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

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Abstract:
Omalizumab was shown to reduce exacerbation rate in moderate to severe allergic asthma.

Objective: To evaluate omalizumab efficacy and safety in a real life setting in severe asthmatic children.

Methods: 104 children (6-18y), followed-up in paediatric pulmonary tertiary care centres were included at omalizumab onset. Asthma control levels, exacerbations, inhaled corticosteroids (ICS) dose, lung function and adverse events (AEs) were evaluated over one year.

Results: Children were characterized by allergic sensitisation to ≥ 3 allergens (66%), high IgE levels (mean: 1125 kU/l), high rate of exacerbations (4.4/year) and health care use during the previous year, high ICS dose (mean: 703 µg equivalent fluticasone/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 %. At 12 months, FEV1 improved by 4.9% (p = 0.023), and ICS dose decreased by 30% (p<0.001). Six patients stopped omalizumab for related significant AEs.

Conclusion: 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.

Key words: severe asthma, omalizumab, asthma control, exacerbation, allergy, children
Introduction

The management of severe asthma in children still remains a challenge, with a prevalence being estimated at 5% of the asthmatic population. The term of problematic severe asthma has been recently preferred to describe these school-aged children who have poorly controlled asthma despite a maintenance therapy with ≥400 µg/day fluticasone or equivalent of inhaled corticosteroids (ICS) plus inhaled long-acting β-agonist (LABA) or leukotriene receptor antagonist or theophylline. Those children are characterized at various degrees by daily symptoms, severe or frequent exacerbations, high rates of health care utilization, 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 to-79 years), and then of specific paediatric trials. These studies have shown a significant decrease in exacerbations and health care use, improvement in quality of life but nonetheless a modest effect on symptoms and lung function tests (LFTs). The French Health Authority has limited the utilization of omalizumab to allergic children with uncontrolled persistent asthma and/or severe exacerbations, severe airway obstruction evaluated by LFTs when aged > 12y, despite being administered high doses of ICS or oral corticosteroids in association with at least LABA. In France, omalizumab was available in 2006 for children over 12 years old and with total IgE ≤ 700 kU/l and since 2009 for those older than 6 and with total IgE ≤ 1500 kU/l. A few real life studies have been conducted in adults. The latter have not only confirmed but also extended previous drug efficacy and safety observed in randomized trials. Conversely, knowledge on omalizumab utilization and safety has remained limited in childhood. This was marked in adolescents (12-18 years) who were diluted in the large primary study. Moreover, the effect of omalizumab on disease control has not yet been assessed as an efficacy outcome.

This one 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 GINA 2011. We also assessed other outcomes of efficacy (exacerbation rate, health care utilization, ICS sparing effect and change in lung function), as well as safety.
Material and methods:

Design:
This is a one year real life multicenter survey conducted in 12 paediatric pulmonology and allergy tertiary care centres (figure 1).

Subjects:
All patients with confirmed allergic severe asthma for whom omalizumab treatment has been initiated from January 2006 to June 2009 and aged less than 18 years were included in the study. They have received a long term follow-up (> 12 months in the tertiary care center). This allowed characterising their asthma phenotype and evaluating 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 on 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, intensive care unit (ICU) admission ever], asthma severity over the past year assessed using rate of exacerbations requiring systemic corticosteroids and/or health care utilization [emergency department (ED) visits and hospitalisation], allergic sensitisation assessed by skin prick tests (SPT), specific and total IgE levels, and co-morbidities (allergic rhinitis, atopic dermatitis, food allergy, overweight determined by BMI > 97th percentile for age and sex).

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 in poor, partial and good control according to the GINA 3 levels: controlled, partly controlled and uncontrolled asthma (www.ginasthma.org). 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 Health care 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 second (FEV₁) and forced expiratory flow rate at 25% to 75% of forced vital capacity (FEF 25-75) were expressed as % predictive values, and FEV₁/ forced vital capacity (FEV₁/FVC) ratio as a
percentage. Data on maintenance therapy were collected at each visit and ICS doses were standardized as fluticasone equivalent dose per day (FP µg/day), 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 a good asthma control over the year of treatment. We defined the good asthma control according to the GINA criteria of controlled asthma (daytime symptoms: twice or less/week, limitation of activities: none, nocturnal symptoms/awakening: none, need for reliever/rescue treatment: twice or less/week, and normal FEV1 - www.ginasthma.org). The secondary criteria were the reduction in severe exacerbation rate and health care 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 frequencies and percentages for qualitative variables and as mean and 95% confidence interval (CI 95%) for quantitative variables (mean [CI 95%]). Comparisons between V0, V1 and V2 were performed by a Mac Nemar test for qualitative variables and by a Student t-test for paired samples for quantitative variables.

In this population, bivariate analysis was performed to examine potential factors that may affect the response to omalizumab at V1 and V2. The relationship between age (< or ≥ 12 years old), VEMS/CVF (< or ≥ 0.8), number of exacerbation in the previous year (< 3 or ≥ 3), sensitizations (< or ≥ 3), allergic co-morbidities (present/absent), IgE level (< or > 700 kU/l), dosing regimen (every 2 or 4 weeks) and the response to omalizumab were investigated by Chi-squared tests. To determine the relation between 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 analyzed all the outcomes in the subgroup of patients with IgE level > 700 kUI/l. P-value ≤ 0.05 was considered significant.
All analyses were performed using SAS software version 9.2 (SAS Institute Inc., Cary, NC 25513).

Results

Descriptive data: One hundred and four children were included, all fulfilling the criteria of severe asthma (Table 1). Forty four per cent of them had been hospitalised during the previous year, 20 children requiring more than one admission, leading to 87 stays, 8 of which being in ICU. Six children (5.8%) required continuous oral corticosteroid therapy. This atopic population was characterised by (i) very high IgE levels, with a value above the threshold of 700 kIU/l in 57 (55%) children; IgE levels between 1500-3000 kU/l in 20 children and > 3000 kIU/l in 7 children; 16 of these 27 children with the highest IgE levels were under 12 years; (ii) polysensitisation: 66% had allergic sensitisation to at least 3 allergens; (iii) high frequency of food allergies (35%) ; (iii) high frequency of allergic rhinitis (85 %). (Table I and Figure 2). Lung function tests revealed airway obstruction with FEV₁ < 80% predicted value in 36%, or FEF 25-75% < 60% % predicted value in 51%, FEV₁/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 (figure 1). At V1, treatment was discontinued in 8 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/l according to weight. Thus, the children with IgE levels above this threshold received the maximum recommended dose of 375 mg every 2 weeks. Sixty eight percent 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 2 injection sites for 76% of children and the number rose to 3 sites for 6% of patients. Overall, 58% required local anesthetics by lidocaine/procaine application at the sites of injections.

Asthma control: Control of asthma clearly improved over the year of treatment (Figure 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). Twenty patients (20%) with partially controlled (n=16) or uncontrolled (n=4) asthma at V1 became in good control at V2. Conversely, 6 children improved
at V1, and then lost control between V1 and V2. In addition, 11 (11%) 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 kU/L [385; 1797] vs 1040 kU/L [380; 1445] respectively (p=0.32). V2: 1173 kU/L [365; 1714] vs 891 kU/L [276; 1061], respectively (p=0.21)].

**Exacerbations:** A significant decrease in the number of exacerbations was observed under treatment, when compared to the previous year (Figure 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 %.

**Lung function tests:** FEV₁ was available in 78 and FEF₂₅₋₇₅% in 64 children over the year of follow up (Figure 5). The mean improvement of lung function assessed at V2 was 4.9% of predicted values  [0.69; 9.19] (p=0.023) and 9.5% of predicted values  [3.7; 15.2] (p=0.002) for FEV₁ and FEF₂₅₋₇₅%, respectively.

**Inhaled steroid sparing effect:** Over the year on treatment, ICS sparing effect was -212 µg [-284;-140], equivalent to a 30% reduction in ICS dose (Figure 6). The mean administered dose of FP or equivalent was 703 µg [642; 764] at V0, 592 µg [528; 656] at V1 and 481µg [412; 551] 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 the 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 less than 12 years old were less frequently controlled at V2 than older children (53.5 % vs. 76 %, p=0.02) and exacerbation were more frequent under treatment (1.85 [0.33;3.38] versus 0.76 [0.45;1.08]; p = 0.049) (Table s1 and table s2). Neither characteristics detailed above nor allergic comorbidities (allergic rhinitis, atopic dermatitis, and food allergy) and rate of allergenic sensitizations were predictive of good control.
at V1 or V2. We also analyzed the administration frequency (every 2 weeks versus every 4 weeks) and we did not find any difference in all outcomes (Table s1 and table s3).

Then, we repeated the analysis in the subgroup of children with high IgE levels (> 700 kU/l). We did not find any relation between IgE level and all the outcomes (Table s4).

**Safety:** Overall, at least one AE was reported in 47 children (Figure 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 (5 at V1 and 1 at V2) resulted in treatment discontinuation in 6 patients: extended urticaria (n=1), anaphylaxis (n=1), systemic reactions associating 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 then 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 to have a precise characterization 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 health care utilization, a greater steroid sparing effect, a greater reduction in exacerbation rates and health care utilization than that reported in efficacy trials. Notably, the children studied appeared more severe, 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 [GINA 2011 criteria; www.ginasthma.org], thus providing new data of clinical relevance. The clinical trials have definitely shown omalizumab efficacy on exacerbation rates. By contrast,
this effect was less marked on 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 one year enabled two thirds of these children to achieve good control. These data suggest that the recommended mean recognized time interval of 4 months for drug response evaluation has to be considered on a case to 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 non responders. A reduction in night symptoms and use on demand of bronchodilators was observed by Milgrom \textit{et al} \(^6\), but was not by Lanier \textit{et al} \(^5\). In less severe asthmatic children, Busse \textit{et al}. \(^4\) reported a decrease of 25% of symptom score, comprising day and night symptoms, school absenteeism and activity interference, per 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 group. 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 admitted to ICU when receiving omalizumab. A reduction in exacerbation rate was the most significant effect attributed to omalizumab and was estimated to 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 \(^4,^7\). In addition, the effect on exacerbations was obtained during the first months of treatment, in accordance with the 28-week and 16-week studies by Milgrom \textit{et al}. \(^6\) and Brodlie \textit{et al}. \(^8\) respectively. By contrast, Kulus \textit{et al}. \(^7\) observed the highest reduction of exacerbation during the final 6 months in their one 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, could stop 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 \textit{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 decrease of 109µg/day (FP equivalent) between the omalizumab and placebo groups, which was greater in those children exposed and sensitized to cockroaches, and those with a more severe asthma.

Lastly, both large (FEV₁) and small airway (FEF 25-75%) 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 provided however a positive outcome, as a decline in lung function has been described in severe asthmatic children followed up for many years 14. 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 to inhaled corticosteroids drugs.

This improvement in asthma control was observed despite the fact that nearly half of patients might be considered as receiving sub optimal dose of omalizumab, since the European dosing table at time of study was limited to an IgE level of < 700 kU/l. Nonetheless, response to treatment depends on the reduction of free IgE levels 15, which is not related to measured IgE levels and cannot be routinely evaluated. Finally, response to treatment was not modified by administration frequency. That supports the proposal to decrease the frequency of the injections every 4 weeks when the total dose is ≤ 600 mg/4 weeks.

We cannot definitely exclude that improvement may be linked to the subcutaneous mode of omalizumab administration that improved the compliance in comparison with that known on inhaled drugs. However, our population was comprised of poorly controlled children, followed up since many years in tertiary care centers, where compliance was routinely assessed 2, 13. This suggests that most of them belonged to a true therapy resistant asthma profile. As compared to the children included in US paediatric trials 4-7, the patients included in this study were more severe with higher rates of exacerbation needing oral steroids (4.4/year vs. 1.9-2.7/year), hospitalisations (74% vs. 18-52%) and requiring high rates of health care utilization. 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 often in severe childhood asthma, the associated alteration of lung function remained moderate, but with a wide range of variation 14, 16. Half of the children however displayed a diminished FEF₂₅₋₇₅, which appeared to be the most sensitive markers of functional alteration in severe asthma 1, 17.
These children featured a peculiar severe atopic phenotype. Total IgE concentration was more than twofold that previously reported in omalizumab trials, two third of the children were poly-sensitized, one third had food allergy, and rhinitis co-morbidity was nearly constant. An elevated production of total IgE was demonstrated as a marker of asthma severity in children, and related to greater health care utilization, altered lung function and airway hyper-responsiveness. In contrast, such a severe allergic profile has not yet been clearly individualized as a risk group in problematic severe asthma either in previous cohorts or in recent guidelines. A poly-sensitisation ≥ 3 allergens has nevertheless been associated with severe or uncontrolled asthma. This is in accordance with recent findings, which defined a specific phenotype of severe asthma in children with multiple sensitizations not only to inhaled but also to food allergens. Food allergies have been determined as a risk factor of life threatening asthma exacerbations, and also appear to be involved in cases of difficult asthma. Lastly, a sensitization to Alternaria, an allergen previously associated with severe asthma, was also over represented within this cohort. The rate was eight fold higher than the 2.8% recently determined in a large French study.

The proportion of systemic reactions or general symptoms was comparable to that recently detailed by Milgrom et al. 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 time of the survey. These AEs are currently diminishing with the recent modification of the drug composition. Compared to this safety review, fewer cases of urticaria, headaches and only one related anaphylaxis were reported. 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 characterized by high IgE production, poly-sensitizations 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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Table I: Characteristics of the total population (n=104)

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td></td>
<td>11.9  [11.3;12.5]</td>
</tr>
<tr>
<td>Gender (Male)</td>
<td></td>
<td>47 (45%)</td>
</tr>
<tr>
<td>Overweight (BMI&gt; 97 percentile)</td>
<td></td>
<td>60 (58%)</td>
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<tr>
<td>History of asthma</td>
<td></td>
<td>20 (19%)</td>
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<tr>
<td>Duration of asthma (years)</td>
<td></td>
<td>9.1    [8.3;9.9]</td>
</tr>
<tr>
<td>Exercise induced asthma</td>
<td></td>
<td>89 (86%)</td>
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<tr>
<td>≥ 1 ED attendance ever</td>
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<td>70 (68%)</td>
</tr>
<tr>
<td>ever hospitalised</td>
<td></td>
<td>77 (74%)</td>
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<tr>
<td>ever hospitalised in ICU</td>
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<td>17 (16.5%)</td>
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<tr>
<td>Allergy and allergic co-morbidities</td>
<td></td>
<td>88 (84.5%)</td>
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<tr>
<td>Allergic rhinitis</td>
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<td>35 (34%)</td>
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<tr>
<td>Atopic dermatitis</td>
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<td>36 (35%)</td>
</tr>
<tr>
<td>Food allergy</td>
<td></td>
<td>1125 [934;1315]</td>
</tr>
<tr>
<td>Total IgE levels (kU/l)</td>
<td></td>
<td>101 (97%)</td>
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<tr>
<td>Sensitisation to aeroallergens</td>
<td></td>
<td>69 (66%)</td>
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<tr>
<td>≥ 2 sensitisations</td>
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<td>68 (65.5%)</td>
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<tr>
<td>Asthma-related events in the previous year</td>
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<tr>
<td>Exacerbation rate</td>
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<td>46 (44%)</td>
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<tr>
<td>&gt; 2 oral steroid course</td>
<td></td>
<td>20 (19%)</td>
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<tr>
<td>ED visit</td>
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<td>8 (7.7%)</td>
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<tr>
<td>Hospitalisation</td>
<td></td>
<td>93 (89.5%)</td>
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<tr>
<td>&gt; 1 hospitalisation</td>
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<td>48 (46%)</td>
</tr>
<tr>
<td>Hospitalisation in ICU</td>
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<td>6 (5.5%)</td>
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<tr>
<td>Asthma medication at baseline</td>
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<td>104 (100%)</td>
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<tr>
<td>Inhaled corticosteroids</td>
<td></td>
<td>703 [642;764]</td>
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<tr>
<td>Dose of ICS (fluticasone equivalent, µg/day)</td>
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<td>98 (94%)</td>
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<tr>
<td>Association with LABA</td>
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<td>93 (89.5%)</td>
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<tr>
<td>&gt; 2 long term controller medication</td>
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<td>48 (46%)</td>
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<td>Daily SABA</td>
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<td>6 (5.5%)</td>
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<tr>
<td>Lung function tests</td>
<td>FEV1, % predicted</td>
<td>88 [83.8;92.2]</td>
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<td></td>
<td>FEV1/FVC, %</td>
<td>75.8 [72.5;79.1]</td>
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<tr>
<td></td>
<td>FEF25-75, % predicted</td>
<td>65.1 [58.8;71.4]</td>
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<tr>
<td>Asthma control</td>
<td>Poor</td>
<td>85 (82%)</td>
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<tr>
<td></td>
<td>Partial</td>
<td>9 (18%)</td>
</tr>
<tr>
<td></td>
<td>Good</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

Results are expressed in number (%) or mean [95%CI] as required.
ICU: intensive care unit. ED: emergency department.
SABA: short acting β2 agonists. LABA : long acting β2 agonists
Figure 1: flow chart
**Figure 1: Flow chart**

**Enrollment**
- 104 children enrolled
  - January 2006 to June 2009

**Drug not given n=1**
- Parental refusal to carry on n=1
- Lost of follow-up n=1

**20 weeks**
- 101 children treated by Omalizumab
  - PFT\(^1\) = 100
  - Reported AEs\(^2\) n=39

**Serious AEs\(^2\) n=5**
- Treatment failure n=3
- No compliance n=1
- Lost of follow-up n=1

**52 weeks**
- 92 children treated with Omalizumab
  - PFT\(^1\) = 78
  - Reported AEs\(^2\) n=18

\(^1\)PFT = Pulmonary Function Tests

\(^2\)AE = Adverse Event
Figure 2:
Allergen sensitisations detected at baseline in the overall population (n=104).
Food allergies, alternaria and cockroach sensitizations were over represented in these severe asthmatic children.

Figure 3
Asthma control levels at baseline (V0; n=104), at 20±4 weeks (V1; n=101) and at 52±4 weeks (V2; n=92) after the initiation of add-on omalizumab treatment.
Figure 4
Change in exacerbation rates over a period of 52 weeks with add-on omalizumab treatment in children with uncontrolled severe allergic asthma.
Figure 5
Changes in prebronchodilator FEV1 and FEF$_{25-75}$ percent predicted (means, 95% CI) from baseline during the treatment with omalizumab.
Figure 6
Changes in daily inhaled corticosteroids dose (fluticasone propionate equivalent) from baseline during the treatment with omalizumab (means, 95% CI).
References


