

Real-World Clinical Characteristics, Treatment Patterns, and Exacerbations in US Patients With Asthma Newly Treated With Omalizumab

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ABSTRACT

Purpose: The objective of this study was to examine patient characteristics, treatment patterns, and exacerbations among patients with asthma newly treated with omalizumab.

Methods: Data for this study were obtained from administrative claims and medical records. The index date was the date of the first claim for omalizumab. All patients had ≥ 12 months of continuous health plan eligibility before and after the index date. Demographic and clinical characteristics were obtained 12 months before the index date. Treatment patterns of asthma medications, including omalizumab, and asthma exacerbations were evaluated in the preindex and postindex periods.

Findings: The study included 1564 patients. Asthma-related medication use decreased from the pre-index to the postindex periods (oral corticosteroids, 83.3%–66.4%, $P < 0.001$; inhaled corticosteroids [ICSs], 33.1%–26.8%, $P < 0.001$; long-acting β_2 -adrenergic agonists [LABAs], 6.6%–5.2%, $P = 0.009$; ICS-LABA combination, 69.3%–64.3%, $P < 0.001$; leukotriene modifiers, 67.8%–59.7%, $P < 0.001$). The proportion of patients with any asthma exacerbations decreased by 33.6% (66.6%–44.2%, $P < 0.001$). Notably, the relative decreases in hospitalization and emergency department exacerbations were 79.3% and 72.2%, respectively. A total of 930 patients (59.5%) discontinued omalizumab treatment during the entire postindex period (maximum, 3400 days

[approximately 9 years]), with 353 (38.0%) restarting omalizumab treatment.

Implications: In this real-world analysis, patients newly initiating omalizumab therapy for allergic asthma used fewer concomitant asthma medications, while experiencing significant reductions in asthma exacerbations, especially hospitalization- and emergency department-specific exacerbations, from pre- to post-omalizumab treatment initiation periods. (*Clin Ther.* 2018;■:1–23) © 2018 Elsevier Inc. All rights reserved.

Key words: allergic asthma, omalizumab, treatment pattern, exacerbation, real-world evidence, medical record.

INTRODUCTION

Of the 24 million people in the United States who have asthma,¹ approximately two-thirds have allergic asthma, which is triggered by inhaled allergens.^{2–5} Allergic (or extrinsic) asthma is associated with a greater burden of illness than nonallergic asthma. In a recent study, most patients with allergic asthma had poorly or not well-controlled symptoms, higher exacerbation rates, increased health care resource use and

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greater expenditures.^{5,6} Half of all patients diagnosed with severe asthma have allergic asthma.^{3–5}

The standard care for asthma includes bronchodilators, inhaled corticosteroids (ICSs), and other anti-inflammatory drugs.^{7,8} Although these medications are effective for most patients, some patients with an allergic phenotype or who have symptoms that are allergic in nature may not achieve adequate asthma control.⁸ Poorly controlled asthma can lead to exacerbations, hospitalizations, lost time from work or school, and reduced quality of life.⁹ The monoclonal antibody omalizumab is indicated for patients ≥ 6 years of age who have moderate-to-severe persistent asthma with an allergic component whose asthma symptoms are not controlled by inhaled corticosteroids.¹⁰ The clinical efficacy of omalizumab in treating moderate-to-severe allergic asthma has been found in a number of clinical trials and in real-world clinical practice.^{11–13} However, there is a lack of real-world data on long-term treatment patterns and outcomes of omalizumab therapy among US patients with moderate-to-severe asthma.⁹

To address this research gap, the present study used a unique research environment that combined administrative claims and medical record data. Objectives of

the study included the exploration of patient demographic and clinical characteristics, medication treatment patterns, and exacerbations before and after omalizumab treatment initiation among patients with asthma newly treated with omalizumab.

METHODS

Study Design and Population

This was a retrospective observational cohort study that used administrative claims data augmented with medical record data. Data were obtained from the HealthCore Integrated Research Database (HIRD®). HIRD contains longitudinal administrative claims data for members of 14 major US commercial health plans, and it is largely representative of the general US Census population.¹⁴ The index date was the date of the first claim for omalizumab between January 1, 2007, and May 2, 2015 (the intake period) (Figure 1). The intake period was based on data availability. Patients with ≥ 1 claims for omalizumab in the 12-month preindex period were excluded so that only patients newly initiating omalizumab treatment were included in the study.

Patients treated with omalizumab were defined as those who had at least 4 medical or pharmacy claims

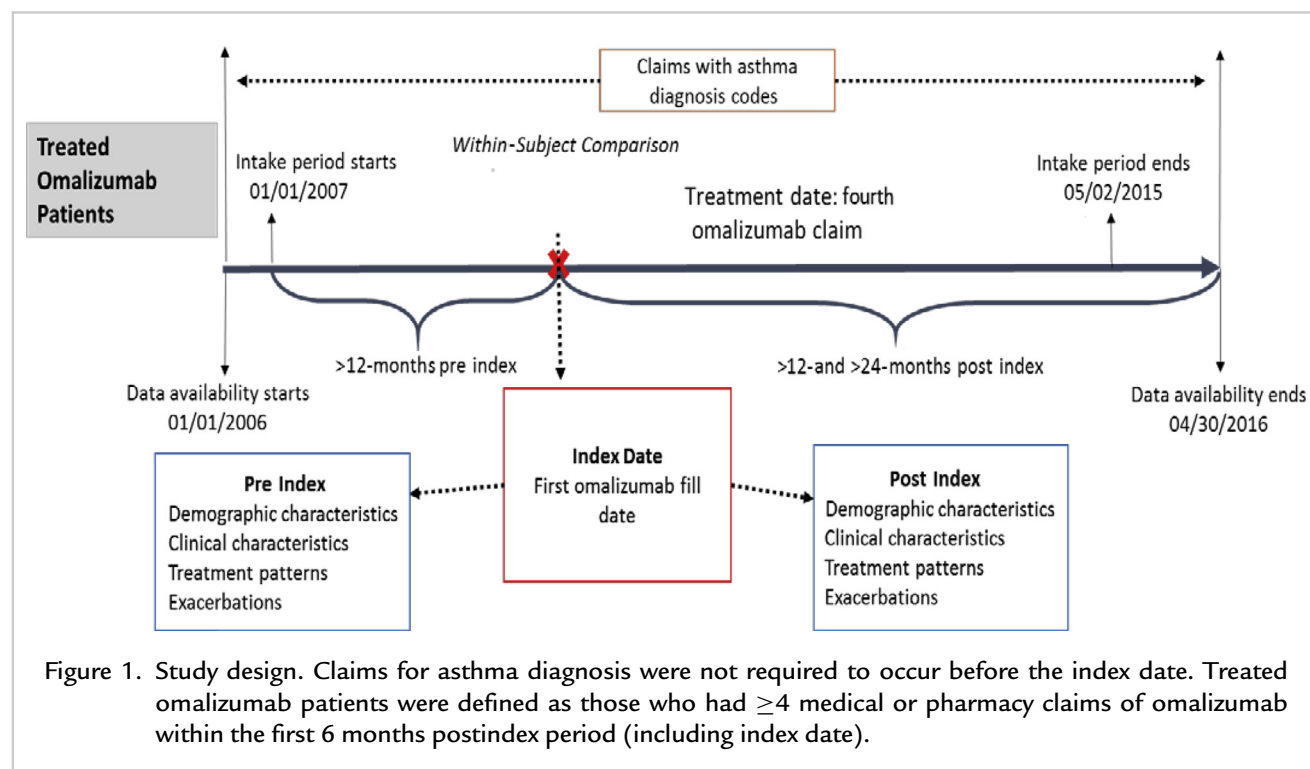


Figure 1. Study design. Claims for asthma diagnosis were not required to occur before the index date. Treated omalizumab patients were defined as those who had ≥ 4 medical or pharmacy claims of omalizumab within the first 6 months postindex period (including index date).

of omalizumab (*Current Procedural Terminology* code J2357, Generic Product Identifier code 44603060002120) to ensure that we evaluated only patients who were provided omalizumab therapy that was sufficient for a meaningful determination of effect.^{15–17} The number of omalizumab medical or pharmacy claims were counted based on distinct claim dates for omalizumab from the index date through 6 months after the index date.

All patients included in the study had a diagnosis of asthma, defined as at least 1 medical claim for an inpatient stay or emergency department (ED) visit with an *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) or *International Classification of Diseases, Tenth Revision, Clinical Modification* (ICD-10-CM) diagnosis code for asthma (ICD-9-CM diagnosis codes 493.xx; ICD-10-CM diagnosis codes J45.20–J45.998) in the primary diagnosis position or as ≥ 2 medical claims with distinct service dates for asthma in any setting.^{5,18,19} All patients had at least 12 months of continuous health care plan eligibility before and after the index date and had enrollment in only commercial or Medicare Advantage plans during the entire study period. A subset of patients with at least 24 months postindex continuous health plan eligibility was also analyzed.

Medical Record Population

For a subset of eligible patients, additional clinical data were abstracted from medical records obtained from providers by trained reviewers using a standardized extraction form. Patients were eligible for medical record request and abstraction if they belonged to the medical record eligible population, had at least 1 outpatient claim that had omalizumab codes or asthma codes and were associated with the same allergy/immunology, pulmonary medicine, or primary care provider within the 12-month preindex period and up to 24 months after the index date, respectively; and had valid provider contact information. The medical record-based subanalysis was institutional review board approved, and the study complied with state and federal privacy regulations, including the Health Insurance Portability and Accountability Act.

Study Measures

Demographic and clinical characteristics were obtained 12 months before the index date. Clinical characteristics were also collected during the 2

postindex follow-up periods: 1 to 12 months and 13 to 24 months (for the subset of patients with ≥ 24 months of follow-up).

Treatment patterns of overall asthma medications, including asthma controller and rescue medications and allergen immunotherapy, were evaluated during the 12-month preindex period and the first (1–12 months) and second (13–24 months) years after the index date. Controller medications included ICSs, long-term oral corticosteroids (OCSs), long-acting β_2 -adrenergic agonists (LABAs), leukotriene modifiers, monoclonal antibodies, long-acting muscarinic antagonists (LAMAs), mast cell stabilizers, and short-acting β_2 -adrenergic agonists (SABAs). Rescue medications included SABAs. Use of short-term OCSs for presumed exacerbations were also assessed. Omalizumab treatment discontinuation, defined by a gap of ≥ 90 days (60 days for sensitivity analysis) between omalizumab administrations, and treatment persistence were reported for the 12- and 24-month postindex periods and for the entire study period. The discontinuation date was defined as the last omalizumab administration date within the first continuous therapy segment plus 1 day for medical claims and the last omalizumab fill date plus days of supply of the last fill for pharmacy claims. Persistence was defined as the length of the entire postindex follow-up period or length of time between the index date and discontinuation date for those who discontinued omalizumab treatment. Omalizumab treatment restart was limited to the first restart from the first discontinuation and was defined as the date of the first omalizumab claim after the first discontinuation and were reported at 6, 12, and 24 months after the index date.

Asthma exacerbations were evaluated during the preindex period and the first and second years of the postindex period (for the subset of patients with ≥ 24 months of follow-up). Exacerbations were classified as follows: a hospital asthma exacerbation was a hospitalization with asthma as the primary diagnosis, an ED asthma exacerbation was an ED visit with asthma as the primary diagnosis, and an outpatient asthma exacerbation was an outpatient visit with an asthma diagnosis in any position of a medical claim and receipt of oral corticosteroids within 7 days after the outpatient visit. A 30-day clean period (ie, no asthma-related hospitalization, ED, or outpatient visits and no use of any oral corticosteroid) was applied to differentiate 2

consecutive asthma exacerbation episodes. The following hierarchy was applied to assign type for an exacerbation episode: hospitalization asthma exacerbation followed by ED asthma exacerbation followed by outpatient asthma exacerbation.

Statistical Analysis

Descriptive statistics, including means (standard deviation (SD), median, interquartile range) for continuous variables and relative frequencies for categorical variables were reported.

For the preindex and postindex comparisons among patients treated with omalizumab and for the subset of patients with at least 24 months of postindex follow-up, the paired *t* test or Wilcoxon signed rank sum test was used for normally distributed and nonnormally distributed continuous variables during bivariate analysis; a McNemar test (or Bowker test of symmetry for square tables larger than 2×2) was used for categorical variables during bivariate analysis. The Kaplan-Meier method was used to examine (1) omalizumab treatment persistence from omalizumab treatment initiation until first discontinuation or end of study follow-up (whichever came first) and (2) omalizumab restart from first discontinuation date until the occurrence of first restart or the end of the study follow-up (whichever came first) among a subset of patients who discontinued omalizumab treatment.

Generalized estimating equation logistic regression models were developed to examine the changes in occurrence of asthma exacerbations from 12 months before the index date through the first and second years after the index date (for the subset of patients with ≥ 24 months of follow-up).

All analyses were performed with SAS Enterprise Guide, version 7.1 (SAS Institute, Cary, North Carolina). A 2-sided 5% significance level was used for all statistical tests.

RESULTS

The study included 1564 patients with at least 12 months of postindex follow-up and a subset of 970 patients with at least 24 months of postindex follow-up. A subset of 259 patients had additional clinical information abstracted from their medical records. The mean postindex follow-up times were 1181.4 days (median, 938.5 days) for patients with 12 months of

postindex follow-up and 1577.2 days (median 1388.5 days) for the subset of patients with 24 months of postindex follow-up (Table I). Of the patients with 12 months of postindex follow-up, the mean (SD) age was 44.9 (15.67) years, and 61.8% were women. Similarly, in the subset of patients with 24 months of postindex follow-up, the mean (SD) age was 44.7 (15.70), years and 61.8% were women (Table I). A slightly higher proportion of patients were from the southern region of the United States in both the main study population and the subset with 24 months of postindex follow-up. The index dates were largely spread across the seasons in both groups, although a slightly higher proportion of index dates fell in the spring months (March to May).

Clinical Characteristics

In both the preindex and postindex periods, most patients were seen by allergists/immunologists (77% in both the preindex and postindex periods), followed by pulmonologists (20.9% preindex, 21.0% postindex) (Table II). The comorbidity burden remained relatively low from the preindex to the postindex period, with most patients (62.3% preindex, 64.3% postindex) reporting a Quan-Charlson Comorbidity Index (QCI) score of 1 (Table II). The most commonly reported comorbidity in the QCI was chronic pulmonary disease (99.7% in both time frames; data not shown), followed by diabetes (18.4% in both time frames; data not shown). Health care encounters with the claims for the following diagnoses decreased from the preindex to the postindex periods: allergic rhinitis (75.8%–72.5%, $P = 0.002$), anaphylaxis (4.9%–3.3%, $P = 0.001$), food allergy (4.8%–2.6%, $P < 0.001$), urticaria (15.2%–13.1%, $P = 0.002$), angioedema (5.3%–3.9%, $P = 0.006$), chronic obstructive pulmonary disease (21.8%–18.9%, $P = 0.003$), acute (33.8%–28.6%) or chronic (37.2%–30.6%) sinusitis (both $P < 0.001$), nasal polyps (10.6%–8.9%, $P = 0.008$), acute bronchitis (30.2%–19.7%, $P < 0.001$), and respiratory infection (72.4%–69.1%, $P = 0.015$). Similar findings were observed in patients with 24 months of postindex follow-up (Supplemental Table I).

Of the 259 patients who had their medical records abstracted, 175 had prebronchodilator forced expiratory volume in 1 second (FEV₁) percent predicted results reported in their medical records in the preindex period (Table II). Roughly equal proportions of patients had prebronchodilator FEV₁ percent predicted

Table I. Demographic characteristics for patients with asthma newly treated with omalizumab.*

Demographic Characteristics	Patients With ≥ 12 Months of Postindex Follow-up (n = 1564)	Patients With ≥ 24 Months of Postindex Follow-up [†] (n = 970)
Female	966 (61.8)	599 (61.8)
Age at index, mean (SD), y	44.9 (15.67)	44.7 (15.70)
Age, median (IQR), y	47.5 (20.0)	48.0 (19.0)
Age categories, y		
6–11	23 (1.5)	12 (1.2)
12–17	123 (7.9)	88 (9.1)
18–39	331 (21.2)	191 (19.7)
40–64	988 (63.2)	621 (64.0)
65–74	78 (5.0)	45 (4.6)
≥ 75	21 (1.3)	13 (1.3)
Health plan type		
PPO	1031 (65.9)	663 (68.4)
HMO	408 (26.1)	241 (24.8)
CDHP	125 (8.0)	66 (6.8)
Medicare Advantage	59 (3.8)	36 (3.7)
Geographic region of patient		
South	470 (30.1)	276 (28.5)
Midwest	383 (24.5)	233 (24.0)
West	369 (23.6)	243 (25.1)
Northeast	342 (21.9)	218 (22.5)
Season of index date		
Spring (March–May)	422 (27.0)	257 (26.5)
Summer (June–August)	381 (24.4)	239 (24.6)
Fall (September–November)	379 (24.2)	238 (24.5)
Winter (December–February)	382 (24.4)	236 (24.3)
Length of postindex follow-up (including index date), d		
Mean (SD)	1181.4 (748.56)	1577.2 (696.00)
Median (IQR)	938.5 (1020.0)	1388.5 (1006.0)

CDHP = consumer-driven health plan; HMO = health maintenance organization; IQR = interquartile range; PPO = preferred provider organization; y = years; d = days.

* Characteristics were assessed on the index date. Data are expressed as number (percentage) unless otherwise indicated.

[†] Subset of total patient population

>60% (32.0%), between 60% and 80% (32.0%), and $\geq 80\%$ (36.0%). A total of 140 patients had total serum IgE results reported in the medical records in the preindex period. IgE levels between 30 and 300 IU/mL were observed in 50% of the patients with available results (Table II).

Omalizumab Treatment

Omalizumab dosing and dosing frequency information was obtained from the medical records review. Among 180 patients with documented dosing information, the most common index dosages of omalizumab were 300 mg every 4 weeks for 20.6% of the patients and 150 mg every 4 weeks for 20.0% of the patients

Table II. Preindex and postindex clinical characteristics for patients with asthma newly treated with omalizumab.

Clinical Characteristic	Patients (n = 1564)*		<i>P</i> [†] [A vs B]
	12 Months Preindex Period [A]	12 Months Postindex Period [B]	
Prescribing or treating physician specialty [‡]			
Allergist or immunologist	1204 (77.0)	1204 (77.0)	>0.99
Pulmonologist	327 (20.9)	328 (21.0)	0.317
Primary care physician	22 (1.4)	21 (1.3)	0.317
Others	8 (0.5)	8 (0.5)	>0.99
Unknown	3 (0.2)	3 (0.2)	>0.99
Asthma or urticaria diagnosis associated with omalizumab treatment initiation [§]			
Asthma	1261 (80.6)	—	—
Urticaria	63 (4.0)	—	—
Both asthma and urticaria	39 (2.5)	—	—
Neither asthma nor urticaria	201 (12.9)	—	—
Comorbidities, QCI			
Mean (SD)	1.5 (1.07)	1.6 (1.17)	0.001
Median (IQR)	1.0 (1.0)	1.0 (1.0)	—
Asthma-associated comorbidities			
Allergic rhinitis	1186 (75.8)	1134 (72.5)	0.002
Respiratory infection	1133 (72.4)	1081 (69.1)	0.015
Chronic sinusitis	582 (37.2)	478 (30.6)	<0.001
Acute sinusitis	529 (33.8)	447 (28.6)	<0.001
Gastroesophageal reflux disease	476 (30.4)	460 (29.4)	0.402
Acute bronchitis	472 (30.2)	308 (19.7)	<0.001
COPD	341 (21.8)	296 (18.9)	0.003
Eczema/dermatitis	262 (16.8)	259 (16.6)	0.857
Urticaria	237 (15.2)	205 (13.1)	0.002
Conjunctivitis	176 (11.3)	170 (10.9)	0.641
Nasal polyposis	166 (10.6)	139 (8.9)	0.008
Angioedema	83 (5.3)	61 (3.9)	0.006
Anaphylaxis	77 (4.9)	52 (3.3)	0.001
Food allergy	75 (4.8)	41 (2.6)	<0.001
Tests of interest			
Any allergy test	1287 (82.3)	349 (22.3)	<0.001
Total IgE	1179 (75.4)	158 (10.1)	<0.001
Skin test for allergen specific IgE	579 (37.0)	215 (13.7)	<0.001
Blood test for allergen specific IgE	570 (36.4)	73 (4.7)	<0.001
Spirometry	1269 (81.1)	1017 (65.0)	<0.001
CBC	976 (62.4)	807 (51.6)	<0.001
Fractional exhaled nitric oxide	111 (7.1)	113 (7.2)	0.864
Medical record review	259 (16.6)	—	—
Documented prebronchodilator FEV ₁ results	175 (67.6)	—	—

(continued)

Table II. (Continued)

Clinical Characteristic	Patients (n = 1564)*		<i>P</i> [†] [A vs B]
	12 Months Preindex Period [A]	12 Months Postindex Period [B]	
Prebronchodilator FEV ₁ results [‡]			
Mean (SD), % predicted	71.1 (21.67)	—	—
Median (IQR), % predicted	72.0 (32.0)	—	—
<60%	56 (32.0)	—	—
60%–80%	56 (32.0)	—	—
≥80%	63 (36.0)	—	—
Documented total serum IgE results, IU/mL ^{¶,§,***}	140 (54.1)	—	—
<30	10 (7.1)	—	—
30–100	26 (18.6)	—	—
>100–200	23 (16.4)	—	—
>200–300	21 (15.0)	—	—
>300–400	11 (7.9)	—	—
>400–500	9 (6.4)	—	—
>500–600	5 (3.6)	—	—
>600–700	5 (3.6)	—	—
>700	30 (21.4)	—	—

CBC = complete blood cell count with differential; CIU = chronic idiopathic urticaria; COPD = chronic obstructive pulmonary disease; FEV₁ = forced expiratory volume in 1 second; IQR = interquartile range; PCP = primary care physician; QCI = Quan-Charlson Comorbidity Index.

* Data are expressed as number (percentage) unless otherwise indicated.

[†] *P* values were estimated from the paired *t* test or Wilcoxon signed rank sum test for normally distributed and nonnormally distributed continuous variables, respectively, and from the McNemar test (or Bowker test of symmetry for square tables larger than 2 × 2) for categorical variables.

[‡] The following hierarchy was applied when multiple specialties existed: allergy/immunology followed by pulmonary medicine followed by family/general practice followed by internal medicine followed by others or unknown. PCP includes family/general practice and internal medicine.

[§] For patients who had omalizumab medical claims on the index date, asthma or urticaria diagnoses were identified based on those medical claims on the index date; for patients who had only omalizumab pharmacy claims on the index date, asthma or urticaria diagnoses were identified from medical claims between (index date – 14 days) and (index date + 14 days).

[¶] To obtain eosinophil level.

[¶] The test result with the date closest to the index date was selected.

[#] The denominator was the number of patients with medical records abstracted (n = 259).

^{***} The valid denominator was the number of patients with specific laboratory results documented in medical records (n = 140).

(Table III). The 300-mg dose, regardless of dosing intervals, was used in more than one-third of the patients (38.9%, data not shown). Subsequent doses remained the same as the index dose for 73.3% of patients, whereas 8.9% of patients received a dose increase and <5% of patients received a dose decrease. In terms of dosing frequency, among 163 patients with documented dosing frequency, >50% of patients received omalizumab every 4 weeks and 47.9%

received omalizumab every 2 weeks. The subsequent dosing frequency remained the same as the index dose for 63.8% of patients, with 9.8% of patients receiving an increase in frequency and 9.8% receiving a decrease in frequency (Table III).

Omalizumab treatment discontinuations were observed among 32.3% and 59.5% of patients in the 12-month postindex period and the entire postindex period (maximum, 3400 days [approximately 9 years]),

Table III. Postindex omalizumab treatment patterns for patients with asthma newly treated with omalizumab.

Omalizumab Treatment Pattern	Patients Treated With Omalizumab (n = 1564)	Subset of Patients Treated With Omalizumab With ≥ 24 Months of Postindex Follow-up (n = 970)
	No. (%) [*]	No. (%) [*]
Medical record review	259 (16.5)	—
Documented index dose [†]	180 (69.5)	—
Index dosage, mg [‡]		
150 mg every 4 wk	36 (20.0)	—
300 mg every 4 wk	37 (20.6)	—
225 mg every 2 wk	10 (5.6)	—
300 mg every 2 wk	22 (12.2)	—
375 mg every 2 wk	28 (15.6)	—
Other	47 (26.1)	—
Dose titration: index vs subsequent dose [‡]		
Mean subsequent dose equal to index dose	132 (73.3)	—
Mean subsequent dose increase from index dose	16 (8.9)	—
Mean subsequent dose decrease from index dose	8 (4.4)	—
Unknown/not documented	24 (13.3)	—
Documented index dosing frequency ^{†,§}	163 (62.9)	—
Every 2 weeks	78 (47.9)	—
Every 4 weeks	84 (51.5)	—
Other	1 (0.6)	—
Dosing frequency, index vs subsequent doses [§]		
Mean subsequent dosing frequency equal to index	104 (63.8)	—
Mean subsequent dosing frequency increase from index	16 (9.8)	—
Mean subsequent dosing frequency decrease from index	16 (9.8)	—
Unknown/not documented	27 (16.6)	—
Claims-based analysis	1564	—
First omalizumab discontinuation		
Within 12 months after the index date	505 (32.3)	311 (32.1)
Within 24 months after the index date	—	513 (52.9)
Within the entire postindex period	930 (59.5)	691 (71.2)
Omalizumab treatment persistence, mean (SD)/median (IQR), d	645.7 (528.0)/489.5 (547.0)	790.0 (613.4)/672.0 (787.0)

(continued)

Table III. (Continued)

Omalizumab Treatment Pattern	Patients Treated With Omalizumab (n = 1564)	Subset of Patients Treated With Omalizumab With ≥ 24 Months of Postindex Follow-up (n = 970)
	No. (%) [*]	No. (%) [*]
Patients with treatment persistence within 12 months of the postindex date	1059.0 (67.7)	659.0 (67.9)
Patients with treatment persistence within 24 months of the postindex date	—	457.0
Patients with treatment persistence within the entire postindex period	634 (40.5)	279.0 (28.8)
Time to first discontinuation, mean (95% CI), d [†]	1058.5 (998.3–1118.7)	1047.1 (981.9–1112.2)
Probability of treatment persistence [‡]		
12-Month postindex period (95% CI)	0.676 (0.653–0.699)	0.679 (0.649–0.708)
24-Month postindex period (95% CI)	0.481 (0.454–0.508)	0.471 (0.439–0.502)
Omalizumab treatment restart [#]	353 (38.0)	290 (42.0)
Time to first restart from discontinuation, mean (95% CI), d ^{**}	1183.4 (1124.9–1241.8)	1156.8 (1091.8–1221.9)
Probability of restart ^{**}		
6 Months since first discontinuation date (95% CI)	0.271 (0.243–0.301)	0.283 (0.251–0.318)
12 months since first discontinuation date (95% CI)	0.356 (0.325–0.389)	0.373 (0.338–1.410)
24 months since first discontinuation date (95% CI)	0.402 (0.369–0.438)	0.418 (0.381–0.457)

IQR = interquartile range; CI = confidence interval; SD = standard deviation; wk = week; d = days.

^{*} Values are expressed as number (percentage) unless otherwise indicated.

[†] Assessed only in patients included in the medical record review (n = 259).

[‡] The denominator was the number of patients with index dose documented.

[§] The denominator was the number of patients with index dosing frequency documented.

^{||} Omalizumab treatment discontinuation was limited to first discontinuation from the index date and was defined as patients who had a ≥ 90 -day gap between omalizumab administrations/fills (days covered by a specific fill from pharmacy claims were not considered as the gap). The gap of ≥ 90 days was selected based on medical adviser input. A sensitivity analysis using gap of ≥ 60 days was also conducted.

[¶] The Kaplan-Meier method was used to examine omalizumab persistence until first discontinuation or end of study follow-up, whichever occurred first.

[#] Within the entire study period, among a subset of patients with omalizumab treatment discontinuation.

^{**} The Kaplan-Meier method was used to examine omalizumab treatment restart from first discontinuation date until the occurrence of first restart or end of study follow-up, whichever occurred first for a subset of patients with omalizumab treatment discontinuation.

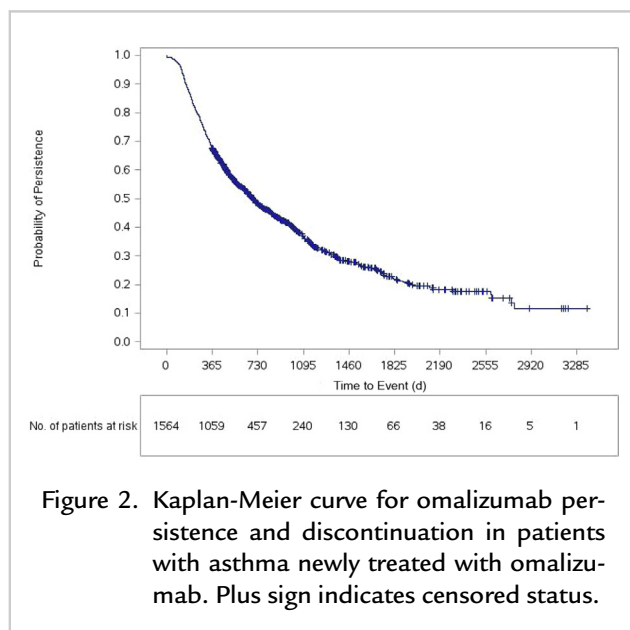


Figure 2. Kaplan-Meier curve for omalizumab persistence and discontinuation in patients with asthma newly treated with omalizumab. Plus sign indicates censored status.

respectively (Table III). Among patients with 24 months of postindex follow-up, omalizumab treatment discontinuations were observed among 32.1%, 52.9%, and 71.2% patients in the 12-month, 24-month, and the entire postindex periods, respectively (Table III).

Among patients with 12 months of postindex follow-up, the mean time to first discontinuation was 1058.5 days (95% CI, 998.3–1118.7 days); the probability of persistence was 0.676 (95% CI, 0.653–0.699) and 0.481 (95% CI, 0.454–0.508) in the 12- and 24-month postindex periods, respectively (Table III and Figure 2). Among patients with 24 months of postindex follow-up, the mean time to first discontinuation was 1047.1 days (95% CI, 981.9–1112.2); the probability of persistence was 0.679 (95% CI, 0.649–0.708) and 0.471 (95% CI, 0.439–0.502) in the 12- and 24-month postindex periods, respectively (Table III and Supplemental Figure 1).

Among the 930 patients (59.5%) who discontinued omalizumab treatment during the entire postindex period, 353 (38.0%) restarted omalizumab treatment (Table III). Among patients with 24 months of postindex follow-up, 691 (71.2%) discontinued omalizumab treatment, with 290 (42.0%) restarting within the postindex period (Table III).

For patients with 12 months of postindex follow-up, the probability of restart was 0.271 (95% CI,

0.243–0.301), 0.356 (95% CI, 0.325–0.389), and 0.402 (95% CI, 0.369–0.438) within the 6, 12, and 24 months after first discontinuation, respectively (Table III). Among patients with 24 months of postindex follow-up, the probability of restart was 0.283 (95% CI, 0.251–0.318), 0.373 (95% CI, 0.338–0.410), and 0.418 (95% CI, 0.381–0.457) in the 6, 12, and 24 months after first discontinuation, respectively (Table III).

A sensitivity analysis of omalizumab treatment patterns using a 60-day gap period showed similar trends as the main analysis results above, with lower estimated probability of persistence and higher estimated probability of restart (data not shown).

Concomitant Asthma Medication Use

Asthma-related medication use (excluding omalizumab) decreased after the initiation of omalizumab treatment (Table IV). Specifically, ICS use decreased 19% (33.1% preindex to 26.8% postindex, $P < 0.001$), LABA use decreased 21.4% (6.6% preindex to 5.2% postindex, $P = 0.009$), ICS-LABA combination (free or fixed dose) use decreased 7.3% (69.3%–64.3%, $P < 0.001$), leukotriene modifier use decreased 12.0% (67.8% preindex to 59.7% postindex, $P < 0.001$), and overall OCS use decreased 20.3% (83.3% preindex to 66.4% postindex, $P < 0.001$). Inhaled SABA use decreased 12.6% (76.3% preindex to 66.7% postindex, $P < 0.001$); however, use of allergen immunotherapy increased 20.6% (27.9% preindex to 33.7% postindex, $P < 0.001$).

Similar trends were observed among patients with 24 months of postindex follow-up, with the exception of longer term LAMA use. As in patients with 12 months of postindex follow-up, LAMA use remained unchanged for months 1 to 12 for patients with 24 months postindex follow-up (13.2% preindex to 13.1% postindex, $P = 0.909$) before experiencing a decrease to 10.9% in months 13 to 24 ($P = 0.036$) (Supplemental Table II).

Asthma Exacerbations

The proportion of patients with any asthma exacerbation (hospitalization, ED, or outpatient) decreased significantly between the preindex and postindex periods (66.6% and 44.2%, respectively; relative difference, 33.6%; $P < 0.001$) (Table V). Notably, hospitalization- and ED-specific exacerbations had a 79.3% and 72.2% relative decrease from preindex to postindex follow-up,

Table IV. Preindex and postindex asthma-related medications and treatment for patients with asthma newly treated with omalizumab.

Asthma-Related Medication and Treatment	No. (%) of Patients Treated With Omalizumab (n = 1564)			
	12-Month Preindex Period [A]	12-Month Postindex Period [B]	P* [A vs B]	Relative Change, % [(B – A)/A]
Asthma controller medications				
ICS	517 (33.1)	419 (26.8)	<0.001	–19.0
Low dose [†]	93 (5.9)	89 (5.7)	0.695	–4.3
Medium dose [†]	234 (15.0)	177 (11.3)	<0.001	–24.4
High dose [†]	123 (7.9)	87 (5.6)	0.001	–29.3
Unspecified dose [†]	191 (12.2)	173 (11.1)	0.125	–9.4
LABA	103 (6.6)	81 (5.2)	0.009	–21.4
ICS-LABA combination (fixed-dose combination)	1047 (66.9)	968 (61.9)	<0.001	–7.5
Low-dose ICS [†]	128 (8.2)	76 (4.9)	<0.001	–40.6
Medium-dose ICS [†]	617 (39.5)	488 (31.2)	<0.001	–20.9
High-dose ICS [†]	618 (39.5)	542 (34.7)	<0.001	–12.3
Unspecified dose ICS [†]	6 (0.4)	10 (0.6)	0.157	66.7
ICS-LABA combination (free- [‡] or fixed-dose combination)	1084 (69.3)	1005 (64.3)	<0.001	–7.3
Any ICS (single or ICS-LABA fixed dose combination)	1228 (78.5)	1149 (73.5)	<0.001	–6.4
Any LABA (single or ICS-LABA fixed-dose combination)	1093 (69.9)	1018 (65.1)	<0.001	–6.9
Leukotriene modifiers	1061 (67.8)	934 (59.7)	<0.001	–12.0
Methylxanthine	100 (6.4)	98 (6.3)	0.796	–2.0
LAMA	222 (14.2)	213 (13.6)	0.439	–4.1
Mast cell stabilizers	19 (1.2)	10 (0.6)	0.039	–47.4
Bronchodilators (long-acting albuterol)	13 (0.8)	9 (0.6)	0.157	–30.8
Asthma rescue medications				
Inhaled SABA	1194 (76.3)	1043 (66.7)	<0.001	–12.6
Noninhaled SABA	17 (1.1)	15 (1.0)	0.655	–11.8
SAMA	105 (6.7)	71 (4.5)	0.001	–32.4
SABA-SAMA combination (fixed dose)	230 (14.7)	162 (10.4)	<0.001	–29.6
OCS	1303 (83.3)	1039 (66.4)	<0.001	–20.3
Long course [§]	124 (7.9)	134 (8.6)	0.345	8.1
Short course	1179 (75.4)	905 (57.9)	<0.001	–23.2

(continued)

Table IV. (Continued)

Asthma-Related Medication and Treatment	No. (%) of Patients Treated With Omalizumab (n = 1564)			
	12-Month Preindex Period [A]	12-Month Postindex Period [B]	<i>P</i> * [A vs B]	Relative Change, % [(B – A)/A]
No. of types of asthma medications (listed above) [†]	4.0 (1.60)	4.5 (1.70)	<0.001	12.5
0	60 (3.8)	0 (0)	<0.001	–100.0
1	86 (5.5)	106 (6.8)	0.089	23.3
2	147 (9.4)	122 (7.8)	0.073	–17.0
≥3	1271 (81.3)	1336 (85.4)	<0.001	5.1
Allergen immunotherapy	437 (27.9)	527 (33.7)	<0.001	20.6

ICS = inhaled corticosteroid; LABA = long-acting β_2 -adrenergic agonist; LAMA = long-acting muscarinic antagonist; OCS = oral corticosteroid; PDE4 = phosphodiesterase 4; SABA = short-acting β_2 -adrenergic agonist; SAMA = short-acting muscarinic antagonist.

* *P* values were estimated from the paired *t* test or Wilcoxon signed rank sum test for normally distributed and nonnormally distributed continuous variables, respectively, and from McNemar test (or Bowker test of symmetry for square tables larger than 2 × 2) for categorical variables.

[†] Presence of any fill/administration with specific dose, not necessarily mutually exclusive. Certain ICS use may not fall into low, medium, and high categories as defined by the National Heart, Lung, and Blood Institute guidelines (eg. no definition for specific ICS or dose not within the defined ranges) and were captured under the unspecified dose category.

[‡] Free-dose combination was defined as having ≥14 days of continuous overlap of days of supply of specific medications within the period of interest.

[§] Based on days of supply (≥180 sum of days of supply in a 12-month period).

^{||} Based on days of supply (<180 sum of days of supply in a 12-month period).

[¶] The mean (SD) numbers of types of asthma medications were 4.0 (1.60) (median, 4.0; interquartile range, 2.0) in the 12-month preindex period and 4.5 (1.70) (median, 5.0; interquartile range, 3.0) in the 12-month postindex period (relative change, 12.5).

respectively (hospitalization exacerbations: 11.4% preindex to 2.4% postindex, *P* < 0.001; ED exacerbations: 11.3% preindex to 3.1% postindex, *P* < 0.001). Out-patient exacerbations had a 30.3% relative decrease from the preindex period (57.5% preindex to 40.1% postindex, *P* < 0.001). Similar trends were observed among patients with 24 months of postindex follow-up (Supplemental Table III).

Multivariable analysis found that the odds of exacerbation occurrence during the 12-month postindex period was 86% less than during the 12-month preindex period, after adjusting for age, sex, and a series of time-variant variables, including provider specialty, comorbidities of interest, QCI, laboratory test of interest, and medications of interest (Table VI). Among patients with 24 months of postindex follow-up, multivariable analysis found that the odds of exacerbation occurrence was 86% less and 87% less in postindex

months 1 to 12 and postindex months 13 to 24, respectively, compared with the 12-month preindex period after adjusting for age, sex, and a series of time-variant variables (Table VI). Use of ICS-LABA combination therapy, leukotriene modifiers, or methylxanthines was associated with decreased odds of exacerbations (85%, 61%, and 71%, respectively, and 84%, 56%, and 70%, respectively, for patients with 24 months of postindex follow-up) (Table VI).

DISCUSSION

This real-world analysis described treatment patterns and the demographic and clinical profiles, including asthma exacerbations, of patients with asthma newly treated with omalizumab. The study was conducted using a unique combination of integrated administrative claims and medical record data. This approach allowed

Table V. Preindex and postindex asthma exacerbations for patients with asthma newly treated with omalizumab.

	Patients Treated With Omalizumab (n = 1564)		P* [A vs B]	Relative Change,% [(B – A)/A]
	12 Months Preindex Period [A]	12 Months Postindex Period [B]		
Asthma Exacerbations				
Any asthma exacerbation, No. (%) [†]	1041 (66.6)	691 (44.2)	<0.001	–33.6
No. of episodes, mean (SD)/median (IQR)	1.2 (1.14)/1.0 (2.0)	0.6 (0.75)/0.0 (1.0)	<0.001	–50.0
Hospitalization exacerbations, No. (%)	179 (11.4)	37 (2.4)	<0.001	–79.3
No. of episodes, mean (SD)/median (IQR)	0.1 (0.32)/0.0 (0.0)	0.0 (0.15)/0.0 (0.0)	<0.001	–100.0
No. of	176 (11.3)	49 (3.1)	<0.001	–72.2
ED exacerbations, No. (%)				
No. of episodes, mean (SD)/median (IQR)	0.1 (0.32)/0.0 (0.0)	0.0 (0.17)/0.0 (0.0)	<0.001	–100.0
No. of	900 (57.5)	627 (40.1)	<0.001	–30.3
Outpatient exacerbations, No. (%)				
No. of episodes, mean (SD)/median (IQR)	1.0 (1.06)/1.0 (2.0)	0.5 (0.73)/0.0 (1.0)	<0.001	–50.0

ED = emergency department; IQR = interquartile range; SD = standard deviation.

* P values were estimated from the paired *t* test or Wilcoxon signed rank sum test for normally distributed and nonnormally distributed continuous variables, respectively, and from McNemar test for categorical variables.

[†] Asthma exacerbation was defined as follows: (1) hospitalization asthma exacerbation: an inpatient stay with asthma (*International Classification of Diseases, Ninth Revision, Clinical Modification* [ICD-9-CM] codes: 493.xx; *International Classification of Diseases, Tenth Revision, Clinical Modification* [ICD-10-CM] diagnosis codes: J45.20-J45.998) as the primary diagnosis; (2) ED asthma exacerbation: an ED visit with asthma as the primary diagnosis (ED visits followed by hospitalizations were not included in this category because they would be considered inpatient hospitalizations); and (3) outpatient asthma exacerbation: outpatient visit with asthma diagnosis in any position of a medical claim and receipt of oral corticosteroids within 7 days after the outpatient visit. A clean period (no asthma-related inpatient, ED, or outpatient visits, AND no use of any oral corticosteroids) of 30 days was applied to differentiate 2 consecutive asthma exacerbation episodes. The following hierarchy was applied to create type of asthma exacerbation for an exacerbation episode: hospitalization asthma exacerbation followed by ED asthma exacerbation followed by outpatient asthma exacerbation.

for the assessment of the results of clinical testing, such as spirometry and IgE, which was essential in understanding the treatment and outcomes associated with the care of patients with allergic asthma. After omalizumab treatment initiation, we observed reductions in the number of asthma exacerbations and the use of

concomitant asthma controller and rescue medications. Although these end points have been explored in other studies and our results appear to be consistent with prior research, these data provide further support for the use of omalizumab in patients with allergic asthma with more recent data and longer follow-up time.

Table VI. Generalized estimating equation logistic regression model: the changes in occurrence of exacerbations before and after initiation of omalizumab treatment among patients with asthma newly treated with omalizumab.

Covariates	Patients Treated With Omalizumab (n = 1564)			Subset of Patients Treated With Omalizumab With ≥ 24 Months of Postindex Follow-up (n = 970)		
	Odds Ratio	95% Confidence Interval	P	Odds Ratio	95% Confidence Interval	P
Demographic characteristics on index date						
Age, y						
12–17 vs 6–11	0.55	0.24–1.25	0.152	0.60	0.21–1.67	0.327
18–39 vs 6–11	0.52	0.23–1.17	0.114	0.55	0.20–1.50	0.242
40–64 vs 6–11	0.55	0.25–1.22	0.141	0.57	0.21–1.55	0.271
65–74 vs 6–11	0.68	0.28–1.65	0.394	0.71	0.24–2.11	0.533
≥ 75 vs 6–11	0.49	0.15–1.60	0.238	0.36	0.11–1.19	0.094
Female vs male	1.25	1.04–1.49	0.015	1.28	1.06–1.55	0.010
Time variant variables						
Time frame of interest						
12 months postindex vs 12 months preindex	0.14	0.12–0.18	<0.001	0.14	0.11–0.17	<0.001
13–24 months postindex vs 12 months preindex	—	—	—	0.13	0.10–0.17	<0.001
Provider specialty						
Allergist/immunologist vs PCP	0.69	0.32–1.49	0.348	0.88	0.41–1.89	0.734
Pulmonologist vs PCP	0.70	0.32–1.53	0.372	0.95	0.44–2.08	0.904
Others/unknown vs PCP	0.35	0.13–0.97	0.044	0.30	0.10–0.94	0.039
Conditions of interest						
Urticaria (yes vs no)	0.66	0.51–0.84	0.001	0.92	0.66–1.27	0.596
COPD (yes vs no)	1.03	0.81–1.30	0.830	1.11	0.86–1.43	0.433
Nasal polyps (yes vs no)	1.87	1.29–2.73	0.001	1.83	1.25–2.67	0.002
QCI						
2 vs 0–1	0.90	0.69–1.18	0.463	0.94	0.71–1.24	0.653
≥ 3 vs 0–1	0.92	0.70–1.21	0.547	0.82	0.60–1.11	0.197
Laboratory tests						
FeNO (yes vs no)	1.19	0.84–1.70	0.332	1.06	0.76–1.48	0.727
Spirometry (yes vs no)	1.20	0.98–1.48	0.078	1.18	0.97–1.44	0.101
Therapy						
ICS-LABA combination (including free- or fixed-dose combination) (yes vs no)	0.15	0.11–0.20	<0.001	0.16	0.12–0.22	<0.001
Leukotriene modifiers (yes vs no)	0.39	0.31–0.49	<0.001	0.44	0.34–0.56	<0.001
Methylxanthine (yes vs. no)	0.29	0.19–0.43	<0.001	0.30	0.20–0.44	<0.001

(continued)

Table VI. (Continued)

Covariates	Patients Treated With Omalizumab (n = 1564)			Subset of Patients Treated With Omalizumab With ≥ 24 Months of Postindex Follow-up (n = 970)		
	Odds Ratio	95% Confidence Interval	P	Odds Ratio	95% Confidence Interval	P
Number of fills/administrations of inhaled SABA	1.00	0.98–1.02	0.919	0.99	0.97–1.01	0.360
Number of types of asthma medications*	3.22	2.84–3.67	<0.001	2.98	2.62–3.38	<0.001

COPD = chronic obstructive pulmonary disease; FeNO = fractional exhaled nitric oxide; ICS = inhaled corticosteroid; LABA = long-acting β_2 -adrenergic agonist; PCP = primary care physician; QCI = Quan-Charlson Comorbidity Index; SABA = inhaled short-acting β_2 -adrenergic agonist; y = years.

* Counted based on distinct number of the following types of asthma medications: ICS, LABA, leukotriene modifiers, methylxanthine, omalizumab, LAMA, mast cell stabilizers, long-acting albuterol, inhaled SABA, noninhaled SABA, or OCS. ICS-LABA combination (free or fixed dose) was counted as 2.

Omalizumab dosing frequency was almost evenly split between 2 weeks (47.9%) and 4 weeks (51.5%), with most patients receiving ≥ 300 mg. Ours is the first study to report omalizumab dose and frequency in a real-world setting and provide insight into how omalizumab is used in everyday practice. At 12 months after treatment initiation, approximately a third of patients discontinued omalizumab therapy, which is similar to the 32.5% 6-month discontinuation rate in a published postmarketing surveillance study²⁰ and more favorable than the 46% 1-year discontinuation rate found in a previous claims analysis.²¹ These previous analyses included all patients who had at least 1 dose of omalizumab, whereas we required patients to have at least 4 doses. Clinical trial evidence recommends evaluating a patient's response after 16 weeks of omalizumab therapy, with treatment continuing only in those who have shown a response.^{15,17,22} Our discontinuation rates, however, were higher than the 7% to 19% reported in randomized controlled trials but consistent with previous real-world studies that reported discontinuation rates from 0% up to 46%.²³ Omalizumab persistence has been associated with improved outcomes, including reduced exacerbation rates and ED visits, and decreased use of concomitant asthma medications.^{9,17,24}

Reductions in use of both asthma controller and rescue medications were also observed in the present

study. Corticosteroid burden was reduced after initiation of omalizumab treatment, as reflected by decreased use of both ICSs and OCSs. Most notably, overall OCS use decreased by 20.3%, and overall ICS use decreased 19.0%. Combined ICS and LABA treatment, which was the most commonly used controller therapy, decreased 7.3%. Because systemic corticosteroids are associated with serious adverse effects,^{25–30} easing a patient's reliance on these medications for maintenance or rescue therapy is particularly important. Numerous studies have reported decreases in concomitant corticosteroid therapy after omalizumab treatment initiation, with more recent studies finding marked reductions in OCS and ICS use after omalizumab treatment initiation.^{9,24,31–33} Reductions in ICS use have ranged from 10% to 56%, whereas OCS use reductions have ranged from 30% to 66% in previous studies, depending on the length of follow-up,^{9,24,31} with one small study reporting that all patients decreased their ICS dose and all discontinued OCS use 3 years after omalizumab treatment initiation.³⁴ Decreased use of inhaled bronchodilator asthma rescue medications and leukotriene modifiers was also observed after initiation of omalizumab treatment in our study. Decreases in asthma medication use suggests that asthma symptoms may be improved after initiating omalizumab treatment.

Assessment of asthma exacerbations provides a means to gauge asthma control,³⁵ but exacerbations are also associated with increased costs attributable to ED visits or hospitalizations and may result in death.^{12,36,37} Omalizumab treatment was associated with significant decreases in asthma exacerbations in the present study, ranging from a relative decrease of 79.3% for hospitalization exacerbations to 30.3% for outpatient exacerbations. Such reductions have been reported in omalizumab clinical trials,^{12,35} pooled analyses,^{9,36,38} and real-world observational studies.^{17,20,24,39} In these prior publications, the decreases in overall asthma exacerbations ranged from 26%¹² to 82%; ED exacerbations, including unscheduled physician visits, decreased between 44%¹² and 81%²⁰; and hospitalization exacerbations decreased between 28%¹⁷ and 78%.²⁰ The relative reductions observed in the present study decreased in the midrange or lower, with the exception of hospitalization exacerbations (79.3%). In the multivariate analyses that adjusted for meaningful patient and treatment characteristics of interest, exacerbations were >85% less likely to occur after omalizumab treatment initiation in both the 1- and 2-year periods. This significant decrease in exacerbations indicates the real-world effectiveness of omalizumab on this very important marker of asthma control.

Reductions in the medical claims for asthma-related comorbidities from the preindex to the postindex periods were observed in the study. This finding may reflect the typical diagnostic workup performed before initiating omalizumab treatment, the cyclic nature of the conditions, and variations in medical billing and coding practices. Data abstracted from medical records enriched the information available in claims. Approximately 50% of the patients with preindex IgE results available had IgE levels between 30 and 300 IU/mL. Previous research has identified baseline IgE levels as an important predictor of omalizumab response.^{40,41} However, approximately 46% of medical record patients did not have preindex IgE levels documented in their medical records. Because IgE levels are necessary before administration of omalizumab, it is possible that IgE levels were obtained but not documented in the records. In addition, approximately two-thirds of patients with available spirometry results had a pre-bronchodilator level of >80% of the predicted value, with equal proportions of patients having values >60% and between 60% and 80% of the predicted value (32% each). Similar to the IgE levels with regard

to the level of data capture, the missing spirometry results may be also due to lack of documentation in the medical records.

Limitations

This study benefited from a large, geographically dispersed population and a follow-up period longer than that used in clinical trials. However, certain limitations should be noted. The presence of a diagnosis code on a medical claim is not proof a condition is present because the diagnosis may be incorrectly coded or included as a rule-out criterion. In addition, a small number of patients may have had a concomitant diagnosis of urticaria, for which omalizumab is also indicated, so we cannot definitely determine the indication for administration of omalizumab in these patients. The comorbidity measures in this study may have been overestimated by requiring ≥ 1 medical claims with any ICD-9-CM or ICD-10-CM diagnosis code for specific conditions of interest from all places of service. The presence of a claim for a filled prescription does not indicate that the medication was consumed or that it was taken as prescribed. Although this limitation is not applicable to omalizumab, which is administered in the office, it does pertain to other concomitant medications. Furthermore, any medications filled over-the-counter or provided as samples by the physician are not captured in claims data, which may underestimate use of medications.

The study sample was identified from a large US administrative claims database and consisted of patients with commercial and Medicare Advantage insurance. These results may not be generalizable to patients with different types of health insurance, patients with no insurance, or those living outside the United States. Lastly, because this study included only patients treated with at least 4 claims for omalizumab within 6 months after treatment initiation, which was consistent with clinical guidelines on the use of omalizumab,^{15,17,22} the study population may be different from the population with <4 claims for omalizumab.

CONCLUSION

This long-term study is unique in that it combined data from both claims and medical records, allowing for the inclusion of information, such as dosing and IgE values. The results of this real-world analysis indicate that in patients newly initiating omalizumab therapy for

allergic asthma, significant reductions were observed in asthma exacerbations, especially hospitalization- and ED-specific ones, from before to after omalizumab treatment initiation. In addition, patients receiving omalizumab had a reduction in concomitant asthma medications, most specifically with regard to use of both OCSs and ICSs and inhaled bronchodilator rescue medications. Reductions in both exacerbations and concomitant asthma medication after initiating omalizumab treatment in this cohort suggest that the efficacy of omalizumab observed in clinical trials is also observed in real-world clinical practice.

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CONFLICTS OF INTEREST

D. Wertz, Q. Huang, L. Wang, V.J. Willey, and J.J. Stephenson are employees of HealthCore Inc, an independent research organization that received funding from Novartis Pharmaceuticals Corporation for the conduct of the study. X. Ke was an employee of HealthCore Inc, when the study was conducted. A. Kavati and B. Ortiz are employees of Novartis Pharmaceuticals Corporation. R.A. Panettieri Jr is affiliated with Rutgers, The State University of New Jersey, under contract with Novartis Pharmaceuticals Corporation to provide consulting services to the study. J. Corren is affiliated with David Geffen School of Medicine at University of California, Los Angeles, under contract with Novartis Pharmaceuticals Corporation to provide consulting services to the study. The authors have indicated that they have no other conflicts of interest regarding the content of this article.

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X. Ke, Q. Huang and L. Wang contributed to study design, literature search, data collection, analysis and interpretation of data, figure/table creation, manuscript writing and revision. A. Kavati, D. Wertz, V.J. Willey, J.J. Stephenson, B. Ortiz, R.A. Panettieri Jr and J.

Corren contributed to study design, manuscript writing and revision. All authors are involved in the decision to submit the manuscript for publication. Cheryl Jones, HealthCore Inc, provided writing and editorial support for the manuscript. Patrick W. Sullivan, PhD, professor at Regis University School of Pharmacy, provided critical reviews in the preparation of the manuscript.

SUPPLEMENTARY MATERIALS

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Supplemental Table 1. Pre- and Post-Index Clinical Characteristics for Patients With Asthma Newly Treated With Omalizumab and With ≥ 24 Months Post-Index Follow-Up

Clinical Characteristics	Subset of Patients Treated With Omalizumab With ≥24 Months Post-Index Follow-Up (n=970)						p-Value ^b [A vs B]	p-Value ^b [A vs C]
	12 Months Pre-Index [A]		12 Months Post-Index [B]		13 – 24 Months Post-Index [C]			
	n (%) ^a	Median (IQR)	n (%) ^a	Median (IQR)	n (%) ^a	Median (IQR)		
Prescribing/treating physician specialty ^c							1.000	.891
Allergist/immunologist	749 (77.2)		749 (77.2)		745 (76.8)		—	.046
Pulmonologist	196 (20.2)		197 (20.3)		195 (20.1)		.317	.317
Primary care physician	18 (1.9)		17 (1.8)		23 (2.4)		.317	.025
Other	6 (0.6)		6 (0.6)		6 (0.6)		—	—
Unknown	1 (0.1)		1 (0.1)		1 (0.1)		—	—
Asthma or urticaria diagnosis associated with omalizumab initiation								
Asthma	814 (83.9)							
Urticaria	8 (0.8)							
Both asthma and urticaria	17 (1.8)							
Neither asthma nor urticaria	131 (13.5)							
Comorbidities								
QCI, mean (SD)	1.5 (1.01)	1.0 (1.0)	1.6 (1.12)	1.0 (1.0)	1.6 (1.24)	1.0 (1.0)	.012	.011
Asthma-associated comorbidities								
Allergic rhinitis	746 (76.9)		733 (75.6)		683 (70.4)		.312	<.001
Respiratory infection	716 (73.8)		698 (72.0)		668 (68.9)		.270	.007
Chronic sinusitis	383 (39.5)		328 (33.8)		277 (28.6)		<.001	<.001
Acute sinusitis	357 (36.8)		295 (30.4)		279 (28.8)		<.001	<.001
Gastroesophageal reflux disease	296 (30.5)		279 (28.8)		262 (27.0)		.253	.025
Acute bronchitis	293 (30.2)		194 (20.0)		201 (20.7)		<.001	<.001
COPD	215 (22.2)		173 (17.8)		171 (17.6)		.001	.001
Eczema/dermatitis	145 (14.9)		152 (15.7)		152 (15.7)		.590	.603
Conjunctivitis	114 (11.8)		106 (10.9)		91 (9.4)		.419	.032
Nasal polyposis	109 (11.2)		98 (10.1)		90 (9.3)		.185	.039
Urticaria	98 (10.1)		73 (7.5)		67 (6.9)		.002	<.001
Food allergy	52 (5.4)		28 (2.9)		22 (2.3)		.001	<.001
Anaphylaxis	48 (4.9)		32 (3.3)		25 (2.6)		.009	.001
Angioedema	44 (4.5)		34 (3.5)		23 (2.4)		.096	.001
Tests of interest								
Any allergy test	805 (83.0)		215 (22.2)		206 (21.2)		<.001	<.001
Total IgE	738 (76.1)		98 (10.1)		95 (9.8)		<.001	<.001
Skin test for allergen-specific IgE	353 (36.4)		130 (13.4)		120 (12.4)		<.001	<.001
Blood test for allergen-specific IgE	334 (34.4)		45 (4.6)		44 (4.5)		<.001	<.001
Spirometry	813 (83.8)		657 (67.7)		595 (61.3)		<.001	<.001
CBC ^d	601 (62.0)		493 (50.8)		500 (51.5)		<.001	<.001
Fractional exhaled nitric oxide	50 (5.2)		61 (6.3)		74 (7.6)		.179	.007

Abbreviations: CBC=complete blood count with differential; CIU=chronic idiopathic urticaria; COPD=chronic obstructive pulmonary disease; IgE=immunoglobulin E; IQR=interquartile range; QCI=Quan-Charlson Comorbidity Index; SD=standard deviation

^a Values are expressed as n (%) unless otherwise noted

^b P-values were estimated from paired t-test or Wilcoxon signed rank sum test for normally distributed and non-normally distributed continuous variables, respectively; and from McNemar test (or Bowker's test of symmetry for square tables larger than 2×2) for categorical variables

^c The following hierarchy was applied when multiple specialties existed: allergy/immunology > pulmonary medicine > family/general practice > internal medicine > others or unknown. PCP includes family/general practice, and internal medicine

^d To obtain eosinophil level

Supplemental Table 2. Pre- and Post-Index Asthma-Related Medications and Treatment for Patients With Asthma Newly Treated With Omalizumab and With ≥ 24 Months Post-Index Follow-Up

Subset of Treated Omalizumab Patients with ≥24 Months of Post-Index Follow-up (N=970)										
Asthma Related Medication and Treatment	12 Months Pre-Index [A]		12 Months Post-Index [B]		13-24 Months Post-Index [C]		p-Value ^b [A vs B]	Relative Change (%) [(B-A)/A]	p-Value ^b [A vs C]	Relative Change (%) [(C-A)/A]
	n (%) ^a	Median (IQR)	n (%) ^a	Median (IQR)	n (%) ^a	Median (IQR)				
Asthma controller medications										
ICS	334 (34.4)		269 (27.7)		253 (26.1)		<.001	-19.5	<.001	-24.3
Low dose ^c	53 (5.5)		51 (5.3)		51 (5.3)		.811	-3.8	.829	-3.8
Medium dose ^c	144 (14.8)		106 (10.9)		101 (10.4)		.001	-26.4	.001	-29.9
High dose ^c	91 (9.4)		65 (6.7)		55 (5.7)		.003	-28.6	<.001	-39.6
Unspecified dose ^c	130 (13.4)		123 (12.7)		106 (10.9)		.482	-5.4	.037	-18.5
LABA	75 (7.7)		60 (6.2)		42 (4.3)		.032	-20.0	<.001	-44.0
ICS-LABA combination (fixed-dose combination)	675 (69.6)		627 (64.6)		580 (59.8)		<.001	-7.1	<.001	-14.1
Low dose ICS ^c	84 (8.7)		56 (5.8)		56 (5.8)		.004	-33.3	.008	-33.3
Medium dose ICS ^c	400 (41.2)		331 (34.1)		287 (29.6)		<.001	-17.3	<.001	-28.3
High dose ICS ^c	394 (40.6)		353 (36.4)		306 (31.5)		.001	-10.4	<.001	-22.3
Unspecified dose ICS ^c	2 (0.2)		1 (0.1)		6 (0.6)		.317	-50.0	.157	200.0
ICS-LABA combination (including free ^d or fixed-dose combination)	705 (72.7)		654 (67.4)		598 (61.6)		<.001	-7.2	<.001	-15.2
Leukotriene modifiers	662 (68.2)		577 (59.5)		509 (52.5)		<.001	-12.8	<.001	-23.1
Methylxanthine	69 (7.1)		72 (7.4)		62 (6.4)		.647	4.3	.362	-10.1
Omalizumab	—		970 (100.0)		749 (77.2)		—	—	—	—
LAMA	128 (13.2)		127 (13.1)		106 (10.9)		.909	-0.8	.036	-17.2
Mast cell stabilizers	10 (1.0)		6 (0.6)		6 (0.6)		.206	-40.0	.285	-40.0
Bronchodilators (long acting albuterol)	9 (0.9)		7 (0.7)		6 (0.6)		.414	-22.2	.180	-33.3
Asthma rescue medications										
Inhaled SABA	757 (78.0)		654 (67.4)		628 (64.7)		<.001	-13.6	<.001	-17.0
Non-inhaled SABA	11 (1.1)		12 (1.2)		10 (1.0)		.796	9.1	.782	-9.1
SAMA	70 (7.2)		40 (4.1)		45 (4.6)		<.001	-42.9	.004	-35.7
SABA-SAMA combination (fixed-dose)	137 (14.1)		91 (9.4)		81 (8.4)		<.001	-33.6	<.001	-40.9
OCS	814 (83.9)		628 (64.7)		610 (62.9)		<.001	-22.9	<.001	-25.1
Long-course ^e	80 (8.2)		86 (8.9)		75 (7.7)		.491	7.5	.579	-6.3
Short-course ^f	734 (75.7)		542 (55.9)		535 (55.2)		<.001	-26.2	<.001	-27.1
Number of types of asthma medications (listed above), mean (SD)	4.1 (1.56)	4.0 (2.0)	4.6 (1.66)	5.0 (2.0)	4.1 (1.85)	4.0 (3.0)	<.001	12.2	.556	0.0
0	37 (3.8)		0 (0)		32 (3.3)		<.001	-100.0	.508	-13.5
1	39 (4.0)		58 (6.0)		78 (8.0)		.022	48.7	<.001	100.0
2	85 (8.8)		69 (7.1)		102 (10.5)		.127	-18.8	.172	20.0
≥3	809 (83.4)		843 (86.9)		758 (78.1)		.001	4.2	<.001	-6.3
Other asthma treatment										
Allergen immunotherapy	308 (31.8)		367 (37.8)		308 (31.8)		<.001	19.2	1.000	0.0

Abbreviations: ICS=inhaled corticosteroids; IQR=interquartile range; LABA= long-acting beta-2 adrenergic agonist; LAMA= long-acting muscarinic antagonist; OCS=oral corticosteroids; PDE4=phosphodiesterase-4; SABA=short-acting beta-2 adrenergic agonist; SAMA=short-acting muscarinic antagonist; SD=standard deviation

^a Values are expressed as n (%) unless otherwise noted

^b P-values were estimated from paired t-test or Wilcoxon signed rank sum test for normally distributed and non normally distributed continuous variables, respectively; and from McNemar test for categorical variables

^c Presence of any fill/administration with specific dose, not necessarily mutually exclusive. Certain ICS use may not fall into low/med/high categories as defined by the National Heart, Lung, and Blood Institute (NHLBI) guidelines (eg, no definition for specific ICS or dose not within the defined ranges), and were captured under the unspecified dose category

^d Free-dose combination was defined as having ≥ 14 days of continuous overlap of days of supply of specific medications within the period of interest

^e Based on days of supply (≥ 180 sum of days supply in a 12-month period)

^f Based on days of supply (< 180 sum of days supply in a 12-month period)

Supplemental Table 3. Pre- and Post-Index Asthma Exacerbations for Patients With Asthma Newly Treated With Omalizumab and With ≥ 24 Months Post-Index Follow-Up

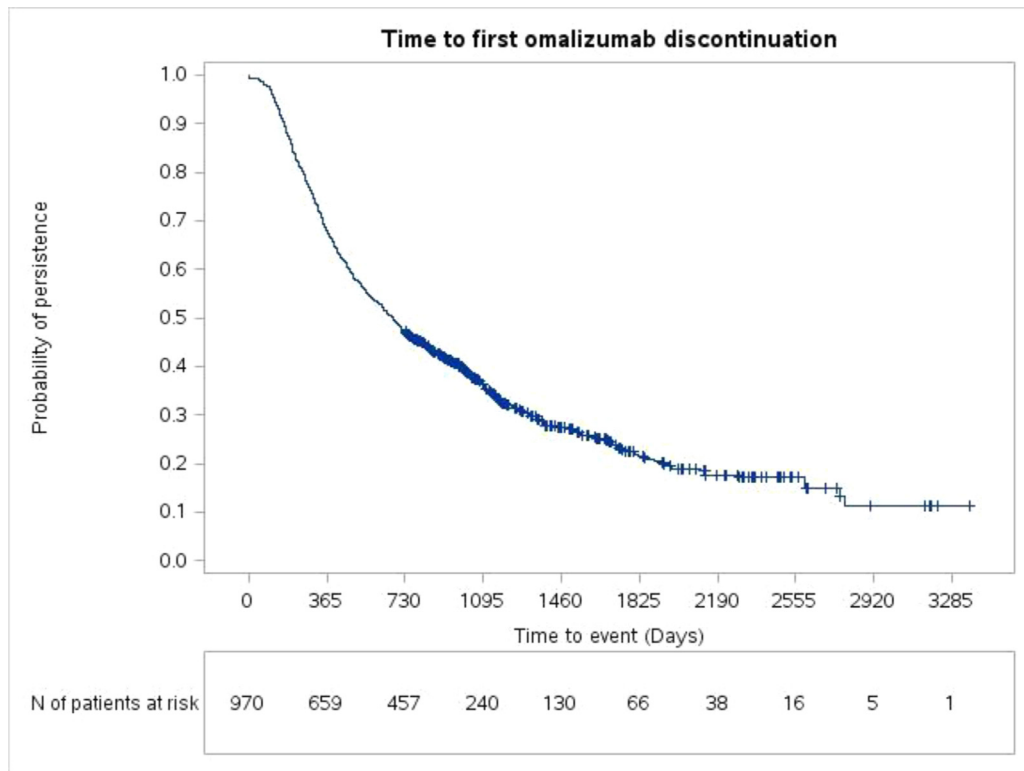
Subset of Patients Treated With Omalizumab With ≥ 24 Months Post-Index Follow-Up (N=970)										
	12 Months Pre-Index [A]		12 Months Post-Index [B]		13–24 Months Post-Index [C]			Relative		Relative
Asthma Exacerbations	n (%) ^a	Median (IQR)	n (%) ^a	Median (IQR)	n (%) ^a	Median (IQR)	p-Value ^b [A vs B]	Change (%) [(B-A)/A]	p-Value ^b [A vs C]	Change (%) [(C-A)/A]
Any asthma exacerbations ^c	668 (68.9)		420 (43.3)		353 (36.4)		<.001	-37.1	<.001	-47.2
Number of episodes, mean (SD)	1.2 (1.12)	1.0 (2.0)	0.6 (0.76)	0.0 (1.0)	0.5 (0.73)	0.0 (1.0)	<.001	-50.0	<.001	-58.3
Hospitalization exacerbations	111 (11.4)		19 (2.0)		6 (0.6)		<.001	-82.9	<.001	-94.6
Number of episodes, mean (SD)	0.1 (0.32)	0.0 (0.0)	0.0 (0.14)	0.0 (0.0)	0.0 (0.08)	0.0 (0.0)	<.001	-100.0	<.001	-100.0
ED exacerbations	114 (11.8)		33 (3.4)		20 (2.1)		<.001	-71.1	<.001	-82.5
Number of episodes, mean (SD)	0.1 (0.32)	0.0 (0.0)	0.0 (0.18)	0.0 (0.0)	0.0 (0.14)	0.0 (0.0)	<.001	-100.0	<.001	-100.0
Outpatient exacerbations	577 (59.5)		381 (39.3)		336 (34.6)		<.001	-34.0	<.001	-41.8
Number of episodes, mean (SD)	1.0 (1.05)	1.0 (2.0)	0.5 (0.74)	0.0 (1.0)	0.5 (0.71)	0.0 (1.0)	<.001	-50.0	<.001	-50.0

Abbreviations: ED=emergency department; IQR=interquartile range; SD=standard deviation; n=number

^a Values are expressed as n (%) unless otherwise noted

^b p-Values were estimated from paired t-test or Wilcoxon signed rank sum test for normally distributed and non normally distributed continuous variables, respectively; and from McNemar test for categorical variables

^c Asthma exacerbation was defined as follows: (1) Hospitalization asthma exacerbation: an inpatient stay with asthma (ICD-9-CM codes: 493.xx; ICD-10-CM diagnosis codes: J45.20-J45.998) as the primary diagnosis; (2) ED asthma exacerbation: an ED visit with asthma as the primary diagnosis (ED visits followed by hospitalizations were not included in this category as they would be considered inpatient hospitalizations); (3) Outpatient asthma exacerbation: outpatient visit with asthma diagnosis in any position of a medical claim and receipt of oral corticosteroids within 7 days following the outpatient visit. A clean period (no asthma-related inpatient, ED, or outpatient visits AND no use of any oral corticosteroids) of 30 days was applied to differentiate two consecutive asthma exacerbation episodes. The following hierarchy was applied to create type of asthma exacerbation for an exacerbation episode: hospitalization asthma exacerbation > ED asthma exacerbation > outpatient asthma exacerbation



Supplemental Figure 1. Kaplan-Meier Curve for Omalizumab Persistence/Discontinuation in Patients With Asthma Newly Treated With Omalizumab and With ≥ 24 Months Post-Index Follow-Up

Note: “+” symbols indicated censored status.

Supplemental Table 1: Pre- and Post-Index Clinical Characteristics for Patients With Asthma Newly Treated With Omalizumab and With ≥24 Months Post-Index Follow- Up

Subset of Patients Treated With Omalizumab With ≥24 Months Post-Index Follow-Up (N=970)								
Clinical Characteristics	12 Months Pre-Index [A]		12 Months Post-Index [B]		13 – 24 Months Post-Index [C]		p-Value ^b [A vs B]	p-Value ^b [A vs C]
	n (%) ^a	Median (IQR)	n (%) ^a	Median (IQR)	n (%) ^a	Median (IQR)		
Prescribing/treating physician specialty ^c							1.000	.891
Allergist/immunologist	749 (77.2)		749 (77.2)		745 (76.8)		–	.046
Pulmonologist	196 (20.2)		197 (20.3)		195 (20.1)		.317	.317
Primary care physician	18 (1.9)		17 (1.8)		23 (2.4)		.317	.025
Other	6 (0.6)		6 (0.6)		6 (0.6)		–	–
Unknown	1 (0.1)		1 (0.1)		1 (0.1)		–	–
Asthma or urticaria diagnosis associated with omalizumab initiation								
Asthma	814 (83.9)							
Urticaria	8 (0.8)							
Both asthma and urticaria	17 (1.8)							
Neither asthma nor urticaria	131 (13.5)							
Comorbidities								
QCI, mean (SD)	1.5 (1.01)	1.0 (1.0)	1.6 (1.12)	1.0 (1.0)	1.6 (1.24)	1.0 (1.0)	.012	.011
Asthma-associated comorbidities								

Allergic rhinitis	746 (76.9)	733 (75.6)	683 (70.4)	.312	<.001
Respiratory infection	716 (73.8)	698 (72.0)	668 (68.9)	.270	.007
Chronic sinusitis	383 (39.5)	328 (33.8)	277 (28.6)	<.001	<.001
Acute sinusitis	357 (36.8)	295 (30.4)	279 (28.8)	<.001	<.001
Gastroesophageal reflux disease	296 (30.5)	279 (28.8)	262 (27.0)	.253	.025
Acute bronchitis	293 (30.2)	194 (20.0)	201 (20.7)	<.001	<.001
COPD	215 (22.2)	173 (17.8)	171 (17.6)	.001	.001
Eczema/dermatitis	145 (14.9)	152 (15.7)	152 (15.7)	.590	.603
Conjunctivitis	114 (11.8)	106 (10.9)	91 (9.4)	.419	.032
Nasal polyposis	109 (11.2)	98 (10.1)	90 (9.3)	.185	.039
Urticaria	98 (10.1)	73 (7.5)	67 (6.9)	.002	<.001
Food allergy	52 (5.4)	28 (2.9)	22 (2.3)	.001	<.001
Anaphylaxis	48 (4.9)	32 (3.3)	25 (2.6)	.009	.001
Angioedema	44 (4.5)	34 (3.5)	23 (2.4)	.096	.001
Tests of interest					
Any allergy test	805 (83.0)	215 (22.2)	206 (21.2)	<.001	<.001
Total IgE	738 (76.1)	98 (10.1)	95 (9.8)	<.001	<.001
Skin test for allergen-specific IgE	353 (36.4)	130 (13.4)	120 (12.4)	<.001	<.001
Blood test for allergen-specific IgE	334 (34.4)	45 (4.6)	44 (4.5)	<.001	<.001
Spirometry	813 (83.8)	657 (67.7)	595 (61.3)	<.001	<.001
CBC ^d	601 (62.0)	493 (50.8)	500 (51.5)	<.001	<.001
Fractional exhaled nitric oxide	50 (5.2)	61 (6.3)	74 (7.6)	.179	.007

Abbreviations: CBC=complete blood count with differential; CIU=chronic idiopathic urticaria; COPD=chronic obstructive pulmonary disease; IgE=immunoglobulin E; IQR=interquartile range; QCI=Quan-Charlson Comorbidity Index; SD=standard deviation

^aValues are expressed as n (%) unless otherwise noted

^bP-values were estimated from paired t-test or Wilcoxon signed rank sum test for normally distributed and non-normally distributed continuous variables, respectively; and from McNemar test (or Bowker's test of symmetry for square tables larger than 2×2) for categorical variables

^cThe following hierarchy was applied when multiple specialties existed: allergy/immunology > pulmonary medicine > family/general practice > internal medicine > others or unknown. PCP includes family/general practice, and internal medicine

^dTo obtain eosinophil level

Supplemental Table 2. Pre- and Post-Index Asthma-Related Medications and Treatment for Patients With Asthma Newly Treated With Omalizumab and With ≥ 24 Months Post-Index Follow- Up

Subset of Treated Omalizumab Patients with ≥24 Months of Post-Index Follow-up (N=970)										
Asthma Related Medication and Treatment	12 Months Pre-Index [A]		12 Months Post-Index [B]		13-24 Months Post-Index [C]		p-Value ^b [A vs B]	Relative Change (%) [(B-A)/A]	p-Value ^b [A vs C]	Relative Change (%) [(C-A)/A]
	n (%) ^a	Median (IQR)	n (%) ^a	Median (IQR)	n (%) ^a	Median (IQR)				
Asthma controller medications										
ICS	334 (34.4)		269 (27.7)		253 (26.1)		<.001	-19.5	<.001	-24.3
Low dose ^c	53 (5.5)		51 (5.3)		51 (5.3)		.811	-3.8	.829	-3.8
Medium dose ^c	144 (14.8)		106 (10.9)		101 (10.4)		.001	-26.4	.001	-29.9
High dose ^c	91 (9.4)		65 (6.7)		55 (5.7)		.003	-28.6	<.001	-39.6
Unspecified dose ^c	130 (13.4)		123 (12.7)		106 (10.9)		.482	-5.4	.037	-18.5
LABA	75 (7.7)		60 (6.2)		42 (4.3)		.032	-20.0	<.001	-44.0
ICS-LABA combination (fixed-dose combination)	675 (69.6)		627 (64.6)		580 (59.8)		<.001	-7.1	<.001	-14.1
Low dose ICS ^c	84 (8.7)		56 (5.8)		56 (5.8)		.004	-33.3	.008	-33.3
Medium dose ICS ^c	400 (41.2)		331 (34.1)		287 (29.6)		<.001	-17.3	<.001	-28.3
High dose ICS ^c	394 (40.6)		353 (36.4)		306 (31.5)		.001	-10.4	<.001	-22.3
Unspecified dose ICS ^c	2 (0.2)		1 (0.1)		6 (0.6)		.317	-50.0	.157	200.0
ICS-LABA combination (including free ^d or fixed-dose combination)	705 (72.7)		654 (67.4)		598 (61.6)		<.001	-7.2	<.001	-15.2

Leukotriene modifiers	662 (68.2)		577 (59.5)		509 (52.5)		<.001	-12.8	<.001	-23.1
Methylxanthine	69 (7.1)		72 (7.4)		62 (6.4)		.647	4.3	.362	-10.1
Omalizumab	–		970 (100.0)		749 (77.2)		–	–	–	–
LAMA	128 (13.2)		127 (13.1)		106 (10.9)		.909	-0.8	.036	-17.2
Mast cell stabilizers	10 (1.0)		6 (0.6)		6 (0.6)		.206	-40.0	.285	-40.0
Bronchodilators (long acting albuterol)	9 (0.9)		7 (0.7)		6 (0.6)		.414	-22.2	.180	-33.3
Asthma rescue medications										
Inhaled SABA	757 (78.0)		654 (67.4)		628 (64.7)		<.001	-13.6	<.001	-17.0
Non-inhaled SABA	11 (1.1)		12 (1.2)		10 (1.0)		.796	9.1	.782	-9.1
SAMA	70 (7.2)		40 (4.1)		45 (4.6)		<.001	-42.9	.004	-35.7
SABA-SAMA combination (fixed-dose)	137 (14.1)		91 (9.4)		81 (8.4)		<.001	-33.6	<.001	-40.9
OCS	814 (83.9)		628 (64.7)		610 (62.9)		<.001	-22.9	<.001	-25.1
Long-course ^e	80 (8.2)		86 (8.9)		75 (7.7)		.491	7.5	.579	-6.3
Short-course ^f	734 (75.7)		542 (55.9)		535 (55.2)		<.001	-26.2	<.001	-27.1
Number of types of asthma medications (listed above), mean (SD)	4.1 (1.56)	4.0 (2.0)	4.6 (1.66)	5.0 (2.0)	4.1 (1.85)	4.0 (3.0)	<.001	12.2	.556	0.0
0	37 (3.8)		0 (0)		32 (3.3)		<.001	-100.0	.508	-13.5
1	39 (4.0)		58 (6.0)		78 (8.0)		.022	48.7	<.001	100.0
2	85 (8.8)		69 (7.1)		102 (10.5)		.127	-18.8	.172	20.0
≥3	809 (83.4)		843 (86.9)		758 (78.1)		.001	4.2	<.001	-6.3
Other asthma treatment										
Allergen immunotherapy	308 (31.8)		367 (37.8)		308 (31.8)		<.001	19.2	1.000	0.0

Abbreviations: ICS=inhaled corticosteroids; IQR=interquartile range; LABA= Long acting beta-2 adrenergic agonist; LAMA=long-acting muscarinic antagonist; OCS=oral corticosteroids; PDE4=phosphodiesterase-4; SABA=short-acting beta-2 adrenergic agonist; SAMA=short-acting muscarinic antagonist; SD=standard deviation

^aValues are expressed as n (%) unless otherwise noted

^bP-values were estimated from paired t-test or Wilcoxon signed rank sum test for normally distributed and non-normally distributed continuous variables, respectively; and from McNemar test for categorical variables

^cPresence of any fill/administration with specific dose, not necessarily mutually exclusive. Certain ICS use may not fall into low/med/high categories as defined by the National Heart, Lung, and Blood Institute (NHLBI) guidelines (eg, no definition for specific ICS or dose not within the defined ranges), and were captured under the unspecified dose category

^dFree-dose combination was defined as having ≥ 14 days of continuous overlap of days of supply of specific medications within the period of interest

^eBased on days of supply (≥ 180 sum of days supply in a 12-month period)

^fBased on days of supply (< 180 sum of days supply in a 12-month period)

Supplemental Table 3. Pre- and Post-Index Asthma Exacerbations for Patients With Asthma Newly Treated With Omalizumab and With ≥24 Months

Post-Index Follow- Up

Subset of Patients Treated With Omalizumab With ≥24 Months Post-Index Follow-Up (N=970)										
Asthma Exacerbations	12 Months Pre-Index [A]		12 Months Post-Index [B]		13–S24 Months Post-Index [C]		p-Value ^b [A vs B]	Relative Change (%) [(B-A)/A]	p-Value ^b [A vs C]	Relative Change (%) [(C-A)/A]
	n (%) ^a	Median (IQR)	n (%) ^a	Median (IQR)	n (%) ^a	Median (IQR)				
Any asthma exacerbations ^c	668 (68.9)		420 (43.3)		353 (36.4)		<.001	-37.1	<.001	-47.2
Number of episodes, mean (SD)	1.2 (1.12)	1.0 (2.0)	0.6 (0.76)	0.0 (1.0)	0.5 (0.73)	0.0 (1.0)	<.001	-50.0	<.001	-58.3
Hospitalization exacerbations	111 (11.4)		19 (2.0)		6 (0.6)		<.001	-82.9	<.001	-94.6
Number of episodes, mean (SD)	0.1 (0.32)	0.0 (0.0)	0.0 (0.14)	0.0 (0.0)	0.0 (0.08)	0.0 (0.0)	<.001	-100.0	<.001	-100.0
ED exacerbations	114 (11.8)		33 (3.4)		20 (2.1)		<.001	-71.1	<.001	-82.5
Number of episodes, mean (SD)	0.1 (0.32)	0.0 (0.0)	0.0 (0.18)	0.0 (0.0)	0.0 (0.14)	0.0 (0.0)	<.001	-100.0	<.001	-100.0
Outpatient exacerbations	577 (59.5)		381 (39.3)		336 (34.6)		<.001	-34.0	<.001	-41.8
Number of episodes, mean (SD)	1.0 (1.05)	1.0 (2.0)	0.5 (0.74)	0.0 (1.0)	0.5 (0.71)	0.0 (1.0)	<.001	-50.0	<.001	-50.0

Abbreviations: ED=emergency department; IQR=interquartile range; SD=standard deviation

^aValues are expressed as n (%) unless otherwise noted

^bp-Values were estimated from paired t-test or Wilcoxon signed rank sum test for normally distributed and non-normally distributed continuous variables, respectively; and from McNemar test for categorical variables

^cAsthma exacerbation was defined as follows:

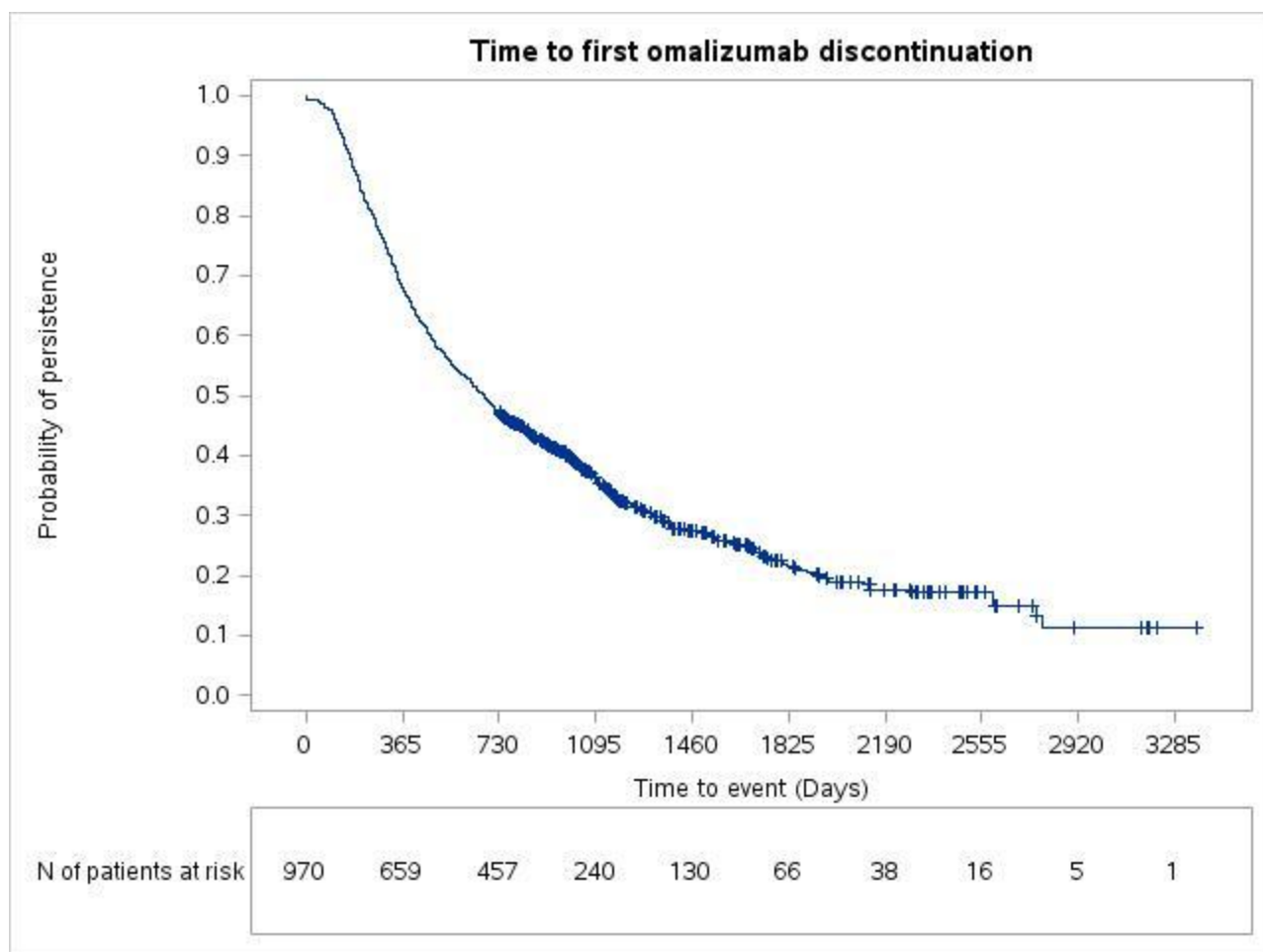
(1) Hospitalization asthma exacerbation: an inpatient stay with asthma (ICD-9-CM codes: 493.xx; ICD-10-CM diagnosis codes: J45.20-J45.998) as the primary diagnosis

(2) ED asthma exacerbation: an ED visit with asthma as the primary diagnosis (ED visits followed by hospitalizations were not included in this category as they would be considered inpatient hospitalizations)

(3) Outpatient asthma exacerbation: outpatient visit with asthma diagnosis in any position of a medical claim and receipt of oral corticosteroids within 7 days following the outpatient visit
A clean period (no asthma related inpatient, ED, or outpatient visits AND no use of any oral corticosteroids) of 30 days was applied to differentiate two consecutive asthma exacerbation episodes.
The following hierarchy was applied to create type of asthma exacerbation for an exacerbation episode: hospitalization asthma exacerbation > ED asthma exacerbation > outpatient asthma exacerbation

Supplemental Figure 1. Kaplan-Meier Curve for Omalizumab

Persistence/Discontinuation in Patients With Asthma Newly Treated With Omalizumab and With ≥ 24 Months Post-Index Follow- Up



Note: "+" symbols indicated censored status.