Methods: We examined the proportion of patients in each category when evaluated by CAT categories A, B, C, and D, patients were using a long-acting β₂-agonist and when evaluated by mMRC was 39, 20, 13 and 28%. By CAT evaluation in classification parameters were analyzed. The proportion of patients in categories A, B, C, and D, respectively, were using a long-acting β₂-agonist (LABA) alone (8, 6, 0 and 1%), long-acting muscarinic antagonist (LAMA) alone (37, 25, 8 and 5%), inhaled corticosteroid plus LABA (ICS/LABA) alone (22, 18, 9 and 8%), and ICS/LABA plus LAMA only (11, 20, 46, 43%).

Conclusion: CAT assessment increased the number of patients in the more symptomatic categories (B and D), compared with mMRC. Contrary to the GOLD 2011 Strategy classifies COPD patients into 4 categories (A: low risk, less symptoms; B: low risk, more symptoms; C: high risk, less symptoms; D: high risk, more symptoms) based on risk (FEV₁ < 50% predicted and/or exacerbation history < or ≥ 2 per year) and symptoms (CAT score < or ≥ 10 or moderate). The Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2011 criteria were applied to a real-world international COPD population sampled from the Adelphi Respiratory Disease Specific Programme undertaken June to September 2011. Physicians and patients completed matched questionnaires.

Results: 2392 patients completed a questionnaire, of which 1508 with all 4 GOLD classification parameters were analyzed. The proportion of patients in categories A, B, C, and D, respectively, were using a long-acting β₂-agonist (LABA) alone (8, 6, 0 and 1%), long-acting muscarinic antagonist (LAMA) alone (37, 25, 8 and 5%), inhaled corticosteroid plus LABA (ICS/LABA) alone (22, 18, 9 and 8%), and ICS/LABA plus LAMA only (11, 20, 46, 43%).

Conclusion: CAT assessment increased the number of patients in the more symptomatic categories (B and D), compared with mMRC. Contrary to the GOLD 2011 recommendations, by CAT assessment, a high proportion of low-risk patients (A and B) were using ICS/LABA.

P2877

Differential dropout may affect exacerbation risk estimates differently in moderate-to-very severe COPD

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Background: Differential withdrawal of patients from clinical trials (dropout) complicates interpretation of the effect of intervention on the exacerbation frequency in COPD studies. We examined the impact of differential dropout on exacerbations in moderate-to-very severe COPD (GOLD grades 2-4).

Methods: Patients in 3 pooled COPD studies¹,²,³ were randomised to budesonide/formoterol (B/F 320/9 μg bid) or placebo (P) via Turbuhaler. Exacerbations, dropouts and a composite of the two outcomes were examined over the first 3 months of treatment.

Results: 1583 COPD patients were studied (24% moderate; 61% severe, 14% very severe). B/F improved time to first exacerbation in moderate and severe but not very severe COPD (HRadj: 0.43 [95% CI 0.25–0.72]; 0.45 [0.33–0.63] and 0.58 [0.32–0.95]) vs. P. Time to dropout was improved by B/F vs. P, the differences being larger with increasing COPD severity (HRadj: 0.62 [0.34–1.11]; 0.56 [0.39–0.81] and 0.38 [0.18–0.80]). A composite measure of time to first exacerbation or dropout showed a significant effect of B/F in all severities.

Conclusions: Differential study dropout (greater with P than B/F) increased as the severity of COPD worsened. This should be considered when interpreting clinical COPD trial data.

References:
Effects of high dose N-acetylcysteine in COPD patients
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Aim: Studies suggest that NAC can reduce inflammation and hyperinflation in COPD patients, but little data is published about effects of high dose NAC (3x600mg daily) on airway remodeling. Since hdNAC may induce high levels of GSH, this study focuses on the effect of hdNAC on airway structure/function in relation to GSH.

Method: A double blind randomized placebo-controlled 2way crossover pilot study in 12 GOLDII patients was performed. Patients were treated twice for 3m with either hdNAC or placebo (provided by Zambon S.p.A.) on top of their usual treatment periods.

Result: A clear drop in iRaw is seen in patients with a higher anti-oxidant reserve (i.e. low baseline GPs) despite lack of overall improvement in the entire population. This drop in iRaw is observed in patients that were already treated according (i.e. low baseline GPx) despite lack of overall improvement in the entire population. The re sults demonstrate the potential of using RFI to assess anti-inflammatory characteristics of existing and newly developed compounds.

Introduction: Acute exacerbations of chronic obstructive pulmonary disease (AE-COPD) are frequent cause of hospital admission and associated to high risk of recurrence. Preventing exacerbations is a key treatment goal.

Objectives: To evaluate the effect of erdosteine, an anti-oxidant mucolytic agent, given on acute setting during hospitalization for severe AE-COPD to prevent subsequent recurrence of exacerbations.

Methods: 15 COPD patients hospitalized for severe AE-COPD randomly received erdosteine 900mg daily or placebo for 10 days in combination with standard treatment. Recurrence of exacerbations after hospital discharge was assessed at 30 and 60 days. Data were correlated to pulmonary function indices and serum C-reactive protein (CRP) measured at 10 and 30 days after hospitalization.

Results: Table 1. The mean exacerbation recurrence was significantly higher (p<0.05) in the placebo group. The recurrence of exacerbation was inversely correlated to FEF25–75% value at 10d (p<0.05), 30d (p<0.05) and positively correlated to serum CRP marker of systemic inflammation at 10d (p<0.05) and 30d (p<0.05).

Table 1

<table>
<thead>
<tr>
<th>Treatment</th>
<th>CRP, mg/100ml</th>
<th>FEF25–75%, mL/sec</th>
<th>No. exacerbations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endosteine</td>
<td>0.38 0.29</td>
<td>619 811</td>
<td>0 0.25*</td>
</tr>
<tr>
<td>Placebo</td>
<td>1.36 0.67</td>
<td>375 472</td>
<td>0 1.14</td>
</tr>
</tbody>
</table>

Data are mean values. *p<0.05 vs. placebo.

Conclusions: Treatment with erdosteine plus standard therapy in severe AE-COPD reduced their early recurrence after hospital discharge. These results were related to improvement in small airway obstruction and decrease of serum CRP at recovery from AE-COPD. Mucolytic agents with relevant antioxidant activity may improve clinical outcome after AE-COPD by reducing the burst of airway inflammation.
once daily for 4 weeks (NCT 01040403). The primary end point was trough FEV1 response (L) at the end of week 4.

Results: In total, 232 COPD patients (133 male: 99 female) received treatment FEV1, response trough and up to 6 h post-dose for 5 and 10 μg monotherapy were similar. For all doses of T, FEV1 responses were significantly increased when added to 5 and 10 μg. Dose ordering for T when added to O was evident. No safety or tolerability concerns were identified.

Conclusions: Addition of T to O resulted in significant improvements in FEV1 versus O alone. These data support further investigation of T 2.5 and 5 μg combined with O 5 μg in the Phase III Tyg0 clinical trial programme.

P2885
Anti-inflammatory effects of add-on atorvastatin therapy during the treatment of COPD patients

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Introduction: NVA237 (glycopyrronium bromide) is a safe and effective once daily (QD) inhaled long-acting muscarinic agonist for the maintenance treatment of COPD.

Methods: This is a pooled analysis of the GL(C)pyromyron bromide in COPD airWays clinical studies (GLOW1 and 2) which assessed the efficacy of NVA237 50μg QD vs placebo (PBO) and open-label tiotropium 18 μg QD (TIO) over 26 to 52 wks in COPD patients. Results include exacerbations, symptoms (transition dyspnea index (TDE)) and Health Status (St George’s Respiratory Questionnaire [SGRQ]).

Results: 1854 patients were analyzed (NVA237=1059, TIO=627, PBO=582). NVA237 significantly prolonged the time to first moderate/severe exacerbation vs PBO (Wk 26: hazard ratio [HR] 0.64; Wk 52: HR 0.67, both p<0.001), which was comparable to TIO (Wk 26: HR 0.70, p=0.026; Wk 52: HR 0.61, both p<0.001). NVA237 had a statistically significantly lower rate of moderate/severe exacerbations vs PBO (Wk 26: rate ratio [RR] 0.66; Wk 52: RR 0.66; both p<0.005), while TIO was not significantly different from PBO (Wk 26: RR 0.74, p=0.085 and Wk 52: RR 0.80, p=0.179). Treatment difference in TDI total score was significant for NVA237 (Wk 26: 0.93 and Wk 52: 0.57) and TIO (Wk 26: 1.05 and Wk 52: 066) vs PBO, all p<0.05. SGRQ score (LS Mean [SE]) was significant for NVA237 (Wk 52: -2.32 [1.04], p<0.001) and TIO (Wk 26: -2.43 [1.04] and Wk 52: -2.84 [1.155]; p<0.05) vs PBO.

Conclusion: NVA237 once daily significantly reduced COPD exacerbations and improved symptoms vs PBO over 52 wks. Overall, the effects of NVA237 were similar to tiotropium.

P2886
Cigarette smoke retention and bronchodilation in patients with COPD: A controlled randomized trial

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Many COPD patients use bronchodilators while continuing cigarette smoking. We hypothesized that these agents interact with cigarette smoking and hence affect the risk to develop smoking-related (cardiovascular) disease. In this study we explored if bronchodilation increases pulmonary retention of cigarette smoke and smoking-related biomarkers in patients with COPD.

Methods: We performed a double-blinded, placebo-controlled, randomized crossover trial. COPD patients smoked cigarettes during undiluted conditions at one session and maximal bronchodilated conditions at the other session. Cigarette smoke was measured by pulmonary proportional retention of tar and nicotine. Secondary outcomes included smoke inhalation patterns, and the biomarkers C-reactive protein and fibrinogen. We excluded measurements with possible contamination in a secondary analysis.

P2887
Once-daily NVA237 reduces exacerbations and improves symptoms in COPD patients: A pooled analysis of the GLOW1 and GLOW2 studies

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Introduction: NVA237 (glycopyrronium bromide) is a safe and effective once daily (QD) inhaled long-acting muscarinic agonist for the maintenance treatment of COPD.

Methods: This is a pooled analysis of the GL(C)pyromyron bromide in COPD airWays clinical studies (GLOW1 and 2) which assessed the efficacy of NVA237 50μg QD vs placebo (PBO) and open-label tiotropium 18 μg QD (TIO) over 26 to 52 wks in COPD patients. Results include exacerbations, symptoms (transition dyspnea index (TDE)) and Health Status (St George’s Respiratory Questionnaire [SGRQ]).

Results: 1854 patients were analyzed (NVA237=1059, TIO=627, PBO=582). NVA237 significantly prolonged the time to first moderate/severe exacerbation vs PBO (Wk 26: hazard ratio [HR] 0.64; Wk 52: HR 0.67, both p<0.001), which was comparable to TIO (Wk 26: HR 0.70, p=0.026; Wk 52: HR 0.61, both p<0.001). NVA237 had a statistically significantly lower rate of moderate/severe exacerbations vs PBO (Wk 26: rate ratio [RR] 0.66; Wk 52: RR 0.66; both p<0.005), while TIO was not significantly different from PBO (Wk 26: RR 0.74, p=0.085 and Wk 52: RR 0.80, p=0.179). Treatment difference in TDI total score was significant for NVA237 (Wk 26: 0.93 and Wk 52: 0.57) and TIO (Wk 26: 1.05 and Wk 52: 066) vs PBO, all p<0.05. SGRQ score (LS Mean [SE]) was significant for NVA237 (Wk 52: -2.32 [1.04], p<0.001) and TIO (Wk 26: -2.43 [1.04] and Wk 52: -2.84 [1.155]; p<0.05) vs PBO.

Conclusion: NVA237 once daily significantly reduced COPD exacerbations and improved symptoms vs PBO over 52 wks. Overall, the effects of NVA237 were similar to tiotropium.

P2888
An audit of oxygen prescribing practices in a district general hospital

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Introduction: Oxygen is a drug and should be prescribed. Yet the attitudes about oxygen prescription are extremely different to that of other prescription only medications. We wished to evaluate that a) correct prescription was filled out for patients receiving oxygen in hospital and b) patients with COPD oxygen saturation (SpO2) was maintained at 88-92% (1).

Methods: On a single day in January 2012 all patients on 14 wards (medical and surgical) were observed for supplemental oxygen therapy. All patients receiving oxygen therapy had their prescription charts and clinical notes assessed for quality of the oxygen prescription and presence of COPD.

Results: Out of a total of 250 patients seen, 51 (19.6%) were on oxygen. Of these 21 (41%) patients had the oxygen prescribed correctly. Seventeen patients were diagnosed to have COPD; in 6 (46%) the actual bedside oxygen saturations matched the correct safe target set by BTS guideline, but in only 3 (23%) the target oxygen saturations was correctly specified.

Conclusions: This audit highlights significant gaps in oxygen prescribing in secondary care. Almost half of COPD patients receiving supplemental oxygen remain at risk of oxygen toxicity. Education of doctors and nurses on oxygen prescription should be reinforced regularly.

Reference:
Results: In 35 patients analyzed, bronchodilation did not significantly increase 
tar retention (-4.5%, p=0.20), or nicotine retention (-2.6%, p=0.11). 
Bronchodilation did not significantly affect our secondary outcomes. Secondary 
analysis revealed a potentially less retention due to bronchodilation: tar retention 
-3.8% (p=0.13), and nicotine retention -3.4% (p=0.01).

Conclusions: Our results do not support the hypothesis that bronchodilation in 
cigarette tar and nicotine retention in COPD patients. Instead, we observed a 
possibility for less retention.

P2887

Lung function effects and safety of fluticasone furoate (FF)/vilanterol (VI) in 
patients with COPD: Mid-high dose assessment

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Research, Union, United States; 3Clinical Research, S. Carolina Pharmaceutical 
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Rationale: FF/VI is a novel once-daily (OD) inhaled corticosteroid/long-acting 
beta2 agonist in development as combination therapy for COPD.

Objective: To evaluate the efficacy and safety of FF/VI (200/25 and 100/25) vs 
PBO, FF (200 and 100mcg) and VI (25mcg), given OD via novel dry powder 
hailer in moderate-severe COPD patients for 168 days.

Methods: A multicentre, randomised, PBO-controlled, double-blind, parallel-
group study (N=1224 (ITT)). Co-primary endpoints: weighted mean (wm) FEV1 
0–4h (Day 168) to assess the contribution of VI, and trough FEV1, (Day 169) 
to assess the contribution of FF and 24h duration of VI. Additional endpoints 
included CRQ-SAS dyspnea, and safety.

Results: Co-primary endpoints, see Figure. Treatment differences from PBO 
dyspnea scores were -0.12, -0.01, 0.07, 0.24 and 0.10 for FF 100, 200, VI 25, 
FF/VI 100/25, 200/25, respectively. On-treatment AEs were similar between active 
treatment groups (38–47%) and PBO (47%). No treatment effects on 24h urinary 
cortisol, laboratory values, or cardiac monitoring parameters were seen.

Conclusions: Addition of FF to VI reduced the annual rate of MSE and time to 	onest of 1st MSE, with evidence of a consistent effect of the 100/25mcg strength 
in individual studies and the pooled analysis. Lung function improved at all strengths 
of FF/VI vs VI in pooled analysis. The safety of the combination is reported 
separately.

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P2889

Efficacy of combination fluticasone furoate/vilanterol (FF/VI) and 
salmeterol/fluticasone propionate (SFC) over 12 weeks in patients with COPD

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Kingdom; 6Medicine, McGill University Health Centre, Montreal, QC, Canada

Introduction: The novel combination of FF, an inhaled corticosteroid and VI, a 
long-acting beta2 agonist, is under development as a once-daily (OD) therapy for 
COPD and asthma.

Objectives: To compare the efficacy of OD FF/VI and twice-daily (BD) SFC in 
moderate-to-severe COPD.

Methods: In a randomised, double-blind, double-dummy, parallel-group study, 
COPD patients (mean post-bronchodilator (predicted FEV1, = 43%) received 
FF/VI 100/25mcg OD AM (N=266) via a novel dry powder inhaler or SFC 
50/500mcg BD (N=262) via DISKUSTM. Primary efficacy: change from baseline 
to 24h weighted mean (wm) FEV1. Secondary endpoints included time to 
treatment failure (TF) via FEV1 assessment on Day 1 (speed of onsets, SGRQ-C, 
safety endpoints included adverse events (AEs)).

Results: There were no significant trends favouring FF/VI (130mL) versus SFC 
(110mL) for wmFEV1 (22mL [95%CI: –18,63], p=0.282) and speed of onset; 
FF/VI=161mL, SFC=28min (p=0.280). A clinically meaningful improvement 
(4.8) in SGRQ-C score was seen with FF/VI, but not SFC (–3.3), though the 
difference (–1.5 [95%CI: –3.9, 0.9]) was not statistically significant (p=0.215).
Both treatments were well tolerated. 3 (1%) and 6 (2%) patients in the FF/VI and 
SFC arms experienced serious AEs; the same numbers withdrew as a result of 
on-treatment AEs. Safety profiles, including pulse rate, were similar.

Conclusions: OD FF/VI and BD SFC improved lung function in patients with 
moderate-to-severe COPD without substantial safety concerns. Primary and sec-
Introduction: Aclidinium is a novel, long-acting muscarinic antagonist being investigated for maintenance treatment of COPD. Pooled analyses of lung function data from the ACCORD and ATTAIN trials are presented here.

Methods: Patients (N=1389) were randomized to aclidinium 200 μg, 400 μg, or pbo BID for 12- and 24-weeks for ACCORD and ATTAIN, respectively. Endpoints included change from baseline in FEV1 over 3h postdose on Day 1 as well as trough and peak FEV1 at Week 12.

Results: Mean (SD) baseline and % predicted FEV1 were 1.4±0.52L and 400 μg (13.2%) respectively. Significant improvements in lung function were seen following the first dose, as measured by change from baseline in FEV1 at 0.5h postdose (first time point assessed) on Day 1 (200 μg, 99 mL; 400 μg, 128 mL; both p<0.0001 vs pbo). The lung function improvements seen after the first dose were sustained throughout the study. Both doses resulted in statistically significant improvements from baseline to Week 12 in trough FEV1; a greater improvement and a clinically significant effect in trough FEV1, was seen with the higher dose (200 μg, 80 mL; 400 μg, 112 mL; both p<0.0001 vs pbo). Mean change from baseline to Week 12 in peak FEV1 was 167 mL and 191 mL for 200 μg and 400 μg respectively (both p<0.0001 vs pbo), with numerically greater improvements in the 400 μg vs 200 μg dose at all measured time points from 0.5h to 3h postdose.

Conclusions: Both doses of aclidinium produced significant improvements in lung function in COPD patients, with the 400 μg dose being consistently more effective. Maximal improvements in lung function were seen at Day 1 and were maintained over 12 weeks.

P2892

Twice-daily aclidinium bromide in COPD patients: A pooled analysis of lung function in the ACCORD-COPD I and ATTAIN trials

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Introduction: Aclidinium is a novel, long-acting muscarinic antagonist being investigated for maintenance treatment of COPD. Pooled analyses of lung function data from the ACCORD and ATTAIN trials are presented here.

Methods: Patients (N=1389) were randomized to aclidinium 200 μg, 400 μg, or pbo BID for 12- and 24-weeks for ACCORD and ATTAIN, respectively. Endpoints included change from baseline in FEV1 over 3h postdose on Day 1 as well as trough and peak FEV1 at Week 12.

Results: Mean (SD) baseline and % predicted FEV1 were 1.4±0.52L and 400 μg (13.2%) respectively. Significant improvements in lung function were seen following the first dose, as measured by change from baseline in FEV1 at 0.5h postdose (first time point assessed) on Day 1 (200 μg, 99 mL; 400 μg, 128 mL; both p<0.0001 vs pbo). The lung function improvements seen after the first dose were sustained throughout the study. Both doses resulted in statistically significant improvements from baseline to Week 12 in trough FEV1; a greater improvement and a clinically significant effect in trough FEV1, was seen with the higher dose (200 μg, 80 mL; 400 μg, 112 mL; both p<0.0001 vs pbo). Mean change from baseline to Week 12 in peak FEV1 was 167 mL and 191 mL for 200 μg and 400 μg respectively (both p<0.0001 vs pbo), with numerically greater improvements in the 400 μg vs 200 μg dose at all measured time points from 0.5h to 3h postdose.

Conclusions: Both doses of aclidinium produced significant improvements in lung function in COPD patients, with the 400 μg dose being consistently more effective. Maximal improvements in lung function were seen at Day 1 and were maintained over 12 weeks.

P2893

Long-term efficacy of twice-daily aclidinium bromide in COPD patients: A one-year study

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Introduction: Aclidinium bromide is a long-acting muscarinic antagonist currently under investigation for the long-term maintenance treatment of COPD. In this study, the long-term efficacy and safety of twice-daily (BID) aclidinium 200 μg and 400 μg in moderate-to-severe COPD patients were assessed. The efficacy results are reported here.

Methods: Patients were randomized (1:1) to receive aclidinium 200 μg or 400 μg BID in a double-blind manner. The primary endpoint was change from baseline to Week 52 in trough FEV1. Other efficacy parameters included change from baseline to Week 52 in peak FEV1, trough and peak FEV1, by study visit, normal-
ized FEV₁, AUC₀₋₃, and change from baseline to Week 52 in SGRQ and EuroQoL scores.

**Results:** A total of 605 patients were randomized to this study. Both aclidinium 200 μg and 400 μg BID resulted in improvements from baseline to Week 52 in trough and peak FEV₁ (Table), with numerically larger increases seen with the 400 μg dose. At study end, change from baseline in normalized AUC₀₋₃ FEV₁ was also improved for both groups, with greater improvements seen with the higher aclidinium dose (Table). Both treatment groups showed clinically significant improvements in SGRQ Total score and improvements in EuroQoL parameters from baseline to Week 52 (Table).

**Conclusions:** Treatment with aclidinium 200 μg or 400 μg BID results in benefits in lung function and health status in COPD patients over 1 year.