Management of Uncontrolled Asthma: A Framework for Novel and Legacy Biologic Treatments

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Abstract: Asthma continues to be a complex respiratory disease to control for many despite optimal standard inhaler therapy. The increased dependence on steroid-sparing biologic treatments in the 21st century has created a dilemma between identifying the patient’s intrinsic biomarkers and their “life markers.” With Tezepelumab being the most recent FDA-approved biologic for asthma, it is even more critical for asthma specialists to better understand and establish a framework to determine which biologic would work best for their patients. While cost and payor approvals limit access to certain asthma biologics, medical decisions on which biologic to select should be centered around shared decision-making, the rationale for biologic initiation, and critical biologic education to help achieve successful asthma control.

Keywords: severe asthma, Tezepelumab, asthma biologic, shared decision making, asthma

Introduction

Asthma is a heterogeneous disease with varying degrees of airway inflammation and airflow limitation that affects 1–18% of the population in different countries.¹,² Of those with asthma, refractory disease can range from 5% to 10%. Unfortunately, this group of refractory asthmatics also disproportionately contributes significantly to the overall economic and healthcare burden on the total cost of asthma.³ To address this disparity and provide best practice evidence-based recommendations and guidelines, NAEPP (National Asthma Education and Prevention Program) and GINA (Global Initiative for Asthma) were formed.²,⁴,⁵ With the help of NAEPP and GINA, most asthmatics are well controlled with conventional pharmacotherapy of inhaled corticosteroids combined with long or short-acting B-agonist bronchodilators (LABA or SABA) or long-acting muscarinic antagonists with the occasional addition of leukotriene antagonists (LTRAs). However, for those with severe refractory disease, these current modalities are not sufficient to control their asthma. Gaps in medical knowledge, deficiencies in the identification of severe asthma, barriers to clinical restraints in coordination, integration, resources, and access to bronchial thermoplasty (BT) as well as advanced treatments in legacy and novel asthma biologics (ie, Tezepulumab)⁶ could all be contributing factors as to why control of severe asthmatics continues to be problematic. Therefore, a framework for understanding, discussing, and determining the best treatment options is critical, especially for biologics. While there are many new biologics in the pipeline for asthma, the same framework should hold true for other novel biologics as they become available. In addition to the framework, in this paper, we will review the prospects for treating severe refractory asthmatics with a novel biologic agent (ie, Tezepelumab).

Understanding Phenotyping and Endotyping in Asthma

Asthma historically was thought to manifest as two major phenotypes, non-atopic or “non-allergic” asthma, and atopic or “allergic” asthma. Most prevalent was early-onset atopic asthma which was typically seen during childhood and into young adulthood. Evidence has shown that non-atopic asthma predominates among older age groups.⁷ Additional asthma phenotypes were also identified based on age of onset, asthma triggers, disease severity,
exacerbations, and airflow limitation. A significant limitation with this approach arose because distinguishing groups based on observation was complex, overlap exists between clinical phenotypes and it does not address the underlying pathobiology.

While the historical idiom of “what you see is what you get” is great to help identify the variable clinical presentations of asthmatics (phenotype), it still falls short of defining the specific mechanistic pathway (endotype) that leads to the phenotypic presentation. Understanding these mechanistic pathways is critical to asthma management due to their therapeutic and prognostic implications.

Endotyping in asthma was once deep-rooted in understanding that CD4+ T-cell responses are heterogenous and promote many inflammatory pathways. More importantly, within the subsets of T-helper1 (Th1) and T-helper2 (Th2) subpopulations, it was once accepted that Th2 cells were the principal driver of airway inflammation by generating interleukins (IL), more specifically IL-4, IL-5, and IL-13.

It is now better understood as Type 2 inflammation since various cell types can also produce the characteristic and key cytokines (IL-4, IL-5, IL-13), which are often produced by the adaptive immune system on recognizing allergens.

In addition to Th2-driven airway inflammation, group 2 innate lymphoid cells (ILC2) have also been found to play a critical role in type 2 immune responses that do not participate in the classic allergen-specific activation. ILC2 also produces vast amounts of prototypic type 2 cytokines, IL-5 and IL-13, which are found to be widespread within lung tissue and are mediated by alarmins. ILC2 mediated inflammation occurs when airway epithelial cells release alarmins in response to stressors (ie, infection, noxious irritation) or inflammation. ILC2 appears to play an early and critical role in augmenting asthma’s type 2 (T2) responses. This mechanistic pathway highlights the intimate connection between the adaptive and innate immunity.

The body’s first line of defense in asthma or innate immune pathway is the airway epithelium, which is complex and dynamically orchestrates the immune responses in T2 asthma. Previous studies have shown that asthmatic airways have dysregulated airway epithelial barriers. Dysfunction in barrier integrity caused by damage from various inhaled noxious stimuli results in access to stromal tissue by allergens and microbes, which is integral to asthma pathogenesis. Damaged airway epithelium also releases innate immune cytokines known as alarmins (TSLP, IL-25, IL-33). These airway epithelium cytokines initiate multiple T2 pathways in response to allergen and infection-driven inflammation. IL-33 and IL-25 are known to mainly activate ILC2s. Thymic stromal lipoproteins (TSLP), on the other hand, have been shown to promote antigen-presenting cells (APCs) that lead to the activation of T cells and B cells.

In addition to the more commonly mentioned T2 cytokines, IL-25, IL33 and TSLP should also be recognized in the pathogenesis of inflammatory airway diseases. Elevated bronchial mucosal expression of TSLP could be found in some subsets of asthma and COPD, both heterogeneous conditions with the overlapping features, with increased expression correlating with severity. Understanding asthma phenotype and endotype is essential as asthma biologic treatments continue to grow even though commercially available endotype testing is not yet readily available. Therefore, it is foundational for asthma specialists to comprehend the inflammatory pathophysiology and the pathway targeted by each asthma biologic (see Table 1).

**Why is Shared Decision-Making Critical for All Asthmatic Patients? First, Identify the “Life Markers” of All Asthmatics**

Shared decision-making (SDM) is important in the treatment plan for all asthmatics (ie, understanding asthma, inhaler technique, and adherence to treatment plan). This is especially crucial since the severity of the disease is defined by the level of treatment required to maintain asthma control and depends on the patient’s understanding and adherence to therapy. In a survey of 300 patients who attended an allergy clinic, 53% indicated they had searched online for allergy information before their consultation. Asthmatic patients are becoming more aware of their therapy regimens. In the era of personalized medicine, patient-centered asthma care should not be implemented without going beyond the phenotypic biomarkers and exploring a patient’s needs, values and preferences. The combination of the aforementioned has been previously published as “life-markers” and should be addressed with all asthmatics early and throughout their asthma journey.
When and Why Should the Discussions About Biologics Occur, and What Should the Biologic Discussion Entail?

While the majority of asthmatics can be managed with inhalers that contain ICS with LABA, long-acting anti-muscarinic (LAMA) and SABA,

Existing biologic therapies have been found to have a greater response among those with eosinophilic asthma (ie, blood eosinophil count of ≥300 cells/mL).

Unfortunately, approximately 50% of patients with severe asthma are non-eosinophilic and some patients with eosinophilic asthma respond suboptimally to standard therapy and the available biologic therapies or lose control of their asthma after an initial response.

Because of these reasons, discussions with patients on biologic options should occur very early on when first establishing care with asthma specialists. Then, it should continue throughout their lifelong asthma journey, especially if their symptoms are not well uncontrolled.

Asthmatic Patients Should Understand the Rationale for Biologics

Since the 1950s, oral corticosteroids (OCS) have been the preferred treatment for acute asthma exacerbations. Previous publications have demonstrated the effectiveness of OCS for treating asthma exacerbations, reducing relapses, lowering short-acting beta2-agonist (SABA) use, and decreasing hospital admissions. There are also overwhelming data that show repeated and continued OCS use is a major cause of serious drug-related adverse effects (AE), contributes to significant morbidity and substantially increases healthcare costs.

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**Table 1 Available Asthma Biologic Therapies**

<table>
<thead>
<tr>
<th>Asthma Biologic Therapy</th>
<th>FDA Approval</th>
<th>Mechanism of Action</th>
<th>Asthma Exacerbation</th>
<th>Lung Function</th>
<th>Corticosteroid Weaning</th>
<th>SQ and IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omalizumab</td>
<td>2003</td>
<td>Anti-IgE; binds to IgE</td>
<td>Reduces by ~25%</td>
<td>Minimal or equivocal improvement</td>
<td>Decreases use of ICS</td>
<td>Subcutaneous Every 2–4 weeks</td>
</tr>
<tr>
<td>Mepolizumab</td>
<td>2015</td>
<td>Anti–IL-5; binds to IL-5 ligand</td>
<td>Reduces by ~50%</td>
<td>Nominal improvement</td>
<td>Decreases total use of OCS and has been shown to facilitate complete weaning from chronic OCS (14%)</td>
<td>Subcutaneous every 4 weeks</td>
</tr>
<tr>
<td>Reslizumab</td>
<td>2016</td>
<td>Anti–IL-5; binds to IL-5 ligand</td>
<td>Reduces by ~50–60%</td>
<td>Improved</td>
<td>Has not been specifically evaluated for this indication</td>
<td>Intravenous every 4 weeks</td>
</tr>
<tr>
<td>Benralizumab</td>
<td>2017</td>
<td>Anti–IL-5; binds to IL-5 receptor α</td>
<td>Reduces by ~25–60%</td>
<td>Improved</td>
<td>Decreases total use of OCS and has been shown to facilitate complete weaning from chronic OCS (50%)</td>
<td>Subcutaneous every 4 weeks for 3 doses then every 8 weeks</td>
</tr>
<tr>
<td>Dupilumab</td>
<td>2018</td>
<td>Anti–IL-4R; binds to IL-4 receptor α</td>
<td>Reduces by ~50–70%</td>
<td>Improved</td>
<td>Decreases total use of OCS and has been shown to facilitate complete weaning from chronic OCS (50%)</td>
<td>Subcutaneous every 2 weeks</td>
</tr>
<tr>
<td>Tezepelumab</td>
<td>2021</td>
<td>Anti-TSLP; binds to TSLP ligand</td>
<td>Reduces by ~50 – 70%</td>
<td>Improved</td>
<td>Did not demonstrate a statistically significant reduction in maintenance OCS dose compared with placebo.</td>
<td>Subcutaneous every 4 weeks</td>
</tr>
</tbody>
</table>


**Abbreviations:** IgE, immunoglobulin; IL, interleukin; ICS, inhaled corticosteroids; TSLP, thymic stromal lymphopoietin; OCS, oral corticosteroids; SQ, subcutaneous; IV, intravenous; FDA, Federal Drug Administration.
Patients who cannot achieve asthma control despite being on maximal ICS combination therapy and LTRAs often experience multiple asthma exacerbations requiring continued or repeated courses of OCS. Over the past decade, an improved understanding of the complex pathophysiology of asthma has led to the development of new treatment options for asthma. Today, patients with uncontrolled severe asthma are routinely considered for steroid-sparing treatments such as biologic therapies as well as bronchial theromplasty.

It is also important to highlight that the majority of the randomized controlled trials on biologics in patients with uncontrolled severe asthma have demonstrated a significant response to placebo with reductions in exacerbations, improvement in lung function, and improvement in patient-reported outcomes. It suggests that some asthmatics are not intrinsically severe but often poorly controlled and would benefit from the following: Improving affordability, availability, and accessibility to ICS combination therapy, as well as emphasizing the principles of asthma management, such as shared decision-making, encouraging adherence, good inhaler technique, and allergen avoidance, are sufficient to control symptoms and prevent asthma exacerbations.

**Critical Biologic Administration Information for the Asthma Specialist and Patient**

**Understanding Types of Injectors (Prefilled vs Autoinjector)**

A prefilled syringe is a single dose disposable syringe that contains medication to which a needle has been fixed by the manufacturer. Autoinjector syringes are similar to prefilled syringes but are designed to help self-administration with the assistance of a spring-loaded syringe. With the advent of 6 asthma biologics, preference for injector type can vary among the available options. It is difficult to conclude which injection type is superior, but there is growing evidence to support that patients prefer autoinjector syringes, in addition to minimal errors occurring when using autoinjectors (See Table 2).

**Injection Site**

Injection sites for asthma biologics can vary (typically in the arms, abdomen, and thighs). Still, it ultimately depends on the patients’ preference for injection and the route of administration (ie, intravenous, subcutaneous). These are all critical points for education and could also assist in achieving better compliance and tolerance. Asthma specialists should also be familiar with the various approved regions for subcutaneous biologic injections (see Table 2). Arm injections can be challenging to perform without the help of a family member, especially in rheumatologic/arthritic or neurologic conditions (ie, tremor). These conditions cause impediment to choosing a self-administration option and will need to be considered in the overall choice of an asthma biologic. This is a key “life marker” point that is often missed without exploring if someone is available to assist the patient with arm injections.

**Biologic Temperature Considerations and Expiration Countdown**

Additional critical information that asthma specialists and patients should be aware of are the varying recommended time for asthma biologic medications to warm up before administration, maximum storage temperature after being taken out of the refrigerator, and how long a biologic medication can be stored at room temperature. Air conditioning may be scarce in high-temperature regions with low socioeconomic status, and during hot months room temperatures may exceed asthma biologics’ recommended maximum room temperature. While it is not clear on the effectiveness of a biologic that has exceeded the manufacturer’s recommended room temperature (see Table 2), this may result in suboptimal biologic responders. Another knowledge gap of high importance is the manufacturer time for how long a biologic can be stored at room temperature before injection. This time frame can range from 2 to 30 days. Finally, with the growing number of approved asthma biologics, asthma specialists and patients will need to focus more on when a biologic medication will expire after being taken out of the refrigerator. Although, the majority of patients should be instructed to keep their biologic medication in the fridge until it is time for their injection, there will likely be some patients that will take their biologic medication on trips, may have prematurely taken their biologic medications out of the refrigerator or...

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**Table 2**

<table>
<thead>
<tr>
<th>Injection Site</th>
<th>Critical Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arms</td>
<td>Preference for injection</td>
</tr>
<tr>
<td>Abdomen</td>
<td>Assistance of a family member</td>
</tr>
<tr>
<td>Thighs</td>
<td>Pain management</td>
</tr>
</tbody>
</table>

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**References**

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forgot to administer their biologic medication. Asthma specialists and clinic staff will also likely receive questions from patients seeking advice on whether their biologic medication is effective after so many days of being outside the refrigerator. Patients may inadvertently inject biologic medications that have gone past the recommended time after being thawed to room temperature. This will be especially problematic for patients during biologic switches. The importance of proper inhaler technique and adherence is still a priority in asthma care, but so should biologic knowledge, technique, and adherence. Without asthma specialists knowing these nuances which will likely be complicated further due to payor and coverage on the route of biologic administration, it will be much more difficult for patients to understand and adhere to proper biologic techniques.

### Table 2 Critical Biologic Administration Information

<table>
<thead>
<tr>
<th>Asthma Biologic Therapy</th>
<th>Type of Injector</th>
<th>Region for Injection</th>
<th>Room Temperature-Time Recommendations</th>
<th>Biologic Expiration after Being at Room Temperature</th>
<th>Home Storage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omalizumab</td>
<td>Prefilled Syringe</td>
<td>Front and middle of the thighs and the stomach area (abdomen). The outer area of the upper arms may also be used if a caregiver is giving the injection.</td>
<td>Set aside the carton for at least 13 to 30 minutes so the prefilled syringe can warm up on its own to room temperature.</td>
<td>The total combined time out of the refrigerator may not exceed 2 days. If the prefilled syringe is exposed to temperatures above 77 °F (25 °C), do not use it and throw it away in a sharps disposal container.</td>
<td>Store in the refrigerator between 36°F and 46°F (2°C to 8°C).</td>
</tr>
<tr>
<td>Mepolizumab</td>
<td>Autoinjector and Prefilled Syringe</td>
<td>Front and middle of the thighs and the stomach area (abdomen). The outer area of the upper arms may also be used if a caregiver is giving the injection.</td>
<td>Wait 30 minutes (and no more than 8 hours) before use.</td>
<td>If necessary, an unopened carton can be stored outside the refrigerator at up to 86°F (30°C) for up to 7 days.</td>
<td>Store in the refrigerator between 36°F to 46°F (2°C to 8°C).</td>
</tr>
<tr>
<td>Reslizumab</td>
<td>Not available for home administration</td>
<td>Intravenous, is given in a clinic or infusion center</td>
<td>N/a</td>
<td>N/a</td>
<td>N/a</td>
</tr>
<tr>
<td>Benralizumab</td>
<td>Autoinjector and Prefilled Syringe</td>
<td>Front and middle of the thighs and the stomach area (abdomen). The outer area of the upper arms may also be used if a caregiver is giving the injection.</td>
<td>Warm-up at room temperature between 68°F to 77°F (20°C to 25°C) for about 30 minutes before giving the injection</td>
<td>May be kept at room temperature between 68°F to 77°F (20°C to 25°C) for a maximum of 14 days.</td>
<td>Store in the refrigerator between 36°F to 46°F (2°C to 8°C).</td>
</tr>
<tr>
<td>Dupilumab</td>
<td>Autoinjector and Prefilled Syringe</td>
<td>Front and middle of the thighs and the stomach area (abdomen). The outer area of the upper arms may also be used if a caregiver is giving the injection.</td>
<td>Let it naturally warm to room temperature for at least 45 minutes.</td>
<td>It may be stored at room temperature up to 77°F (25°C) up to 14 days.</td>
<td>Store in the refrigerator between 36°F to 46°F (2°C to 8°C).</td>
</tr>
<tr>
<td>Tezepelumab</td>
<td>Prefilled Syringe</td>
<td>Front and middle of the thighs and the stomach area (abdomen). The outer area of the upper arms may also be used if a caregiver is giving the injection.</td>
<td>Allow it to reach room temperature. This generally takes 60 minutes.</td>
<td>May be kept at room temperature between 68°F to 77°F (20°C to 25°C) for a maximum of 30 days</td>
<td>Store in the refrigerator between 36°F to 46°F (2°C to 8°C).</td>
</tr>
</tbody>
</table>

Abbreviations: F, Fahrenheit; C, Celsius.
Novel Asthma Biologic: Tezepelumab
Mode of Action of Tezepelumab

Thymic stromal lymphopoietin (TSLP) is a commonly overexpressed cytokine in asthmatics responsible for the inflammatory response seen in asthma. Predominant in lung epithelial cells, TSLP exerts its biological effects through binding high-affinity heteromeric receptor complexes of TSLPR and IL-7 receptor α. Once expressed, TSLP induces the release of cytokines and chemokines, activation of functional T-helper type 2 cells, and eosinophils, mediating a broad range of immunological pathologies pertaining to asthma. As TSLP has been shown to play a relevant role in mediating the asthma response, Tezepelumab was developed as a human monoclonal antibody anti-TSLP that advantageously binds to TSLP. Upon the binding of Tezepelumab to TSLP, Tezepelumab, while not necessarily resulting in a conformational change of TSLP, does result in the blockage of the required binding site relevant to asthma pathologies. This high-affinity binding of Tezepelumab to TSLP occurs via its variable heavy-chain domain. Consequently, it inhibits the formation of the TSLP receptor complex necessary for the pathological responses prevalent in asthmatics. More specifically, Tezepelumab actively inhibits the dendritic cell maturation as well as chemokine production responsible for inflammatory cell trafficking into tissue.38

Tezepelumab Clinical Trials

As Tezepelumab becomes more prevalent as a potential biologic therapy to combat severe uncontrolled asthma, there have been various Phase 2 and 3 trials to evaluate the safety and efficacy of Tezepelumab in patients. First, the PATHWAY study was established as a phase 2b trial to analyze patient-reported outcomes after administration of a subcutaneous dosage of Tezepelumab. Patient-reported outcomes (PROs) were assessed through reports of asthma control from the Asthma Control Questionnaire-6, health-related quality of life from the Asthma Quality of Life Questionnaire (standardized) for patients aged 12 years or older, as well as daily asthma-related health issues from the Asthma Daily Diary questionnaire. An analysis of responses from PROs, the PATHWAY study indicates that treatment with Tezepelumab reduced the exacerbation median time to first well-controlled or partially controlled asthma and improved daily asthma-related health issues compared to baseline. However, due to the nature of this study, the PROs may not be reflective of the true treatment benefit.39

In response, a pivotal Phase 3 trial was designed to investigate further and build on the observations gained from the previous studies. This study, NAVIGATOR, is a phase 3 trial with the primary objective of assessing Tezepelumab's effect on asthma exacerbations via the annualized asthma exacerbation rate (AAER). Additionally, the effects on PROs, type 2 inflammatory biomarkers, asthma control, and patient health status were assessed. Overall, the NAVIGATOR study demonstrated that administration of Tezepelumab resulted in a significantly reduced annualized rate of asthma exacerbations as well as significant improvements in forced expiratory volume in one second, PROs, and reductions in exacerbations resulting in hospitalization.19 Thus, confirming the findings established in the PATHWAY study.39 In further examinations, Tezepelumab shows promise in reducing blood eosinophil count and levels of FENO and IgE, indicating inhibition of the inflammatory response and suppression of TSLP. There were no significant reported difference in the frequency or type of adverse events compared to the placebo groups in both the NAVIGATOR and PATHWAY studies. With regard to the safety profile of Tezepelumab, there were no reports of treatment-related anaphylactic reactions or development of neutralizing antibodies.19,40,41

SOURCE is yet another phase 3 trial analyzing the effects of Tezepelumab in asthma patients. However, this trial focuses on using oral corticosteroids (OCS) to treat severe asthma and asthma exacerbations and how Tezepelumab may lead to OCS dose reduction, and determining Tezepelumab’s efficacy in reducing asthma exacerbations via AAER. An analysis of data found that although the use of Tezepelumab in treatment for patients diagnosed with OCS-dependent asthma did reduce AAER, it did not result in a significant reduction in OCS dosage compared to placebo.42 Additionally, one other Phase 4 extension trial (initially started as a phase 3 trial prior to Tezepelumab FDA approval), DESTINATION, aims to examine the long-term effect and safety of Tezepelumab. With the primary criteria of having completed the NAVIGATOR and SOURCE studies, patients enrolled in DESTINATION will continue to receive administration of Tezepelumab over an additional one-year period. The long-term effects of Tezepelumab will be assessed via adverse events (AEs), AEs of particular interest, and serious AEs. Subjects previously randomized in one
of the predecessor studies to Tezepelumab will be assigned and remain on Tezepelumab dosing in the DESTINATION study. Subjects randomized to the placebo arm in the predecessor studies will be re-randomized in a 1:1 ratio to either Tezepelumab or placebo. Given the randomization scheme of subjects in the predecessor studies, this will result in an overall subject distribution of 3:1 (Tezepelumab: placebo), assuming a similar number of subjects rollover from each arm in the predecessor studies. An additional extended follow-up period will be assessed following treatment cessation to investigate any improvements in lung function and changes in blood eosinophil count, FENO levels, and IgE. At this time, there are no results available for DESTINATION.43

Where Does Tezepelumab Fit in the Biologic Treatments for Asthma?
Prior to the approval of Tezepelumab, various asthma biologics have been used to downregulate the pathological effects of asthma. These have included, but are not limited to, anti-IgE, anti-IL5, anti-IL4, and anti-IL13 biologics. On the other hand, Tezepelumab directly binds and inhibits upstream TSLP, thus preventing the induction of numerous downstream targets. In reviewing the National Asthma Education and Prevention Program (NAEPP) step guidelines for asthma management, asthma biologics should be considered in a treatment plan during steps 5 and 6 for individuals ages 12 and older, with discussions about biologics occurring much sooner. In addition to NAEPP, Global Initiative for Asthma (GINA) step guidelines for asthma management and prevention, it is noted that anti-IgE, anti-IL5, anti-IL4, and anti-IL13 are recommended to be added to the treatment plan during step 5, which would also apply for Tezepelumab.1,2,5

Conclusion
Patients who suffer from asthma typically respond well to standard inhaler therapy and do not need asthma biologics to control their asthma. Unfortunately, some asthmatics continue to suffer despite being adherent to their inhaler regimen that should be considered for biologic therapy. Informing and educating patients about biologic treatments early in their asthma journey is essential and can help identify “life markers” that could be barriers to specific biologic therapy. In recognizing patients who have severe uncontrolled asthma with luminal obstruction and asthma severity predominantly mediated by eosinophils, anti–IL-5 mAbs are the therapy of choice. In moderate-to-severe asthmatic patients with severity driven by mucus production, eosinophils, and smooth muscle contraction and remodeling, an anti–IL-4R mAb may be the therapy of choice. Severe asthmatic patients who are clearly atopic driven by elevated IgE are candidates for anti-IgE therapy; however, anti–IL-5 mAbs have also been effective in these patients as well and have beneficial effects on lung function.32 In severe asthmatics that have luminal obstruction with non-eosinophilic or T2-low disease, anti-TSLP mAb should be considered as a therapy of choice.40 The early identification of biomarkers, “life-markers,” and biologic discussions will help facilitate an earlier initiation of biologics in hopes of altering the disease progression of asthma. In addition to the aforementioned, the success of biologics in controlling asthma will depend not only on adherence to inhaler therapy and biologic therapy but also on asthma specialists and patients having an in-depth understanding of proper biologic administration and the nuances of each biologic (see Table 2).

Disclosure
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