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ORIGINAL ARTICLE

Patient-Reported Outcomes among Omalizumab and Salmeterol/Fluticasone Combination Therapy Patients

DAVE P. MILLER, M.S.,[1,*] GLADYS TOM, M.S.,[1] LAWRENCE RASOULIYAN, M.P.H.,[1] AND BRADLEY CHIPPS, M.D.[2]

[1]*ICON Clinical Research, San Francisco, CA*
[2]*Capital Allergy and Respiratory Disease Center, Sacramento, CA*

Background. Some asthma patients remain poorly controlled despite receiving care consistent with treatment guidelines. *Objective*. This study compared the ability to sleep, work, and participate in leisure activities among subjects with immunoglobulin E–mediated (allergic) asthma initiating omalizumab (omalizumab start group) with subjects receiving moderate-to-high doses of salmeterol/fluticasone combination therapy, who continued on salmeterol/fluticasone combination therapy for at least a year without adding omalizumab (salmeterol/fluticasone combination continuation group). *Methods*. Subjects completed an Internet-based screener and, if eligible, an Internet-based questionnaire. A propensity score model was utilized in the analysis. Group differences were assessed through logistic and linear regression models. Analyses were adjusted for propensity score quintile, how subjects heard about the study, and responses to retrospective single-item questions. *Results*. The analysis population included 86 omalizumab start group subjects and 436 salmeterol/fluticasone combination continuation subjects, recruited from June to November 2006. In the adjusted analyses, the omalizumab start group was more than twice as likely to have controlled asthma as measured by the Asthma Control Test (odds ratio, 2.62; $p = 0.005$). The omalizumab start group had significantly fewer sleep disturbances as measured by the Jenkins Sleep Evaluation Questionnaire (least-square means difference, -1.65; $p = 0.004$), less activity impairment as measured by the Work Productivity Activity Impairment-Asthma Scale (least-square means difference, -13.36; $p < 0.001$), and less difficulty in activities as measured by the Valued Life Activities Questionnaire (least-square means difference, -0.24; $p < 0.001$). *Conclusion*. Asthma subjects who started taking omalizumab reported more improvement in asthma control, fewer sleep problems, less activity impairment, and less difficulty with activities than a similar cohort of subjects who continued taking salmeterol/fluticasone combination therapy.

Keywords asthma, productivity, omalizumab, fluticasone, salmeterol

INTRODUCTION

Asthma affects 300 million people worldwide (1). Approximately 20 million people in the United States have asthma, of whom half have immunoglobulin E (IgE)–mediated (allergic) asthma (2, 3). Allergic asthma sufferers produce IgE, a class of antibodies associated with allergic reactions, when they come into contact with allergens (4). The recommended treatment for patients with moderate-to-severe asthma is combination therapy with inhaled corticosteroids and a long-acting inhaled beta$_2$-agonist (5, 6). One such combination therapy is salmeterol and fluticasone (7). Many patients with moderate-to-severe asthma remain poorly controlled despite receiving care that is consistent with the 2002 National Heart, Lung, and Blood Institute treatment guidelines (8, 9). Patient-reported data from previous studies have indicated that moderate-to-severe allergic asthma can cause significant impairment (8, 10). It is recommended that asthma patients be routinely assessed for absences from work, reductions in usual occupational and recreational activities, and disturbances in sleep (11).

Omalizumab is the first US Food and Drug Administration–approved allergic asthma therapy that treats asthma by binding to circulating IgE (12), inhibiting the inflammatory reaction associated with the pathogenesis of asthma (4). Omalizumab reduces allergic symptoms of asthma by preventing the binding of IgE to the cellular receptors on the surface of mast cells and basophils. Reduction in surface-bound IgE on these cells limits the degree of release of mediators of the allergic response (13). Omalizumab is indicated for patients 12 years of age and older with moderate-to-severe persistent IgE-mediated (allergic asthma) (14). Patient-reported data from several studies have shown that treatment in moderate-to-severe asthma patients with omalizumab leads to a reduction in asthma exacerbations and improves symptom control (4, 15).

The objective of the study was to assess and compare the ability to sleep, work, and to participate in leisure activities among subjects with moderate-to-severe IgE-mediated (allergic asthma) initiating omalizumab and a similarly poorly controlled cohort of subjects receiving moderate-to-high doses of salmeterol/fluticasone combination (SFC) therapy, who continued on SFC for at least a year without the addition of omalizumab. It was expected that many of the omalizumab patients would remain on SFC, in addition to initiating omalizumab, so the objective is not to compare 2 treatments but rather to develop the understanding of omalizumab as an add-on therapy.

A substantial challenge in conducting a naturalistic study based on this comparison of strategies is that 2 strategies are not pursued with equally severe or poorly controlled patients. The study was designed to use propensity score methodology to adjust for group differences and assess outcomes for comparable cohorts.

*Corresponding author: Dave P. Miller, ICON Clinical Research, 188 Embarcadero, Suite 200, San Francisco, CA 94105, USA; E-mail: dave.miller@iconplc.com

METHODS

Study Design

A cross-sectional study design was utilized. Potential subjects completed an Internet-based screener to determine their eligibility, and then eligible subjects were immediately asked to complete an Internet-based questionnaire.

To be eligible to participate, subjects must have had patient-reported in vitro reactivity to a perennial allergen known to trigger allergic asthma and they must have either been on omalizumab for the past 4 to 12 months (omalizumab start group), hereafter referred to as (OSG) or on SFC (250/50 or 500/50 mcg/puff, one puff twice daily) for at least the past 12 months (SFC continuation group). In addition, subjects had to be between 18 and 55 years of age and a nonsmoker for at least 6 months. As a function of the study design, subjects also needed to have Internet access and be willing to provide online informed consent.

The screener and questionnaire were developed based on literature reviews and expert opinion from clinicians and outcomes researchers. The instruments were pretested in 10 subjects and modifications were made based on feedback received.

Four primary outcomes, each based on validated measures, were included in the final questionnaires to assess impact on sleep, work productivity, activity level, and asthma control. The Jenkins Sleep Evaluation Questionnaire (16) is a 4-item measure that evaluates the impact of therapies on sleep problems, with a 1-month recall period and scoring range of 0 to 20. Work Productivity Activity Impairment-Asthma (17) is a 9-item measure that assesses the percentage of work impairment and activity impairment because of the asthma during the past 7 days. The Valued Life Activities (VLA) Questionnaire (18) is a 32-item measure that assesses ability to perform activities that individuals enjoy or find meaningful with a 1-week recall period and scoring range of 0 to 3. The Asthma Control Test (ACT) (19) is a 5-item measure of asthma control with a 1-month recall period and scoring range of 5 to 25. An ACT score of 20 or higher is considered controlled asthma.

In addition, the final questionnaire included original single-item questions regarding the primary outcomes (i.e., asthma control, ability to sleep, ability to participate in leisure activities, and work productivity) in which subjects were asked to recall their status one year ago. These items served as baseline data in the analysis and were used as covariates in the models comparing the OSG and SFC groups on the 4 main outcomes. Items also were included in the final questionnaire regarding asthma medication use.

The screener, questionnaire, protocol, and relevant supporting materials were approved by Copernicus IRB Group, an independent review board. All subjects who met the eligibility criteria were required to provide informed consent online before proceeding to the questionnaire.

Subject Recruitment

A convenience sample of subjects was recruited via the Internet and through the distribution of paper flyers. E-mail announcements about the study were distributed through the Harris Poll Online Panel (HPOL), a multimillion member panel of prerecruited respondents who indicated a willingness to participate in research studies, and to members of AsthmaMatters™, an Internet resource for asthma patients. In addition, advertisements about the study were posted in online discussion groups. Paper flyers were distributed through OptionCare, a specialty pharmacy that distributes omalizumab, and through nurses and physicians in offices with omalizumab training and frequent omalizumab use. All respondents received $25 in cash or merchandise credit upon completion of the questionnaire.

Statistical Methods

A propensity score model was developed to address selection bias that may be present in nonrandomized studies (20). Covariates that were possibly associated with the treatment group and that were likely to differentiate omalizumab and SFC subjects in a random sample were included as candidate variables in the development of the propensity score. The score was derived from a stepwise multivariable logistic regression analysis in which the treatment group was modeled as a function of the statistically significant covariates. Based on the coefficients of the final model, a propensity score was calculated for each subject.

The propensity score indicates the likelihood that any given subject would be a member of the OSG based on the associated covariates. Subjects were ranked based on their propensity scores and categorized into quintiles. An important step in evaluating the fitted propensity score is assessing overlap of the 2 treatment groups (21). Because, we expected there to be a group at one end of the propensity spectrum with virtually no chance of receiving omalizumab, the protocol specified that the analysis be limited to potentially comparable patients, with the exclusions based on a propensity score threshold.

Propensity scores allow for an adjustment for differential probabilities of being in one group or the other, but subjects who were nearly certain to be in one particular group did not contribute substantively to the adjustment and were excluded. Specifically, subjects who had a low propensity for receiving omalizumab (ie, subjects in the bottom 3 quintiles) were excluded from the final analysis. This exclusion ensured that there was substantial overlap with respect to the level of control and severity between the SFC continuation group and the OSG, allowing for a robust statistical adjustment for the remaining group differences. Descriptive statistics were generated for demographics, medication use, and single-item patient-reported outcomes from one year ago.

In the analysis of primary outcomes, to assess asthma control, subjects were dichotomized into controlled (ACT $\geq$ 20) and uncontrolled (ACT $<$ 20), and logistic regression models were generated to calculate the unadjusted and adjusted odds ratios (ORs) (OSG *vs.* SFC continuation group). For the remainder of the outcomes (mean sleep problems scale score, mean percent overall work impairment, mean percent activity impairment, mean VLA average difficulty rating), linear regression models were generated to calculate the unadjusted and adjusted least-square means (LSM) differences between treatment groups. Analyses were adjusted for propensity score quintile, how the subject heard about the study, and the relevant single-item questions pertaining to the primary outcomes from one year ago. For

TABLE 1.—Propensity score models for OSG *vs.* SFC continuation group.

	OSG *vs.* SFC continuation group*					
	Univariable			Multivariable Stepwise Logistic Regression		
Variable	OR†	95% CI	*p*	OR†	95% CI	*P*
Age (per 10 years)	0.98	(0.78, 1.23)	0.8609			
Male	1.17	(0.70, 1.94)	0.5468	1.94	(1.07, 3.52)	0.0301
Non-White	1.26	(0.69, 2.28)	0.451			
Hispanic	0.72	(0.41, 1.27)	0.2617			
College degree or higher	0.98	(0.64, 1.49)	0.9131			
Pet(s)	0.63	(0.41, 0.99)	0.0427			
Physician type						
Allergist	19.6	(9.26, 41.47)	<.0001	17.38	(8.04, 37.54)	<0.0001
Pulmonologist	11.3	(4.98, 25.67)	<.0001	9.45	(4.02, 2.17)	<0.0001
Insurance type						
Commercial/PPO	2.42	(1.18, 4.97)	0.0159	3.54	(1.56, 8.04)	0.0025
HMO	2.08	(0.96, 4.50)	0.0634	2.41	(1.01, 5.76)	0.0476
Asthma control self-rated 1 year ago‡	0.34	(0.27, 0.43)	<0.0001	0.43	(0.31, 0.59)	<0.0001
Sleep ability affected 1 year ago§	1.24	(1.16, 1.33)	<0.0001			
Work productivity affected 1 year ago§,‖	1.29	(1.19, 1.38)	<0.0001			
Activity impairment affected 1 year ago§	1.27	(1.17, 1.38)	<0.0001			
Leisure impairment affected 1 year ago§	1.35	(1.25, 1.45)	<0.0001	1.15	(1.03, 1.28)	0.0119

CI = confidence interval; HMO = health maintenance organization; OSG = omalizumab start group; PPO = preferred provider organization; SFC = salmeterol/fluticasone combination.
*OSG (n = 92), SFC continuation group (n = 1220).
†Denotes the odds of being in the OSG relative to the odds of being in the SFC continuation group.
‡Based on scale from 1–5, where 1 denotes not controlled and 5 denotes completely controlled.
§Based on scale from 0-10, where 0 denotes no effect and 10 denotes complete prevention of activities.
‖Since this question was only asked of a subset of subjects (those currently employed) it was not considered in the construction of the propensity score model.

example, in the analysis of the sleep problems scale score, the relevant single-item question that was included in the adjustment asked subjects how much their asthma affected their ability to sleep approximately one year ago, on a scale from 0 (no effect) to 10 (completely prevented me from sleeping). Sensitivity analyses were conducted using a 1:1 match on propensity score rather than adjusting for propensity quintile as a covariate.

Missing data were rare. Three subjects had missing data for the single-item work impairment question in reference to 1 year ago, and 3 SFC continuation subjects had missing data with respect to change in medication dose. These subjects were excluded from relevant analyses. All other data were nonmissing.

RESULTS

A total of 92 OSG subjects and 1220 SFC continuation subjects were enrolled in the study between June and November 2006.

Propensity Modeling: Likelihood of Being in the OSG

Table 1 contains unadjusted and adjusted ORs that represent the likelihood of being in the OSG versus the SFC continuation group for various subject characteristics. The adjusted results control for variables such as demographics and level of functioning one year ago. Subjects were more likely to be in the OSG if they were male (adjusted OR, 1.94; $p = 0.030$), if they were treated by an allergist or pulmonologist (adjusted OR, 17.38, $p < 0.001$, and 9.45, $p < 0.001$, respectively), and if they had commercial/preferred provider organization (PPO) or health maintenance organization (HMO) health insurance (adjusted OR, 3.54, $p = 0.003$, and 2.41, $p = 0.047$, respectively). Subjects with greater asthma control were less likely to be in the OSG (adjusted OR, 0.43; $p < 0.001$) while subjects with greater leisure impairment were more likely to be in the OSG (adjusted OR, 1.15; $p = 0.012$). Subjects with greater sleep and activity impairment appeared to have a greater propensity for being in the OSG in the unadjusted analysis; however, these variables were not significant in the adjusted analysis because of at least in part to their high correlations with leisure ability (ranging from $r = 0.774$ to 0.83) and asthma control (ranging from $r = -0.63$ to -0.68).

Based on these results, each subject was assigned a propensity score, indicating the likelihood of that subject being in the OSG based solely on his or her demographic or clinical characteristics from one year ago. As described in the methods section, subjects in quintiles 1 to 3, with the lowest likelihood of receiving omalizumab, were excluded. The excluded population had 790 subjects, 6 in the OSG and 784 in the SFC continuation group. The excluded population did not differ from the analysis population with respect to age, gender, race, or ethnicity. As expected, and in agreement with the OR analysis, fewer subjects in the excluded population were treated by a specialist for their asthma and more subjects in the excluded population had an insurance type other than commercial/PPO or HMO. In addition, subjects in the excluded population had better asthma control and less impairment caused by asthma on their ability to sleep, their productivity, and their ability to do regular daily activities.

Subjects who were excluded as a result of the propensity model results all had a predicted probability of being in the OSG of less than 2.92%. The following results were based on the remaining analysis population of 522 subjects, with 86 subjects in the OSG and 436 subjects in the SFC continuation group. As a sensitivity analysis, the adjusted models were regenerated without excluding patients on the basis of propensity score and similar results were obtained across all outcomes.

TABLE 2.—Demographic characteristics of treatment groups.

Characteristic	OSG (n = 86)	SFC continuation group (n = 436)	p*
Age, Mean (SD)	40.9 (9.9)	41.4 (9.2)	0.6539
Gender, *N* (%)			
Male	19 (22.1%)	94 (21.6%)	0.9126
Female	67 (77.9%)	342 (78.4%)	
Hispanic origin, *N* (%)†			
Yes	5 (5.8%)	22 (5.1%)	0.7983
No	81 (94.2%)	406 (94.9%)	
Race/Ethnicity, *N* (%)†			
White	75 (87.2%)	379 (88.1%)	0.9709
Black or African American	6 (7.0%)	28 (6.5%)	
All Other	5 (5.8%)	23 (5.3%)	
Asthma physician type, *N* (%)			
Allergist or immunologist	61 (70.9%)	252 (57.8%)	0.0119
Pulmonologist	22 (25.6%)	122 (28.0%)	
All others	3 (3.5%)	62 (14.2%)	
Health care insurance, *N* (%)			
Commercial/PPO	55 (64.0%)	247 (56.7%)	0.2065
HMO	25 (29.1%)	130 (29.8%)	
All other	6 (7.0%)	59 (13.5%)	
Which of the following medications, if any, were you taking to control your asthma? *N* (%)‡			
Inhaled corticosteroid + long-acting beta-agonist	66 (76.7%)	436 (100.0%)	<0.0001§
Inhaled corticosteroid	24 (27.9%)	46 (10.6%)	0.0033
Long-acting beta-agonist	4 (4.7%)	24 (5.5%)	1.000§
Leukotriene modifier	59 (68.6%)	222 (50.9%)	0.0026
Other	39 (45.3%)	113 (25.9%)	0.0003
None	3 (3.5%)	11 (2.5%)	0.7120§

HMO = health maintenance organization; OSG = omalizumab start group; PPO = preferred provider organization; SFC = salmeterol/fluticasone combination.

*P values derived from chi-square and Student's t-test for categorical and continuous variables, respectively, unless otherwise indicated

†There were eight subjects (for the Hispanic origin question) and six subjects (for the race/ethnicity question) marked "Decline to Answer." These subjects were treated as missing and excluded from calculations of percentages and p values.

‡This question was based on the one-year-prior timeframe. Respondents could select as many responses as relevant.

§Fisher's exact test.

Descriptive Statistics

Demographic characteristics were computed by treatment group (Table 2). The groups did not differ with respect to age, gender, or race/ethnicity. Significant differences were found between treatment groups in the type of physician that primarily treats their asthma. More subjects in the OSG (70.93%) were treated by an allergist or an immunologist. For both treatment groups, the most common health insurance type was commercial/PPO, followed by HMO.

The median number of months since initiating therapy was 8 for OSG subjects and 38 for SFC continuation subjects. How subjects heard about the study differed as expected because of the recruitment scheme. Most SFC continuation subjects (63.99%) were recruited online through HPOL. Other sources of recruitment for SFC continuation subjects (of which more than one could apply) included other Internet sources (34.63%), health-care providers (1.38%), paper flyers (0.23%), and other sources (0.46%). The most common sources of recruitment among OSG subjects were other Internet sources (47.67%), paper flyers (20.93%), health-care providers (16.28%), and HPOL (16.28%).

In the OSG, 76.74% of subjects were on SFC from one year ago. In the SFC continuation group, by design, 100% of subjects were on SFC from one year ago. Over 60% of subjects in the SFC continuation group were on the 250/50 mcg/puff (one puff twice daily) strength medication, and 69.95% had been on the same strength medication for at least a year.

Self-Reported Outcomes From One-Year Ago

The results of single-item questions related to the primary outcome measures from one year ago are presented in Table 3. Subjects in the OSG reported being significantly worse off one year ago to starting omalizumab than subjects in the SFC continuation group in terms of asthma control, sleep, work productivity, regular daily activities, and leisure activities.

Primary Outcomes

Figure 1 presents the current primary outcomes for the OSG versus the SFC continuation group as measured by multi-item validated scales, after adjustments for propensity score quintile, how the subject heard about the study, and the relevant single-item score from one year ago. The OSG was more than twice as likely to have controlled asthma than the SFC continuation group (OR, 2.62; $p = 0.005$). In addition, the OSG had less activity impairment (24.33% *vs* 37.69%) (LSM difference, 13.36; $p < 0.001$) and less work impairment (17.47% *vs* 22.74%) compared with the SFC continuation group. There were no statistically significant differences on the work impairment scale ($p = 0.163$). With scores of 3.14 versus 4.80 on the Jenkins Sleep scale, which ranges from 0 to 20, the OSG had fewer sleep problems than the SFC continuation group (LSM difference, –1.65; $p = 0.004$) and, with VLA scores of 0.42 versus 0.66 on a scale of 0 to 3, the OSG also had less difficulty in valued life activities than

TABLE 3.—Single-item patient-reported outcomes from one year prior.

Characteristic*	OSG (n = 86)	SFC continuation group (n = 436)	$p^{\dagger}$
How would you rate your asthma control? (1–5)‡	2.16 (0.80)	2.80 (0.98)	<0.0001
How much did asthma affect your ability to sleep? (0–10)§	5.21 (3.11)	4.01 (3.13)	0.0013
How much did asthma affect your productivity while you were working? (0–10)§	4.42 (3.22)	3.16 (2.90)	0.0025
How much did asthma affect your ability to do regular daily activities? (0–10)§	5.98 (2.86)	4.67 (3.09)	0.0003
How much did your asthma affect your ability to participate in leisure activities? (0–10)§	5.42 (3.01)	3.81 (2.96)	<0.0001

OSG = omalizumab start group; SFC = salmeterol/fluticasone combination.
*Mean (SE), unless otherwise indicated.
† P values derived from Student's t-test and chi-square test for continuous and categorical variables, respectively, unless otherwise indicated.
‡Based on scale from 1–5, where 1 denotes not controlled and 5 denotes completely controlled.
§Based on scale from 0–10, where 0 denotes no effect and 10 denotes complete prevention of activities.

the SFC continuation group (LSM difference, –0.24; $p < 0.001$).

Sensitivity analyses, using propensity score matching instead of a model-based adjustment for propensity score produced generally similar results. Based on this method the estimated effect of OSG on control was slightly lessened compared to the primary protocol-specified analysis, but remained statistically significant (OR = 2.1, $p = 0.038$). Effects on sleep, daily activities, and leisure activities were comparable between the two analyses. Additionally, the relationship between SFC continuation and work impairment was estimated to be somewhat greater (estimated difference of 11 percentage points, $p = 0.015$) using the matching approach.

DISCUSSION

Concurrent with the completion of this study, new guidelines were issued stating that "Omalizumab is used as

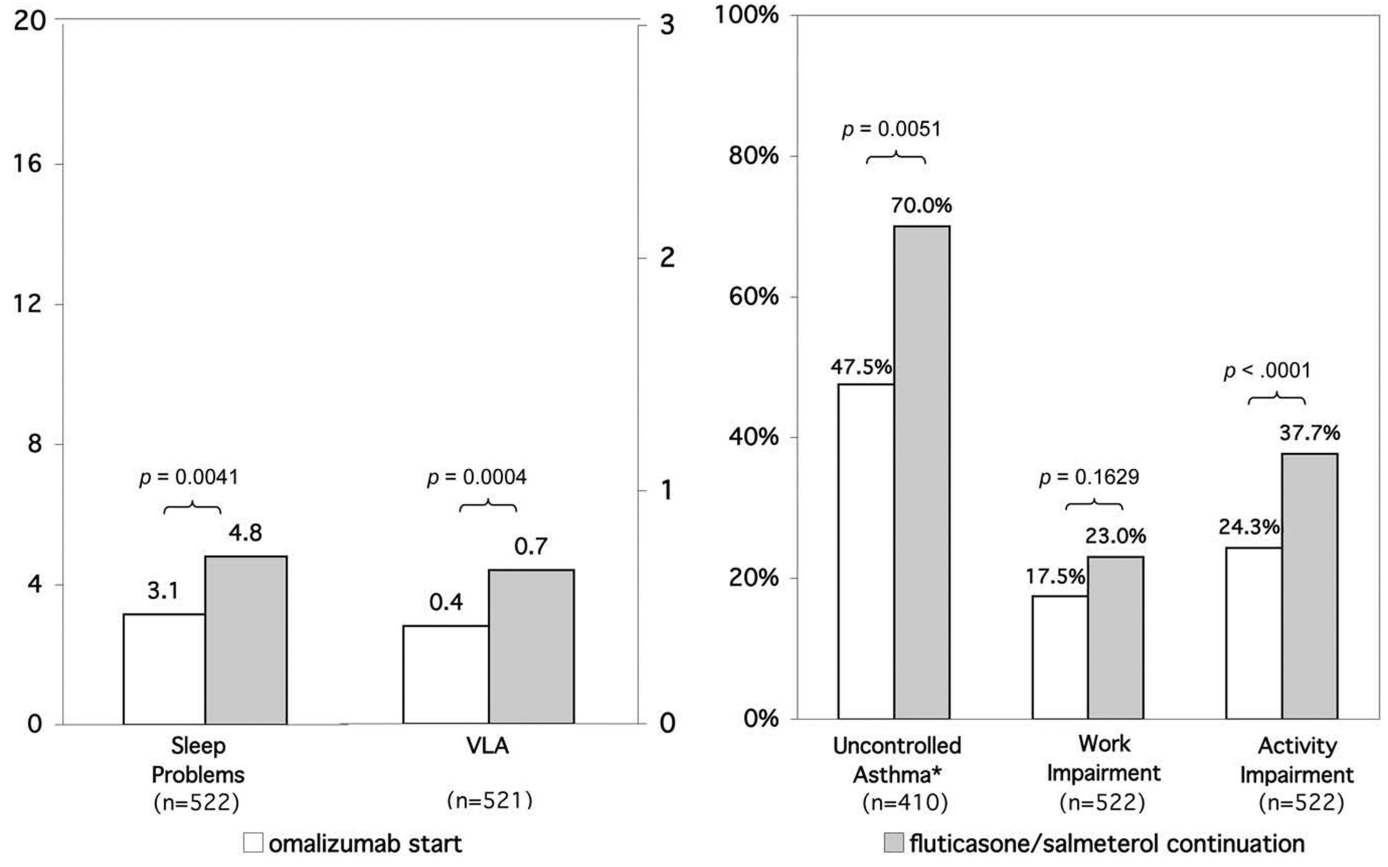

FIGURE 1.—Current patient-reported outcomes for omalizumab start group *vs.* salmeterol/fluticasone combination continuation group 1a) Sleep problems because of asthma and difficulty with valued life activities. 1b) Percentage uncontrolled and impairment because of asthma. ACT = Asthma Control Test; VLA = Valued Life Activities.

adjunctive therapy for patients 12 years of age who have sensitivity to relevant allergens (e.g., dust mite, cockroach, cat, or dog) and who require step 5 or 6 care (for severe persistent asthma) i.e., patients who are uncontrolled on Step 4" (22). Because OSG is specifically recommended for poorly controlled patients, identifying an appropriate comparison group in an observational study is a challenge. The objective of this study was to assess and compare patient-reported outcomes among subjects with IgE-mediated (allergic asthma) initiating omalizumab and a similarly poorly controlled cohort of subjects receiving moderate-to-high doses of SFC, who continued on SFC for at least a year without adding omalizumab. Results from an adjusted analysis of multi-item, validated instruments showed that subjects in the OSG reported greater asthma control, fewer sleep problems, less activity impairment, and less difficulty with valued life activities.

Future research may address some of the limitations of this study. The generalizability is limited by the use of an on-line questionnaire and a convenience sample. Because the questionnaire was administered online, the responses may not be representative of subjects who do not have Internet access or who are less familiar with the Internet. This limitation could be addressed by replicating the study with a paper questionnaire or personal interview. The extent to which the use of a convenience sample limits the generalizability is unknown and would best be addressed through a study with probability sampling. Selection bias may have been introduced into the study by the use of different recruitment sources for the OSG and SFC groups. Because of the difficulty in identifying OSG patients through traditional sources, OSG patients were primarily recruited through a specialty pharmacy. This limitation was addressed through the multivariable analysis. The study design is limited by the ascertainment of baseline data through patient recall of asthma status one year ago. Patients were asked a series of single-item questions regarding the primary outcomes, including asthma control, ability to sleep, ability to participate in leisure activities, and work productivity. This limitation could be addressed with a prospective study design.

Subjects who were identified as having a very low propensity for receiving omalizumab were excluded from the analysis, which resulted in the exclusion of 6 OSG subjects and 784 SFC continuation subjects. This raises the possibility that a more comprehensive approach to collecting baseline data could have identified additional subjects who were nearly certain to be treated with one strategy or the other. The success of the propensity score adjustment depends on having groups that are overlapping if not comparable. Furthermore, the success of a propensity score analysis depends on accounting for all important covariates. In this analysis, an effort was made to include all important covariates, but it is possible that one or more were omitted. In particularly, insufficient smoking data were collected to identify possible chronic obstructive pulmonary disease patients, and data on other comorbidities such as gastroesophageal reflux disease were not collected. Data were collected on emergency room visits and hospitalizations, but the timing relative to starting omalizumab was not collected, so the data could neither be used as a pre-treatment covariate or a post-treatment outcome. A prospective, randomized study would avoid selection bias while addressing these limitations of a propensity score analysis.

This study should not be misconstrued as a comparison of SFC versus omalizumab. Omalizumab is not a substitute for SFC. Many of the subjects in the OSG were also taking SFC, which reflects current practice patterns. Thus, the results of this study may help clinicians better understand the potential benefits of omalizumab as an add-on therapy.

Despite the limitations of this study, there is value in the use of a naturalistic design comparing 2 common treatment strategies. That is, continuation of SFC without omalizumab versus initiation of omalizumab. Research that mirrors how subjects are treated in the real world is helpful for health-care providers and decision makers.

In conclusion, subjects with allergic asthma who started taking omalizumab reported more improved outcomes than similar subjects who continued taking SFC therapy with regard to asthma control, sleep problems, activity impairment, and difficulty with valued life activities.

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