A REVIEW ON ANTIASTHMATIC DRUGS

Nitish Choudhary[1], Kirti Kaushal[2], Shalini Vashisht[3], Jyoti Gupta[4]

1. Nitish Choudhary, Student of Bachelors of Pharmacy, IEC University, Baddi.
2. Kirti Kaushal , Assistant Professor , School of Pharmacy , IEC University, Baddi.
3. Shalini Vashisht , Assistant Professor , School of Pharmacy , IEC University, Baddi.
4. Jyoti Gupta , Associate Proffesor , Head of Department , IEC University, Baddi.

Abstract

Asthma is a chronic respiratory condition that affects millions of people worldwide, characterized by inflammation and narrowing of the airways, resulting in recurrent episodes of wheezing, coughing, chest tightness, and shortness of breath. Despite the availability of numerous medications, a significant number of asthma patients still experience symptoms that are inadequately controlled, highlighting the need for new treatments. A new drug, Dupilumab, recently has been approved for the treatment of asthma. Dupilumab is a monoclonal antibody that targets the interleukin-4 receptor alpha (IL-4Ra), which is involved in the inflammatory response in asthma. It has been shown to reduce asthma exacerbations and improve lung function in patients with moderate-to-severe asthma.Clinical trials has shown that Dupilumab, used in combination with other asthma medications, significantly reduces the frequency of exacerbations, improves lung function, and reduces symptoms in patients with moderate-to-severe asthma. Additionally, it has also been shown to improve quality of life and reduce the need for oral corticosteroids. Despite its potential benefits, Thus, careful patient selection and monitoring the drug.The pathogenic process begins with the inhalation of an allergen or an irritant, such as cold air, which causes bronchial hypersensitivity and, as a result, causes the airways to become inflamed and produce more mucus As a result, there is a notable rise in airwa y resistance, which is most noticeable during expiration. Benralizumab is a type of biologic medication that was approved by the U.S. Food and Drug Administration for the treatment of severe asthma. It is designed to target a specific type of white blood cell called eosinophils, which are involved in the inflammatory response in asthma. Dupilumab is a monoclonal antibody medication that was approved for the treatment of moderate to severe asthma. It works by blocking two proteins involved in the inflammatory response in asthma: interleukin-4 (IL-4) and interleukin-13 (IL-13). Tezepelumab is a monoclonal antibody medication that was approved for the treatment of severe asthma. It works by blocking a protein called thymic stromal lymphopoietin (TSLP), which is involved in the allergic response in asthma. Bronchial thermoplasty is a non-medication treatment for severe asthma that was approved by the . It involves the use of a catheter inserted through the nose or mouth to deliver controlled heat energy to the airway walls, reducing the amount of muscle tissue and decreasing airway responsiveness these all medications helps to treat asthma..

Key Words: *Asthma, Adverse Effect, Inflammation, Clinical trial, medication.*

INTRODUCTION:

It can be challenging to breathe when someone has asthma because it affects the airways, making them small and irritated. Asthma is a chronic respiratory disorder. Wheezing, coughing, tightness in the chest, and shortness of breath are just a few of the symptoms of asthma that may be brought on by several things including allergen exposure, exercise, and cold air. People of all ages frequently suffer from asthma, which can range in severity from moderate to severe and, in some circumstances, necessitate hospitalisation. Asthma cannot be cured, but it may be controlled with medicine, a change in lifestyle, and avoidance of triggers. People with asthma may live healthy, active lives with the right care. The symptoms of asthma can vary in severity from mild to life-threatening. The most common symptoms of asthma include wheezing, coughing, shortness of breath, and chest tightness. These

symptoms can be triggered by a variety of factors, such as allergens (e.g. dust mites, pet dander), irritants (e.g. cigarette smoke, air pollution), exercise, stress, and infections (e.g. colds, flu).

The exact cause of asthma is not fully understood, but it is believed to be the result of a complex interaction between genetic and environmental factors. Research has shown that people who have a family history of asthma or allergies are more likely to develop asthma themselves. Additionally, exposure to certain environmental factors, such as air pollution and secondhand smoke, can increase the risk of developing asthma or worsening asthma symptoms.

Asthma is diagnosed through a combination of medical history, physical examination, and lung function tests. The medical history will include questions about symptoms, triggers, and family history of asthma or allergies. The physical examination will involve listening to the lungs with a stethoscope and checking for signs of inflammation, such as wheezing or coughing. Lung function tests, such as spirometry, measure how much air a person can exhale and how quickly they can do so.

There is no cure for asthma, but there are many treatment options available to help manage its symptoms and reduce the risk of flare-ups. The most common treatments for asthma include inhaled bronchodilators, inhaled corticosteroids, combination inhalers, and oral medications. These medications work to reduce inflammation in the airways, relax the muscles around the airways, and improve lung function.

In addition to medication, there are several non-medication treatments that can be effective for asthma. These include avoiding triggers, using a peak flow meter to monitor lung function, and practicing breathing techniques, such as deep breathing and pursed lip breathing.[1,2,3,4,5]

HISTORY:

In India, asthma has long been recognised as a medical problem. Ayurveda books from antiquity mention an ailment termed "Swas Roga" that is comparable to modern-day asthma. Traditional Indian medicine has traditionally employed herbal treatments, yoga, and breathing techniques to treat respiratory diseases, including asthma. Asthma is a chronic respiratory disease that has been recognized for thousands of years. The first recorded description of asthma-like symptoms can be found in ancient Egyptian medical texts dating back to 2600 BCE. Throughout history, asthma was thought to be caused by various factors, including bad air, emotional stress, and poor diet.[6]

It wasn't until the 19th century that asthma began to be understood as a disease of the lungs. In 1872, British physician Salter first described asthma as a constriction of the airways. Later, in the early 20th century, allergists identified asthma triggers such as dust, pollen, and animal dander.[7]

The use of inhaled bronchodilators to treat asthma was first introduced in the 1950s, followed by the development of inhaled corticosteroids in the 1960s. These medications revolutionized the treatment of asthma and allowed patients to control their symptoms more effectively.[8]

Over the years, there has been a significant increase in the prevalence of asthma worldwide. In the 20th century, asthma was primarily considered a disease of developed countries, but it has since become a global health issue affecting people of all ages and socioeconomic backgrounds. The causes of this increase are not entirely clear, but factors such as air pollution, changes in lifestyle, and genetics are thought to play a role.[9]

Pathophysiology:

Acute, fully treatable airway inflammation characterises asthma, which frequently develops after exposure to an env ironmental cause.

The pathogenic process begins with the inhalation of an allergen or an irritant, such as cold air, which causes bronch ial hypersensitivity and, as a result, causes the airways to become inflamed and produce more mucus.
As a result, there is a notable rise in airway resistance, which is most noticeable during expiration.[10,11]

Combinations of:

1. Infiltration of inflammatory cells cause airway blockage.
2. Hypersecretion of mucus together with mucus plug development. 3.Muscle contraction that is smooth.[12,13]

As a result of:

1.Basement membrane thickening, collagen deposition, and epithelial desquamation, these irreversible alterations m ay eventually become irreversible.

2. Chronic illness accompanied by smooth muscle hypertrophy and hyperplasia results in airway remodeling. [14,15]. If asthma is not treated right away, it could get worse because the formation of mucus keeps the inhaled me dication from getting to the mucosa.

The swelling from the inflammation also gets worse, Beta2 agonists (such as salbutamol, salmeterol, and albuterol) a nd muscarinic receptor antagonis (such as ipratropium bromide) can help resolve this process (complete resolution is necessary in asthma, but in practise, this is not checked or tested). These medications work to reduce inflammation and relax the bronchial musculature while also decreasing mucus production.[17,18,19]

Classification of Asthma Level of Severity:

The grading of the severity of the asthma influences the level of pharmaceutical therapy.
The severity degree of ANY of the following should be determined by the frequency of symptoms episodes: Coughing fits, chest tightness, dyspnea, and wheezing fits. [35,36]

Type of Asthma:

According to how severe your asthma is, there are four different types of asthma. Your level of asthma is based on how frequently you get symptoms and how well your lungs are working. the following questions:

Intermittent asthma: You wake up less than two nights per month and experience symptoms less than twice per week. You only take quick-relief medications (like albuterol) twice a week or less. All of your regular activities are possible. Your lungs are operating normally.

Mild persistent asthma: You experience symptoms at least twice a week and experience sleep disturbances three to four nights per month. Daily symptoms are not present in you. More than two days a week are spent using a quick-relief medication. Your symptoms affect some of your daily activities. Most of your lung function is normal. [32]

Moderate persistent asthma: You wake up at least once a week and experience symptoms at least once a day. You need your quick-relief medicine daily. Your symptoms limit some of your everyday usual activities. There is some decline in your lung function.

Severe chronic asthma: You suffer symptoms during the day and wake up every night owing to asthma. You need your quick-relief medicine several times a day for asthma symptoms. Your symptoms put extreme limitations on your daily activities. There are significant decreases in your lung function. [37]

Symptoms:

Symptoms of asthma might differ from person to person. You may experience rare asthma attacks, only experience symptoms sometimes, such as when you exercise, or experience constant symptoms. [20,21]

One of the first signs of Asthma is:

1. Shortness of breath.

2. Chest pain or tightness

3. Having trouble falling asleep due to shortness of breath, coughing, or wheezing.

4. Wheezing when exhaling, which is a common indication of asthma in youngsters.

5. Attacks of coughing or wheezing that are made worse by a respiratory virus, such as the flu or a cold. [22,23,24]

Warning sign of asthma

1. More frequent and troublesome asthmatic signs and symptoms.

2. Increased difficulty breathing as determined by a tool that measures how well your lungs are functioning.

3. The requirement to use a fast-acting inhaler more frequently. Some persons experience an asthma attack or symptom flare-up when:

- Asthma brought on by exercise, which may be worse by the cold and dry weather.
- Occupational asthma, triggered by industrial irritants such as chemical fumes, gases or dust.
- Asthma brought on by allergies that are brought on by airborne items like pollen, mould spores, cockroach faeces, or dried saliva and skin fragments from animals. [25,26,27]

Treatment:

Men and women of all ages can have asthma, a lower respiratory tract illness. Asthma is diagnosed clinically, however there is no one gold standard test available, the pathogenesis and clinical manifestation of the disease are highly heterogeneous, and clinical overdiagnosis can happen, especially in those lacking spirometric proof. Hence, a comprehensive historyand physical examination together with spirometryare crucial for the diagnosis of asthma. [28]

Diagnosis of asthma:

The three following circumstances are the most common ones when diagnosing asthma:

1. There are sporadic signs of airflow blockage

2. At least a portion of the airflow restriction is reversible.

3. A history and physical exam rule out any additional potential reasons of this airflow blockage. [29,30]

In the presence of the following symptoms, the diagnosis of asthma (showing episodic airflow restriction and some evidence of this obstruction's reversibility) should be highly evaluated. Asthma symptoms can be highly changeable throughout the day and occasionally only present at night, therefore the absence of symptoms at the time of assessment does not rule out an asthma diagnosis. [31]

1. The patient complains of occasional wheezing, tightness in the chest, shortness of breath, or coughing, esp ecially at night.
2. The symptoms change during the day or week.
3. Previous history of allergic rhinitis or atopic dermatitis;
4. Development of wheezing in response to particular triggers.
5. These triggers differ from person to person but are generally the same for each person.
6. Some people may only have one or two triggers that have been discovered, while others may have many.
7. The patient has a family history of sinusitis, chronic rhinitis, asthma, or skin or respiratory allergies. [32,33,34]

Anti-Asthma Drugs:

Asthma is a chronic respiratory condition that affects millions of people worldwide. While there is no cure for asthma, there are a variety of medications available to help manage its symptoms and reduce the risk of flare-ups. In recent years, several new drugs have been developed for the treatment of asthma that offer improved efficacy and fewer side effects compared to older medications. Here are some of the recent drugs for asthma:

1.Benralizumab:

Benralizumab is a type of biologic medication that was approved by the U.S. Food and Drug Administration (FDA) in 2017 for the treatment of severe asthma. It is designed to target a specific type of white blood cell called eosinophils, which are involved in the inflammatory response in asthma. By binding to these cells and triggering their destruction, benralizumab can reduce airway inflammation and improve asthma control. Benralizumab is administered as a subcutaneous injection every four weeks, and studies have shown it to be effective in reducing asthma exacerbations and improving lung function in people with severe eosinophilic asthma.[38]

Benralizumab: Mechanism of Action

AstraZeneca/MedImmune used hybridoma technology to develop and manufacture benralizumab (MEDI-563) [41–43]. This biological substance is an IgG1k monoclonal antibody that has been humanised and was produced in mice. Its distinctive property is that it binds only to the amino acid residue isoleucine-61 found in domain 1 of the human IL-5R. Benralizumab interacts with an extracellular IL-5R epitope that is located close to the IL-5 binding site via this linkage [44,45]. Benralizumab's high-affinity association with IL-5R prevents IL-5 from binding to its receptor and the ensuing heterodimerization of the and subunits which prevents the complex signalling pathways connected to IL-5 receptor activation from being stimulated.

Benralizumab binds to the FcRIIIa receptor, which is found on the cell membrane of natural killer (NK) cells, in addition to connecting with IL-5R through its Fab sections (Figure 2) [46,47]. Benralizumab was created in Chinese hamster ovary cells that did not express the enzyme -1,6-fucosyltransferase, which is significant in this context. Benralizumab's affinity for the NK cell FcRIIIa receptor is noticeably increased (5–50 times) as a result of the absence of the fucose molecule in the sugar component of the CH2 domain of the constant segment of the monoclonal antibody [59]. Benralizumab, in instance, can cause an approximately 1000-fold increase in the apoptotic process known as antibody-dependent cell-mediated cytotoxicity when compared to the original fucosylated antibody (ADCC). Given that NK cells secrete the proapoptotic proteins perforin and granzyme B, benralizumab is a powerful inducer of eosinophil apoptosis [46]. Benralizumab-induced increases in eosinophil staining with annexin V, a well-known indicator of apoptosis, have also been used to establish afucosylation-dependent ADCC [46].

2.Tezepelumab:

Tezepelumab is a monoclonal antibody medication that was approved by the FDA in 2021 for the treatment of severe asthma. It works by blocking a protein called thymic stromal lymphopoietin (TSLP), which is involved in the allergic response in asthma. By inhibiting TSLP, tezepelumab can reduce inflammation in the airways and improve asthma control. Tezepelumab is administered as a subcutaneous injection every four weeks, and studies have shown it to be effective in reducing asthma exacerbations and improving lung function in people with severe asthma.

3.Bronchial thermoplasty:

Bronchial thermoplasty is a non-medication treatment for severe asthma that was approved by the FDA in 2010. It involves the use of a catheter inserted through the nose or mouth to deliver controlled heat energy to the airway walls, reducing the amount of muscle tissue and decreasing airway responsiveness. Bronchial thermoplasty is typically performed in three sessions, with each session treating a different part of the lungs. Studies have shown

that bronchial thermoplasty can improve asthma control and reduce asthma exacerbations in people with severe asthma.[40,41]

4.Dupilumab:

Dupilumab is a monoclonal antibody medication that was approved by the FDA in 2018 for the treatment of moderate to severe asthma. It works by blocking two proteins involved in the inflammatory response in asthma: interleukin-4 (IL-4) and interleukin-13 (IL-13). By inhibiting these proteins, dupilumab can reduce airway inflammation and improve asthma control. Dupilumab is administered as a subcutaneous injection every two weeks, and studies have show it to be effective in reducing asthma exacerbations and improving lung function in people with moderate to severe asthma.[39,40]

Dupilumab: Mechanism of Action

The etiology of allergy illnesses is heavily influenced by the Th2 cytokines interleukin 4 (IL-4) and IL-13 as well as the heterodimeric IL-4 receptor (IL-4R) complexes that they interact with. A humanised IgG4 monoclonal antibody known as dupilumab specifically targets the IL-4 receptor alpha chain (IL-4R), which is present in both type 1 (IL-4R/c; IL-4 specific) and type 2 (IL-4R/IL-13R1; IL-4 and IL-13 specific) IL-4R complexes. In this study, we go through the present state of knowledge on the many signalling pathways connected to IL-4R complexes, look at potential mechanisms of action for dupilumab, and assess the clinical effectiveness of dupilumab in treating various allergy illnesses. The advancement of Dupilumab and the expanding range of its clinical applications are pertinent given the current focus on precision medicine methods for pathway blocking.

Conclusion

In conclusion, asthma is a chronic respiratory condition that affects millions of people worldwide. It is characterized by airway inflammation, bronchial hyperresponsiveness, and recurrent episodes of wheezing, coughing, and shortness of breath. While there is no cure for asthma, there are many medications and treatment options available to help manage its symptoms and reduce the risk of flare-ups. The most common treatments for asthma include inhaled bronchodilators, inhaled corticosteroids, combination inhalers, and oral medications. These medications work to reduce inflammation in the airways, relax the muscles around the airways, and improve lung function. In addition to medication, there are several non-medication treatments that can be effective for asthma, such as avoiding triggers, using a peak flow meter, and practicing breathing techniques. In recent years, several new drugs have been developed for the treatment of asthma that offer improved efficacy and fewer side effects compared to older medications. These drugs include benralizumab, dupilumab, tezepelumab, and bronchial thermoplasty. These new drugs target specific aspects of the inflammatory response in asthma, offering improved asthma control and fewer side effects. Overall, the key to managing asthma is to work closely with your healthcare provider to find a treatment plan that works best for you. This may involve a combination of medications and non-medication treatments, as well as regular monitoring of your lung function and symptoms. With proper management, most people with asthma are able to lead active and healthy lives. Asthma is a chronic respiratory condition that affects millions of people worldwide. The prevalence of asthma has been increasing steadily in recent years, and it is now one of the most common chronic diseases among children and adults. Asthma is characterized by inflammation and narrowing of the airways, which can lead to symptoms such as wheezing, coughing, shortness of breath, and chest tightness. The management of asthma involves a combination of pharmacological and non-pharmacological interventions. The most commonly used medications for asthma include inhaled corticosteroids, beta-agonists, leukotriene modifiers, and anticholinergics. These medications are used to control inflammation and bronchospasm, which are the underlying causes of asthma symptoms. Non-pharmacological interventions such as avoiding triggers, regular exercise, and maintaining a healthy lifestyle can also help manage asthma symptoms.The diagnosis of asthma involves a detailed medical history, physical examination, and pulmonary function tests. The medical history should include a description of the symptoms, triggers, and family history of asthma. A physical examination can reveal signs of asthma, such as wheezing and decreased lung function. Pulmonary function tests, such as spirometry, can help confirm the diagnosis of asthma and assess the severity of the condition.

REFRENCE

1.Lee J, McDonald C. Review: Immunotherapy improves some symptoms and reduces long-term medication use in mild to moderate asthma. Ann Intern Med. 2018 Aug 21.

2.Tesfaye ZT, Gebreselase NT, Horsa BA. Appropriateness of chronic asthma management and medication adherence in patients visiting ambulatory clinic of Gondar University Hospital: a cross-sectional study. World Allergy Organ J. 2018.

3.Salo PM, Cohn RD, Zeldin DC. Bedroom Allergen Exposure Beyond House Dust Mites. Curr Allergy Asthma Rep. 2018 Aug 20.

4.Scirica CV, Celedón JC. Genetics of asthma: potential implications for reducing asthma disparities. Chest. 2007 Nov.

5.Yii AC, Soh AZ, Chee CBE, Wang YT, Yuan JM, Koh WP. Asthma, Sinonasal Disease, and the Risk of Active Tuberculosis. J Allergy Clin Immunol Pract. 2019 Feb;7(2):641-648.e1.

6.D'Amato M, Molino A, Calabrese G, Cecchi L, Annesi-Maesano I, D'Amato G. The impact of cold on the respiratory tract and its consequences to respiratory health. Clin Transl Allergy. 2018;8:20.

7.Burrows B, Barbee RA, Cline MG, Knudson RJ, Lebowitz MD. Characteristics of asthma among elderly adults in a sample of the general population. Chest. 1991 Oct;100(4):935-42. [

8.Martin AJ, Landau LI, Phelan PD. Lung function in young adults who had asthma in childhood. Am Rev Respir Dis. 1980 Oct;122(4):609-16.

9.Southworth T, Kaur M, Hodgson L, Facchinetti F, Villetti G, Civelli M, Singh D. Anti-inflammatory effects of the phosphodiesterase type 4 inhibitor CHF6001 on bronchoalveolar lavage lymphocytes from asthma patients. Cytokine. 2019 Jan

10. Global Initiative for Asthma (GINA): Global strategy for asthma management and prevention. 2009, Available at: http://www.ginasthma. com Accessed July 15, 2010.

11. Lemanske RF, Busse WW: Asthma: Clinical expression and molecular mechanisms. J Allergy Clin Immunol 2010

12.American Thoracic Society. What constitutes an adverse health effect of air pollution? Official statement of the American Thoracic Society. Am J Respir Crit Care Med 2000

13. Barnes PJ. Cytokine modulators as novel therapies for asthma. Annu Rev Pharmacol Toxicol 2002.

14. Bateman ED, Boushey HA, Bousquet J, Busse WW, Clark TJ, Pauwels RA, Pedersen SE; GOAL Investigators Group. Can guideline-defined asthma control be achieved? The Gaining Optimal Asthma ControL study. Am J Respir Crit Care Med 2004

15 .Boyce JA. Mast cells: beyond IgE. J Allergy Clin Immunol 2003

16. Brightling CE, Bradding P, Symon FA, Holgate ST, Wardlaw AJ, Pavord ID. Mast-cell infiltration of airway smooth muscle in asthma. N Engl J Med 2002.

17.Busse W, Corren J, Lanier BQ, McAlary M, Fowler-Taylor A, Cioppa GD, van As A, Gupta N. Omalizumab, anti-IgE recombinant humanized monoclonal antibody, for the treatment of severe allergic asthma. J Allergy Clin Immunol 2009

18. Busse WW. The role of leukotrienes in asthma and allergic rhinitis. Clin Exp Allergy 2019

19. Castro-Rodriguez JA, Holberg CJ, Wright AL, Martinez FD. A clinical index to define risk of asthma in young children with recurrent wheezing. Am J Respir Crit Care Med 2000.

20. To T, Stanojevic S, Moores G, Gershon AS, Bateman ED, Cruz AA, et al. Global asthma prevalence in adults: findings from the cross-sectional world health survey. BMC Public Health 2012

21. Calciano L, Corsico AG, Pirina P, Trucco G, Jarvis D, Janson C, et al. Assessment of asthma severity in adults with ever asthma: a continuous score. PloS One. 2017

22. Gillis RME, van Litsenburg W, van Balkom RH, Muris JW, Smeenk FW. The contribution of an asthma diagnostic consultation service in obtaining an accurate asthma diagnosis for primary care patients: results of a real-life study. NPJ Prim Care Respir Med 2017.

23. DAlonzo GE, Ciccolella DE. Nocturnal asthma: physiologic determinants and current therapeutic approaches. Curr Opin Pulm Med 2018.

24. Greenberg H, Cohen RI. Nocturnal asthma. Curr Opin Pulm Med 2012. 102. Soler-Catalun˜a JJ, Sauleda J, Valde´s L, Marin P, Aguero R, Perez M, et al. Prevalence and perception of 24-hour symptom patterns in patients with stable chronic obstructive pulmonary disease in Spain. Arch Bronconeumol 2016.

25. Globe G, Martin M, Schatz M, Wiklund I, Lin J, von Maltzahn R, et al. Symptoms and markers of symptom severity in asthma—content validity of the asthma symptom diary. Health Qual Life Outcomes 2015.

27. Juniper EF et al. Development and validation of a questionnaire to measure asthma control. Eur Respir J. 2007

28. Nathan RA et al. Development of the asthma control test: A survey for assessing asthma control. J AllergyClin Immunol. 2004

29. Juniper EF et al. Development and validation of the Mini Asthma Quality of Life Questionnaire. Eur Respir J.2017

30. Ignacio-Garcia JM, GonzalezSantos P. Asthma self-management education program by home monitoring of peak expiratory flow. Am J Respir Crit Care Med. 2013

31. Lahdensuo A et al. Randomised comparison of guided self management and traditional treatment of asthma over one year. BMJ. 2015

32. Haldar P et al. Cluster analysis and clinical asthma phenotypes. Am J Respir Crit Care Med. 2008

33. Douwes J et al. Non-eosinophilic asthma: Importance and possible mechanisms. Thorax. 2002

34. Bonsignore MR et al. Advances in asthma pathophysiology: Stepping forward from the maurizio vignola experience. Eur Respir Rev. 2015

35. Siroux V et al. Identifying adult asthma phenotypes using a clustering approach. Eur Respir J. 2011

36. Moore WC et al. Identification of asthma phenotypes using cluster analysis in the severe asthma research program. Am J Respir Crit Care Med. 2010

37. https://www.webmd.com/asthma/newer-asthma-medications-treatments Nov 12 2022.

38. 55. Koike M., Nakamura K., Furuya A., et al. Establishment of humanized anti-interleukin-5 receptor alpha chain monoclonal antibodies having a potent neutralizing activity. 2009;18(1-2):17–27. doi: 10.3233/HAB-2009-0198.

39. Ghazi A., Trikha A., Calhoun W. J. Benralizumab - A humanized mAb to IL-5Rα with enhanced antibody-dependent cell-mediated cytotoxicity - A novel approach for the treatment of asthma. 2012.

40. Menzella F., Lusuardi M., Galeone C., Facciolongo N., Zucchi L. The clinical profile of benralizumab in the management of severe eosinophilic asthma. 2016;10(6):534–548. doi: 10.1177/1753465816667659.

41. Ishino T., Pasut G., Scibek J., Chaiken I. Kinetic Interaction Analysis of Human Interleukin 5 Receptor α Mutants Reveals a Unique Binding Topology and Charge Distribution for Cytokine Recognition. 2004;279(10):9547–9556. doi: 10.1074/jbc.M309327200]

42. Kolbeck R., Kozhich A., Koike M., et al. Medi-563, a humanized anti-IL-5 receptor a mAb with enhanced antibody-dependent cell mediated cytotoxicity function. 2010;125(6):1344–1353. doi: 10.1016/j.jaci.2010.04.00443. Shields R. L., Lai J., Keck R., et al. Lack of fucose on human IgG1 N-linked oligosaccharide improves binding to human FcγRIII and antibody-dependent cellular toxicity 2002.

44. Shinkawa T., Nakamura K., Yamane N., et al. The absence of fucose but not the presence of galactose or bisecting N-acetylglucosamine of human IgG1 complex-type oligosaccharides shows the critical role of enhancing antibody-dependent cellular cytotoxicity. 2003.

45. Busse W. W., Katial R., Gossage D., et al. Safety profile, pharmacokinetics, and biologic activity of MEDI-563, an anti-IL-5 receptor *α* antibody, in a phase I study of subjects with mild asthma. 2010;125(6):1237–1244. doi: 10.1016/j.jaci.2010.

46. Laviolette M., Gossage D. L., Gauvreau G., et al. Effects of benralizumab on airway eosinophils in asthmatic patients with sputum eosinophilia. 2013;132(5):1086–1096. doi: 10.1016/j.jaci.2013.05.02047. Assa'ad A. H., Rothenberg M. E. Eosinophilic asthma: Insights into the effects of reducing IL-5 receptor-positive cell levels. 2013.