A review and international expert opinion on effective management asthma with biological medications in old patients

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ABSTRACT

Despite excellent therapies and evidence-based guidelines, severe asthma is frequently uncontrolled. The most relevant clinical characteristics to manage severe asthma in adult patients and guide treatment choice were reviewed by a group of worldwide specialists in asthma and biologic drugs from nine countries. Biomarker levels (blood eosinophil count and fractional concentration of exhaled nitric oxide [FeNO]), clinical features (oral corticosteroid [OCS] dependence, specific comorbid disease entities associated with severe type 2 asthma), and safety considerations are all addressed in the recommendations. Biomarkers, such as blood or sputum eosinophil counts, as well as FeNO, appear to have prognostic and predictive value, and should be assessed in all patients with severe asthma, according to current research.

Key Words: *Cardiac rehabilitation; Core components; Guidelines; Heart valve surgery; Heart valve replacement*

INTRODUCTION

OCS use is an essential consideration in biologic selection, especially since some biologics have been shown to minimise minimise OCS reliance. Comorbid disorders and safety concerns specific to each biologic should also be taken into account. More data is needed to assess whether biomarker profiles identify people who are better suited to one biologic over another, as there is currently insufficient evidence to support differential response predictions [1].There is a need for more prospective head-to-head studies and post-hoc assessments of clinical trial data. These suggestions, according to the authors, are valuable because they provide expert advice to help health care practitioners make challenging decisions about the quality of care in severe, type 2 asthma treated with biologic drugs. Due to a paucity of head-to-head comparisons, they remain conditional and are based on restricted data.

Chronic asthma

Asthma is a chronic inflammatory illness that affects 339 million people worldwide, with severe asthma affecting 5% to 10% of those affected. Severe asthma creates persistent symptoms that have a negative impact on one's Quality Of Life (QoL) and can lead to life-threatening exacerbations.

Although severe asthma affects a tiny percentage of the total asthma population, it is associated with much higher health-care expenses and indirect costs, with severe exacerbations in these patients resulting in significant health-care costs as well as psychological load [2]. When maximal, high-intensity medication is required for management or when it remains uncontrolled despite treatment adherence, asthma is classed as severe. To maintain disease control and decrease exacerbations, severe asthma requires maintenance treatment with high-dose Inhaled Corticosteroids (ICS) with supplementary controller medication(s) or systemic corticosteroids. Despite the availability of effective asthma treatments, severe exacerbations remain a significant health concern that can result in serious consequences such as hospitalisation or death, with asthma exacerbations occurring three times more frequently in individuals with uncontrolled asthma. About a quarter of people with severe asthma have four or more exacerbations per year. Different phenotypes of severe asthma have been identified. Identification of a patient's specific asthma phenotype is important not only for research or clinical trials, but also in clinical practise to guide therapy in the implementation of a successful treatment plan to improve QoL, reduce exacerbations, and limit hospitalizations in this persistent, often uncontrolled disease. In numerous asthma phenotypes, including those with both allergic and nonallergic traits, the eosinophil granulocyte has been identified as a significant

mediator of airway inflammation. Eosinophils have a variety of biological roles, including serving as antigen-presenting cells and releasing type 2 (T2) cytokines, as well as promoting dendritic cell development by the production of eosinophil-derived neurotoxic. Furthermore, there is a strong link between nasal and pharyngeal eosinophil peroxidase (EPX) levels and the eosinophil percentage of induced sputum, with EPX-produced oxidants linked to mucus plug development and chronic airflow restriction in severe asthma. Eosinophils are also key players in immunity, as their cytokines and growth factors play a role in proinflammatory responses. T2 asthma accounts for over 70% of severe asthma cases, according to the International Severe Asthma Registry [3]. T2 asthma is characterised by the pathophysiology of InterLeukin (IL)-4, IL-5, and IL-13, which results in both eosinophilic and allergic illness. Eosinophils concentrate in the airway wall and the airway lumen in eosinophilic asthma, where their activation and degranulation contribute to airway inflammation, mucus hypersecretion, mucus plugging, bronchoconstriction, and airway remodelling. Increased Blood Eosinophil Counts (BECs) are linked to more severe asthma, increased exacerbation frequency, and asthma mortality. Several asthma biologic medicines target eosinophil-associated airway inflammation as a therapeutic target.

The FDA has approved five biologics to treat severe T2 asthma (containing both allergic [total IgE with a set range] and eosinophilic asthma), each with its own mechanism of action. Omalizumab is used to treat moderate-to-severe persistent asthma in children aged 6 and above who have a positive skin test or in vitro reactivity to a perennial aeroallergen and symptoms that are not well managed with inhaled corticosteroids (ICS. Omalizumab is a recombinant humanised IgG1 monoclonal antibody (mAb) therapy that targets and binds free IgE, interrupting the IgE-mediated asthma inflammatory cascade at an early stage, reducing both early and late asthmatic responses and improving exacerbations, lung function, and asthma control, with a stronger effect on exacerbations. Mepolizumab, reslizumab, and benralizumab are three immunomodulator Monoclonal Antibody (mAb) medicines that diminish eosinophilic inflammation and are suggested as add-on therapies for individuals with severe, uncontrolled asthma who have an eosinophilic phenotype. Mepolizumab is a fully humanised Monoclonal Antibody (mAb) that binds to IL-5, blocking its action as a key inflammatory cytokine in eosinophil development, activation, and survival; in clinical trials, it reduces exacerbation rates, improves lung function, reduces OCS exposure, and shows clinically significant improvement for patients with a BEC of 150 cells/L at baseline, as well as better outcomes in those with adult asthma [4-5]. Dupilumab is a fully human mAb directed against the α-subunit of the IL-4 receptor and blocks both IL-4 and IL-13 signal transduction, which significantly lowers rates of severe asthma exacerbations and OCS use and demonstrates improvement in lung function versus placebo, with the greatest treatment benefits observed for patients with elevated BEC and/or FeNO levels. In actual practise, clinicians face a difficult problem in determining which of these five biologics is the best therapy option for any given patient, due to the high overlap in patient features among those who qualify for different biologics. There are no direct comparisons between biologics, and meta-analyses and network analysis have yielded equivocal results [6]. Over the last five years, several algorithms for the selection of biologics in severe asthma have been published, with some of them predating currently accessible molecules. In severe asthma that is still uncontrolled, there is a definite need for a planned therapeutic approach. It's critical to make a solid first choice in order to minimise unfavourable switching, avoid unnecessary exposure to expensive medications, reduce the risk of patient distrust, and lower the cost of care.

Treatment of asthma

In severe asthma that is still uncontrolled, there is a definite need for a planned therapeutic approach. It's critical to make a solid first choice to minimise unfavourable switching, eliminate unnecessary exposure to expensive medications, reduce the danger of patient distrust, and reduce the chance of antidrug antibodies. Some of the existing therapy algorithms are complicated, and they don't fully address the best anti-IgE, anti-IL-5, anti-IL-5 receptor, and anti-IL-4 receptor treatments [7]. Due to the restrictions and availability of biologic therapy, as well as the ease of switching between biologic drugs, individual country reimbursement practises may also dictate decisions. For optimum, customised therapy of this patient population, updated clinical treatment recommendations are required. The goal of this summary and expert opinion is to look into biomarker levels (BEC and FeNO), clinical features (OCS dependence and specific comorbid disease entities associated with severe T2 asthma [e.g., severe atopic dermatitis, CRSwNP, perennial allergy, eosinophilic granulomatosis with polyangiitis (EGPA), and eosinophilic pneumonia]), and research into biomarker levels (BEC and FeNO) and safety issues, some of which haven't been addressed in prior clinical guidelines. All advice and comments should be understood with the particular patient in mind, as well as their clinical conditions, perceptions, values, and preferences. Biologics that target important inflammatory pathways have recently emerged as new therapy alternatives for severe asthma. At the moment, existing drugs target diverse components of T2 immunity, and their indications frequently overlap. The proposed treatment guidelines for the initial choice and potential switch between biologic medications for the management of adult patients with severe asthma are based on current evidence, including clinical trial data and analyses, because direct head-to-head clinical studies for biologics are lacking. This guidance also takes into account the essential difficulties, as well as a grasp of the key aspects of the various treatment alternatives, as well as clinical practise experience. New information on severe asthma phenotyping and treatment choices has come from recent research and clinical studies. The roundtable's goal was to come up with treatment recommendations that took into account Biomarker concentrations (BEC and FeNO levels), clinical features (OCS dependence and comorbid disease entities associated with severe T2 asthma [perennial allergy, CRSwNP, and severe atopic dermatitis]), and biologic medication safety concerns [8]. An expert opinion on treatment recommendations for people with severe asthma who are using biologic drugs was developed. In clinical practise, BEC and FeNO levels can be utilised to aid in the selection of anti-IL-5, anti-IL-5R, and anti-IL-4/13 medications for patients with severe T2 asthma. If a patient's response to first-line medication isn't satisfactory, another therapeutic option targeting a different T2 inflammatory pathway or the potential of non-T2 disease would be considered. In order to determine therapy responsiveness for biologic drugs in individuals with severe asthma, an appropriate trial of at least 4 to 6 months is required. Physicians should evaluate patient response to treatment based on predetermined goals provided with the patient at the start of treatment. Treatment is usually evaluated using a multimodal approach that includes OCS reduction, symptom control, lung function, and exacerbations. Exacerbations are the most crucial of the outcomes when any of the predetermined goals is considered therapeutic success Graft (CABG). Patients with a BEC count of 150 cells per litre Persistently low BEC and FeNO levels who are not taking systemic Sensitization to perennial allergens alone does not suggest T2 airway inflammation or the potential

efficacy of biologic treatment in the absence of high BEC (but within the normal range) and FeNO levels [9]. Physicians should investigate the patient's clinical history and examination to determine the underlying cause of the patient's clinical condition if there is no evidence of a clear T2 inflammatory signal. Treatment with anti-IgE could be recommended for individuals with FeNO 25 ppb and confirmation of perennial allergy, as well as a history of proven allergy-provoked asthma symptoms. Although there is a lack of clinical trial data to support efficacy in this group, real-world data and clinical experience have shown that anti-IgE treatment is useful for individuals with allergen sensitivity (including those with high FeNO and BEC levels) that may benefit from anti-IgE therapy. Treatment with anti-IL-4/13 or anti-IgE is advised for patients with FeNO 25 ppb and confirmation of perennial allergy, as well as a clear history of proven allergy-provoked asthma symptoms. If an allergy history cannot be established, anti-IL-4/13 therapy is advised because they provide energy, help patient regain strength, boost immunity and as a results enhance.

REFERENCES

1. TTo, S. Stanojevic, G. Moores, et al. Asthma prevalence in adults: findings from the cross-sectional world health survey. BMC Public Health. 2012;12(1):204.

2. K.F Chung, SE. Wenzel, JL Brozek, et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. Eur Respir J. 2014;44:343-373.

3. P.P. Hekking, R.R. Wener, M. Amelink, et al. The prevalence of severe refractory asthma. J Allergy Clin Immunol. 2015;896-902.

4. E. Zervas, K. Samitas, A.I. Papaioannou, et al. An algorithmic approach for the treatment of severe uncontrolled asthma. ERJ Open Res. 2018;(1):125.

5. BE Chipps, J Corren, E Israel, et al. Asthma Yardstick: practical recommendations for a sustained step-up in asthma therapy for poorly controlled asthma. Ann Allergy Asthma Immunol. 2017;118 :133-142.

6. R.S. Zeiger, M. Schatz, A.A. Dalal, et al. Utilization and costs of severe uncontrolled asthma in a managed-care setting. J Allergy Clin Immunol Pract. 2016;4:120-129.

7. M. Kerkhof, TNTran, JB Soriano, et al. Healthcare resource use and costs of severe, uncontrolled eosinophilic asthma in the UK general population. Thorax. 2018;73:116-124

8. El Badrawy MK, Elela MA, Yousef AM, et al. Effect of sodium bicarbonate 8.4% on respiratory tract pathogens. Chest Lung Res. 2018;1(1):3-7.

9. Sharma MV. Early diagnosis of viral pneumonia. J Pulmon. 2019;3(1):1-3.