



A Critical Review of Cinqair (Reslizumab) in the Treatment of Severe Asthma Patients

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ABSTRACT

CINQAIR works in a way that is different from inhalers or steroids. Biologics are believed to be more effective for those suffering from severe, unmanageable allergic Asthma than other treatments. Patients with poorly managed, severe Asthma who also had elevated eosinophil levels As soon as four weeks after being introduced to their previous asthma medications, CINQAIR relieved the severe asthmatic patients. Also, benefits were observed at the end of the one-year study. Comparatively, people who added CINQAIR to their asthma treatments reported a higher quality of life than those who did not take reslizumab. Those who took CINQAIR had better control over their symptoms. If we look at the cinqair review, it has improved QoL and better effectiveness, absorption, and results from clinical trial data. Immediately following your CINQAIR infusion, severe allergic responses might occur. These responses might be fatal. Sometimes Allergic responses might not always happen immediately. After receiving your CINQAIR infusion, your medical professional will watch for reactions. Your body may experience abnormal cell or tissue development that might be cancer (malignancy) but may not be cancer. Additional diagnosis is required to declare. There is a limited public-private collaboration with Cinqair that needs to have more because the prevalence of the disease is rising compared to the last decade.



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INTRODUCTION

Asthma is a chronic lung disease. In this disease, lung airways are more impacted [1]. The two major characterized issues of this disease are congestion and excessive mucous (inflammation) in the bronchi and tightening of muscles around the bronchi, known as bronchospasm [Figure 1].

Symptoms

It is one of the most prevalent chronic, non-communicable illnesses in children and adults [2]. Fluctuating respiratory distress, wheezing, persistent cough, Chronic airway inflammation, non-specific bronchial hyperreactivity, and reversible airflow obstruction are the well-known hallmarks of Asthma [Figure 2].

Eosinophils influence exacerbations of Asthma. Recent research shows that mucus and blood eosinophil levels may be crucial indicators for predicting asthma severity. Individuals with Asthma who have blood eosinophil counts above 400 cells per μL had worse asthma control and more severe exacerbations [3]. Asthma is usually categorized in adults and children [Figure 3].

Factors that Influence Asthma Attacks

It is a heterogeneous disease in which many lung

inflammatory cells are activated due to this systemic condition [Figure 4].

Presently the worldwide burden of Asthma remains high; the disease's incidence and prevalence do not appear to be increasing clinically or economically in terms of health loss and death [4].

Death and Disability-Adjusted Life Years

The asthma rate was 43.12 million new cases per year (0.56%) in 2017, while prevalence and mortality were 272.68 million cases (3.57%) and 0.49 million deaths (0.006%) in the same year, respectively [5]. Deaths and disability-adjusted life years (DALYs) have steadily declined over the past 25 years, despite a considerable increase in asthma patients. While asthma mortality considerably decreased during the past 25 years, there were no noticeable improvements in asthma incidence, prevalence, or DALYs after adjusting for global demographic diversity. When compared to prevalence and DALYs, asthma incidence peaks before age five, whereas DALYs peak between 0 and 14 years. By 80 years of age, asthma mortality peaks [6]. Asthma mortality increases with aging. Women have a more considerable epidemiologic burden and death rate from Asthma than males. The sociodemographic index has an inverse, very significant connection with asthma incidence ($r = 0.98$) or death ($r = 0.96$) [7].

Compared to HIV/AIDS and T.B. combined, Asthma has higher global economic consequences. In several Western nations, the financial burden on people with Asthma varies from \$300 to \$ 1,300 per patient annually. The entire direct medical and indirect economic expenses of Asthma in the United States were over \$12 billion in 1994, an increase of more than 50% in only ten years. The overall annual cost of Asthma in Europe is 17.7 billion euros (\$21.65 billion). In 2019, Asthma afflicted an estimated 262 million individuals and killed 455 000 people [8].

The National Heart, Lung, and Blood Institute, National Institutes of Health, USA, and the World Health Organization developed the Global Initiative for Asthma guideline (GINA) to create a worldwide strategy for asthma care and prevention in 1993 [9].

Anti-Asthmatic Classification

In the current treatment, Bronchodilators and anti-inflammatory drugs are the two main medications used to treat Asthma. In bronchodilators, there are sympathomimetics, methylxanthines, and anticholinergics. In Anti-inflammatory, we have corticosteroids divided into systemic and inhaled corticosteroids. To treat moderate to severe chronic allergic Asthma, monoclonal antibodies targeting

IgE, such as omalizumab injection, are utilized [10]. It is used when other asthma medications have failed to manage a patient's Asthma [Figure 5] adequately.

Management of Asthma

It is advisable to assess the severity of Asthma before starting treatment. The GINA guidelines use four categories, intermittent, persistent-mild, persistent-moderate, and persistent-severe, to categorize the severity of Asthma. The most severe kind of Asthma is persistent-severe Asthma [11]. In this type of patient, symptoms appear daily for those with this ailment. Moreover, they can have difficulties daily and often. Based on the severity of Asthma and the patient's symptoms, the treatment course typically increases gradually [Figure 6].

Current Treatment for Severe Asthma

FDA-approved anti-IL-5 treatment medications for severe Asthma. Between 5–10% of asthmatic patients utilize large doses of ICS and/or systemic glucocorticoids, yet this does not sufficiently control their severe Asthma. Six different monoclonal antibodies are approved for treating severe persistent Asthma [12]. The first approved drug is Omalizumab, which has been widely used for the past ten years. The present treatment for severe persistent Asthma is Omalizumab, sold under the brand name Xolair. Omalizumab's mechanism of action is Omalizumab binds to IgE and creates immune complexes that lower levels of free [13].

IgE in the blood and stop them from interacting with high-affinity IgE receptors ($Fc\epsilon RI$) expressed by dendritic cells, mast cells, basophils, and eosinophils. As a result, eosinophil infiltration, mast cell/basophil degranulation, and IgE-dependent antigen presentation are all blocked [14]. Anti-IgE treatment with Omalizumab reduces $Fc\epsilon RI$ expression as well. All of these actions contribute to a reduction in allergic airway inflammation and asthma symptoms and exacerbations [Figure 7].

Cinqair and its Mechanism of Action

The drug reslizumab are sold under the trade name CINQAIR. Reslizumab is humanized monoclonal antibody against interleukin-5 that impairs eosinophil maturation, proliferation, and chemotaxis [Figure 8]. It is a biological agent, and the dosing type is injectable. It is administered intravenously [15]. Reslizumab is administered intravenously (IV) over 20–50 minutes at a dose of 3 mg/kg dependent on the patient's weight once every four weeks. Future asthma exacerbations are more likely when blood eosinophil levels are elevated [16].

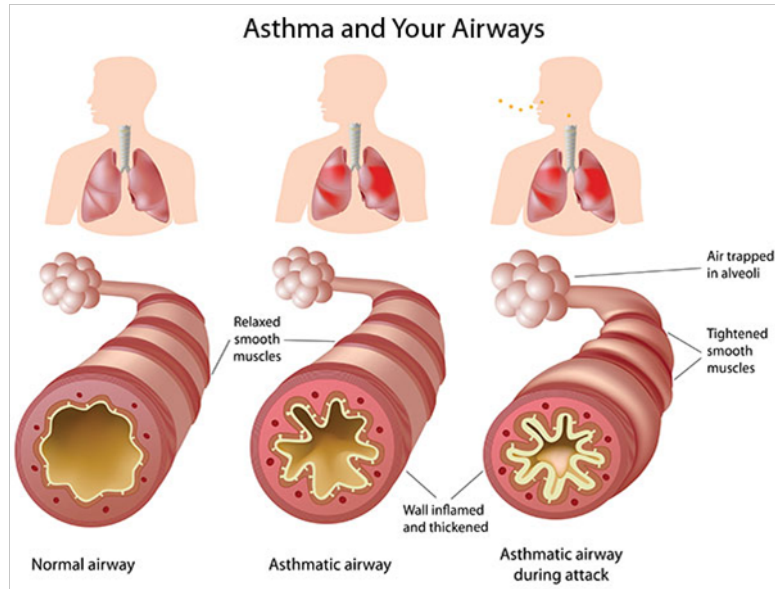


Figure 1: Pathophysiology of Asthma Disease



Figure 2: Symptoms of Asthma

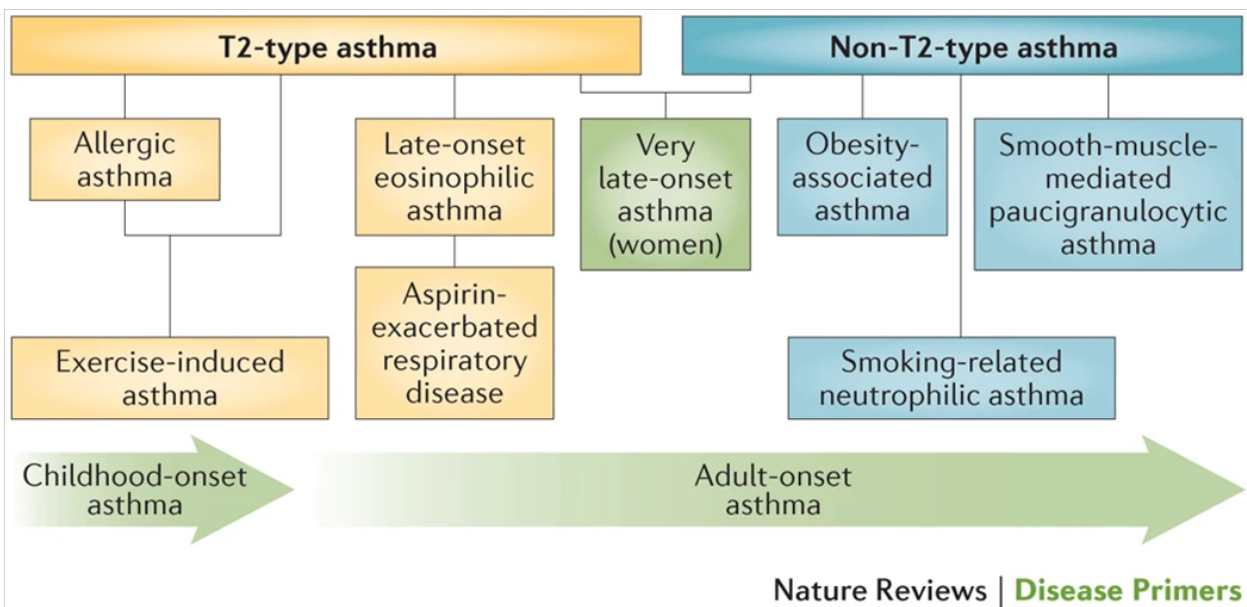


Figure 3: Categorization of Onset of Asthma in Childhood and Adult

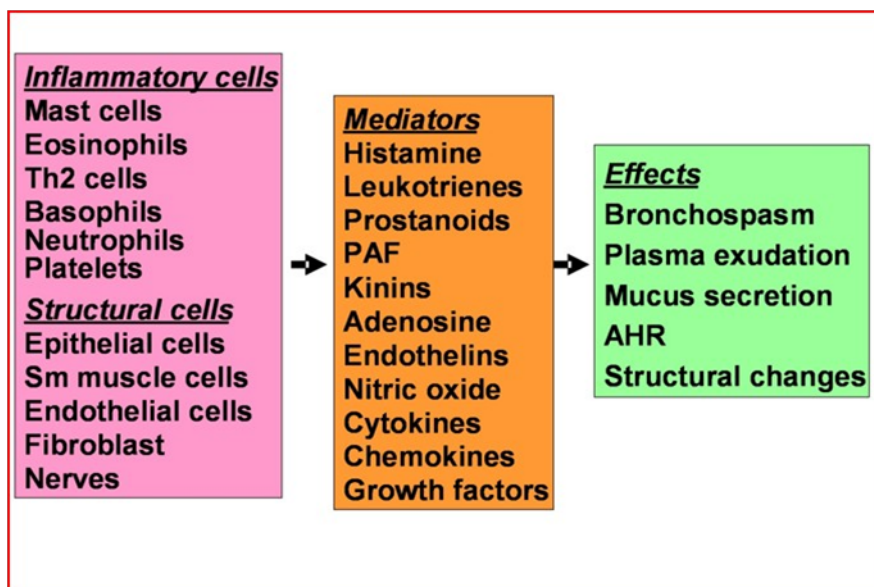


Figure 4: Different Inflammatory Cells and Mediators and Their Effects (PAF =Platelet Activating Factor, AHR = Airway Hyper Responsiveness)

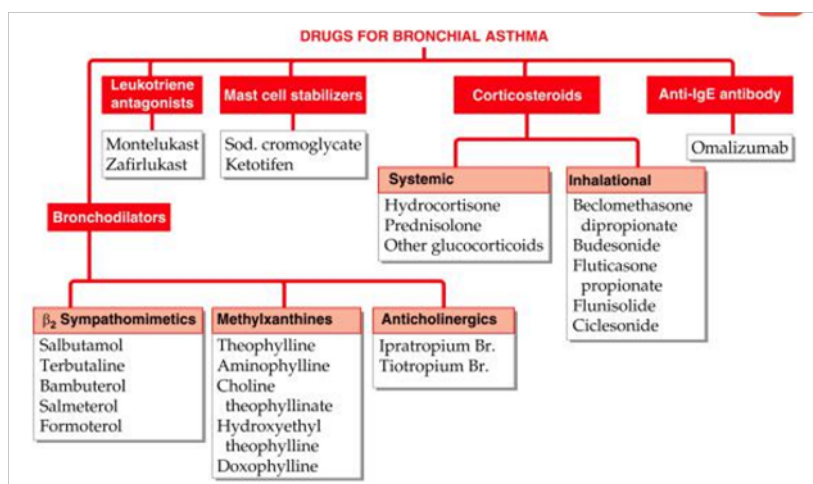


Figure 5: Anti-Asthmatic Drugs

CINQAIR is an asthma drug used to treat severe, uncontrolled eosinophilic Asthma. CINQAIR is a prescription add-on medication for adults over the age of 18. Those with high eosinophil levels and Asthma that are not controlled by available asthma medicines. CINQAIR is the only anti-IL-5 medication with a weight-based dosage [17]. Weight-based dosing enables your doctor to adapt a dosage to your unique requirements. Your weight during therapy determines your customized dose.

Clinical Trails

Based mainly on the data from four clinical studies including 1758 people with severe Asthma, the FDA authorized CINQAIR [18]. Trials occurred in the United States, Canada, Europe, Russia, Israel, Mexico, Argentina, Brazil, Peru, Chile, Columbia, the Philippines, South Africa, Korea, Taiwan, and Aus-

tralia [Figure 9].

Patients with severe asthma and elevated blood eosinophilic counts participated in four clinical studies to assess the effectiveness and side effects of CINQAIR. Every patient was taking their standard asthma medications. Patients got new therapy for 16 to 52 weeks, either with CINQAIR or a placebo [19]. When the experiment was over, neither the patients nor the medical staff knew which new medicine was being administered. The drug's effectiveness in Men and women who took CINQAIR experienced similar effects. Throughout the tested racial groups, CINQAIR performed equally [20]. Both individuals under and over 65 years old experienced the same impact from CINQAIR.

Exacerbations of Asthma were counted to see how effective CINQAIR was, and FEV1 was improved

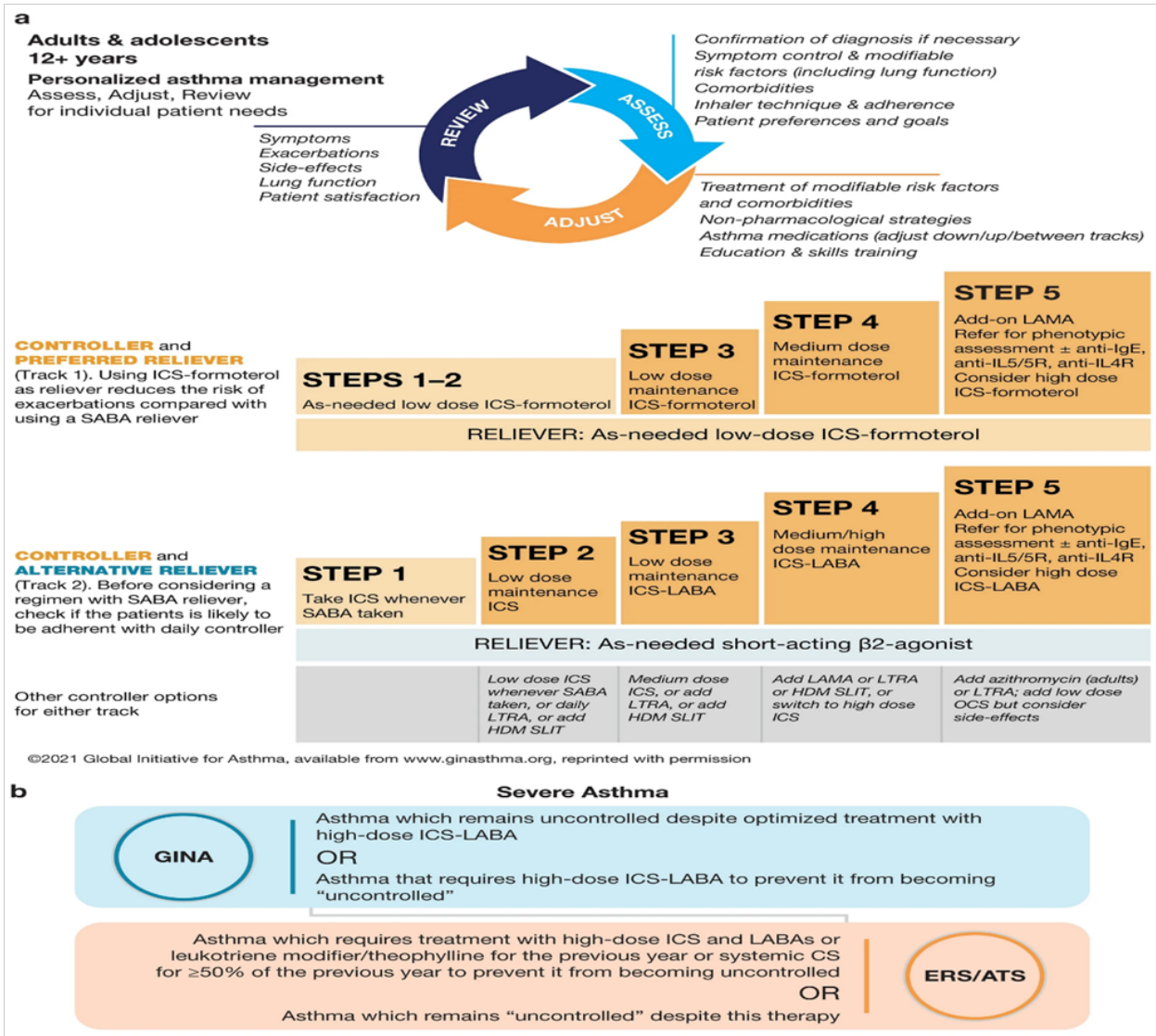


Figure 6: Management of Asthma (ICS= Inhaled Corticosteroids, OCS= Oral Corticosteroids, LAMA=Long-Acting Muscarinic Antagonists, LABA=Long-Acting Beta Agonists, HDM SLIT= House Dust Mite Sub Lingual Immunotherapy, LTRA= Leukotriene Receptor Antagonists)

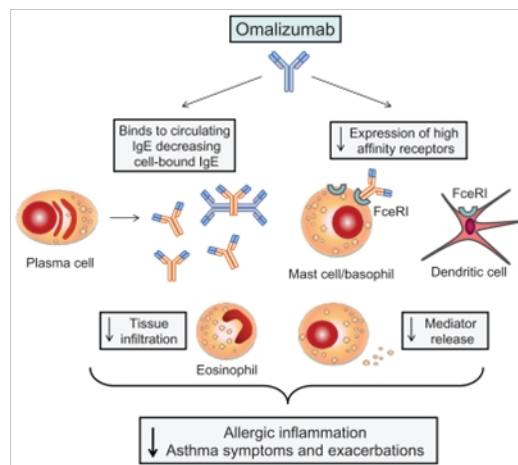


Figure 7: Mechanism of Action of Omalizumab

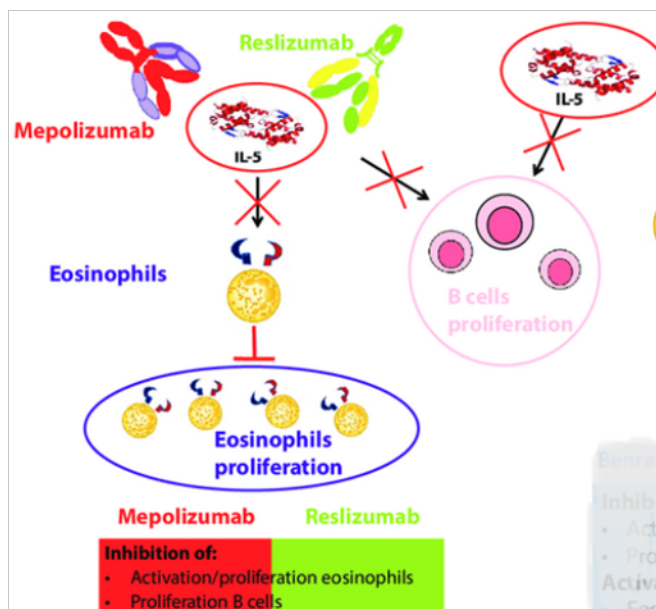


Figure 8: Cinqair and its Mechanism of Action

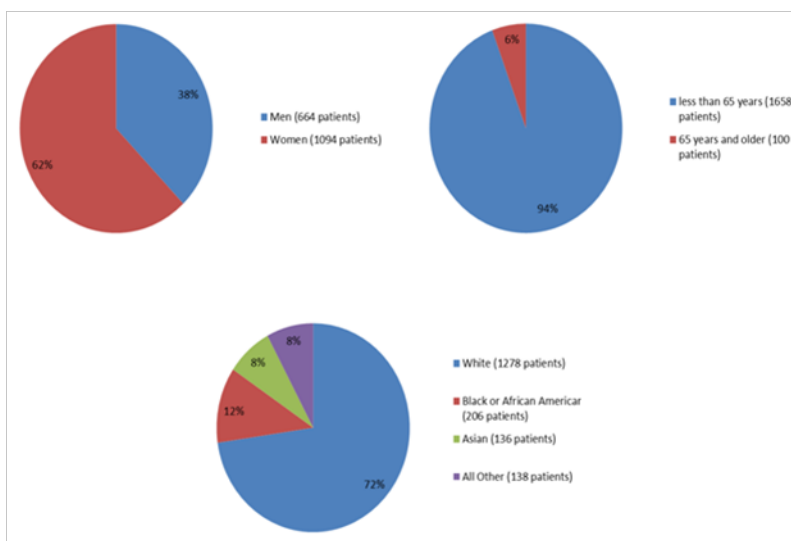


Figure 9: Baseline Demographics of the Clinical Trials

(forced expiratory volume in one second). Individuals on CINQAIR saw fewer asthma attacks and better lung airflow [21].

Peak blood concentrations of reslizumab are frequently recorded toward the end of an infusion. A biphasic decrease in serum concentration occurs. Multiple dosage administrations cause an increase in serum concentrations. (wherein body) Metabolism of Reslizumab is degraded by enzymatic proteolysis into tiny peptides and amino acids, just as other monoclonal antibodies. The elimination of Cinqair and the half-life of reslizumab are 24 days, and it is eliminated at a rate of roughly 7 mL per hour [22].

Cinqair can have substantial adverse effects, including allergic responses (hypersensitivity). These

responses have the potential to be fatal. In clinical studies for Cinqair, the most prevalent side events were anaphylaxis, malignancy, and muscular discomfort.

This real-world observational investigation examined one of the research data from 134 persons with severe eosinophilic Asthma who were registered with the Netherlands severe asthma registry (RAP-SODI). These people underwent at least a six-month follow-up after beginning reslizumab therapy before April 2020. Clinical asthma specialists responded to surveys about their experiences with reslizumab therapy. Therefore, 59.2 percent of the patients reacted strongly or excellently to reslizumab. Following shifting from another biologic, physician surveys revealed that reslizumab had an additional

impact [23].

Quality Adjusted Life Years

The cost of Asthma in Europe between the ages of 15 and 64 has been calculated at €19,000 million per year. Asthma costs the economy 0.2% of its GDP in Italy alone each year, whereas it costs £880 million in the U.K. each year. Asthma prevalence is rising in emerging nations, representing a significant economic burden.

Nations such as Mexico spend \$32-\$35 million to cover the immediate costs of the sickness. In Canada, the indirect expenses of Asthma may exceed 50% of the total price of the illness. Over the course of a year, the Asthma Cost research project investigated 627 adult asthmatic patients. Those with intermittent Asthma will pay €959 in associated charges, while those within assessments of the expenditures paid by 1098 asthmatic patients aged 18 to 65 were made. The impact of illness on work productivity was evaluated in addition to clinical information, lung function, and asthma control level. In addition to the mean job performance, lost workday equivalents (LWDEs), and missed workdays, the study included the number of days worked while experiencing asthma symptoms. The average cost per LWDE was €285.8/month, with indirect expenses increases with age patients (€405/month), patients with more severe illness (€698/month), and those with worse asthma control (€466.8/month). As a result, the average cost per asthmatic patient over three months would be €1317, while this figure would rise to €3301 for older patients, increasing disease severity and poorer asthma management [24].

Public-Private Partnerships

The Minnesota Department of Human Services is a state government organization that provides some services to Minnesota citizens, including healthcare coverage and assistance programs. The Minnesota Department of Human Services covers CINQAIR as part of its healthcare coverage programs.

Teva Canada Innovation has announced that Health Canada has approved CINQAIR. Teva Canada Innovation is dedicated to developing medicines that meet the unmet needs of patients, healthcare professionals, carers, and payers in our major therapeutic areas. Asthma is one of them [25]. With a Novel Biologic for Add-On Maintenance Therapy of Adult Patients with Severe Eosinophilic Asthma, the Organization Starts a Respiratory Franchise in Canada.

CONCLUSION

For those suffering from severe, unmanageable allergic Asthma, biologics are believed to be more effective than other treatments. CINQAIR works in a way that is different from inhalers or steroids. Patients with poorly managed, severe Asthma who also had elevated eosinophil levels As soon as four weeks after being introduced to their previous asthma medications, CINQAIR relieved the severe asthmatic patients. Also, benefits were observed at the end of the one-year study. The usage of oral corticosteroids and asthma exacerbations are decreased by reslizumab, an increase in better lung flow, and a decrease in asthma attacks seen in patients with severe eosinophilic Asthma, according to real-world data. This is true for biologic-naive patients and those who switched from another type 2 biologic. Reslizumab is unlikely to be cost-effective at the WTP due to the improvement in QoL and exacerbation rates coupled with high expenses. Quality of life and symptom management were both enhanced with CINQAIR. Comparatively, people who added CINQAIR to their asthma treatments reported a higher quality of life than those who did not take reslizumab. Those who took CINQAIR had better control over their symptoms. If we look at the cinqair review, it has improved QoL and better effectiveness, absorption, and results from clinical trial data. Immediately following your CINQAIR infusion, severe allergic responses might occur. These responses might be fatal. Sometimes Allergic responses might not always happen immediately. After receiving your CINQAIR infusion, your medical professional will watch for reactions. Your body may experience abnormal cell or tissue development that might be cancer (malignancy) but not cancer; an additional diagnosis must be declared. There is a limited public-private collaboration with Cinqair that needs to have more because the prevalence of the disease is rising compared to the last decade.

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Conflict of Interest

The authors declare no conflict of interest, financial or otherwise.

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