td>89.93</td>
<td>238.8</td>
<td>83.69</td>
<td>222.2</td>
</tr>
<tr>
<td>/[1]</td>
<td>0.62</td>
<td></td>
<td>0.45</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>/[1]</td>
<td>1.60</td>
<td></td>
<td>1.96</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>[s]</em></td>
<td>0.96</td>
<td>0.96</td>
<td>7.87</td>
<td>818.4</td>
<td>6.01</td>
<td>625.2</td>
</tr>
<tr>
<td><em>[s]</em></td>
<td>1.04</td>
<td>1.04</td>
<td>0.13</td>
<td>12.2</td>
<td>0.17</td>
<td>16.0</td>
</tr>
</tbody>
</table>
Diagnosis

• Severe emphysema
• Gas trapping
• Reversible hyperinflation
What are the treatment options?

1. Inhaled corticosteroids
2. Inhaled LABA
3. LAMA
4. LABA/LAMA combination
5. ICS/LABA
6. Lung volume reduction surgery
Management

- Check A1AT
- Eosinophil count
- Assess for LTOT
- Pulmonary rehabilitation
- Maximise therapy
  - LABA/LAMA
- Consider LVRS/bullectomy/single lung transplantation
Progress

• Low eosinophils:
  • Commenced on tiotropium/olodaterol therapy
  • Completed pulmonary rehabilitation
  • Maximised exercise tolerance

• Now runs Marathons!
How to treat COPD

• Diagnose early and stop smoking
• Bronchodilate to the maximum:
  - LAMA; LAMA/LABA
• Assess risk
  - Exacerbation
  - CVS
• Give inhaled steroids to the RIGHT patients (eos)
• Pulmonary rehabilitation for all
Thank you for listening
ARE YOU A SMOKER?
THIS IS THE AMOUNT OF TAR
IN YOUR LUNGS AFTER 3 YEARS