Patient Characteristics and Individualization of Biologic Therapy

Steven Draikiwicz, MD[1], John Oppenheimer, MD*

KEYWORDS

• Biologics • Patient characteristics • Asthma • Urticaria • Phenotypes

KEY POINTS

- An overview is provided of the current status of therapy for outlined disease states and the role for biologic therapy in treatment.
- Current literature is reviewed regarding studied patient characteristics and the effect on outcome in patients with asthma and urticaria.
- The need for appropriate patient phenotyping is identified and guidance on evidence-based biologic selection is provided.

INTRODUCTION

Progress in the understanding of disease processes has provided additional therapeutic targets. This progress is best exemplified by the increasing role of biologics in the clinical armamentarium. Biologic agents are therapeutics synthesized by living organisms and directed against a specific determinant.[1] This article provides a focused review of current treatment paradigms and pathophysiology for asthma and urticaria. A table highlighting the mechanisms of action of individual therapeutics is presented after each section in which they are introduced. The goal is to elucidate for practicing physicians the populations in which biologics were studied for the aforementioned disease states, emphasizing characteristics to consider when selecting therapy.

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Division of Allergy and Immunology, New Jersey Medical School, Newark, NJ, USA
[1] Present address: 57 Mounthaven Drive, Livingston, NJ 07039.
* Corresponding author. Pulmonary and Allergy Associates, 1 Springfield Avenue, Summit, NJ 07901, USA.
E-mail address: nallopp@optonline.net

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ASTHMA

Asthma is an ongoing public health concern with more than 24 million individuals, approximately 7.3% of the total population, affected in the United States and an increase in prevalence between 2001 and 2010.[2,3] Total incremental cost of asthma in the United States was estimated to be $56 billion in 2007.[4] Current National Heart Blood and Lung Association and Global Initiative for Asthma guidelines recommend a stepwise approach to therapy.[5,6] Even with adherence to guideline therapy, including combination inhaled corticosteroids (ICS) and long-acting beta-agonist (LABA) therapy, as many as 50% of patients may continue to have suboptimal control.[7,8] Suboptimal control has been associated with lower physical and mental health–related quality of life, increased health care use, lower overall work productivity, and activity impairment.[9]

Studies show that a significant amount of uncontrolled asthma can be attributed to lack of adherence to prescribed therapy. Although approximately 60% to 70% of patients evaluated in an acute care setting fill initial prescriptions for asthma medication, one study suggests that only 14% to 16% of patients may maintain satisfactory ($\geq$80% medication availability) adherence over a 6-month period.[10,11] Beyond intentional nonadherence, failure of medication delivery may affect as many as 40% to 80% of adherent asthmatics because of inappropriate inhaler technique (nonintentional nonadherence).[12,13] Attaining control may also be impeded by obesity, active smoke exposure, allergies, psychiatric conditions, low socioeconomic status, as well as other underlying health conditions.[14,15] Accounting for these comorbidities still leaves approximately 10% or less of asthmatics on appropriate therapy who continue to have severe refractory asthma.[16] Severe asthma is classified as asthma that requires treatment with high-dose ICS plus a second controller and/or systemic corticosteroids to prevent it from becoming uncontrolled or that remains uncontrolled despite this therapy.[17] Patients with severe or difficult-to-treat asthma have higher health care use, with research showing as much as 3 times the direct medical costs and 10 times greater indirect medical costs compared with mild asthma.[18] Taken together, these patients may account for approximately 50% of direct expenditure on asthma care.[19]

Advances in the understanding of the pathophysiology of asthma have revealed that asthma is a heterogeneous disorder.[20] Multiple subgroups have been identified within the severe asthma population, which can further be stratified into specific phenotypes and endotypes.[21] The goal of phenotyping is to correlate cellular and clinical features with individual patient disease characteristics in an attempt to improve the choice of therapy.[22] Coinciding with the better understanding of the pathophysiology of asthma, the advent of immunomodulatory biologic therapy has emerged as a potential treatment option for individuals with severe refractory asthma. Omalizumab was the first monoclonal antibody approved for treatment in asthmatics in 2003, followed by mepolizumab in 2015, and reslizumab in March 2016. Multiple additional biologics are under study and are likely soon to be available for use in severe asthmatics. Choosing the optimal individual biologic requires a thorough understanding of the severe asthmatic's clinical characteristics and correlating with the patient's phenoendotype.

ASTHMA PHENOTYPING

The severe asthma phenotype characteristically has a reduced or refractory response to corticosteroid therapy.[23] Although there is no current biomarker to definitively delineate this group of individuals and classification depends on clinical course, to optimize the likelihood of clinical efficacy of biologic therapy additional phenotyping is required. Many different phenotypes of asthma have been described, including classifications