Add-on omalizumab in children with severe allergic asthma: a 1-year real life survey

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ABSTRACT Omalizumab has been shown to reduce exacerbation rates in moderate to severe allergic asthma. Our aim was to evaluate omalizumab efficacy and safety in a real-life setting in severe asthmatic children.

104 children (aged 6–18 years), followed up in paediatric pulmonary tertiary care centres, were included at the beginning of omalizumab treatment. Asthma control levels, exacerbations, inhaled corticosteroid dose, lung function and adverse events were evaluated over 1 year.

Children were characterised by allergic sensitisation to three or more allergens (66%), high IgE levels (mean 1125 $kU \cdot L^{-1}$), high rate of exacerbations (4.4 per year) and healthcare use during the previous year, and high inhaled corticosteroid dose (mean 703 μg equivalent fluticasone per day). Asthma control levels defined as good, partial or poor, improved from 0%, 18% and 82% at entry to 53%, 30% and 17% at week 20, and to 67%, 25% and 8% at week 52, respectively ($p<0.0001$). Exacerbation and hospitalisation rates dropped by 72% and 88.5%, respectively. At 12 months, forced expiratory volume in 1 s improved by 4.9% ($p=0.023$), and inhaled corticosteroid dose decreased by 30% ($p<0.001$). Six patients stopped omalizumab for related significant adverse events.

Omalizumab improved asthma control in children with severe allergic asthma and was generally well tolerated. The observed benefit was greater than that reported in clinical trials.

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Introduction

The management of severe asthma in children remains a challenge, with its prevalence being estimated at 5% of the asthmatic population [1]. The term ''problematic severe asthma'' has been recently preferred to describe these school-aged children who have poorly controlled asthma despite maintenance therapy with $\geqslant$400 μg of fluticasone per day or equivalent of inhaled corticosteroids (ICSs) plus inhaled long-acting β-agonist (LABA) or leukotriene receptor antagonist or theophylline [2]. Those children are characterised at various degrees by daily symptoms, severe or frequent exacerbations, high rates of healthcare utilisation, persistent lung function alteration and altered quality of life. Problematic severe asthma is therefore a costly disease in childhood despite its fairly low frequency. Omalizumab is a recent and expensive treatment designed as an add-on therapy in difficult-to-treat patients with allergic asthma. Children included in clinical trials have been part of a wide age group including mainly adults in the first clinical trial (age range 12–79 years) [3], and then of specific paediatric trials [4–8]. These studies have shown a significant decrease in exacerbations and healthcare use, and an improvement in quality of life, but nonetheless a modest effect on symptoms and lung function tests (LFTs). The French Health Authority has limited the utilisation of omalizumab to allergic children with uncontrolled persistent asthma and/or severe exacerbations, severe airway obstruction evaluated by LFTs when aged >12 years, despite being administered high doses of ICS or oral corticosteroids in association with at least LABA. In France, omalizumab has been available since 2006 for children aged >12 years and with total IgE $\leqslant$700 kU·L^{-1} and since 2009 for those aged >6 years and with total IgE $\leqslant$1500 kU·L^{-1}. A few real-life studies have been conducted in adults [9, 10]. The latter have not only confirmed but also extended previous drug efficacy and safety observed in randomised trials. Conversely, knowledge on omalizumab utilisation and safety has remained limited in childhood [11, 12]. This was marked in adolescents (12–18 years) who were diluted in the large primary study [3]. Moreover, the effect of omalizumab on disease control has not yet been assessed as an efficacy outcome [4–7].

This 1-year observational study reports the real-life efficacy and safety of add-on treatment with omalizumab in a large group of children with allergic severe asthma. The primary objective was to evaluate the effect of add-on omalizumab on asthma control, as mentioned in step 5 of the Global Initiative for Asthma (GINA) guidelines [13]. We also assessed other outcomes of efficacy (exacerbation rate, healthcare utilisation, ICS sparing effect and change in lung function), as well as safety.

Material and methods

Design

The study was a 1-year real-life multicentre survey conducted in 12 paediatric pulmonology and allergy tertiary care centres (fig. 1).

Subjects

All patients with confirmed allergic severe asthma for whom omalizumab treatment was initiated between January 2006 and June 2009, and who were aged <18 years were included in the study [14]. They had received long term follow-up (>12 months in the tertiary care centre). This allowed characterisation of their asthma phenotype and evaluation of treatment efficacy and compliance. The survey was approved by the Nord Pas de Calais Human Protection Committee for Clinical Research as well as the National Committee for Freedom of Information (Commission Nationale de l'Informatique et des Libertés).

Methods

Baseline characteristics were collected from medical files: demographic data, asthma history (age at diagnosis of asthma, hospitalisation for asthma ever and intensive care unit (ICU) admission ever), asthma severity over the past year assessed using rate of exacerbations requiring systemic corticosteroids and/or healthcare utilisation (emergency department (ED) visits and hospitalisation), allergic sensitisation assessed by skin prick tests, specific and total IgE levels, and comorbidities (allergic rhinitis, atopic dermatitis, food allergy, and overweight determined by body mass index >97th percentile for age and sex).

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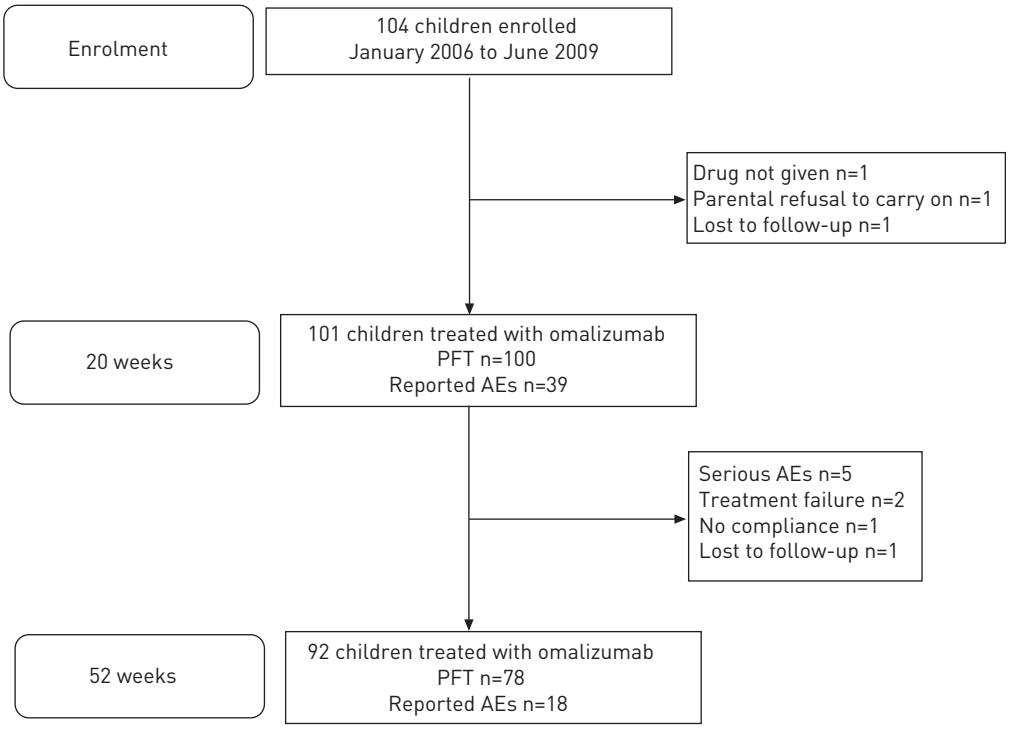

FIGURE 1 Flow chart showing the course of study. PFT: pulmonary function test; AE: adverse event.

Assessment of efficacy and safety

Data were collected and recorded on a standardised file at the time of the first administration (V0), at 20±4 weeks (V1) and at 52±4 weeks (V2). Level of asthma control was assessed over the 4 weeks preceding each visit, and classified as poor, partial or good according to the GINA 3 levels: controlled, partly controlled and uncontrolled asthma [13]. Exacerbations were quantified separately and only those needing systemic steroid bursts ⩾3 days were retained in the evaluation, as highlighted in previous trials [4–7]. Healthcare utilisation was estimated by the number of ED visits or hospitalisation or admission to ICU for asthma. LFTs comprised a flow–volume curve pre- and post-inhaled β2-agonists, and were routinely performed in each centre. Forced expiratory volume in 1 s (FEV_1) and forced expiratory flow at 25–75% of the forced vital capacity (FVC) ($FEF_{25–75\%}$) were expressed as % predicted values, and the FEV_1/FVC ratio as a percentage. Data on maintenance therapy were collected at each visit and ICS doses were standardised as fluticasone equivalent dose per day (fluticasone propionate $\mu g \cdot day^{-1}$), according to French guidelines. At each visit, any significant adverse events (AEs) were reported to evaluate the safety of the drug. They were described in a narrative form and then classified in significant or serious AEs, as required by the European Medicines Agency. Significant AE resulted in any intervention, *e.g.* treatment discontinuation, and serious AE resulted in hospitalisation, any life-threatening events or incapacity.

Analyses

The primary outcome criterion of omalizumab responsiveness was to achieve good asthma control over the year of treatment. We defined good asthma control according to the GINA criteria of controlled asthma (daytime symptoms: twice or less per week; limitation of activities: none; nocturnal symptoms/awakening: none; need for reliever/rescue treatment: twice or less per week, and normal FEV_1 according to the GINA guidelines [13]). The secondary criteria were the reduction in severe exacerbation rate and healthcare use in comparison with that observed during the previous year, the reduction in ICS dose, and the lung function improvement over the year of treatment. Safety was analysed separately.

Statistics

Data are presented as n (%) for qualitative variables and as mean (95% confidence interval) for quantitative variables. Comparisons between V0, V1 and V2 were performed by a MacNemar test for qualitative variables and by a t-test for paired samples for quantitative variables.

In our population, bivariate analysis was performed to examine potential factors that may affect the response to omalizumab at V1 and V2. The relationship between age (<12 or ⩾12 years), FEV_1/FVC (<0.8 or ⩾0.8),

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number of exacerbation in the previous year (<3 or ⩾3), sensitisations (<3 or ⩾3), allergic comorbidities (present or absent), IgE level (⩽700 or >700 kU·L^{-1}), dosing regimen (every 2 or 4 weeks) and the response to omalizumab were investigated by Chi-squared tests. To determine the relation between a good response to omalizumab and IgE level, a Mann–Whitney test was used. The correlations between continuous variables were measured by Pearson's correlation coefficient. We also analysed all the outcomes in the subgroup of patients with IgE level >700 kUI·L^{-1}. A p-value ⩽0.05 was considered significant. All analyses were performed using SAS software version 9.2 (SAS Institute Inc., Cary, NC, USA).

Results

Descriptive data

104 children were included, all fulfilling the criteria of severe asthma (table 1). 44% of them had been hospitalised during the previous year, with 20 children requiring more than one admission, leading to 87 stays, eight of which were in the ICU. Six (5.8%) children required continuous oral corticosteroid therapy. This atopic population was characterised by: 1) very high IgE levels, with a value above the threshold of 700 kIU·L^{-1} in 57 (55%) children, IgE levels between 1500–3000 kU·L^{-1} in 20 children and >3000 kIU·L^{-1}

TABLE 1 Characteristics of the total population[#]

Age years	11.9 (11.3–12.5)
Age <12 years	47 (45)
Sex male	60 (58)
Overweight[¶]	20 (19)
History of asthma	
Duration of asthma years	9.1 (8.3–9.9)
Exercise induced asthma	89 (86)
⩾1 ED attendance ever	70 (68)
Ever hospitalised	77 (74)
Ever hospitalised in ICU	17 (16.5)
Allergy and allergic comorbidities	
Allergic rhinitis	88 (84.5)
Atopic dermatitis	35 (34)
Food allergy	36 (35)
Total IgE levels kU·L^{-1}	1125 (934–1315)
Sensitisation to aeroallergens	101 (97)
>2 sensitisations	69 (66)
Asthma-related events in the previous year	
Exacerbation rate	4.4 (3.7–5.2)
>2 oral steroid courses	68 (65.5)
ED visit	70 (67)
Hospitalisation	46 (44)
>1 hospitalisation	20 (19)
Hospitalisation in ICU	8 (7.7)
Asthma medication at baseline	
ICS	104 (100)
Dose of ICS fluticasone equivalent μg·day^{-1}	703 (642–764)
Association with LABA	98 (94)
>2 long-term controller medication	93 (89.5)
Daily SABA	48 (46)
Maintenance oral corticosteroids	6 (5.5)
Lung function tests	
FEV_1 % pred	88 (83.8–92.2)
FEV_1/FVC %	75.8 (72.5–79.1)
$FEF_{25–75\%}$ % pred	65.1 (58.8–71.4)
Asthma control	
Poor	85 (82)
Partial	19 (18)
Good	0 (0)

Data are presented as mean (95% CI) or n (%). BMI: body mass index; ED: emergency department; ICU: intensive care unit; ICS: inhaled corticosteroid; LABA: long-acting β_2-agonists; SABA: short-acting β_2-agonists; FEV_1: forced expiratory volume in 1 s; % pred: % predicted; FVC: forced vital capacity; $FEF_{25–75\%}$: forced expiratory flow at 25–75% of FVC. [#]: n=104; [¶]: BMI >97th percentile.

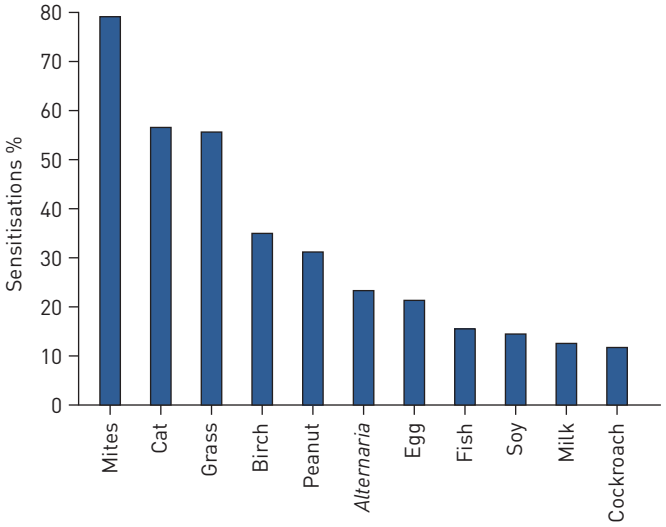

FIGURE 2 Allergen sensitisations detected at baseline in the overall population (n=104). Food allergies, *Alternaria* and cockroach sensitisations were overrepresented in these severe asthmatic children.

in seven children; 16 of these 27 children with the highest IgE levels were aged <12 years; 2) polysensitisation: 66% had allergic sensitisation to at least three allergens; 3) a high frequency of food allergies (35%); and 4) a high frequency of allergic rhinitis (85%) (table 1 and fig. 2). Lung function tests revealed airway obstruction with FEV_1 <80% pred in 36%, or $FEF_{25–75\%}$ <60% pred in 51%, FEV_1/FVC <0.8 in 53% and <0.7 in 26% of children.

The outcomes were available in 101 patients at V1 and 92 patients at V2 (fig. 1). At V1, treatment was discontinued in eight children by the physician. One more patient was lost to follow-up between V1 and V2.

Omalizumab dosage

Omalizumab was administered as required by the dosing table available at the time of the initial prescription, establishing doses for up to IgE level <700 $kU \cdot L^{-1}$ according to weight. Thus, the children with IgE levels above this threshold received the maximum recommended dose of 375 mg every 2 weeks. 68% of children were administered omalizumab every 2 weeks and the remaining 32% received the treatment every 4 weeks. Due to the high IgE levels encountered in this population, there were two injection sites for 76% of children and the number rose to three sites for 6% of patients. Overall, 58% required local anaesthetic by lidocaine/prolicaine application at the sites of injections.

Asthma control

Control of asthma clearly improved over the year of treatment (fig. 3). Asthma control levels were good in 0%, partial in 18% and poor in 82% of the population at treatment initiation and improved to 53%, 30% and 17% at week 20, and to 67%, 25% and 8% at week 52, respectively ($p<0.0001$). 20 (20%) patients with partially controlled (n=16) or uncontrolled (n=4) asthma at V1 became in good control at V2. Conversely, six children improved at V1, and then lost control between V1 and V2. In addition, 11 (10.5%) children with poor asthma control at V0 moved to partial control at V1 and V2. Thus, only 14% of the children did not improve over the year. Mean baseline IgE levels were not different between patients with good control and without control (partial or poor control) at V1 or V2 (V1: 1214 (385–1797) $kU \cdot L^{-1}$ *versus* 1040 (380–1445) $kU \cdot L^{-1}$, respectively, p=0.32; V2: 1173 (365–1714) $kU \cdot L^{-1}$ *versus* 891 (276–1061) $kU \cdot L^{-1}$, respectively, p=0.21).

Exacerbations

A significant decrease in the number of exacerbations was observed under treatment, when compared with the previous year (fig. 4). The mean rate of severe exacerbations decreased from 4.4 (3.7–5.2) per patient during the previous year to 1.25 (0.55–1.95) during the year of treatment ($p<0.0001$). This represented a reduction of 72% over the year. A low rate of exacerbation (0.66 (0.33–0.99) per patient) was early observed over the period V0–V1, and was maintained at 0.57 (0.23–0.93) per patient over the period V1–V2. In addition, the percentage of children requiring hospitalisation decreased from 44% in the past year to 6.7% (n=7, 10 admissions), with none necessitating a stay in ICU during the year on treatment ($p<0.001$). Hospital admissions were reduced by 88.5%.

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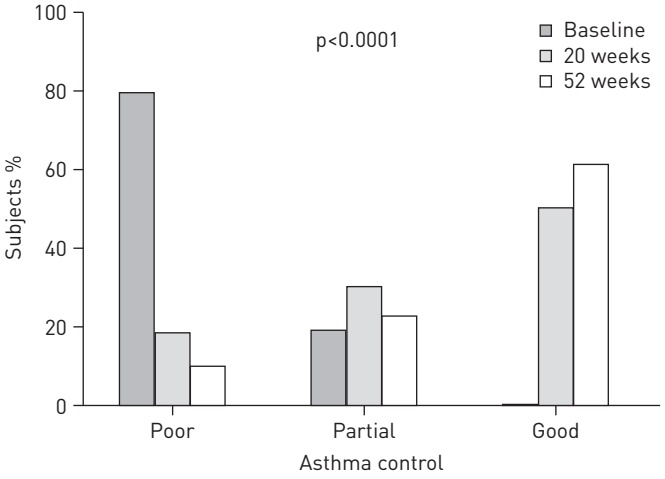

FIGURE 3 Asthma control levels at baseline (n=104), at 20±4 weeks (n=101) and at 52±4 weeks (n=92) after the initiation of add-on omalizumab treatment.

Lung function tests

FEV_1 was available in 78 and $FEF_{25–75\%}$ in 64 children over the year of follow-up (fig. 5). The mean improvement of lung function assessed at V2 was 4.9% pred (95% CI 0.69–9.19; p=0.023) and 9.5% pred (95% CI 3.7–15.2; p=0.002) for FEV_1 and $FEF_{25–75\%}$, respectively.

Inhaled steroid sparing effect

Over the year on treatment, the ICS sparing effect was -212 (-284– -140) µg, equivalent to a 30% reduction in ICS dose (fig. 6). The mean administered dose of FP or equivalent was 703 (642–764) µg at V0, 592 (528–656) µg at V1 and 481 (412–551) µg at V2 (p<0.0001). 46.7% of patients achieved ⩾50% reduction in the administered dose, and only 5.4% maintained unchanged ICS doses between V0 and V2. Oral corticosteroids were withdrawn in all six children with this maintenance therapy at baseline.

Effect modifiers of the response to omalizumab

The only significant factor associated with a good response to omalizumab was age. Children aged <12 years were less frequently controlled at V2 than older children (53.5% *versus* 76%; p=0.02) and exacerbations were more frequent under treatment (1.85 (0.33–3.38) *versus* 0.76 (0.45–1.08); p=0.049) (tables S1 and S2). Neither of the characteristics detailed above, allergic comorbidities (allergic rhinitis, atopic dermatitis and food allergy) and rate of allergenic sensitisations, were predictive of good control at V1 or V2. We also analysed the administration frequency (every 2 weeks *versus* every 4 weeks) and we did not find any difference in all outcomes (table S1 and S3).

Next we repeated the analysis in the subgroup of children with high IgE levels (>700 $kU \cdot L^{-1}$). We did not find any relation between IgE level and all the outcomes (table S4).

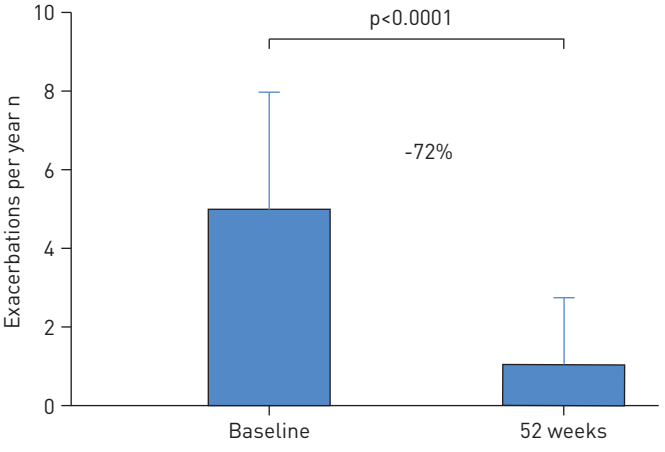

FIGURE 4 Change in exacerbation rates over a period of 52 weeks with add-on omalizumab treatment in children with uncontrolled severe allergic asthma. Data are presented as mean (95% confidence interval).

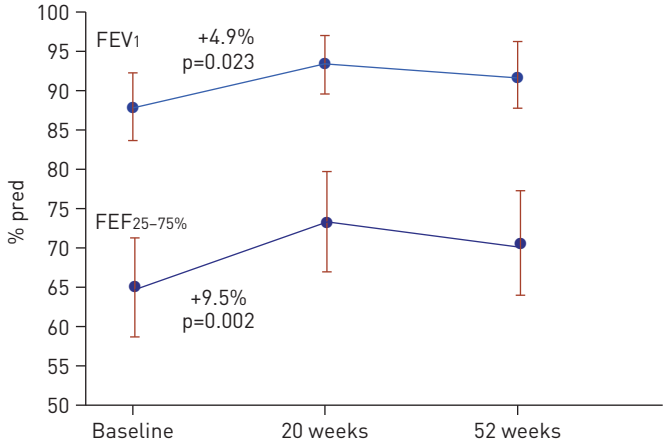

FIGURE 5 Changes in mean (95% confidence interval) pre-bronchodilator forced expiratory volume in 1 s (FEV_1) and forced expiratory flow at 25–75% of forced vital capacity ($FEF_{25–75\%}$) from baseline during the treatment with omalizumab.

Safety

Overall, at least one AE was reported in 47 children (fig. 1). The most frequent AEs were pain at injection site (n=23), which led to discontinuation in one patient, and local reaction in 10 others. Symptoms such as asthenia after injections (n=6), headache (n=3), abdominal pain (n=3) and vagal malaise (n=3) were also reported. Serious AEs due to omalizumab according to physician's assessment, which allowed a precise characterisation (five at V1 and one at V2), resulted in treatment discontinuation in six patients, as follows: extended urticaria (n=1), anaphylaxis (n=1), and systemic reactions associated with abdominal and muscular pain, fatigue and headache (n=4). Omalizumab was successfully reinitiated under medical supervision in two of these patients. The last declared event was a case of anaphylaxis linked to exotic fruit allergy, and was unrelated to omalizumab.

Discussion

We report an observational survey of 104 atopic children and adolescents with severe allergic asthma, who benefited from omalizumab treatment as an add-on therapy to high level maintenance treatment. All children in this series had received long-term follow-up in tertiary care centres, which allowed them to have a precise characterisation of their asthma, and to target the associated co-factors with poor asthma control, such as compliance or environmental exposures. The interest of observational studies is to provide complete real-life data, which might differ from that obtained in clinical trials (table S5). Our survey showed a greater improvement in asthma control, a greater reduction in exacerbation rates and healthcare utilisation and a greater steroid-sparing effect than that reported in efficacy trials. Notably, the children studied appeared to be more severely affected, less controlled and more atopic than those in the previous clinical trials, suggesting a specific clinical profile targeted by omalizumab. These results in childhood are in agreement with those recently observed in other observational studies in adults and adolescents with severe allergic persistent asthma [9, 10]. The primary outcome point of this survey was the number of children who achieved good control level (according to the GINA criteria [13]), thus providing new data of clinical relevance. The clinical trials have definitely shown omalizumab efficacy on exacerbation rates. By contrast,

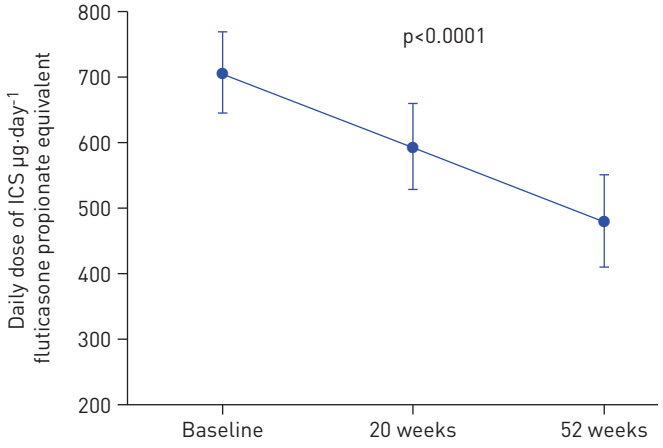

FIGURE 6 Changes in daily inhaled corticosteroid (ICS) dose ($\mu g \cdot day^{-1}$ fluticasone propionate-equivalent) from baseline during the treatment with omalizumab. Data are presented as mean (95% confidence interval).

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this effect was less marked in the control of symptoms [4–7]. In this survey, control was obtained for half of the children during the first 20 weeks of drug administration. In addition, prolonged treatment of up to 1 year enabled two-thirds of these children to achieve good control. These data suggest that the recommended mean recognised time interval of 4 months for drug response evaluation has to be considered on a case-by-case basis. Taking into account those who moved from poor to partial control, only 14% of the children did not improve. That means that one in six should be considered as nonresponders. A reduction in night symptoms and use on demand of bronchodilators was observed by MILGROM *et al.* [6], but not by LANIER *et al* [5]. In less severe asthmatic children, BUSSE *et al.* [4] reported a decrease of 25% of symptom score, comprising day and night symptoms, school absenteeism and activity interference, over 2 weeks. These authors observed a significant gain of asthma control, assessed by the Asthma Control Test, only in the 6–11-year-old age range. In our survey, the response was also observed in this age group, but was less pronounced. Young age should not delay anti-IgE treatment when required.

The other main finding was a 72% reduction in the rate of severe exacerbations, with only a few participants needing hospitalisation and none being admitted to the ICU when receiving omalizumab. A reduction in exacerbation rate was the most significant effect attributed to omalizumab and was estimated to lead to a 43–45% reduction in a recent meta-analysis [11]. Our results reinforced the previous 43–50% reduction reported in children with moderate or severe asthma [5, 7]. In addition, the effect on exacerbations was obtained during the first months of treatment, in accordance with the 28- and 16-week studies by MILGROM *et al.* [6] and BRODLIE *et al.* [8], respectively. In contrast, KULUS *et al.* [7] observed the highest reduction of exacerbation during the final 6 months in their 1-year trial.

One of the additional benefits observed in this survey of severe allergic asthmatics was the corticosteroid-sparing effect. The drop in oral steroid bursts was an expected consequence of the dramatic reduction in exacerbations. Furthermore, all six children who had previously required daily oral steroid treatment were able to stop taking them, in accordance with a recent report [8]. It was possible to decrease the ICS dose in almost all patients. This contrasts with the modest 4% reduction in ICS dosing reported in children with similar high ICS doses, but less severe asthma [5]. Conversely, MILGROM *et al.* [6] reported a 100% decrease in the median ICS dose in young patients exposed to a dose five times lower than in this and other series [5]. Although limited, these current data support the fact that the step down was not related to the ICS dose administered at the onset of omalizumab. BUSSE *et al.* [4] also reported a significant difference in the ICS dose of 109 $\mu g \cdot day^{-1}$ budesonide-equivalents between the omalizumab and placebo groups, which was greater in those children exposed and sensitised to cockroaches and those with a more severe asthma.

Lastly, both large (FEV_1) and small ($FEF_{25–75\%}$) airway functional parameters improved over the year of treatment, which was not observed in previous trials [4, 6]. Although the increase was small and may be not clinically relevant, it did provide a positive outcome, as a decline in lung function has been described in severe asthmatic children followed up for many years [15]. The persistence of this positive impact on lung function over time may illustrate a modifier effect on long-term disease progression in patients with severe asthma unlike that of inhaled corticosteroids drugs.

This improvement in asthma control was observed despite the fact that nearly half of patients might be considered as receiving a suboptimal dose of omazilumab, as the European dosing table at the time of study was limited to an IgE level of <700 $kU \cdot L^{-1}$. Nonetheless, response to treatment depends on the reduction of free IgE levels [16], which is not related to measured IgE levels and cannot be routinely evaluated. Finally, response to treatment was not modified by administration frequency. This supports the proposal to decrease the frequency of the injections every 4 weeks when the total dose is $\leqslant 600$ mg every 4 weeks.

We cannot definitely exclude that improvement may be linked to the subcutaneous mode of omalizumab administration, which improved compliance in comparison with that of inhaled drugs. However, our population was comprised of children with poorly controlled asthma, followed up over many years in tertiary care centres where compliance was routinely assessed [2, 14]. This suggests that most of them belonged to a true therapy-resistant asthma profile. Compared with the children included in US paediatric trials [4–7], the patients included in our study had more severe asthma and with higher rates of exacerbation needing oral steroids (4.4 per year *versus* 1.9–2.7 per year), hospitalisations (74% *versus* 18–52%) and requiring high rates of healthcare utilisation. In fact, European omalizumab approbation was more restrictive than US approbation, limiting administration in poorly controlled severe asthma treated with high doses of ICS or oral steroids in association with at least a LABA. As is often the case in severe childhood asthma, the associated alteration of lung function remained moderate, but with a wide range of variation [15, 17]. Half of the children, however, displayed a diminished $FEF_{25–75\%}$, which appeared to be the most sensitive marker of functional alteration in severe asthma [1, 18].

These children featured a peculiar severe atopic phenotype. Total IgE concentration was more than twofold that previously reported in omalizumab trials [5, 6], two-thirds of the children were polysensitised, one-third had food allergy, and rhinitis comorbidity was nearly constant. An elevated production of total IgE was demonstrated to be a marker of asthma severity in children [19] and was related to greater healthcare utilisation, altered lung function and airway hyperresponsiveness [20, 21]. In contrast, such a severe allergic profile has not yet been clearly individualised as a risk group in problematic severe asthma either in previous cohorts [15, 17] or in recent guidelines [2]. A polysensitisation to three or more allergens has nevertheless been associated with severe [22, 23] or uncontrolled asthma [24]. This is in accordance with recent findings, which defined a specific phenotype of severe asthma in children with multiple sensitisations not only to inhaled but also to food allergens [25]. Food allergies have been determined as a risk factor of life-threatening asthma exacerbations [26], and also appear to be involved in cases of difficult asthma. Lastly, a sensitisation to *Alternaria*, an allergen previously associated with severe asthma [27], was also overrepresented within this cohort. The rate was eightfold higher than the 2.8% recently determined in a large French study [28].

The proportion of systemic reactions or general symptoms was comparable to that recently detailed by MILGROM *et al.* [29] in a safety review, where no difference in the number or categories of AEs between the drug and control groups was revealed in the previous trials. Pain or local reaction after injection was not only the most frequent but also the most expected phenomenon, given the viscosity of the product at the time of the survey. These AEs are currently diminishing with the recent modification of the drug composition. Compared with this safety review [29], we report fewer cases of urticaria, headaches and only one related anaphylaxis. Six patients presented with serious adverse effects and discontinued treatment administration. According to the benefit response to omalizumab, two patients were successfully retreated at hospital and no adverse effect occurred. This suggests that the benefit/risk balance should be reassessed in children with therapy resistant asthma.

In conclusion, omalizumab is an effective and safe add-on therapy in uncontrolled severe asthmatic and allergic children. Those characterised by high IgE production, polysensitisations and/or food allergy were revealed to form a subpopulation of true highly allergic severe asthma, and responded well to omalizumab.

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