

PHARMCOTHERAPY

## A 36-Month Study on the Cost/Utility of Add-On Omalizumab in Persistent Difficult-to-Treat Atopic Asthma in Italy

ROBERTO WALTER DAL NEGRO, M.D.,<sup>1,2</sup> SILVIA TOGNELLA, M.D.,<sup>1</sup> AND LORENZO PRADELLI, M.D.<sup>3,\*</sup>

<sup>1</sup>Lung Unit, Orlandi General Hospital, Bussolengo, Verona, Italy.

<sup>2</sup>Centro Nazionale Studi di Farmacoeconomia e Farmacoepidemiologia Respiratoria—CESFAR, Verona, Italy.

<sup>3</sup>AdRes Health Economics & Outcomes Research, Torino, Italy.

**Objective.** Omalizumab is a biological treatment for difficult-to-treat allergic asthma. Its mechanism of action relies on impeding the binding of immunoglobulin E (IgE) to specific cellular receptors, thus blocking the inflammatory cascade. At present, no long-term data are available on its cost/effectiveness. The aim of this study is to assess long-term clinical outcomes and to measure the cost/utility of long-term omalizumab use in difficult-to-treat allergic asthmatics. **Methods.** The clinical, economic, and quality-of-life (QoL) outcomes of 36-month add-on omalizumab therapy were compared to equivalent outcomes for the year before the therapy's introduction in a cohort ( $n = 16$ ) of adults with severe uncontrolled atopic asthma on chronic high-dose antiasthma treatments. The variables considered were lung function, IgE levels, health status, Asthma Control Test (ACT) score, QoL (St. George Questionnaire), general practitioner (GP) and specialist visits, number and duration of hospitalizations, emergency room admission, and pharmacological treatment (both dose and duration). Derived calculated indicators were changes in health-related QoL, total healthcare costs, and incremental cost/utility. Data from the two periods were tested for statistically significant differences according to Student's  $t$  test and  $p < .05$  was accepted. **Results.** Add-on omalizumab significantly and progressively improved asthma control and patient health-related QoL. Symptomatic drug and hospital care costs for these patients dropped significantly. A €450 increase in overall monthly costs was observed; however, when health benefits were considered, this cost increase translated into an incremental cost/utility ratio of €23,880 per quality-adjusted life year gained, which is quite a favorable and convenient figure in terms of the willingness to pay for health benefits in industrialized countries. **Conclusions.** The 36-month add-on omalizumab therapy persistently improved all clinical outcomes in difficult-to-treat asthmatic patients. Costs were also optimized and related to the extent of long-term health benefits achieved.

**Keywords** cost/utility, difficult-to-treat atopic asthma, effectiveness, healthcare costs, omalizumab

### INTRODUCTION

Asthma is a chronic inflammatory disease that affects 300 million patients all over the world, a figure which is expected to increase even further over the next 15 years (1). Most atopic asthmatics respond very well to inhaled corticosteroids (ICS) and/or bronchodilators; nevertheless, 5–10% of asthma patients suffer from a much more severe disease that does not respond as satisfactorily to these basic therapeutic options (2).

Omalizumab is a recombinant monoclonal antibody that selectively binds to the high-affinity C-epsilon 3 site of human immunoglobulins E (IgEs). The binding of the drug prevents the IgEs from binding to mastocytes and other effector cells, thus inhibiting the inflammatory cascade that occurs as a response to antigenic stimuli. A systematic review of omalizumab in asthmatic patients showed that the drug is significantly more effective in reducing both ICS use and the exacerbation rate than placebo treatments (3). Common therapeutic doses are in the 150–375 mg range, administered via subcutaneous (SC) injection and to be repeated every 2–4 weeks. The individual dose is defined on the basis of body weight and baseline serum IgE levels.

Omalizumab has proved to be effective in children, adolescents, and adults at doses which are able to guarantee at least 0.016 mg/kg/IU/ml of IgE for a minimum of 4 weeks (4).

The clinical efficacy of add-on omalizumab in persistent, difficult-to-treat atopic asthma has already, fundamentally, been established. The majority of international trials have provided evidence, notwithstanding the various different experimental designs utilized, to support the recommendation of this therapeutic strategy for patients whose asthma is difficult to manage and whose asthma proves to be resistant to high doses of the internationally recommended therapeutic options (3, 5–14). Several 1-year studies have shown that the drug is effective in the long term in moderate-to-severe, difficult-to-treat atopic asthma, when it is given in addition to the patient's regular antiasthma therapy (mainly ICS + long-acting  $\beta$ -agonists (LABAs), and/or anti-leukotrienes, and/or periodic oral steroid courses). In these studies, a significant drop in annual exacerbation rate and respiratory symptom severity was coupled with significant amelioration of both lung function indices and quality-of-life (QoL) scores (5–14).

In these more severe cases, which represent at least 5% of all asthmatics (12), clinical benefits were usually reported in terms of recovery of lung function (i.e., forced expiratory volume in 1 second (FEV<sub>1</sub>)), a reduction in day- and night-time asthma symptoms, a reduction in the use of rescue medications and corticosteroids (both inhaled and systemic),

\*Corresponding author: Lorenzo Pradelli, M.D., AdRes Health Economics & Outcomes Research, Piazza Carlo Emanuele II, 19, I-10123 Torino, Italy; Tel: +39 011 7651239; Fax: +39 011 5186892; E-mail: l.pradelli@adreshe.com

and a reduction in exacerbations, in particular of the most severe episodes leading to hospitalization (3, 5–14).

A couple of 1-year studies have also documented the pharmacoeconomic convenience of add-on omalizumab (8, 14). To the best of our knowledge, no economic data taken over longer omalizumab treatment periods are available.

The aim of this study is to calculate the cost/utility of 36 months of omalizumab treatment in a sample of patients who suffer from severe, difficult-to-treat atopic asthma.

## METHODS

Patient files were extracted from the institutional database (DB) that holds more than 300,000 records which include patient history and clinical signs and symptoms, lung function, biological markers, treatment and related side effects, adherence scores to treatment, annual hospitalization and exacerbation rates, Asthma Control Test (ACT) scores, St. George's Respiratory Questionnaire (SGRQ) scores, general practitioner (GP) and specialist visits, and absenteeism of all the patients who have been referred to the Lung Unit since 1983. The DB operates in agreement with the current national law on privacy and according to the strict procedures of ISO-9001-2000 protocols (15). All subjects signed an informed consent form. The study protocol was approved by the local (Verona Province) Ethical Committee on 19 January 2010, Protocol no.1489. Boolean selection criteria were as follows: subjects were of both genders, AND older than 12 years old, AND with severe, persistent atopic asthma according to the Global Initiative for Asthma (GINA) guideline definition, AND sensitized to perennial allergens (as assessed by specific IgE testing, Immulite<sup>®</sup> System, Diagnostic Product Corp., Los Angeles, CA, USA), AND resistant to their daily high-dose antiasthma drugs (i.e., lung function, asthma signs, and clinical outcomes persisted substantially unchanged over the high-dose antiasthma treatment), AND add-on omalizumab was administered for at least 36 months AND data were available for at least 12 months preceding omalizumab treatment.

Sixteen patients (eight females) complying with these criteria were identified and T<sub>0</sub> corresponded to the start of omalizumab treatment (Table 1).

TABLE 1.—Demographics and characteristics of the patient sample at T<sub>0</sub> (start of add-on omalizumab).

| Characteristic                  | Value                           |
|---------------------------------|---------------------------------|
| Gender                          | 8 Females                       |
| Age (mean, min–max)             | 45.4 (31–64)                    |
| BMI (mean, min–max)             | 25.2 (19.8–37.5)                |
| Smoking habit                   | 12 never, 4 ex-smokers          |
| IgE (mean, 95% CI)              | 271 (77–712) UI/mL              |
| FEV <sub>1</sub> (mean, 95% CI) | 56.6 (37.8–71.1) % of predicted |
| Var % (mean, 95% CI)            | 21.4 (9.5–41.7)                 |
| MMEF (mean, 95% CI)             | 25.3 (13.4–43.6) L/s            |

Notes: BMI, body mass index; FEV<sub>1</sub>, forced expiratory volume in 1 second; Var %, reversibility of obstruction; MMEF, maximal mid-expiratory flow.

The variables considered were lung function indices (such as pre-bronchodilator FEV<sub>1</sub>, maximal mid-expiratory flow (MMEF), and % FEV<sub>1</sub> reversibility after salbutamol 400 mcg), serum IgE levels, and annual exacerbations (exacerbations were defined as conditions that lead to a substantial change in the usual antiasthma therapy, in particular the addition of systemic steroids and/or antibiotics, and/or an Emergency Room (ER) visit or hospitalization). Subjective measures of asthma control were also considered (these included the ACT—symptom score), together with the patient's record of disease-related days of inactivity. Annual healthcare consumption (including variables such as the number and duration of hospitalizations for respiratory causes, the number of ER visits, the number of visits by specialists and GPs, and consumption of inhaled and systemic corticosteroids, bronchodilators, anti-leukotrienes, xanthines, antibiotics, and other respiratory compounds) was also calculated.

Spirometric recordings (FEV<sub>1</sub> and MMEF), serum IgE levels, and ACT scores were collected every 6 months and drug consumption records quarterly during both the pre-omalizumab and omalizumab observational periods. The SGRQ was administered at the beginning of omalizumab treatment (T<sub>0</sub>) and every 6 months during the 36-month survey.

The study was designed as a pre–post comparison of clinical outcomes and healthcare consumption in the selected cohort of subjects. The data measured in the year preceding omalizumab introduction were taken as a reference to assess the impact of omalizumab treatment.

Descriptive statistics (mean, 95% confidence interval (CI), and minimum–maximum range) of data from the two periods were calculated and tested using the Student's *t*-test for paired data and *p* < .05 was accepted as the minimum level of statistical significance.

Data related to clinical events and healthcare consumption during the omalizumab observational period (36 months) were normalized to 1 year in order to enable a homogeneous comparison with data related to the pre-omalizumab observational period (12 months). Healthcare resources consumed were converted into economic values according to the Regional Health System (RHS) whenever possible. Consequently, hospitalizations were valued according to the Diagnosis-related group-based remuneration tariff granted to hospitals in the Veneto region (16), specialist visits were valued on the basis of the most recent update of the regional specialist tariffs (17), and GP visits were valued as opportunity cost according to the findings of the Dysthymia Costs study by Garattini et al. (18).

Drug prices for drugs that are only to be used in a hospital (i.e., omalizumab) were ex-factory prices (19) and reference prices (20) were used for reimbursed off-patent drugs and retail prices (21) for reimbursed patent-covered drugs (Table 2—price update on June 2011).

On the basis of the collected data, cost/effectiveness and cost/utility calculations were performed. Incremental cost/effectiveness and cost/utility ratios were calculated as the ratio of the pre–post differential costs over differential

TABLE 2.—Unit costs used for the analysis.

| Type of resource                                                                                                                          | Price, tariff, or cost (€) | Source |
|-------------------------------------------------------------------------------------------------------------------------------------------|----------------------------|--------|
| Drugs                                                                                                                                     |                            |        |
| Omalizumab 150 mg, 1 vial                                                                                                                 | 351.12                     | 18     |
| Salmeterol 25 mcg, 120 puffs                                                                                                              | 32.7                       | 18     |
| Formoterol 12 mcg, 60 puffs                                                                                                               | 17.64                      | 19     |
| Montelukast 10 mg, 28 tablets                                                                                                             | 43.94                      | 18     |
| Prednisone 25 mg, 10 tablets                                                                                                              | 6.18                       | 18     |
| Betamethasone 4 mg, 3 vials                                                                                                               | 2.41                       | 19     |
| Theophylline 200 mg, 30 tablets                                                                                                           | 2.31                       | 18     |
| Salbutamol 100 mcg, 200 puffs                                                                                                             | 2.51                       | 19     |
| Amoxicillin + clavulanate 875 + 125 mg, 12 tablets                                                                                        | 7.92                       | 19     |
| Ciprofloxacin 500 mg, 6 tablets                                                                                                           | 6.79                       | 19     |
| Levofloxacin 500 mg, 5 tablets                                                                                                            | 22.37                      | 18     |
| Clarithromycin 500 mg, 14 tablets                                                                                                         | 10.35                      | 19     |
| Cetirizine 10 mg, 20 tablets                                                                                                              | 3.60                       | 19     |
| Hospital                                                                                                                                  |                            |        |
| Hospitalization for asthma exacerbation (DRG 96 and 97, weighted for their relative frequency in Veneto according to 2005 discharge data) | 1713.42                    | 15, 20 |
| Emergency unit accesses (brief observation)                                                                                               | 200.00                     | 15     |
| Visits                                                                                                                                    |                            |        |
| Specialist visit                                                                                                                          | 20.50                      | 16     |
| GP visit                                                                                                                                  | 15.09                      | 17     |

Note: GP, general practitioner.

effectiveness/utility and reported as mean and 95% CI. Moreover, pre-post FEV<sub>1</sub> percentage points and ACT points gained were used as a measure of the effectiveness of omalizumab addition. The calculation of utility was based on SGRQ total scores, for the cost/utility analysis, according to the analytic relationship between them and the EQ-5D utility index reported by Stahl et al. (22, 23). Increases in utility are relative to the difference between mean starting values (T<sub>0</sub>) and mean post-omalizumab measurements (T<sub>6-36</sub>).

## RESULTS

Clinical efficacy data (Table 3) indicate that overall asthma control improves during omalizumab treatment. FEV<sub>1</sub> increased substantially in 15 of 16 patients (the difference was +3% in the remaining one), and ACT scores also improved significantly in all patients. The effect in terms of exacerbation frequency and severity clearly indicates the therapy's benefits. While in the year preceding omalizumab treatment all patients reported exacerbations (an average of two per patient per year), and 12 of them were hospitalized for a total of 15 admissions (Table 5), no exacerbation caused hospitalizations during omalizumab treatment. All patients still experienced at least one exacerbation in the first year, with a mean frequency of 1.9 per year, but in the second and third years of omalizumab therapy, exacerbations were observed in 38% of patients, with a mean annual frequency of 0.56 and 0.38, respectively; most importantly, however, no episodes were severe enough to require hospitalization (Table 5). Moreover, respiratory symptoms occasionally forced 15 of 16 patients to inactivity (on average, 19 days per year) in the pre-omalizumab year, while no days off work were reported during omalizumab observation period (Table 3).

Improved asthma control was also mirrored by the dramatic drop in "rescue" medication use. All patients were using salbutamol (for an average of 2.6 puffs daily) in the year preceding omalizumab administration, whereas only 7.6% patients needed an average of 1.4 daily puffs over the following 3 years. Systemic corticosteroid consumption presented a fairly similar trend, with 5 of 16 (2 per year) and 0 of 16 patients needing oral and parenteral corticosteroids, respectively, during the omalizumab observation, as compared to 16 of 16 and 6 of 16, respectively, during the pre-omalizumab period. Finally, local (at the injection site) and systemic tolerability of omalizumab proved to be

TABLE 3.—Clinical outcomes expressed as per patient mean (SD).

| Parameter (measure unit)       | Pre-omalizumab observation period | Omalizumab observation period | Pre-post difference | p-Value |
|--------------------------------|-----------------------------------|-------------------------------|---------------------|---------|
| FEV <sub>1</sub> (% predicted) | 57 (12)                           | 76 (19)                       | 19 (12)             | <.01    |
| ACT (score)                    | 11.56 (3.22)                      | 19.91 (4.12)                  | 8.34 (3.83)         | <.01    |
| Exacerbations (n/year)         | 2.06 (1.12)                       | 0.94 (0.46)                   | -1.13 (1.05)        | <.01    |
| Inactivity (days/year)         | 19 (21)                           | 0 (0)                         | -19 (21)            | <.01    |

Notes: ACT, asthma control test; FEV<sub>1</sub>, forced expiratory volume in 1 second; n the number of exacerbations.

TABLE 4.—Mean (SD) results of the SGRQ (period T<sub>0</sub>-T<sub>36</sub>).

| Time points     | Symptom score  | Activity score | Impact score   | Total score    |
|-----------------|----------------|----------------|----------------|----------------|
| T <sub>0</sub>  | 69.38 (23.69)  | 52.91 (25.06)  | 42.58 (19.67)  | 50.16 (20.60)  |
| T <sub>6</sub>  | 46.18 (23)*    | 43.46 (20.54)  | 22.47 (13.59)* | 32.77 (15.87)* |
| T <sub>12</sub> | 44.61 (23.91)* | 40.68 (16.03)  | 22.04 (14.38)* | 31.44 (14.43)* |
| T <sub>18</sub> | 50.25 (22.94)  | 38.88 (21.22)  | 21.44 (15.2)*  | 31.51 (15.94)* |
| T <sub>24</sub> | 44.06 (20.63)* | 31.66 (18.25)* | 20.25 (14.2)*  | 27.66 (14.43)* |
| T <sub>30</sub> | 43.23 (24.97)* | 35.59 (21.9)   | 20.84 (14.77)* | 29.03 (17.11)* |
| T <sub>36</sub> | 46.52 (24.72)* | 31.77 (22.22)* | 21.56 (16.17)* | 28.8 (17.94)*  |

\*p < .01 versus T<sub>0</sub>.

TABLE 5.—Healthcare resources consumed before and after omalizumab initiation.

| Resource                   | Pre-omalizumab period | Omalizumab period | Pre-post difference | <i>p</i> -Value |
|----------------------------|-----------------------|-------------------|---------------------|-----------------|
| Hospitalizations (n/year)  | 0.94 (0.68)           | 0 (0)             | −0.94 (0.68)        | <.01            |
| EU accesses (n/year)       | 0.69 (0.95)           | 0.25 (0.31)       | −0.44 (0.65)        | <.05            |
| GP visits (n/year)         | 3.38 (2.03)           | 1.42 (0.67)       | −1.96 (1.88)        | <.01            |
| Specialist visits (n/year) | 2.06 (1.24)           | 1.10 (0.65)       | −0.96 (1.08)        | <.01            |

Notes: EU, Emergency Unit; GP, general practitioner.  
Values are expressed as annual per patient mean (SD).

excellent and no adverse events were reported during omalizumab treatment; the dropouts that did occur over the period were due to work-related issues.

The time course of serum IgE levels proved to be consistent with the monoclonal antibody action mechanism. Serum IgE levels increased substantially during the first semester ( $T_6$ ; in particular in the first months) due to IgE displacement by competitive binding, whereas concentrations showed only slight oscillations around their mean values over the remaining 30 months (Figure 1).

SGRQ data were available for all patients and at all checkpoints. All four SGRQ scores improved (i.e., diminished) significantly ( $p < .01$ ) after 36 months of omalizumab treatment. In particular, all the scores, except the activity score, improved significantly from the first semester of omalizumab treatment and this significant change persisted for 36 months (Table 4).

Significant differences in mean utility (before vs. after omalizumab addition) clearly emerged when the analytical relationship between SGRQ total score and the EQ-5D-based utility index, as reported by Stahl et al. (22), was applied to the data. As presented in Table 6, patients gained

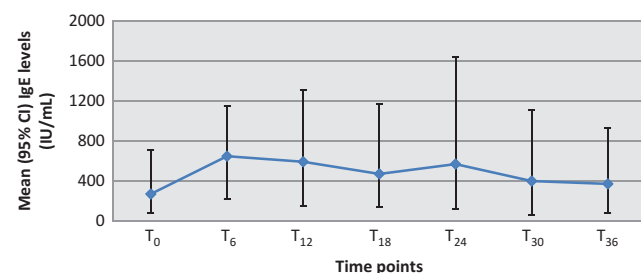


FIGURE 1.—Mean (95% CI) serum IgE time course during the 36-month survey.

TABLE 6.—Summary of utility and economic results.

| Annual means (SD)                       | Costs (€)   | Utility (QALY) |
|-----------------------------------------|-------------|----------------|
| Pre-omalizumab                          | 2869 (1383) | 0.56 (0.22)    |
| Post-omalizumab                         | 8038 (2096) | 0.78 (0.19)    |
| Increment                               | 5169 (2752) | 0.22 (0.16)    |
| Incremental cost/utility ratio (€/QALY) | 23,880      |                |

an average of 0.22 Quality-adjusted life year (about one-fifth of a year in the best imaginable health state) in each year of omalizumab treatment.

As already mentioned, the most dramatic changes in healthcare consumption were seen in the lack of exacerbation that caused hospitalizations over the 3-year omalizumab observation period.

In general, there was a substantial drop in drug consumption during omalizumab treatment. In particular, a slight increase in LABA use corresponded to a significant reduction in prn relievers (short-acting bronchodilators (SABAs)), all maintenance therapies (other than anti-leukotrienes), and the drugs needed to manage exacerbations (mainly oral and parenteral corticosteroids, and antibiotics).

The acquisition cost of omalizumab was only minimally offset by the reduction in other drug costs, leading to a substantial and significant increase (almost €600 per month) in mean pharmaceutical expense (Table 8).

The same was true for total healthcare costs. Despite the significant decrease in mean hospital costs, the omalizumab-based strategy proved to be significantly more expensive by €430 per month (Table 7).

Superior clinical performance and higher concomitant costs are typical features of innovative drugs which emphasize the scope of incremental cost/utility analyses that allow the quantification of the cost increase needed to obtain a unitary increase in utility.

TABLE 7.—Economical outcomes.

| Annual costs (€)         | Pre-omalizumab | Post-omalizumab | Difference   | <i>p</i> -Value |
|--------------------------|----------------|-----------------|--------------|-----------------|
| Drugs                    | 1032 (404)     | 7944 (2134)     | 6912 (2097)  | <.01            |
| Hospital costs, of which | 1744 (1194)    | 50 (62)         | −1694 (1181) | <.01            |
| Hospitalizations         | 1606 (1165)    | 0 (0)           | −1606 (1165) | <.01            |
| EU accesses              | 138 (189)      | 50 (62)         | −88 (130)    | <.05            |
| Visits, of which         | 93 (56)        | 44 (24)         | −49 (32)     | <.01            |
| GP                       | 51 (31)        | 21 (10)         | −30 (28)     | <.01            |
| Specialist               | 42 (25)        | 23 (13)         | −20 (22)     | <.01            |
| Total costs              | 2869 (1383)    | 8038 (2096)     | 5169 (2752)  | <.01            |

Note: Values are expressed as annual means (SD).

TABLE 8.—Mean annual pharmaceutical costs (€) before and after omalizumab initiation.

|               | Pre-omalizumab | Post-omalizumab | Delta       | <i>p</i> -Value |
|---------------|----------------|-----------------|-------------|-----------------|
| Omalizumab    | 0 (0)          | 7132 (2116)     | 7132 (2116) | <.01            |
| LABAs         | 251 (155)      | 339 (103)       | 87 (183)    | <.05            |
| ICS           | 262 (100)      | 166 (20)        | −96 (98)    | <.01            |
| OCS           | 139 (41)       | 16 (10)         | −123 (34)   | <.01            |
| Anti-LTs      | 255 (281)      | 286 (270)       | 32 (195)    | NS              |
| Antibiotics   | 100 (98)       | 1 (3)           | −99 (98)    | <.01            |
| SABAs         | 12 (3)         | 3 (3)           | −9 (5)      | <.01            |
| Parenteral CS | 2 (2)          | 0 (0)           | −2 (2)      | <.01            |
| Xanthines     | 11 (22)        | 0 (0)           | −11 (22)    | <.05            |
| Total         | 1032 (404)     | 7944 (2134)     | 6913 (2097) | <.01            |

Notes: LABAs, long-acting  $\beta$ -agonists; ICS, inhaled corticosteroids; Anti-LTs, anti-leukotrienes; (O)CS, (oral) corticosteroids; SABAs, short-acting  $\beta$ -agonists; NS, not significant.

Values are expressed as mean (SD).

The estimated value of €23,880 per QALY for add-on omalizumab indicates that this treatment can be considered cost/effective for persistent difficult-to-treat asthma patients according to the standards of the willingness to pay for health benefits in industrialized countries. In reality, the threshold for acceptable incremental cost/utility ratio in these countries usually lies in the \$27,000–165,000 per QALY gained range (24), with values for biologic treatments such as omalizumab tending to lie toward the upper limit of the range.

## DISCUSSION

Severe, difficult-to-treat atopic asthma is characterized by dramatic, long-term morbidity and is associated with a striking economic impact that can be up to 70% of the total cost of illness. Nevertheless, studies specifically designed to assess the pharmacoeconomic performance of omalizumab have usually only occurred over a short time period (maximum 12 months) (14), even when they were supposed to provide a crucial contribution to the definition of a cost/utility estimate stemming from real-life data.

In this study, all clinical outcomes (such as respiratory symptoms, lung function, and drug use) progressively improved and then stabilized over the 36 months of add-on omalizumab therapy. In particular, both the annual exacerbation and hospitalization rates diminished considerably, as long-term QoL that involved all SGRQ domains. In other words, the results of this study are in agreement with and confirm those obtained in previous studies which, however, were focused on the short-term (maximum 1-year) effects of add-on omalizumab in difficult-to-treat atopic asthma. In addition, this study showed that these benefits persist for a much longer period—up to 3 years.

The overall clinical response to omalizumab obtained in this study may appear to be much higher than that described in a previous pivotal study (25). This difference can be mainly attributed to differences in the experimental design (namely a monocentric, retrospective investigation on the same sample of 16 patients vs. a multicenter, double-blind, randomized, placebo-controlled phase III study on 1070 subjects) and duration (36 months vs. 16 weeks, respectively) of these two studies.

In economic terms, the first expected consequence of such long-term clinical results was clearly the substantial change in healthcare resource consumption which was mainly caused by the dramatic drop in hospitalization rates. As was found in previous, shorter studies (6), no hospitalization occurred over the 36 months of add-on omalizumab treatment. It is plausible that such a remarkable outcome produced the dramatic improvement in QoL in the patient cohort.

In strict financial terms, the therapeutic add-on omalizumab-based regimen involves a significant cost increase (about €430 per month) despite the systematic reduction in all other healthcare costs. The true pharmacoeconomic value of this treatment, however, emerges only when the wider perspective of the incremental cost/utility analysis is adopted.

From this point of view, the estimated €23,880 per QALY for the triennial omalizumab treatment indicates that this therapeutic strategy can be considered cost/effective when compared to the willingness-to-pay values that are usually reported in industrialized countries.

To the best of our knowledge, this is the only long-term (3-year) cost/utility study on omalizumab treatment available to date. We were, therefore, able to compare the economic effect of a shorter (12-month) and of a longer (36-month) duration strategy. In particular, the cost per QALY calculated for the triennial treatment proved to be lower by 8.1% when compared to that of 1-year add-on omalizumab therapy in the same kind of asthma patients (14). This gives weight to the argument that the pharmacoeconomic convenience of this strategy increases with the duration of add-on omalizumab therapy in this patient population, even considering the potential weaknesses of this study, mainly the lack of a reference group.

## CONCLUSION

In conclusion, based on this retrospective study, the efficacy of omalizumab given on top of all other high-dose respiratory drugs needed for controlling severe, difficult-to-treat atopic asthma was further supported in terms of long-term clinical outcomes, health-related QoL, and overall economic impact. Moreover, the economic convenience is also suggested to increase in proportion to the duration of add-on omalizumab therapy.

## ACKNOWLEDGMENTS

The authors would like to thank O. Zaniolo for the assistance in retrieving unit cost data and D. Lawson for the language edit.

## DECLARATION OF INTEREST

LP is an employee of AdRes, which has received a grant from Novartis S.p.A., market authorization holder for omalizumab in Italy. The other authors report no conflict of interest.

## REFERENCES

1. Bousquet J, Dahl R, Khaltaev N. Global alliance against chronic respiratory diseases. *Eur Respir J* 2007; 29:233–239.
2. Adcock IM, Caramori G, Chung KF. New targets for drug development in asthma. *Lancet* 2008; 372:1073–1087.
3. Walker S, Monteil M, Phelan K, Lasserson TJ, Walters EH. Anti-IgE for chronic asthma in adults and children (Cochrane Review). *The Cochrane Library* Issue. Vol 2. Chichester: Wiley, 2005.
4. FDA Omalizumab Product Approval Information Sheet 20-06-2003.
5. Niven R, Chung KF, Panahloo Z, Blogg M, Ayre G. Effectiveness of omalizumab in patients with inadequately controlled severe persistent allergic asthma: an open-label study. *Respir Med* 2008; 102: 1371–1378.
6. Solèr M, Matz J, Townley R, Buhl R, O'Brien J, Fox H, Thirlwell J, Gupta N, Della Cioppa G. The anti-IgE antibody omalizumab reduces exacerbations and steroid requirement in allergic asthmatics. *Eur Respir J* 2001; 18:254–261.
7. Busse WW. Anti-immunoglobulin E (omalizumab) therapy in allergic asthma. *Am J Respir Crit Care Med* 2001; 164:S12–S17.
8. Vignola AM, Humbert M, Bousquet J, Boulet LP, Hedgecock S, Blogg M, Fox H, Surrey K. Efficacy and tolerability of anti-immunoglobulin E therapy with omalizumab in patients with concomitant allergic asthma and persistent allergic rhinitis: SOLAR. *Allergy* 2004; 59:709–717.
9. Diukanovic R, Wilson SJ, Kraft M, Jarjour NN, Steel M, Chung KF, Bao W, Fowler-Taylor A, Matthews J, Busse WW, Holgate ST, Fahy JV. Effects of treatment with anti-immunoglobulin E antibody omalizumab on airway inflammation in allergic asthma. *Am J Respir Crit Care Med* 2004; 170:583–593.
10. Ayers JG, Higgins B, Chilvers ER, Ayre G, Blogg M, Fox H. Efficacy and tolerability of anti-immunoglobulin E therapy with omalizumab in patients with poorly controlled (moderate-to-severe) allergic asthma. *Allergy* 2004; 59: 701–708.
11. Holgate ST, Chuchalin AG, Hébert J, Lötval J, Persson GB, Chung KF, Bousquet J, Kerstjens HA, Fox H, Thirlwell J, Cioppa GD. Efficacy and safety of a recombinant anti-immunoglobulin E antibody (omalizumab) in severe allergic asthma. *Clin Exp Allergy* 2004; 34:632–638.
12. Humbert M, Beasley R, Ayers J, Slavin R, Hébert J, Bousquet J, Beeh KM, Ramos S, Canonica GW, Hedgecock S, Fox H, Blogg M, Surrey K. Benefits of omalizumab as add-on therapy in patients with severe persistent asthma who are inadequately controlled despite best available therapy (GINA 2002 step 4 treatment): INNOVATE. *Allergy* 2005; 60:309–316.
13. Hanania NA, Alban O, Hamilos DL, Condemi JJ, Reyes-Rivera I, Zhu J, Rosen KE, Eisner MD, Wong DA, Busse W. Omalizumab in severe allergic asthma inadequately controlled with standard therapy: a randomized trial. *Ann Intern Med* 2011; 154(9):573–582.
14. Dal Negro RW, Pradelli L, Tognella S, Micheletto C, Iannazzo S. Cost-utility of add-on omalizumab in difficult-to-treat allergic asthma in Italy. *Eur Ann Allergy Clin Immunol.* 2011; 43(2):45–53.
15. Tognella S, Dal Negro RW. Omalizumab: una risposta terapeutico-gestionale per il controllo dell'asma grave resistente. *It J Chest Dis* 2007; 61:390–394.
16. Regional DRG Tariffs. Aggiornamento del tariffario per la remunerazione delle prestazioni di assistenza Ospedaliera. Regione Veneto. Deliberazione della Giunta n. 916 del 28-03-2006.
17. Regional Specialist Tariffs. Nomenclatore Tariffario Regionale delle prestazioni di assistenza specialistica ambulatoriale: aggiornamento tariffe di cui alla D.G.R. n.61 del 21-01-05. Regione Veneto. Deliberazione della Giunta n. 917 del 28-03-2006.
18. Garattini L, Castelnuovo E, Lanzeni D, Viscarra C. Durata e costo delle visite in medicina generale: il progetto DYSCO. *Farmeconomia e percorsi terapeutici* 2003; 4(2):109–114.
19. Italian Drugs Formulary. Informatore Farmaceutico—68a edizione 2008. Elsevier Masson, 2008.
20. Off-Patent Drugs Reference Price System. Lista di trasparenza dei medicinali inseriti nell'elenco dei farmaci equivalenti (Legge 178/2002) con i relativi prezzi di riferimento aggiornati a giugno 2011. Available at: <http://www.agenziafarmaco.gov.it/it/content/liste-di-trasparenza-e-rimborsabilita>. Accessed September, 2011.
21. National Hospital Discharge Database. Statistiche sui ricoveri ospedalieri. Available at: [http://www.ministerosalute.it/programmazione/sdo/ric\\_informazioni/default.jsp](http://www.ministerosalute.it/programmazione/sdo/ric_informazioni/default.jsp). Accessed December, 2008.
22. Ståhl E, Lindberg A, Jansson SA, Rönmark E, Svensson K, Andersson F, Löfdahl CG, Lundbäck B. Health-related quality of life is related to COPD disease severity. *Health Qual Life Outcomes* 2005; 3:56.
23. Oba Y. Cost-effectiveness of long-acting bronchodilators for chronic obstructive pulmonary disease. *Mayo Clin Proc* 2007; 82(5): 575–582.
24. Hirth RA, Chernew ME, Miller E, Fendrick AM, Weissert WG. Willingness to pay for a quality-adjusted life year: in search of a standard. *Med Decis Making* 2000; 20(3):332–342.
25. Bousquet J, Wenzel S, Holgate S, Lumry W, Freeman P, Fox H. Predicting response to omalizumab, an anti-IgE antibody, in patients with allergic asthma. *Chest* 2004; 125(4):1378–1386.

Copyright of Journal of Asthma is the property of Taylor & Francis Ltd and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.