Original Article

Trends in Omalizumab Utilization for Asthma: Evidence of Suboptimal Patient Selection

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What is already known about this topic? Omalizumab has been available as a treatment for asthma in the United States for 14 years.

What does this article add to our knowledge? Many omalizumab users have low or very low adherence to inhaled corticosteroid and/or inhaled corticosteroid-long-acting β-agonist inhalers in the 12 months before omalizumab initiation.

How does this study impact current management guidelines? The study findings highlight the need for control, risk, and adherence assessments when considering omalizumab for patients with asthma.

BACKGROUND: Utilization trends of omalizumab, a first-in-its-class asthma biologic approved in 2003 for individuals not controlled by inhaled corticosteroids (ICSs), may reveal lessons in patient selection.
OBJECTIVE: To describe utilization patterns for omalizumab since its introduction in 2003, with a focus on patient-level characteristics of patients for whom omalizumab was initiated.
METHODS: Using a large US database of administrative claims, we identified privately insured and Medicare Advantage beneficiaries with asthma between 2003 and 2015. Characteristics of incident (no omalizumab use in the previous 12 months) and prevalent users of omalizumab for asthma were described and omalizumab use trends graphed. A comparison cohort (1:5 matching proportion) of nonomalizumab users was compared with incident omalizumab users on demographic characteristics, medication adherence (medication possession ratio [MPR]) for ICSs and/or ICS/long-acting β-agonist (ICS-LABA), exacerbation frequency, and asthma control in the 6 months before omalizumab initiation.
RESULTS: We identified 7,658 prevalent and 3,399 incident omalizumab users. Omalizumab incidence peaked in the second quarter of 2004 at 0.65 per 1,000 individuals with asthma, whereas prevalence peaked in the fourth quarter of 2006 at 3.22; as of fourth quarter 2015, rates were 0.14 and 1.96, respectively. In the 12 months before omalizumab initiation, 72.5% had low adherence (MPR ≤ 0.75) and 48.6% had very low adherence (MPR ≤ 0.5) to ICSs and/or ICS-LABA. In the period 2003 to 2015, the mean number of exacerbations in the 12 months before incident use ranged from 1.50 to 2.11 and the proportion that had poor asthma control (≥3 rescue inhalers dispensed) ranged from 54% to 67%. Incident omalizumab users were less likely to have good asthma control than the matched cohort of nonusers (adjusted odds ratio, 0.53 [0.48-0.59]).
CONCLUSIONS: Omalizumab use for asthma has been gradually decreasing following a peak shortly after its market availability. Many omalizumab users have low or very low adherence rates for ICSs and/or ICS-LABA in the 12 months before omalizumab initiation. © 2017 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2017;■:■-■)

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Omalizumab, a biologic mAb targeting IgE, was first approved by the US Food and Drug Administration for use in individuals 12 years and older with allergic asthma not controlled by inhaled

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Abbreviations used
CIU- Chronic idiopathic urticaria
COPD- Chronic obstructive pulmonary disease
ED- Emergency department
EXCELS- Evaluating Clinical Effectiveness and Long-term Safety in Patients with Moderate-to-Severe Asthma
HEDIS- Healthcare Effectiveness Dataset Information Set
ICS- Inhaled corticosteroid
ICS-LABA- Inhaled corticosteroid/long-acting β-agonist
MPR- Medication possession ratio
OLDW- OptumLabs Data Warehouse

corticosteroids (ICSs) in 2003.[1] Recently, 2 additional asthma biologics have been approved, both targeting IL-5: mepolizumab in 2015[2] and reslizumab in 2016.[3] In addition, in 2016 an indication for asthma in 5- to 11-year-olds has been added for omalizumab.[4] A systematic review and meta-analysis of 25 clinical trials concluded that omalizumab reduces asthma exacerbations when used as an adjunctive therapy to ICSs.[5] Given the findings from clinical trials and the drug's label, one would expect to find individuals who start omalizumab to have frequent asthma exacerbations despite being highly adherent to ICSs and/or inhaled corticosteroid/long-acting β-agonist (ICS-LABA). However, trial conditions may be different than real-world clinical practice in important ways, including patient selection.[6] Evidence from secondary data sources such as administrative claims can be useful to understand patient-level factors associated with medication use in clinical practice settings.[7] The objective of this study was to describe utilization patterns for omalizumab since its introduction in 2003, with a focus on patient-level characteristics of patients for whom omalizumab was initiated.

METHODS

Data source

We conducted a retrospective cohort analysis using administrative claims from OptumLabs Data Warehouse (OLDW), which includes more than 110 million privately insured and Medicare Advantage enrollees throughout the United States, with highest representation from the South and Midwest.[8] This study was deemed exempt from institutional board review because only deidentified data were used.

Cohort selection

Population. We identified all beneficiaries in OLDW with at least 12 months of continuous enrollment in both medical and pharmacy coverage between 2003 and 2015; 55 million unique individuals contributed 590 million person-quarters of coverage to the population denominator. Medicare Advantage beneficiaries accounted for 9% of person-quarters of coverage in the OLDW population (17.5% of person-quarters for people with asthma).

Asthma population. From the population, we identified 14,634,621 people with at least 1 asthma diagnosis code. We applied a modified version of the Healthcare Effectiveness Dataset Information Set (HEDIS) criteria for persistent asthma (described in more detail in this article's Online Repository available at www.jaci-inpractice.org) to yield a population of 1,702,300 people with asthma.[9]

Prevalent cohort. From the total population we identified 17,327 individuals who had a claim for omalizumab in pharmacy claims or medical claims (using Healthcare Common Procedure Coding System [HCPCS] codes C2917, S0107, and J2357). Among these omalizumab users, we applied the same modified HEDIS definition of asthma described above to create a cohort of 7,658 prevalent users of omalizumab.

The only other current clinical indication for omalizumab use is for treatment of chronic idiopathic urticaria (CIU). To avoid describing trends related to the treatment of CIU, we excluded all patients who had a CIU diagnosis (*International Classification of Diseases, Ninth Revision* code 708.1 and *International Classification of Diseases, Tenth Revision* code L50.1) after January 1, 2013, the year when the new indication was approved.

Incident cohort. To create the omalizumab incident cohort, we selected individuals from the prevalent cohort who had continuous medical and pharmacy insurance coverage for at least 12 months before the first recorded omalizumab use; this requirement ensures that we do not capture individuals who may have switched insurance and were continuing omalizumab use (and therefore reduces contamination of the cohort with prevalent users). There were 3399 incident users of omalizumab.

Comparison cohort. To better understand how incident omalizumab users may differ from other people with asthma, we created a comparison group of 1.7 million nonomalizumab users with asthma: (1) For each incident omalizumab user i, we calculated S_i: the number of days from meeting the modified HEDIS definition for asthma to the first use of omalizumab. (2) Then, each omalizumab user was matched to all nonomalizumab users who met the modified HEDIS definition for asthma in the same year and quarter and were still covered S_i days after meeting the modified HEDIS definition for asthma. (3) An anchor date was defined for each omalizumab user to be the date of first use and for each nonomalizumab user to be that user's asthma definition date plus the matched omalizumab user's value of S_i. (4) We calculated the number of asthma exacerbations (defined below) for each incident omalizumab user and matched nonomalizumab user in the 12 months before the anchor date. (5) Finally, where possible, we selected 5 nonuser matches for each omalizumab user with the same number of asthma exacerbations in the 12 months before the anchor date of omalizumab use. A single nonuser could be matched to multiple users of omalizumab, and therefore be included in the comparison analysis multiple times over different time periods. We did not follow a similar matching procedure for prevalent omalizumab users because we are unable to determine key information about these users' initiation of the drug and therefore cannot create a suitable comparison sample.

Variable definitions

Medication possession ratio. Asthma medications were identified using National Drug Codes (NDCs) from the HEDIS definition criteria as we have previously described using OLDW data.[10,11] Medication adherence was assessed using medication possession ratio (MPR) and was calculated using the HEDIS asthma criteria to define medication dispensing events.[10] The MPR is a measure of a patient's adherence to prescribed medication. It is equal to the sum of the number of days of medication the patient has from prescription fills divided by the number of days in the period. For example, a patient filling one 30-day prescription over a period of 60