Ann Allergy Asthma Immunol 127 (2021) 655–660

Contents lists available at ScienceDirect

Asthma biologics

Real-world effectiveness, impact of switching biologics, and predictors of response

Farrukh Abbas, MD, FACP*; Steve Georas, MD*,†; Xueya Cai, PhD‡; Sandhya Khurana, MD*,†

* Pulmonary and Critical Care Medicine, University of Rochester School of Medicine and Dentistry, Rochester, New York
† Mary Parkes Center for Asthma, Allergy & Pulmonary Care, University of Rochester Medical Center, Rochester, New York
‡ Department of Biostatistics and Computational Biology, University of Rochester School of Medicine and Dentistry, Rochester, New York

ARTICLE INFO

Article history:
Received for publication June 5, 2021.
Received in revised form July 30, 2021.
Accepted for publication August 30, 2021.

ABSTRACT

Background: Confirmation of effectiveness of asthma biologics in the real world is desirable because patient characteristics and experiences may differ from those included in randomized controlled trials.
Objective: To evaluate real-world effectiveness of asthma biologics and identify predictors of response.
Methods: We performed a retrospective study in patients with severe asthma receiving biologics. The primary outcome was change in clinically significant exacerbations at 12 months after starting biologic therapy, compared with 12 months before. Secondary outcomes were change in severe exacerbations, maintenance oral corticosteroid (OCS) dose, prebronchodilator forced expiratory volume in 1 second (FEV1), and asthma control test scores. Subgroup analyses were performed for subjects who were biologic naive or not. A stepwise logistic regression model was performed to compare responders to nonresponders.
Results: A total of 112 patients were included. Biologic therapy was associated with a 59% reduction in clinically significant exacerbations ($P < .001$), 65% reduction in severe exacerbations ($P < .001$), and 54% reduction in maintenance OCS dose ($P = .001$) in the 12 months after starting therapy. Biologics also resulted in improvement in prebronchodilator FEV1 ($P = .002$) and Asthma Control Test score ($P < .001$). Subjects who were previously on another biologic also experienced significant improvements in exacerbation frequency, maintenance OCS dose, and asthma control. Responders were more likely to be nonsmokers and have higher baseline FEV1, gastroesophageal reflux disease, and eosinophil counts greater than 500 cells/μL.
Conclusion: In a real-world setting, biologic therapy in asthma is effective in improving exacerbations, asthma control, and lung function. Patients who have a suboptimal response to 1 biologic can still benefit from treatment with a different biologic.

Introduction

Asthma is a heterogeneous disease usually characterized by chronic airway inflammation, variable airflow limitation, and respiratory symptoms, including dyspnea, wheezing, chest tightness, and cough.[1] Severe asthma is defined as asthma that requires treatment with high-dose inhaled corticosteroids plus a second controller or systemic corticosteroids (CS) to maintain asthma control (or remains poorly controlled despite this therapy). Although severe asthma makes up for less than 5% of all asthma, it accounts for most of asthma-associated morbidity and health care costs.[2] The heterogeneity in severe asthma has become increasingly relevant as several biologic treatments targeting specific asthma phenotypes have recently become available. Omalizumab, an anti–immunoglobulin E (IgE) monoclonal antibody, was the first biologic to receive approval from the US Food and Drug Administration (FDA) in 2003 as add-on treatment in moderate to severe allergic asthma. With almost 2 decades of experience, a large body of evidence has accumulated, revealing efficacy and safety of omalizumab in both controlled clinical trials and real-world settings.[3-8] Mepolizumab, an anti–interleukin (IL)-5 antibody, was the next biologic to receive FDA approval as add-on treatment in severe eosinophilic asthma in 2015.[9-11] This was followed closely by FDA approval of reslizumab (anti–IL-5),[12] benralizumab (anti–IL-5 receptor),[13-15] and dupilumab (anti–IL-4/IL-13 receptor).[16-18]

These advanced biologic treatments were found to have efficacy in decreasing asthma exacerbations, reducing systemic corticosteroid exposure, and improving asthma control in randomized controlled trials (RCTs) of patients with severe uncontrolled asthma.[10-19] Although data from RCTs are essential to confirm safety and efficacy, RCTs have strict inclusion and exclusion criteria and close monitoring of participants for adherence and adverse effects. Confirmation of effectiveness of these therapies in the real-world settings is desirable as patient characteristics and experiences may differ from those

Reprints: Farrukh Abbas, MD, FACP, Pulmonary and Critical Care Medicine, University of Rochester School of Medicine and Dentistry, 601 Elmwood Avenue, Box 692, Rochester, NY 14642. E-mail: drfarrukhabbas@live.com.
Disclosures: The authors have no conflicts of interest to report.
Funding: This study was supported by a grant from the Parkes Family Foundation, which has no bearing on the views expressed in this study. Dr Georas reports receiving other funding support from National Institutes of Health grant numbers R01 AI1444241 and T32HL066988.

https://doi.org/10.1016/j.anai.2021.08.416
1081-1206/

included in RCTs. Real-world studies can also help reveal responder profile and impact of comorbidities that may have been excluded in RCTs. For example, mepolizumab data from 6 severe asthma clinics in Northwestern Italy found that patients receiving the biologic were older, had higher lung function, higher prednisone dose requirement, higher blood eosinophil count, and higher prevalence of nasal polyposis when compared with the patients included in RCTs.[19]

The purpose of this study was to evaluate the real-world effectiveness of all FDA-approved asthma biologics in patients with severe asthma seen at our severe asthma referral center. We further analyzed the impact on asthma outcomes when patients were switched from 1 biologic to another for suboptimal response. We also tried to identify predictors of response to asthma biologic therapies.

Methods

Study Design and Approval

As illustrated in Figure 1, we performed a retrospective, single-center study at the University of Rochester Mary Parkes Asthma Center. Approval for the study was obtained from the institutional review board at the University of Rochester. Patients for whom biologic therapy was started between January 2014 and December 2020 were included in the study. Patients' electronic medical records were reviewed for data on demographics, lung function, medications, comorbidities, exacerbations, and Asthma Control Test (ACT) score. Exacerbation frequency was confirmed after review of provider notes and medication prescription history in electronic medical records.

Clinical Outcomes and Analysis

Primary outcome was the change in clinically significant asthma exacerbations during the 12 months after starting the biologic compared with historical control during 12 months before starting the biologic. Clinically significant asthma exacerbation was defined as a composite of exacerbations requiring treatment with oral corticosteroids (OCS), emergency department or urgent care visits, or hospitalization for asthma. The secondary outcomes included reduction in severe exacerbations (emergency department or urgent care visits or hospitalization) during 12 months after starting the biologic, reduction in maintenance OCS (mOCS) dose during 12 months after starting the biologic, change in prebronchodilator forced expiratory volume in 1 second 1 (FEV1) during 3 to 12 months after starting the biologic, and change in ACT score during 3 to 12 months after starting the biologic.

Subgroup analyses were performed for patients who were switched from 1 biologic to another for suboptimal response, as determined by the treating clinician. Paired *t* test was used to calculate the *P* value using GraphPad Prism version 9.0.2. The entire patient cohort was grouped into responders or nonresponders. Unpaired *t* test and contingency χ^2 test were used to determine difference between the 2 groups using GraphPad Prism version 9.0.2. A stepwise logistic regression model was performed in SAS to compare responders to nonresponders regarding patient characteristics, in which patient characteristics having significant associations in bivariate analysis were included. Sensitivity analyses were performed when only patients having at least 12-month follow-up were included.

Patients were classified as "responders" if they met any 1 of the following 3 criteria:

- greater than or equal to 50% reduction in clinically significant exacerbations;
- greater than or equal to 50% reduction in mOCS dose;

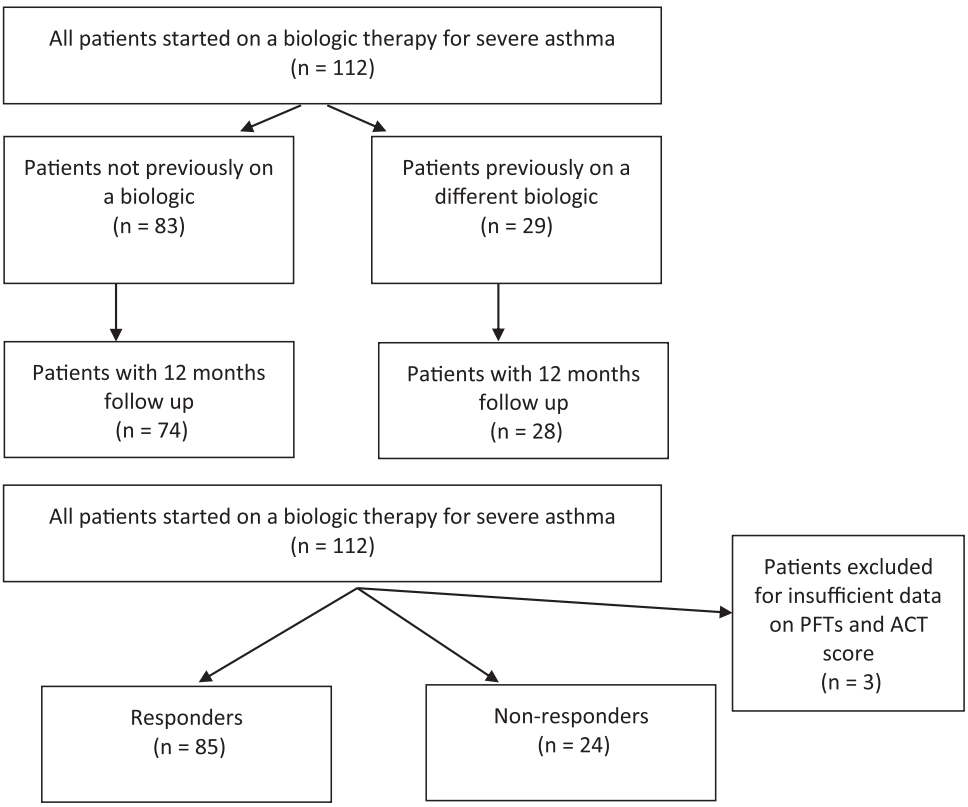

Figure 1. Of 112 patients who were included in the study, 83 were previously biologic naive and 29 were switched to another biologic for suboptimal response. The entire patient cohort was then divided into responders and nonresponders to identify the differences between the 2 groups. ACT, asthma control test; PFT, pulmonary function test.

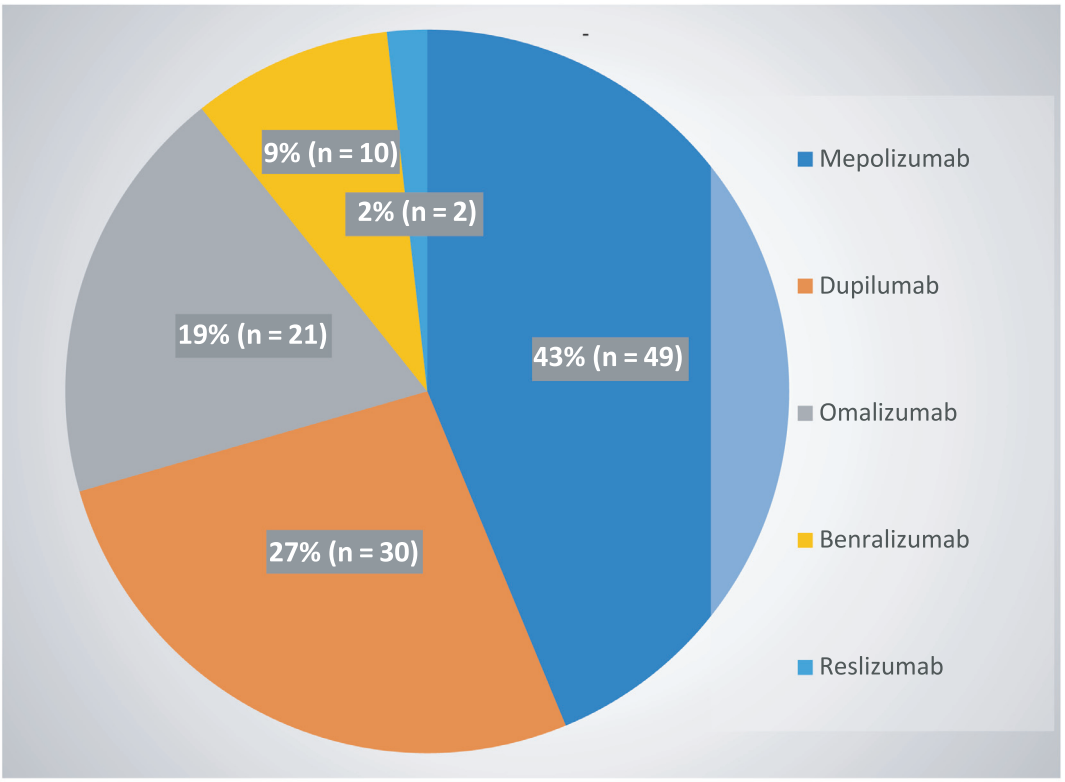

Figure 2. Distribution of asthma biologics. Mepolizumab and dupilumab were the 2 most often used biologics.

- greater than or equal to 120 mL increase in FEV1 and greater than or equal to 3-point increase in ACT score.

Results

We identified 112 patients who were initiated on asthma biologic therapy between January 2014 and December 2020 and for whom follow-up data were available between 3 and 12 months afterward. The distribution of biologic therapies is summarized in Figure 2. Mepolizumab (49, 43%) and dupilumab (30, 27%) were the most frequently used biologics. Table 1 provides baseline patient characteristics. The mean age of our patient cohort was 57 years with 55% female. The mean body mass index was 32.8 kg/m^2. All patients were receiving inhaled corticosteroids, and 44% our patients were requiring maintenance OCS. Asthma control was poor with an average ACT score of 14. Biologics were switched in 26% of the patients for suboptimal response to the initial therapy, as determined by the treating physician. Of the subjects included for analyses, 103 completed 1-year follow-up (92%). The remainder of the patients had follow-up data available between 3 and 12 months of initiation of biologic therapy. Only those patients who had 1-year follow-up data available were included in the analysis for reduction in clinically significant exacerbations, severe exacerbations, and mOCS dose.

Treatment with any biologic therapy was associated with a 59% reduction in clinically significant exacerbations from mean 4.50/y in the 12-month period preceding initiation of biologic therapy to 1.83/y in the 12-month period after initiation of therapy (Table 2, $P < .001$). All the secondary outcomes also reached statistical significance. Severe exacerbations were decreased by 65% from 1.62/y to 0.57/y ($P < .001$). Biologic therapy also led to improvement in mean FEV1 (180 mL, $P = .002$) and mean ACT score (4 points, $P < .001$) as found in Figures 3 and 4. Mean mOCS dose reduction of 54% (prednisone equivalent 11 mg to 5 mg, $P = .001$) was observed, with 31% (15/49) of patients able to discontinue mOCS. Of note, 26% (13/49) of patients

Table 1
Baseline Patient Characteristics (N = 112)

Mean age, y (range)	57 (28-92)
Female, n (%)	62 (55)
Body mass index, kg/m^2 (range)	32.8 (16.47-59.21)
Race, n (%)	
White	86 (77)
African American	19 (17)
Asian	2 (1.8)
Other	5 (4.5)
Mean blood eosinophil count, cells/μL (range)	624 (0-3400)
Mean blood eosinophil percentage, (range)	7 (0-30)
Mean FEV1 pre-BD, L (range)	2.05 (0.56-3.67)
Mean FEV1 pre-BD, % predicted (range)	69 (25-110)
Mean ACT score (range)	14 (5-25)
Patients with history of asthma related-intubations, n (%)	14 (12.5)
Medications, n (%)	
Inhaled corticosteroids	112 (100)
LABA	96 (86)
LAMA	76 (68)
LTM	81 (72)
Nasal corticosteroids	66 (59)
Theophylline	6 (5)
Patients previously on a biologic, n (%)	29 (26)
Patients on maintenance OCS, n (%).	49 (44)
Mean daily OCS dose, mg (range)	11 (2.5-60)
Comorbidities, n (%)	
GERD	87 (77)
Allergies	69 (62)
Allergic rhinitis	63 (56)
OSA	47 (42)
Depression	40 (36)
Nasal polyposis	23 (20)
Vocal cord dysfunction	16 (14)
Frequent respiratory tract infections	15 (13)
Aspirin allergy	4 (3)

Abbreviations: ACT, asthma control test; GERD, gastroesophageal reflux disease; LABA, long-acting beta-agonist; LAMA, long-acting muscarinic antagonist; LTM, leukotriene modifier; OSA, obstructive sleep apnea; OCS, oral corticosteroid; pre-BD, prebronchodilator.

Table 2
Response to Biologics in All Patients (n = 112)

Outcomes	Mean baseline	Mean follow-up	*P* value
Rate of clinically significant exacerbations (n = 103)	4.50	1.83	< .01
Rate of severe exacerbations (n = 103)	1.62	0.57	< .01
mOCS-mg prednisone equivalent (n = 50)	11	5	< .01
FEV1 L (n = 77)	2.05	2.23	< .01
FEV1 (% predicted) (n = 77)	69.49	77.39	< .01
ACT score (n = 83)	14	18	< .01

Abbreviations: ACT, asthma control test; FEV1, forced expiratory volume in 1 second; mOCS, maintenance oral corticosteroid.

were unable to reduce or required an increase in mOCS dose despite biologic therapy. Table 2 summarizes the results for the entire study cohort.

Previously Biologic Naive vs Biologic Treatment Failure

We compared outcomes between patients who were previously not on an asthma biologic and those who were switched from a previous biologic for suboptimal response (Tables 3 and 4). The effect size for the outcomes was better in the subgroup wherein the initial biologic was continued (n = 74) with 80% reduction in mean clinically significant exacerbations (5.0-1.0; $P < .01$), 100% reduction in severe exacerbations from 2.0 to 0 ($P < .01$), and improvements in ACT score. Improvement in FEV1 was not observed in this subgroup. A 53% reduction in mOCS dose was seen in this group of patients with 30% (11/36) able to discontinue mOCS.

A total of 29 patients were switched from an initial biologic to another by the treating physician, because of lack of efficacy in reducing exacerbation frequency, improving lung function, or improving symptoms. The biologic therapies chosen initially in this subgroup were mepolizumab (n = 11), omalizumab (n = 10), benralizumab (n = 7), and reslizumab (n = 1). Patients were switched to dupilumab

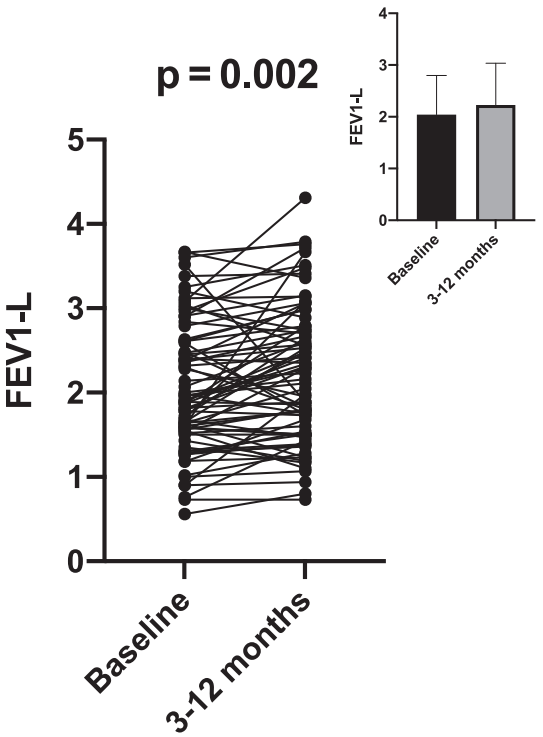

Figure 3. Mean prebronchodilator FEV1 improved by 180 mL in 3 to 12 months after starting biologic therapy. FEV1, forced expiratory volume in 1 second.

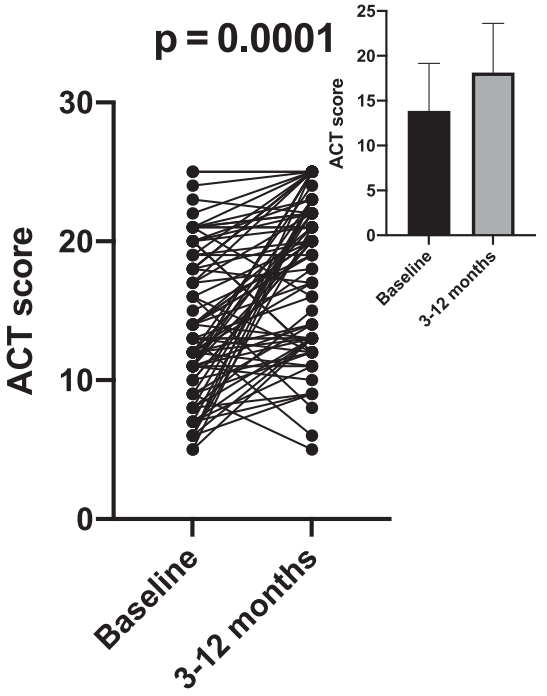

Figure 4. Mean ACT score improved by 4 points in 3 to 12 months after starting biologic therapy. ACT, asthma control test.

Table 3
Response to Biologics in Patients Previously Not on a Biologic (N = 83)

Outcomes	Mean baseline	Mean follow-up	*P* value
Rate of clinically significant exacerbations (n = 74)	5.0	1.0	< .01
Rate of severe exacerbations (n = 74)	2.0	0.0	< .01
mOCS-mg prednisone equivalent (n = 36)	13.7	6.4	< .01
FEV1 L (n = 58)	2.08	2.00	.05
ACT score (n = 56)	13	18	< .01

Abbreviations: ACT, asthma control test; FEV1, forced expiratory volume in 1 second; mOCS, maintenance oral corticosteroid.

Table 4
Response to Biologics in Patients Previously on a Different Biologic (N = 29)

Outcomes	Mean baseline	Mean follow-up	*P* value
Rate of clinically significant exacerbations (n = 28)	3.46	2.07	< .01
Rate of severe exacerbations (n = 28)	1.28	0.78	.09
mOCS-mg prednisone equivalent (n = 14)	8.82	5.07	.16
FEV1 L (n = 19)	1.94	2.27	.01
ACT score (20)	15	18	.04

Abbreviations: ACT, asthma control test; FEV1, forced expiratory volume in 1 second; mOCS, maintenance oral corticosteroid.

(n = 16), benralizumab (n = 7), and mepolizumab (n = 6) as summarized in eTable 1. There was a 40% reduction in clinically significant exacerbations in this cohort (3.46-2.07; P = .01). Improvements in FEV1 (330 mL, P = .01) and ACT score (3, P = .04) were observed. No significant reduction in severe exacerbations was observed. There was a 42% reduction in mOCS dose that was not statistically significant (P = .16) and 36% (5/14) of patients were able to discontinue mOCS. In the subgroup of patients (n = 5) in whom anti–IL-5 therapy (mepolizumab) was switched to anti–IL-5R therapy (benralizumab), the switch seemed to be effective although statistical significance was not achieved likely owing to small sample size.

Responders vs Nonresponders

Patients were assigned to "responder" (n = 85) and "nonresponder" (n = 24) subgroups, using criteria listed in the methods section (eTable 2). There were 3 patients excluded from this analysis owing to insufficient data on lung function and ACT score within 3 to 12 months after initiating biologics. A greater proportion of nonresponders had lower baseline prebronchodilator FEV1 (2.17 L vs 1.62 L; P = .01). More patients in the "responder" subgroup had an absolute blood eosinophil count greater than or equal to 500 cells/μL (65% vs 37%; P = .01) and had a history of gastroesophageal reflux disease (GERD) (82% vs 58%; P = .01). Nonresponders had higher proportion of females and ever smoker.

The 2 groups did not differ significantly in terms of body mass index, mean blood eosinophil count, serum IgE, ACT score, mOCS dose, or percentage of patients on mOCS.

The multivariable stepwise logistic regression model (eTable 3) revealed that ever-smokers were less likely to be responders (odds ratio [OR], 0.01; P = .01), patients with higher baseline FEV1 (OR, 1.05; P = .01) and eosinophil counts greater than or equal to 500 cells/μL (OR, 1.24; P = .02) were more likely to be responders, and patients having a history of GERD were marginally more likely to be responders (OR, 4.55; P = .06). Sensitivity analyses revealed same conclusions based on patients having at least 12-month follow-up.

Discussion

We report here our real-world experience with biologic therapies in patients with severe asthma at a high-risk asthma referral clinic. In previous real-world studies, mepolizumab was found to have reduction in asthma exacerbations and OCS dose in severe eosinophilic asthma with efficacy similar to RCTs.[20-22] Similarly, benralizumab had significant improvement in all relevant clinical outcomes in a real-world setting.[23,24] Reslizumab also had improved real-world clinical outcomes in severe eosinophilic asthma.[25] Approximately 24% to 42% of patients with severe eosinophilic asthma have suboptimal or no response to anti–IL-5/IL-5R therapy and require mOCS in real-world effectiveness studies.[26,27] Limited data are available on characteristics of this subgroup and the mechanisms underlying lack of response to biologic therapy. It is also unclear whether a patient who has failed 1 asthma biologic will respond to a different biologic. In 1 study, switching to dupilumab from anti-IgE or anti–IL-5/IL-5R therapy resulted in improvement in asthma control and reduction in exacerbations and systemic corticosteroid requirement.[29] In another study, reslizumab had reduction in OCS requirement from 72% to 52% and an improvement in asthma control when switched from mepolizumab.[30] Post hoc analysis of OSMO study revealed beneficial response in uncontrolled severe eosinophilic asthma on omalizumab when switched to mepolizumab,[31]

In our study, treatment with any biologic therapy was associated with significant improvement in asthma exacerbations, OCS dependence, lung function, and asthma control. The magnitude of effect observed in our study is comparable to other real-world effectiveness studies.[20,21,23,24] At our center, approximately 1 in 4 patients on an asthma biologic was switched to another biologic for suboptimal response. This finding is consistent with previous reports.[27-29] Global Initiative for Asthma guidelines suggest switching to a different T2-targeted asthma therapy if the response to a biologic is not sufficient. It is important to better characterize this group of "nonresponders" and assess effectiveness of switching to a different biologic. We found that in this subgroup of patients, switching to a different biologic was still effective in improving asthma exacerbations, OCS dependence, lung function, and ACT score. Interestingly, the improvement in asthma outcomes in the patients who switched biologic therapy was not as large as found in biologic-naive patients. The most likely explanation for this finding is that, compared with biologic-naive patients, patients who were on a biologic during the preceding 12 months experienced fewer baseline clinically significant exacerbations (3.46 vs 5.0) or had a lower baseline mean mOCS dose requirement (8.82 vs 13.7 mg), suggesting that they had achieved some improvement in asthma control on the initial biologic. Alternatively, these subjects may have different underlying pathobiology of severe asthma rendering them resistant to the effects of targeted biologics.

These finding are consistent with other studies[29,30] that have revealed benefits of switching to dupilumab or reslizumab in patients when an initial biologic was ineffective. Our study also suggests that a switch to anti–IL-5R therapy (benralizumab) can also be effective for patients with suboptimal response to anti–IL-5 therapy (mepolizumab).

We also studied the differences between "responders" and "nonresponders." We found that nonresponders were more likely to be of female sex, ever smoker, and had lower baseline prebronchodilator FEV1. Responders were more likely to be never smokers, have a history of GERD, and have a higher baseline prebronchodilator FEV1. Association of GERD with response to biologic therapy was an interesting finding and, to the best of our knowledge, has not been previously reported. This may be related to underdiagnosis of GERD in nonresponders or undiagnosed eosinophilic esophagitis in responders who also improved with biologic therapy. The responder subgroup also had higher percentage of patients with eosinophil count greater than 500 cells/μL, although there was no difference in mean eosinophil count between the 2 groups. In a previous study, fractional exhaled nitric oxide (FeNO) greater than 25 ppb was predictive of a response to dupilumab when switched from another biologic.[29] This was not reproduced in our study although our study was limited by the fact that we did not have FeNO data available for all patients.

Our study has many strengths. It is one of the largest real-world studies on effectiveness of biologics in severe asthma in the United States, which not only includes all classes of biologics but also evaluates effectiveness of switching between various different biologics instead of a single biologic switch. We also looked for predictors of treatment response. Our follow-up period of 1 year was also longer than most other similar studies.[22,24,27,29]

There are several limitations to our study. This is a retrospective study and affected by the limitations of a retrospective single-center study. Our patient cohort was less diverse. We had FeNO data available for only 40% of the patients. The follow-up was less than 12 months for 8% of the patients.

In summary, asthma biologics can significantly improve disease control in a real-world clinic setting. Further study of the determinants of response to individual biologics will help in targeting the right drug to the right subjects with severe asthma.

Supplementary Data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.anai.2021.08.416.

References

1. Chung KF, Wenzel SE, Brozek JL, et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *Eur Respir J*. 2014;43 (2):343–373.
2. Hekking P-PW, Wener RR, Amelink M, Zwinderman AH, Bouvy ML, Bel EH. The prevalence of severe refractory asthma. *J Allergy Clin Immunol*. 2015;135(4):896–902.
3. Alhossan A, Lee CS, MacDonald K, Abraham I. "Real-life" effectiveness studies of omalizumab in adult patients with severe allergic asthma: meta-analysis. *J Allergy Clin Immunol Pract*. 2017;5(5):1362–1370.e2.
4. Canonica GW, Rottoli P, Bucca C, et al. Improvement of patient-reported outcomes in severe allergic asthma by omalizumab treatment: the real life observational PROXIMA study. *World Allergy Organ J*. 2018;11(1):33.
5. Normansell R, Walker S, Milan SJ, Walters EH, Nair P. Omalizumab for asthma in adults and children. *Cochrane Database Syst Rev*. 2014;1:(1):CD003559.
6. Milgrom H, Fick Jr RB, Su JQ, et al. Treatment of allergic asthma with monoclonal anti-IgE antibody. rhuMAb-E25 Study Group. *N Engl J Med*. 1999;341(26): 1966–1973.
7. Busse W, Corren J, Lanier BQ, et al. Omalizumab, anti-IgE recombinant humanized monoclonal antibody, for the treatment of severe allergic asthma. *J Allergy Clin Immunol*. 2001;108(2):184–190.
8. Soler M, Matz J, Townley R, et al. The anti-IgE antibody omalizumab reduces exacerbations and steroid requirement in allergic asthmatics. *Eur Respir J*. 2001;18 (2):254–261.
9. Ortega HG, Liu MC, Pavord ID, et al. Mepolizumab treatment in patients with severe eosinophilic asthma. *N Engl J Med*. 2014;371(13):1198–1207.
10. Bel EH, Wenzel SE, Thompson PJ, et al. Oral glucocorticoid-sparing effect of mepolizumab in eosinophilic asthma. *N Engl J Med*. 2014;371(13):1189–1197.
11. Pavord ID, Korn S, Howarth P, et al. Mepolizumab for severe eosinophilic asthma (DREAM): a multicentre, double-blind, placebo-controlled trial. *Lancet*. 2012;380 (9842):651–659.
12. Castro M, Zangrilli J, Wechsler ME, et al. Reslizumab for inadequately controlled asthma with elevated blood eosinophil counts: results from two multicentre, parallel, double-blind, randomised, placebo-controlled, phase 3 trials. *Lancet Respir Med*. 2015;3(5):355–366.
13. FitzGerald JM, Bleecker ER, Nair P, et al. Benralizumab, an anti-interleukin-5 receptor α monoclonal antibody, as add-on treatment for patients with severe, uncontrolled, eosinophilic asthma (CALIMA): a randomised, double-blind, placebo-controlled phase 3 trial. *Lancet*. 2016;388(10056):2128–2141.
14. Bleecker ER, FitzGerald JM, Chanez P, et al. Efficacy and safety of benralizumab for patients with severe asthma uncontrolled with high-dosage inhaled corticosteroids and long-acting β 2-agonists (SIROCCO): a randomised, multicentre, placebo-controlled phase 3 trial. *Lancet*. 2016;388(10056):2115–2127.
15. Nair P, Wenzel S, Rabe KF, et al. Oral glucocorticoid-sparing effect of benralizumab in severe asthma. *N Engl J Med*. 2017;376(25):2448–2458.
16. Wenzel S, Ford L, Pearlman D, et al. Dupilumab in persistent asthma with elevated eosinophil levels. *N Engl J Med*. 2013;368(26):2455–2466.
17. Wenzel S, Castro M, Corren J, et al. Dupilumab efficacy and safety in adults with uncontrolled persistent asthma despite use of medium-to-high-dose inhaled corticosteroids plus a long-acting β2 agonist: a randomised double-blind placebo-controlled pivotal phase 2b dose-ranging trial. *Lancet*. 2016;388 (10039):31–44.
18. Castro M, Corren J, Pavord ID, et al. Dupilumab efficacy and safety in moderate-to-severe uncontrolled asthma. *N Engl J Med*. 2018;378(26):2486–2496.
19. Bagnasco D, Milanese M, Rolla G, et al. The North-Western Italian experience with anti IL-5 therapy and comparison with regulatory trials. *World Allergy Organ J*. 2018;11(1):34.
20. Pelaia C, Busceti MT, Solinas S, Terracciano R, Pelaia G. Real-life evaluation of the clinical, functional, and hematological effects of mepolizumab in patients with severe eosinophilic asthma: results of a single-centre observational study. *Pulm Pharmacol Ther*. 2018;53:1–5.
21. Renner A, Marth K, Patocka K, Idzko M, Pohl W. Effectiveness of mepolizumab therapy in patients with severe eosinophilic asthma: Austrian real-life data. *Pulm Pharmacol Ther*. 2020;64: 101946.
22. Pertzov B, Unterman A, Shtraichman O, Shitenberg D, Rosengarten D, Kramer MR. Efficacy and safety of mepolizumab in a real-world cohort of patients with severe eosinophilic asthma. *J Asthma*. 2021;58(1):79–84.
23. Kavanagh J, Roxas C, Thomson L, et al. *Real-World 1 Year Effectiveness of Benralizumab in Severe Eosinophilic Asthma*. P89. Thorax; 2019:A38.
24. Di Bona D, Minenna E, Albanesi M, Nettis E, Caiaffa MF, Macchia L. Benralizumab improves patient reported outcomes and functional parameters in difficult-to-treat patients with severe asthma: data from a real-life cohort. *Pulm Pharmacol Ther*. 2020;64: 101974.
25. Wechsler ME, Peters SP, Hill TD, et al. Clinical outcomes and health-care resource use associated with reslizumab treatment in adults with severe eosinophilic asthma in real-world practice. *Chest*. 2021;159(5):1734–1746.
26. Kavanagh JE, Hearn AP, Dhariwal J, et al. Real-world effectiveness of benralizumab in severe eosinophilic asthma. *Chest*. 2021;159(2):496–506.
27. Mukherjee M, Forero DF, Tran S, et al. Suboptimal treatment response to anti-IL-5 monoclonal antibodies in severe eosinophilic asthmatics with airway autoimmune phenomena. *Eur Respir J*. 2020;56(4):2000117.
28. Drick N, Seeliger B, Welte T, Fuge J, Suhling H. Anti-IL-5 therapy in patients with severe eosinophilic asthma—clinical efficacy and possible criteria for treatment response. *BMC Pulm Med*. 2018;18(1):119.
29. Mümmler C, Munker D, Barnikel M, et al. Dupilumab improves asthma control and lung function in patients with insufficient outcome during previous antibody therapy. *J Allergy Clin Immunol Pract*. 2021;9(3):1177–1185.e4.
30. de Llano LAP, Cosío BG, Domingo C, et al. Efficacy and safety of reslizumab in patients with severe asthma with inadequate response to omalizumab: a multicenter, open-label pilot study. *J Allergy Clin Immunol Pract*. 2019;7(7):2277–2283.e2.
31. Liu MC, Chipps B, Munoz X, et al. Benefit of switching to mepolizumab from omalizumab in severe eosinophilic asthma based on patient characteristics. *Respir Res*. 2021;22(1):144.

Supplementary data

eTable 1
Biologic Switch Group (N = 29)

Previous biologic	New biologic
Mepolizumab (6)	Dupilumab (16)
Benralizumab (7)	
Omalizumab (2)	
Reslizumab (1)	
Mepolizumab (5)	Benralizumab (7)
Omalizumab (2)	
Omalizumab (6)	Mepolizumab (6)

eTable 3
Multivariate Logistic Regression Comparing Responders and Nonresponders

Effect	OR	*P* value
Ever smoker vs never smoker	0.01	.01
GERD vs no GERD	4.55	.06
Patients with eosinophil count ≥500 vs <500 cells/μL	1.24	.02
Baseline FEV1	1.05	.01

Abbreviations: FEV1, forced expiratory volume in 1 second; GERD, gastroesophageal reflux disease; OR, odds ratio.

eTable 2
Bivariate Analysis Comparing Responders and Nonresponders

Characteristics	Responders mean (N = 85)	Nonresponders mean (N = 24)	*P* value
Age (y)	57	54	.22
Female	49% (42/85)	66% (16/24)	.13
Never smoker	59% (50/85)	37% (9/24)	.06
Ever smoker	41% (35/85)	62% (15/24)	.06
BMI (kg/m^2)	32.91	33.5	.61
GERD	82% (70/85)	58% (14/24)	.01
Nasal polyposis	21% (18/85)	21% (5/24)	.9
Vocal cord dysfunction	13% (11/85)	21% (5/24)	.3
Blood eosinophil count (cells/μL)	664	468	.12
Blood eosinophil ≥500 cells/μL	65% (55/85)	37% (9/24)	.01
IgE (kU/L)	382	549	.42
Baseline FEV1 (L)	2.17	1.62	.01
Baseline FEV1 % predicted	72.8	55.38	<.01
Positive bronchodilator response[a]	21/52 (40%)	7/16 (44%)	.41
FENO (ppb)	39.85 (34/85)	43.10 (10/24)	.83
FENO ≥25 ppb	17/34	5/10	>.99
ACT	13.53	14.73	.44
Rate of clinically significant exacerbations	4.78	4.45	.88
Rate of severe exacerbation	1.6	2.1	.53
Patients on mOCS	45% (38/85)	37% (9/24)	.6
mOCS dose-mg prednisone equivalent	10	16.94	.19

Abbreviations: ACT, asthma control test; BMI, body mass index; FENO, fractional exhaled nitric oxide; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; ppb, parts per billion; GERD, gastroesophageal reflux disease; IgE, immunoglobulin E; mOCS, maintenance oral corticosteroid.
[a]An increase of ≥12% and ≥200 mL as an absolute value compared with a baseline in either forced expiratory volume at 1 second or FVC.