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Cost-utility of add-on Omalizumab in difficult-to-treat allergic asthma in Italy

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Key words

Difficult-to-treat asthma, allergic asthma; omalizumab, effectiveness, health care costs, cost/utility

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Summary

Objective: *Omalizumab (OM), an innovative biological treatment for difficult asthma with perennial sensitisations, is an humanized monoclonal anti-IgE antibody that binds free circulating IgE; inhibits mast cell and basophil activation by combining free IgE, leads to IgE receptor down-regulation, thus blocking the inflammatory cascade. AIM of the study was to assess real-world cost-utility of add-on OM in Italy.* ***Methods:*** *changes in clinical and economical outcomes, and in quality of life (QoL) associated with add-on OM in adults (n=23) with severe difficult asthma were compared with those recorded before OM in the same subjects. Variables were: lung function; IgE levels; health status; ACT score; QoL (SGRQ); n. GP and specialist visits; emergency visits; hospitalizations, and concomitant pharmacological treatments. Further indices were: changes in Health-related QoL; total health-care costs, and incremental cost/utility. Data were statistically compared (Student's T test), and $p < 0.01$ was accepted for statistical significance.* ***Results:*** *asthma clinical outcomes and patients' health-related quality of life improved significantly by adding OM, and both costs for drugs and hospital care dropped significantly ($p<0.01$). The net economic effect was a 350 € increase in overall monthly costs; when related to health benefits, it corresponded to an incremental cost/utility ratio of about 26,000 €/QALY, which represents a quite favourable figure in terms of willingness to pay for health benefits in industrialised countries.* ***Conclusions:*** *Omalizumab added to an optimised therapy significantly improves clinical outcomes in difficult-to-treat, persistent allergic asthma. Costs also increased, but proved justified by health benefits achieved.*

Introduction

Asthma is a chronic inflammatory disease that affects more than 300 million subjects in the world, and its prevalence is presumed to be further increasing in the next fifteen years. In Italy, asthma has a prevalence of 6% and induces high social costs (1).

The majority of asthmatics respond very well to inhaled corticosteroids (ICS) and/or bronchodilators. However, a small proportion of persistent asthmatics (5-10%) do not respond sufficiently to usual therapies, even though optimized; this may reflect the role of different pathogenic mechanisms in these asthma phenotypes, as suggested by their better response to drugs affecting leukotriene production or to monoclonal antibodies targeting immunoglobulin E (IgE) (2).

Omalizumab is a recombinant monoclonal antibody which selectively binds the high affinity C-epsilon 3 site of human IgE. The binding of the drug prevents IgE from binding to mastocytes and other effector cells, thus inhibiting the inflammatory cascade in response to antigenic stimuli. A review of 14 trials evaluating the role of omalizumab in 3,143 asthmatic patients highlighted significant reductions in inhaled corticosteroid use and exacerbation rate (3). Common therapeutic doses for Omalizumab are in the range 150-375 mg/subcutaneous injection, repeated every 2 to 4 weeks; the individual dose is to be determined on the basis of body weight and baseline free IgE serum levels (Table 1).

Omalizumab efficacy has been proved in children, adolescents and adults for doses able to guarantee at least 0.016 mg/kg/IU/ml of IgE for a minimum of 4 weeks (4). Several studies on patients with moderate to severe allergic asthma proved the clinical efficacy of omalizumab in addition to the standard optimised therapy (ICS + long-acting beta-agonists – LABA), and demonstrated significant reductions in annual exacerbation rates and severity of respiratory symptoms, together with increased FEV1 and quality-of-life scores (5-12).

The aim of the present study was the real-life survey of clinical outcomes, quality-of-life (QoL), and health resources use in a sample of patients with persistent atopic asthma, resistant to common therapies (optimised according to present GINA guidelines), treated with add-on Omalizumab. Data collected were then used to infer an estimate of the economic value of such a therapy in the Italian healthcare setting.

Methods

Data collection and subjects

The database (DB) available in the Lung Department of the Orlandi General Hospital - ULSS 22 of Veneto Region (North-Eastern Italy) represents the institutional tool operating since 1983 for officially collecting and centralizing data from all respiratory patients (in- and out-patients) referring from inside and outside the district (13). At present, the DB currently holds more than 350,000 records corresponding to visits; diagnostic procedures; results of respiratory and biological test; hospitalizations; visits; compliance to treatments, and treatments of more than 53,000 patients.

Data collection is based on the current national legal framework (Italian Privacy Law – sensitive data on subjects) and according to a strict internal procedural protocol, which is ISO-9001-2000 certified since 1999 (14). All subjects included in the present study signed their informed consent written form. DB records were analyzed to select patients sensitised to perennial antigens with severe and resistant asthma, which started the treatment with omalizumab in addition to their optimised therapeutic regimen. Patients with at least 12 months of clinical history preceding the beginning of Omalizumab (pre-omalizumab observation period) were filtered.

Twenty-three patients (14 females and 9 males) were identified with an average of a 10-month complete follow-up (Omalizumab observation period) from the treatment start (T_0); patients' characteristics before adding Omalizumab are reported in Table 2.

Table 1 - Dose in milligrams for asthmatic subjects over 12 years. Administration every two weeks. (*) administration every four weeks.

Serum IgE (UI/mL)	Body weight (Kg)			
	30-60	60-70	70-90	90-150
≥ 30-100	150(*)	150(*)	150(*)	300(*)
> 100-200	300(*)	300(*)	300(*)	225
> 200-300	300(*)	225	225	300
> 300-400	225	225	300	
> 400-500	300	300	375	
> 500-600	300	375		
> 600-700	375			

Table 2 - Characteristics measured at T0 (Omalizumab start) of the selected patients' sample

Characteristic	Value
Gender	9 m, 14 f
Age (mean, min - max)	46.5 (27 - 70)
BMI (mean, min - max)	25.75 (19.8 - 37.5)
Smoking habit	16 never, 5 ex, 2 current
IgE (mean, CI 95%)	240 (34 - 622) UI/mL
FEV1 (mean, CI 95%)	57.6 (33.5 - 89.7) % of predicted
Var % (mean, CI 95%)	22.6 (10.2 - 44.5)
MMEF (mean, CI 95%)	26.5 (9.6 - 55.3) L/s
Follow-up (mean, CI 95%)	10 (2 – 22) months

BMI: body mass index; FEV1: forced expiratory volume/1 sec; Var %: reversibility of obstruction; MMEF: maximal mid-expiratory flow

Variables

Data included clinical parameters, such as: Forced Expiratory Volume in one second (FEV1); maximal mid-expiratory flow (MMEF); reversibility of airway obstruction; n. exacerbations, and serum IgE levels. Exacerbations were defined as moderate when leading to a substantial implementation of previous daily treatment (mainly by adding systemic steroids), and severe when also requiring hospitalization.
Subjective measures of asthma control were also considered, like the Asthma Control Test (ACT) symptom score and a patient's registration of the illness-related inactivity days.

Health care

Health care resource consumption in terms of number and duration of hospitalizations due to respiratory causes; drug use (inhaled and systemic corticosteroids, bronchodilators, antileukotrienes, xantines, and antibiotics), and both specialist's and GP's examinations were also calculated.
Spirometric values (FEV1 and MMEF) and serum IgE concentrations were measured, and ACT scored monthly, while drug consumption was assessed every four months in both the pre-Omalizumab and the Omalizumab observational period. The St. George Respiratory Questionnaire (SGRQ) was administered immediately before the Omalizumab treatment (T_0) and every six months during the follow-up.

The study was designed as a pre-post comparison of clinical outcomes and of consumed healthcare resources value assessed in the selected cohort. The figures measured in the year preceding Omalizumab were taken as reference values to investigate and compare the impact of the Omalizumab treatment. Descriptive statistics (mean, 95% CI and minimum-maximum range) of data from the two observational periods were compared by Student's T test for paired data, and $p<0.01$ accepted as the level for the statistical significance.
In each patient, data relating to clinical events and resource consumption during the Omalizumab period were normalized to one year, in order to consent the homogeneous comparison with data of the pre-Omalizumab observation period (12 months).

Pharmaco-economic procedures

Healthcare resources consumed were converted into economic values by adopting the perspective of the Regional Health System (RHS) whenever possible. Consequently, costs due to hospitalizations were calculated according to the DRG-based remuneration tariff granted to hospitals in the Veneto Region (15), and specialist visits valued on the base of the last update of the regional specialist's tariffs (16). GP visits were valued as opportunity cost according to the findings of the DYSCO study by Garattini et al. (17).
Drug prices considered were ex-factory prices (18) for drugs of exclusive hospital use (i.e. omalizumab), reference prices (19) for reimbursed off-patent drugs and retail price (18) for reimbursed patent-covered drugs (price update October 2008) (Table 3).
On the basis of data collected, both the cost/effectiveness and the cost/utility calculation were performed. Incremental cost/effectiveness and cost/utility ratios were constructed as the ratio of the pre-post differential costs over differential effectiveness/utility, and presented as mean and 95% CI.
The pre-post FEV1 percentage points gained and the ACT points gained were considered as effectiveness measures. For the cost/utility analysis, calculation of the utility is based on SGRQ Total Scores, according to the analytic relationship among these and the EQ-5D utility index reported by Stahl et al. (21, 22). The considered utility increments are related to the difference between the start of the treatment values (T_0) and the last available measurement (LO). In other words, for the calculation of cost/QALY, it was assumed that the utility measured at T_0 was representative of the mean utility during the pre-Omalizumab year, and that the last available value represented the mean utility in the Omalizumab observation period.

Table 3 - Unit costs used for the analysis

Type of resource		Price, tariff or cost (€)	Source
Drugs	Omalizumab 150 mg, 1 vial	315.12	18
	Salmeterol 25mcg, 120 puffs	32.7	18
	Formoterol 12mcg, 60 puffs	19.41	19
	Fluticasone250 mcg, 120 puffs	53.07	18
	Budesonide 400 mcg, 50 puffs	16.71	19
	Montelukast 10 mg, 28 tablets	43.94	18
	Prednisone 25 mg, 10 tablets	5.13	18
	Betamethasone 4 mg, 3 vials	2.65	19
	Theophylline 200 mg, 30 tablets	2.31	18
	Theophylline 300 mg, 30 tablets	3.26	18
	Salbutamol 100 mcg, 200 puffs	4.54	18
	Ipratropium 20 mcg, 200 puffs	4.78	18
	Tiotropium 18 mcg, 30 puffs	50.8	18
	Amoxicillin + clavulanate 875+125 mg, 12 tablets	8.72	19
	Moxifloxacin 400 mg, 5 tablets	22.81	18
Hospital	Hospitalization for asthma exacerbation (DRG 96 and 97, weighted for their relative frequency in Veneto according to 2005 discharge data)	1759.20	15,20
	Emergency unit accesses (brief observation)	200	15
Visits	Specialist visit	14.25	16
	GP visit	12.32	17

GP: general practitioner

Results

Asthma control

Present data on the clinical effectiveness indicates a general improvement in asthma control following the add-on Omalizumab: FEV1 increased in 21/23 patients (in the two remaining, the difference is less than 3%), and ACT scores improved in all patients. During Omalizumab, exacerbations were recorded in 35% of patients (9/23), without any episode severe enough to require hospitalization, while in the preceding year all patients reported at least one exacerbation, and 18/23 were hospitalized, for a total of 21 admissions.

Respiratory symptoms forced 22/23 patients to some absenteeism in the pre-Omalizumab year, while no day off work was reported during Omalizumab (Table 4).

The substantial improvement in asthma symptom control was also mirrored by the dramatic drop in the consumption of "rescue" medications: only 1/23 patients continued using short-acting beta-agonists (SABAs) during Omalizumab, as compared to 21/23 patients using an average of 3.4 puffs daily in the preceding year. Also the use of systemic corticosteroid showed a similar trend, with only 1/23 and 0/23 patients respectively needing oral and parenteral corticosteroids during the add-on Omalizumab, as compared to 23/23 and 5/23 in the pre-Omalizumab period.

Both the local (such as in the site of injection) and the systemic tolerability of Omalizumab proved excellent because no significant adverse event was recorded during the corresponding observational period.

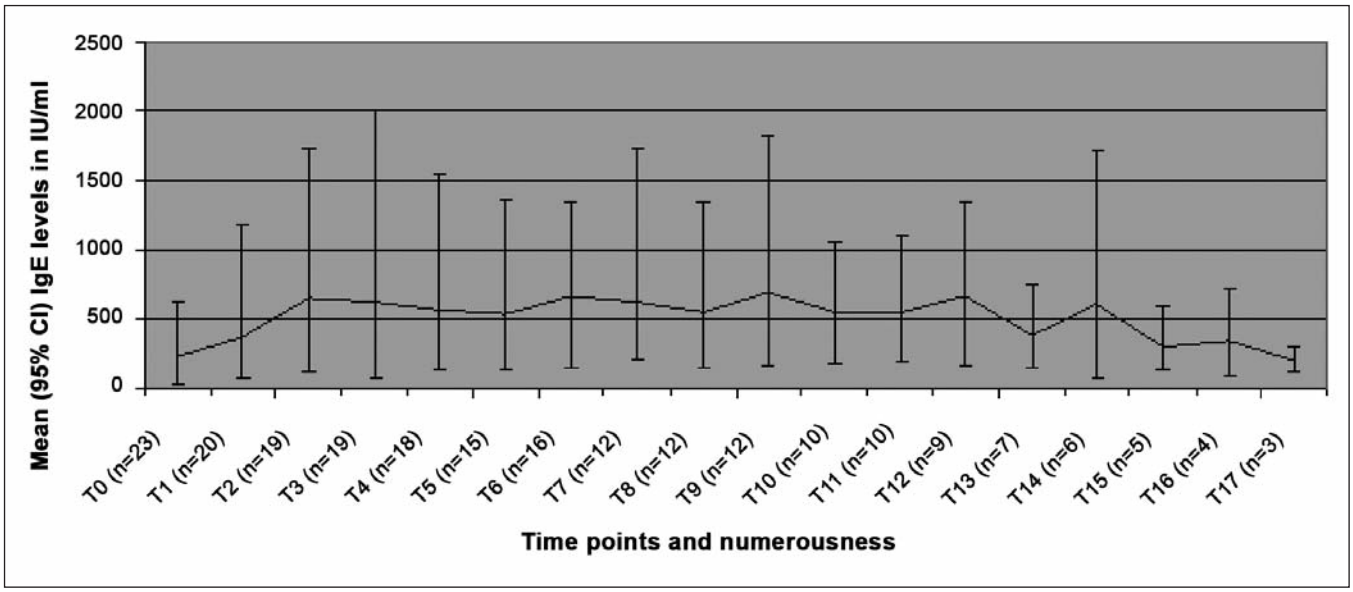
The time course of mean serum IgE levels was peculiar: IgE levels increased during the first month (T_1), and more markedly after the second month of add-on Omalizumab due to the IgE displacement by competitive binding, while the remaining trend for IgE concentrations showed only slight further variations around the mean value. The

Table 4 - Clinical outcomes expressed as mean (95%CI)

Parameter (measure unit)	Pre-Omalizumab period	Add-on Omalizumab period	Pre-post difference	p
FEV1(% predicted)	57.61 (33.55 – 89.70)	75.46 (45.10 – 104.29)	17.85 (-2.30 – 43.63)	< 0.01
ACT (score)	11.87 (7.55 – 17)	19.40 (13.16 – 23.64)	7.53 (2.89 – 15.22)	< 0.01
Exacerbations (n/year)	2 (1 – 4)	0.52 (0 – 3)	-1.48 (-4.00 – 1.45)	< 0.01
Inactivity (days/year)	17.61 (0.55 – 58.15)	0	-17.61 (-58.15 – 0.55)	< 0.01

ACT: asthma control test; FEV1: forced expiratory volume/1 sec

Figure 1 - Mean (95% CI) serum IgE levels during the add-on Omalizumab period



apparent reduction observed in the last months of the survey is a false effect due to some subjects characterised by a shorter duration of treatment. Actually, the analysis of all individual time courses (data not shown) does not indicate any tendency of IgE level reduction over the treatment period (Figure 1).

Quality of life and Pharnacoeconomic outcomes

The scores of all the four SGRQ domains also improved (i.e. diminished) significantly ($p<0.01$) after 6 months of add-on Omalizumab (Table 5). At the further measurements (such as, after 12^{h} and 18^{h} months), the difference in mean scores did not reach the statistical significance mainly because of the drop in the patients' number (tab.5). On Starting from empirical data, Stahl et al. reported an analytical relationship between SGRQ total score and the EQ-5D based utility index (21):

Utility (EQ-5D): 1.102 – 0.01083 × SGRQTS

where SGRQTS is the total score obtained from the SGRQ.

Moreover, in the present study, a significant difference in mean utility emerges when this formula is applied to data collected before and after add-on Omalizumab (Table 6). Assuming that T_0 utility represents the mean utility experienced in the pre-Omalizumab year, and that data of last observation (LO) represent the subsequent quality of life, it can be estimated that patients gained an average of 0.21 QALYs (about one fifth of a year in the best imaginable health state) in one year of add-on Omalizumab.

Table 5 - Results of the St. George's Respiratory Questionnaire

Mean (95%CI)	SS	AS	IS	TS
T0 (n=23)	71.4 (22.7 - 95.1)	57.4 (3.4 - 100.0)	45.2 (5.8 - 79.9)	53.2 (8.9 - 85.0)
T6 (n=21)	53.9 (16.7 - 94.0)*	44.6 (11.7 - 73.3)*	28.0 (4.3 - 64.8) *	37.3 (13.1 - 68.2)*
T12 (n=10)	45.5 (15.4 - 77.8)	46.2 (13.4 - 59.5)	26.6 (4.4 - 47.9)	35.7 (9.2 - 53.6)
T18 (n=3)	55.5 (46.8 - 61.6)	53.8 (48.0 - 59.2)	26.2 (22.1 - 31.7)	39.7 (34.6 - 43.1)
LO (n=21)	51.2 (15.3 - 90.5)	45.0 (14.7 - 62.8)	28.3 (7.0 - 52.5)	37.2 (11.7 - 59.3)
Delta T0 – LO (n=21)	23.4 (-21.7 - 68.1)*	16.2 (-6.6 - 54.5)*	19.8 (-11.4 - 57.8) *	19.2 (-6.8 - 51.2)*

SS: Symptom score, AS: Activity score, IS: Impact score, TS: Total Score *p < 0.01

T0: enrolment, T6: first semester, T12: second semester, T18: third semester, LO: last observation

Table 6 - Utility (EQ-5D) before and after add-on Omalizumab

Utility at T0	Utility at LO	Incremental Utility	p
0.53 (0.18 – 1)	0.70 (0.46 – 0.98)	0.21 (- 0.07 – 0.55)	< 0.01

T0: enrolment, LO: last observation

Table 7 - Health care resources consumed before and after add-on Omalizumab. Values expressed as mean (95% CI)

Resource	Pre-omalizumab observation period	Omalizumab observation period	Pre-post difference	p
Hospitalizations (n/year)	0.91 (0 – 2)	0 (0-0)	-0.91 (-2 – 0)	< 0.01
Hospital days/year	8.17 (0 – 26.1)	0 (0-0)	-8.17 (-26.1 – 0)	< 0.01
EU accesses (n/year)	0.65 (0 – 2.45)	0 (0-0)	-0.65 (-2.45 – 0)	< 0.01
GP visits (n/year)	3.74 (0.55 – 14.5)	0.14 (0 – 1.56)	-3.60 (- 14.5 – 0.56)	< 0.01
Specialist visits (n/year)	1.65 (1 – 3.45)	0.54 (0 – 2.82)	-1.11 (-3.45 – 1.67)	< 0.01

EU: Emergency Unit, GP: General Practitioner

The most relevant drop in the consumption of health care resources related to treatment of asthma and of its complications should be mainly related to the drop in both exacerbation and hospitalisation rate (Table 7).

Furthermore, drug consumption changed substantially during Omalizumab treatment, with a significant reduction in all other maintenance therapies (ICSs, antileukotrienes, xantines, and anticholinergics), including those needed to control exacerbations (SABAs, oral corticosteroids, and antibiotics) (Table 8).

The acquisition cost for Omalizumab is only minimally offset by the reduction in other drug costs, leading to a considerable and statistically significant increase (about 500 € monthly) in mean pharmaceutical expense (Table 9). The same trend was observed for total sanitary costs: despite the substantial and significant reduction in mean hospital costs, the Omalizumab-based strategy resulted significantly more expensive (an increment of about 350 € per month).

This kind of performance (i.e. a superior clinical performance and concomitant greater costs) is typical of innovative drugs and defines the field of incremental cost/effectiveness and cost/utility analyses that leads to the quantification of the cost increase necessary to obtain a unitary increase in effectiveness/utility. The incremental cost per month with one FEV1% predicted point gained and with one ACT point gained are, however, difficult to interpret for both the clinician and the health care decision-maker, due to the surrogate nature of these clinical outcomes.

Table 8- Mean monthly pharmaceutical costs before and after add-on omalizumab. Values expressed as mean (95% CI)

Drug costs (€/month)	Pre-omalizumab observation period	Omalizumab observation period	Pre-post difference	p
Omalizumab	N/A	526.68 (351.12 -702.24)	526.68 (351.12 -702.24)	< 0.01
LABAs	22.97 (0 – 32.70)	25.99 (0 – 32.70)	3.02 (- 32.70 – 32.70)	NS
ICSs	34.66 (0 – 53.07)	23.02 (0 – 53.07)	-11.64 (- 53.07 – 26.54)	NS
Anti-LTs	22.52 (0 – 47.08)	10.23 (0 – 47.08)	-12.28 (-47.08 – 21.19)	NS
OCS	3.71 (1.95 – 7.10)	0.03 (0 – 0.32)	-3.68 (-6.71 – -1.75)	< 0.01
Theophylline	1.17 (0 – 6.52)	0 (0 – 0)	-1.17 (-6.52 – 0)	NS
SABAs	2.10 (0 – 4.39)	0.18 (0 – 1.84)	-1.92 (-4.39 – 0)	< 0.01
Anticholinergics	1.21 (0 – 5.74)	0.50 (0 – 5.74)	-0.50 (- 5.74 – 0)	NS
Antibiotics	2.84 (0 – 7.27)	0.70 (0 – 3.56)	-2.15 (-7.27 – 1.31)	< 0.01
Total	90.97 (13.68 – 150.01)	585.93 (390.58 – 773.41)	494.96 (265.32 – 725.57)	< 0.01

N/A: not applicable, LABAs: long-acting bronchodilators, ICSs: inhaled corticosteroids, Anti-LTs: anti-leukotrienes, OCS: oral corticosteroids, SABAs: short-acting bronchodilators, NS: not significant.

Table 9- Economic outcomes. Values expressed as mean (95% CI)

Monthly Costs (€)	Pre –omalizumab	Post –omalizumab	Pre-post difference	p
Drugs	90.97 (13.68 – 150.01)	585.93 (390.58 – 773.41)	494.96 (265.32 – 725.57)	< 0.01
Hospital costs, of which	144.72 (0 – 317.37)	0 (0 – 0)	-144.72 (- 317.37 – 0)	< 0.01
Hospitalizations	133.85 (0 – 293.20)	0 (0 – 0)	-133.85 (- 293.20 – 0)	< 0.01
EU accesses	10.87 (0 – 40.83)	0 (0 – 0)	-10.87 (-40.83 – 0)	< 0.01
Visits, of which	5.80 (1.75 – 18.98)	0.79 (0 – 4.95)	-5.01 (- 18.98 – 2.56)	< 0.01
GP	3.84 (0.56 – 14.89)	0.14 (0 -1.60)	-3.70 (-14.89 – 0.57)	< 0.01
Specialist	1.96 (1.19 – 4.10)	0.64 (0 – 3.34)	-1.32 (-4.10 – 1.98)	< 0.01
Total costs	241.49 (69.08 – 464.95)	586.71 (392.15 – 773.41)	345.22 (33.01 – 677.68)	< 0.01

The cost/QALY here calculated on the basis of the variation in quality of life as measured on the SGRQ is much more informative, due to reference values and the richness of specialised literature on the topic. The estimated value of about 26,000 €/QALY for add-on Omalizumab (Table 10) indicates that this treatment should be considered cost/effective according to the standards of the willingness to pay for health benefits in industrialised countries. Actually. the maximum threshold is usually in the range 27,000-165,000 $/QALY gained (23).

Table 10- Incremental cost/effectiveness and cost/utility

Indicator	Mean (95%CI)
Cost/FEV	21.9 (dominant – 104.0) €/%FEV1
Cost/ACT	57.3 (0.96 – 154.9) €/ ACT point
Cost/QALY	25,983.33 (dominant – 94.010) €/QALY

Cost/FEV: cost per month with one FEV1 predicted percentage point gained; cost/ACT: cost per month with one ACT point gained

Discussion

Several international studies have focused the role of add-on Omalizumab and confirmed the effectiveness and the therapeutic value of this option particularly in severe persistent, difficult-to-treat allergic asthma, when the disease proves resistant to high doses of the internationally recommended therapeutic options.

Clinical benefits reported in these studies were in terms of recovery of functional impairment (FEV1); reduction of day- and night-time asthma symptoms; reduction in rescue medications and corticosteroids (both inhaled and systemic) use; reduction of exacerbations, and particularly of those leading to hospitalization (3, 5-12).

These subjects, who represent at least 5% of all asthmatics (12), are at elevated risk of severe exacerbations, which in turn cause a significantly increase of asthma morbidity and mortality. The consequent economic impact is quite cumbersome, reaching up to 50% of the total cost of illness.

At present, no study had been specifically designed to asses in real-life the Omalizumab pharmacoeconomic impact in terms of cost-utility analysis the Italian framework, and data from the present study could represent the first contribution to this particular topic available in this context.

On the other hand, clinical outcomes obtained with the add-on Omalizumab in the present study are in good agreement with those shown in previous international trials. In other words, when compared to pre-Omalizumab period, a dramatic reduction in respiratory symptoms, functional impairment and drug consumption (SABAs and corticosteroids) was observed following the Omalizumab treatment. Moreover, both the frequency and the severity of exacerbations, and the consequent n. hospital admissions dropped substantially, and also the patients' quality of life was systematically improved, as indicated by the amelioration of the scores for all SGRQ domains.

Obviously, such positive clinical outcomes had to lead to a significant change in the health care resource consumption, which is mainly driven by the reduction in hospitalization rates. Consistent with the findings from another study (6), also the present survey showed no hospitalization during the Omalizumab treatment period for any of the subjects recruited. It is very likely that such a strong outcome has driven the dramatic increase reported by all patients in their perceived quality of life.

Generally speaking and from a strict financial point of view, the therapeutic regimen including also the add-on Omalizumab proves significantly more expensive (about 350€ /month), despite the systematical reduction of all other sanitary costs.

The pharmacoeconomic value of this treatment only emerges if one adopts the wider perspective of an incremental cost/utility analysis. From this point of view, the estimated 26,000 €/QALY induced by a one-year omalizumab treatment indicates that this strategy can be considered very cost/effective according to the accepted willingness-to-pay thresholds in industrialized countries, such as in Italy.

The World Health Organization considers those health interventions whose cost per life year gained is lower than the per capita gross domestic product (GDP) as being very cost/effective. The interventions which cost between 1 and 3 per capita GDPs per life year saved are considered cost/effective (24). One QALY corresponds to a life year in the best imaginable health state; in 2007, the Italian per capita GDP was of 25,968 € (25).

In conclusion, data from the present study are confirming that add-on Omalizumab to subjects with severe, persistent allergic asthma, uncontrolled by standard optimised treatments, leads to a substantial and systematic improvement in clinical outcomes and in health-related quality of life. In these patients, and in a time horizon sufficiently long, the systematic extension of both the symptom-free and the hospitalization-free periods reflects the achievement of a good and stable asthma control, and highly contributes to the very favourable and acceptable incremental cost/utility value.

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