Effectiveness of indacaterol and tiotropium in patients with severe dyspnoea

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Introduction: Dyspnoea is a common, troublesome symptom of COPD. It is useful to know how patients (pts) with varying degrees of breathlessness respond to treatment.

Aim: We explored the effectiveness of the once-daily (od) long-acting inhaled bronchodilators indacaterol (IND) and tiotropium (TIO) in COPD pts according to baseline dyspnoea severity (median modified Medical Research Council (mMRC) score <2.0 or ≥2.0 (ie less or more dyspnoea)).

Methods: Data were pooled from three randomized studies of double-blind IND 150 µg od(n=745), IND 300 µg od(n=849) and placebo (PBO: n=1171) and open-label (o/l) TIO 18 µg od(n=411) in pts with moderate-to-severe COPD. Trough FEV₁, transition dyspnoea index (TDI), St George’s Respiratory Ques-
The improvement in FEV1 with NVA237 was seen immediately after the first dose on Day 1 (90mL at 5min and 144mL at 15min versus PBO, p < 0.001) and was sustained throughout the 52 Wk period. FEV1 AUC for 0-4h, 0-12h, 0-24h and 12-24h for NVA237 was significantly greater than PBO (p < 0.05) and numerically greater than TIO on Day 1, Wk 12, 26 and 52. Conclusion: NVA237 50µg QD provided rapid, sustained and clinically meaningful bronchodilation over 52 Wks with efficacy similar to tiotropium.

P2104
Sputum neutrophil monitoring is useful for long-term oxygen therapy in patients with COPD

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Introduction: Long-term oxygen therapy (LTOT) is the treatment proven to improve survival in chronic respiratory failure patients, especially chronic obstructive pulmonary disease (COPD). Participation of airway neutrophil inflammation is suggested to be a part of illness, such as COPD. The aim of this study is to evaluate whether sputum neutrophil monitoring is useful for LTOT in patients with COPD exacerbations.

Twenty two patients, mean age were 72 years, were participated in this study. Twenty patients survived to the follow-up after 14 months of this study. Before receiving LTOT, mean sputum neutrophil was 8%. However, after LTOT administration, sputum neutrophil was decreased to approximately 3% and reduced the number of hospitalizations including outpatient service. Also St George’s Respiratory Questionnaire score (SGRQ) was significantly improved. In peripheral blood, downward tendency was seen, but not so significant. Before outpatient service in COPD patients, average neutrophil percentage in the sputum was gradually raised up to 18% at 60% or more. We could respond for COPD exacerbations at an early stage using corticosteroid and antibiotic drugs. While this neutrophil participate mechanism is still unknown, further study should be needed including cytokine evaluation. However, this study indicates that in patients with COPD, long-term oxygen therapy is associated with airway sputum neutrophil reduction.

P2105
The effect of high dose N-acetylcysteine (1200mg daily) on airway function and airway trapping in COPD patients – A double blinded randomized placebo controlled trial

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Introduction: High dose N-acetylcysteine (NAC) has both antioxidant and mucolytic effect. However, there was a lack of study to demonstrate its beneficial use in COPD patients. Aims: To investigate the effect of high dose NAC (1200mg daily) on airflow function in stable COPD patients.

Methods: This is a 16-week double-blinded randomized placebo-controlled trial conducted in a government hospital in Hong Kong. Spirometry confirmed COPD patients (FEV1/FVC < 70%) were recruited and randomized into treatment (NAC 1200mg daily) and placebo groups. Both patients and doctors were blinded for treatment allocation.

P2106
Safety and efficacy of NVA237 once daily in Japanese patients: The GLOW4 trial

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

Methods: The primary objective of the 52-week, multi-center, randomized, open label, parallel group GLOW4 clinical trial was to assess the safety and tolerability of NVA237 50µg QD for 52 wks in Japanese patients with moderate-to-severe COPD. A secondary objective was to compare the safety and efficacy of NVA237 to open-label tiotropium 18 µg QD (TIO).

Results: 163 patients were randomized (NVA237=123, TIO=40); 84% completed. Mean age was 68.7 yrs, 97.5% male. Overall adverse events (AE) incidence was similar between NVA237 and TIO. The only AEs with >10% incidence in any group were COPD worsening (24.4 and 32.5%) and nasopharyngitis (30.9 and 32.5%) for NVA237 and TIO, respectively. Serious AEs occurred in 13 and 15 patients for NVA237 and TIO, respectively, with no deaths. There were no reports of notable pulse rate (>130 bpm, or >120 and +15 bpm from baseline) and QTc interval (Fidericia) >500ms over 52 wks. Dry mouth incidence was less frequent with NVA237 (1.6%) vs TIO (5%). A clinically significant increase from baseline in pre-dose FEV1 was observed for NVA (101 mL) and TIO (173 mL) at Wk 12. The event-free rate for moderate or severe COPD exacerbation was 78.9% for NVA237 and 76.6% for TIO at Wk 52.

Conclusion: NVA237 once daily had a safety and tolerability and efficacy profile similar to tiotropium in Japanese patients with moderate-to-severe COPD over 52 weeks.
P2106 Cost-effectiveness of adding budesonide/formoterol to tiotropium in severe COPD patients in four Nordic countries

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Objective: To assess the cost-effectiveness of budesonide/formoterol (B/F)+tiotropium (TIO) versus placebo (PBO)+TIO for the treatment of chronic obstructive pulmonary disease (COPD) patients eligible for inhaled corticosteroid monotherapy aged 50-75 years, from societal and healthcare perspectives in Denmark, Finland, Norway and Sweden.

Methods: The cost-effectiveness analysis was based on the 12-week, randomised, double-blind, parallel-group, phase III study (NCT01696289) in 651 COPD patients with moderate-to-severe COPD (mean FEV1 40.3% pred, mean pack-year history 40 pack-years). The primary outcome was the proportion of patients with a ≥50% improvement from baseline in pre-bronchodilator FEV1 (P/B-FEV1). The key secondary outcomes were death, exacerbation and hospitalisation. The last observation carried forward principle was used for missing values. The incremental cost-effectiveness ratios (ICERs) were estimated using bootstrapping.

Results: From a societal perspective, the ICER was estimated at €174 per additional quality-adjusted life-year (QALY) gained in Denmark, €126 per QALY gained in Finland, €138 per QALY gained in Norway and €152 per QALY gained in Sweden. From a healthcare perspective, B/F+TIO was dominant in Norway and the ICERs were estimated at DKK 1,580 (€212), €307, SEK 1,573 (€165) and DKK 1,580 (€212) for Denmark, Finland and Sweden, respectively. Including antibiotics decreased ICERs by 8-15%. Sensitivity analyses showed that results were overall robust.

Conclusion: The results indicate that B/F+TIO represents a clinical and economic benefit to healthcare systems and society for the treatment of COPD in the Nordic countries.

P2107 Effect of once-daily indacaterol in a predominantly Chinese COPD population: A 26-week Asia-Pacific study

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Rationale: The efficacy and safety of indacaterol (IND) once-daily (qd) inhaler LABA for the treatment of COPD, was investigated in a predominantly Chinese COPD population.

Methods: This double-blind placebo (PBO)-controlled 26-week study, randomized pts with moderate-to-severe COPD (FEV1 <40, post-bd FEV1/FVC ≥70%, FEV1 ≥30 to ≤80% pred, smoking history ≥10 pack-years) to IND 150 μg or IND 300 μg or PBO qd. Variables included trough FEV1 (mean of 23h 10min and 23h 45min post-dose) at Wk12 (primary) and 26, and health status (St George's Respiratory Questionnaire: SGRQ) and transition dyspnea index (TDI) at Week 26.

Results: Of 563 pts randomized (98.9% Chinese, 94.3% male, mean age 65.4 yrs, post-bd FEV1 49.9% pred), 85.6% completed. Both IND doses significantly improved trough FEV1 vs PBO (p<0.001), with IND-PBO diffs exceeding the prespecified MCID (0.12L) at Wk12 (0.15 ± 0.13L for 150 & 300 μg) and Wk26 (both 0.13L). TDI total score at Wk26 was superior to PBO for both IND doses (0.82 ± 1.11L) vs PBO (0.68 ± 1.04L). A significant reduction in time to exacerbation (56.5% vs 65.3% for IND 150, 300 μg vs PBO). Both doses provided improvements (i.e., decreases) from baseline in SGRQ total score of ≥4 units at Wk26 that were numerically greater than with PBO (raw mean changes: 9.6 ± 8.8 vs -7.0 units), with a similar pattern in the % pts with a clinically relevant gain in SGRQ score (≤-4 units; 65.9% ± 61.5% vs 66.0%). The incidence of AEs was 49.2%, 53.4% & 56.2% for IND 150, 300 μg & PBO.

Conclusions: Indacaterol provided effective bronchodilation in this predominantly Chinese population, with significant improvements in breathlessness and a trend towards improved health status.

P2108 Budesonide/formoterol vs formoterol, both via Turbuhaler® 4, in patients with moderate to severe COPD: PHASE III study results

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Background: This study evaluated the efficacy and tolerability of budeso- nide/formoterol (BUD/FORM) vs formoterol (FORM) in patients with moderate to severe COPD.

Methods: In this randomised, double-blind, parallel-group, phase III study (NCT01696289) patients with moderate to severe COPD for ≥2 years received either BUD/FORM 160/4.5 μg 2 inhalations twice daily via Turbuhaler® or FORM 4.5 μg 2 inhalations twice daily via Turbuhaler® for 12 weeks. The primary endpoint was exacerbation avoidance (pEA) in Finland while B/F+TIO was dominant in the other countries. Resource use from the treatment period in predose FEV1; secondary outcome measures included lung function time to first exacerbation, tolerability. Results: 1293 patients were randomised. Both BUD/FORM and FORM improved predose FEV1 (improvements of 4.6% and 1.5%, respectively); the change from baseline was significantly greater with BUD/FORM vs FORM (BUD/FORM:FORM ratio: 1.072; 95% CI: 1.013–1.032; p=0.0011). Significantly greater improvements in other lung function measures were also observed. BUD/FORM patients had a statistically significantly prolonged time to first exacerbation vs FORM patients (hazard ratio: 0.679; 95% CI: 0.507–0.909; p=0.004). Both treatments were well tolerated. The incidence and type of adverse events were similar in both groups; most commonly reported adverse events (BUD/FORM vs FORM): COPD (8.0% vs 9.4%), nasopharyngitis (5.5% vs 4.9%) and bronchitis (2.3% vs 2.3%).

Conclusions: BUD/FORM 160/4.5 μg 2 inhalations twice daily was more effective than FORM 4.5 μg 2 inhalations twice daily in patients with moderate to severe COPD. Both treatments were well tolerated. Funding: AstraZeneca.
P2110
The effect of tiotropium on lung dynamic hyperinflation and treadmill exercise capacity in mild to moderate COPD
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Rationale: In previous studies tiotropium improved cycle exercise duration in GOLD II-IV COPD patients. This double-blind crossover study (NOTCH2396) compared tiotropium with placebo in GOLD I and II COPD using treadmill exercise testing.

Methods: Patients were current or ex-smokers aged ≥40 y with post-bronchodilator FEV1/FVC <70%, FEV1 ≥50% predicted, and dynamic hyperinflation (>100 mL inspiratory capacity [IC] decrease during incremental treadmill exercise). Patients received tiotropium 18 µg gid and placebo for 6 weeks each (random order, 4-week washout). Patients performed constant work rate treadmill exercise at 80% of peak incremental work rate before and after each treatment period. The primary endpoint was the difference in exercise isometric IC change from baseline to Week 6 between tiotropium and placebo. Secondary endpoints included change in exercise duration.

Results: Patients (n=126, 52% male) had mean age 61 y, post-bronchodilator FEV1/FVC 59% and FEV1 77% predicted. Baseline IC was 2.27 L and exercise duration 447 s. The difference in change in isometric IC from baseline to Week 6 between tiotropium and placebo was statistically significant (65 mL, P=0.009). The difference in change in baseline exercise duration between tiotropium and placebo was not significant in the combined GOLD I+II (29.3 s, P=0.100) and GOLD I (23.5 s, P=0.415) groups, but was statistically significant for GOLD II (63.0 s, P=0.007).

Conclusions: Tiotropium was associated with reduced lung hyperinflation at rest and during exercise in GOLD I and II COPD patients. Significantly improved exercise duration was observed in GOLD II patients but not the combined or GOLD I groups.

P2111
Pretreatment with inhaled procaterol improves symptoms of dyspnea and quality of life in patients with severe COPD
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Objectives: To investigate the efficacy of the inhaled supplementary short-acting beta2-agonist (SABA) administered before the performance of daily activity (the SABA Assist Use) in patients with COPD.

Methods: Thirty outpatients with moderate to severe COPD (Stage II-IV), regular use of tiotropium bromide alone, and dyspnea during daily activities, were enrolled. Subjects self-administered 20µg of inhaled procaterol hydrochloride before daily activities no more than four times daily. Dyspnea symptom scores, St George’s Respiratory Questionnaire (SGRQ) activity domains, impulse oscillometry system parameters, and pulmonary function tests were recorded at the beginning and end of the 2-week study.

Results: More than 80% of subjects reported dyspnea when performing the following activities: walking up a slope (100.0%), climbing stairs (100.0%), gardening (93.3%), walking on flat ground (90.0%), bathing (86.7%), getting on a bus or train (83.5%), and changing clothes (80.0%). After 2 weeks, subjects with Stage III significantly improved dyspnea scores (walking up a slope (p=0.047), climbing stairs (p=0.014), gardening (p=0.034), walking on flat ground (p=0.006), getting on a bus or train (p=0.039), and changing clothes (p=0.045)). Both symptoms and activity SGRQ domains significantly improved in subjects with Stage III (p<0.036 and p<0.028, respectively). Resistance of small airways (R5-R20) and low-frequency reactance area (AX) significantly improved in subjects with Stage III (p=0.003 and p=0.004, respectively). No significant changes were found in pulmonary function tests.

Conclusion: The SABA Assist Use improved dyspnea symptoms in subjects with Stage III COPD.

P2112
The impact of treatment of chronic obstructive pulmonary disease (COPD) on function and quality of life of patients
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Purpose: To determine a possible correlation between objective laboratory data on the health of patients with Chronic Obstructive Pulmonary Disease (COPD) and the subjective perception of disease and quality of life by patients themselves. Also to investigate whether these two factors are consistent and whether there are corresponding changes over time after therapeutic intervention.

Methods: We studied 100 patients with COPD who completed the general health questionnaire SF-36 and the qualified for COPD questionnaire St. George’s (SGRQ) and were classified into four groups (four stages of COPD by GOLD) based on their spirometric performance (FEV1) during the first session of the investigation. After 6 months of specific treatment for each group the patients returned for a new spirometry and completed the two questionnaires again. The same changes happened with 20 controls who received absolutely no treatment.

Results: There was a direct correlation between FEV1 values with the scores of both SGRQ and SF-36 questionnaires in all study groups during sessions. Following the therapeutic intervention, improvement of FEV1 values with corresponding changes in the scores of questionnaires were observed in all patient groups. However, statistically significant differences emerged only in two groups of patients raising issues of medication revision taken by the other two groups.

Conclusion: It was confirmed that the subjective perception of COPD patients are consistent with objective findings that characterize them in course, and therefore both questionnaires used to measure the quality of life are reliable and record the changes.

P2113
Safety of fluticasone furoate (FF), an inhaled corticosteroid in combination with vilanterol (VI), a long-acting beta agonist in management of COPD exacerbations
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Introduction: FF and VI are in development as combined once-daily (OD) therapy for COPD.

Objectives: Assess the safety of FF/VI (3 strengths) and VI in COPD.

Methods: In two replicate 1 year studies, after a 28 day run-in with ADVAIR DISKUS® 250/50mcg, subjects received FF/VI 50/25, 100/25, 200/50mcg or VI 25mcg OD. Primary endpoint: annual rate of moderate/severe exacerbations (described separately). Safety endpoints included all, serious and fatal Adverse Events (AEs), Local Steroid Effects (LSE, including candidiasis), bone disorders (BD, including fractures) and pneumonia.

Results: Pooled safety findings are shown in the table.

<table>
<thead>
<tr>
<th>VI</th>
<th>PFVI</th>
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<tr>
<td>TTAE (%)</td>
<td>25 (N=818)</td>
</tr>
<tr>
<td>SAE (%)</td>
<td>50/25 (N=820)</td>
</tr>
<tr>
<td>FSAE (%)</td>
<td>100/25 (N=806)</td>
</tr>
<tr>
<td>FSFSAE (%)</td>
<td>200/25 (N=811)</td>
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AE*: drug-related
AE*: on-treatment, † on-/post-treatment
HR, Hazard Ratio. *On-treatment, † On-/Post-treatment. HR for LSE and BD were significantly higher for FF/VI vs VI in all comparisons except LSE at 010/25 (p=0.065).

Conclusions: In COPD patients FF/VI exhibited similar rates of serious and fatal AEs to VI, although rates of AE, BD, LSE and pneumonia were greater with FF/VI than VI alone. The efficacy of the combination is supported Funded by GSK: HZC102871-NCT011099463, HZC102970-NCT01107952.
P2114

Inhaled corticosteroid/long-acting beta-2 agonist (ICS/LABA) combination can decrease mortality of COPD patients, a nationwide population-based cohort study in Taiwan

Background: Chronic Obstructive Pulmonary Disease (COPD) remains a major public health problem. Current treatments, including pharmacological and non-pharmacological, can only alleviate symptoms, prevent exacerbation and improve quality of life. Previous large-scale studies failed to demonstrate benefit of mortality reduction which is also important for a chronic illness.

Objective: The aim of this study is to determine whether ICS/LABA combination can reduce mortality of COPD by using Taiwan National Health Insurance Database.

Method: This was a nationwide population-based cohort study. A total of 1989 COPD patients were identified from one million sampling cohort dataset between January to December in 2005. Patients with diagnosed in 2005 as COPD were grouped as non-controller user (n=1638), ICS/LABA (n=265) and LAMA (n=86). Cox regression model was used to evaluate the incidence of mortality and pneumonia in the following 3 years to December 2008.

Result: The incidence of pneumonia was not different among three groups. However, COPD patients with older age (H.R. 1.398 for every increase of 10 years, p < 0.0001) and male gender (H.R. 1.411, p < 0.001) had higher incidence to have pneumonia. The mortality rate was lower in patients who used ICS/LABA combination as compared with non-controller group (H.R. 0.694, p = 0.0165)

Conclusion: In the selected Taiwanese population, COPD mortality was lower among patients who used ICS/LABA. Incidence of pneumonia was not increased with ICS/LABA, but significantly related increased age and male gender.

P2116

Effect of formoterol alone and in combination with aclidinium on electrocardiograms in dogs

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Introduction: Co-administration of a long-acting β-agonist with an anticholinergic is common clinical practice for the management of COPD, but there are concerns that systemic exposure to both drugs could cause undesirable pharmacodynamic effects on the heart.

Aims: To evaluate the cardiovascular safety of formoterol alone and in combination with aclidinium in conscious dogs.

Methods: Formoterol (1, 3, 10 μg/kg iv), aclidinium (50, 167 μg/kg iv) and formoterol+aclidinium (1:1, 3:5:10, 10:167 μg/kg iv) were administered to fasting, male Beagle dogs (n=4; 16-16 kg) in a 3-min perfusion. Each dog received each dose with 6-day washout. Electrocardiograms were recorded at baseline (for 1 h) and 24 h post-administration (for 90 min) and assessed for ventricular tachycardia (VT) and premature ventricular complexes (PVC).

Results: Formoterol alone showed a dose-dependent trend to induce VT. VT was observed in 0, 1 and 4 animals treated with formoterol 1, 3 and 10 μg/kg, respectively. Aclidinium alone induced VT. The combination of formoterol-aclidinium resulted in VT in a similar number of animals as formoterol alone (2 and 3 animals with 3:50 and 10:167 μg/kg, respectively). Similar results were observed for PVC. At the highest doses of formoterol and aclidinium, the plasma concentrations corresponded to 32 and 4000 times those reported in human plasma after clinically relevant doses.

Conclusions: Addition of aclidinium does not alter the incidence or rate of formoterol-induced VT or PVC in dogs. These results suggest that aclidinium has no synergistic interaction on cardiac function with β-agonists.

This study was supported by Almirall S.A., Barcelona, Spain.

P2117

Risk of pneumonia related to budesonide use in COPD: An updated pooled analysis

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Introduction: Aclidinium bromide is a novel, long-acting muscarinic antagonist currently under investigation for the maintenance treatment of COPD. Safety data from a long-term efficacy and safety trial of twice-daily (BID) aclidinium are presented here.

Methods: In this 52-week study, moderate-to-severe COPD patients were randomised (1:1) to receive aclidinium 200 μg or 400 μg BID. Safety was assessed via adverse events (AEs), vital signs, and 12-lead ECG.

Results: A total of 605 patients were randomized, and 602 (99.5%) were in the safety population. Postbronchodilator FEV1, and percent predicted at screening were (mean ±SD) 1.55 ±0.54 L and 52.3 ±13.2 L. The incidence of AEs was similar across the aclidinium 200 μg and 400 μg groups and most were mild or moderate. The most common AE and most frequently reported AE leading to discontinuation was COPD exacerbation, with a similar percentage of patients between groups who discontinued due to exacerbations (200 μg 9 (2.9%); 400 μg 8 (2.7%)). The incidence of typically expected anticholinergic AEs was low and similar between groups (e.g. dry mouth: 200 μg, 1.3%; 400 μg, 2.7%; constipation: 200 μg, 2.9%; 400 μg, 1.7%). Cardiac and cerebrovascular AEs did not occur in a dose-related manner. The 200 μg and 400 μg groups had similar incidences of serious AEs, with values [n (%)] of 29 (9.3) and 29 (10.0), respectively. One patient in each treatment group died during the study (200 μg, biliary sepsis; 400 μg, subarachnoid hemorrhage), but neither death was deemed to be related to treatment.

Conclusions: Twice-daily aclidinium 200 μg and 400 μg were safe and well tolerated over 52 weeks with a similar safety profile for both doses.

P2119

Effect of augmentation therapy on immune function of patients with severe Alpha-1 antitrypsin deficiency

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Introduction: Augmentation therapy with human plasma derived AAT, and comparing them to ZZ individuals with early-onset emphysema. Approximately 5% of AATD individuals have other deficiency alleles including Null alleles which do not express AAT. Although AAT production in monocytes is relatively small in comparison with hepatocytes, local regulation of the antiprotease shield represents an important first line of defense during infection and inflammation.

Our aim was to investigate the anti-inflammatory properties of AAT by studying individuals homozygous for Null mutations who were receiving augmentation therapy with human plasma derived AAT, and comparing them to ZZ individuals and MM healthy controls.

We isolated peripheral blood monocytes from Null/Null and ZZ patients (with/without therapy), and MM controls. To investigate cytokine production, monocytes were maintained for 24 hours in the presence/absence of LPS. ELISAs and quantitative RT-PCRs were used to evaluate cytokine expression. Superoxide production and chemotactic activity were measured in monocytes.

Augmentation therapy was associated to interleukin IL-6 and IL-8 production from ZZ monocytes at both. Moreover, we noted a reduced chemotactic activity and superox-
ide production in AATD individuals receiving augmentation therapy in comparison to untreated AATD patients. Augmentation therapy in AATD individuals (ZZ and Null/Null) appears to modulate immune function and may provide a rationale for reduced exacerbations in subjects receiving augmentation therapy.

P2120 NFAT subtypes in regulating Th2 lymphocytes
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Background: Nuclear factor of activate T cells (NFAT), consists of five members and plays a pivotal role in regulating T lymphocyte activation. Among the five subtypes of NFAT, NFAT1, NFAT2 and NFAT4 were recognized as the key family members associated with allergic diseases. However, evidence regarding the functions of NFAT1 and NFAT2 in Th2 cells are still conflicting.

Aims and objectives: Therefore, we explored the functions of NFAT1 and NFAT2 on Th2 lymphocytes.

Methods: Knockdown of NFAT1 and NFAT2 using small interfering RNA (siRNA) was performed in the murine Th2 lymphocyte cell line (D10.G4.1). Real-time qPCR, Western Blotting and ELISA were performed to test the relatively expression of Th2 cytokine mRNA and protein in cells and culture supernatant.

Results: D10 cells express IL-4, IL-5, IL13 and GATA3 mRNA level. NFAT1 siRNA and NFAT2 siRNA selectively suppressed the expression of NFAT1 and NFAT2 respectively at both the mRNA and protein level. Higher levels of IL-4, IL-5 and IL-13 were seen in NFAT1 siRNA treated Th2 cells. This suggests that NFAT1 may play a negative role in Th2 cytokine expression. Interestingly, the opposite effect was seen with NFAT2 siRNA. NFAT2 siRNA down-regulated the expression of IL-4, IL-5 and IL13 mRNA levels. This was associated with a reduction in the expression of GATA3 mRNA and protein.

Conclusions: NFAT1 may play a negative role in regulating Th2 cytokines whilst NFAT2 may have the opposite effect.