Transcript Details

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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

A Look at Allergic Asthma and a Potential Treatment Option

Announcer:
Welcome to ReachMD. This medical industry feature, titled “A Look at Allergic Asthma and a Potential Treatment Option” is sponsored by Novartis Pharmaceuticals Corporation and Genentech. This program is intended for healthcare professionals.

Here’s your host, Dr. Charles Turck.

Dr. Turck:
This is ReachMD, and I'm Dr. Charles Turck. Joining me today to discuss allergic, or IgE-mediated asthma and treatment with XOLAIR, or omalizumab, is Dr. Sridhar Reddy and Dr. Stanley Goldstein. Dr. Reddy is chief medical officer at Lake Huron Medical Center in Port Huron, Michigan. Dr. Goldstein is an allergy and asthma specialist with Allergy and Asthma Care of Long Island in Rockville Center.

Dr. Reddy and Dr. Goldstein, thanks for being here to share your insights on how we help manage moderate to severe allergic asthma, sometimes known as IgE-mediated asthma, in patients who are not adequately controlled on inhaled corticosteroids.

Dr. Reddy:
Thank you. Happy to be here.

Dr. Goldstein:
Thanks for having me.

Dr. Turck:
Before we begin, let's take a moment to review some important safety information for XOLAIR.

Announcer:
INDICATION

XOLAIR® (omalizumab) is indicated for adults and pediatric patients 6 years of age and older with moderate to severe persistent asthma who have a positive skin test or in vitro reactivity to a perennial aeroallergen and whose symptoms are inadequately controlled with inhaled corticosteroids.

Limitations of Use: XOLAIR is not indicated for the relief of acute bronchospasm, status asthmaticus, or for treatment of other allergic conditions.

IMPORTANT SAFETY INFORMATION

WARNING: Anaphylaxis
Anaphylaxis presenting as bronchospasm, hypotension, syncope, urticaria, and/or angioedema of the throat or tongue, has been reported to occur after administration of XOLAIR. Anaphylaxis has occurred as early as after the first dose of XOLAIR, but also has occurred beyond 1 year after beginning regularly administered treatment. Because of the risk of anaphylaxis, initiate XOLAIR therapy in a healthcare setting and closely observe patients for an appropriate period of time after XOLAIR administration. Health care providers administering XOLAIR should be prepared to manage anaphylaxis which can be life-threatening. Inform patients of the signs and symptoms of anaphylaxis and instruct them to seek immediate medical care should symptoms occur. Selection of patients for self-administration of XOLAIR should be based on criteria to mitigate risk from anaphylaxis.

Dr. Turck:

I want to start by discussing XOLAIR's time on market. Considering how many biologics have become available over the years in the respiratory space, how has XOLAIR, which was approved about 17 years ago in patients 12 and older, managed to stay relevant in treating patients with allergic, or IgE-mediated asthma.

Dr. Reddy:
A key differentiator for XOLAIR is that it's the only FDA-approved biologic designed to inhibit IgE, which is a key driver of inflammation in patients 6 years and older with allergic asthma.

Dr. Goldstein:
Now, when you consider any type of treatment, efficacy and safety are extremely important. With respect to XOLAIR on the market, it has a well-documented safety profile within allergic asthma. And there are actually some big firsts for XOLAIR. It was the first biologic approved for the treatment of allergic asthma. It was the first biologic approved for the treatment of 6-year-olds who have uncontrolled asthma despite taking their inhaled corticosteroids. There's extensive world experience with using XOLAIR. It has been prescribed to over 300,000 allergic asthma patients. And also, it's the first asthma biologic to have completed a published pregnancy registry study.

Dr. Reddy:
You know, I'd also like to mention self-injection with XOLAIR. This was approved in 2021. We can determine if self-injection with XOLAIR prefilled syringe by the patient or administration by a caregiver is appropriate. And this is based on careful assessment of the risk of anaphylaxis and mitigation strategies allowing for the flexibility of administration that can be done outside of the healthcare setting.

Dr. Turck:
In regard to helping patients lower exacerbation risk with their allergic, or IgE-mediated asthma, how has XOLAIR had an impact on your practice?

Dr. Goldstein:
Well, when I consider treating allergic asthma, I want to consider two very important facts. I want to consider the mechanism of the disease. In other words, what is driving that airway inflammation? And that is what we know as the endotype. And at the same time, I want to consider the mechanism of action of what we want to use. In this case, we're talking about the mechanism of action of XOLAIR. So, we now understand that IgE is a key driver of inflammation in allergic asthma. So, here we have an IgE-mediated disease, and XOLAIR is an IgE targeted treatment. It's designed to block IgE, and it blocks IgE regardless of eosinophil counts, whether they're high or low.

Dr. Reddy:
Agree, Dr. Goldstein. To expand on the mechanism of action of XOLAIR, I'd like to add the preclinical evidence behind its mechanism of action. With XOLAIR's inhibition of IgE-mediated inflammation, we see reduced blood and tissue eosinophils as well as reduction in inflammatory mediators, including interleukin-4, interleukin-5, and interleukin-13.

Dr. Turck:
Let's move on to patient identification. How do you recognize if a patient's asthma is allergic or IgE-mediated and therefore, potentially appropriate for a treatment with XOLAIR?

Dr. Reddy:
In any of my asthma patients, I look for a treatable trait to essentially minimize side effects from other medications, but also decrease the risk of exacerbation. I always want to consider the possibility of IgE involvement. Allergic asthma is in fact the most common phenotype, affecting about 60% of the adult and adolescent patients 12 years and older, and 80% of pediatric patients ages 6 to 12. For these patients, sensitivity to one or more aeroallergens can put them at risk for exacerbation.

Dr. Goldstein:
What I'd like to know is, does my patient have other signs of allergic disease? And therefore, I may look at the comorbid conditions. Do they have allergic rhinitis? Another example of allergy. Do they have chronic rhinosinusitis, which also can be caused by allergic mechanisms. I want to know, is there a family history of allergy, because we know that runs in families. At the same time, I'm looking at their symptoms and exacerbations. I want to know if they are made worse when exposed to triggers. Now we know allergic triggers can include year-round allergens, such as dust mites, pet dander. At the same time, we know that allergic asthma can also be triggered by respiratory infections and environmental irritants. If these answers are yes, then I know I'm dealing with allergic asthma. And I lean forward to trying to help the patient understand why XOLAIR may be right for them.

Dr. Reddy:
A specific IgE level of more than 0.35 IUA/mL, which is international units, allergen-specific, supports an allergic asthma diagnosis. Allergen sensitivity is then confirmed using a skin or blood test. When you have a patient with sensitivity to one or more perennial

aeroallergens, a diagnosis of IgE-mediated asthma can be confirmed.

To figure out the XOLAIR dosing for adult allergic asthma patients, a total IgE level is performed. XOLAIR dosing starts at total IgE levels of 30 IU/mL, regardless of eosinophil levels.

Dr. Turck:
What other factors go into determining if your allergic asthma patients are appropriate XOLAIR candidates? Knowing XOLAIR has a black box warning for anaphylaxis, how do you balance the efficacy and safety of a biologic treatment? And what else do you consider before prescribing XOLAIR?

Dr. Reddy:
It really comes down to shared decision-making. I talk with my patients about how XOLAIR can help reduce their exacerbations from their IgE-mediated asthma. But I'm careful to balance that conversation by discussing the potential for adverse events.

Dr. Goldstein:
So, I'd like to echo that shared decision-making thought, Dr. Reddy, because we know many of our allergic asthma patients are of childbearing age, and we know that there are risks associated with poorly to moderately controlled asthma in pregnancy. And it's, therefore, important to consider the use of medications in select patients and review the risk information regarding exposure during pregnancy. There is a pregnancy registry study for XOLAIR, which is available in the prescribing information. It's important to note that the registry study cannot definitively establish the absence of any risk because of methodological limitations.

So, treatment modality is part of the conversation regarding shared decision-making. Once we have patients on established XOLAIR therapy, we now have the availability of a self-injection with a prefilled syringe. And it's important to consider in patients that you may deem appropriate for using this method, the self-injection prefilled syringe, so they can be treated at home. And having that flexibility is very important for our patients. The flexibility of at-home administration, but we want to make sure that these are appropriate patients for that consideration in prescribing treatment with XOLAIR at home.

Dr. Turck:
In closing, is there anything else you'd like to add?

Dr. Goldstein:
Yes, something very important when you think about allergic asthma. And as you've heard, we also know it as IgE-mediated asthma. So, number one, it's making that diagnosis. And healthcare providers have to understand that when you think about making a diagnosis of allergic asthma, you're looking at the specific IgE. What is that IgE that is indicating that they have allergic asthma? When you think about treatment, and you've decided they have allergic asthma, that's when you look at the total IgE, which helps in the dosing of XOLAIR. And we need to focus on the fact that the IgE is the key driver of inflammation in allergic asthma.

Dr. Reddy:
You know, as a patient advocate, I always look for a treatable trait to decrease the risk of exacerbation as well as the risk of adverse events and side effects of other medications. It's really about considering and focusing in on the IgE component of allergic asthma. XOLAIR is designed to inhibit IgE, which is a key driver of inflammation in patients with allergic asthma.

Dr. Turck:
It's a great perspective to round out our discussion on allergic, or IgE-mediated asthma and treatment with XOLAIR. I want to thank my guests, Dr. Reddy and Dr. Goldstein, for helping us better understand this important topic. Dr. Reddy, Dr. Goldstein, it was great speaking with you today.

Dr. Goldstein:
Thank you for having me today and letting me share my thoughts and insights on allergic asthma.

Dr. Reddy:
Thank you for having me today and giving me this opportunity to share my thoughts regarding allergic asthma.

Dr. Turck:
I'm Dr. Turck. And before we close, let's take a moment to review some important safety information for XOLAIR.

Announcer:
IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS
XOLAIR is contraindicated in patients with a severe hypersensitivity reaction to XOLAIR or to any ingredient of XOLAIR.

WARNINGS AND PRECAUTIONS

Anaphylaxis: Anaphylaxis has been reported to occur after administration of XOLAIR in premarketing clinical trials and in postmarketing spontaneous reports. In premarketing clinical trials in patients with asthma, anaphylaxis was reported in 3 of 3507 (0.1%) patients. Anaphylaxis occurred with the first dose of XOLAIR in two patients and with the fourth dose in one patient. The time to onset of anaphylaxis was 90 minutes after administration in two patients and 2 hours after administration in one patient.

A case-control study showed that, among XOLAIR users, patients with a history of anaphylaxis to foods, medications, or other causes were at increased risk of anaphylaxis associated with XOLAIR, compared to those with no prior history of anaphylaxis.

In postmarketing spontaneous reports, the frequency of anaphylaxis attributed to XOLAIR use was estimated to be at least 0.2% of patients based on an estimated exposure of about 57,300 patients from June 2003 through December 2006. Approximately 60% to 70% of anaphylaxis cases have been reported to occur within the first three doses of XOLAIR, with additional cases occurring sporadically beyond the third dose.

Initiate XOLAIR only in a healthcare setting equipped to manage anaphylaxis which can be life-threatening. Observe patients closely for an appropriate period of time after administration of XOLAIR, taking into account the time to onset of anaphylaxis seen in premarketing clinical trials and postmarketing spontaneous reports. Inform patients of the signs and symptoms of anaphylaxis, and instruct them to seek immediate medical care should signs or symptoms occur.

Once XOLAIR therapy has been established, administration of XOLAIR Prefilled Syringe outside of a healthcare setting by a patient or a caregiver may be appropriate for selected patients. Patient selection, determined by the healthcare provider in consultation with the patient, should take into account the pattern of anaphylaxis events seen in premarketing clinical trials and postmarketing spontaneous reports, as well as individual patient risk factors (e.g. prior history of anaphylaxis), ability to recognize signs and symptoms of anaphylaxis, and ability to perform subcutaneous injections with XOLAIR Prefilled Syringe with proper technique according to the prescribed dosing regimen and Instructions for Use.

Discontinue XOLAIR in patients who experience a severe hypersensitivity reaction.

Malignancy: Malignant neoplasms were observed in 20 of 4127 (0.5%) XOLAIR-treated patients compared with 5 of 2236 (0.2%) control patients in clinical studies of adults and adolescents (≥12 years of age) with asthma and other allergic disorders. The observed malignancies in XOLAIR-treated patients were a variety of types, with breast, non-melanoma skin, prostate, melanoma, and parotid occurring more than once, and five other types occurring once each. The majority of patients were observed for less than 1 year. The impact of longer exposure to XOLAIR or use in patients at higher risk for malignancy (e.g., elderly, current smokers) is not known.

A subsequent 5-year observational study of 5007 XOLAIR-treated and 2829 non-XOLAIR-treated adolescent and adult patients with moderate to severe persistent asthma and a positive skin test reaction or in vitro reactivity to a perennial aeroallergen found that the incidence rates of primary malignancies (per 1000 patient years) were similar in both groups (12.3 vs 13.0, respectively). Study limitations which include the observational study design, the bias introduced by allowing enrollment of patients previously exposed to XOLAIR (88%), enrollment of patients (56%) while a history of cancer or a premalignant condition were study exclusion criteria, and the high study discontinuation rate (44%) preclude definitively ruling out a malignancy risk with XOLAIR.

Acute Asthma Symptoms and Deteriorating Disease: XOLAIR has not been shown to alleviate asthma exacerbations acutely. Do not use XOLAIR to treat acute bronchospasm or status asthmaticus. Patients should seek medical advice if their asthma remains uncontrolled or worsens after initiation of treatment with XOLAIR.

Corticosteroid Reduction: Do not discontinue systemic or inhaled corticosteroids abruptly upon initiation of XOLAIR therapy for asthma. Decrease corticosteroids gradually under the direct supervision of a physician.

Eosinophilic Conditions: In rare cases, patients with asthma on therapy with XOLAIR may present with serious systemic eosinophilia, sometimes presenting with clinical features of vasculitis consistent with Churg-Strauss syndrome. These events usually, but not always, have been associated with the reduction of oral corticosteroid therapy. Physicians should be alert to eosinophilia, vasculitic rash, worsening pulmonary symptoms, cardiac complications, and/or neuropathy presenting in their patients. A causal association between XOLAIR and these underlying conditions has not been established.

Fever, Arthralgia, and Rash: In post-approval use, some patients have experienced a constellation of signs and symptoms, including arthritis/arthralgia, rash, fever, and lymphadenopathy with an onset 1 to 5 days after the first or subsequent injections of XOLAIR. These signs and symptoms have recurred after additional doses in some patients. Physicians should stop XOLAIR if a patient develops this constellation of signs and symptoms.

Parasitic (Helminth) Infection: Monitor patients at high risk of geohelminth infection while on XOLAIR therapy. Insufficient data are available to determine the length of monitoring required for geohelminth infections after stopping XOLAIR treatment.

Laboratory Tests: Due to formation of XOLAIR:IgE complexes, serum total IgE levels increase following administration of XOLAIR and may remain elevated for up to 1 year following discontinuation of XOLAIR. Do not use serum total IgE levels obtained less than 1 year following discontinuation to reassess the dosing regimen for asthma patients, because these levels may not reflect steady state free IgE levels.

ADVERSE REACTIONS

Asthma: In patients ≥12 years of age, the most common adverse reactions (≥1% more frequent in XOLAIR-treated patients) were: arthralgia (8%), pain (general) (7%), leg pain (4%), fatigue (3%), dizziness (3%), fracture (2%), arm pain (2%), pruritus (2%), dermatitis (2%), and earache (2%). In pediatric patients 6 to <12 years of age, the most commonly observed adverse reactions (≥3% more frequent in XOLAIR-treated pediatric patients) were: nasopharyngitis, headache, pyrexia , upper abdominal pain, pharyngitis streptococcal, otitis media, viral gastroenteritis, arthropod bite, and epistaxis.

Injection Site Reactions: In adults and adolescents with asthma, injection site reactions of any severity occurred at a rate of 45% in XOLAIR-treated patients compared with 43% in placebo-treated patients. Severe injection site reactions occurred more frequently in XOLAIR-treated patients compared with patients in the placebo group (12% vs 9%, respectively). The types of injection site reactions in asthma studies included: bruising, redness, warmth, burning, stinging, itching, hive formation, pain, indurations, mass, and inflammation.

Cardiovascular and Cerebrovascular Events from Clinical Studies in Patients with Asthma: A 5-year observational study was conducted in 5007 XOLAIR-treated and 2829 non-XOLAIR-treated patients ≥12 years of age with moderate to severe persistent asthma and a positive skin test reaction to a perennial aeroallergen to evaluate the long term safety of XOLAIR, including the risk of malignancy. Similar percentages of patients in both cohorts were current (5%) or former smokers (29%). Patients had a mean age of 45 years and were followed for a mean of 3.7 years. More XOLAIR-treated patients were diagnosed with severe asthma (50%) compared to the non-XOLAIR-treated patients (23%). A higher incidence rate (per 1000 patient-years) of overall cardiovascular and cerebrovascular serious adverse events (SAEs) was observed in XOLAIR-treated patients (13.4) compared to non-XOLAIR-treated patients (8.1). Increases in rates were observed for transient ischemic attack (0.7 vs 0.1), myocardial infarction (2.1 vs 0.8), pulmonary hypertension (0.5 vs 0), pulmonary embolism/venous thrombosis (3.2 vs 1.5), and unstable angina (2.2 vs 1.4), while the rates observed for ischemic stroke and cardiovascular death were similar among both study cohorts. The results suggest a potential increased risk of serious cardiovascular and cerebrovascular events in patients treated with XOLAIR, however the observational study design, the inclusion of patients previously exposed to XOLAIR (88% for a mean of 8 months), baseline imbalances in cardiovascular risk factors between the treatment groups, an inability to adjust for unmeasured risk factors, and the high study discontinuation rate (44%) limit the ability to quantify the magnitude of the risk.

Pregnancy: Data with XOLAIR use in pregnant women are insufficient to inform on drug associated risk.

You may report side effects to the FDA at (800) FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Genentech at (888) 835-2555 or Novartis Pharmaceuticals Corporation at (888) 669-6682.

Please see full Prescribing Information, including Boxed WARNING and Medication Guide for additional Important Safety Information.

Announcer:
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