Effects of formoterol-budesonide combination on residual eosinophilic inflammation in distal airway of patients with well-controlled moderate asthma

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Aims: To investigate whether formoterol-budesonide combination (FBC, Symbicort TM) controls residual eosinophilic inflammation in the distal airways of well-controlled asthmatic patients more effectively than salmeterol-fluticasone propionate combination (SFC).

Methods: Twenty eight outpatients (58.4±19.7yrs) with well-controlled moderate asthma who had used SFC for more than 3 months were the subjects. Evidence of eosinophilic cationic protein (ECP) and surfactant protein D (SP-D) in 10% hypertonic saline-induced sputum was assessed, together with pulmonary function testing, impulse oscillometry system (IOS) and exhaled nitric oxide (FeNO).

Results: Eosinophilic inflammation was detected in the distal airway of eleven patients (39.3%) and they were switched to FBC (4.5/160ug, 2 inhalations twice daily). As higher levels of sputum SP-D were obtained from the nearer peripheral airway area, significantly higher ECP levels in late-phase sputum may indicate...
residual asthma inflammation in the peripheral airway. The ECP levels in late-phase sputum (255.2±297.1 fg/ml) at study entry) significantly decrease 60.6±43.7 (p=0.038) and 50.7±48.4 (p=0.049) at 4 and 8 weeks after switching to treatment with the FBC, respectively. The FeNO levels (76.0±69.4 ppb at study entry) also significantly decreased 29.1±15.7 (p=0.017) at 8 weeks. The R5-R20 and AX values of IOS parameters also significantly improved after 8 weeks.

Conclusions: This study suggests that the FBC may give better control of residual eosinophilic inflammation in the distal airway compared to SFC therapy.

P3952
Montelukast as add-on therapy may improve some indices of small airways involvement in uncontrolled asthmatics

Gert-Jan Braunstahl1, João Leão2, Chien-Wei Chen3, Robert Maykut 4, and Panayiotis Georgiou2, Guy Peachey 2.

Background: Several studies suggest an involvement of small airways in asthma that are poorly controlled. The aim of the study was to assess the added value of montelukast in uncontrolled asthma.

Aim: To assess whether montelukast improves indices of small airways involvement and clinical outcomes in asthmatics in regular therapy with medium-high doses of inhaled corticosteroids and long-acting β2-agonist.

Subjects and methods: 240 uncontrolled asthmatics underwent, at baseline and after one-month open label therapy with montelukast. FEV1, Single Breath Nitrogen WhasAuthent for phase III slope (DN2); multiple flows exhaled nitric oxide (NO); eosinophils in sputum (EOs); and alveolar-arterial differences of respiratory gases (AaDO2, AaDCO2); asthma control obtained by symptoms (S) and variability of peak expiration flow (AEPF) monitoring.

Results: Patients were divided in controlled (n=7 well controlled, n=10 partially controlled) and non-controlled (n=7) according to GINA guidelines. After one-month therapy with montelukast: a) in controlled group, therapy significantly reduced AEPF (18.2±9.3 vs 13.1±5.6; p<0.007); b) in non-controlled group, therapy significantly reduced only AaD2 (32.1±7.9 vs 25.8±7.7 mmHg, p=0.034). Patients were also divided in other two groups according to the number of abnormal indices of small airways involvement (DN2, CaNO and AaDO2) at baseline: 0-1 vs 2-3 abnormalities. Montelukast reduced AEPF (21.4±7.8 vs 17.3±4.1; p<0.001) only in patients with 2-3 abnormalities in small airways indices.

Conclusions: Montelukast might improve both functional and clinical indices of small airways involvement, in controlled and non-controlled asthmatics and this might be associated with some effects on small airways.

P3953
The exPenrience registry: Monitoring the “real-world” effectiveness of omalizumab in allergic asthma

Ger Jan Braunstahl1, J. L. Lee2, Chien-Wei Chen3, Robert Maykut 4, Panayiotis Georgiou2, Guy Peachey 2.

Background: Several studies suggest an involvement of small airways in asthma that are poorly controlled. The aim of the study was to assess the added value of montelukast in uncontrolled asthma.

Aim: To assess whether montelukast improves indices of small airways involvement and clinical outcomes in asthmatics in regular therapy with medium-high doses of inhaled corticosteroids and long-acting β2-agonist.

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Conclusions: Montelukast might improve both functional and clinical indices of small airways involvement, in controlled and non-controlled asthmatics and this might be associated with some effects on small airways.

P3954
Omalizumab and malignancy: Interim results from the EXCELS study

Mark Eisner, Mary Miller, Will Chou, Abdelkader Rahmaoui, Mary Bradley.

Objective: The EXCELS study is an FDA postmarketing commitment to evaluate the long-term safety of omalizumab.

Methods: EXCELS is an ongoing prospective observational study of approximately 5000 omalizumab-treated and 2500 non-omalizumab-treated moderate to severe persistent allergic asthma patients aged ≥12 years from 448 US centers who are followed up for up to 5 years. All reported potential malignancies are reviewed by an independent oncology panel. The primary analysis includes confirmed, incident study-emergent primary malignancies.

Results: This analysis of malignancy rates was based on interim study report 6 (data through 11/30/2010) which comprises 18, 860 person-years in the omalizumab cohort and 10, 947 person-years in the non-omalizumab cohort. Both cohorts had an average follow-up of 3.8 person-years. The incidence of study-emergent primary malignancy was 12.78 and 14.48 per 1000 person-years in the omalizumab and the non-omalizumab cohorts, respectively, corresponding to a rate difference of 1.70 per 1000 person-years (95% CI: 6.43 to 2.21).

Conclusions: In this analysis, the incidence of malignancy was similar in the omalizumab and non-omalizumab cohorts. These interim results are preliminary and the study is still ongoing. Because the study is observational, selection and other biases cannot be excluded.

Funding Source: Genentech Inc and Novartis Pharmaceuticals Corp.

P3955
Factors influencing the relative effect of leukotriene receptor antagonists (LTRA) and inhaled corticosteroids (ICS) as monotherapy in persistent asthma: A systematic review

Bhupenrasinh Chauhan, Franckie Ducharme. Clinical Research Unit on Childhood Asthma (CRUCA), CHU Ste-Justine Hospital Research Center, Montreal, QC, Canada.

Objectives: To compare the safety and efficacy of LTRA with ICS in patients with asthma across age groups, over time, baseline severity and ICS dose.

Methods: In a systematic review until Dec 2010, we included randomised controlled trials comparing LTRA to ICS for ≥30 days in children and adults with asthma. The primary outcome was exacerbation requiring systemic steroids. Secondary outcomes included lung function, asthma control, adverse effects and withdrawals.

Results: The 54 included trials comprised 13,460 patients (2,795 children) with mild (42%) or moderate (58%) airway obstruction. In 84% of trials, LTRA was compared to a low ICS dose over 4-52 weeks. Compared to ICS, 48% more patients treated with LTRA suffered exacerbations requiring systemic steroids (RR 1.48; 95% CI 1.18, 1.85). There was no significant difference in the magnitude of effect between children and adults, ICS dose, and over time. The benefit of ICS over LTRA was greater in patients with moderate vs. mild airway obstruction (RR=2.03 vs. 1.25, p<0.001). Exacerbations, mean (SD). Medical healthcare uses‡ 6.2 (7.08) 0.3 (0.91).

Conclusions: ICS remains superior to LTRA to prevent exacerbations and improve asthma control, irrespective of age group, ICS dose, and duration of treatment. However, the benefit of ICS is significantly greater in patients with moderate airway obstruction.

P3956
Real-life effectiveness of beclomethasone dipropionate/formoterol extra-fine combination in adult patients with persistent asthma

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Background: Omalizumab is a biologic for the treatment of moderate-to-severe persistent allergic asthma that is inadequately controlled with inhaled corticosteroids. At the time of FDA approval, the incidence of malignant neoplasms was higher among patients who had received omalizumab (0.5%) compared to placebo (0.2%) in clinical trials.

Objective: The EXCELS study is an FDA postmarketing commitment to evaluate the long-term safety of omalizumab.

Methods: EXCELS is an ongoing prospective observational study of approximately 5000 omalizumab-treated and 2500 non-omalizumab-treated moderate to severe persistent allergic asthma patients aged ≥12 years from 448 US centers who are followed up for up to 5 years. All reported potential malignancies are reviewed by an independent oncology panel. The primary analysis includes confirmed, incident study-emergent primary malignancies.

Results: This analysis of malignancy rates was based on interim study report 6 (data through 11/30/2010) which comprises 18, 860 person-years in the omalizumab cohort and 10, 947 person-years in the non-omalizumab cohort. Both cohorts had an average follow-up of 3.8 person-years. The incidence of study-emergent primary malignancy was 12.78 and 14.48 per 1000 person-years in the omalizumab and the non-omalizumab cohorts, respectively, corresponding to a rate difference of 1.70 per 1000 person-years (95% CI: 6.43 to 2.21).

Conclusions: In this analysis, the incidence of malignancy was similar in the omalizumab and non-omalizumab cohorts. These interim results are preliminary and the study is still ongoing. Because the study is observational, selection and other biases cannot be excluded.

Funding Source: Genentech Inc and Novartis Pharmaceuticals Corp.

Abstract printing supported by Chiesi. Visit Chiesi at Stand D.30
gium from December 2008 till December 2010. Patients were enrolled by pneumologists and general practitioners (GP). Visit 1 (Day 0): demographic and baseline asthma control data collection, initiation of BDPF treatment; Visit 2 (Day 61-240) and Visit 3 (Day 241-420): evaluation of asthma control by patients (Juniper ACQ7) and investigators (GINA asthma control score), assessment of BDPF safety/tolerability.

Results: 619 patients were enrolled: mean age 48±16.9 years, 54% female, 22.8% smokers, mean FEV1% pred 78.6±20.0. At visit 3 the mean daily beclomethasone dose was 266±127 μg.

Table 1. Evolution of ACQ7 and GINA asthma control scores

<table>
<thead>
<tr>
<th>Visit 1</th>
<th>Visit 2</th>
<th>Visit 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACQ7 (mean ± SD)</td>
<td>2.24±1.13</td>
<td>1.05±0.82*</td>
</tr>
<tr>
<td>GINA score (%)</td>
<td>46.8</td>
<td>49.3</td>
</tr>
<tr>
<td>GINA score (μg)</td>
<td>41.7</td>
<td>41.7</td>
</tr>
</tbody>
</table>

Methods: Patients (ages 18-55 years, with asthma ≥1 year, FEV1 ≥ 60%, 90%-95% predicted, airway reversibility ≥12%, and active smoking [≥0.5 to ≤ 2 pack/day]) were randomized (after a 3-week, single-blind, placebo run-in) to 1 of 3 parallel, 6-month, double-blind treatment arms. Primary efficacy endpoint was percent of days with Asthma Control (% days/AC) during treatment; AC was defined as a composite: β-agonist (SABA) ≥ 2 puff/day, no night-time symptoms (N-Sxs), and no unscheduled healthcare (U/Hc) or systemic-CS use. Adverse events (AEs) were also evaluated.

Results: The % days/AC over 6 months of treatment was 45% (Mont [N=347]), 39% (FP [N=336]) and 39% (Pro [N=336]; p-values for Mont and FP (each vs Pro) were p<0.05 and p<0.001, respectively. The difference between Mont and FP was not significant (p=0.14). Components of % days/AC (SABA and N-Sxs) also showed significant differences from Pro, but Asthma Attacks (defined as U/Hc or systemic-CS use) were infrequent and not significantly different. AEs occurred in similar proportions among treatment groups.

Conclusion: In a population of asthmatic patients actively smoking cigarettes, both montelukast 10mg daily and fluticasone 500 μg bid significantly increased the percent of days with asthma control, compared with placebo.

P3957

Effect of budesonide/formoterol, budesonide and terbutaline on exercise-induced bronchoconstriction in mild intermittent asthma

Nikolaos fort Vousontas1, Nikolaos Kafatos2, Katerina Raptopoulou3, Erika Niakas4, Christos Politis5, Marinos Vlahopoulos6, Thomas VlahopoulosJ, Dimitra Zonnios1, Tatiana Skordou1, Fotini Kaka1, Tommi Ekström4, Gunilla Hedlin4, Leif Jörgensen1, Jörgen Jørgensen4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J абсолютны4, Maria J absol...
Results: The peak median urinary concentration was found after 4hrs reaching 0.38±0.26 ng mL⁻¹ in A and 0.38±0.22 ng mL⁻¹ in C. Peak median plasma concentration was 0.07±0.03 ng mL⁻¹ for A and 0.06±0.03 ng mL⁻¹ in C. No difference was found between the groups.

Conclusions: There was no significant difference between symptom and satisfaction scores. There was a difference in scores when compared to the usual guideline group. IgE levels less than 30 iu/ml and IgE >30 iu/ml were p=0.774777 and p=0.774777 respectively. After admission the symptom level in group 1 decreased to 9.0±0.1 μM (p=0.11) as well as in control group it was at the same border (7.7±1.4 μM).

Conclusion: The results obtained demonstrate that liposome inhalation administered once a day during 14-days period has a significant antioxidant effect in patients with mild-to-moderate bronchial asthma.

P3962
Quantitative IgE levels in asthma and implications for treatment with omalizumab. Are the cutoffs to narrow? Mary Lynn Zaremba, Kristin Elliott, Alicia Redford, Nipurn Shah, Syed Ali, Sridhar Reddy. 3Div. of Pulmonary, Critical Care & Cardiology, 1210 18th Avenue, Port Huron, MI, United States

The use of omalizumab is constrained by the narrow quantitative parameters in its use. This study looks at experience in a small pulmonary practice as regards comparison study. All patients were divided in two groups: group 1 contains 25 patients, who received a liposome inhalation by compression nebulizer once a day (300 mg of phospholipids in each admission); group 2 contains 25 patients, who received a traditional therapy (control). Antioxidant activity was determined by the estimation of the exhaled nitric oxide level (ENDO) and total nitrite/nitrate (TNN) in exhaled breath condensate before and after the investigation period.

Results: There was a significant decrease of ENO level in group 1 from 31.8±2.4 to 7.1±1.4 ppb (p=0.001) after the observing period. In group 2 the ENO level was decreased from 29.7±3.9 ppb to 25.0±2.5 ppb (not significant). Patients in both groups had significantly higher levels of TNN before the study (7.9±0.8 μL/M and 8.4±1.1 μL/M respectively). After admission the symptom level in group 2 decreased to 9.8±0.0 μM (p=0.01) as well as control group it was at the same level (7.7±1.4 μM).

Conclusion: The results obtained demonstrate that liposome inhalation administered once a day during 14-days period has a significant antioxidant effect in patients with mild-to-moderate bronchial asthma.

P3963
The effect of liposome inhalation on non-invasive oxidative stress markers in patients with bronchial asthma

Alexander Listina, Igor Klimanov, Svetlana Soodaeva. Clinical and Experimental Biophysics, Pulmonology Research Institute, Moscow, Russian Federation

Background: The liposome inhalation demonstrates an antioxidant activity in the treatment of various diseases, confirmed both by experimental and clinical studies. The aim is to carry out a prospective study of antioxidant features of liposome administration in patients with the exacerbation of bronchial asthma.

Materials and methods: We enrolled 50 patients (age=37.6±7.5 year, men=64%) with bronchial asthma (FEV1>70%, steroid-naïve) in prospective comparison study. All patients were divided in two groups: group 1 contains 25 patients, who received a liposome inhalation by compression nebulizer once a day (300 mg of phospholipids in each admission); group 2 contains 25 patients, who received a traditional therapy (control). Antioxidant activity was determined by the estimation of the exhaled nitric oxide level (ENDO) and total nitrite/nitrate (TNN) in exhaled breath condensate before and after the investigation period.

Methods: All patients were divided in two groups: group 1 contains 25 patients, who received a liposome inhalation by compression nebulizer once a day (300 mg of phospholipids in each admission); group 2 contains 25 patients, who received a traditional therapy (control). Antioxidant activity was determined by the estimation of the exhaled nitric oxide level (ENDO) and total nitrite/nitrate (TNN) in exhaled breath condensate before and after the investigating period.

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Conclusion: The results obtained demonstrate that liposome inhalation administered once a day during 14-days period has a significant antioxidant effect in patients with mild-to-moderate bronchial asthma.

P3964
Stability and achievement of asthma control with higher doses of inhaled corticosteroids regular treatment Shih-Lung Cheng. Internal Medicine, Far Eastern Memorial Hospital, Taipei, Taiwan

Background: Uncontrolled asthma is characterized by variability. Previous GOAL study demonstrated that once asthma is achieved, the future risk of instability is greatly reduced. Higher stability (lower variability) in asthma control is also associated with a lower future possibility of unmatched healthcare resource use. In the study, we attempted to increase inhaled combined agents doses initially and hypothesized that stability was positively associated with the level of control achieved.

Methods: This was a prospective study and new diagnosed asthma patients were included and randomized into two groups. One group was treated with higher doses (HD) one month then shifted to guideline-practice (GP) treatment and another was treated with GP therapy model. Peak expiratory flow (PEF) asthma control test (ACT) and exacerbation frequency were measured. The follow-up time was 1/2 year.

Results: 39 patients were treated with HD and 40 patients were GP therapy policy. PEF change were significantly improved in HD group compared with GP (56±17 vs. 45±19, p=0.04). The obvious improvement especially in initial 2 months (77±39 vs. 52±23, p=0.01). There were significantly different in ACT change and exacerbation frequency in patients with mild and moderate persistent asthma using HD therapy.

Conclusion: Our findings demonstrated that patients with HD treatment were more improved and stabilized than patients with previous conventional therapy policy. Further evaluation should be performed more patients and long term follow-up to confirm the higher doses’ efficiency.

P3965
Comparison of the efficacy of ciclesonide with budesonide in mild to moderate asthma patients after step-down therapy Shih-Lung Wang1, Han-Pin Kuo2,3, Chun-Hua Wang2, 4, Chen-Hua Kang1,3,2, Chun-Hua Wang4, Ben-Ting Liu5,6, Wee-Ton Lin4, Chun-Hua Wang5, Han-Pin Kuo2,3, 1Division of Chest, Department of Internal Medicine, Saint Mary’s Hospital, Tainan City, Taiwan; 2Division of Chest, Department of Internal Medicine, Tainan Veterans General Hospital, Tainan, Taiwan; 3Division of Chest, Department of Internal Medicine, Chiayi Christian Hospital, Chiayi, Taiwan; 4Department of Thoracic Medicine, Chang Gung Memorial Hospital, Taoyuan, Taiwan

Inhaled corticosteroids are the most widely used controller treatment for asthma, and is the stepping down level when asthma is controlled with combination therapy. Ciclesonide is an inhaled corticosteroid with on-site lung activation that provides anti-inflammatory activity. The aim of this study was to compare the efficacy of ciclesonide (CIC) with budesonide (BUD) in 142 adult patients with mild to moderate asthma who were well-controlled with a combination of inhaled corticosteroids and long-acting β2-agonist. They were randomized to receive once-daily ciclesonide 320mg (n=73) or twice-daily inhaled corticosteroid 200mg (n=69) for 12 weeks. The forced expiratory volume in one second (FEV1), maximum mid-expiratory flow (MMEF) and asthma control test (ACT) score were evaluated. Tolerability and ranked stratification of patient and physician were assessed. At the end of study, the withdrawal rate of CIC group (26.4%) was significantly less than that of BUD group (42.7%, p=0.02). There was no difference of FEV1 and MMEF throughout 12-week treatment period in CIC group. In BUD group, FEV1 decreased significantly at 4-week (1.8±0.1 L, n=59, p=0.0006) and 12-week of treatment (1.9±0.1 L, n=59, p=0.01) compared with baseline (2.0±0.1 L, n=69). MMEF decreased significantly at 4-, 8- and 12-week compared to baseline in BUD group. ACT score decreased significantly at 4-week of treatment in BUD group compared with baseline. There was no difference of ACT score over the 12-week period in CIC group. In conclusion, ciclesonide was more effective and better drug adherence than budesonide in the stepping-down treatment of asthma from combination therapy.

TUESDAY, SEPTEMBER 27TH 2011
Hall 2-21 - 12:50-14:40

721s
Abstract printing supported by Chiesi. Visit Chiesi at Stand D.30
The effect of GSK2190915, a 5-lipoxygenase activating protein inhibitor, on the early asthmatic response to inhaled allergen.

P3966

Thematic Poster Session
Abstract printing supported by Chiesi. Visit Chiesi at Stand D.30

Morning PEF remained above 95% predicted throughout the study, though absolute 87% of patients. Equivalence was shown in morning PEF at the end of treatment pMDI 400/24 μg and Diskus 1000/100 one/salmeterol (FP/S) either DPI or pMDI entered a 2-month run-in with FP/S to evaluate whether lung function and asthma control can be maintained control.

Rationale:
Department, University of Pisa, Pisa, Italy; 2Medical Affairs, Chiesi Italy; 3Research Center on Asthma and COPD, University of Ferrara, Ferrara, Italy; 4Respiratory Medicine, Medicine Evaluation Unit, Manchester, United Kingdom; 5Department of Medical Statistics, Clinical Epidemiology and Biostatistics, Academic Medical Centre, Amsterdam, Netherlands; 6Department of Respiratory Medicine, University of Catania, Catania, Italy; 7Section of Respiratory Diseases, University of Ferrara, Ferrara, Italy; 8Resident Center on Asthma and COPD, University of Ferrara, Ferrara, Italy

Rationale:
Guidelines recommend asthma treatment to be adjusted to the lowest dose maintaining control.

Objectives:
To evaluate whether lung function and asthma control can be maintained in patients treated with high dose ICS/LABA combination after step-down.

Methods:
Prospective, multinational, randomized, open label, parallel group controlled trial. Patients treated with high dose (1000/100 μg daily) fluticasone/salmeterol (FP/S) either DPI or pMDI entered a 2-month run-in with FP/S Diskus 1000/100 μg daily. Controlled patients (GINA) were treated with either FP/S Diskus 500/100 μg daily or extrafine beclometasone/formoterol (BDP/F) pMDI 400/24 μg daily for 6 months. Morning PEF was the primary outcome.

Secondary outcomes included asthma control.

Conclusion: This retrospective analysis of all double-blind trials with BUD in asthmatic patients did not demonstrate any increased risk of diabetes mellitus/hyperglycaemia with BUD treatment. Funded by AstzA.Zeneca.

P3967

Asthma control and lung function after step down from high dose ICS/LABA combination therapy

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Pulmonary embolism, which is associated with exacerbation frequency and chronic OCS use. All VTE events were objectively diagnosed. Data were compared with the available incidence (ages 50-54 yr) in the general population (Naess 2007).

Results: Deep vein thrombosis (DVT) occurred in 3 and 2 patients with severe and mild-moderate asthma resp. and pulmonary embolism (PE) in 11 and 3. Overall risks were not increased.

Methods: 166 Outpatients with mild-moderate asthma (mean (range) age 49yr (18-80), 56% female, all using ICS), and 139 patients with severe asthma (52yr (18-77), 62% female, 39% using OCS) from 3 clinics in the Netherlands and Davos, Switzerland, were consecutively included in a cross-sectional study. Patients completed a questionnaire about previous VTE, risk factors and medication use. All VTE events were objectively diagnosed. Data were compared with the available incidence (ages 50-54 yr) in the general population (Naess 2007).

Hypothesis: The incidence of VTE is increased in asthma, and associated with asthma severity and OCS use.

Introduction: Many patients with severe asthma need inhaled (ICS) and chronic oral (OCS) corticosteroids for asthma control. OCS are associated with hypercoagulability and increased risk of venous thromboembolism (VTE). Also asthma itself is associated with a prothrombotic state (Brims 2009).

P3969

Increased incidence of pulmonary embolism in severe asthma

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Methods:
166 Outpatients with mild-moderate asthma (mean (range) age 49yr (18-80), 56% female, all using ICS), and 139 patients with severe asthma (52yr (18-77), 62% female, 39% using OCS) from 3 clinics in the Netherlands and Davos, Switzerland, were consecutively included in a cross-sectional study. Patients completed a questionnaire about previous VTE, risk factors and medication use. All VTE events were objectively diagnosed. Data were compared with the available incidence (ages 50-54 yr) in the general population (Naess 2007).

Results: Deep vein thrombosis (DVT) occurred in 3 and 2 patients with severe and mild-moderate asthma resp. and pulmonary embolism (PE) in 11 and 3. Overall risks were not increased.

Hypothesis: The incidence of VTE is increased in asthma, and associated with asthma severity and OCS use.

P3968

Risks of diabetes mellitus and hyperglycaemic adverse events in patients with asthma taking inhaled corticosteroids

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Background: A recent study of patients with lung disease and with prescriptions for inhaled corticosteroids (ICS) detected a 34% increased risk of diabetes mellitus.

Methods: A retrospective analysis evaluated the double-blind, placebo-controlled, clinical trials in asthma (duration 24 years of age, involving budesonide (BUD) or BUD/formoterol (26 trials, n=9067 for BUD; n=9526 for placebo). A supplementary dataset evaluated all double-blind, non-placebo controlled trials in asthma (duration >3 months), involving the use of ICS (60 trials, n=33496 for BUD, n=2773 for fluticasone propionate [FP]). Cox proportional hazards regression modelling, both adjusted and not adjusted by study, was used to estimate the relative risk of diabetes mellitus/hyperglycaemia adverse events (AEs) or serious adverse events (SAEs) in both the primary and supplementary datasets.

Results: In the primary dataset, the occurrence of diabetes mellitus/hyperglycaemia AEs was 0.13% for BUD and 0.15% for placebo (RR 0.98 [95% CI 0.38–2.50] p=0.96); the occurrence of diabetes mellitus/hyperglycaemia SAEs was 0% for BUD and 0.05% for placebo. In the supplementary dataset, the occurrence of diabetes/hyperglycaemia as AE and SAE was 0.19% and 0.03%, respectively. There was no increased risk with higher doses of BUD, nor any difference between BUD and FP. The risk for diabetes mellitus/hyperglycaemia increased with age, BMI and disease severity.

Conclusion: This retrospective analysis of all double-blind trials with BUD in asthmatic patients did not demonstrate any increased risk of diabetes mellitus/hyperglycaemia with BUD treatment.

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P3970
Effects of hydrocortisone on acute beta-blocker and histamine induced bronchoconstriction
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Introduction and objectives: The benefits of chronic beta-blockade in asthma have recently been questioned, however concerns of bronchoconstriction persist with the greatest risk after first dose. We investigated the safety of acute exposure to propranolol in asthmatics, sequentially challenged with histamine to mimic an asthma exacerbation and evaluated the role of hydrocortisone in potentiating salbutamol reversibility.

Methods: Persistent atopic asthmatics, ≤1000μg/day budesonide performed a randomised double-blind placebo-controlled crossover study. Following 10mg or 20mg of oral propranolol, patients received 400mg iv. hydrocortisone or placebo, followed by histamine challenge with nebulised salbutamol 5mg and ipratropium 500mcg recovery.

Results: 13 patients completed per protocol. Hydrocortisone did not potentiate salbutamol recovery post-propranolol and histamine challenge. Beta-blocker induced bronchoconstriction was demonstrated by spirometry and IOS. For the placebo visit, FEV1% fell 4.7% 2hrs post-propranolol whilst R5% increased 31.3%. On both visits FEV1% and R5% returned to baseline after salbutamol post-histamine.

Conclusion: Nebulised salbutamol produced a full recovery after propranolol and histamine induced bronchoconstriction, independent of hydrocortisone use. Our findings offer reassurance to those undertaking further evaluation of chronic beta-blockade as a potential treatment for asthma.