A prospective 10-year-follow-up study has been designed to evaluate the natural history of LAR and the new incidence of systemic atopy. The majority of LAR patients were non-smoker women with moderate/severe persistent perennial rhinitis, without family history of atopy and city dwelling. At initial evaluation conjunctivitis (52.3%) and asthma (18.8%) were the most frequent comorbidities, and D. pteronyssinus (51.1%) the main specific aeroallergen detected by NAPT. After 5 years a worsening of rhinitis was detected in 26.2% patients, with increase in persistence and severity of symptoms. New associations to conjunctivitis (7.9%) and asthma (5.6%) were also detected. Systemic atopy was detected by SPT and/or serum specific IgE in LAR (12/176, 6.81%) and control group (4/88, 4.5%), without significant differences.

Conclusions: The results of the first 5-year-follow-up study show that a similar proportion of LAR patients and healthy controls developed systemic atopy, suggesting LAR and classical AR can be two independent entities. However, in order to ensure these findings, it is necessary to wait for the conclusion of the 10-year-follow-up study actually in progress.

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ORAL PRESENTATIONS

O1 Local allergic rhinitis: natural history
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Background: Local allergic rhinitis (LAR) is a common respiratory disease with a prevalence of 25.7% in rhinitis population. However, whether LAR is a first step in the development of classical allergic rhinitis (AR) with systemic atopy or not, needs to be explored. The objectives of this study were to evaluate the natural history of LAR and the new incidence of systemic atopy.

Methods: A prospective 10-year-follow-up study has been designed to evaluate 194 LAR patients and 97 healthy controls. All LAR patients had positive response to nasal allergen provocation test (NAPT) with at least one aeroallergen. Demographic and clinical questionnaire, spirometry, skin prick testing, and serum specific IgE antibodies to common aeroallergens were evaluated yearly, and NAPT were performed at initial evaluation and after 5 and 10 years of evolution.

Results: These data represent the results of the first 5 years of the follow-up. The majority of LAR patients were non-smoker women with moderate/severe persistent perennial rhinitis, without family history of atopy and city dwelling. At initial evaluation conjunctivitis (52.3%) and asthma (18.8%) were the most frequent comorbidities, and D. pteronyssinus (51.1%) the main specific aeroallergen detected by NAPT. After 5 years a worsening of rhinitis was detected in 26.2% patients, with increase in persistence and severity of symptoms. New associations to conjunctivitis (7.9%) and asthma (5.6%) were also detected. Systemic atopy was detected by SPT and/or serum specific IgE in LAR (12/176, 6.81%) and control group (4/88, 4.5%), without significant differences.

Conclusions: The results of the first 5-year-follow-up study show that a similar proportion of LAR patients and healthy controls developed systemic atopy, suggesting LAR and classical AR can be two independent entities. However, in order to ensure these findings, it is necessary to wait for the conclusion of the 10-year-follow-up study actually in progress.
O3
A historical cohort study of eosinophilic inflammation in chronic rhinosinusitis with nasal polyps in Okayama, Japan
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Clinical and Translational Allergy 2013, 3(Suppl 2):O3

Background: CRSwNP (chronic rhinosinusitis with nasal polyps) is characterized with eosinophil infiltration into sinonasal tissues in Caucasian patients. In Japan, this condition was thought to be an infectious disease (so called "empyema") for a long time. However, after a clinical profile of ECRS (eosinophilic chronic rhinosinusitis) was first introduced by Moniyama in 2002, the prevalence of ECRS in CRSwNP seems to be increasing in clinical setting. In the present study, we examined a historical cohort study and determined the alteration of eosinophilic inflammation in sinonasal tissues in Japanese CRS.

Method: Specimens of the sinonasal tissues from adult patients with CRSwNP were collected at the time of paranasal sinus surgery. We selected surgery specimens between 1961 and 1984 (Group A: n=100) and all subjects in 2012 (Group B: n=104 ), for a comparative assessment used historical cohort study. The lamina propria just beneath the epithelial layer was observed under a light microscope, and the number of infiltrated eosinophils per visual field at ~400 magnification was counted.

Result: The number of eosinophils infiltrating the nasal or paranasal sinus mucosa was significantly larger in Group B (2012) than Group A (1961-1984).

Conclusion: This result was consistent with the report that patients with ECRS have been increased in Japan. The increase of co-morbidity including allergic rhinitis or bronchial asthma may cause an increase of patients with ECRS. Secondely, macrolide therapy for CRS became popular in the previous two decades in Japan. Therefore, the decrease of infectious CRS which requires surgical treatment may affect the increase of ECRS.

O4
Quality of life and use of medication in chronic allergic and non-allergic rhinitis patients
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Introduction: In contrast to the significant number of studies indicating the impairment of QoL in AR, the degree of impairment in Quality of Life (QoL) in NAR remains underexposed. Again in contrast to AR, almost no evidence-based therapies for NAR patients exist. We assessed QoL in NAR compared to healthy controls and AR patients as positive controls and investigated whether the use of treatment in patients with NAR and AR had effect on QoL.

Methods: An observational cohort study with 585 AR and 408 NAR patients was performed. Patients filled in the mini-RQLQ, assessing QoL related to symptoms of rhino-conjunctivitis. For the purpose of validation of the mini-RQLQ in NAR patients, 35 healthy controls working at the Otorhinolaryngology department were recruited. Both AR and NAR were defined as two or more of the following symptoms for >1 hour on most days: watery anterior rhinorhoea, (paroxysmal) sneezing, nasal obstruction, nasal pruriitus and/or conjunctivitis. For AR, these clinical findings had to be combined with one or more positive results on skin prick testing, relevant to the symptoms of rhinitis and/or conjunctivitis. For NAR, these clinical findings had to be combined with negative skin prick test results. A factor analysis assessing influence of age, gender, ARIA and use of medications performed.

Results: Validation of the mini-RQLQ for NAR showed that this questionnaire is able to discriminate between NAR and healthy controls. Analysis of a total of 111 NAR patients compared to 167 AR patients, showed a significant higher impairment of QoL in NAR compared to AR patients, both on overall symptom score as on different sub domains. The mean overall symptom score (2.45) of NAR patients was significantly higher (p = 0.002) compared to the overall symptom score of AR patients (1.94). A factor analysis showed no influence of any factors assessed on QoL, including use of medication.

Conclusion: NAR patients had a significant higher impairment of QoL compared to AR patients. Use of medication did not influence QoL in AR and NAR.

O5
Sinonasal ultrastructure of the transplant hematopoietic stem cell and chronic graft-versus-host disease with rhinosinusitis
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Background: It is believed that immunosuppression is the sole cause for the occurrence of rhinosinusitis in hematopoietic stem cell transplant (HSCT). There is a high incidence of sinusitis in recipient’s patients, especially those with Chronic Graft Versus Host disease (GVHD). Histopathological abnormalities were described in recipient’s sinus mucosa comparing to the immunocompetents patients. There are also mucosal abnormalities related to the cytotoxicity in the transplanted patients with chronic GVHD, but no difference in ultrastructure between HSCT patients with and without GVHD, except increased goblet cells in patients without GVHD. The relation between the sinonasal mucosa abnormalities of patients with and without GVHD and rhinosinusitis is not well established yet.

Objective: To verify the ultrastructure of the sinonasal mucosa of HSCT with and without GVHD with rhinosinusitis in order to understand the cause of high sinusitis incidence in recipients with and without GVHD.

Method: A preliminary prospective study with statistical analysis of data obtained from the evaluation of the mucosa of the unicinate process by transmission electron microscopy of those recipients with (10) and without GVHD (9) with rhinosinusitis.

Results: 93% of transplanted patients with GVHD and 62% of those without GVHD had 2 or more rhinosinusitis. Only the presence of microvilli was significantly increased in patients without GVHD. There was no significant difference in the cilia number, cilia ultrastructure, squamous metaplasia, goblet cells or ciliatedastic vacuolization between those groups.

Conclusion: The recurrence of rhinosinusitis seems to be higher in chronic GVHD patients, however no abnormalities were found in the ultrastructure of their sinonasal mucosa, except increased microvilli in those without GVHD. This is a preliminary study and an increased sample might modify statistical analysis, as well as the comparison of recipients without rhinosinusitis.

O6
Platelet activating factor-induced mast cell degranulation is inhibited by rupatadine, and to a lower extent by levocetirizine and desoratadine, in a mast cell line (LAD-2)
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Background: Platelet activating factor (PAF) is a lipid mediator that appears to be involved in the pathophysiology of several allergic reactions such as anaphylaxis and potentially urticaria and allergic rhinitis. The role of rupatadine, a drug with dual antihistamine and anti-PAF effect, in mast cell (MC) degranulation is not known. The objective of this study was to investigate the expression of PAF receptors and the effect of rupatadine on PAF-induced MC degranulation compared with other second generation antihistamines (desloratadine, levocetirizine) and a pure specific PAF inhibitor in a human mast cell line (LAD-2).

Methodology: MC degranulation was evaluated by the a-hexosaminidase and histamine release while PAF receptor expression was evaluated by western blot. After stimulation with PAF in a dose-response and time course manner, the optimal PAF conditions to induce LAD-2 degranulation were identified (10 µM and 30 minutes). The effects of rupatadine, desloratadine, and levocetirizine (from 1 µM to 100 µM) on PAF-induced LAD-2 degranulation were investigated. The inhibitory effect of CV6209 (specific anti-PAF) at 2 µM was used as positive control in all experiments.
Results: Protein expression of the PAF receptor was found in LAD-2 cells. Rupatadine (5 to 10 µM, p<0.05) and levocetirizine (5 µM, p<0.01) but not desloratadine inhibited PAF-induced α-hexosaminidase release. Rupatadine (1 to 10 µM, p<0.01), levocetirizine (1 to 25 µM, p<0.05), and desloratadine (10 µM, p<0.05) all inhibited PAF-induced histamine release.

Conclusions: This study shows that the anti-H1 compounds rupatadine, and to a lower extent levocetirizine and desloratadine, have an anti-PAF effect in the mast cell line LAD-2, suggesting that rupatadine could be more effective than other antihistamine drugs in those allergic disorders where PAF may act as an important inflammatory mediator.

07 Two year persistent treatment effect in reducing nasal symptoms of cat allergy after 4 doses of Cat-PAD, the first in a new class of synthetic peptide immuno-regulatory epitopes
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Background: Treatment with Cat-PAD (also known as Tolerumune® Cat, the first in a new class of synthetic peptide immuno-regulatory epitopes), in an Environmental Exposure Chamber (EEC) model of cat allergy showed a persistent treatment effect one year [1] and two years [2] after administration of only 4 injections over 12 weeks. Here we report the differences in Total Nasal Symptom Scores (TNSS) between Cat-PAD treatment arms and placebo two years after treatment started.

Method: Originally 202 subjects were randomised to 4 × 6nmol Cat-PAD 4 weeks (wk) apart, 8 × 3nmol Cat-PAD 2 wk apart, or placebo. EEC challenges were performed at baseline and 18-22 wk. 89 subjects were recruited into a follow-on study one year after the start of treatment. Of the subjects who completed the one year EEC challenge, 50 subjects were recruited for a further EEC challenge 100-144wk after the start of treatment. All EEC challenges consisted of 4 consecutive days of 3 hours of allergen exposure with Fel d1 levels of circa 50 ng/m3. The 4 day challenge was designed to ensure late phase responses were present in the nasal airway. Subjects scored each of 4 symptoms (Running nose; Sneezing; Blocked nose; Itchy nose) on a scale of 0-3 every 30 minutes during the EEC challenge. These scores were summed to give a TNSS on a scale of 0-12.

Results: The least squares (LS) mean TNSS was significantly lower (p<0.05) for 4x6nmol Cat-PAD vs placebo at the following EEC challenge: Day 1 at 2 h and 2.5 h; Day 2 at 2 h, 2.5h and 3h; Day 3 at 1 h, 1.5 h, 2 h, 2.5 h and 3 h. On Day 4 of EEC Challenge, when the cumulative allergen challenge is greatest and late phase responses in the nose are likely to be maximal, LS mean TNSS was significantly lower for 4 × 6nmol Cat-PAD vs placebo at 2 h (4.818 vs 7.762, p=0.0090), 2.5 h (5.091 vs 7.667, p=0.0290) and 3 h (4.818 vs 7.952, p=0.0080) time points. No significant reductions in LS mean TNSS were observed for 8 × 3nmol Cat-PAD vs placebo.

Conclusion: Treatment with 4 injections of 6nmol Cat-PAD over 12 wk showed a substantial reduction in patients’ TNSS that persisted two years after starting treatment. The treatment effect is substantial under conditions where late phase responses are expected to be present in the nasal airway. Cat-PAD is the first in a new class of synthetic peptide immuno-regulatory epitopes and may confer long-term disease-modification in chronic nasal airway disease due to cat allergy.

References

08 Expression of the epithelial polymeric immunoglobulin receptor is decreased in allergic rhinitis and eosinophilic rhinosinusitis
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Clinical and Translational Allergy 2013, 3(Suppl 2):O8

Background: Transcytosis of immunoglobulin A (IgA) through polarized bronchial and sinonasal epithelial cells is mediated by the polymeric immunoglobulin receptor (pIgR), which represents the rate-limiting factor for this frontline protective mechanism in the airways. pIgR expression is decreased in COPD, lung cancer and nasopharyngeal carcinoma, while its role in sinonasal chronic inflammatory diseases has not been explored. The aim of this study was thus to assess pIgR expression in sinonasal mucosa of patients with chronic rhinosinusitis with (CRSwNP) or without polyps (CRSsNP) and in allergic rhinitis (AR), as well as IgA and SC (the released soluble part of the pIgR) in nasal secretions.

Methods: Nasal and ethmoidal biopsies, as well as nasal fluid, were collected from patients with CRSwNP, CRSsNP and AR, as compared to control subjects. pIgR expression was analyzed by RT-qPCR and immunohistochemistry. IgA and SC were measured in nasal secretions by ELISA. Quantification of mucosal eosinophils was performed following hematoxylin-eosin staining.

Results: RT-qPCR showed a significant reduction of pIgR expression in ethmoidal biopsies from CRSwNP (p = 0.01) and AR (p = 0.04). This reduction was confirmed at the protein level by immunohistochemistry, and resulted into reduced levels of SC and trends for reduced IgA in nasal secretions from these patients. Decreased pIgR expression was mainly observed in patients with increased mucosal eosinophils.

Conclusion: Epithelial pIgR expression is decreased in patients with CRSwNP and AR, results in decreased SC (and IgA) in nasal secretions, and closely correlates to Th2-type eosinophilic inflammation. Whether this defect leads to impaired defense of the upper airways against pathogens remains to be explored.

09 Downregulation of epithelial MHC II expression in chronic rhinosinusitis with polyps
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Clinical and Translational Allergy 2013, 3(Suppl 2):O9

Background: Inflammation in the nasal mucosa has been shown to correlate with the development of CRSwNP (chronic rhinosinusitis with nasal polyps). The mechanism behind this is not fully understood but changes in the activity of the immune system might contribute to the growth of polyps. The present study focuses on the potential role of MHC II (major histocompatibility complex class II) in the cell surface proteins of chronic rhinosinusitis with nasal polyps development.

Methods: Biopsies from polyops were obtained from patients with CRSwNP (with and without local steroid treatment during at least six consecutive weeks) as well as from the mucosa (concha inferior) of healthy control subjects. The obtained specimens were homogenized and subsequently analysed with flow cytometry.

Results: Preliminary data indicates a downregulation of MHC II expression in polyop epithelial cells from patients with CRSwNP compared to healthy patients (healthy controls: 60.2 ± 7.8; polyps 31.1 ± 7.4; p < 0.05). This reduction seems to be independent of the steroid treatment. In contrast, the level MHC II/CD86+ on epithelial cells was downregulated in patients receiving steroid treatment but not in those without treatment. The mechanisms involved are presently investigated in mice.

Conclusion: Expression of MHC II and its co-receptor CD86 can be seen on epithelial cells in the mucosa of healthy controls as well as within the polyps of CRSwNP patients. This suggests a role for epithelial cells in the antigen-presenting procedure. Change of the MHC II expression, altering the inflammatory activity in response to invading microorganisms, might contribute to the development of polyps.

O10 Matrix metalloproteinases, tissue inhibitor of metalloproteinase and transforming growth factor A1 in the remodeling of chronic rhinosinusitis in North China
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http://www.ctajournal.com/supplements/3/S2
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Background: To evaluate the expression and roles of matrix metalloproteinases (MMPs), tissue inhibitor of metalloproteinase (TIMP) 1, 2, 3, 4, and transforming growth factor-α (TGF-α) in chronic rhinosinusitis with or without nasal polyps (CRSsNP) and with nasal polyps (CRSwNP) in North China.

Method: 100 cases of NP tissue, 25 cases of sinus mucosa of CRSsNP and 25 cases of control were enrolled in the present study. ELISA was used to measure MMP-1,2,3,7,8,9,12,13 and TGF-α1 in homogenization.

Results: MMP-8,9 were the highest among all above MMPs. MMP-8 of NP tissue was much higher than that of CRS and control tissue (P<0.001). MMP-9 of NP tissue was also significantly higher than that of CRSsNP and control tissue (P<0.05). MMP-7 of NP tissue and CRSsNP were much higher than that of control tissue (P<0.001). MMP-2 of CRSsNP tissue was much higher than that of NP and control tissue (P<0.001). TIMP-1, 2, 3 were the highest among all the four TIMPs. TIMP-1 of CRSsNP was much higher than that of NP and control tissue (P<0.001 and P<0.05 respectively). TIMP-2 of NP and CRSsNP tissue were much higher than that of control tissue (P<0.01). TIMP-3 of CRSsNP tissue was much higher than that of NP and control tissue (P<0.01 and P<0.05 respectively). There were no significantly difference of TGF-α1 among the three groups.

Conclusion: Different MMPs and TIMPs may play different roles in the remodeling of CRSsNP and CRSwNP.

Background: The association between smoking and lower airway inflammation and disease is well documented; however, it is not established whether smoking also induces disease of the upper airways.

Method: A cross-sectional study of a random population sample (n=3762; age 18-69 years) was conducted in Copenhagen, Denmark. Study subjects were invited to a general health examination that included questions related to nasal symptoms (SNOT-22) and to other HRQL measures, like Sino-Nasal Outcome Test-22 (SNOT-22). Mean spirometric values were not significantly decreased in any group. The association with chronic bronchitis was stronger in non-allergic chronic rhinosinusitis than in allergic rhinitis, whereas the opposite was observed for asthma.

Conclusion: This study confirms that both smoking and chronic bronchitis are associated with non-allergic sinus disease. We conclude that smoking, at least in some cases, can be a triggering factor for the development of non-allergic sinus disease.

Background: Patients with chronic rhinosinusitis with or without nasal polyps (CRSsNP/CRSwNP) benefit from endoscopic sinus surgery (ESS), with an estimated success rate of 80%. At present, it remains unclear to what extent the presence of eosinophils, eosinophilic mucin (EM) and fungal hyphae (FH) in secretions influence the clinical outcome and recurrence of disease after ESS.

Objective: By delineating CRS groups and subgroups based on the finding of eosinophils, EM and FH, differences in the frequency of recurrent disease after ESS over a longer period of time were investigated.

Methods: A prospective mono-centre study including 221 CRS patients who were unresponsive to medical treatment and underwent ESS, was performed. All tissue and sinonasal secretions were microscopically examined for the presence of eosinophils, EM and FH. Patients were followed for 3 years after surgery. Recurrence was defined according to the EPOS clinical control assessment, based on nasal endoscopy, symptoms and the need for systemic treatment.

Results: In total, 96 CRSwNP and 125 CRSsNP patients were included. Eosinophils were found in 78% of CRSwNP patients compared to 42% in CRSsNP. Eosinophilic mucin was observed in 52% of the CRSwNP group versus 20% of the CRSsNP group. Furthermore, secretion analysis revealed FH in 11% CRSwNP patients compared to 3% CRSsNP patients. Recurrence in the total group was 22% over 3 years. CRSwNP patients with eosinophilic involvement showed a recurrence rate of 48%. When the airway mucus secretions were positive for EM and FH the recurrence rate was even 73%.

Conclusion: The presence of eosinophilic greatly increases the risk of recurrent disease in CRSwNP patients. The finding of EM and FH in the collected sinonasal airway mucus secretions provides valuable information regarding the clinical outcome and the increased likelihood of CRS recurrence after ESS.

Background: Chronic rhinosinusitis (CRS) is a common disorder with a significant impact on health-related quality of life (HRQL). Due to symptoms based diagnosis, disease severity is usually estimated using questionnaires which evaluate subjective scores on severity of symptoms and deterioration of HRQL, like Sino-Nasal Outcome Test-22 Questionnaire (SNOT-22). Objective severity staging is rather based on computerized tomography (CT) scores than on severity of inflammation. There is recent evidence that perceived stress has significant impact on asthma incidence and hospitalization, as well as on allergic rhinitis. As CRS is comorbidity of asthma and allergic rhinitis, we hypothesized that perceived stress may have impact on severity of CRS. The aim of the study is to correlate objective and subjective outcome measures with perceived stress.

Method: The study was conducted in 29 patients with CRS, with and without nasal polyps, scheduled for surgical treatment. After giving their informed consent, patients filled in SNOT-22 and Measure of Psychological Stress for assessment of perceived stress. We divided SNOT-22 Questionnaire into 6 subgroups related to nasal symptoms (SNOT-22 nasal) and to other symptoms (HRQL SNOT-22). These results were correlated with Lund-Mackay CT score and semi-quantitative scoring of inflammatory cells infiltration of sinus mucosa.

Results: There are significant positive correlations between HRQL SNOT-22 set of questions and MPS score (Pearson test, r =0.49, p=0.008) and between total SNOT-22 and MPS score (r=0.45, p=0.013).
between scores of nasal and HRQL SNOT-22 is also significant (r=0.53, p=0.003). There is also significant correlation between scores of eosinophilic and mononuclear of infiltration (r=0.63, p=0.001). The only difference between CRSwNP and CRSsNP patients is significantly higher mononuclear infiltration in CRSsNP, and higher CT score in CRSwNP.

**Conclusion:** Results are suggesting that subjective scoring of disease severity is related to perceived stress in CRS patients. As no correlation was found between perceived stress and inflammation severity or CT severity scores, further research in order to evaluate possible cause-and-effect relationship should be undertaken. Our results suggest that CRS staging based on combined symptoms and HRQL scoring, may be moderated by patients’ stress exposure and perception.

**O14**

**Nasal allergen provocation test in nasal polyposis with and without allergy**

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**Clinical and Translational Allergy 2013, 3(Suppl 2):O14**

**Background:** CRSwNP is characterised by eosinophilic inflammation and local IgE production. The amount of local tissue IgE in CRSwNP is independent of the atopic status and serum IgE of the patient. Moreover patients with CRSwNP and pollen allergy do not show prominent symptoms during season.

**Methods:** Four groups of patients (n=48) underwent nasal allergen provocation test for grass pollen. We included 12 patients with allergic rhinitis based on grass allergy, 12 patients with CRSwNP without grass allergy, 12 patients with CRSwNP with grass allergy, and 12 control patients. The diagnosis of grass allergy was based on skin prick test and RAST. The test was positive based on change in nasal airflow measured by active anterior rhinometry and symptoms. In annex, VAS scores were performed before and after NAPT.

**Results:** The nasal allergen provocation test was positive in 19 % of the patients with CRSwNP without allergy and in 54% of the patients with CRSwNP with allergy. In contrast 100% of the patients with allergic rhinitis developed a positive provocation test whereas in the control group 9% of the patients developed a positive provocation test. CRSwNP without allergy did not show a significant increase in VAS scores of complaints. In contrast, allergic rhinitis patients and CRSwNP patients with grass allergy developed a significant increase in nasal obstruction and nasal drip. However, in allergic CRSwNP patients the symptoms after provocation were significantly lower compared to AR patients.

**Conclusion:** This suggests that local IgE present in these patients are functional in allergic provocation with grass pollen. However there is a reduced reactivity after grass pollen stimulation in CRSwNP compared to allergic rhinitis. This reduced reactivity is most likely due to the polyclonality of local IgE or IgG4 blocking activity in CRSwNP.

**O15**

**Short and long-term safety of MP29-02*; a new therapy for the treatment of allergic rhinitis**

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**Clinical and Translational Allergy 2013, 3(Suppl 2):O15**

**Background:** MP29-02*, a novel intranasal formulation of azelastine hydrochloride [AZE] and fluticasone propionate (FP) provides significantly superior symptom relief to current first line therapy in patients with seasonal allergic rhinitis (SAR) and with chronic rhinosinusitis (CRS) [1,2].

**Objective:** To evaluate the short- and long-term safety of MP29-02*.

**Method:** 4022 patients (>=12 years old) were randomized into 4, 14-day double-blind, placebo-controlled SAR trials to receive MP29-02*, AZE, FP or placebo nasal sprays (all given as 1 spray/nostril bid). 612 patients (>=12 years old) were randomized into 1-1 year, open-label, active-controlled, parallel-group chronic rhinitis trial to receive MP29-02* (1 spray/nostril bid) or FP nasal spray (2 sprays/nostril qd). For all studies the total daily dose of AZE and FP was 548 µg and 200 µg respectively. Safety was assessed by incidence, type, and severity of adverse events, vital signs and nasal examination.

**Results:** In all SAR studies, the treatment-related adverse events (TRAEs) observed were those usually reported with AZE (dysesthesia) and FP (headache and epistaxis), did not exceed placebo in many instances (Table 1 shows results from a representative SAR study) and were ‘mild’ in the vast majority of cases. In the long-term study there was no evidence for an accumulation of TRAEs over time, any occurrence of late AEs and none were considered severe. <3% of subjects discontinued from the study due to an AE. A SAE was reported by 3 MP29-02 subjects and 1 FP subject, but none were considered treatment-related. For all studies, changes in vital signs and nasal examinations were similar in all groups.

**Conclusion:** MP29-02* was well tolerated following 14 day’s use in SAR patients with a similar safety profile as standard therapies and placebo. MP29-02* is also safe for long-term use.

*Dymista

**References**


**O16**

**A new therapy (MP29-02*) effectively controls nasal symptoms of seasonal allergic rhinitis irrespective of severity**

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**Clinical and Translational Allergy 2013, 3(Suppl 2):O16**

**Background:** It is important to show efficacy in allergic rhinitis (AR) patients regardless of symptom severity since most AR patients presenting to a doctor have moderate-to-severe disease.

**Objective:** To assess the efficacy of MP29-02* [a novel intranasal formulation of azelastine hydrochloride (AZE) and fluticasone propionate (FP)] compared to AZE, FP or placebo nasal sprays in seasonal AR (SAR) patients according to severity.

**Methods:** 610 patients (>= 12 years old) with moderate-to-severe SAR were randomized into a double-blind, placebo-controlled, 14-day, parallel-group trial to receive MP29-02*, commercially-available AZE or FP nasal sprays or placebo (all given as 1 spray/nostril bid; total daily dose: 548 µg AZE; 200 µg FP). The primary efficacy variable was change from baseline in rTNSS (AM + PM). This primary endpoint was assessed post-hoc according to symptom severity. All patients had moderate-to-severe disease. Patients were categorized into two severity groups according to their median baseline rTNSS. Those with a baseline rTNSS > 18.9 points were defined as more severe and those with a baseline rTNSS <= 18.9 points were defined as less severe.

**Results:** MP29-02* was significantly superior to either FP or AZE in alleviating patients’ rTNSS regardless of disease severity. For those patients with less severe disease (<18.9) MP29-02* reduced the rTNSS from baseline by -4.68 compared to -3.21 for FP (Diff: -1.46; 95% CI: -2.68, -0.25; p=0.0184), -2.41 for AZE (Diff: -2.26; 95% CI: -3.42, -1.10; p=0.0000) and -1.16 for placebo (Diff: -3.51; 95% CI: -4.78, -2.24; p<0.0001), corresponding to a relative treatment difference of 42% vs FP and 64% vs AZE. Patients with more severe disease (>18.9) experienced a -6.24 point reduction in their rTNSS with MP29-02*, significantly more than -4.73 with FP (Diff: -1.52; 95% CI: -2.99, -0.04; p=0.0436), -4.11 with AZE (Diff: -2.13; 95% CI: -3.55, -0.71; p=0.0035) and -3.18 with placebo (Diff: -3.06; 95% CI: -4.34, -1.80).

**Conclusion:** Results from a representative SAR study (Table 1) show that MP29-02* was well tolerated following 14 day’s use in SAR patients with a similar safety profile as standard therapies and placebo. MP29-02* is also safe for long-term use.
Table 1 (abstract O15)

<table>
<thead>
<tr>
<th>MP4002 SAR study (14 days)</th>
<th>MP29-02* (n=207)</th>
<th>FP (n=207)</th>
<th>AZE (n=208)</th>
<th>Placebo (n=210)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRAE n (%)</td>
<td>17 (8.2%)</td>
<td>14 (6.8%)</td>
<td>16 (7.7%)</td>
<td>8 (3.8%)</td>
</tr>
<tr>
<td>Dygeusia</td>
<td>5 (2.4%)</td>
<td>2 (1.0%)</td>
<td>7 (3.4%)</td>
<td>1 (0.5%)</td>
</tr>
<tr>
<td>Epistaxis</td>
<td>2 (1.0%)</td>
<td>5 (2.4%)</td>
<td>4 (1.9%)</td>
<td>2 (1.0%)</td>
</tr>
<tr>
<td>Headache</td>
<td>1 (0.5%)</td>
<td>5 (2.4%)</td>
<td>1 (0.5%)</td>
<td>3 (1.4%)</td>
</tr>
<tr>
<td>Chronic rhinitis study (52 weeks)</td>
<td>MP29-02* (n=404)</td>
<td>FP (n=207)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TRAE n (%)</td>
<td>38 (9.4%)</td>
<td>23 (11.1%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dygeusia</td>
<td>10 (2.5%)</td>
<td>1 (0.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epistaxis</td>
<td>5 (1.2%)</td>
<td>1 (0.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>4 (1.0%)</td>
<td>9 (4.3%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

-1.77; p<0.0001). For these more severe patients, the relative treatment effect was 49% to FP and 70% to AZE.

Conclusion: MP29-02* provided benefits for all patients, offering significantly greater relief from nasal symptoms compared to two first-line therapies regardless of disease severity and is the drug of choice for the treatment of AR.

Dymista

O17 The role of nasal trigeminal nerves expressing TRP channels in modulation of cough threshold and urge to cough – possible clinical application
Jana Plevkova1, Zuzana Bringerová2, Silvia Gavliakova2, Eva Hanusková2, Tomas Buday3, Mariana Brozmanova2
1Comenius University, Jessenius Faculty of Medicine, Martin, Slovakia; 2Comenius University, Jessenius Faculty of Medicine, Department of Pathophysiology, Martin, Slovakia

Cough is a phenomenon frequently associated with upper airway diseases and as a reflex is modulated by many afferent inputs either from respiratory tussigenic areas, but also by afferent drive from other organs. Modulation of cough by nasal afferent inputs could either facilitate cough response or inhibit it in animal models, depending on the type of trigeminal afferents which are stimulated. In recent study we focused on afferents expressing TRPA1, TRPM6 & TRPV3 channels – channels known as relevant for airway irritants (TRPA1), menthol and other cooling substances (TRPM8) and thymol (TRPV3). Particularly menthol and thymol are substances which are frequently used in over-the-counter medication for cough and common cold based on empirical approach. Objective evidence regarding the modulation of cough in humans has never been reported. 60 human healthy volunteers participated in the study, and they have been challenged by intranasal drops containing agonists of selected ion channels: isocyanate (AITC) & cinnamaldehyde for TRPA1, (-) menthol and (+) menthol for TRPM8 and thymol for TRPV3 ion channels in randomized order (all 10-3 M). Nasal symptom score, cough threshold (C2), urge to cough (Cu) and cumulative cough response had been assessed using capsaicin cough challenge tests.

Nasal challenges of TRPA1 relevant agonists induced considerable nasal symptoms, significantly enhanced urge to cough (p<0.05) but modulation of C2 and cumulative cough response did not reach significance level. Both TRPM8 agonists and TRPV3 agonist thymol administered to the nose significantly modulated all parameters including C2 (p<0.05), Cu (p<0.01) and cumulative cough response (p<0.01) documenting strong anti irritating and antitusis potential of menthol isomers and thymol. Nasal afferent drive modulates cough reflex in human healthy volunteers and this knowledge could have clinical application involved in relieving lower airway symptoms in subjects with upper airway diseases. The role of trigeminal afferents, olfactory nerve endings, smell perception process and other supramedullar influences have to be taken into consideration as relevant enough to modulate cough response in humans.

O18 Subjects with local allergic rhinitis can be identified by basophil activation test
Paloma Campo1, Carmen Rondon1, Enrique Gomez2, Natalia Blanca-Lopez2, M Jose Torres1, Esther Barrionuevo1, Rocío Herrera1, Luisa Galindo1, Cristobalina Mayorga1, Miguel Biancal
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Clinical and Translational Allergy 2013, 3(Suppl 2):O18

Background: Local allergic rhinitis (LAR) is characterized by negative skin testing and serum specific IgE. Diagnosis is based on nasal provocation test (NPT), very sensitive but time-consuming, and/or presence of local synthesis of specific IgE (sIgE) which shows low sensitivity (22%). The aim of the study was to evaluate the presence of specific D. pteronyssinus (DP) activation of basophils by basophil activation test (BAT) in subjects with confirmed LAR.

Methods: BAT was performed in 43 subjects: 16 with confirmed LAR (positive NPT with DP, negative skin testing and sIgE to DP), 13 with allergic rhinitis (AR)(positive NPT with DP, positive skin testing and sIgE to DP) and 14 healthy controls (negative NPT, negative skin testing and sIgE to DP). To demonstrate a specific IgE mechanism of basophil activation, BAT with wortmannin pre-treatment was performed in four LAR patients.

Results: BAT with DP was positive in 85% of AR patients and 50% of LAR subjects. BAT showed a substantial correlation with NPT in AR subjects (kappa index: 0.78, p<0.0001). The positive responses of the 4 LAR samples that underwent BAT with wortmannin became negative when this substance was added to the assay.

Conclusions: BAT was able to detect 50% of LAR subjects to DP, being more sensitive than detection of nasal specific IgE. Responses were IgE-specific demonstrated by BAT-wortmannin assay. Further studies are needed to test this assay with other allergens.

O19 Chemoattractant levels in nasal secretions as indicators of clinical severity in chronic polyposis rhinosinusitis
Aleksandar Peric1, Danilo Vojodic2, Nenad Baletic1, Vesna Radulovic3
1Faculty of Medicine, Military Medical Academy, Department of Otorhinolaryngology, Belgrade, Serbia; 2Faculty of Medicine, Military Medical Academy, Department of Clinical and Experimental Immunology, Belgrade, Serbia; 3Municipal Institute for Lung Diseases, Department of Pneumology, Belgrade, Serbia

Clinical and Translational Allergy 2013, 3(Suppl 2):O19

Background: The local accumulation of activated eosinophils in the nasal mucosa is a feature of chronic polyposis rhinosinusitis (CPRS). However, the pathogenesis of chronic hypereosinophilia in nasal polyps is still unknown. An increased production of several chemoattractants, responsible for guiding the inflammatory process, has been reported in this disease.
The aim of this study was to evaluate nasal secretion levels of several chemokines and to correlate those levels with clinical characteristics and degree of eosinophilia in asthmatic and non-asthmatic patients with polypous sinusitis.

**Method:** Fourteen non-atopic non-asthmatic patients with CPRS and 14 CPRS patients with co-morbid atopic asthma were recruited for this cross-sectional study. Fourteen healthy subjects were included as controls. The concentrations of GM-CSF, MCP-1, MCP-3, MIP-1alpha, MIP-1beta, and RANTES in nasal secretions were measured using flow-cytometric method. Eosinophil counts were performed by percentage of differential granulocyte counts during cytological examination of scraped nasal mucosa obtained from the inferior turbinate by rhinprobe. Therefore, we scored clinically each of the 28 nasal polyt patients according to the nasal symptom score, endoscopic score, and Lund-Mackay CT score.

**Results:** We found significantly higher concentrations of MCP-1 (p<0.0001), MCP-3 (p=0.018) and RANTES (p<0.0001) in nasal fluid of asthmatic CPRS patients compared to non-asthmatic. In non-asthmatic patients, we found positive correlation between MCP-1 alpha levels and nasal symptom score, at the 0.01 level (p=0.01). Therefore, the concentrations of RANTES were positively correlated with nasal symptom score, nasal endoscopic score, CT score, and eosinophil counts (p=0.01). On the other hand, in asthmatic patients, the concentrations of MCP-1 were associated with nasal symptom score, nasal endoscopic score, Lund-Mackay score, and percentage of eosinophils (p=0.01). The concentration of RANTES in asthmatic CRS patients also correlate with all clinical parameters, and with degree of eosinophilia (p=0.01).

**Conclusion:** CRS in asthmatics is characterized by higher degree of eosinophilic inflammation than in non-asthmatics. RANTES and MCP-1 levels correlate well with clinical severity of CRS. The measurement of chemokines in nasal secretions could be useful in evaluating the degree of sinonasal inflammation in nasal polyt patients.

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**POSTER PRESENTATIONS**

**P1**
Abstract not presented and not submitted for publication

**P2**
Abstract not presented and not submitted for publication

**P3**
Evaluation of birch pollen sensitization profile in allergic rhinoconjunctivitis patients from Bucharest region using component-resolved diagnosis

Floriar-Dan Popescu, Mariana Vieru, Adriana Mihaela Tudose
University of Medicine and Pharmacy "Carol Davila", Department of Allergology, Bucharest, Romania

**Clinical and Translational Allergy 2013, 3(Suppl 2)p3**

**P4**
Abstract not presented and not submitted for publication

**P5**
Rhinitis prevalence and incidence in a cohort of children with recurrent wheezing: from preschool age to adolescence

Ana Pereira, Ângela Gaspar, Mário Morais-Almeida
Hospital CUF-Deicobertas, Immunology Department, Lisbon, Portugal

**Clinical and Translational Allergy 2013, 3(Suppl 2)p5**

**Background:** The aims of this study were 1) to estimate baseline rhinitis prevalence in a cohort of preschool children with recurrent wheezing...
This cohort study included 308 children observed as first and 20% of the children with rhinitis in adolescence had the previous year’s prevalence of eczema was 29% and that of wheezing was 45% vs. 31%, respectively, p=0.009).

Conclusions: Current rhinitis and rhinoconjunctivitis were highly prevalent in school aged children. The presence of eye symptoms was associated with a greater persistence and impact of nasal disease in daily activities and with a higher prevalence of wheezing and eczema.

P7
The effect of nasal breathing on the exercise induced bronchospasm in children with allergic asthma and rhinitis
Mirjana Turkolić1,2, Martina Canaki1, Robert Magdic1, Marcel Lipej2, Sandra Bulat2, Jelena Zivkovic2, Davor Plavec2
1 Children’s Hospital Srebrnjak, Zagreb, Croatia; 2 Children’s Hospital Srebrnjak, Allergy Department, Zagreb, Croatia

Clinical and Translational Allergy 2013, 3(Suppl 2) P7

Background: Allergic rhinitis (AR) is very common in children and it affects 10–40% of children world-wide. Asthma and AR commonly coexist and we can find up to 30% of asthma in patients with AR and up to 90% of AR in patients with asthma. Moreover, these two disorders seem to influence each other’s activity and intensity. Physical activity is commonly prescribed as a rehabilitation treatment for asthma in children although there is a high percentage of asthmatics with exercise-induced bronchospasm (EIB) at that age and recent studies show beneficial effects of aerobic training on allergic inflammation. EIB can be one of the reasons for low adherence to physical training. The aim of this study was to test if a nose clip during a 6 minute free running test changes the magnitude of EIB according to the severity of AR.

Methods: The study was conducted in 55 children (24 girls, mean age 12.6 yrs) with moderate persistent asthma and AR in an Asthma Camp, at island Lolinj. Their asthma was controlled under their regular treatment and they were daily participating in an aerobic fitness program. They were divided in two subgroups according to the median of intensity of their nasal symptoms (less nasal symptoms – LNS; more nasal symptoms – MNS). Spirometry was performed before, 3 and 20’ after 2 exercises (6 minutes free running with and without a nose clip) done a day apart.

Results: Two subgroups (LNS and MNS) were not significantly different according to their demographic characteristics, sensitization profile, asthma control, lung function and exhaled NO measurements and physical fitness (p>0.05 for all). There was a significantly greater fall in FEV1 3’ after exercise with a nose clip in the LNS subgroup than in the MNS subgroup (p<0.001) and compared to testing without the nose clip (LNS, p=0.009; MNS, p=0.010). Contrary to the testing with the nose clip there were no significant differences in the FEV1 fall after exercise when the same patients were tested without the nose clip during exercise (p=0.068).

Conclusion: It seems that regular mouth breathing due to nasal congestion somehow protects patients with asthma and AR from EIB.

P8
Abstract not presented and not submitted for publication

P1
Prevalence and burden of rhinitis and rhinoconjunctivitis in 9- to 11-year-old children
Ana Pereira1, Angela Gaspar, Mário Moreira-Almeida
Hospital CUF-Descobertas, Immunology Department, Lisbon, Portugal

Clinical and Translational Allergy 2013, 3(Suppl 2) P1

Background: The aims of this study were: 1) to estimate current rhinitis (CR) prevalence in school aged children using the ISAAC definitions; 2) to characterize children with CR; and 3) to estimate rhinitis incidence over a 13 years follow-up period.

Methods: This cohort study included 308 children observed as first appointments in a tertiary hospital’s outpatient clinic in 1993. All children aged <7 years old and with RW (≥3 wheezing episodes responsive to bronchodilator in the previous year with symptom-free intervals in-between) were included. Evaluations included an allergy consultation and skin-prick tests (SPT). In 1993, the participant’s mean (SD) age was 3.7 (1.7) years, 61% were male, 48% had positive SPT, 22% had personal history of atopic eczema and 6% of food allergy. Children were reassessed in 2001 (n=249) and 2006 (n=170); no significant differences were found between the characteristics of the children assessed in each evaluation (p>0.049). A multiple logistic regression model was developed to study risk factors for rhinitis at preschool age; results were presented as odds ratio (OR) with 95% confidence interval (CI).

Results: In 1993, the prevalence of rhinitis was 60% (95%CI(55-65)). Rhinitis at preschool age was positively associated with atopy (19.6(9.1-42.4)), maternal asthma (2.6(1.6-6.3)), personal history of food allergy (13.2(1.2-120.6)) and atopic eczema (2.6(1.6-6.4)); kindergarten attendance before the age of 12 months presented a negative association (0.4(0.2-0.8)). Recurrent respiratory infections, parental rhinitis and paternal asthma were not significantly associated with rhinitis diagnosis. When considering the period from 1993 to 2001, 10 children (out of the 93 previously without rhinitis) had new rhinitis diagnosis (incidence: 11%). The 1993-2001 incidence was highest in atopic children (33% vs. 7% in non-atopic, p=0.007). Most of the children with rhinitis at preschool age persisted with rhinitis diagnosis in 2001 (96%). In 2001-2006, 11 new rhinitis cases (out of 65) were reported (incidence: 17%); the incidence was also highest in atopic children (56%). In 2006, 87% of those with rhinitis had it since preschool age.

Conclusion: The prevalence of rhinitis in preschool children with recurrent wheezing was high and atopy presented the strongest association with rhinitis diagnosis. Most of the children with rhinitis in adolescence had rhinitis since preschool age.

P2
Abstract not presented and not submitted for publication

P3
Allergic profile of Congolese individuals exposed to flour dust as compared with a non-exposed work group
Dieudonné Nyembue Tshipukane1, Elise Kembia1, Léone Lusamba2, Marie Jeanne Nkoy3, Jeroen Vanhove1,2, hans Sneeers2, Frank Buntinx3, Peter Hellings2, Marie Jorrisen2
1 University of Kinshasa, Otorhinolaryngology Department, Kinshasa, Congo; 2 Hospital Sino-Congolais, ENT Service, Kinshasa, Congo; 3 University of Kinshasa, Médecine Physique, Kinshasa, Congo; 4 University of Kinshasa, Pneumologie, Kinshasa, Congo; 5 KU Leuven, Occupational, Environmental Medicine, Leuven, Belgium; 6 KU Leuven, Academic Center for General Medicine, Leuven, Belgium

Clinical and Translational Allergy 2013, 3(Suppl 2) P3

Background: It seems that regular mouth breathing due to nasal breathing change the magnitude of EIB according to the severity of AR.

Methods: The study was conducted in 55 children (24 girls, mean age 12.6 yrs) with moderate persistent asthma and AR in an Asthma Camp, at island Loliunj. Their asthma was controlled under their regular treatment and they were daily participating in an aerobic fitness program. They were divided in two subgroups according to the median of intensity of their nasal symptoms (less nasal symptoms – LNS; more nasal symptoms – MNS). Spirometry was performed before, 3’ and 20’ after 2 exercises (6 minutes free running with and without a nose clip) done a day apart.

Results: Two subgroups (LNS and MNS) were not significantly different according to their demographic characteristics, sensitization profile, asthma control, lung function and exhaled NO measurements and physical fitness (p>0.05 for all). There was a significantly greater fall in FEV1 3’ after exercise with a nose clip in the LNS subgroup than in the MNS subgroup (p<0.001) and compared to testing without the nose clip (LNS, p=0.009; MNS, p=0.010). Contrary to the testing with the nose clip there were no significant differences in the FEV1 fall after exercise when the same patients were tested without the nose clip during exercise (p=0.068).

Conclusion: It seems that regular mouth breathing due to nasal congestion somehow protects patients with asthma and AR from EIB.
Primary ciliary dyskinesia and humoral immunodeficiency - what is the missing link?

Niekke Boon1, Mark Jorissen2, Kris De Boeck3, Isabelle Meys3

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Background: Primary ciliary dyskinesia (PCD) is a rare disorder (prevalence 1/20000), caused by congenital dysmotility of the respiratory cilia. Humoral immunodeficiency (HID) often presents in a similar way with recurrent ear, nose and sinopulmonary infections, not seldom evolving to chronic lung disease. Although isolated IgG subclass deficiencies and IgA deficiency are common conditions, Common Variable Immunodeficiency (CVID) is more rare with a prevalence ranging from 1/10000 to 1/50000.

Methods: We examined the coincidence of PCD with HID in a large cohort of patients with PCD. The diagnosis of PCD was confirmed by functional and structural evaluation of the cilia, including evaluation after ciliogenesis in culture, excluding secondary ciliary dyskinesia.

Results: We report the coincidence of PCD with HID in 8 patients (4.6%).

Conclusion: We have no explanation for this remarkable finding, but hypotheses can be postulated. Hematopoietic cells lack primary cilia, but they do express certain intraflagellar transport proteins needed for the formation of the immune synaps. Dysfunction of one of these proteins might cause PCD as well as HID. Ciliary proteins might play a role in B-cell proliferation or immunoglobulin class-switch and normal ciliary function might be needed for a fully intact immune response to antigen presentation. PCD could cause cytokine dysfunction, which could disturb the immunoglobulin secretion indirectly. Immune dysfunction may be a feature of PCD and explain part of the symptom complex. PCD genes could be modifier genes for HID genes or vice versa. Of course, it can be pure coincidence that some patients present with both disorders and that no causal relation is present. The diagnosis of HID can be important since immunoglobulin substitution is an effective treatment and therefore checking antibody titers should be recommended.

Conclusion: Patients with PCD may be at increased risk for coincident HID and a underlying link between both disorders might be present.

Longer treatment duration with SLIT leads to higher patient satisfaction and clinical improvement. Outcomes of the SAMITES study

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Clinical and Translational Allergy 2013, 3(2)P12

Background: Sublingual immunotherapy (SLIT) is considered as a valid alternative in treatment of patients suffering house dust mite (HDM) allergic rhinitis. No evaluation of the patients’ satisfaction on treatment and its relationship with clinical improvement and compliance was previously described.

Methods: An observational cross-sectional study was carried out to compare patients’ satisfaction after 4-6 months (group A) or 9-12 months (group B) of SLIT treatment by the use of a validated Spanish satisfaction questionnaire (ESPIA) consisting of 16 items on a 5-point Likert scale (scale 16-80, higher score indicating more satisfaction). Secondary objectives were to investigate relation between satisfaction and both clinical improvement and compliance. Patients were classified in terms of compliance into <25%; 25-50%, 51-75%; >76% group.

Results: Data from 232 patients (162 in A and 70 in B) were collected. In group A, 72% of them had persistent and 96% moderate-severe rhinitis before starting immunotherapy. Similarly in group B, 68% of them had persistent and 97% moderate-severe rhinitis. Treatment duration was 5.5±1.7 months in A and 12.3±2.5 months in B. Median total satisfaction was 60 and 73 points in A and B respectively. In those patients reporting compliance > 76% (n=191) higher median values of satisfaction (ESPIA score) were found in group B (P<0.0001). Patients changing from
<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (y)</th>
<th>Clinical presentation</th>
<th>Immuno deficiency</th>
<th>Laboratory results (before start of replacement therapy)</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>IgG (g/l) IgG2 (g/ml) IgG3 (g/l) IgA (g/l) IgM (g/l) Pneumococcal antibodies (before-after vaccination) (U/ml)</td>
<td></td>
</tr>
<tr>
<td>1*</td>
<td>13</td>
<td>SI, C, B, CR, E</td>
<td>CVID</td>
<td>7.54 (6.35-14.89) 0.5 (0.63-3.0) 0.13 (0.17-0.88) 0.29 (0.46-2.51) 0.23 (0.47-2.2) Type 3: 33-114, type 4: 38-23, type 9N: 6-33</td>
<td>SCIG</td>
</tr>
<tr>
<td>2*</td>
<td>16</td>
<td>C, B, CR</td>
<td>CVID</td>
<td>8.55 (4.78-11.29) 0.38 (0.72-3.4) 0.27 (0.13-1.33) 0 (0.35-1.9) 0.41 (0.34-1.34) Type 3: 26-57, type 4: 8-54, type 9N:7-66</td>
<td>SCIG</td>
</tr>
<tr>
<td>3</td>
<td>32</td>
<td>SI, C, B, CR, E</td>
<td>IgG2 and IgG3 deficiency</td>
<td>8.3 (7-16) 1.8 (2.42-7.0) 0.18 (0.22-1.76) 1.37 (0.7-4.0) 0.37 (0.4-2.3)</td>
<td>SCIG</td>
</tr>
<tr>
<td>4</td>
<td>43</td>
<td>C, B, CR</td>
<td>IgG3 deficiency</td>
<td>9.34 (7.51-15.6) 3.38 (1.50-6.40) 0.11 (0.20-1.10)</td>
<td>Intermittent IVIG</td>
</tr>
<tr>
<td>5</td>
<td>62</td>
<td>SI, C, B, CR</td>
<td>IgG2 deficiency</td>
<td>6.64 (7.51-15.6) 1.14 (1.5-6.4) 0.96 (0.2-1.1) 1.43 (0.82-4.53) 2.71 (0.46-3.04)</td>
<td>Intermittent IVIG</td>
</tr>
<tr>
<td>6</td>
<td>33</td>
<td>C, B, CR, E</td>
<td>IgG3 deficiency</td>
<td>14.0 (7.51-15.6) 4.06 (1,17-7.47) 0.29 (0.41-1.29)</td>
<td>No IG treatment</td>
</tr>
<tr>
<td>7#</td>
<td>10</td>
<td>SI, C, B, CR, E</td>
<td>IgA deficiency, SPAD</td>
<td>14.5 (5.3-13.06) 1.27 (0.98-4.8) 0.59 (0.15-1.49) 0.29 (0.6-2.7) 2.56 (0.43 -2.7) Type 3: 30-21, type 4: 9-7, type 9N: 8-6</td>
<td>No IG treatment</td>
</tr>
<tr>
<td>8#</td>
<td>14</td>
<td>C, B, CR, E</td>
<td>IgA deficiency</td>
<td>12.6 (5.76-12.65) 0.56 (0.81-2.32) 1.28 (0.3-1.59)</td>
<td>No IG treatment</td>
</tr>
</tbody>
</table>

persistent to intermittent rhinitis between start of SLIT and current situation were 49% and 60% in A and B respectively. Concerning severity according to ARIA guidelines, patients changing from moderate-severe to mild were 43% and 72% in A and B respectively (group effect, p=0.0003). In those patients reporting clinical improvement in terms of rhinitis frequency (n=108) higher median values of satisfaction were found in group B (P=0.0007) and similarly, patients reporting clinical improvement in terms of rhinitis severity (n=151), higher median values of satisfaction were found in group B (P<0.0001).

Conclusions: Almost 50% of the patients treated 5.5 months experienced an improvement of their rhinitis in terms of frequency (49%) and severity (43%), this percentage is higher in patients treated 12.3 months 60% and 72% respectively following ARIA classification. The SAMITES study demonstrates a clear relationship between patients’ satisfaction with SLIT for HDM allergic rhinitis with the duration of treatment, compliance and clinical improvement.

Introduction: Chronic Rhinosinusitis with Nasal Polyps (CRSwNP) presents a Th2 profile predominance, with a remarkable eosinophil infiltration and IL-5 secretion. The influence of molecular markers on both histology and recurrence is still misunderstood.

Aims: To evaluate the gene expression of IL-5, IL-8 and TGF-beta in patients with nasal polyps and control patients, as well as its correlation to tissue cellularity and diseases relapsing.

Methods: The mRNA expression of the IL-5, IL-8 and TGF-beta protein was analyzed using qRT-PCR in 32 nasal polyps and 7 control samples comparing it with medium turbinate control samples (obtained from patients undergoing aesthetic rhinoplasty). The numbers of eosinophils and neutrophils were counted in samples obtained during surgical procedure, and stained with hematoxylin eosin in an optical microscope. The patients were followed up to three years after surgery, and considered with relapsing disease if there was polyp in the medium meatus through nasal endoscopy.

Results: IL-5 and IL-8 expressions were increased whereas TGF-beta was decreased in the nasal polyps when compared to the control mucosa from medium turbinates. There was no correlation between these molecules expression and tissue’s cellularity, nor to relapsing of the disease.

Conclusion: Brazilians’ nasal polyps present an increased Th2 and a decreased Treg profile, as Europeans’. The expression of none of these molecules correlated to tissue cellularity, neither to recurrence of the disease. Future research is still needed to observe the real impact of these molecules in CRSwNP, especially when regarding its therapy.

Anaphylaxis by inhalation of allergenic proteins from Anisakis simplex

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Background: Anaphylaxis can affect 20% of patients sensitized to Anisakis simplex. There have been reports of occupational asthma due to inhalation of allergens in patients who handle raw fish. Anisakis has several proteins which are capable of producing sensitizations, primarily by ingestion, but may also occur by contact or inhalation.

Method: We report a 50 year old patient, who works as a cook. A year ago she presented two episodes of anaphylaxis after eating undercooked fresh fish. Thereafter she removed raw fish from her diet. Ten months later after handling fish (escaverting it), an hour after hand injury, she presented itching hands and head, epigastic pain, nausea and severe generalized urticaria. Attended the emergency room with adrenaline, corticosteroids, antihistamines, with good response. She manipulates fish daily with gloves because of her profession. Prick test (PT) with allergenic extracts of fish, Anisakis, food (Alk Abelló).Total and specific IgE to Anisakis, white and blue fish (Thermo Fisher). Gastroscopy.

Results: Negative PT both raw and cooked whitening. Anisakis simplex PT positive both immediate and 48h later reading. Allergic response test against aeroallergens negative. Total IgE 1821KU/l. Specific IgE levels were always kept high Anisakis:> 100KU/l. Normal Gastroscopy: Anisakis larvae not observed. Not taking biopy.

Conclusion: We report a case of anaphylaxis following ingestion, contact and inhalation of various Anisakis simplex proteins in a patient previously sensitized by digestive tract. The positivity of tests carried out in vivo and in vitro against Anisakis with negativity against fish proteins, confirms the diagnosis of anaphylaxis by inhalation, because the patient had not returned to eating fish.

Allergic fungal rhinosinusitis (AFRS) is characterized by the growth of fungi, mostly Aspergillus sp., in the paranasal sinuses together with the formation of nasal polyps, peanut-butter like “allergic mucin” with fungal hyphae and typical CT-findings, as well as increased serum total IgE and Aspergillus-specific IgE concentrations. We here hypothesize that the increase in serum total IgE is caused by the local symbiosis of Asp. sp. with Staphylococcus aureus, a germ which is known for the production of enterotoxins with superantigenic properties. We demonstrate the presence of S. aureus specific IgE antibodies in the sera of AFRS patients, correlating with total serum IgE concentrations, as well as the coexistence of both, A. fumigatus and S. aureus, in biofilm-like formations on the sinus mucosa. Similar mechanisms and findings may apply for Allergic Broncho-Pulmonary Aspergillosis/Mycosis (ABPA/AI). This knowledge may result in new diagnostic and therapeutic approaches including anti-IgE strategies.

Changes in paranasal sinus mucosa due to the nasopharyngian obstruction

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Background: The purpose of the study is to determine the effects of the artificially induced mechanical obstruction on the physiopathology of the paranasal sinus mucosa, taking into consideration an experimental model on animals (rabbit).

Methods: The study was performed on 20 New Zealand white rabbits, distributed into two equal groups. In the case of the first group of 10 experimental animals, we induced the model of ipsilateral double obstruction, the opposite side being left intact as term of comparison. Thus we produced the mechanical obstruction of the nasopharynx at the level of the choanal orifices as well as the obstruction at the level of ostiomeatal complex. In the case of the second experimental group we induced the model of the double counterlateral obstruction: the obstruction of the nasopharynx at the level of the choanal orifice and the counterlateral...
obstruction of the ostiomeatal complex. We studied and determined the qualitative changes of the pH and the microbiology of the paranasal sinus mucosa.

Results: The study determines: 1. pH statistical average and standard deviations of the maxillary sinus mucosa. 2. The isolated germs were Staphylococcus aureus, Streptococcus pneumoniae, Haemophilus influenzae. Multigerm association was present in the case of the double ipsilateral obstruction. 3. The reversed correlation between the pH values and the presence of multiple germs in the sinus mucosa.

Conclusions: The experimentally induced obstruction of the nasopharynx, modifies the ventilation of the nasal fossae and leads to morphophysiological changes in sinus mucosa, causing inflammation. As compared to the normal values, the pH average values of the maxillary sinus mucosa in the obstructed side are significantly lower (p<0.001). It is noticeable that there are no significant statistic differences between maxillary sinus mucosa pH values in the double ipsilateral obstruction and the obstruction of the ostiomeatal complex (p>0.05), thus certifying that the nasopharynx contributes indirectly to the ventilation of the paranasal sinuses.

P17
The correlation between chronic sinusitis and chronic adenoiditis in children
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Background: The purpose of the study is to evaluate the correlation between chronically sinusitis and chronically adenoiditis in children.

Methods: The study was carried out on two groups of children aged between 6 and 18, diagnosed and treated in the Pediatric Hospital of Oradea in the period 2010-2012. In the first phase of the study, diagnosis was established on clinical and radiological criteria. The first group of 112 patients was submitted to adenoidectomy. The second group of 40 patients was given medicine instead of being submitted to surgical procedures. In the second phase, six months later, patients were re-evaluated clinically and with endoscopy.

Results: 70% of the patients were aged between 10-14 in both groups. There are no statistic differences between the two groups. In both groups the study showed the predominance of ethmoido-maxillary sinusitis. Nasal obstruction prevailed in the case of the first group (surgically treated-adenoidectomy). Rhinorrhea was almost equally distributed in the first phase at patients in both groups; on second evaluation, we noticed its absence in 60% of patients in the first group. Statistically, the difference between the two groups, in the case of second evaluation, is strongly significant. On second evaluation, in the case of the first group, the study showed the reduction of sinus infection in 56% of patients as compared to the second group, where recovery was present in only 24% of patients.

Conclusions: As a result of adenoidectomy, the reduction of the inflammation in the case of sinus infection, can be a proof of the role of the nasopharynx. Chronic hypertrophic adenoiditis can be both a mechanical obstacle and a cause of infection of the paranasal sinuses in children.

P18
Comparative proteomic analysis of tear fluid versus nasal mucus in allergic rhinitis patients and healthy controls
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Background: Allergy is a common disorder in the western world with a prevalence of 15% to 20%. The combination of ocular symptoms in patients with allergic rhinitis occurs frequently. Nasal mucus for the nasal epithelium and tear fluid for the eye are the first defence barrier against various pathogens including aeroallergens. Little is known about the nasal mucus and particularly about the tear fluid proteome. The aim of the study was to analyse both body fluids on a proteome level and detect possible impact of its proteins in the pathophysiology in allergic rhinoconjunctivitis.

Methods: Fifty-eight patients (29 allergic, 29 healthy controls) were included in this study. Allergy status was confirmed through skin prick test (SPT). Patients sensitized to house dust mite or animals were excluded. Nasal mucus was collected with a special suction device, tear fluid was collected with a glass capillary. Specimens then were sent for LC MS/MS mass spectrometry.

Results: In total 86 different proteins could be identified in tear fluid (267 in nasal mucus). 74 proteins could be identified with a peptide count of ≥2. Considering a mean spectral count (SC) of ≥4 in either group 18 different proteins could be identified. Calculating a means SC ration between allergic (A) and healthy (H) (A/H) 6 proteins were elevated in allergies (A/H > 1) two of which were significantly elevated (lactoperoxidase and prolactin inducible protein). Twelve proteins (A/H < 1) were elevated in healthy controls four of which were significantly elevated (serum albumin, secretoglobin family 1-D1), proline-rich protein 4 and mammaglobin-B. With a SC of ≥4 and a peptide count of ≥1, 56 different proteins were found in tear fluid and nasal mucus, 13 of which were found in both fluids, 5 exclusively in tear fluid and 38 exclusively in nasal mucus.

Conclusion: Tear fluid proteome is significantly different between allergies and healthy controls, significantly elevated proteins in allergies reflect exposure to exogenic noxa thorough peroxidase activity and pathological condition of tissue. In healthy controls proteins reflect normal lacrimal gland secretory function and immunemodulation through steroid binding protein activity. A larger number of proteins are found in nasal mucus only (38 vs. 5), the functional differences need to be further determined.

P19
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P20
Dry extract BNO 1011 inhibits human influenza a replication and neuraminidase activity in oseltamivir-resistant and -sensitive viral strains
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Background: Virus infection is the main triggering event for the development of acute rhinosinusitis and human influenza A virus ranks among the most frequent viral causes of infection. Influenza neuraminidase, a key enzyme in viral replication, spread, and pathogenesis, is the primary target in prevention and treatment of influenza infection. Sinupret®, a herbal medicinal product composed of Gentianae radix, Primulae flos, Sambuci flos, Rumicis herba, and Verbenae herba, is frequently used for the treatment of acute rhinosinusitis.

Objective: To investigate the anti-viral activity of the Sinupret® dry extract BNO 1011 in vitro and its potential to inhibit neuraminidase in oseltamivir-resistant and -sensitive human influenza A H1N1 strains of clinical relevance.

Methodology: In vitro, BNO 1011 was tested for its interference with human influenza A infection using a plaque reduction assay in MDCK cells. The impact on two clinically relevant human influenza A H1N1 strains displaying divergent sensitivity against the well-known neuraminidase inhibitor oseltamivir (OS) was studied (OS-resistant: human influenza A/California/07/2009; OS-resistant: human influenza A/ Maryland/04/2011). In addition, BNO 1011 was studied for its inhibitory activity on neuraminidase of the same influenza A strains in a highly sensitive chemiluminescence assay. The in vitro experiments were paralleled by monitoring viability of MDCK cells in the presence of BNO 1011.

Results and conclusions: BNO 1011 efficiently blocked the infectivity of both influenza A H1N1 strains studied in a plaque reduction assay [EC50 8.3
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P21

Anti-inflammatory effect of rebamipide on the ocular surface
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Purpose: The eyelid form of rebamipide was approved in Japan for use in the treatment of dry eye diseases, because it up-regulates mucin secretion and production. Others reported that rebamipide, a gastroprotective drug, could not only increase gastric mucus production but also suppressed gastric mucosal inflammation and that it was dominantly distributed in mucosal tissues. In this study we investigated whether rebamipide has anti-inflammatory effects in the ocular surface.

Methods: We used ELISA and quantitative RT-PCR assay to examine the effects of rebamipide on poly(C)-induced cytokine expression by primary human conjunctival epithelial cells. We studied the effects of rebamipide on ocular surface inflammation in our murine experimental allergic conjunctivitis (EAC) model. Moreover, we also observed their condition of allergic conjunctivitis when we treated the dry eye patients accompanied with allergic conjunctivitis using rebamipide.

Results: Rebamipide could suppress poly(C)-induced cytokine mRNA expression and the production of CXCL10, CXCL11, RANTES, MCP-1, and IL-6 in human conjunctival epithelial cells. The topical administration of rebamipide suppressed conjunctival allergic eosinophil infiltration in our EAC model. Furthermore, the allergic conjunctivitis which accompanied by dry eye patients treated with rebamipide tended to be better.

Conclusions: The topical application of rebamipide on the ocular surface might suppress ocular surface inflammation by suppressing the production of cytokines by ocular surface epithelial cells.

P22

Abstract not presented and not submitted for publication

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P23

Thymosin α1: a novel therapeutic option for patients with refractory chronic purulent rhinosinusitis
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Background: Chronic purulent rhinosinusitis (CPR) is an inflammatory disorder of the nose and paranasal sinuses of unknown cause. Despite various available medical and surgical treatment options still 5 to 10% of patients remain refractory. Immune deficiency is one of the underlying risk factors for CPR and previous studies demonstrated defects in monocyte chemotaxis. Subsequent treatment with the thymic hormone preparation thymostimulin led to in vitro restoration of monocyte chemotaxis and significant clinical improvement in patients. However, thymostimulin became unavailable in recent years. In the present study we evaluated the effects of the thymic peptide thymosin α1 on monocytes from CPR patients as well as aberrant gene expression profiles in these monocytes in order to further elucidate the pathogenesis of CPR.

Method: Monocytes were isolated from 16 patients with CPR and 13 healthy volunteers. Monocyte polarization was assessed using the Cianciolo–Snyderman monocyte polarization assay and the effects of thymosin α1 on monocyte polarization were evaluated. Furthermore, by Affymetrix whole-genome gene expression profiling and Q-PCR analysis we analyzed aberrant gene expression profiles in monocytes from CPR patients.

Results: In 4 out of 16 CPR patients we found diminished monocyte polarization (45%, sd 8%) when compared to healthy volunteers (58%, sd 12.5%)(p=0.078). More interestingly, in vitro treatment with thymosin α1 significantly restored monocyte polarization in these patients (64% sd 10%, p=0.029). In the “poor polarizing” monocytes we found aberrant expression of genes involved in pathways of inflammation, chemotaxis and cell migration.

Conclusion: Patients with CPR show diminished monocyte polarization in vitro that could be restored by thymosin α1. Moreover, these monocytes show an aberrant gene expression profile. We hypothesize that thymosin α1 may be a promising agent in treatment of refractory CPR patients. These effects may be mediated through interference with pathways involving the aberrantly expressed genes.

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P24

Abstract not presented and not submitted for publication

P25

Cellular responses to Staphylococcus aureus alpha-toxin are associated with clinical outcomes in chronic rhinosinusitis with nasal polyps
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Background: In contrast to Staphylococcus aureus-derived superantigenic exotoxins, the role of non-superantigenic exotoxins in the pathogenesis of chronic rhinosinusitis (CRS) remains obscure.

Objective: We sought to characterize S. aureus alpha-toxin–induced Th1-, Th2-, Th17– and Treg-associated cellular responses in CRS with nasal polyps (CRSwNP).

Method: Dispersed nasal polyp cells (DNPCs) and dispersed uncinate tissue cells (DUTCs) were prepared from patients with CRS with and without nasal polyps, respectively. Cells were incubated with various concentrations of alpha-toxin or staphylococcal enterotoxin B (SEB) and then the levels of IL-5, IL-13, IFN-gamma, IL-17A, and IL-10 in the cell supernatants were determined. The effect of blocking the COX pathway and neutralizing HLA-DR and ICAM-1 was examined. The pathophysiological significance of alpha-toxin–induced cytokine production was also determined.

Results: DNPCs produced substantial amounts of IL-5, IL-13, IFN-gamma, IL-17A, and IL-10 in response to alpha-toxin. Proinflammatory effects in the ocular surface.

Conclusion: Patients with CPR show diminished monocyte polarization in vitro that could be restored by thymosin α1. Moreover, these monocytes show an aberrant gene expression profile. We hypothesize that thymosin α1 may be a promising agent in treatment of refractory CPR patients. These effects may be mediated through interference with pathways involving the aberrantly expressed genes.

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**P26**

Early growth response protein 1 and dual specificity protein phosphatase 1 are involved in down-regulation of allergic responses

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**Background:** The airway epithelium is accepted as an active player in immune responses. Besides its role as a physical barrier towards invading pathogens and irritants, epithelium also affects the outcome of the immune response by the production of various pro-inflammatory mediators. We have previously shown that nasal epithelial cells are able to respond to exposure to house dust mite (HDM) allergen and that this response is different for epithelial cells isolated from healthy or from allergic individuals. Expression profiling in allergic individuals relative to healthy ones reveals genes that are permanently activated (e.g. NFKB-1, FOSL-1 and JUN) and genes that fail to be up-regulated (e.g. DUSP-1, EGR-1). As EGR-1 and DUSP-1 have been implicated in the down-regulation of inflammatory responses, we hypothesize that failure of up-regulation of DUSP-1/EGR-1 after exposure to HDM in allergic individuals could be responsible for the sustained activation of the allergic response.

**Methods:** We characterized regulatory responses triggered by allergen and viral stimulation in airway epithelium and the contribution of EGR-1 or DUSP-1 to these responses. The parent human bronchiolar cell line (NCI-H292) together with two mutant cell lines with silenced EGR-1 or DUSP-1 were exposed to HDM or poly(I:C) in a time course of 96 hours. Expression levels of selected transcription factors and cytokines were quantified by the real-time PCR and ELISA.

**Results:** Knock down of EGR-1 significantly enhanced and sustained the production of cytokines (e.g. IL-6, IL-8) after both HDM and poly(I:C) stimulation. The DUSP-1 knock down resulted in enhanced and sustained cytokines production after HDM stimulation. Additionally, in the wild type cell line, we observed a two-phase temporal response after HDM exposure, with EGR-1, DUSP-1, ATF-3 induced rapidly and reaching maximal expression not later than 1 hour after stimulation, while other genes and cytokines reached their maximal expression 4 hours after induction. This early indication of EGR-1, DUSP-1 and ATF-3 is compatible with the notion of an allergen c.q. viral-induced negative feedback loop of the inflammatory response. Furthermore, the high degree of overlap between the poly(I:C) and the HDM response suggests a potential mechanism of viral induced allergic exacerbations.

**Conclusions:** Failure of EGR-1 or DUSP-1 up-regulation in allergic individuals could be responsible for the prolonged activated state observed in vivo.

**P27**

Minimal persistent inflammation in Japanese cedar pollinosis and a prophylactic effect of intranasal corticosteroids

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**Background:** Low doses of allergen exposure can cause an activation of inflammatory cells in nasal mucosa without an onset of nasal symptoms, called MPI (minimal persistent inflammation). MPI contributes to hyperreactivity and subsequently onset of the full-scale symptom. However, little is known whether MPI is present in JCP (Japanese cedar pollinosis). In addition, a prophylactic effect of intranasal corticosteroids on MPI in JCP has not been investigated.

**Method:** We designed a double-blinded, randomized, placebo-controlled, crossover trial. 20 patients with JCP and without perennial allergic rhinitis were enrolled. Nasal provocation test with low dose of allergen (147 µg/disc) was performed once daily for 3 consecutive days. The levels of ECP and tryptase in nasal discharge were examined. Patients started to receive FNS (fluticasone furoate nasal spray) or placebo one day before the first nasal provocation test.

**Result:** In placebo group, only 25% of patients showed positive response to the provocation test on day 1. However, 75% and 68% of patients showed positive response on day2 and day3, respectively. After the first provocation, the levels of ECP and tryptase were both significantly increased. These levels were not significantly different between the positive and negative responders, and the increase was seen even in the negative responders. Pretreatment with FNS significantly suppressed the increase of nasal ECP and tryptase.

**Conclusion:** These results suggest that MPI characterized by the up-regulation of ECP and tryptase is present in JCP, and a prophylactic treatment with intranasal corticosteroids has a potential for controlling MPI in JCP.

**P28**

Abstract not presented and not submitted for publication

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**P29**

Grass pollen nasal challenge is associated with increases in Th2 cytokines, Eotaxin, MDC and IL-6 in nasal fluid

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**Background:** We previously validated a grass pollen nasal challenge model to record clinical outcomes and local biomarkers in nasal fluid [1]. Here we further validate our methods and compare the expression of Th2- and Th1-related cytokines, chemokines and IL-17.

**Methods:** 18 grass pollen allergics underwent nasal allergen challenges; 15 grass allergics had matched diluent challenges. Symptom scores and peak nasal inspiratory flow were recorded; nasal fluid was collected using both polyurethane sponges and Leukosorb filter strips; nasal fluid was analysed by Milliplex cytokine/chemokine magnetic bead multiplex assay.

**Results:** Allergen vs diluent challenges; multi-spot plate assay. A further 6 allergics underwent nasal allergen challenges with collection of fluid using both polyurethane sponges and Leukosorb filter strips; nasal fluid was analysed by Milliplex cytokine/chemokine magnetic bead multiplex assay.

**Conclusions:** Minimal persistent inflammation in Japanese cedar pollinosis and a prophylactic effect of intranasal corticosteroids have been implicated in the down-regulation of inflammatory responses, we hypothesize that failure of up-regulation of DUSP-1/EGR-1 after exposure to HDM in allergic individuals could be responsible for the sustained activation of the allergic response.

**Conclusion:** These results suggest that MPI characterized by the up-regulation of ECP and tryptase is present in JCP, and a prophylactic treatment with intranasal corticosteroids has a potential for controlling MPI in JCP.

**Reference:**
P30
Abstract not presented and not submitted for publication

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P31
The role of mast cells, interleukin-13 and transient receptor potential channels in a mouse model of chemical-induced airway hyperresponsiveness
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Clinical and Translational Allergy 2013, 3(Suppl 2)P31

Background: Occupational asthma is the most common work-related lung disease in industrialized countries. The mechanisms of occupational asthma caused by chemicals are still not completely understood. Therefore, we used a mouse model of chemical-induced asthma to examine the role of the neurogenic system as well as the role of IL-13 and mast cells by using different knock-out mice.

Method: On days 1 and 8, wild type C57Bl/6 mice, IL-13, TRP (Transient Receptor Potential) A1, TRPV1 and mast cell deficient mice were dermally sensitized with 1% TDI (toluene-2.4-diisocyanate) or vehicle (acetone/olive oil) on both ears. On day 15, the mice received a single intranasal challenge with 0.1% TDI or vehicle. In a second experiment TDI or vehicle sensitized wild type C57Bl/6 mice received an intraperitoneal injection of the NK1R antagonist RP67580 (1ug/ml) prior to the challenge. Airway reactivity to methacholine, lung inflammation, lymphocyte subpopulations in the draining auricular lymph nodes and total serum IgE were assessed 24h after the challenge.

Results: IL-13, TRPV1, TRPA1 and mast cell deficient mice showed a significant lower airway hyperreactivity compared to wild type mice, 24h after TDI challenge, without any sign of lung inflammation. Treatment with the NK1R antagonist also resulted in a significant decrease in airway hyperreactivity. In the auricular lymph nodes T-helper cells, T-cytotoxic cells and B-cells were significantly lower in mast cell deficient and IL-13 deficient mice, compared to wild type mice.

Conclusion: These results indicate the importance of IL-13, TRPA1 and TRPV1 channels and mast cells in the development of immune-mediated bronchial hyperreactivity.

P32
Immunocap ISAC as an important diagnostic tool in rhino-sinusitis
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Background: Recent developments in immunology have started to influence clinical allergy by introducing a promising approach of molecular allergy (allergology) - ImmunoCap ISAC.

Aim: We present a unique case of severe allergic rhino-sinusitis in a 39 y.o. female patient that was diagnosed using ISAC.

Method: ISAC is designed to detect specific IgE antibodies to a large number of allergenic epitopes – components of known allergens from a single blood test.

Results: The patient (smoker) complained on a variety of symptoms that were bothering her for more than 3 years: headaches, significant fatigue, nasal blockage, breathlessness on exercise and occasionally at rest. There were no ocular symptoms. She had several courses of antibiotics during this period with slight improvement. Careful history revealed progressive deterioration in her condition; there was no difference in her symptom pattern through the season although she noted that she had more sinus pains in winter. There was a dog, but no dampness in the house. There was no personal or family history of atopy. Anterior rhinoscopy had appearance of acute inflammation with no structural abnormalities. Spirometry showed FEV1 95%, FVC 92% and Peak flow 85% predicted. Skin prick test with valid controls, was negative to a standard panel of aeroallergens including dog. Immunocap ISAC test was offered to broaden the spectrum of allergens tested. This showed - mono-sensitisation to Dog rCan f 5 Arginine esterase 1.5 ISU and negative to all other components.

Conclusion: The spectrum of usually tested dog allergens appears incomplete: Two lipocalins, Can f 1 and Can f 2, and serum albumin, Can f 3, have been characterised in detail but do not fully account for the IgE antibody-binding activity in all dog-allergic patients. Allergen activity has previously been detected in dog urine Can f 5, believed to be produced only in male dogs. ISAC was very beneficial in this case and opened a new insight on the diagnostic process.

P33
Rupatadine oral solution improves rhino-conjunctive symptoms control in children with 6-11 years weighing ≥25 kg with persistent allergic rhinitis
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Background: Clinical trials with the newer 2nd generation antihistamines in children under the age of 12 years have been performed previously but further studies are needed in order to show efficacy and safety in the most unfavourable clinical conditions such as persistent allergic rhinitis (PER). Rupatadine oral solution was developed for children with allergic rhinitis in view of its rapid onset of action and its lack of relevant side effects. These advantages were confirmed previously in a phase III study in children 6-11 years.

Objective: To assess the efficacy and safety of rupatadine (RUP) oral solution in a subgroup of children between 6 and 11 years weighing ≥25 kg with PER.

Methods: A subanalysis was performed from a previous placebo-controlled study carried out in patients between 6-11 years diagnosed as PER according to ARIA criteria. This analysis included patients with a positive prick test, weight ≥25 kg and basal nasal symptoms score (including rhinorrhea, nasal blockage, sneezing and nasal itching assessment) ≥24 obtained in 4 days throughout the 2-week screening period. Patients were allocated to treatment with either RUP oral solution (1 mg/ml) or placebo during 6 weeks. The dose was 5 ml of oral solution. The main efficacy endpoint was the change from baseline of the nasal (4TSS) and global symptoms (5TSS) score at 4 and 6 weeks of treatment. Furthermore the

Table 1 (abstract P33)

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Placebo (n=135)</th>
<th>Rupatadine (n= 131)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>4TSS at 4 weeks</td>
<td>-2.4 (1.9)</td>
<td>-3.1 (2.1)</td>
<td>P &lt; 0.01</td>
</tr>
<tr>
<td>4TSS at 6 weeks</td>
<td>-2.6 (2.0)</td>
<td>-3.4 (2.1)</td>
<td>P &lt; 0.01</td>
</tr>
<tr>
<td>5TSS at 4 weeks</td>
<td>-2.7 (2.4)</td>
<td>-3.7 (2.5)</td>
<td>P &lt; 0.01</td>
</tr>
<tr>
<td>5TSS at 6 weeks</td>
<td>-2.9 (2.5)</td>
<td>-4.0 (2.6)</td>
<td>P &lt; 0.01</td>
</tr>
</tbody>
</table>

PROLOQ overall score showed statistical significant differences between RUP and placebo at 4 weeks (p<0.01) and 6 weeks (p<0.05). Adverse events were scarce in both treatment groups throughout the study. Somnolence was reported with a very low incidence (1.4% RUP) and no serious adverse events were reported.
The subgroup analysed was a total of 266 randomized to rupatadine (n=131) or placebo (n=135). Table 1 summarizes the efficacy results.

**Results:** The subgroup analysis was a total of 266 randomized to rupatadine (n=131) or placebo (n=135). Table 1 summarizes the efficacy results.

**Conclusion:** Rupatadine oral solution (1mg/ml) was significantly more effective than placebo in improving nasal symptoms (ATSS) at 4 and 6 weeks. This is the first clinical evidence of a H1-receptor antagonist efficacy in children between 6-11 years over 25 kg with PER.

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**P34**

Long-term results of functional endoscopic sinus surgery in children with chronic rhinosinusitis with nasal polyps

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**Background:** Chronic rhinosinusitis with nasal polyps (CRSwNP) is rare in children and has a major impact on Quality of Life (QoL). Functional endoscopic sinus surgery (FESS) has proven to be an effective treatment, but it is still unclear what long term outcomes are in children with CRSwNP. Therefore the objective of this study was to assess long term results of FESS in children with CRSwNP.

**Methods:** In this combined prospective and retrospective study a QoL questionnaire was filled in by all children who received FESS because of CRSwNP between the year 2000 and 2010. Almost half of these children also filled in this questionnaire preoperatively. Primary outcome was R-SOM score.

**Results:** 44 Children underwent FESS. From 18 patients we also prospectively collected preoperative QoL questionnaires. The response rate was 82% (36/44) and mean follow-up was 40 years (±2.9). The mean age at surgery was 13 years (±2.9). Of these children 9 had CF (25%) and 10 children asthma (28%). R-SOM scores showed a significant improvement both in general symptoms as well as several different domains when comparing pre- and postoperative questionnaires (p=0.04). Only 14% (S) of the patients needed a subsequent intervention. In children with CF this was 33% (3/9).

**Conclusions:** This study demonstrates that long term results of FESS in children with CRSwNP are good. Overall QoL has improved significantly for the whole group, especially in nasal symptoms, showing that FESS is a good treatment in children with CRSwNP. Furthermore even children with CF show good results.

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**P35**

Chronic rhinosinusitis with nasal polyps in the elderly

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**Background:** To determine the influence of age on the long term results of functional endoscopic sinus surgery (FESS) in patients with chronic rhinosinusitis with nasal polyps (CRSwNP).

**Methods:** In this study we sent all adult patients who received FESS because of CRSwNP between the year 2000 and 2005 in the AMC in Amsterdam a quality of life questionnaire in the year 2012. The Lund- Mackay score was calculated for each patient. We compared postoperative subjective improvement using the SNOT questionnaire. Two different age groups were analysed separately, group 1 (age 18-65) and group 2 (over 65 years).

**Results:** Response rate was 67% (151 out of 225). 104 patients were < 65 years (group 1) and 47 patients > 65 years (group 2). The mean age at the time of questionnaire of the whole group was 56 years old (range 28-84). Mean follow-up time was 7 years (range 12 years). Of these patients 35% had a primary FESS and 65% revision surgery. There was no statistical difference in Lund-Mackay score between the two age groups. The mean postoperative total SNOT score in the whole group was 1.3. We found a tendency to significance with a lower score in the older age group compared to the younger patients (p=0.06) and in several separate SNOT domain scores we found a significant difference. The older patients scored significantly lower in the domains of ear- and head symptoms.

**Conclusion:** Our objective postoperative outcomes show a significant difference in several SNOT domains and a tendency to significance in total SNOT score between the two different age groups. These results could be influenced by a natural decrease in symptoms over time in older patients. There is still not enough evidence for this thought and further research will be needed on this subject.

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**P36**

Early interventional treatment with intranasal corticosteroids is superior to post-onset treatment in Japanese cedar/cypress pollinosis

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**Background:** The usefulness of early interventional treatment (EIT) with INS compared with POT and placebo in Japanese cedar/cypress pollinosis.

**Method:** We designed a three-armed, double-blinded, randomized, placebo-controlled trial. Patients received mometasone furoate nasal spray (EIT group: n=25), placebo (n=25), or 4 weeks of placebo followed by 8 weeks of mometasone (POT group: n=25) for a 12-week period starting on February 1, 2011. The primary endpoint was the comparison of the total nasal symptom score (TNSS) among the three groups. Total ocular symptom score (TOS), total naso-ocular symptom score (TSS), ARIA classification, safety, etc. were secondary endpoints.

**Results:** The placebo and POT groups, but not the EIT group, showed a significant exacerbation of TNSS and TOS soon after the start of pollen counts being high on consecutive days. The 12-week average TSS in the EIT group (score, 2.3) was significantly lower than in the placebo (5.0; P<0.01) and POT (3.9; P=0.03) groups. All subjects in the placebo and POT groups were classified as having persistent rhinitis, while 80% of the EIT group met the ARIA classification criteria (P=0.03). QOL score and nasal ECP levels were lower in the EIT and POT groups as compared with the placebo group. Daytime sleepiness, smell disturbance and the average dose of loratadine taken as the rescue medication were similar. Treatment with mometasone was well tolerated.

**Conclusion:** EIT with INS is superior to POT in controlling pollinosis.

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**P37**

Abstract not presented and not submitted for publication
Azelastine hydrochloride and budesonide (nasal sprays): effectiveness combination therapy monitored by acoustic rhinometry and clinical symptom score in the treatment of allergic rhinitis

P40
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Background: Guidelines therapy for allergic rhinitis (AR) recommends new-generation H1-antihistamines and intranasal corticosteroids as main treatment. The objective of this study was to evaluate the effects of intranasal therapy with azelastine hydrochloride and budesonide (isolated and combined) using nasal provocation test (NPT) and acoustic rhinometry in patients with AR.

Methods: The study population consisted of 28 patients (9 female and 19 males, aged between 18-32 years) with diagnostic of persistent AR (ARIA consensus). This was a randomized, crossover study. Subjects were randomly assigned to receive either azelastine hydrochloride (140 mcg/nostril) or budesonide (64 mcg/nostril) or both drugs. All patients received the three treatments using nasal spray twice daily, each period of treatment lasted 30 days and washout period was 7 days. Subjects were submitted to nasal provocation test (NPT) with histamine before and after each period of treatment. Nasal responsiveness to histamine was monitored based on subjective (symptom score) and objective parameters (acoustic rhinometry) to compare the treatments. After acoustic rhinometry measure (baseline) histamine was instilled in nasal cavity (0.5 mg/mL/nostril) via nasal spray. Minimal cross-area (MCA2) was measured by acoustic rhinometry at times 1; 4; 8; and 12 minutes after NPT for each histamine concentration (0.5; 1; 2; 4 and 6 mg/mL) up to positive response occurs (nasal obstruction). The criteria for a positive response were histamine dose and rhinometric measure time causing at least 20% fall in MCA2 (NPT20). NPT was stopped when a positive response occurred. Statistical significance was assessed by paired t-test.

Results: Baseline MCA2 decreases significantly after azelastine therapy (p=0.01) and did not change with budesonide. Combination therapy demonstrated significantly increasing in baseline MCA2, namely improvement of nasal patency (p=0.005). MCA2 after NPT increased with budesonide (p=0.02) and combined therapy (p=0.002), demonstrating the protective effect of therapy. There was a decrease in MCA2 in asthmatic hydrochloride therapy (p=0.02). Score symptoms during NPT decreases significantly after all treatments (azelastine p=0.04, budesonide and combined drugs p<0.0001).

Conclusion: Azelastine hydrochloride therapy combined with budesonide might provide more therapeutic benefits than isolated drugs in nasal patency and symptoms score in patients with AR.
Objective: To assess the efficacy of MP29-02* (a novel intranasal formulation of azelastine hydrochloride [AZE] and fluticasone propionate [FP]) in providing relief from each of the nasal and ocular symptoms commonly experienced by patients with seasonal AR (SAR) compared to commercially available intranasal AZE or FP nasal sprays or placebo.

Methods: Patients (≥12 years old) with moderate-to-severe SAR (n=610) were randomized into this double-blind, placebo-controlled, 14-day, parallel-group trial to receive MP29-02*, commercially-available AZE or FP nasal sprays, or placebo (all given as 1 spray/nostril bid; total daily dose: AZE 548µg; FP 200µg)). The primary efficacy variable was change from baseline in reflective total nasal symptom score (rTNSS; AM +PM) over 14-days. Secondary endpoints included change from baseline in each of the individual nasal and ocular symptoms.

Results: Defined reduction in nasal congestion by -1.24 vs -0.86 for FP (Diff: -0.39; 95% CI -0.65, -0.13; p=0.0034) and -0.75 for AZE (Diff: -0.49; 95% CI -0.74, -0.24; p=0.0001) and -0.54 for placebo (Diff: -0.70; 95% CI -0.95, -0.45; p=0.0001), with a relative difference of 54% to FP and 70% to AZE. A similar and significant superiority of MP29-02* over FP and AZE was observed for nasal itching (44% to FP, 56% to AZE), rhinorrhea (32% to FP, 65% to AZE) and sneezing (49% to FP, 61% to AZE). The most bothersome ocular symptom of itching was reduced by -1.23 by MP29-02* vs -0.70 for FP (Diff: -0.53; 95% CI: -0.79, -0.26; p=0.0001), -0.88 for AZE (Diff: -0.35; 95% CI: -0.63, -0.08; p=0.0127) and -0.44 for placebo (Diff: -0.79; 95% CI -1.04, -0.54; p<0.0001) with a relative difference of 67% to FP and 44% to AZE. The relative differences to FP and AZE respectively were 51% and 25% for ocular watering, and 53% and 40% for ocular redness.

Conclusion: MP29-02* provides superior relief from each nasal and ocular symptom compared to first line AR therapies, including the most bother-some symptoms of nasal congestion and ocular itching, and can be considered the drug of choice for AR.

*Dymista
The response rate was 54.5% (n = 297). 19.8% were well controlled, but 12.5% had symptoms too, since patients frequently present with symptoms from both nasal and ocular origin. The reflective total of 7 symptom scores (rTNSS) is an endpoint measuring the entire AR symptom complex. It comprises both the reflective total nasal symptom score (rTNSS) and the reflective total ocular symptom score in one global score (max score=42).

Objective: To assess the efficacy of MP29-02* (a novel intranasal formulation of azelastine hydrochloride (AZE) and fluticasone propionate (FP)) in providing relief from the entire AR symptom complex compared to commercially available intranasal AZE or FP nasal sprays and placebo, in patients with seasonal AR (SAR).

Methods: 610 patients (>12 years old) with moderate-to-severe SAR were randomized into this double-blind, placebo-controlled, 14-day, parallel-group trial to MP29-02*, commercially-available AZE or FP nasal sprays, and placebo (all given as 1 spray/nostril bid [total daily doses: AZE = 548 µg; FP=200 µg]). The primary efficacy variable was change from baseline in rTNSS (AM + PM), over 14-days. Change from baseline in rTNSS was assessed post-hoc via an analysis of covariance.

Results: MP29-02* most effectively treated the entire rhinitis symptom complex, reducing the rTNSS from baseline by -8.74 compared to -6.05 for FP (Diff: -2.69; 95% CI: -4.33, -1.06; p=0.0013), -5.83 for AZE (Diff -2.91; 95% CI: -4.52, -1.31; p=0.0004) and -3.55 for placebo (Diff -5.19; 95% CI: -6.17, -3.68; p<0.0001). The relative difference was 52% to FP and 56% to AZE, making MP29-02* twice as effective as either first-line therapy. This benefit was observed during the first day of treatment and was sustained over the entire course of treatment.

Conclusion: Compared to currently available first-line therapy for AR, MP29-02* most effectively treats the entire rhinitis symptom complex, comprising the most commonly reported nasal and ocular symptoms. Such a universal treatment option should preclude the need for concomitant eye drops, and may be considered the drug of choice for AR management.

*Dymista

P45
A new therapy (MP29-02*) effectively targets the entire seasonal allergic rhinitis symptom complex

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Clinical and Translational Allergy 2013, 3(Suppl 2)P45

Background: Over 90% of allergic rhinitis (AR) patients have ocular symptoms during the pollen season, but these are routinely neglected and under-treated. New treatment options should provide relief not only from all nasal symptoms, but all ocular symptoms too, since patients frequently present with symptoms from both nasal and ocular origin. The reflective total of 7 symptom scores (rTNSS) is an endpoint measuring the entire AR symptom complex. It comprises both the reflective total nasal symptom score (rTNSS) and the reflective total ocular symptom score in one global score (max score=42).

Objective: To assess the efficacy of MP29-02* (a novel intranasal formulation of azelastine hydrochloride (AZE) and fluticasone propionate (FP)) in providing relief from the entire AR symptom complex compared to commercially available intranasal AZE or FP nasal sprays and placebo, in patients with seasonal AR (SAR).

Methods: 610 patients (>12 years old) with moderate-to-severe SAR were randomized into this double-blind, placebo-controlled, 14-day, parallel-group trial to MP29-02*, commercially-available AZE or FP nasal sprays, and placebo (all given as 1 spray/nostril bid [total daily doses: AZE = 548 µg; FP=200 µg]). The primary efficacy variable was change from baseline in rTNSS (AM + PM), over 14-days. Change from baseline in rTNSS was assessed post-hoc via an analysis of covariance.

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Conclusion: Compared to currently available first-line therapy for AR, MP29-02* most effectively treats the entire rhinitis symptom complex, comprising the most commonly reported nasal and ocular symptoms. Such a universal treatment option should preclude the need for concomitant eye drops, and may be considered the drug of choice for AR management.

*Dymista
the IT group were significantly lower compared with the non-IT group. 78% of the patients treated with IT was considered as having a mild AR versus 31.5% of the non-IT patients and 81.7% an intermittent AR versus 49.4% in the non-IT group. In the IT group 69.5% of the patients didn’t use any medical treatment 3 years after diagnosis of AR versus 38.9% in the non-IT group.

Conclusions: The AR of 84% of patients three years after treatment with IT is controlled, with significantly better degree of control and less need for medical treatment compared to AR patients who received pharmacotherapy for three years. These date reinforce the need for considering treatment with IT in patients diagnosed with moderate-to-severe AR.

Cite abstracts in this supplement using the relevant abstract number, e.g.: Droesseeert et al. Observational study: evaluating symptom control in allergic rhinitis at three years after starting immunotherapy. Clinical and Translational Allergy 2013, 3(Suppl 2):P46