**249. Translational respiratory medicine in asthma and COPD**

**P2181**

**Comparative in vitro performance of a new reusable breath-actuated nebulizer (BAN) with other high performance systems intended for domiciliary use – I; Table-top compressors**

**Rationale:** Treatments by portable compressor/nebulizer systems can offer very different delivery characteristics. We evaluated a new, reusable BAN (AeroEclipse® XL®, Trudell Medical International) optimized with its table-top (Ombra®) compressor.

**Methods:** Each nebulizer (n=5/group) was filled with 2.5 mL, 1.0 mg/mL albuterol (Ventolin® GSK Canada Inc.), and connected to a breathing simulator (ASL5000, IngMar Medical, Pittsburgh, PA) mimicking adult tidal breathing (Vt= 600 mL; duty cycle = 33%; rate = 10 cycles/min). Emited aerosol was captured on a filter at the mouthpiece, replaced every minute until onset of sputtering, defining run time. Recovery/assay of salbutamol was undertaken by HPLC-UV spectrophotometry. Fine droplet fraction (FDF, <5.0μm) and mass median droplet diameter (MMD) were determined by laser diffractionometry. Total fine droplet mass (FDM, <5.0μm) was the product of total mass and FDF. Comparative measurements were made with the Sprint® (PARL, Germany) and reusable Sidestream® (Philips-Respironics, Germany) air entrainment nebulizers using PARI BOY® SX® and Inspiration Elite® table-top compressors respectively.

**Results:** See Table.

**Nebulizer/Table-top Compressor Performance Data**

<table>
<thead>
<tr>
<th>Mean ± SD</th>
<th>BAN</th>
<th>Sprint</th>
<th>Sidestream</th>
</tr>
</thead>
<tbody>
<tr>
<td>FDF (&lt;5.0μm (%))</td>
<td>70.8 ± 1.0</td>
<td>57.2 ± 3.1</td>
<td>68.6 ± 1.5</td>
</tr>
<tr>
<td>MMD (μm)</td>
<td>3.39 ± 0.05</td>
<td>4.13 ± 0.21</td>
<td>3.43 ± 0.11</td>
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<tr>
<td>FDM (&lt;5.0μm (μg))</td>
<td>530 ± 22</td>
<td>406 ± 22</td>
<td>533 ± 6</td>
</tr>
<tr>
<td>Run time (min)</td>
<td>11</td>
<td>8</td>
<td>10</td>
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</tbody>
</table>

**Conclusions:** The BAN/Ombr system provided highly respirable aerosol with FDM (<5.0μm) greater than the benchmark systems. Its run time reflects the fact that aerosol is only delivered during inhalation and not wasted to the environment.

**P2182**

**Formoterol and fluticasone reduce the deposition of pro-inflammatory collagen**

**Background:** Increased deposition pro-inflammatory collagen I and III has been shown in the sub-epithelial airways in asthma. Formoterol has been reported to reduce collagen deposition, while steroid action depends on the presence of inflammation. Under inflammatory condition, steroids increased collagen deposition.

**Objective:** We investigated the effect of three steroids on the inhibitory effect of formoterol on collagen deposition in TGF-β1 and serum stimulated human airway smooth muscle (ASM) cells.

**Methods:** ASM cells were incubated for 3 days with serum (5%) or TGF-β1 (1ng/ml) in the presence or absence of formoterol, dexamethasone, budesonide or fluticasone (1nM – 1microM). Collagen deposition was determined by an in house ELISA.

**Results:** Serum and TGF-β1 significantly increased the deposition of collagen I and III, while they did not affect the collagen IV content. In non-stimulated cells, all 3 steroids reduced the deposition of collagen I and III dose dependently, while they increased collagen IV. In stimulated cells (TGF-β1, serum) collagen I and III deposition were further increased. Formoterol dose dependently reduced the deposition of all three collagens in non-stimulated and stimulated cells. When combined with steroids the inhibitory of formoterol on collagen I and III deposition was dose dependently increased, but had no effect on collagen IV. The combination with fluticasone achieved more often a stronger inhibitory effect than the other 2 steroids.

**Conclusion:** Our data suggests that formoterol has the potential to reduce airway wall remodelling in asthma and in combination with fluticasone, it is more effective than with other steroids.
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Tiotropium enhances the inhibitory effect of the long-acting β2-agonist olodaterol on the release of IL-6 and IL-8 by primary human lung fibroblasts of asthma patients

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Muscarinic and β2-adrenergic receptors of resident lung cells are modulators of airway inflammation and remodeling. Here, we used human primary lung fibroblasts and asthmatic subjects to investigate the role of β2-adrenergic and muscarinic receptors on the interleukin IL-1β-secretion of IL-6 and IL-8. Fibroblasts were isolated from asthmatic (n=5) and non-asthmatic subjects (n=5) and incubated with IL-1β in the presence or absence of olodaterol (10^{-6} M) and tiotropium (10^{-6} M), or with the combination of olodaterol (10^{-6} M) and tiotropium (10^{-6} M). IL-6 and IL-8 levels in the supernatant were measured by ELISA.

Neither olodaterol nor tiotropium alone affected the secretion of IL-6 and IL-8 in unstimulated cells. Tiotropium reduced the IL-1β-induced secretion of IL-6 and IL-8 in both control and asthmatic cells (p<0.05). Olodaterol reduced IL-1β-induced cytokines in control (IL-6: 52±16%, p<0.05; IL-8: 54±10%, p<0.05) and asthmatic (IL-6: 76±54%, n<0.05; IL-8: 72±22%, p<0.05) fibroblasts. Compared to olodaterol alone the combination of olodaterol (10^{-6} M) with tiotropium (10^{-6} M) further reduced the release of IL-6 (55±7%; p<0.05) and IL-8 (50±6%; p<0.05) from both control and asthmatic patients only.

Both olodaterol and tiotropium exert anti-inflammatory responses in healthy and asthmatic fibroblasts. The combination of olodaterol with tiotropium further improved the anti-inflammatory effect, specifically in asthmatic fibroblasts. These data provide support for combination therapy of long acting β2-agonists plus long acting muscarinic receptor antagonists.

Supported by Boehringer-Ingelheim, Biberach, Germany.

P2185

Low dose inhaled LPS challenge – Reproducibility of the inflammatory response

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Introduction: Inhaled endotoxin (LPS) is used to study pulmonary inflammation. Conventional inhalation models require substantial amounts of LPS (15-30μg) to induce a detectable inflammatory response. Authorities often permit LPS challenges only with GMP-grade LPS, which is of limited availability. Here we studied the reproducibility of the response to a low dose of LPS (0.4μg), which was inhaled by a flow/volume controlled procedure to increase lung deposition.

Methods: Twelve healthy non-smoking volunteers were included. Baseline sputum was evaluated 2-4 weeks prior to the first challenge. On two occasions, separated by a washout period of 2 weeks, volunteers inhaled 3μg LPS (Clinical Center Reference Endotoxin, CCRE, NIH), which was nebulized using an Aeroneb solo (Inspiration Medical). Sputum was induced 6hr after LPS provocation.

Results: The low dose challenge was well tolerated. Both challenges induced a significant (p<0.001) increase in sputum neutrophils (median IQR% of sputum leukocytes at baseline: 24.4(31.2)%, 1.LPS: 52.4(16.0)%, p<0.05) and increased sputum IL-8 and MPO. A significant (p<0.001) increase in sputum monocytes was only detected after the 2 LPS challenge (baseline: 4.3(5.3)%, 1.LPS: 7.7(8.0)%, 2.LPS: 11.8(8.1)%). Despite lower increases of neutrophils in the second challenge, the changes compared to baseline were correlated (r=0.79, p<0.05) and IL-8 (r=0.73, p<0.05) from both patients only.

Conclusion: Low dose LPS causes a reproducible inflammatory response. However, we found evidence for a more pronounced increase in monocytes in the second challenge. This needs to be considered in proof of concept studies for novel inflammatory compounds.

CCRE was kindly provided by Dr. A. Suffredini, NIH, Bethesda.

P2186

Transactivation and transrepression in the repression of inflammatory gene expression by dexamethasone

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Background: The anti-inflammatory activities of glucocorticoids are attributed to the repression of inflammatory gene expression. Dexamethasone (Dex) is a potent synthetic glucocorticoid that has been shown to have a high efficacy in the treatment of asthma and COPD. The exact mechanisms of dexamethasone action are complex and not completely understood.

Methods and results: The effect of Dex on 39 IL-1β-induced genes was examined in human pulmonary A549 cells by real-time PCR. Dex showed a range of activity in terms of the extent (Emax) and potency (EC50) of repression on these genes. These parameters correlated, such that the most highly repressed genes were also the most potently repressed. While all 39 genes were NF-κB-dependent, this did not correlate with repression by Dex. Finally, inhibition of protein translation by cycloheximide (CHX) reduced IL-1β-induced expression of 19 genes (secondary response genes). Of the remaining 21 genes, CHX significantly prevented the Dex-dependent repression of 11 (∼50%), suggesting a role for transcription.

These 11 genes were significantly more sensitive (Emax and EC50) to repression by dexamethasone when compared to genes showing repression that was insensitive to CHX (and which may represent a classical transrepression mechanism).

Conclusions: Repression of inflammatory gene expression by dexamethasone involves multiple mechanisms. Transactivation appears to play a significant role showing both high potency and high level of repression on target genes.

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Tiotropium provides sustained bronchodilation in asthmatics with persistent airflow obstruction uncontrolled despite treatment in accordance with guidelines

Hiub Kerstens1, Pierluigi Paggiaro2, Mark Vanwelken3, Ekkehard Beck4, Michael Engel5, Ralf Sigmund6, Wolfgang Seibold7, Petra Moroni-Zentgraf8, Norbert Krug, Jens M. Hohlfeld9. Inhalated endotoxin (LPS) is used to study pulmonary inflammation. In a recent study, adding a long-acting anticholinergic (tiotropium) showed favourable effects over 8 weeks (wk) (Kerstgens HA, et al. JACI. 2011).

Methods: In 2 replicate 48-wk, doubleblind, parallel-group trials a total of 912 asthmatics with postbronchodilator (BD) FEV1 <80% predicted and asthma control trial questionnaire score ≥1.5 while on at least HD ICS+LABA were randomised to additional tiotropium Respimat® 5 mcg or placebo. Prespecified co-primary endpoints included peak and trough FEV1 at 24 wks. Secondary endpoints were FEV1 at other time-points, FVC, and daily PEFR.

Results: Baseline characteristics were similar between trials and treatment groups (mean post-BD FEV1: 62% ±[13%]. Mean change from baseline tiotropium vs placebo after 24 wks in peak pre-BD FEV1 was 86 (±34) mL (P=0.01) or 154 (±32) mL greater (P<0.001), and in trough FEV1, 88 (±34) mL (P=0.01) or 111 (±30) mL greater (P<0.001) in trials 1 and 2, respectively. Improvements in FVC and daily PEFRs were also significantly greater with tiotropium. There were no new or increased adverse events. The changes were sustained over 48 wks. Tiotropium is likely to improve severe uncontrolled asthma.

Conclusion: In some asthmatics airflow obstruction persists despite high-dose (HD) inhaled corticosteroid (ICS) and long-acting β2-agonist (LABA) use. In a recent study, adding a long-acting anticholinergic (tiotropium) showed favourable effects over 8 weeks (wk) (Kerstgens HA, et al. JACI. 2011).

Supported by Boehringer-Ingelheim, Biberach, Germany.

P2188

The effects of sildenafil on lung function in COPD

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Background: Sildenafil is a pulmonary vasodilator drug used to treat pulmonary hypertension (PH) via PDE5 inhibition. Zaprinast, the precursor to Sildenafil, has moderate bronchodilator effects in exercise induced asthma. A recent study investigating the haemodynamic effects of sildenafil in COPD associated PH (COPD-PH) noted small but significant improvements in FEV1 and FVC.

Aims: To study the effects of sildenafil on bronchodilation and gas trapping in those with COPD-PH.

Methods: COPD patients were invited for echo. RVSP>30mmHg and/or a pulmonary acceleration time of <120ms determined PH. Subjects with COPD-PH were given 50mg of sildenafil/PO. Spirometry was recorded at 0.5, 1 and 3 hours (t0,t1, t3).

Results: A total of 33 patients were studied, 61% male. Baseline spirometry: FEV1(1) 1.13 (SD 0.41), FEV1% 45%(14.7), FVC(l) 2.75(0.76), FVC% 71%.All had significant baseline improvements which were sustained over 48 wks. Tiotropium is likely to improve severe uncontrolled asthma on top of treatment in accordance with guidelines.

Study supported by Boehringer Ingelheim and Pfizer.

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Conclusion: Acute sildainall use resulted in transient airways dilatation and reduced gas trapping. In the absence of placebo control, spirometric changes due to natural variability cannot be ruled out, although the return to normal at 3 hours suggests a real effect.

P2189 Tolerability and efficacy of budesonide/formoterol via Turbuhaler® vs standard treatment in Japanese patients with moderate to severe COPD:

Masakazu Ishimine1, Hiroyuki Nakamura2, Noriharu Shijubo3, Takefumi Saito4, Hirohito Taniguchi5, Toru Tsuda6, Kosho Yoshikawa7, Lars-Goran Carlsson8

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Background: This study evaluated the tolerability and efficacy of budesonide/formoterol via Turbuhaler® vs standard COPD treatment (SCT) in Japanese patients with moderate to severe COPD.

Methods: In this randomised, open-label, parallel-group, phase III study (NCT01070784), patients ≥40 years of age with moderate to severe COPD for ≥2 years received either BUD/FORM 160/4.5 μg 2 inhalations twice daily via Turbuhaler® or SCT (as judged by the investigator) for 52 weeks. Reliever medication: salbutamol via MDI. Primary outcome: increase in FEV1 from 3 to 9 hours. Secondary outcome variables included: COPD symptom, lung function and exacerbations.

Results: 260 patients were randomised. BUD/FORM was well tolerated: 404 AEs were reported by 123 patients (94.6%) receiving BUD/FORM vs. 367 AEs by 112 patients (86.2%) on SCT. The majority of AEs were of mild or moderate intensity and the AE profile was similar in both groups. The most commonly reported AEs (BUD/FORM vs SCT) were nasopharyngitis (42.3% vs 39.2%), COPD (10.8% vs 19.2%) and bronchitis (11.5% vs 11.5%). The frequency of pneumonia-related AEs was similar in both groups (13.1% vs 12.3%) while dysphonia was more frequent with BUD/FORM (5.4% vs 0.8%). Serious AEs were more frequent with SCT (2.8%) vs BUD/FORM (1.9%). No deaths were reported. Efficacy of BUD/FORM was maintained over 52 weeks.

Conclusions: BUD/FORM 160/4.5 μg 2 inhalations twice daily was well tolerated and efficacy was maintained during 52-week treatment in Japanese patients with moderate to severe COPD.

Funding: AstraZeneca.

P2190 Effectiveness of tiotropium in low-risk patients according to new GOLD severity grading:

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1Respiratory Medicine, Royal Devon and Exeter Hospital, Exeter, United Kingdom; 2Respiratory Division, University of Leuven, Belgium; 3Pulmonary Division, Brigham and Women’s Hospital, Boston, MA, United States; 4Allergy and Respiratory Department, Pfizer Inc, New York, NY, United States; 5Medical Affairs, Boehringer Ingelheim Pharma GmbH & Co KG, Ingelheim, Germany; 6Department of Medicine, David Geffen School of Medicine, Los Angeles, CA, United States

Background: GOLD recently updated their COPD severity classification to include risk of exacerbations. Increased risk is typically defined by a FEV1 <50% pred and/or ≥2 exacerbations in the previous year (CHD) and low risk by a FEV1 ≥50% pred and 0-1 exacerbation in the previous year (A+B).

Aims and objectives: To examine the effect of tiotropium 18 μg od via Handihaler® in GOLD low risk patients (pts) using data from a 4-yr, randomised, double-blind, placebo-controlled trial in COPD (UPLIFT).2

Methods: Retrospective analysis of exacerbations, lung function and QoL (SGRQ) in low-risk pts (pts with a baseline postbronchodilator [BD] FEV1 ≤5 pred ≥50% and ≤1 oral steroid/antibiotic course in the previous year). Pts with high risk (FEV1 <5pred <50% or more than 1 course of oral steroids/antibiotics) were also analysed.

Results: 2012 pts were analysed (mean age 64.5±8.6 y, male 74%, mean (±SD) baseline postBD FEV1 1.65 (0.37) L and FEV1 1.5±3.5 pred (±SD) 58.9 (±5.8). The HR (tiotropium vs control) for time to first exacerbation was 0.76 (95% CL 0.68, 0.86; P<0.001). Mean annual exacerbation rates were 0.43 (95% CI, 0.40; 0.48) vs 0.61 (0.56; 0.66); rate ratio 0.72 (0.63; 0.81; P<0.0001). The SGRQ total score after 4 y was significantly improved by tiotropium vs placebo: −3.63 (95% CL −5.14; −2.12; P<0.0001) and the respective increase for trough FEV1 was 110 mL (95% CI, 84; 136; P<0.0001). SGRQ and trough FEV1 were significantly improved at all time points. The above-mentioned endpoints were also significantly improved in the high-risk population.

Conclusion: Tiotropium od was effective throughout 4 y in reducing exacerbations and improving lung function and QoL, in low-risk pts with COPD (GOLD A+B).

P2191 Efficacy and safety of fluticasone/formoterol compared to fluticasone alone in patients with asthma:

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Background: To demonstrate efficacy and safety of fluticasone propionate/formoterol fumarate pMDI (FLUT/FORM) compared with fluticasone (FLUT) alone on the basis of change in FEV1 from morning pre-dose at baseline and 2 hours post-dose at week 12 in GOLD low risk patients (pts).

Methods: Patients included in the study were ≥12 years with symptomatic asthma for ≥1 year; steroid-requiring, had FEV1 ≥50% to 80% [inclusive] of predicted normal values, and documented reversibility within 12 months of the study. Following a 2 week open-label run-in phase with FLUT (100 or 200 μg bd.i.d.), 438 patients were randomised to treatment with FLUT/FORM (250/10 μg b.i.d.) or one of two pMDI formulations of FLUT alone (250 μg b.i.d.). The formulations were Salmeterol/Fluticasone, MDI and Fluticasone/MOFLO (FLUT) with n=146 in all groups. Albuterol/salbutamol was given as rescue medication.

Results: There was a clinically important and statistically significant difference in mean change from pre-dose FEV1, at baseline to 2 h post-dose at week 12 between the FLUT/FORM and both formulations of FLUT (SKP/LS mean difference=0.161 L,P=0.001; FLO/LS mean difference=0.185 LP<0.001). Results from multiple secondary and tertiary efficacy endpoints assessing lung function, asthma symptoms, exacerbations and rescue medication use supported a superior efficacy of the FLUT/FORM combination over FLUT. Treatment-emergent adverse events were lowest in the FLUT/FORM group (32.9%) compared to SKP (39.7%) and FLO (40.4%). FLUT/FORM was generally well tolerated.

Conclusion: FLUT/FORM was superior to FLUT alone in the management of moderate to severe asthma in adolescents and adults. The overall safety profile of FLUT/FORM was consistent with that of FLUT.

P2192 Does eosinophil cationic protein (ECP) predict asthma outcome and response to treatment in asthmatic patients?

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In order to test whether sputum Eosinophil Cationic Protein (ECP) predicts asthma outcome and response to treatment, we studied 119 mild/moderate, steroid-naive asthmatic patients. All patients underwent spirometry, methacholine test, induced sputum analysis before and after treatment, and recorded symptom score and rescue medication use.

Methods: Patients were then treated with inhaled corticosteroids (ICS, n=76) or long-acting β2-agonist (LABA, n=43) based on the change in FEV1 from morning pre-dose at baseline. The concordance between sputum eosinophilic and ECP was poor (r=0.52, p<0.01), although the concordance between sputum eosinophilic and ECP was poor (r=0.52, p<0.01). Patients were then treated with either inhaled corticosteroids (ICS, n=76) or long-acting β2-agonist (LABA, n=43) for 3 to 6 months. In LABA-treated patients, symptom score and beta-2-agonist rescue use improved regardless of baseline sputum ECP levels; after treatment, however, patients with high baseline ECP levels had greater beta-2-agonist use (high-ECP: 16.3 ±17.1; low-ECP: 6.1 ±8.3; p<0.01), although the concordance between sputum eosinophilic and ECP was poor (r=0.52, p<0.01).

Conclusion: ECP could be used as a biomarker for therapy response in asthma.
P2193 Methacholine challenge test as an evaluator of response in bronchial hyperresponsiveness

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3-hydroxy-3-methylglutaryl-CoA reductase inhibitors (statins), are effective serum cholesterol-lowering agents which they may also have anti-inflammatory properties. The objective of this study was to evaluate the effect of atorvastatin on bronchial hyperresponsiveness.

Adult patients (age 14 to 65 years) with bronchial hyperresponsiveness (BHR) diagnosis based on the spirometry with methacholine challenge test were entered into the study. The study was conducted in the National Research Institute of Tuberculosis and Lung Disease. Patients were randomized to receive either atorvastatin 20 mg daily or placebo for 4 weeks. Spirometric parameters were determined at baseline and at completion of the study. Twenty two patients with the age of 32.9±10.30 years completed the trial.

Changes in airway responsiveness categories (moderate to severe, mild, borderline, normal) after the intervention were not significant in atorvastatin group as in placebo group (p=0.13) for atorvastatin group and p = 0.305 for placebo group). Also, changes in methacholine solution number (different concentrations of methacholine) which caused at least 20% decrease in FEV1 were not significant between groups (p = 0.089). Although we could not find a significant difference, the patients’ fall in FEV1 in atorvastatin group was observed in higher concentrations of methacholine. Median before treatment versus after treatment in atorvastatin group was 1 versus 4 mg/ml, while those were 2 versus 1 mg/ml in placebo group.

This study showed a better but no significant hyperresponsiveness control in the treatment group. The result may be presented more pronounced, if we could increase the sample size.

P2194 The GOLDEN-1 study: Safety and bronchodilatory effects of nebulized glycopyrrrolate (EP-101) using high efficiency nebulizer in patients with COPD

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Introduction: EP-101 is a long-acting muscarinic antagonist bronchodilator for nebulization using a high efficiency nebulizer for the treatment of COPD.

Methods: This was a multicenter, randomized, double-blind, placebo-controlled, 4-period cross-over, incomplete block design study. A total of 140 patients with moderate-to-severe COPD were randomized to receive 4 of 7 treatments: EP-101 (placebo, 25, 50, 100, and 200 μg) once daily via high efficiency nebulizer, open-label ipratropium 500 μg three times daily, or placebo. There was a 7-day washout period between treatments.

Results: All doses of EP-101 were well tolerated with similar AE rates between placebo and EP-101 (31.2%, 29.7%, 26.9%, 35.5% and 30.7% for placebo, 25, 50, 100, and 200 μg, respectively). There was no apparent dose-response relationship for incidence and severity of AEs. Mean changes in vital signs and ECG parameters from baseline on Day 7 were comparable between the treatment groups. All doses of EP-101 demonstrated dose-related and significant improvements in FEV1 AUC from baseline on Day 7 were comparable between the treatment groups. All doses of EP-101 were well tolerated with similar AE rates between placebo and EP-101 (31.2%, 29.7%, 26.9%, 35.5% and 30.7% for placebo, 25, 50, 100, and 200 μg, respectively).

Conclusion: The result may be presented more pronounced, if we could increase the sample size.

P2195 Bronchodilator reversibility of FEV1 in asthma and COPD patients

Parisa Adimi1

1 University of Tehran, Tehran, Iran

Introduction: This was a multicenter, randomized, double-blind, placebo-controlled, 7-day treatment period and provided rapid onset of bronchodilation with clinically meaningful and sustained improvement in lung function over 24 hours in patients with COPD.

Funded by Elevation Pharmaceuticals Inc.

P2196 Patterns of bronchodilator reversibility of FEV1 in asthma and COPD patients

Mark Sanders1, Keely Thompson1, Ron Bruin1

1 HQ, Clement Clarke International Ltd, Harlow, United Kingdom; 2 Senior Clinical Research Fellow, Allergy and Respiratory Research Group, Centre for Population Health Sciences, GP Section, University of Edinburgh, Doorway 3, Medical School, Edinburgh, United Kingdom

Introduction: Washing spacers improves drug delivery by reduction of electrostatic charges, and is hygienic. Contamination of spacers and masks has been shown (JAMA 2003;290; 2, 195-196). The ERS/ISAM guideline (ERSI 2011;37:1308-1331) identified a lack of standard instructions for good spacer cleaning practice.

Methods: Online structured interview questionnaires by a market research agency, abstract printing supported by Chiesi Visit Chiesi at Stand B2.10

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Monday, September 3rd 2012

Thematic Poster Session

Halle A-11 - 12:50 - 14:40

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100 asthma patients (Pts) using pMDI with spacer and 50 respiratory nurses (RN) to establish current practice. Pts: 49 adults, parents of children aged 2-9 yrs (n=30) or 10-15 yrs (n=21).

Results: 74% of RN told Pts to wash spacers weekly. 4% instruct daily and 22% instruct < than weekly. RN reported that Pts describe correct washing: 4% always, 42% mostly, 36% sometimes, 14% rarely and 4% never. RN confidence in patients keeping spacers hygienically was low, with 48% not very or not at all confident, this figure increased to 56% in respect of masks. 71% of Pts said their RN or doctor explained how to wash the spacer, and 63% received drying instructions. 54% were told how to wash and dry, but 26% were not told and 8% could not recall being told. 21% of adult Pts don’t wash + dry their spacer (not been told); 6% of children’s spacers were not washed. Of 83 who wash their spacer: 35% do so after each use, 20% every day, 27% once a week and 18% < weekly: 72% report air drying and 27% use a cloth.

Conclusions: RN spacer washing instructions frequently conform to manufacturer’s instructions. Many Pts wash spacers more frequently than instructed but some do not wash at all, many dry with a cloth which may dissipate the electrostatic benefits of air-drying and encourage contamination.
MONDAY, SEPTEMBER 3RD 2012

P2198
The effect of smoking on severity of asthma and quality of life in patients treated with inhaled corticosteroids and long-acting b2-agonist (ICS/LABA)
Galina Sergeeva, Alexander Emelyanov. Lung and Allergy Diseases, Mechnikov North West State Medical University, Saint-Petersburg, Russian Federation

Background: The aim of this study was to assess the effect of smoking on severity of asthma and quality of life in asthmatic patients treated with ICS/LABA in real clinical practice.

Methods: 122 out-patients (aged 20 - 82 yrs, mean age 55 yrs, 28% males) with moderate-to-severe asthma were treated with medium/high doses of ICS (GINA2010) and LABA in one inhaler for ≥ 2 years. Quality of life was measured by using Russian version of St. George’s Respiratory Questionnaire (SGRQ).

Results: Never smoked 36% of patients, former smokers were 31% and current smokers were 33%. Among never smoked asthmatics 80% were treated by medium doses of ICS/LABA and 20% received high doses. Patients with history of smoking (current or previous) have administered medium doses of ICS/LABA in 68% and high doses in 32%. FEV1 differed in nonsmokers and current smokers: 70% vs 56%, p < 0.05. History of smoking was associated with FEV1 level (r=-0.25, p < 0.05) and severity of disease (r=0.3, p < 0.05). The difference of Symptom score between smokers (current or former) and nonsmokers was significant (57,6 versus 66,7, p < 0.05). We revealed the impact of smoking to all scores of SGRQ in females: Symptom (57 vs 65, p < 0.05), Activity (53 vs 51, p < 0.05), Impact (39 vs 40, p < 0.01), and Total score (46 vs 48, p < 0.01) but not in males.

Conclusion: Smoking is common and may decrease effectiveness of ICS and LABA in asthmatic patients in real clinical practice. There were significant correlations between smoking, severity of asthma and SGRQ scores, especially in females.

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The correction of monocyte-derived neohepatocytes from alpha1 antitrypsin deficient patients
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This study explores the culture of monocyte-derived neohepatocytes from PiZ alpha1 antitrypsin deficient (α1ATD) patients and homologous replacement using small DNA fragments (SDFs) to correct the Z defect.

Monocytes from 6 patients were de-differentiated with MCSF and IL3 and then differentiated into neohepatocytes with FGF-4. Albumin, urea and α1AT were measured. SDF enclosing the normal sequence at the PiZ mutation site was generated from genomic DNA of a healthy volunteer. SDFs were transfected into neohepatocytes and cDNA checked for the M or Z message.

No albumin was detected from monocytes. Neohepatocytes secreted 250±50 mg/dL albumin/72h. Monocytes secreted both urea (5±2 μg/dL) and α1AT (272±42 μg/ml) over 72h. Neohepatocytes secreted 103±30 μg/dL urea and 311±34 μg/ml α1AT.

Neohepatocytes produced PCR products from Z primers. M SDF treated neohepatocytes generated bands using M primers, indicating the generation of a corrected transcript.

Neohepatocytes transfected with a monocyte transfection kit but no DNA control produced 163±42μg/ml α1AT in 24h, whereas 20μg M SDF significantly increased secretion (173±41μg/ml/24h, p=0.046, n=3). Using a hepatocyte transfection kit caused further increases in the amount of α1AT released. Control transfected neohepatocytes produced 322μg/ml/24h α1AT and 20μg M SDF significantly increased secretion (590±104μg/ml/24h, p=0.026, n=3). Moreover, 50 μgM SDF caused more α1AT production (886±298μg/ml/24h).

Neohepatocytes can be generated from α1ATD monocytes. The defective gene can be corrected and is associated with an increase in α1AT secretion. Development of this technique could be beneficial and protect both the liver and lungs.

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