Benralizumab (Fasenra™)
Protocol for Severe Eosinophilic Asthma

Background

Severe asthma is present in 5-10% of patients with asthma. These patients have frequent exacerbations that require oral corticosteroids, and an important proportion may need daily use of this therapy to achieve control. Oral corticosteroids are associated with multiple side effects, thus steroid-sparing therapies are essential in severe asthma.

Eosinophils have a central role in the inflammatory pathways of allergic asthma. Activation of this cellular line is mediated through interleukin-5 (IL-5). Activated eosinophils release reactive oxygen species, leukotrienes and other cytokines that promote inflammation and lead to worsening asthma control.

Benralizumab is a humanized afucosylated monoclonal antibody that binds with high affinity to epitope within domain 1 of the α subunit of the IL-5 receptor.[1,2] Afucosylated monoclonal antibodies lack fucose sugars in the Fc region of the antibody, a process that augments the interaction between benralizumab and the IL-5 receptor and increases the antibody-dependent cell-mediated cytotoxicity (ADCC) compared to targeting the IL-5 ligand directly.[2] ADCC may result in a more complete depletion of eosinophils in the airway lumen without degranulation of eosinophils.

Patient selection

Benralizumab is currently approved by the FDA and indicated for severe eosinophilic asthma that is not responding to maximal inhaler therapy. Patients must have persistent exacerbations despite high dose inhaled corticosteroids in combination with a long-acting beta agonist, and a long-acting muscarinic antagonist. Patients that have 3 or more exacerbations in 1 year and have evidence of *peripheral eosinophilia* (serum eosinophils of 300 cells/microliter or greater) will be considered for this therapy. This measurement can be readily obtained with a complete blood count with differential. Patients will be selected from the *UHS Severe Asthma Program* clinic after careful evaluation of their diagnosis is completed, environmental measures are in place, adequate inhaler technique has been addressed and asthma comorbidities have been treated.

Administration

Benralizumab is administered via subcutaneous injection (30mg) every 4 weeks for the first 3 doses and every 8 weeks thereafter. The medication is delivered via a prefilled syringe. After the first dose the patients needs to be observed in the infusion center for side effects for at least 2 hours. In subsequent treatments, if there have been no reactions, the patient can be observed for 1 hour. Hypersensitivity reaction have occurred after administration of benralizumab. These reactions occur typically within hours of administration. Standing orders for Epinephrine 1:1000, 0.3mg/0.3ml IM, methylprednisolone 125mg slow IV push, and diphenhydramine 50mg IV push PRN for anaphylaxis will be in place.

Origination date: 1/2019
Pulmonary Subcommittee Approval: 1/2019
P&T Committee Approval: 1/2019

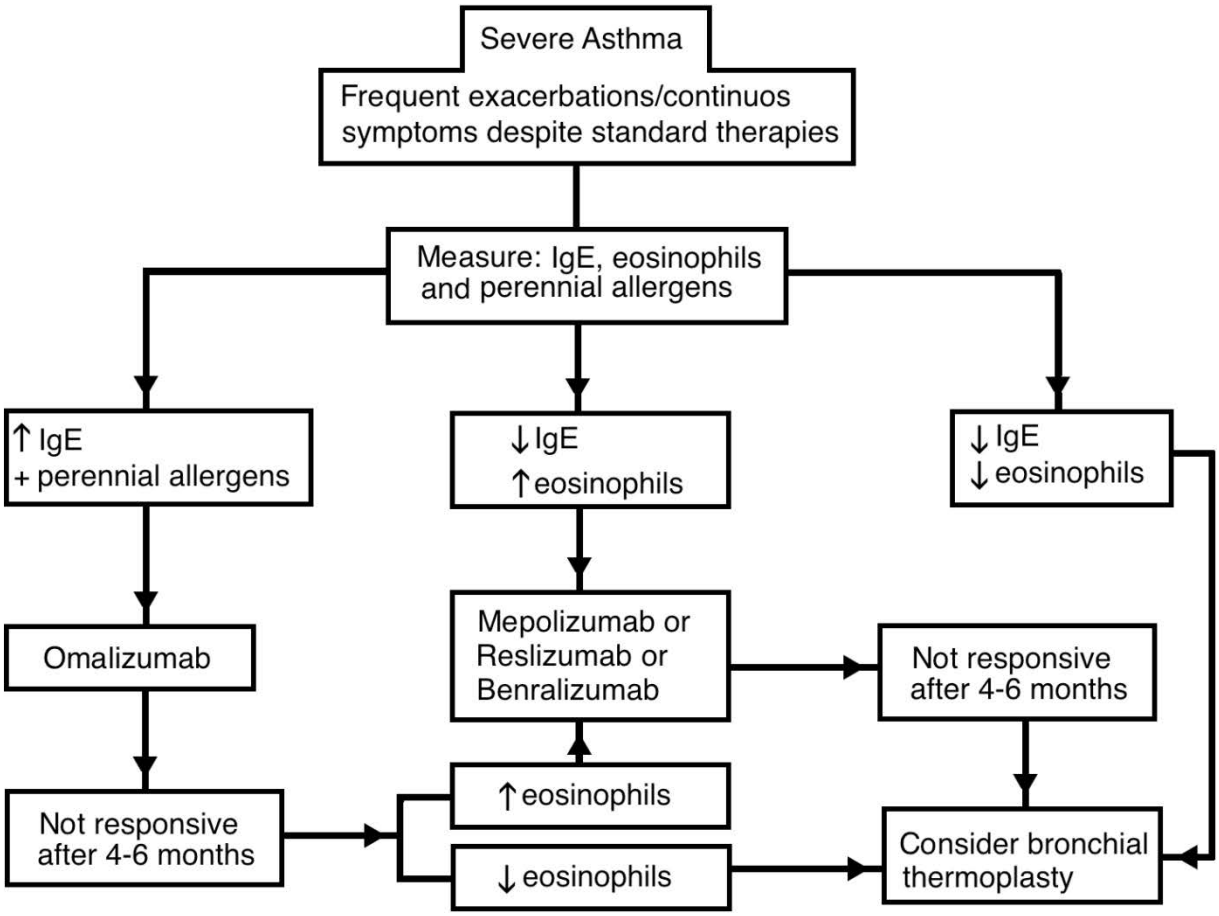
Safety

Administration of benralizumab resulted in similar rates of side effects compared to placebo in 4 large randomized controlled trials.[3-7] Reactions/pain at the site of injection and nasopharyngitis were the most frequently reported side effects and were considered mild.[3-7]

Efficacy

Benralizumab has been shown to decrease exacerbations and reduce oral corticosteroid use in patients with severe eosinophilic asthma in several large, randomized, placebo-controlled, multicenter, phase III trials.[4-7] Additionally, treatment with benralizumab has been associated to significant improvements in health-related quality of life and respiratory symptoms.[4-7]

Treatment pathway



Adapted from: Maselli DJ, et al. J Asthma Allergy. 2016 Aug 31;9:155-62.[8]

References

1. Koike M, Nakamura K, Furuya A, et al. Establishment of humanized anti-interleukin-5 receptor alpha chain monoclonal antibodies having a potent neutralizing activity. Hum Antibodies. 2009;18(1-2):17-27.

2. Kolbeck R, Kozhich A, Koike M, et al. MEDI-563, a humanized anti-IL-5 receptor alpha mAb with enhanced antibody-dependent cell-mediated cytotoxicity function. J Allergy Clin Immunol. 2010;125(6):1344-1353. Ferguson GT,

3. FitzGerald JM, Bleecker ER, et al. Benralizumab for patients with mild to moderate, persistent asthma (BISE): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Respir Med. 2017;5(7):568-576.

4. 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 β2-agonists (SIROCCO): a randomised, multicentre, placebo-controlled phase 3 trial. Lancet. 2016;388(10056):2115-2127.

5. 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.

6. 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.

7. Maselli DJ, Rogers L, Peters JI. Benralizumab, an add-on treatment for severe eosinophilic asthma: evaluation of exacerbations, emergency department visits, lung function, and oral corticosteroid use. Ther Clin Risk Manag. 2018 Oct 23;14:2059-2068.

8. Maselli DJ, Velez MI, Rogers L. Reslizumab in the management of poorly controlled asthma: the data so far. J Asthma Allergy. 2016 Aug 31;9:155-62.