Omalizumab's effectiveness in severe allergic asthma and nasal polyps: a real-life study

Running title : Omalizumab in severe asthma and nasal polyps

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Abstract

Background: Omalizumab is a human anti-IgE antibody approved for the treatment of severe allergic asthma (SAA), but its effectiveness when a chronic rhinosinusitis with nasal polyposis (CRSNP+) is associated is less documented.

Objective: The aim of this study was to evaluate in real-life the effectiveness of omalizumab in patients with SAA and CRSNP+ with or without aspirin intolerance.

Methods: A retrospective, observational, multicentric real-life study was realized including patients with SAA and CRSNP+ treated by omalizumab for 6 months. Asthma outcome parameters (symptoms, number of salbutamol rescue/week, number of moderate/severe exacerbations, Asthma Control Test score, and lung function), sino-nasal outcome parameters (symptoms, number of acute rhinosinusitis, sinus computed tomographic images, nasal endoscopy polyps score), and serum eosinophils levels have been analysed before and after 6 months of treatment by omalizumab.

Results: Twenty-four adult patients were included (nine with a documented aspirin intolerance). All respiratory parameters were significantly improved by the treatment. In parallel, the sino-nasal clinical outcomes and the sinus computed tomographic images were significantly improved without an important effect on the nasal endoscopy polyps score. The serum levels of eosinophils were significantly decreased after 6 months of treatment by omalizumab.

Conclusion: The treatment by omalizumab in SAA improves the associated CRSNP+ outcomes supporting the concept of the one airway disease.

Key words: Severe allergic asthma. CRSNP+. Omalizumab effectiveness.

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Resumen

Antecedentes: el omalizumab es un anticuerpo anti-IgE humanizado aprobado para el tratamiento del asma alérgica grave (SAA), si bien su eficacia, cuando esta se asocia a la rinosinusitis crónica con poliposis nasal (CRSNP +), está menos documentada.

Objetivo: el objetivo de este estudio fue evaluar en "vida real" la eficacia de omalizumab en pacientes con SAA y CRSNP + con o sin intolerancia a la aspirina.

Métodos: se realizó un estudio retrospectivo, observacional y multicéntrico, en vida real que incluyó pacientes con SAA y CRSNP + que fueron tratados con omalizumab durante 6 meses. Las variables de eficacia en relación al asma (síntomas, número de inhalaciones de rescate de salbutamol por semana, número de exacerbaciones moderadas/graves, puntuación de la prueba de control del asma (ACT) y función pulmonar), y de la rinosinusitos (síntomas, número de rinosinusitis aguda, puntuación en tomografía computarizada, puntuación del tamaño de los pólipos en la endoscopia nasal) y el nivel de eosinófilos en sangre se analizaron antes y después de 6 meses de tratamiento con omalizumab.

Resultados: se incluyeron veinticuatro pacientes adultos (nueve con una intolerancia a la aspirina documentada). Todas las variables de eficacia en relación al asma mejoraron significativamente con el tratamiento. Paralelamente, las variables clínicas de eficacia en rinosinusitis y la puntuación de las imágenes tomográficas de los senos paranasales mejoraron significativamente, si bien no se observó un efecto relevante en la puntuación de los pólipos en la endoscopia nasal. El nivel de eosinófilos en sangre disminuyó significativamente después de 6 meses de tratamiento con omalizumab.

Conclusión: el tratamiento con omalizumab en pacientes con SAA induce paralelamente una mejoría clínica y radiológica de la CRSNP + asociada, lo que apoya el concepto de una única enfermedad de las vías respiratorias.

Palabras clave: Asma alérgica grave. CRSNP +. afectividad de omalizumab.

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Introduction

Chronic rhinosinusitis (CRS) is an inflammation of the nasal cavity and paranasal sinuses characterized by symptoms such as nasal obstruction or rhinorrhoea, facial pain, reduction or loss of smell, lasting for ≥12 weeks with objective evidence on nasal endoscopy and sinus CT scan. Based on the presence of nasal polyps (NP) (benign oedematous masses in the nasal cavities), CRS is classified as CRS with nasal polyposis (CRSNP+) and without nasal polyposis (CRSNP-) [1]. NP has a negative impact on quality of life and can lead to an important workplace absenteeism [2]. The standard treatment of CRSNP+ is medical management with nasal saline irrigations and intranasal steroids for maintenance therapy, systemic corticosteroids and antibiotics for exacerbations, and endoscopic sinus surgery in patients with CRSNP+ who fail to medical therapy [3].

Asthma is a heterogeneous inflammatory airway disease comprising several phenotypes driven by different pathways [4]. The diagnosis of asthma is based on the presence of intermittent symptoms of wheeze, cough and chest tightness that vary over time and in intensity with variable expiratory airflow limitation [5]. Inhaled corticosteroid (ICS) therapy remains the cornerstone of treatment and current guidelines recommend a step-up approach with incremental dosing and additonal controller medication in order to achieve symptom control and prevent exacerbations [4–6] . While a majority of patients respond well to these guideline-based treatement approaches, 5-10% remain refractory despite the maximal therapeutic regimen defining the « severe asthma » population [5,7]. The severe allergic asthma (SAA) phenotype is a severe asthma with allergic background and high serum IgE level. The introduction of anti-IgE antibody treatment (omalizumab) at Step 5 of the Global Initiative for Asthma (GINA) guidelines opended the era of personalised medicine in asthma [4].

A strong association between CRS and asthma has been recognised with a higher prevalence of CRSNP+ in asthma patients compared to the general population (7% *vs* 4%) and the presence of asthma in up to 45% of patients with CRSNP+ [8,9]. In addition, approximatively 10% of patients with asthma and CRS reports aspirin-exacerbated respiratory disease (AERD) [10]. Many previous studies have provided consistent evidence from clinical epidemiology, pathophysiology, histology, and treatment outcomes for the phenotype CRSNP+ and asthma sustaining the concept of the “United Airway Disease” [8,9]. Clinical

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phenotype of patients with asthma and associated CRSNP+ has been characterized by adult-onset asthma, higher incidence of allergic rhinitis, longer duration of nasal symptoms, increased risk of exacerbation, airway obstruction, uncontrolled and severe asthma, higher computed tomography and endoscopy scores, higher number of sino-nasal surgeries, and poorer quality of life [8,11] These patients may have a more intense lower airway inflammation and remodelling in relation to the presence of CRSNP+ [12] Upregulation of the Th2 system with predominantly eosinophilic inflammation and elevated serum and nasal levels of IL5 and IgE are found in up to 85% of CRSNP+ [13]. A recent analysis of inflammatory endotypes in CRS [14] found that the cluster associated with high IL5 levels is an exclusive NP phenotype, with highest concentrations of IgE and asthma prevalence, with all samples expressing *Staphylococcus aureus* enterotoxin-specific IgE. Based on these data, omalizumab treatment currently approved for the management of the SAA provides a potential therapeutic target for the management of CRSNP+ in selected patients [3].

Data about the effectiveness of omalizumab in the association SAA and CRSNP+ are limited at the moment to small series and studies with results sometimes contradictory concerning the patients outcomes [15–19]. The aim of this study was to evaluate the effectiveness of omalizumab in real-life in patients with SAA and CRSNP+ with or without aspirin intolerance.

Methods

Patients

This multicentre, noninterventional, retrospective, observational, real-life study was performed in the Departments of Pulmonology of University Hospitals of Besançon, Dijon, Nancy, Strasbourg and the Regional Hospital of Colmar, France from December 1, 2016 to October 31, 2017. The study was approved by the Institutional Review Board of the French learned society for respiratory medicine – Société de Pneumologie de Langue Française, no CEPRO 2017-042 and all patients provided informed consent before extracting and using their data.

Hospital chest physicians with experience in treating severe asthma (based on European Respiratory Society/American Thoracic Society definition [20]) were asked to

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provide data of all their patients with SAA and associated CRSNP+ treated by omalizumab for at less 6 months. Inclusion criteria were: adult patients with SAA uncontrolled despite a treatment by step 4 or 5 of the GINA guidelines [3], for which it was necessary to add omalizumab to improve symptom control and to prevent exacerbations and with associated CRSNP+ evaluated by Ear Nose Throat (ENT) specialist and treated by intranasal corticosteroids. The atopy was proved by skin prick test to common aero-allergens according to the European standards [21] and the sensitization to at least one perennial allergen was documented before starting the treatment by omalizumab.. Total serum Ig E level was between 120 UI/mL and 996 UI/mL. The dose (in milligrams) and dosing frequency (every 2 or 4 weeks) of omalizumab administrated for 6 months were based on total serum IgE levels (UI/mL) and body weight (in kilograms), with a maximum dose of 600 mg every 2 weeks. A documented physician evaluation of response to omalizumab at 6 months of treatment was recorded.

Outcome measures

For asthma outcomes, we analysed clinical parameters (dyspnoea, cough, number of daytime asthma symptom/week, number of nocturnal asthma symptom/week, number of salbutamol rescue/week, number of moderate/severe exacerbations), Asthma Control Test (ACT) score, and lung function variables, 6 months before and after the omalizumab treatment. ACT $\geq$ 20 was considered as well-controlled asthma, ACT $\leq$ 19 as poorly controlled asthma, and change of $\geq$ 3 points clinically important in an individual patient (10). Moderate/severe asthma exacerbation was defined as aggravation of respiratory symptoms requiring systemic corticosteroids for at least 3 days and/or hospitalisation.

The ENT evaluation included symptoms (pruritus, loss of smell, rhinorrhoea, sneezing, nasal obstruction), number of acute rhinosinusitis, sinus computed tomographic (CT) images, endoscopic evaluation of NP score 6 months before and after the initiation of omalizumab therapy. The ENT symptoms severity was evaluated by the VAS scale (0 = not troublesome and 10 = worst possible) [2]. The endoscopic NP score was assessed by mean of endoscopy for each nostril separately and graded based on polyp size, resulting in scores of 0 to 4: 0 = no polyps; 1 = small polyps in the middle meatus not reaching below the inferior border of middle turbinate, 2 = polyps reaching below the lower border of the middle turbinate; 3 = large polyps reaching the lower border of the inferior turbinate or polyps medial

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to the middle turbinate; 4 = large polyps causing complete obstruction of the inferior nasal cavity [18]. Acute rhinosinusitis was defined as the presence of symptoms/signs such as discoloured discharge and purulent secretion in cavum nasi, severe local pain and fever (>38ºC) for at least 5 days requiring antibiotics.

The diagnosis of AERD, documented on clinical history and positive oral aspirin challenge test performed a several years ago was obtain from the medical dossier of patients in each center. The oral aspirin challenge test was impossible to perform more recently in raison of the uncontrolled asthma criteria [10]. The protocole curently used in the North-East of France inludes incremental doses (30mg, 60mg, 100mg, 160mg, 325mg) every 2 hours with monitoring in hospitalization for few hours to one day as recommended by current guidelines [10].

The single biological marker in this study was the serum eosinophils level, measured before and after omalizumab treatment.

Statistical analysis

Statistical analysis was performed using the SPPS progamm version 9.4 (SAS Institute, Cary, NC, USA). Qualitative variables in descriptive analysis are expressed as number or percentage. Quantitative variables are presented as mean ± standard deviation (SD). Comparisons of values between baseline and 6 months after treatment by omalizumab were performed using TTEST for all patients and between patients with and without aspirin intolerance using Fisher test. The limit of significance was $p < 0.05$.

- **Results**

Patients:

Twenty-four patients were included in the study, 15 without aspirin intolerance and 9 with AERD. Many patients (83%) had adult-onset asthma. All patients had atopy with symptoms of asthma and rhinitis. The most frequent allergies were dust mite (75%), pets (cat 37.5%, dog 33.3%) grass pollen (33.3%), and birch pollen (20.8%). Some patients had multiple allergies (41.7%) but all patients had at least one perennial allergen sensitization. Most patients were never smokers (62.5%). The baseline characteristics are summarized in Table I.

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Effectiveness of omalizumab:

Nasal polyposis:

Based on total serum IgE levels and body weight, half of patients received omalizumab every 2 weeks, and the others every 4 weeks. After 6 months of treatment by omalizumab, the ENT symptoms were significantly improved: pruritus ($p=0.002$), loss of smell ($p<0.001$), rhinorrhoea ($p<0.001$), sneezing ($p<0.001$), nasal obstruction ($p<0.001$) in parallel with the decrease of the number of acute rhinosinusitis (4.2 *vs* 1.3, $p<0.001$).

Three quarters of patients had previous surgery for NP. The diagnosis of NP was established and quantified by a ENT specialist during a nasal endoscopy at baseline and 6 months after starting of omalizumab therapy. At baseline, 45.8% of patients had NP stage 2 based on endoscopic nasal criteria, 37.5% stage 3, and 16.7% stage 1. After 6 months, several patients improved the stage of NP (Table II) without statistically significant difference.

At baseline the sinus CT scan showed images of sinusitis with NP in 58.3% of patients, only NP in 29.2% of patients, and sinusitis without NP in 12.5% of patients. Omalizumab therapy improved significantly the sinus CT scan opacities secondary to sinusitis making the images of NP more visible as showed in Table II. The improvement of scan imaging at 6 months was evident in 37.5% of patients in the studied population.

Asthma:

Omalizumab therapy improved significantly respiratory symptoms (dyspnoea $p<0.001$ and cough $p=0.028$), decreased the number of asthma daytime and nocturnal symptoms per week reducing the need for the rescue medication ($p<0.001$). The change in the ACT score mean was significant passing from 12.2 to 19.5 ($p<0.001$). Omalizumab treatment reduced significantly the number of asthma exacerbation at 6 months (4.6 *vs* 1.4, $p<0.001$).

Lung function was significantly improved by the treatment with increase of 12.8% in the FEV1 ($p<0.001$), 10.2% in the FVC ($p<0.001$), and decrease of bronchial obstruction (FEV1/FVC at 61.5% before treatment *vs* 66.7% after, $p=0.017$).

Omalizumab treatment significantly decreased the blood eosinophils level (0.91 G/L at baseline *vs* 0.52 G/L at 6 months, $p=0.006$).

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The clinical, functionnal respiratory, biological and imaging characteristics before and after the treatment are summarized in Table II.

AERD

There was no difference in clinical, functional respiratory, biological and imaging studied parameters at baseline in patients with and without AERD as showed in Table III. The comparative analysis of the same parameters after 6 months of treatment by omalizumab in patients with and without AERD proved a similar evolution on clinical, functional respiratory and biological outcomes. The only significant difference between the groups was a better improvement of sinus opacities secondary to sinusitis in patients with AERD *vs* patients without AERD as showed in Table IV.

- **Discussion**

Our real-life study showed that omalizumab is an effective therapy in patients with SAA and CRSNP+ with improvement of asthma (symptoms, control, lung function, attacks medication rescue and exacerbation), and ENT outcomes (symptoms, CT scan images, acute rhinosinusitis number) independently of the presence of AERD. The studied population is characteristic for the phenotype asthma-CRSNP+ with a predominant adult-onset asthma, high prevalence of allergic rhinitis and previous sino-nasal surgery, high exacerbation rate, poor controlled asthma, airway obstruction, and eosinophilic inflammatory pattern [7,8,12,22].

The prevalence of the AERD is at 37.5% in this study, higher than previously described in the severe asthma (14.9%) [10]. One possible explaination of this fact is the general underestimation of AERD because this prevalence increases at 21% in severe asthma when the asprin challenge test is performed systematically [10]. Similarly, the prevalence of AERD in patients with CRSNP+ is estimated at 8.7% while up to 70% of patients report sensitivity to red wine and other alcoholic beverage which could indicate the diagnosis of AERD but non documented with a challenge test [23]. Further studies on larges cohorts in the association asthma-CRSNP+ are needed to find the real prevalence of the AERD with a systematic documentation by an aspirin challenge test when the clinical history is compatible with the diagnosis.

The present study confirmed the benefit of omalizumab therapy for the persistent allergic rhinitis symptoms (pruritus, loss of smell, rhinorrhoea, sneezing, nasal obstruction) in

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SAA patients as previously reported [24]. In a recent metanalysis including 2870 patients with allergic rhinitis [25], omalizumab treatment reduced both daily nasal symptoms and nasal rescue medication usage. These results are not surprising given that allergic asthma and allergic rhinitis have shared pathogenic mechanisms and common triggers and are considered to be components of a single IgE-mediated inflammatory condition. The allergic profile identified in this study is typical for the North-Eastern region of France.

If for omalizumab therapy and allergic airway disease "big" data are available, for the CRSNP+ the literature data are limited to a few small studies with a short treatment period (usually 16 weeks) [3,26]. Three quarters of the studied population required previous surgical interventions for the NP. In several recalcitrant cases of CRSNP+ with severe ENT symptoms and multiple surgical interventions, additional adjuvant medical therapies such as leukotriene antagonists, low-dose macrolides, topical antibiotics, oral antifungal and biologic agents could be benefitial [3].

In this study, the treatement by omalizumab was effective on both ENT symptoms secondary to CRSNP+ (loss of smell, rhinorrhoea, nasal obstruction) and asthma symptoms (dyspnoea, cough, number of daytime asthma symptom/week, number of nocturnal asthma symptom/week) in line with other published data [15,18]. A previous study including patients with NP and asthma treated by omalizumab for 16 weeks [18], showed a significant improvement of several symptoms such as nasal congestion, rhinorrhoea, loss of smell, dyspnoea and wheeze without a benefice on the cough. The decrease of the cough in patients with SAA and CRSNP+ by omalizumab therapy at 6 months is one original finding of our study.

Similarly, the present study showed a significant improvement of the asthma control (ACT score) at 6 months of treatment by omalizumab in patients with SAA and CRSNP+ in line with the data of a recent real-life study [17]. The last one demonstrated a significant improvement in the sino-nasal outcome (SNOT)-22 and the asthma control (measured by Asthma Control Questionnaire - ACQ7) after 16 weeks of treatment by omalizumab in a similar population. Other previous studies including patients with SAA reported the benefit of omalizumab therapy on the disease control with an improvement of ACQ or ACT score [27,28] but data about the impact of this treatment in patients with the association SAA and CRSNP+ are very limited at the moment.

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Other original results of this study are the significant decrease in the number of acute rhinosinusitis and asthma exacerbations requiring medical treatment, and rescue beta2-agonist medication needs, 6 months after the initiation of omalizumab therapy. To the best of our knowledge, this is the firth study in the literature able to prove these data in the association SAA and CRSNP+. Although, multiples previous studies and metanalysis have showed the positive impact of omalizumab therapy in SAA outcomes [29,30]. For example, a systematic review including 24 real-life effectiveness studies of the omalizumab in SAA [29] confirmed the short- and long-term benefit of anti-IgE therapy in terms of achieving asthma control, reducing symptomatology, severe exacerbations and associated work/school days lost; reducing healthcare resource utilizations, in particular hospitalizations, hospital lengths of stay and accident specialist or emergency department visits; reducing or discontinuing other asthma medications; improving lung function and quality of life.

In the present study, the FEV1 was significantly increased at 6 months of treatment by omalizumab compared to baseline by >10% similarly to data found in the study published recently by Mansur et al. in patients with SAA without CRSNP+ [27]. The improvement in lung function parameters by omalizumab treatment was reported previously in SAA patients independently of the presence of CRSNP+ [27,30] , but our data proves for the first time in the literature this effect in patients with SAA and associated CRSNP+.

The impact of omalizumab therapy on the endoscopic scores of NP is controversial. The present study did not show any significant change in the endoscopic polyp score after 6 months of treatment by omalizumab in line with the study of Pinto et al. [31] but in contradiction with other previous data [15,18]. Two explanations are possible for this fact. The first one is that all published data are the results of series or small cohorts and “big” data are lacking. The second one is that our study is retrospective multicentric and the included patients were not evaluated in endoscopy by the same ENT specialist.

The present study confirms the improvement of CT sinus scan opacities in patients treated by omalizumab as previously described [15,18,31]. Interestingly, in the study of Gevaert [18], omalizumab therapy significantly improved Lund-Mackay CT scan score only in the allergic asthmatic patients with CRSNP+ in contrast to the nonallergic asthmatic patients. All patients included in our study were allergic and, unfortunately, the Lund-Mackay CT scan score was not available for all patients.

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To the best of our knowledge, this is the first study which showed a significant decrease in number of blood eosinophils in SAA patients with CRSNP+ by omalizumab therapy. The blood eosinophils level before omalizumab treatment in the present study was higher (0.91 G/L) than in the study of Gevaert (0.39 G/L) [18]. One possible explanation for this fact could be that in our study all patients were allergic while in the other study the population was mixed: 7 patients were allergic and 8 nonallergic. It is known that the high blood eosinophils level (> 0.3 G/L) in asthmatic patients is associated with lower lung function, higher rate of exacerbations and poorer asthma control [32] and omalizumab therapy decreases the blood eosinophils level in treated patients with SAA [33] as found also in our study. Recent data [28,34] showed that omalizumab effectiveness is similar in « high » (≥ 0.3 G/L) and « low » (< 0.3 G/L) eosinophil subgroups with significant improvement of asthma control and reduction of annual exacerbation/hospitalization rate.

The present study confirms previous data whose reported a similar effectiveness of omalizumab therapy for patients with v*s* without AERD [18]. The mechanisms which could explain the benefit of the omalizumab treatment in the AERD are not fully understood. One of the pathomechanisms recognized in the AERD is the activation of mast cells *via* cysteinyl leukotriene-driven IL-33 [10]. A recent study showed that omalizumab reduces cysteinyl leukotriene overproduction [35], so the activation of mast cells on the IL-33 pathway is decreased as well the role which they play in the persistent type 2 inflammation in patients with AERD.

Our results are in line with the data from a Japanese cohort including 21 patients with AERD treated by omalizumab with a significant improvement of all asthma and ENT symptoms, decrease of asthma exacerbation rate and blood eosinophils level [35]. On the other hand, this study failed to prove a significant improvement of the lung function as found in the present study. In addition, our study showed that omalizumab treatment improved significantly CT scan images of sinusitis for patients with AERD compared to patients without AERD, never described before. In a case series of patients with AERD, omalizumab therapy for 6 months decreased significantly the number of exacerbation with improvement of patients' quality of life and development of tolerance to non-steroidal anti-inflammatory drug [36]. Another recent study confirmed that omalizumab administration in atopic patients with AERD, even for 16 weeks, improved the clinical tolerability to aspirin desensitization [37]. Omalizumab seems to be an interesting therapeutic approach for patients with AERD.

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A recent study [17] showed a comparable effectiveness of omalizumab therapy (16 weeks) *vs* surgery in patients with CRSNP+ and SAA with a parallel improvement of sino-nasal outcomes and asthma control for both groups supporting the concept of the one airway disease hypothesis. The possibility to treat the one airway disease with a single biologic agent (anti-IgE, anti-IL5 or anti-IL4/13) is on the horizon viewing the recent progress in this domain [3,26].

Currently, this study is the largest in the literature which analyse in real-life the effectiveness of omalizumab in patients with SAA and CRSNP+. Omalizumab therapy improved asthma outcomes (symptoms, control, lung function, attacks medication rescue), ENT symptoms, CT scan images, decreased number of acute rhinosinusitis, asthma exacerbations and blood eosinophils level without a significant effect in the NP score.

Patients with AERD have the same outcomes as patients without AERD except the improvement of the sinusitis on CT sinus scan after 6 months of treatment by omalizumab more evident for the first group. These results need to be verified by prospective studies including large cohorts of patients. Biologic therapy could be an alternative in the treatment of recalcitrant CRSNP+ in SAA patients with or without AERD.

Conflict of interest:

A.Tiotiu is member of scientific advisory board of Menarini, Novartis Pharma, and co-investigator in studies for AstraZeneca, Novartis Pharma, Sanofi.

JP. Oster is member of scientific advisory board of Novartis Pharma.

P. Roux is member of scientific advisory board of Novartis Pharma.

PL. Nguyen Thi: none.

G. Peiffert is member of scientific advisory board of Chiesi and Novartis Pharma.

P. Bonniaud is member of scientific advisory board of Novartis Pharma, and co-investigator in studies for AstraZeneca, GSK, Novartis Pharma, Sanofi.

JC. Dalphin is member of scientific advisory board of Novartis Pharma, and Teva.

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F. de Blay is member of scientific advisory board of ALK, AstraZeneca, GSK, Novartis Pharma, Teva and co-investigator in studies for ALK, Astra-Zeneca, GSK, Novartis Pharma, Sanofi.

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Table I. Clinical and demographic characteristics of population at baseline

Age (y), mean (SD)	49 (16)
Men/women (%)	58/42
Smoking (%)	
Never smoker	62.50
Ex-smoker	33.33
Active smoker	4.17
Pack-year mean (SD)	4.21 (7.37)
Family history (%)	
Atopy	12.50
Asthma	12.50
Asthma diagnosis early/late onset (%)	17/83
Allergy (%)	
Dust mite	75
Aspergillus	12.50
Alternaria	8.33
Cat	37.50
Dog	33.33
Birch pollen	20.83
Ash pollen	12.50
Cypress pollen	4.17
Grass pollen	33.33
Plantain pollen	12.50
Mugwort pollen	8.33
AERD (%)	37.50
Previous polyp surgery (%)	75
Sinus CT scan (%)	
Nasal polyposis	29.17
Sinusitis	12.50
Nasal polyposis + Sinusitis	58.33
Total serum Ig E (UI/mL) mean (SD)	494 (337)

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Table II. Clinical characteristics, lung function, biological and imaging challenges before and after 6 months of treatment with omalizumab

Parameter	Before	After	p value
ENT severity VAS symptom score mean (SD)			
Pruritus	1.88 (2.85)	0	0.002
Loss of smell	8.50 (1.58)	5.08 (3.42)	<0.001
Rhinorrhoea	8.00 (2.57)	4.83 (3.27)	<0.001
Sneezing	2.88 (3.20)	0.42 (1.38)	<0.001
Nasal obstruction	7.38 (3.97)	1.17 (3.39)	<0.001
Number of acute rhinosinusitis mean (SD)	4.21 (1.28)	1.29 (1.49)	<0.001
Endoscopic nasal polyp score n (%)			0.415
1	16.67	20.83	
2	45.83	58.33	
3	37.50	20.83	
CT sinus scan (%)			0.006
Nasal polyps	29.17	70.83	
Sinusitis	12.50	4.17	
Nasal polyps + Sinusitis	58.33	25.00	
Respiratory symptom			
Dyspnoea (mMRC) score n (%)			<0.001
0	0	25.00	
1	20.83	41.67	
2	12.50	29.16	
3	62.50	4.17	
4	4.17	0	
Cough n (%)	83.33	62.50	0.028
Number of daytime asthma symptom/week mean (SD)	5.25 (2.95)	1.67 (1.28)	<0.001
Number of nocturnal asthma symptom/week mean (SD)	2.88 (2.09)	0.54 (0.96)	<0.001
Number of salbutamol rescue/week mean (SD)	13.29 (7.51)	3.63 (3.08)	<0.001
ACT score mean (SD)	12.21 (4.09)	19.46 (3.34)	<0.001
Number of asthma exacerbation mean (SD)	4.58 (1.25)	1.42 (1.44)	<0.001
Lung function mean (SD)			
FEV1 (%)	60.08 (18.24)	72.88 (19.43)	<0.001
FVC (%)	83.17 (17.88)	93.38 (17.06)	<0.001
FEV1/FVC (%)	61.50 (13.96)	66.67 (11.21)	0.017
Blood eosinophils level mean (G/L) (SD)	0.91 (0.51)	0.52 (0.38)	0.006

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Table III. Patients' clinical, functional respiratory, biological and imaging characteristics at baseline in patients with/without AERD

Parameter	Without AERD (n=15)	With AERD (n=9)	p value
ENT severity VAS symptom score mean (SD)			
Pruritus	2.00 (2.40)	1.67 (2.59)	0.809
Loss of smell	8.40 (1.44)	8.67 (1.33)	0.701
Rhinorrhoea	7.60 (1.87)	8.67 (1.63)	0.309
Sneezing	3.00 (2.80)	2.67 (2.96)	0.821
Nasal obstruction	7.53 (3.29)	7.11 (3.41)	0.813
Number of acute rhinosinusitis mean (SD)	4.53 (1.10)	3.67 (1.63)	0.276
Endoscopic nasal polyp score n (%)			0.519
1	20.00	33.33	
2	46.67	33.33	
3	33.33	33.33	
Sinus CT scan (%)			0.278
Nasal polyps	33.33	22.22	
Sinusitis	20.00	0	
Nasal polyps + Sinusitis	46.67	77.78	
Respiratory symptom			
Dyspnoea (mMRC) score n (%)			0.837
1	13.33	33.33	
2	20.00	0	
3	66.67	55.56	
4	0	11.11	
Cough n (%)	93.33	66.67	0.167
Number of daytime asthma symptom/week mean (SD)	5.47 (2.49)	4.89 (2.09)	0.660
Number of nocturnal asthma symptom/week mean (SD)	2.93 (1.78)	2.78 (1.48)	0.863
Number of salbutamol rescue/week mean (SD)	15.13 (7.08)	10.22 (4.02)	0.100
ACT score mean (SD)	12.00 (3.33)	12.56 (3.48)	0.759
Number of asthma exacerbation mean (SD)	4.53 (1.10)	4.47 (1.26)	0.818
Lung function mean (SD)			
FEV1 (%)	63.67 (17.33)	54.11 (10.57)	0.182
FVC (%)	84.13 (18.56)	81.56 (5.60)	0.691
FEV1/FVC (%)	63.40 (10.43)	58.33 (13.63)	0.445
Blood eosinophils level mean (G/L) (SD)	0.81 (0.29)	1.07 (0.47)	0.312
Total serum Ig E (UI/mL) mean (SD)	517 (320)	455 (284)	0.679

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Table IV. Patients' clinical, functional respiratory, biological and imaging characteristics after 6 months of treatment by omalizumab in patients with/without AERD

Parameter	**Without AERD (n=15)**	**With AERD (n=9)**	**p value**
ENT severity VAS symptom score mean (SD)			
Pruritus	0	0	
Loss of smell	4.87 (2.59)	5.44 (2.62)	0.703
Rhinorrhoea	4.87 (2.59)	4.78 (2.12)	0.950
Sneezing	0.33 (0.62)	0.56 (0.98)	0.736
Nasal obstruction	4.20 (2.83)	4.11 (2.74)	0.952
Number of acute rhinosinusitis mean (SD)	1.47 (1.29)	1.00 (1.11)	0.454
Endoscopic nasal polyp score n (%)			1.000
1	13.33	33.33	
2	73.33	33.33	
3	13.33	33.33	
Sinus CT scan (%)			0.004
Nasal polyps	53.33	100.00	
Sinusitis	6.67	0	
Nasal polyps + Sinusitis	40.00	0	
Respiratory symptom			
Dyspnoea (mMRC) score n (%)			0.370
0	33.33	11.11	
1	33.33	0	
2	33.33	55.56	
3	0	33.33	
Cough n (%)	73.33	44.44	0.192
Number of daytime asthma symptom/week mean (SD)	1.73 (1.12)	1.56 (0.94)	0.748
Number of nocturnal asthma symptom/week mean (SD)	0.33 (0.53)	0.89 (0.99)	0.255
Number of salbutamol rescue/week mean (SD)	3.87 (2.29)	3.22 (2.47)	0.659
ACT score mean (SD)	18.80 (2.85)	20.56 (2.39)	0.195
Number of asthma exacerbation mean (SD)	1.47 (1.29)	1.33 (1.04)	0.823
Lung function mean (SD)			
FEV1 (%)	76.00 (20.53)	67.67 (7.78)	0.258
FVC (%)	94.60 (17.17)	91.33 (8.00)	0.609
FEV1/FVC (%)	68.53 (8.03)	63.56 (9.73)	0.313
Blood eosinophils level mean (G/L) (SD)	0.51 (0.25)	0.54 (0.39)	0.881

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