Conclusions: Analysis of STIP1 genetic variant rs2236647 serves as an asthma marker. Further investigation with a bigger N is needed to fully validate this study and establish other possible applications of these findings.

P1783
Over-expression of Th17-related cytokines in bronchial and nasal submucosa in severe asthma
Fabio Luigi Massimo Ricciardolo 1, Sabrina Benedetto 1, Antonino Di Stefano 2, GianMario Massaglia 1, Bruno Andreotto 1, Gabriella Favata 1, Salvatore Conticello 1, Giorgio Ciprandi 1
1 Department of Biological and Clinical Science, AOU San Luigi Gonzaga, Orbassano, TO, Italy; 2Division of Respiratory Disease, AOU San Luigi Gonzaga, Orbassano, TO, Italy; 3Intensive Care Unit, AOU San Luigi Gonzaga, Orbassano, TO, Italy; 4Division of Ear, Nose and Throat, AOU San Luigi Gonzaga, Orbassano, TO, Italy; 5IRCCS, AOU San Martino, Genova, GE, Italy

In severe asthma neutrophil recruitment in bronchial submucosa is associated with steroid resistance, and in addition Th17-derived cytokines are important in induction and activation of neutrophils.

We evaluated the differences in inflammatory cells and Th17-related cytokine in bronchial and nasal submucosa between severe asthmatics (SA) and mild asthmatics (MA).

We did not find differences regarding asthma control and the presence of al least one C allele, and a specificity of 100% considering as a diagnostic test, STIP1 SNP analysis showed to have a sensitivity of 100% being homozygous. We did not find differences regarding asthma control and heterozygous and 7/50 did not have the C allele (p<0.05).

POSTER DISCUSSION
MONDAY, SEPTEMBER 3RD 2012
ROOM C8 - 08:30 - 10:30

214. Trials in asthma: asthma exacerbations and severe asthma

P1782
Use of steroid receptor related STIP1 gene analysis as an asthma marker
Helly Ensminger 1, Maria Loreto Reyes 1, Jennifer Angulo 2, Marcelo López-Luca 1, Jaime Cerda 3, José Antonio Castro-Rodríguez 1
1 Pediatrics, Pontificia Universidad Católica de Chile, Santiago, Chile; 2 Medical Investigation Center Pontificia Universidad Católica de Chile, Santiago, Chile; 3 Public Health, Pontificia Universidad Católica de Chile, Santiago, Chile

Introduction: Inhaled steroids are first choice for asthma treatment. However, some patients do not respond, needing higher doses or combined therapies. This difference in responsiveness might be associated to genetic makeup. We evaluated the possible association between variations in treatment requirement and single nucleotide polymorphism (SNP) in importin-13 and STIP1 (steroid receptor related genes).

Aims: Study SNP in inpatient-13 and STIP1, in healthy and asthmatic children.

Methods: Healthy children were enrolled by a public call. Asthmatics treated with <3 months of inhaled steroids were enrolled in outpatient clinics. A clinical questionnaire was applied. SNP were analyzed by PCR-RFLP assay.

Results: 125 children between 2 and 18 years of age were included, 227 healthy and 75 with asthma. Analysis of STIP1 SNP (rs2236647) was obtained in all healthy children and in 63 of the 75 asthmatics. The C allele (minor allele) was present in all asthmatic patients, 46 were heterozygous and 17 homozygous. In contrast, in healthy children, none were homozygous for this allele, 43/50 were heterozygous and 7/50 did not have the C allele (p<0.0001). When considered as a diagnostic test, STIP1 SNP analysis showed to have a sensitivity of 100% with the presence of at least one C allele, and a specificity of 100% considering being homozygous. We did not find differences regarding asthma control and treatment requirement. No association could be established with asthma in patients with severe asthma (SA).

Table 1. Maximal cytokine inhibition achieved by dexamethasone

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>Maximum % inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HNS</td>
</tr>
<tr>
<td>IL-17</td>
<td>54.5</td>
</tr>
<tr>
<td>IL-13</td>
<td>90.9***</td>
</tr>
<tr>
<td>IL-2</td>
<td>63.1**</td>
</tr>
<tr>
<td>INF-γ</td>
<td>63.0</td>
</tr>
</tbody>
</table>

*p<0.05, **p<0.01, ***p<0.001

** Denotes significantly higher inhibition compared to severe asthma patients.

Dexamethasone had a reduced effect on all cytokines in SA compared to HNS and MA.

Conclusions: Use of STIP1 SNP analysis was able to identify a susceptible group of asthmatics.

P1784
Effect of corticosteroids on lymphocytes from severe asthma patients
Manninder Kaur 1, Sophie Reynolds 1, Lucy Smyth 1, Simon Hall 2

1 Karen Simpson 1, Steven Fox 1, Dave Singh 1, 2NIHR Translational Research Facility, University of Manchester, United Kingdom; 3Respiratory Inflammation DPU, Respiratory TAU, GSK Medicine Research Centre, Stevenage, United Kingdom; 4Statistical Consulting, GSK Medicine Research Centre, Stevenage, United Kingdom

Patients with severe asthma have persistent airway inflammation that responds poorly to corticosteroids. Lymphocytes play a central role in disease pathogenesis; we hypothesised that lung lymphocytes from patients with severe asthma are insensitive to the effects of corticosteroids.

We investigated suppression of lung lymphocyte cytokine production by corticosteroids in healthy non-smokers (HNS) and patients with mild asthma (MA) and severe asthma (SA).

We assessed lymphocyte cytokine production in mild asthma (MA) and severe asthma (SA) with steroid resistance, and in addition Th17-derived cytokines are important in the irreversible steroid-resistant inflammatory process.

In nasal sub-mucosa (NS) of SA we found higher number of lymphocytes CD4+, CD8+, mast cells and macrophages, but also of IL-17A+, IL-17F+, IL-21+ and IL-22+ cells. Double staining for CD4 or CD8 and IL17F or IL22 showed that all IL-17F+ and IL22+ cells are also CD4+ or CD8+.

In nasal sub-mucosa (NS) of SA we found higher number of lymphocytes CD4+, CD8+, mast cells and macrophages, but also of IL-17A+, IL-17F+, IL-21+ and IL-22+ cells. Double staining for CD4 or CD8 and IL17F or IL22 showed that all IL-17F+ and IL22+ cells are also CD4+ or CD8+.

NS correlated positively with the equivalent cells in NS. Moreover, the number of CD4+, IL-17F+ and IL-22+cells in BS correlated positively with the equivalent cells in NS.

We should have revealed neutrophil/lymphocyte infiltration in conjunction with an amplified expression of Th17-related cytokines in both bronchial and nasal submucosa suggesting an involvement of IL-17 pathway in the progression to an irreversible steroid-resistant inflammatory process.

Cytokine release was inhibited by dexamethasone in a dose dependent manner. Dexamethasone had a reduced effect on all cytokines in SA compared to HNS or MA. Dexamethasone had the greatest effect on the Th2 cytokine IL-13, but had a lower effect on Th1 and Th17 cytokines.

Cytokine production from BAL lymphocytes show corticosteroid insensitivity compared to cells from controls. This phenomenon may be important in the poor clinical response often observed with corticosteroids. Furthermore, corticosteroids have a reduced effect on Th1 and Th17 cytokines, which may predominate in SA.
P1785
Association of glucocorticoid receptor gene polymorphisms of R23K and R477H and steroid-resistant asthma in Chinese Han population
Feng Zhang1, Changya Wu2, Zhikai Li1. Department of Respiratory, Xijing Hospital, Fourth Military Medical University, Xi'an, Shaanxi, China

Some previous studies have shown that steroid resistance in asthma is associated with the mutation of glucocorticoid receptor (GR) gene. Other studies, however, have reached the opposite conclusion. The aim of this study was to detect the GR polymorphisms of R23K and R477H in steroid-resistant (SR) asthma patients and steroid-sensitive (SS) asthma patients in Chinese Han population, and to elucidate the association between GR polymorphisms and steroid resistance in asthma. Sixty-four SR patients and 68 SS patients were recruited for the detection of R23K and R477H variants, using polymerase chain reaction-sequence specific primers. Cortisol contents in serum were examined. The equilibrium dissociation constants (KD) were calculated by dexamethasone radioligand-binding assay and Scatchard analysis to determine GR affinity to glucocorticoids. No statistically significant difference was found in the distribution of R23K polymorphism between SR patients and SS patients. In R477H variant, the wild genotype GG and AG frequencies were significantly lower in SR patients than in SS patients (P=0.043). The cortisol content in serum was found no significant difference between SR patients and SS patients, and among different genotypes. No significant differences in KD were found between GG genotype and GA genotype of R23K variant, GG genotype and GA+GG genotype of R477H variant. In SR patients, the KD values were significantly higher than in SS patients (P<0.001). These findings suggest that GR polymorphisms of R23K and R477H exist in Chinese Han population. R477H variant is associated with steroid-resistant asthma in this population.

P1786
The effect of single-nucleotide polymorphism in IL-13 on airway hyperresponsiveness in asthmatics
Yu Udagawa1, Takayuki Miyamoto1, Kenshi Sekimura1, Nobuhito Sasaki2, Naomi Suzuki1, Yukata Nakamuta1, Hiroshi Kobayashi1, Kohei Yamauchi1. Internal Medicine, Iwate Medical University School of Medicine, Morioka, Iwate, Japan

Background: Single-nucleotide polymorphism (SNP; rs20541) of IL-13 has been recognized as a risk factor of asthma. We recently demonstrated that FEV1 in asthmatics was significantly higher than in non-asthmatics with IL-13 deciliation (Biallowoz et al Int 2011). However, the effects of the variant IL-13 on airway hyperresponsiveness (AHR) have never been elucidated.

Objectives: To evaluate the effects of SNP (rs20541) in IL-13 on AHR in asthmatics, we analyzed the relationship between SNP and AHR.

Methods: We recruited 182 asthmatics to the current study who visited the asthma out-patient clinic in Iwate Medical University Hospital from 2006 to 2011. Subjects were genotyped using rs20541 by 7500 Fast Real-Time PCR System, (Applied Biosystems USA). Therapeutic steps (GINA 2011), eosinophil counts in peripheral blood and serum IgE concentration in those asthmatics were also studied. AHR to methacholine was measured by Astograph; Jupter 21 (Chest, Japan). AHR was expressed as Dmin (U) (average ± SE). Statistical analysis was performed by one way ANOVA. This study was approved by the ethics committee of Iwate Medical University.

Results: Genotyping of rs20541 showed that 26 A/A, 77 A/G and 79 G/G. D min in the 3 genotypes was proved to be significantly different by Kruskal-Wallis One Way Analysis of Variance (p=0.007). There was no significant difference in therapeutic steps, eosinophil counts or serum IgE concentration among the 3 genotypes of asthmatics.

Conclusion: SNP (rs20541) in IL-13 was associated with AHR, suggesting that IL-13 was involved in the progress of AHR through its biological activity on airway smooth muscles.

P1787
Preventive effect of carbocysteine on exacerbation of asthma, GAIA randomized, placebo-controlled multi-centre study
Hirokazu Sano1, Yuji Tohda2, Mitsuru Adachi2, Takeshi Fukuda3, Ken Ohta4, Shunsuke Shoji5, Terumasa Miyamoto6, 1Department of Respiratory Medicine and Allergology, Kinki University Faculty of Medicine, Osaka-Seiya, Japan; 2Division of Respiratory Medicine and Allergology, Department of Internal Medicine, Showa University School of Medicine, Tokyo, Japan; 3Department of Pulmonary Medicine and Clinical Immunology, Dokkyo Medical University, Tochigi, Japan; 4Division of Respiratory Medicine & Allergology, Dokkyo Medical University, Tochigi, Japan; 5Division of Respiratory Medicine and Allergology, Department of Internal Medicine, Teikyo University School of Medicine, Tokyo, Japan; 6Clinical Department, National Hospital Organization Tokyo National Hospital, Kiyose, Japan; 7Internal Medicine and Allergology, Japan Clinical Allergy Research Institute, Tokyo, Japan

Background: Management of exacerbation is clinically very important in asthma control. Carbocysteine, which improves airway mucus clearance and has anti-inflammatory effects, including antioxidant effect, is expected to prevent asthma exacerbation in addition to COPD exacerbation.

Objective: To evaluate the preventive effect of carbocysteine (C) on exacerbation in asthma patients using placebo (P) as a control.

Methods: A total of 286 patients with mild to moderate asthma were randomly assigned to receive either C (1500mg/day) or P for 48 weeks. Patients were allowed to use long-term asthma control medications. The primary endpoint was annual frequency of exacerbations and the secondary endpoints were pulmonary function and asthma control by ACQ.

Results: At the time of enrollment, the disease type (atopic or non-atopic asthma) was significantly different (p = 0.02) between the two groups (C, n = 140; P, n = 140), but no statistically significant differences were observed in any other baseline characteristics of patients. The frequency of asthma exacerbations, the primary endpoint, was 5.4/year in the C group and 8.0/year in the P group, showing a significant decrease in the C group compared with the P group. The risk ratio of exacerbation was 0.658 (95% CI, 0.595-0.727; p < 0.001). No significant differences were observed in the pulmonary function or in the asthma control between the two groups.

Conclusion: C significantly reduced the frequency of asthma exacerbations and thus provides a new therapeutic concept for long-term asthma management.
P7190
The effect of a single high dose vitamin D3 on neutrophilic airway inflammation in nonatopic asthma
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Rationale: Vitamin D deficiency has been associated with asthma and increased risk of respiratory tract infections. An infectious origin in its turn, has been proposed for nonatopic asthma (Joseph Ann All Asthma Immun 2003) as well as neutrophilic asthma (Simson Thorax 2007). Vitamin D enhances anti-microbial defence and might thereby influence the inflammatory process in the Airways. Therefore, we hypothesized that treatment with high dose vitamin D3 reduces neutrophilic airway inflammation in patients with nonatopic, neutrophilic asthma.

Methods: 18 nonatopic, neutrophilic (≥5% sputum neutrophils (Spanevello, AJRCCM 2000)) stable asthma patients were included in a randomized double-blind placebo controlled trial. Patients received 400000 IU vitamin D3 or placebo orally in single dose. All completed questionnaires, underwent blood sampling, lung function tests and sputum induction at baseline and after 8 weeks.

Results: Baseline characteristics were similar in both arms. Results: see table

<table>
<thead>
<tr>
<th>Placebo</th>
<th>Vitamin D</th>
<th>p between groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin D, nmol/l</td>
<td>59 (30-113)</td>
<td>57 (34-92)</td>
</tr>
<tr>
<td>FEV1, %</td>
<td>74 (63-96)</td>
<td>76 (55-96)</td>
</tr>
<tr>
<td>FEV1/FVC, %</td>
<td>95 (11.1)</td>
<td>92 (9.6)</td>
</tr>
<tr>
<td>ACQ</td>
<td>1.2 (1.0-2.6)</td>
<td>0.9 (0.1-2.6)</td>
</tr>
</tbody>
</table>

Conclusion: Treatment with a single high dose vitamin D3 in nonatopic, neutrophilic asthma, does not reduce neutrophilic inflammation, but improves ACQ as compared to placebo.

Implications: The association between vitamin D and asthma is not explained by its effect on sputum neutrophils. The improvement in asthma control by vitamin D suggests that other beneficial mechanisms might be involved.

P7192
Efficacy and safety of BI 671800, an oral CRTH2 antagonist, as add on therapy in poorly controlled asthma patients prescribed an inhaled corticosteroid

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1Department of Respiratory Disease, University of Nottingham, United Kingdom; 2Clinical Development & Medical Affairs/Therapeutic Area Respiratory Diseases, Boehringer Ingelheim Ltd, Bracknell, United Kingdom; 3Boehringer Ingelheim GmbH, Ingelheim, Germany; 4Department of Chest Disease, Mersin University School of Medicine, Mersin, Turkey; 5Department of Clinical Research, IGF Institut fuer Gesundheitsforderung, Ruesselsdorf, Germany; 6Department of Medicine, University of Cape Town, South Africa; 7Clinical Development & Medical Affairs/Therapeutic Area Respiratory Diseases, Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach an der Riss, Germany

Background: BI 671800 is an antagonist of the PGD2 receptor. CRTH2. PGD2 stimulates bronchoconstriction and allergic airway inflammation in animal models and asthma-related quality of life. BI 671800 reduces airway hyper-responsiveness in vitro and in vivo.

Objective: To investigate the efficacy and safety of BI 671800 versus placebo and montelukast in poorly controlled asthma patients as add on to therapy with fluticasone propionate (FP) MDI (88 μg, bid).

Methods: Adults with asthma (FEV1 60-85% and ACQ ≥ 1.5) were enrolled in a randomized, double-blind, parallel arm study comparing BI 671800 400 μg bid with matching placebo bid or montelukast 10 mg qd for 6 weeks. The primary study outcome was change in trough FEV1.

Results: 243 patients were randomised (mean age 41.6 years, FEV1 72%, ACQ ≥ 2). Improvement in trough FEV1 in adjusted mean (SE) trough morning FEV1, % predicted versus placebo was 3.87% (1.49) for BI 671800 and 2.37% (1.57) for montelukast, (one sided p < 0.025 for BI 671800), achieving the primary efficacy outcome for the study. Change in ACQ mean (SD) scores versus placebo were -0.28 (0.12) and -0.18 (0.12) for BI 671800 and montelukast respectively (one sided p < 0.025 for BI 671800).

Conclusion: BI 671800 was better tolerated at a total daily dose of 800 mg for 6 weeks.

P7193
Improvements in asthma control and quality of life with omalizumab in allergic (IgE-mediated) asthma patients

Gert-Jan Braagshuij1, Marco Deenstra2, Janine Canvin3, Panos Georgiou4, Guy Peachey5, Chien-Wes Chen6.

1Primary Care, Novartis Pharmaceuticals Corporation, East Hanover, United States; 2Department of Pulmonology, St. Franciscus Gasthuis, Rotterdam, Netherlands; 3Department of Pulmonology, Flevozenvenhuis, Almere, Netherlands; 4Critical Care, Novartis Pharmaceuticals UK Limited, Horsham, United Kingdom; 5Critical Care, Novartis Pharmaceuticals Corporation, East Hanover, United States

Introduction: Optimizing asthma control and improving health-related quality of life (QoL) are key goals in the management of asthma. The asthma control test (ACT), the asthma control questionnaire (ACQ), and the asthma quality of life questionnaire (AQLQ) are important patient-reported outcomes often used to evaluate treatment efficacy.

Methods: eXperience is a global, post-marketing, observational registry established to evaluate the efficacy and safety of omalizumab for 2 years during standard clinical practice. Data (means [SD]) are presented for the ACT, ACQ, AQLQ and mini-AQLQ at Months 12 and 24.

Results: Of the 943 patients who entered the registry, 916 were included in the intent-to-treat population (mean age 45.0 ± 15.0 years). Asthma control and QoL scores improved in patients receiving omalizumab at Months 12 and 24 compared with baseline (Table). Improvements exceeded the minimum clinically important difference at both timepoints (≥ 3 point increase for the ACT, ≥ 0.5 point decrease for the ACQ, and ≥ 0.5 point increase for the AQLQ and mini-AQLQ).

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>ACT</th>
<th>ACQ</th>
<th>AQLQ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Month 12</td>
<td>3.87</td>
<td>1.80</td>
<td>1.00</td>
</tr>
<tr>
<td>Month 24</td>
<td>4.27</td>
<td>2.39</td>
<td>1.50</td>
</tr>
</tbody>
</table>

*An increase in score reflects an improvement. †A decrease in score reflects an improvement.

Conclusions: In patients with severe allergic asthma, treatment with omalizumab resulted in sustained and clinically meaningful improvements in asthma control and asthma-related quality of life.

312s

Abstract printing supported by Chiesi Visit Chiesi at Stand B2.10
P1794 Efficacy and safety of fluticasone furoate (FF)/vilanterol (VI) once daily (OD) for 24 weeks in persistent asthma
Paul M. O’Byrne1, Eugene R. Bleecker2, Eric D. Bateman3, William W. Busse4, Ashley Woodcock5, Richard Forbh6, Tom Toler7, Loretta Jacques8, Jan Lotvall9, Michael G DeGroot9 School of Medicine, McMaster University, Hamilton, Canada; Center for Genomics and Personalized Medicine, Wake Forest University Health Sciences, Winston-Salem, United States; 10Department of Medicine, University of Cape Town, South Africa; 11Department of Medicine, University of Wisconsin, Madison, United States; 12School of Translational Medicine, University of Manchester, United Kingdom; 13Quantitative Sciences Division, GlaxoSmithKline, Research Triangle Park, United States; 14Respiratory Medicines Development Center, GlaxoSmithKline, Research Triangle Park, United States; 15Respiratory Medicines Development Center, GlaxoSmithKline, Uxbridge, United Kingdom; 16Krefting Research Centre, University of Gothenburg, Sweden

Introduction: FF and VI are, respectively, a novel inhaled corticosteroid and long-acting β2 agonist, in development as a once-daily treatment for asthma and COPD.

Objectives: To compare the efficacy and safety of FF/VF1 with FF and fluticasone propionate (FP) in patients (≥12 years old; on ICS) with moderate-to-severe persistent asthma.

Methods: Patients (N=586; intent-to-treat) received FF/VF1 200/25mcg OD PM, FF 200mcg OD PM or FP 500mcg twice daily (AM/PM) for 24 weeks. Co-primary endpoints were change from baseline in trough (pre-bronchodilator) FEV1, and mean weight 0–24h serial FEV1. Secondary endpoints were change from baseline in Sensitive-free and symptom-free 24 periods and Asthma Quality of Life Questionnaire (AQLQ) score. Safety assessments included adverse events (AEs), 24h urinary cortisol (UC) excretion, vital signs and ECG.

Results: FF/VF1 improved trough FEV1 (diff. 193mL and 210mL; both p<0.001) and mean serial weight FEV1 (diff. 1.68mL [p=0.048] and 206mL [p=0.003]) vs FF and FP. Significantly more % rescue-free (11.7% [p<0.001]) and % symptom-free (8.4% [p=0.031]) 24h periods were reported with FF/VF1 vs FF. There was no statistical difference between FF/VF1 and FF in AQLQ score. Incidence of AEs was similar across groups. No clinically significant difference was seen across treatments with respect to 24h UC excretion, vital signs or ECG.

Conclusions: Treatment with FF/VF1 over 24 weeks was associated with statistically greater improvements in lung function and asthma stability vs FF and FP, and was well tolerated in this asthmatic population. Funded by GSK (HZA106829; NCT01134042).

P1795 Efficacy and safety of fluticasone furoate (FF)/salmeterol combination (FF/SAL) in adults and adolescents with persistent asthma
Ashley Woodcock1, Eugene R. Bleecker2, Jan Lotvall3, Paul M. O’Byrne4, Eric D. Bateman5, Hilary Medley6, Anna Ellsworth7, Loretta Jacques8, William W Busse9, School of Translational Medicine, University of Manchester, United Kingdom; 10Center for Genomics and Personalized Medicine, Wake Forest School of Medicine, Winston-Salem, United States; 11Krefting Research Centre, University of Gothenburg, Sweden; 12Michael G DeGroot School of Medicine, McMaster University, Hamilton, Canada; 13Department of Medicine, University of Cape Town, South Africa; 14Respiratory Medicines Development Centre, GlaxoSmithKline, Uxbridge, United Kingdom; 15Quantitative Sciences Division, GlaxoSmithKline, Research Triangle Park, United States; 16Department of Medicine, University of Wisconsin, Madison, United Kingdom

Introduction: The combination of FF, a novel inhaled corticosteroid and VI, a long-acting β2 agonist, is under development as a once-daily treatment for asthma and COPD.

Objectives: To compare the efficacy of FF/VF1 with FP/SAL in patients with persistent asthma.

Methods: In a randomised, double-blind, double-dummy, parallel-group study, 806 patients received FF/VF1 (100/25mcg, n=403) or FP/SAL (250/50mcg, n=403) via a new dry powder inhaler, or DISKUS®, respectively. FF/VF1 was taken once daily in the evening, FP/SAL twice daily. Primary efficacy measure was 0–24h serial weighted mean (w) FEV1, after 24 weeks of treatment.

Results: Clinically significant improvements from baseline in 0–24h wFEV1 were seen with both FF/VF1 (341mL) and FP/SAL (377mL); the adjusted mean treatment difference was not statistically significant (~37mL, p=0.162). Changes from baseline in 0–4h wFEV1, and trough FEV1 supported the primary findings, as did AQLQ, ACQ and EQ-5D scores. No differences between treatments in reported exacerbations was found. There were no clinically relevant effects on urinary cortisol excretion or vital signs, and no treatment-related serious adverse events; safety profiles were similar across treatment groups.

Conclusions: Once-daily FF/VF1 was as effective as twice-daily FP/SAL in improving lung function in patients with persistent asthma, and no safety issues were identified. No statistically significant treatment difference in efficacy was observed between the two combination treatments. Funded by GSK (HZA113091; NCT01147848).

P1796 Tiotropium reduces asthma exacerbations in asthmatic patients with persistent airflow obstruction uncontrolled despite treatment in accordance with guidelines
Huib Keijser1, Ronald Dahi2, Ekkehard Beck3, Mark Vandewalker2, Michael Engel2, Ralf Sigmund2, Wolfgang Seibold1, Petra Morenz-Zentgraf1, Eric D. Bateman4, Department of Pulmonary Medicine and Tuberculosis, University Medical Center, Groningen, Netherlands; 5Department of Respiratory Diseases, Aarhus University Hospital, Aarhus C, Denmark; 6Medical Department, JFG - Institut für Gesundheitsfor...
administered was greater with NEXThaler® than other DPIs \( (p < 0.001) \) (Fig. 1B). Additionally, NEXThaler® was superior to both Diskus and Turbohaler in terms of ease of use \( (74 \text{ vs } 17 \text{ and } 9\%) \text{ respectively; } p < 0.001 \) and patient preference \( (75 \text{ vs } 17 \text{ and } 8\% \text{ respectively;} p < 0.001) \).

Overall, effectiveness, efficiency and satisfaction measures each demonstrate that the usability of NEXThaler® is superior to Diskus® and Turbohaler®.

P1798
Beclometasone/formoterol administered via extrafine dry powder inhaler in controlled asthmatic patients: Comparison with pMDI and beclometasone monotherapy
Francesco Sergio¹, Catherine Francisco¹, Annamaria Muraro¹, Frank Kanniess².
¹Corporate Clinical Development, Chiesi Farmaceutici S.p.A., Parma, Italy; ²Gemeinschaftspraxis Reinfeld, Gemeinschaftspraxis Reinfeld, Germany
Background: The fixed combination of beclometasone dipropionate and formoterol fumarate \( (BDP/FF) 100 / 6 \mu \text{g} \text{ pMDI (Foster®) is approved for treatment of adult asthmatic patients. In order to provide physicians and patients with an alternative drug delivery system for BDP/FF, a new dry powder inhaler the NEXThaler® has been developed, able to ensure consistent dosing in patients who prefer the use of dry powder inhalers.}

Aim: To compare efficacy and safety profile of BDP/FF NEXThaler® with BDP/FF pMDI or BDP DPI alone in adult patients with controlled asthma.

Methods: 8-week randomised, double-blind, triple-dummy, 3-arm parallel-group clinical study. After 4-week run-in with BDP/FF pMDI 100/6 bid, 755 patients were randomised to receive bid BDP/FF NEXThaler® 100/6, BDP/FF 100/6 pMDI or BDP DPI 100. The primary end-point was change from baseline to the entire treatment period in average pre-dose morning PEF (mPEF).

Results: Non-inferiority of NEXThaler® vs pMDI was shown for mPEF (LSmeans difference: -1.84L/min; 95%CI [-6.73;3.05]) and lower limit of the 95%CI was above the pre-defined non-inferiority margin of -15L/min. Superiority of both combinations over BDP DPI was shown \( (p < 0.001) \) providing evidence of assay sensitivity of the study. Both BDP/FF formulations were statistically superior to BDP alone in terms of ACQ score \( (p=0.009 \text{ and } 0.008) \) and % of rescue use-free days \( (p=0.033 \text{ and } 0.006) \) as well as pulmonary function tests over the entire treatment period.

No relevant drug related AEs were observed.

Conclusion: NEXThaler® is an effective and well-tolerated alternative delivery device for treatment of asthmatic patients with BDP/FF.

P1799
Improving inhalation parameters through dry powder inhalers (DPIs) after an acute asthma exacerbation
Wahida Azouz¹, Mokhtar El-Soussi², Henry Chrystyn¹.
¹Pharmacy, University of Huddersfield, United Kingdom; ²Respiratory, Tripoli Medical Centre, Tripoli, Libyan Arab Jamahiriya
All DPIs are passive inhalers because they require the generation of an internal energy \( (P) \) from an interaction between the patient’s inhalation and the device’s resistance to deaggregate the formulation in the metered dose. During acute exacerbations patient inspiratory effort will be reduced and thus \( P \) will be reduced. We have measured the inhalation profiles of 18 asthmatics, mean(SD) age 42.0(11.8) years, on days 1-4 following their admission with an acute exacerbation. These measurements have been made using a Diskus (DKS), Easyhaler (EASY) and Turbuhaler (TBH) - inhalers with medium, medium/high and high resistance.

<table>
<thead>
<tr>
<th></th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV(_1) % pred</td>
<td>40.9 (12.5)</td>
<td>47.9 (13.6)</td>
<td>55.6 (12.6)</td>
<td>58.2 (11.8)</td>
</tr>
<tr>
<td>DKS PIF (L/min)</td>
<td>42.3 (8.9)</td>
<td>51.0 (8.7)</td>
<td>65.7 (16.0)</td>
<td>77.0 (15.4)</td>
</tr>
<tr>
<td>PP (kPa)</td>
<td>1.40 (0.74)</td>
<td>2.28 (0.83)</td>
<td>3.91 (2.07)</td>
<td>5.27 (2.10)</td>
</tr>
<tr>
<td>ACC (KPa/sec)</td>
<td>2.33 (1.38)</td>
<td>3.63 (2.49)</td>
<td>6.72 (3.68)</td>
<td>10.26 (8.21)</td>
</tr>
<tr>
<td>IV (L)</td>
<td>0.80 (0.34)</td>
<td>0.90 (0.30)</td>
<td>1.11 (0.36)</td>
<td>1.35 (0.31)</td>
</tr>
<tr>
<td>TBH PIF (L/min)</td>
<td>35.1 (4.9)</td>
<td>41.4 (5.60)</td>
<td>45.3 (6.3)</td>
<td>50.9 (7.2)</td>
</tr>
<tr>
<td>PP (kPa)</td>
<td>1.42 (0.41)</td>
<td>1.98 (0.52)</td>
<td>2.38 (0.66)</td>
<td>3.00 (0.83)</td>
</tr>
<tr>
<td>ACC (KPa/sec)</td>
<td>2.55 (1.12)</td>
<td>4.29 (1.21)</td>
<td>4.53 (1.71)</td>
<td>6.23 (3.06)</td>
</tr>
<tr>
<td>IV (L)</td>
<td>0.55 (0.25)</td>
<td>0.64 (0.29)</td>
<td>0.72 (0.26)</td>
<td>0.84 (0.26)</td>
</tr>
<tr>
<td>EASY PIF (L/min)</td>
<td>31.3 (3.7)</td>
<td>38.3 (4.7)</td>
<td>43.3 (6.5)</td>
<td>48.2 (7.6)</td>
</tr>
<tr>
<td>PP (kPa)</td>
<td>2.33 (0.53)</td>
<td>3.51 (0.85)</td>
<td>4.52 (1.35)</td>
<td>5.59 (1.74)</td>
</tr>
<tr>
<td>ACC (KPa/sec)</td>
<td>4.60 (1.78)</td>
<td>6.94 (2.32)</td>
<td>9.06 (3.77)</td>
<td>11.35 (4.91)</td>
</tr>
<tr>
<td>IV (L)</td>
<td>0.53 (0.18)</td>
<td>0.63 (0.17)</td>
<td>0.77 (0.26)</td>
<td>0.86 (0.34)</td>
</tr>
</tbody>
</table>

All parameters improved. PIF should not be considered in isolation and provides the wrong message, especially for high resistance DPIs, as PP and ACC are more important. The significance of the IV results needs to be investigated.