P860 Efficacy of indacaterol in COPD is maintained irrespective of inhaled corticosteroid (ICS) use

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Introduction: Indacaterol is a once-daily inhaled β2-agonist bronchodilator for COPD.

Aim: Pooled analysis to determine if efficacy of indacaterol was maintained in subgroups of COPD patients (pts) receiving ICS or not.

Methods: Data from 4088 pts with moderate-to-severe COPD in 3 randomized, double-blind, placebo-controlled studies of indacaterol 150 and 300 µg od, tiotropium 18 µg od (open-label), formoterol 12 µg bid & salmeterol 50 µg bid were pooled: 44% of pts had baseline ICS use, 56% no ICS use. Endpoints at 6 months: trough FEV1, transition dyspnoea index (TDI) and St George’s Respiratory Questionnaire (SGRQ) total scores. The % of pts with clinically important difference in TDI and SGRQ were analysed as odds ratios (OR).

Results: Differences vs placebo (n=661 not on ICS, 524 on ICS) (⁎p<0.05, †⁎⁎⁎p<0.001, †††⁎⁎⁎p<0.0001) in pts not on ICS (“no”) or on ICS (“ICS”) (‡p<0.05 vs tiotropium, §p<0.05 vs formoterol, ¶p<0.05 vs salmeterol, †p<0.05 vs indacaterol 150 µg).

<table>
<thead>
<tr>
<th></th>
<th>Indacaterol 150 µg</th>
<th>Indacaterol 300 µg</th>
<th>Tiotropium 18 µg od</th>
<th>Formoterol 12 µg bid</th>
<th>Salmeterol 50 µg bid</th>
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<td>308</td>
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<tr>
<td>Trough FEV1 (mL)</td>
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<td>130***</td>
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<tr>
<td>TDI score</td>
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<td>1.2***</td>
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<td>0.9†</td>
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<td>1.0***</td>
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<tr>
<td>SGRQ OR</td>
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<td>1.85***</td>
<td>1.41</td>
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Conclusions: Indacaterol improved FEV1, & clinical outcomes after 6 mo irrespective of COPD severity. Indacaterol 300 µg was notably effective for breathlessness in the more severe subgroup.

P862 The efficacy of the assistant use of short-acting β2 stimulant procaterol on the daily activity in COPD patients. Niigata multicenter study

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Background and purpose: COPD patients have some dyspnoea on exertion in spite of medication. Guidelines suggest the use of short-acting β2 antagonist (SABA) as necessary. There are few reports to see whether the supplementary use of SABA inhalation improves their physical activity, ADL and QoL in the daily life. We evaluated the efficacy and safety of assistant use of procaterol inhalation.

Methods: COPD patients were enrolled and asked to keep as active as possible. Physical activities were measured by the uni-axial accelerometer. COPD patients were divided into two groups. One was the group as controls (Group C) and the other group was the assistant use of SABA (Group A).

Results: Differences vs placebo (n=675 “mod”, n=509 “sev”) (⁎p<0.05, †⁎⁎⁎p<0.001, †††⁎⁎⁎p<0.0001) in subgroups with “mod” and “sev” COPD severity. (p<0.05 vs TIO, †p<0.05 vs formoterol, ‡p<0.05 vs SABA, §p<0.05 vs indacaterol 150 µg).

<table>
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<tr>
<th></th>
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<td>Trough FEV1 (mL)</td>
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<td>140**</td>
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<td>120**</td>
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<td>TDI score</td>
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<td>SGRQ OR</td>
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<td>1.91***</td>
<td>1.72</td>
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Conclusions: Indacaterol improved FEV1, & clinical outcomes after 6 months in patients not receiving ICS and those on ICS.
Thematic Poster Session

P685

Efficacy and safety of nebulized glycopyrrolate (EP-101) for administration using high efficiency nebulizer in patients with COPD

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Introduction: EP-101 is a long-acting muscarinic antagonist formulation of glycopyrrolate optimized for nebulization in development for the treatment of COPD. To date dose-ranging study assessed the efficacy and safety of single doses of nebulized EP-101 in patients with COPD.

Methods: This was a randomized, double-blind, placebo-controlled, 6-period cross-over study in 42 patients with moderate-to-severe COPD. Patients were randomized to receive single doses of EP-101 (12.5, 50, 100, 200 and 400 μg) and placebo via a high efficiency nebulizer, with a 5-12 days of washout between treatments. Plasma PK was assessed in a subset of patients.

Results: The study patients had a mean age of 62 years. COPD duration of 7.5 years, post-bronchodilator FEV1 of 54% predicted normal, FEV1/FVC of 44.9%, FEV1 reversibility of 27.3%. All treatments were well tolerated with similar AE rates between all treatments and no clinically relevant changes in vital signs (heart rate, systolic and diastolic blood pressure) and ECG parameters including QTc interval. Following treatment with EP-101 at all doses there was a rapid bronchodilatory response at 5 minutes. Statistically significant improvements in mean change in trough FEV1 at 24 hours were reported at doses ≥50 μg compared with placebo (37 mL, 72mL, 104mL, 118mL and 95mL at doses 12.5, 50, 100, 200 and 400 μg respectively).

Conclusion: Single doses of EP-101 ranging from 12.5 μg to 400 μg were well tolerated. EP-101 demonstrated rapid onset of bronchodilatation with clinically meaningful improvements in lung function over 24 hours following nebulization in these patients with COPD.

Funded by Elevation Pharmaceuticals Inc.

P686

NVA237 once daily provides rapid, clinically meaningful and sustained 24-h bronchodilatation in patients with COPD: The GLOW1 trial

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Introduction: NVA237 (glycopyrronium bromide) is a once-daily (QD) inhaled long-acting muscarinic antagonist in development for the treatment of COPD.

Methods: Patients with moderate-to-severe COPD were randomized (2:1) to double-blind NVA237 50 μg QD or placebo (PBO) for 26 wks. Study medication was administered via a low-resistance single-dose dry powder inhaler (Concept1 device). The primary efficacy endpoint was trough FEV1 (mean of 23 h 15 min and 23 h 45 min post-dose values) vs PBO after 12 wks.

Results: A total of 822 patients were randomized; 80.5% completed the study. Mean age was 63.9 yrs, mean post-bronchodilator FEV1 was 55% predicted. At Wk 12 there was a statistically significant and clinically relevant difference between NVA237 vs PBO mean change in trough FEV1 (108 mL; p<0.001). Trough FEV1 was also significantly higher at Day 1 and Wk 26 (treatment difference: 105 mL and 113 mL, respectively; p<0.001). At all time points on Day 1, Wk 12 and Wk 26, NVA237 demonstrated statistically superior (p<0.001) and clinically meaningful improvement in FEV1 compared with PBO. NVA237 had a rapid onset of action with an increased FEV1 of 93 mL at 5 min and 144 mL at 15 min vs PBO after the first dose on Day 1 (p<0.001). The incidence of adverse events (AEs) was similar between NVA237 and PBO (57.5% vs 65.2%, respectively). Serious AEs were reported by 7.5% of NVA237- vs 9.0% of PBO-treated patients.

Conclusion: NVA237 50 μg once daily was safe and well tolerated, and produced clinically meaningful bronchodilatation that was rapid in onset and maintained for 24 hrs throughout the study.

P867

NVA237 once daily improves dyspnea and health-related quality of life (HRQoL) in patients with COPD: The GLOW1 trial

J.A. van Noord1, K. Hirata2, A. Fururo3,4, C. Martin5, K. Horton6, Y. Lu7, T. Overend4. 1Respiratory Medicine, Artium Medisch Centrum, Heerlen, Netherlands; 2Respiratory Medicine, Osaka City University, Abeno-ku, Osaka, Japan; 3Department of Emergency Medicine, University of Brown, ON, Canada; 4Respiratory Medicine, Novartis Horsham Research Centre, Horsham, West Sussex, United Kingdom; 5Respiratory Medicine, Novartis Pharmaceuticals Corporation, East Hanover, NJ, United States

Introduction: A high level of unmet need exists in the treatment of COPD patients. NVA237 (glycopyrronium bromide) is a once-daily (QD) long-acting muscarinic antagonist in development for the treatment of COPD.

Methods: Patients with moderate-to-severe COPD were randomized (2:1) to 26

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Abstract printing supported by Chiesi. Visit Chiesi at Stand D.30
Exceeding the minimum clinically important difference (MCID) β Efficacy and safety of AZD3199, an inhaled ultra long-acting vs PBO (56.3% vs 46.0%; p=0.006). Improvement in SGRQ (p=0.005). SGRQ total score was significantly reduced with NV A237 vs PBO post-dose FEV1 values from 0–4 hrs (E0-4, peak) and FEV1 values from 24–26 hrs (E24-26, trough). Use of Tiotropium Respimat® is a newly developed device which delivered the drug with patients with COPD Pulmonology, Medical University Pleven, Pleven, Bulgaria; 3Department of Healthcare Unit, Barlicki University Hospital, Lodz, Poland; 4Dept of Pulmonary, Medical University Pleven, Pleven, Bulgaria; 1Department of Hospital Therapy, Pavlov State Medical University, St. Petersburg, Russian Federation; 2Research and Development, AstraZeneca R&D, Lund, Sweden; 3Centre de Pneumologiu, Institutu Universitario de Cardiología et de Pneumologiu de Quebec, Quebec, Canada

Objective: To study the efficacy and safety of three once-daily doses of AZD3199 inhaled via Turbuhaler compared with twice-daily formoterol and placebo over 4 weeks in COPD patients.

Methods: This was a 4-week randomised, double-blind, parallel-group multicentre Phase II study to compare once-daily inhaled doses of AZD3199 (200, 400 and 800 µg delivered) with formoterol (9 µg bid) and placebo in 329 adults with moderate/severe COPD (NCT00970098). Bronchodilation was assessed by average post-dose FEV1, values from 0–4 hrs (E0-4, peak) and FEV1; values from 24–26 hrs (E24-26, trough). Use of β2-agonist releiver medication, salbutamol reversibility, symptom scores (CCQ) and safety were also assessed.

Results: AZD3199 bid was superior to placebo for FEV1; p<0.001 and symptom score in stable COPD patients. AZD3199 did not impact on the acute bronchodilating effect of salbutamol. All AZD3199 groups showed a reduction in symptom scores with the 800 µg dose reaching significance vs. formoterol and placebo. AZD3199 was well tolerated with no safety concerns.

Conclusions: AZD3199 is a safe and effective uLABA with a 24-hour duration of action.

P668 Efficacy and safety of AZD3199, an inhaled ultra-long acting β2-agonist, in patients with COPD

Piotr Kuna1, Yavor Ivanov2, Vasily Trofimov3, Ola Beckman4, Thomas Bengtsson5, Carin Jorup6, Francois Malais3; 1Autonomous Public Healthcare Unit, Barlicki University Hospital, Lodz, Poland; 2Dept of Pulmonology, Medical University Pleven, Pleven, Bulgaria; 3Department of Hospital Therapy, Pavlov State Medical University, St. Petersburg, Russian Federation; 4Research and Development, AstraZeneca R&D, Lund, Sweden; 5Centre de Pneumologiu, Institutu Universitario de Cardiología et de Pneumologiu de Quebec, Quebec, Canada

Influence of tiotropium bromide on airway inflammation and symptom in COPD patients

Guoy Gao1, Harun Karaman1, Recep Akgedik1, Sema Uysal2, Ramazan Yigitoglu3, Zeki Yildirim1; 1Department of Pulmonology, 2Department of Biochemistry, Faith University Faculty of Medicine, Ankara, Turkey

Aim: Chronic obstructive pulmonary disease (COPD) is characterized by abnormal inflammatory response of lungs to noxious particles or gases. The aim of this study is to analyze effect of tiotropium bromide treatment on airway inflammation and symptom in stable COPD patients.

Methods: Tiotropium bromide treatment with 18 mgq daily dose, was started in newly diagnosed, consecutive mild–moderate stable COPD patients. Peroxynitrite, interleukin-6 (IL-6), 8-isoprostane and tumour necrosis factor alpha (TNF-α) were measured in the expired breath condensate fluid before the treatment and at the end of first month. Each symptom (cough, sputum production and dyspnea) was evaluated on a 4-point scale by the patients.

Results: Twenty-two patients (81% men), with a mean age 65.4±10.1 years were included in the study. The mean nitrotyrosine and 8-isoprostane levels for oxidative stress marker in EBC before and after treatment were 4.5±2.3, 3.5±1.9 pg/ml (p=0.06) and 7.3±10.8, 8.1±11.7 pg/ml (p=0.36) respectively. Peak expiratory flow was significantly improved after changed the device (4.5±3.03 to 4.77±0.28,p=0.004).

Conclusion: Tiotropium Respimat® was a simple and comfortable device and it may improve the pulmonary function for the patients with COPD.

P870 Influence of tiotropium bromide on airway inflammation and symptom in COPD patients

Duygu Grol1, Harun Karaman1, Recep Akgedik1, Sema Uysal2, Ramazan Yigitoglu3, Zeki Yildirim1; 1Department of Pulmonology, 2Department of Biochemistry, Faith University Faculty of Medicine, Ankara, Turkey

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Conclusion: Tiotropium Respimat® was a simple and comfortable device and it may improve the pulmonary function for the patients with COPD.

P871 The impact of tiotropium on mortality when added to inhaled corticosteroids and long-acting beta agonist therapy in COPD

Philip Short1, Douglas Elder2, Peter Williamson1, Samuel Lipworth1, Stuart Schembri1, Brian Lipworth1; 1Asthma and Allergy Research Group, University of Dundee, Dundee, United Kingdom; 2Department of Clinical Pharmacology, University of Dundee, Dundee, United Kingdom; 3Bute Medical School, University of St Andrews, St. Andrews, United Kingdom; 4Department of Respiratory Medicine, Perth Royal Infanry, Perth, United Kingdom

Background and objectives: Tiotropium (TIO) has been shown to improve lung function, quality of life and reduce mortality and exacerbations in COPD. However, it remains unclear whether such benefits are seen when TIO is used in conjunction with inhaled corticosteroid (ICS) plus long acting beta-2 agonists (LABA).

Methods: Retrospective Cohort study using linked NHS databases on hospital admissions, COPD outcomes, prescribing and mortality. Cox proportional hazard regression analysis was used to assess the addition of TIO to ICS+LABA on mortality and exacerbations. History of respiratory and cardiovascular disease, Sex, Age and smoking history were used as covariates. We observed lung function in each group over the study period.

Results: 3044 COPD patients were included in the study. 2082 patients were prescribed ICS+LABA+Tio and 922 were prescribed ICS+LABA. Mean follow up 4.65 years. Mean age 68.5 years. 1035 patients died during the study. The adjusted hazard ratio for all-cause mortality for ICS+LABA+Tio vs ICS+LABA was 0.67 (95% CI 0.58-0.76) p<0.001. Adjusted hazard ratios for respiratory hospital admissions and oral corticosteroid use were 0.86 (95% CI 0.74-0.99) p=0.043 and 0.72 (95% CI 0.65-0.81) p<0.001. In the ICS+LABA group (mean FEV1% pred 66.8%), mean first and last FEV1 and FVC (L) were 1.56 ±1.37 and 2.64 ±2.72. In the ICS+LABA+Tio group, (mean FEV1% pred 51.6%), mean first and last FEV1 and FVC (L) were 1.24 ±1.20 and 2.47 ±2.50.

Conclusion: There were no significant changes for inflammatory and oxidative stress markers in expired breath condensate fluid after a tiotropium treatment of one month, but tiotropium treatment helps to control symptoms in COPD with an increase in FEV1.
Conclusions: We have shown that the addition of TIO to ICS+LABA reduces all-cause mortality in our COPD population. Reductions in COPD exacerbations and oral steroid use reaffirm findings of previous studies.

P872 Assessments of protective effects of tiotropium bromide against methacholine- and neurokinin A-induced bronchoconstriction in patients with asthma

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1Respiratory Medicine, Ghent University Hospital, Ghent, Belgium; 2Respiratory Medicine, CHU Sart Tilman, Liége, Belgium

Rationale: Previous studies using short-acting anticholinergics have suggested a possible protective effect on bronchoconstriction induced by the sensory neuropeptide neurokinin A (NKA).

Aim: To assess the effect of tiotropium bromide, a long-acting anticholinergic agent, on NKA-induced bronchoconstriction.

Methods: Patients with asthma were investigated in asthmatic patients after 20 days of treatment with tiotropium bromide (18 μg/god) or placebo. PC20 was expressed in log2 doubling concentrations (DC). Values were reported as median with 25th-75th percentiles. Paired comparisons of the log2 PC20 values at screening and at the end of active and placebo treatments were performed.

Results: 16 patients with asthma (9 male; age: 14 (13-63) years) were included. PC20 NKA was 0.18 (0.06 - 0.29) μmol/ml at screening, 0.34 (0.09 - 3.34) μmol/ml after placebo, and 0.77 (0.08 - 3.34) μmol/ml after tiotropium bromide. Differences in baseline and screening log2PC20 were 0.4 (0.4 - 3.2) DC for NKA (p = 0.06) and 7.6 (4.8 – 9.0) DC for methacholine (p < 0.0001). Differences between placebo treatment and screening for log2PC20 NKA and log2PC20 methacholine were not observed.

Conclusions: Inhaled tiotropium bromide protects against methacholine-induced bronchoconstriction, but not against bronchoconstriction induced by NKA, suggesting that cholinergic mechanisms are not involved in the contractile effects of NKA in patients with asthma.

P873 ACCORD COPD I: Improvements in nighttime symptoms and rescue medication use in COPD with twice-daily aclidinium bromide

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Introduction: Nighttime symptoms in COPD patients can reduce quality of life. In this Phase III study, nighttime symptoms and rescue medication use were assessed for twice-daily (BID) treatment with aclidinium bromide, a long-acting muscarinic antagonist in development for COPD.

Methods: In this 12-week, double-blind study, COPD patients (FEV1/FVC <70%) were randomised (1:1) to aclidinium 200 μg, 400 μg, or placebo. Nighttime symptoms were recorded daily using electronic diaries via a COPD Nighttime Symptom Diary (TDI) and assessed during twice-daily treatment with aclidinium bromide, a long-acting muscarinic antagonist in development for COPD.

Results: Of 561 randomised patients, 467 completed the study. At Week 12, aclidinium 200 μg and 400 μg reduced night-time symptom scores vs placebo (p = 0.005 and p = 0.005, respectively). Both aclidinium doses reduced severity and impact of night-time breathlessness and cough on morning activities vs placebo (p = 0.01 and p = 0.05, respectively). Severity of early morning breathlessness and activity restriction due to breathlessness were reduced with aclidinium 200 μg (p = 0.01) and 400 μg (p < 0.001) vs placebo. Compared to placebo, 24-h sputum production was significantly reduced with the 200 μg (p = 0.05) and 400 μg (p = 0.001) doses at Week 12 but not sputum production during sleep. Aclidinium 400 μg improved the severity and impact of breathing symptoms on sleep vs placebo at 12 weeks (p < 0.01). Both aclidinium doses reduced total daily rescue medication use vs placebo (p = 0.001 for both).

Conclusions: Aclidinium 200 μg and 400 μg BID significantly reduced night-time/early morning symptoms and daily rescue medication use.

P874 Improvement in symptoms and rescue medication use with aclidinium bromide in patients with chronic obstructive pulmonary disease: Results from ACCORD COPD II

Alvar Agustí1, Paul W. Jones2, Eric Bateman3, David Singh4, Rosa Lamarca5, Gonzalo de Miguel6, Cynthia Caracta7, Esther García Gil5
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Introduction: The ACCORD COPD II study investigated the efficacy and safety of two twice-daily doses of aclidinium bromide, a long-acting muscarinic antagonist, in patients with moderate to severe chronic obstructive pulmonary disease (COPD).

Methods: In this 24-week, double-blind trial, 828 patients were randomised (1:1:1) to twice-daily aclidinium (200 μg or 400 μg) or placebo. COPD symptoms were assessed using the Transition Dyspnoea Index (TDI) patient-reported, electronic diaries and Total Exact score. Relief medication use was also assessed.

Results: Baseline characteristics were similar between the groups; FEV1% predicted 56.8±12.8%, FVC 66.4±9.2%. One patient treated with aclidinium 200 μg or 400 μg had a clinically meaningful improvement in TDI focal score (≥2 units) vs placebo at Week 24 (53.3% and 56.9% vs 45.5%; p=0.032 and 0.004, respectively). Aclidinium dose-dependently improved TDI focal score at Week 24, with clinical meaningfulness for aclidinium 400 μg (1.0 unit) and statistically significant for both doses vs placebo (200 μg, p<0.05; 400 μg, p<0.001). Over the study period, aclidinium (both doses) was associated with a lower incidence of night-time (p<0.0001) and early-morning (p<0.0001) COPD symptoms, a greater reduction in Total Exact score (p<0.0001) and more days without reliever medication (p=0.0003) vs placebo.

Conclusions: Aclidinium 200 μg and 400 μg twice-daily provided statistically significant and clinically meaningful improvements in COPD symptoms in patients with moderate to severe COPD.

This study was supported by Almirall S.A., Barcelona, Spain, and Forest Laborato- ries, Inc, New York, USA.

P875 The ATTAIN study: Bronchodilatory effect of aclidinium bromide in chronic obstructive pulmonary disease (COPD)

David Singh1, Eric D. Bateman2, Paul W. Jones3, Alvar Agustí4, Rosa Lamarca5, Gonzalo de Miguel6, Cynthia Caracta7, Esther García Gil5
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Clinical Development, Forest Research Institute, NJ, United States

Introduction: Aclidinium bromide is a long-acting muscarinic antagonist in clinical development for the treatment of COPD.

Aim: To assess the bronchodilatory effect of aclidinium 200 μg and 400 μg in patients with COPD.

Methods: In this 24-week, double-blind, Phase III study (NCT01001494), patients were randomised to aclidinium 200 μg, 400 μg or placebo BID. The primary endpoint was change from baseline in trough FEV1 at Week 24. Other endpoints included: trough response over time; change from baseline in peak FEV1; time to peak FEV1; and normalised AUCtrough FEV1.

Results: A total of 828 patients were randomised and 737 (89.0%) patients completed the study. Aclidinium 200 μg and 400 μg significantly improved trough FEV1 vs placebo; these improvements were maintained throughout the 6-month treatment period. At Week 24, increases in trough FEV1, from baseline vs placebo for aclidinium 200 μg and 400 μg were 99 mL and 128 mL, respectively (both p<0.0001). Aclidinium 200 μg and 400 μg increased peak FEV1 vs placebo (185 mL and 111 mL to aclidinium; both p<0.0001). Time to peak FEV1 was <2 h post-dose (aclidinium 200 μg, 108 min; aclidinium 400 μg, 100 min). Aclidinium 200 μg and 400 μg significantly improved normalised AUCtrough FEV1 vs placebo at Week 24 (183 mL and 210 mL, respectively, both p<0.0001).

Conclusions: Aclidinium 200 μg and 400 μg twice-daily significantly improved bronchodilation in patients with moderate to severe COPD.

This study was supported by Almirall S.A., Barcelona, Spain, and Forest Laborato- ries, Inc, New York, USA.

P876 ACCORD COPD I: Twice-daily aclidinium bromide improves quality of life and dyspnea in COPD patients

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4Clinical Development, Forest Research Institute, Jersey City, United States

Introduction: Aclidinium bromide is a long-acting muscarinic antagonist in development for treatment of COPD. In this Phase III study, the effects of twice-daily aclidinium on health outcomes were assessed.

Methods: In this 12-week, double-blind study, moderate to severe COPD patients were randomised to receive aclidinium 200 μg, 400 μg or placebo BID. Health outcomes were assessed monthly via SGRO and TDI.

Results: Of the 561 patients randomised, 467 (83%) completed the study. At
baseline, the mean (SD) pre-bronchodilator FEV₁ and percent predicted were 1.36 (0.54) L and 47.2 (14.1)%, respectively. Baseline mean (SD) SGRO total score and BDI focal score were 46.5 (17.1) and 6.4 (2.1), respectively. Adjusted mean differences vs placebo in change from baseline in SGRO total score at Week 12 were -2.7 (p=0.01) and -2.5 (p=0.02) for aclidinium 200 μg and 400 μg, respectively. At all time points, statistically greater percentages of aclidinium patients achieved clinically significant improvements in SGRO vs placebo (≥4 points; p<0.05) for all except Week 12. 400 μg group. Both aclidinium doses provided significant improvements vs placebo at TDI focal score (p<0.05, range 0.6 to 1.4) throughout the study; with the exception of aclidinium 200 μg at Week 8 (p=0.06). Significantly greater percentages of patients achieved clinically meaningful improvements in TDI (≥1 unit) with both aclidinium doses at all time points vs placebo (p<0.05).

Conclusions: This 12-week study, aclidinium 200 μg and 400 μg BID significantly improved quality of life and reduced dyspnea for patients with moderate to severe COPD.

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Aclidinium bromide in patients with chronic obstructive pulmonary disease: Improvement in health status in ATTAIN

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Introduction: The ATTAIN study investigated the efficacy and safety of two twice-daily doses of aclidinium bromide, a long-acting muscarinic antagonist, in patients with moderate to severe chronic obstructive pulmonary disease (COPD).

Methods: In this 24-week, double-blind, placebo-controlled trial, patients were randomised (1:1:1) to receive aclidinium (200 μg or 400 μg) or placebo, twice-daily. Health status was assessed using the St George’s Respiratory Questionnaire (SGRO) and the EuroQol Questionnaire (EQ-5D; both the weighted health status index and the visual analogue scale [VAS]).

Results: There were 819 patients in the intent-to-treat population; forced expiratory volume in 1 second [FEV₁, %] predicted 56.8±12.8%, baseline SGRO total score 46.3±16.8 units. At Week 24, more patients had a clinically significant improvement in SGRO total score (decrease of ≥4 units) with aclidinium 200 μg and 400 μg than placebo (54.9% and 54.3% vs 39.5%; p=0.0004 and 0.0014, respectively). At Week 24, the improvement with aclidinium 400 μg was 4.3 units, p<0.0001. SGRO domain scores (Symptoms, Activity, Impacts) were also significantly improved with both doses vs placebo at Week 24 (p<0.05 all domains). Aclidinium 200 μg and 400 μg also improved the EQ-SD weighted index and VAS compared with placebo at Week 24; the 400 μg dose reached statistical significance for the weighted index (p=0.0041) and VAS (p=0.0005) vs placebo.

Conclusion: Both doses of GFF-MDI were superior to PL and Tio for morning pre-dose trough assessments (255mL, 271mL and 166mL, respectively; P<0.0004 all comparisons) and for Peak IC assessments (265mL, 291mL and 170 mL, respectively; P<0.0016 all comparisons). Both GFF-MDI 729.6 μg and GFF-MDI 369.6 μg were superior to Tio for pre-dose trough IC (90nd, 105mL, respectively; P<0.05 both doses) and Peak IC on Day 7 (95mL, and 124mL, respectively; P<0.05 both doses).

Conclusion: Both doses of GFF-MDI were superior to PL and Tio for morning pre-dose trough assessments. These findings support the further development of GFF-MDI in patients with COPD.

Rationale: In COPD, IC is inversely correlated to dyspnea with exercise. Tio is an inhaled anticholinergic that improves IC. GFF-MDI is an inhaled bronchodilator comprised of glycopyrrolate and formoterol fumarate. Pearl evaluated improvements in IC of GFF-MDI compared to Tio and placebo (PL) following chronic dosing in a large Phase Ib study.

Methods: Randomized, double-blind, customized, unbalanced, incomplete block, crossover study was conducted in patients with moderate to very severe COPD. One objective was to assess changes in IC on Day7 between 2 doses of GFF-MDI, Tio and PL. MDIs were administered BID for 1 week; Tio was administered QD for 1 week.

Results: 118 patients randomized. GFF-MDI (729.6 and 369.6 μg) and Tio were superior to PL on morning pre-dose trough assessments (255mL, 271mL and 166mL, respectively; P<0.0004 all comparisons) and for Peak IC assessments (265mL, 291mL and 170 mL, respectively; P<0.0016 all comparisons). Both GFF-MDI 729.6 μg and GFF-MDI 369.6 μg were superior to Tio for pre-dose trough IC (90nd, 105mL, respectively; P<0.05 both doses) and Peak IC on Day 7 (95mL, and 124mL, respectively; P<0.05 both doses).

Conclusion: Both doses of GFF-MDI were superior to PL and Tio for morning pre-dose trough assessments. These findings support the further development of GFF-MDI in patients with COPD.

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Dose-related efficacy of GSK573719, a new long-acting muscarinic receptor antagonist (LAMA) offering sustained 24-hour bronchodilation, in COPD

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Introduction: GSK573719 is an inhaled LAMA with sustained 24-hour activity under development as a once-a-day therapy for COPD.

Objective: To evaluate the dose response of GSK573719 in patients with COPD.

Methods: This was a multicentre, randomised, double-blind, placebo-controlled, parallel-group study evaluating GSK573719 administered once daily via a novel single-step activation dry powder inhaler in patients with COPD (FEV₁ of ≥35 and ≤70% predicted). The primary endpoint was morning pre-dose (trough) FEV₁ after 28 days of treatment.

Results: All doses of GSK573719 significantly increased trough FEV₁ compared with placebo, with improvement ranging from 150 to 168mL (p<0.001). All doses significantly increased 0-6 hour weighted mean FEV₁ compared with placebo with differences ranging from 113 to 211mL (p<0.001). Additionally, all doses demonstrated significant improvements over placebo in serial FEV₁ at each measured time point over 24 hours (p<0.038). Reductions in albuterol use and improvements in FVC were also noted for all doses. All doses were well tolerated.

Conclusion:Once-daily dosing with GSK573719 provides clinically significant and sustained improvement in lung function and is well tolerated over 24 hours in patients with COPD. Funded by GSK (AC4113589; NCT0130965).

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Fixed combination of glycopyrrolate and formoterol MDI (GFF-MDI) demonstrates superior inspiratory capacity (IC) compared to tiotropium DPI (Tio) following 7 days dosing, in a randomized, double-blind, placebo-controlled phase 2b study in patients with COPD

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