REVIEWS

ISSN 2307-9266 e-ISSN 2413-2241

Scientific and Practical Journal
PHARMACY & PHARMACOLOGY
(ФАРМАЦИЯ И ФАРМАКОЛОГИЯ)

Targeted therapy of bronchial asthma in children and adolescents: A narrative review

M.S. Matevosova[1], L.I. Agapitov[1], I.A. Averina[1, 2], I.V. Sokolova[2], S.V. Zotova[2], R.A. Chernigovsky[1, 2]

[1] Pyatigorsk Medical and Pharmaceutical Institute – branch of Volgograd State Medical University, 11 Kalinin Ave., Pyatigorsk, Russia, 357532

[2] Clinical Hospital No. 10 – branch of North Caucasus Federal Scientific and Clinical Center, 26 Lenin Str., Lermontov, Russia, 357341

E-mail: milalean2001@gmail.com

Received 05 Nov 2024 After peer review 23 Dec 2024 Accepted 30 Dec 2024

The aim. To evaluate the results of clinical studies on the efficacy and safety of bronchial asthma (BA) therapy with genetically engineered biologicals (GEBP) in children and adolescents.

Materials and methods. For writing this review article, a search for full-text publications was conducted in the PubMed database. Studies on the efficacy and safety of biologicals — monoclonal antibodies, in the treatment of BA refractory to therapy with inhaled glucocorticosteroids and beta-2-agonists, in children and adolescents from 2010 to 2025 were analyzed using the following key queries"bronchial asthma", "monoclonal antibodies", "anti-IgE antibody", "anti-IL-receptor antibody", "anti-thymic stromal lymphopoietin antibody", "adolescents", "children".

Results. The observed continuing and steady increase in the incidence of BA, the involvement of several organ systems in the pathological process, the difficulty in choosing treatment tactics, the high cost of therapy, and the need to monitor the patient's condition place this disease in a special place among modern medical problems. To date, advances in genetic engineering have made it possible to introduce GEBPs — monoclonal antibody drugs, into medical practice as one of the steps in the treatment of poorly controlled and resistant to first-line therapy BA of moderate and severe severity. According to recent clinical studies among children and adolescents, biologicals to varying degrees can affect symptom control, lung function, frequency of exacerbations, requests for emergency medical care and hospitalizations, as well as reducing the dosages of glucocorticosteroids and beta-2-agonists used.

Conclusion. To date, positive results have been noted in the use of monoclonal antibodies in the treatment of BA, but clinical trial data among children and adolescents are limited. There is also insufficient information about the consequences of the mechanism of influence of these drugs in relation to long-term inhibition of the immune system and a decrease in the content of eosinophils in the blood serum in the developing child's body. To formulate a final conclusion, further study of the long-term efficacy and safety of biologicals in pediatric practice is necessary in order to combat this serious public threat.

Keywords: bronchial asthma; monoclonal antibodies; immunoglobulin E; interleukins; thymic stromal lymphopoietin; pediatrics

Abbreviations: BA — bronchial asthma; GEBP — genetically engineered biological products / biologicals; GCs — glucocorticosteroids; GINA — Global Initiative for Asthma; IgE — immunoglobulin E; FEV1 — forced expiratory volume in 1 second; IFN-α — interferon-alpha; IL — interleukin-4; TSLP — thymic stromal lymphopoietin.

For citation: M.S. Matevosova, L.I. Agapitov, I.A. Averina, I.V. Sokolova, S.V. Zotova, R.A. Chernigovsky. Targeted therapy of bronchial asthma in children and adolescents: A narrative review. *Pharmacy & Pharmacology.* 2024;12(5):362-373. **DOI:** 10.19163/2307-9266-2024-12-5-362-373

Для цитирования: М.С. Матевосова, Л.И. Агапитов, И.А. Аверина, И.В. Соколова, С.В. Зотова, Р.А. Черниговский. Таргетная терапия бронхиальной астмы у детей и подростков: описательный обзор. *Фармация и фармакология.* 2024;12(5):362-373. **DOI:** 10.19163/2307-9266-2024-12-5-362-373

Научно-практический журнал
ФАРМАЦИЯ И ФАРМАКОЛОГИЯ
(PHARMACY & PHARMACOLOGY)

ОБЗОРЫ

DOI: 10.19163/2307-9266-2024-12-5-362-373

Таргетная терапия бронхиальной астмы у детей и подростков: описательный обзор

М.С. Матевосова[1], Л.И. Агапитов[1], И.А. Аверина[1,2], И.В. Соколова[2], С.В. Зотова[2], Р.А. Черниговский[1,2]

[1] Пятигорский медико-фармацевтический институт – филиал федерального государственного бюджетного образовательного учреждения высшего образования «Волгоградский государственный медицинский университет» Министерства здравоохранения Российской Федерации, Россия, 357532, г. Пятигорск, пр-кт Калинина, д. 11

[2] Клиническая больница № 10 – филиал федерального государственного бюджетного учреждения «Северо-Кавказский федеральный научно-клинический центр Федерального медико-биологического агентства России», Россия, 357341, г. Лермонтов, ул. Ленина, д. 26

E-mail: milalean2001@gmail.com

Получена 05.11.2024 После рецензирования 23.12.2024 Принята к печати 30.12.2024

Цель. Провести оценку результатов клинических исследований, посвящённых изучению эффективности и безопасности терапии бронхиальной астмы (БА) генно-инженерными биологическими препаратами (ГИБП) у детей и подростков.

Материалы и методы. Для написания данной обзорной статьи был проведён поиск полнотекстовых публикаций в базе данных PubMed. Были проанализированы работы по изучению эффективности и безопасности применения биологических препаратов — моноклональных антител, в лечении БА, рефрактерной к терапии ингаляционными глюкокортикостероидами и бета-2-агонистами, у детей и подростков с 2010 по 2025 гг. с использованием следующих ключевых запросов: «bronchial asthma», «monoclonal antibodies», «anti-IgE antibody», «anti-IL-receptor antibody», «anti-thymic stromal lymphopoietin antibody», «adolescents», «children».

Результаты. Наблюдаемый продолжающийся и неуклонный рост заболеваемости БА, вовлечённость нескольких систем органов в патологический процесс, сложность выбора тактики лечения, высокая стоимость терапии и необходимость в мониторинге состояния пациента ставят рассматриваемое заболевание на особое место среди современных проблем медицины. На сегодняшний день достижения в области генной инженерии позволили внедрить в медицинскую практику ГИБП — препараты моноклональных антител, в качестве одной из ступеней лечения плохо контролируемой и резистентной к терапии препаратами первой линии БА средней и тяжёлой степени тяжести. По данным последних клинических исследований среди детей и подростков, биологические препараты в разной степени способны влиять на контроль симптомов, функцию лёгких, частоту обострений, обращений за неотложной медицинской помощью и госпитализаций, а также снижение дозировок применяемых глюкокортикостероидов и бета-2-агонистов.

Заключение. На сегодняшний день отмечаются положительные результаты применения моноклональных антител в терапии БА, однако данные клинических исследований среди детей и подростков ограничены. Также недостаточно информации о последствиях механизма действия данных препаратов в отношении длительного ингибирования иммунной системы и снижения содержания эозинофилов в сыворотке крови в развивающемся организме ребенка. Для формулирования окончательного вывода необходимо дальнейшее изучение долгосрочной эффективности и безопасности применения биологических препаратов в педиатрической практике в целях борьбы с этой серьезной общественной угрозой.

Ключевые слова: бронхиальная астма; моноклональные антитела; иммуноглобулин Е; интерлейкины; тимический стромальный лимфопоэтин; педиатрия

Список сокращений: БА — бронхиальная астма; ГИБП — генно-инженерные биологические препараты; ГКС — глюкокортикостероиды; GINA — Глобальная инициатива по борьбе с астмой; IgE — иммуноглобулин Е; ОФВ1 — объём форсированного выдоха за 1 секунду; ИФН-α — интерферон-альфа; ИЛ — интерлейкин-4; ТСЛП — тимический стромальный лимфопоэтин.

INTRODUCTION

Bronchial asthma (BA) is a heterogeneous disease characterized by chronic airways inflammation. Currently, BA is one of the most common pathologies among children and adolescents. The basis for the disease development is a hyperactive immune response of the body to the effects of specific environmental factors — causally significant triggers [1].

To date, the observed tendency of increasing asthma incidence is directly related to the level of urbanization and the environmental situation in the

ISSN 2307-9266 e-ISSN 2413-2241

Scientific and Practical Journal
PHARMACY & PHARMACOLOGY
(ФАРМАЦИЯ И ФАРМАКОЛОГИЯ)

world [2]. Thus, according to epidemiological data, in 2019, the disease was observed in 262 million people [3]. In 2020, the Centers for Disease Control and Prevention published data on the prevalence of BA in the United States: the disease is noted in 25.25 million patients, of which 4.2 million are children. Already in 2021, there is an increase in the latter indicator — 4.68 million people. In Russia[1], as of 2022, 313 thousand children suffering from this pathology were registered[2]. According to the forecasts of the World Health Organization (WHO), there will be a further increase in the number of patients, and already in 2025 there will be more than 400 million people suffering from BA in the world [4].

The disease significantly reduces the quality of life of patients, having a negative impact not only on indicators of physical health, but also on daily activities: academic performance in school and additional sections, playing sports, interacting with peers, socialization in society, which is an important and integral stage in the life of every child [5, 6]. Undoubtfully, this affects the mental state of the growing organism, causing such symptoms as depressed mood, increased fatigue, and loss of strength. The connection between the disease and mental disorders in adulthood is under consideration, it finds its confirmation again in one of the recent studies: major depressive disorder, bipolar affective disorder, generalized anxiety disorder, panic disorder, specific phobias, as well as post-traumatic stress disorder, overeating and alcohol abuse are more common in patients suffering from BA than in the general population [7].

A significant number of patients (10% of patients according to the latest epidemiological data [8], of which 5% are children and adolescents [9]) have refractory asthma, the therapy with first-line drugs — high doses of inhaled glucocorticosteroids (GCs) and beta-2-agonists — does not lead to proper symptom control, which requires the search for new, more effective drugs [10]. In addition, the mechanism of action of GCs is characterized by its non-selectivity — hormonal drugs have a negative impact on many organs and tissues. Long-term use of this pharmacological group entails the development of a number of undesirable reactions and side effects, significantly reducing the quality of life of patients. Thus, studies among people taking GCs show an increased risk of complications from a number of organ systems: musculoskeletal (fractures, osteoporosis, myopathy), cardiovascular (arterial hypertension, heart failure, coronary heart disease, myocardial infarction), endocrine (obesity, diabetes mellitus, amenorrhea), digestive (gastric and duodenal ulcer). Vision organs complications are noted — glaucoma and cataracts. Growth retardation is most often observed in children. Acne appears on the skin, dryness and peeling are observed. Taking GCs is associated with the risk of developing mental disorders such as depression and anxiety. Cases of increased infectious diseases are also described, which is associated with the immunosuppressive effect of this group of drugs [11]. Daily intake of GCs in high doses contributes to the suppression of adrenal function according to the mechanism of negative feedback due to exogenous hormones in the body [12]. It was found that even short-term therapy can lead to the development of these adverse events [13]. Therapy with high doses of beta-2-agonists also demonstrates ambiguous results in a number of studies. To date, a conclusion has been formulated about the minimum effective dose of drugs for this pharmacological group in the treatment of BA in adults and adolescents, but it has not yet been determined in young children [14]. Moreover, taking this group of drugs can lead to side effects associated with a stimulating effect on the sympathetic nervous system, which is especially dangerous in patients of the age group under consideration.

Currently, International Clinical Guidelines for the treatment of asthma in children and adolescents consider the prescription of biologicals — monoclonal antibodies — depending on the phenotype of the disease, in order to achieve BA control that has not been achieved with drugs recommended in previous stages of treatment. The creation of genetically engineered biological products (GEBPs) is undoubtedly a revolutionary breakthrough and one of the main achievements of modern medicine. Their introduction into clinical practice has opened up new opportunities and made a major step forward in the treatment of many pathologicals. The mechanism of action of this pharmacological group lies in their interaction with specific molecules that are key links in pathogenesis, which prevents the development of pathology and improves the quality of life of patients.

THE AIM. To evaluate the results of clinical studies on the efficacy and safety of monoclonal antibody therapy for bronchial asthma in children and adolescents.

MATERIALS AND METHODS

The search of full-text publications was conducted in the PubMed database. Studies on the use of

[1] Most Recent Asthma Data. CDC. Available from: https://www.cdc.gov/asthma/most_recent_data.htm
[2] Russian Research Institute of Health. Available from: https://mednet.ru

DOI: 10.19163/2307-9266-2024-12-5-362-373

monoclonal antibodies in the treatment of BA refractory to therapy with inhaled GCs and beta-2-agonists in children and adolescents from 2010 to 2025 were analyzed using the following key queries: “bronchial asthma”, “monoclonal antibodies”, “anti-IgE antibody”, “anti-IL-receptor antibody”, “anti-thymic stromal lymphopoietin antibody”, “adolescents”, “children”. As a result, 1296 sources were found. Exclusion criteria were: non-full-text articles (*n*=21), as well as works that do not directly address the topic of the review (*n*=1 222). As a result, 53 scientific works were included in this review.

RESULTS AND DISCUSSION

Monoclonal antibodies to immunoglobulin E

In the International Clinical Guidelines of the Global Initiative for Asthma (GINA), children over 6 years of age with refractory moderate to severe BA, uncontrolled by high doses of inhaled GCs and long-acting beta-2-agonists, are recommended to take a humanized monoclonal antibody to immunoglobulin E (IgE) — omalizumab[3]. Omalizumab not only interacts with IgE, reducing their content in the blood serum, but also inhibits the binding of these molecules to high-affinity FCER1 receptors on mast cells, basophils and dendritic cells (Fig. 1.). Thus, the release of biologically active substances — inflammatory mediators — by the listed immunocompetent cells is prevented [15].

Nowadays, there are a number of scientific papers on the evaluation of the efficacy and safety of this drug in pediatric practice. In a study involving 38 children aged 7 to 16 years, 35 of whom (92.1%) completed it, children were injected with omalizumab subcutaneously at a dosage of 75 to 375 mg every 2 or 4 weeks. As a result, 29 patients (76.3%) had good BA control, based on the results of the Japanese pediatric BA Control Program Questionnaire [16].

After 6 months of treatment, according to the results of a study among children and adolescents with severe BA, a decrease in the number of exacerbations was recorded during omalizumab therapy compared to the previous year (1.03 and 7.2, respectively). After another year of observation, the number of exacerbations was 0.8. In addition, it was noted that the frequency of hospitalizations decreased by 96%. No adverse events were reported [17].

Omalizumab also demonstrated efficacy and safety in study involving 6 patients with moderate to severe BA aged 10 to 13 years. The drug was administered subcutaneously at a dosage of 150 to 600 mg every 2 or 4 weeks. Already after 16 weeks, an increase in the score in the Asthma Control test was registered by 55%, and one of the subjects had complete symptom control. In 3 patients, the dosage of inhaled GCs used decreased by 28.2%. The number of exacerbations decreased in 76.93% of participants, and no hospitalizations were observed [18].

According to the latest clinical observations, viral respiratory infections contribute to the exacerbation of BA symptoms. In studies, omalizumab has demonstrated an enhanced response of the non-specific immune system defense factor — interferon-alpha (IFN-α), which reduced the frequency of virus-induced respiratory infections, as well as their duration in children and adolescents with BA [19, 20].

However, despite the fact that omalizumab therapy has demonstrated high efficacy, and studies examining its safety have not found statistically significant differences in the incidence of adverse events among patients taking this monoclonal antibody and placebo (p <0.05) [21, 22], further research is needed to study the development of side effects, as well as the long-term effect of the drug in pediatric practice.

Monoclonal antibodies to interleukin-4 and interleukin-13

The GINA also consider the use of a humanized monoclonal antibody to the α-chain of the interleukin-4 (IL-4) receptor, capable of, among other things, inhibiting the activity of interleukin-13 (IL-13) — dupilumab, in children over 6 years of age with BA. IL-4, being a signaling molecule, activates T-helpers involved in the implementation of the inflammatory reaction, and IL-13 stimulates the synthesis of periostin by epithelial cells of the bronchi (Fig. 2). Periostin participates in the contraction of smooth muscles of the bronchi and hyperplasia of cells of endoepithelial glands [23]. Consequently, exposure to these targets prevents the development of bronchospasm and mucus hypersecretion, which makes it impossible to implement a hyperactive reaction of the upper respiratory tract in response to a specific allergen or other causative triggers [24].

To date, there are few studies on the efficacy of dupilumab, limited to adult and adolescents patients. According to the results of one such scientific work, 0.46 exacerbations per year were recorded in subjects older than 12 years who took the drug at a dosage of 200 mg every 2 weeks. Among patients who took placebo, this figure was 0.87 per year. Also, in the group of subjects taking dupilumab, an improvement in lung function

[3] Global Initiative for Asthma. Global strategy for asthma management and prevention. Available from: https://ginasthma.org/wp-content/uploads/2024/05/GINA-2024-Strategy-Report-24_05_22_WMS.pdf

ISSN 2307-9266 e-ISSN 2413-2241
Scientific and Practical Journal
PHARMACY & PHARMACOLOGY
(ФАРМАЦИЯ И ФАРМАКОЛОГИЯ)

was noted: the value of forced expiratory volume in 1 sec (FEV1) increased by 0.32 L. The drug showed its effectiveness regardless of the initial content of eosinophils in the serum of studied participants [25]. The most common side effects of dupilumab were injection site reactions (pain, tissue swelling, hyperemia and itching), inflammation of the mucous membrane of the eyes, herpetic infection of the oral cavity, and joint pain [26]. In a study among patients with GCs-dependent BA, a decrease in the dosage of GCs used was recorded (70.1%) compared with the results in the placebo group (41.9%): 80% of individuals in the control group reduced the dosage by 50%, and 48% of subjects completely stopped taking hormone therapy [27].

It was also found that taking dupilumab helps to improve the quality of life in patients with concomitant allergic diseases. Thus, in patients with severe uncontrolled BA and concomitant allergic rhinitis, taking dupilumab at a dosage of 300 mg 2 times/week contributed to a significant improvement in symptoms [28]. Recent studies have revealed that taking dupilumab for concomitant atopic dermatitis contributes to a significant improvement in the clinical picture. The mechanism of alleviating the symptoms of concomitant atopic dermatitis with dupilumab is that systemic blockade of the α-chain of the IL-4 receptor helps to reduce the level of type 2 memory B cells — precursors of B-lymphocytes, and, consequently, IgE in the blood serum [29]. Thus, in one study among children aged 6 months to 5 years suffering from concomitant moderate to severe atopic dermatitis, relief of symptoms was observed as early as 16 weeks of the trial: improvement in the area of eczema and severity index by ≥75% [30]. Among patients with chronic rhinosinusitis with nasal polyps, taking dupilumab demonstrated an improvement in the quality of life of participants. During the survey of patients, there was a significant decrease in the severity of obstruction and discharge from the nose, impaired sense of smell, and a feeling of facial pressure [31]. There is a need for further evaluation of the effectiveness of this monoclonal antibody among children under 12 years of age.

Earlier studies have also been conducted on a drug capable of directly inhibiting IL-13 — lebrikizumab. This humanized monoclonal antibody demonstrated a significant improvement in the clinical picture, according to the results of a recent study among adolescents aged 12 to 17 years with refractory and uncontrolled BA. Over 52 weeks, 113 asthma exacerbations were observed: 31 cases in patients receiving lebrikizumab at a dosage of 125 and 37.5 mg, and 51 cases in participants from the placebo group. As a result, it was concluded that taking lebrikizumab at a dosage of 125 mg contributed to a 51% reduction in the frequency of exacerbations, and at a dosage of 37.5 mg — a 40% reduction. The number of patients with adverse events was the same in both groups of subjects [32]. However, in studies among adult patients, a significant number of subjects experienced adverse events (79%), serious adverse events (8%), and adverse events leading to drug withdrawal (3%). In addition, phase 3 clinical trials did not demonstrate a significant improvement in the clinical picture and a decrease in the frequency of BA exacerbations, even in the group of patients with higher levels of diagnostic markers, therefore, further work with this monoclonal antibody was no longer carried out [33].

Further study of the efficacy and safety of the drug from this group of monoclonal antibodies — tralokinumab — was also discontinued, as this GEBP did not have a significant effect on the frequency of BA exacerbations (only 44%) and improvement in lung function (12.2%) in patients with severe refractory BA compared with placebo [34]. To date, lebrikizumab and tralokinumab are not used in the treatment of BA in children and adolescents due to limited and inconsistent data on their efficacy and safety.

Monoclonal antibodies to interleukin-5

Interleukin-5 (IL-5) is a pro-inflammatory cytokine that promotes the activation and increased lifespan of eosinophils, which is one of the key links in the pathogenesis of BA. Studies on this group of monoclonal antibodies are limited to BA with eosinophilia, as this factor is considered to be prognostic [35]. The IL-5 inhibitor — reslizumab, as well as a humanized monoclonal antibody to the α-chain of the receptor of this signaling molecule — benralizumab, demonstrated mixed results in clinical studies among patients older than 12 years.

The use of reslizumab, according to the results of phase 3 studies among patients aged 12 years and older, contributed to a decrease in the annual frequency of BA exacerbations by 50–59% compared with placebo [36]. However, a number of trials have reported adverse events and side effects, including an increase in the content of the enzyme creatine phosphokinase in the blood serum [37], which confirms the need for further monitoring. Benralizumab was used among patients older than 12 years. During a phase 3 trial involving 728 people (866 patients received benralizumab, and 440 received placebo), it was concluded that the use of this monoclonal antibody led to a decrease in the frequency of exacerbations in the control group (*n*=221). The most common side effect was nasopharyngitis — 39% in the

DOI: 10.19163/2307-9266-2024-12-5-362-373

control group, 21% in the placebo group [38]. However, data on its safety among children and adolescents are limited. To date, in clinical practice, reslizumab and benralizumab are used in the treatment of BA in patients older than 18 years.

From the group of humanized monoclonal antibodies to IL-5 receptors, mepolizumab is the drug of choice for the treatment of BA in children older than 6 years. The mechanism of action is shown in Figure 3.

The study of phase 2 was conducted to evaluate the efficacy and safety of this humanized monoclonal antibody in 36 children with severe BA and eosinophilic airway inflammation. Mepolizumab was administered subcutaneously at a dose of 40 mg (for children weighing less than 40 kg) and 100 mg (for children weighing more than 40 kg) once every 4 weeks. On the 12 weeks, the content of eosinophils in serum and sputum in patients receiving the drug under consideration at a dosage of 40 mg was reduced by 89%, and in patients receiving a dosage of 100 mg, by 83% from the baseline level. More than one exacerbation of BA was observed in 10 patients, 4 of them were hospitalized, and 6 patients reported adverse events [39]. In 2024, the results of work on evaluating the effectiveness of this drug among 16 patients aged 7 to 17 years were published. During therapy with mepolizumab, 3 patients had oral GCs treatment canceled, and another 3 patients had their daily dosage reduced. A decrease in the level of eosinophils in the blood serum was also recorded (on average, by 0.85×109/L) [40]. Data from a study examining the risk/benefit ratio of mepolizumab have also recently been published — in most children, this indicator remained favorable for 10 years of therapy [41]. However, further research is needed to formulate a final conclusion regarding the efficacy and safety of mepolizumab among patients for this age group.

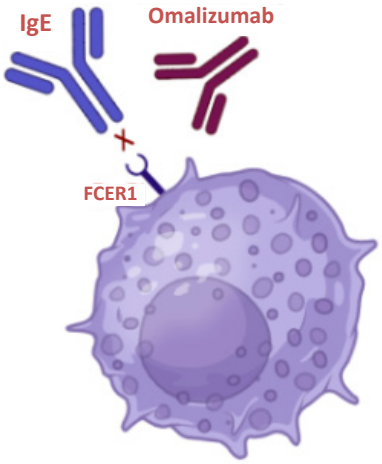

Figure 1 – Mechanism of action of omalizumab
Note: Drawn using the “BioRender” program.

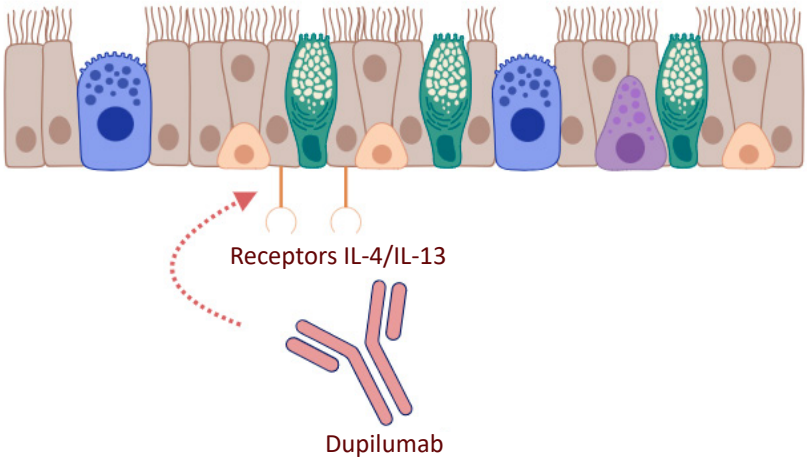

Figure 2 – Mechanism of action of dupilumab
Drawn using the “BioRender” program.

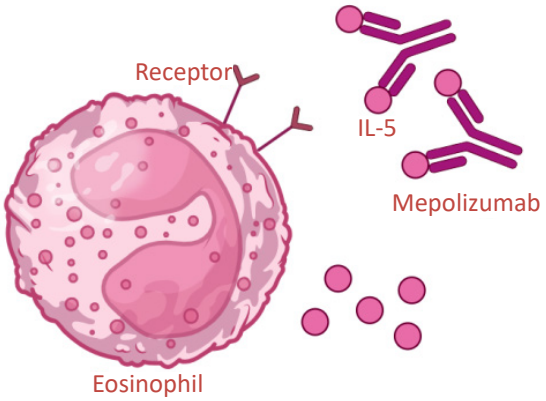

Figure 3 – Mechanism of action of mepolizumab
Note: Drawn using the “BioRender” program.

ISSN 2307-9266 e-ISSN 2413-2241

Scientific and Practical Journal
PHARMACY & PHARMACOLOGY
(ФАРМАЦИЯ И ФАРМАКОЛОГИЯ)

Table 1 – Results of studies of monoclonal antibodies for the treatment of asthma in children and adolescents

Drug	Mechanism of action	Age of participants	Dose	Result	Reference
Omalizumab	Binds to IgE, reducing its content in the blood serum, inhibits the binding of IgE to FCER1 receptors on mast cells, basophils and dendritic cells.	From 7 to 16 years	75–375 mg every 2 or 4 weeks	Good BA control was recorded in 76.3% of patients. The frequency of hospitalizations decreased by 88%. Among the undesirable phenomena, infectious diseases of the upper respiratory tract were observed, but their frequency did not increase with prolonged use of the drug.	[16]
		From 6 years	75–375 mg every 2 or 4 weeks	After 6 months of treatment, a decrease in the number of exacerbations was noted compared to the previous year (1.03 and 7.2, respectively). After a year, the number of exacerbations was 0.8. The frequency of hospitalizations decreased by 96%. No adverse events were observed.	[17]
		From 10 to 13 years	150–600 mg every 2 or 4 weeks	After 16 weeks, an increase in the sum of points in the BA control test by 55% was recorded, one of the subjects had complete symptom control. In 50% of patients, the dosage of GCs used decreased by 28.2%. The number of exacerbations decreased in 76.93% of participants, no hospitalizations were observed.	[18]
Dupilumab	Binds to the α-chain of the IL-4 receptor, inhibits the activity of IL-13	From 12 years	200 mg every 2 weeks	0.46 exacerbations per year were recorded in subjects compared with the placebo group – 0.87 per year. The FEV1 indicator increased by 0.32 liters.	[25]
		From 6 to 11 years	200 mg every 2 weeks	Adverse events were observed: reactions at the injection site of the drug, inflammation of the conjunctiva, herpetic infection of the oral cavity, joint pain, increased levels of eosinophils in the blood serum.	[26]
		From 6 months to 5 years		After 16 week of testing, symptomatic relief was observed: improvement in eczema area and severity index by ≥75%.	[30]
Mepolizumab	Binds to the α-chain of the IL-5 receptor	From 6 to 11 years	40 mg (with body weight <40 kg) and 100 mg (with body weight >40 kg) 1 time every 4 weeks	At week 12, the content of eosinophils in the blood serum and sputum in patients taking the drug at a dosage of 40 mg was reduced by 89%, in patients receiving a dosage of 100 mg—by 83% of the initial level. More than one BA exacerbation was observed in 10 children out of 36, 4 of them were hospitalized, and adverse events were recorded in 6 patients.	[39]
		From 7 to 17 years	40 mg (with weight <40 kg) and 100 mg (with body weight >40 kg) 1 time every 4 weeks	3 out of 16 patients discontinued GCs treatment, and in another 3 patients, their daily dosage was reduced. The drug contributed to a decrease in the frequency of hospitalizations. A decrease in the content of eosinophils in the blood serum was recorded (on average by 0.85×109/L).	[40]
Tezepelumab	Binds to TSLP of the airways	From 12 years old	210 mg every 4 weeks	The exacerbation rate was 0.93 per year in the tezepelumab group and 2.1 in the placebo group. The FEV1 index at week 52 of the trial was 0.23 l in patients taking the drug and 0.09 l in patients taking placebo. The effect of therapy was recorded at 2 week of the study and tended to persist throughout the treatment period.	[47]
		From 12 years old	210 mg every 4 weeks	In 4 out of 65 participants, adverse events from the cardiovascular system (atrial fibrillation) were recorded, as well as the addition of viral and bacterial infectious diseases (gastroenteritis, tonsillitis, lung abscess). 39 patients experienced side effects, the most common of which was nasopharyngitis.	[48]

Note: BA — bronchial asthma; IL — interleukin; GCs — glucocorticosteroids; FEV1 — forced expiratory volume in 1 second; TSLP — thymic stromal lymphopoietin.

DOI: 10.19163/2307-9266-2024-12-5-362-373

Monoclonal antibodies to thymic stromal lymphopoietin

Updated International Clinical Guidelines also include the use of humanized monoclonal antibody thymic stromal lymphopoietin (TSLP), the main regulator of inflammatory processes of the respiratory tract — tezepelumab, in children over 12 years of age with severe refractory asthma. TSLP is a mediator synthesized in large quantities by epithelial cells of the respiratory tract when exposed to environmental factors [42]. It was found that basophils, dendritic and mast cells are also involved in the synthesis of this signaling molecule [43]. TSLP participates in the differentiation of T-helpers, and also promotes the activation of Janus kinase 1 and 2, which, in turn, transmit activating signals to a number of pro-inflammatory cytokines — IL-4, IL-5 and IL-13 [44]. Thus, inhibition of TSLP, a potential therapeutic target in severe asthma, by a monoclonal antibody prevents the production of these signaling molecules, thereby preventing the development of an inflammation [45].

Tezepelumab has shown its effectiveness in the treatment of refractory and uncontrolled BA among adult patients. Participants were divided into 4 groups: 145 patients used the drug at a dose of 70 mg every 4 weeks, 145 patients — at a dose of 210 mg every 4 weeks, 146 patients — 280 mg every 2 weeks, 148 patients made up the placebo group. As a result, a decrease in the frequency of exacerbations was observed for 52 weeks of the study — by 61, 71 and 66% in each group, respectively, in comparison with placebo. Indicators of external respiration also improved: the value of FEV1 before taking a bronchodilator was higher in all groups receiving tezepelumab than in the placebo group (the difference was 0.12, 0.11 and 0.15 L, respectively) [46]. According to the results of a recent study among patients aged 12 years and older to assess the effectiveness of the drug under consideration at a dosage of 210 mg, the frequency of BA exacerbations was 0.93 per year in the tezepelumab group and 2.1 in the placebo group. There was also an improvement in lung function: the FEV1 indicator at 52 weeks of the trial was 0.23 L in patients taking the drug and 0.09 L in patients taking placebo. This effect of therapy was recorded on the 2nd week of the study and tended to persist throughout the treatment period [47]. However, according to the results of clinical trials to assess the safety of this monoclonal antibody among 65 subjects, 4 had adverse events from the cardiovascular system (atrial fibrillation), as well as the addition of viral and bacterial infectious diseases, such as gastroenteritis, tonsillitis and lung abscess. 39 patients experienced side effects, the most common of which was nasopharyngitis [48]. These data confirm the need for further study of the efficacy and safety of this GEBP in children and adolescents.

Genetic Engineering is constantly evolving, developing new promising biologicals for more effective and safer therapy for severe treatment-resistant asthma. Currently, research is being conducted on the first inhaled humanized monoclonal antibody to TSLP — ecleralimab. The inhaled route of administration has several advantages over intravenous and subcutaneous injections — low probability of side effects due to non-systemic administration, the presence of an effect and a high rate of its achievement when administered in small doses, as well as ease of use and lack of trauma [49]. Ecleralimab has shown its effectiveness in a study among adult patients with BA: a decrease in sputum eosinophil content by 64% was observed as early as 7 h and by 52% 24 hours after exposure to the provoking factor [50].

In addition, the use of GIBPs therapy in the treatment of BA helps to improve the mental well-being of patients [51, 52]. Thus, one recent study found that patients responding to monoclonal antibody therapy experienced a reduction in symptoms and a decrease in the severity of major depressive and generalized anxiety disorders [53].

The summary of the results of clinical studies on the use of monoclonal antibodies for the treatment of BA in children and adolescents shown in Table 1.

CONCLUSION

Thus, the creation of GEBPs — monoclonal antibodies, has created new opportunities for the treatment of patients with refractory and uncontrolled BA. The use of monoclonal antibodies as targeted therapy contributes to proper symptom control, improved clinical picture, improved quality of life, as well as socialization and realization of their abilities in studies, creativity, sports, in many other areas of activity. It allows us to conclude that GEBPs have a positive impact not only on physical well-being, but also on the mental health of patients.

However, despite the fact that there are positive results of the usage of these drugs, an important question remains open about the consequences of prolonged inhibition of non-specific immune defense factors and a decrease in the content of eosinophils in the context of the developing immune system of the child's body. Unfortunately, the data from modern clinical trials and scientific research papers in this area are limited to adult patients, which does not allow us to formulate a final conclusion about the long-term effectiveness and safety of using monoclonal antibodies in pediatric practice today.

ISSN 2307-9266 e-ISSN 2413-2241

Scientific and Practical Journal
PHARMACY & PHARMACOLOGY
(ФАРМАЦИЯ И ФАРМАКОЛОГИЯ)

FUNDING

This study did not have financial support from third-party organizations.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS' CONTRIBUTION

All authors made an equivalent and equal contribution to the preparation of the publication.
All authors confirm that their authorship meets the international ICMJE criteria (all authors made a significant contribution to the development of the concept and preparation of the article, read and approved the final version before publication). Milana S. Matevosova, Irina V. Sokolova, Svetlana V. Zotova, Roman A. Chernigovsky — development of the concept and design, study planning, data collection, literature analysis, analysis and interpretation of the data obtained, preparation of a draft manuscript; Leonid I. Agapitov, Irina A. Averina — verification of critical intellectual content, final approval for publication of the manuscript.

REFERENCES

1. Abdel-Aziz MI, Hashimoto S, Neerincx AH, Haarman EG, Cecil A, Lintelmann J, Witting M, Hauck SM, Kerssemakers N, Verster JC, Bang C, Franke A, Dierdorp BS, Dekker T, Metwally NKA, Duitman JW, Lutter R, Gorenjak M, Toncheva AA, Kheiroddin P, Harner S, Brandstetter S, Wolff C, Corcuera-Elosegui P, López-Fernández L, Perez-Garcia J, Martin-Almeida M, Sardón-Prado O, Pino-Yanes M, Potočnik U, Kabesch M, Vijverberg SJH, Kraneveld AD, Maitland-van der Zee AH; SysPharmPediA Consortium. Metabotypes are linked to uncontrolled childhood asthma, gut microbiota, and systemic inflammation. J Aller Clin Immun. 2025;25:457–9. DOI: 10.1016/j.jaci.2025.04.017
2. Kuruvilla ME, Vanijcharoenkarn K, Shih JA, Lee FE. Epidemiology and risk factors for asthma. Resp Med. 2019;149:16–22. DOI: 10.1016/j.rmed.2019.01.014
3. GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet. 2020;396(10258):1204–22. DOI: 10.1016/S0140-6736(20)30925-9
4. GBD 2015 Chronic Respiratory Disease Collaborators. Global, regional, and national deaths, prevalence, disability-adjusted life years, and years lived with disability for chronic obstructive pulmonary disease and asthma, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet Resp Med. 2017;5(9):691–706. DOI: 10.1016/S2213-2600(17)30293-X
5. Montalbano L, Ferrante G, Montella S, Cilluffo G, Di Marco A, Bozzetto S, Di Palmo E, Licari A, Leonardi L, Caldarelli V, Ghezzi M, La Grutta S, Rusconi F. Italian Pediatric Severe Asthma Network (IPSAN) Program of Italian Paediatric Respiratory Society (IPRS). Relationship between quality of life and behavioural disorders in children with persistent asthma: a Multiple Indicators Multiple Causes (MIMIC) model. Sci Rep. 2020;10(1):6957. DOI: 10.1038/s41598-020-62264-9
6. van den Bemt L, Kooijman S, Linssen V, Lucassen P, Muris J, Slabbers G, Schermer T. How does asthma influence the daily life of children? Results of focus group interviews. Health Qual Life Outcomes. 2010;8:5. DOI: 10.1186/1477-7525-8-5
7. Alonso J, de Jonge P, Lim CC, Aguilar-Gaxiola S, Bruffaerts R, Caldas-de-Almeida JM, Liu Z, O'Neill S, Stein DJ, Viana MC, Al-Hamzawi AO, Angermeyer MC, Borges G, Ciutan M, de Girolamo G, Fiestas F, Haro JM, Hu C, Kessler RC, Lépine JP, Levinson D, Nakamura Y, Posada-Villa J, Wojtyniak BJ, Scott KM. Association between mental disorders and subsequent adult onset asthma. J Psy Res. 2014;59:179–88. DOI: 10.1016/j.jpsychires.2014.09.007
8. Chandrasekara S, Wark P. Biologic therapies for severe asthma with persistent type 2 inflammation. Aust Prescr. 2024;47(2):36–42. DOI: 10.18773/austprescr.2024.015
9. Bush A, Fitzpatrick AM, Saglani S, Anderson WC 3rd, Szefler SJ. Difficult-to-Treat Asthma Management in School-Age Children. J Aller Clin Immunol. 2022;10(2):359–75. DOI: 10.1016/j.jaip.2021.11.010
10. Rank M.A., Oppenheimer J.J. Asthma biologics: Underuse, overuse, and best use?. Ann Allergy Asthma Immunol. 2019;122(4):358–9. DOI: 10.1016/j.anai.2018.12.016
11. Lefebvre P, Duh MS, Lafeuille MH, Gozalo L, Desai U, Robitaille MN, Albers F, Yancey S, Ortega H, Forshag M, Lin X, Dalal AA. Acute and chronic systemic corticosteroid-related complications in patients with severe asthma. J Aller Clin Immunol. 2015;136:1488–95. DOI: 10.1016/j.jaci.2015.07.046
12. Kachroo P, Stewart ID, Kelly RS, Stav M, Mendez K, Dahlin A, Soeteman DI, Chu SH, Huang M, Cote M, Knihtilä HM, Lee-Sarwar K, McGeachie M, Wang A, Wu AC, Virkud Y, Zhang P, Wareham NJ, Karlson EW, Wheelock CE, Clish C, Weiss ST, Langenberg C, Lasky-Su JA. Metabolomic profiling reveals extensive adrenal suppression due to inhaled corticosteroid therapy in asthma. Nature Med. 2022;28(4):814–22. DOI: 10.1038/s41591-022-01714-5
13. Price DB, Trudo F, Voorham J, Xu X, Kerkhof M, Ling Zhi Jie J, Tran TN. Adverse outcomes from initiation of systemic corticosteroids for asthma: long-term observational study. J Asthma Allergy. 2018;11:193–204. DOI: 10.2147/JAA.S176026
14. Mukhopadhyay S, Seddon P, Earl G, Wileman E, Symes L, Olden C, Alberti C, Bremner S, Lansley A, Palmer CN, Beydon N. How can we optimise inhaled beta2 agonist dose as 'reliever' medicine for

wheezy pre-school children? Study protocol for a randomised controlled trial. Trials. 2016;17(1):541. DOI: 10.1186/s13063-016-1437-7

15. Hoch HE, Anderson WC III, Szefler SJ. Kendig and chernick's disorders of the respiratory tract in children, 9th ed; Missouri: Elsevier Publishing; 2019. DOI:10.1016/C2011-0-05011-1
16. Odajima H, Ebisawa M, Nagakura T, Fujisawa T, Akasawa A, Ito K, Doi S, Yamaguchi K, Katsunuma T, Kurihara K, Teramoto T, Sugai K, Nambu M, Hoshioka A, Yoshihara S, Sato N, Seko N, Nishima S. Long-term safety, efficacy, pharmacokinetics and pharmacodynamics of omalizumab in children with severe uncontrolled asthma. Allergolog Inter. 2017;66(1):106–15. DOI: 10.1016/j.alit.2016.06.004
17. Licari A, Castagnoli R, Denicolò C, Rossini L, Seminara M, Sacchi L, Testa G, De Amici M, Marseglia GL. Omalizumab in Childhood Asthma Italian Study Group. Omalizumab in Children with Severe Allergic Asthma: The Italian Real-Life Experience. Curr Respir Med Rev. 2017;13(1):36–42. DOI: 10.2174/1573398X13666170426094536
18. Caminiti L, Galletta F, Foti Randazzese S, Barraco P, Passanisi S, Gambadauro A, Crisafulli G, Valenzise M, Manti S. Early Assessment of Efficacy and Safety of Biologics in Pediatric Allergic Diseases: Preliminary Results from a Prospective Real-World Study. Children (Basel). 2024;11(2):170. DOI: 10.3390/children11020170
19. Esquivel A, Busse WW, Calatroni A, Togias AG, Grindle KG, Bochkov YA, Gruchalla RS, Kattan M, Kercsmar CM, Khurana Hershey G, Kim H, Lebeau P, Liu AH, Szefler SJ, Teach SJ, West JB, Wildfire J, Pongracic JA, Gern JE. Effects of Omalizumab on Rhinovirus Infections, Illnesses, and Exacerbations of Asthma. Am J Resp Critic Care Med. 2017;196(8):985–92. DOI: 10.1164/rccm.201701-0120OC
20. Gill MA, Liu AH, Calatroni A, Krouse RZ, Shao B, Schiltz A, Gern JE, Togias A, Busse WW. Enhanced plasmacytoid dendritic cell antiviral responses after omalizumab. J Aller Clin Immunol. 2018;141(5):1735–43.e9. DOI: 10.1016/j.jaci.2017.07.035
21. Teach SJ, Gill MA, Togias A, Sorkness CA, Arbes SJ Jr, Calatroni A, Wildfire JJ, Gergen PJ, Cohen RT, Pongracic JA, Kercsmar CM, Khurana Hershey GK, Gruchalla RS, Liu AH, Zoratti EM, Kattan M, Grindle KA, Gern JE, Busse WW, Szefler SJ. Preseasonal treatment with either omalizumab or an inhaled corticosteroid boost to prevent fall asthma exacerbations. J Aller Clin Immunol. 2015;136(6):1476–85. DOI: 10.1016/j.jaci.2015.09.008
22. Kulus M, Hébert J, Garcia E, Fowler Taylor A, Fernandez Vidaurre C, Blogg M. Omalizumab in children with inadequately controlled severe allergic (IgE-mediated) asthma. Curr Med Res Opin. 2010;26(6):1285–93. DOI: 10.1185/03007991003771338
23. Sonnenberg-Riethmacher E, Miehe M, Riethmacher D. Periostin in Allergy and Inflammation. Front Immunol. 2021;12:722170. DOI: 10.3389/fimmu.2021.722170
24. Anderson WC, Szefler SJ. New and future strategies to improve asthma control in children. J Aller Clin Immunol. 2015;136(4):848–59. DOI: 10.1016/j.jaci.2015.07.007
25. Castro M, Corren J, Pavord ID, Maspero J, Wenzel S, Rabe KF, Busse WW, Ford L, Sher L, FitzGerald JM, Katelaris C, Tohda Y, Zhang B, Staudinger H, Pirozzi G, Amin N, Ruddy M, Akinlade B, Khan A, Chao J, Martincova R, Graham NMH, Hamilton JD, Swanson BN, Stahl N, Yancopoulos GD, Teper A. Dupilumab Efficacy and Safety in Moderate-to-Severe Uncontrolled Asthma. New Eng J Med. 2018;378(26):2486–96. DOI: 10.1056/NEJMoa1804092
26. Bacharier LB, Maspero JF, Katelaris CH, Fiocchi AG, Gagnon R, de Mir I, Jain N, Sher LD, Mao X, Liu D, Zhang Y, Khan AH, Kapoor U, Khokhar FA, Rowe PJ, Deniz Y, Ruddy M, Laws E, Patel N, Weinreich DM, Yancopoulos GD, Amin N, Mannent LP, Lederer DJ, Hardin M; Liberty Asthma VOYAGE Investigators. Dupilumab in Children with Uncontrolled Moderate-to-Severe Asthma. New Eng J Med. 2021;385(24):2230–40. DOI: 10.1056/NEJMoa2106567
27. Rabe KF, Nair P, Brusselle G, Maspero JF, Castro M, Sher L, Zhu H, Hamilton JD, Swanson BN, Khan A, Chao J, Staudinger H, Pirozzi G, Antoni C, Amin N, Ruddy M, Akinlade B, Graham NMH, Stahl N, Yancopoulos GD, Teper A. Efficacy and Safety of Dupilumab in Glucocorticoid-Dependent Severe Asthma. New Eng J Med. 2018;378(26):2475–85. DOI: 10.1056/NEJMoa1804093
28. Weinstein SF, Katial R, Jayawardena S, Pirozzi G, Staudinger H, Eckert L, Joish VN, Amin N, Maroni J, Rowe P, Graham NMH, Teper A. Efficacy and safety of dupilumab in perennial allergic rhinitis and comorbid asthma. J Aller Clin Immunol. 2018;142(1):171–7. DOI: 10.1016/j.jaci.2017.11.051
29. Starrenburg ME, Bel Imam M, Lopez JF, Buergi L, Nguyen NT, Nouwen AEM, Arends NJT, Caspers PJ, Akdis M, Pasmans SGMA, van de Veen W. Dupilumab treatment decreases MBC2s, correlating with reduced IgE levels in pediatric atopic dermatitis. J Aller Clin Immunol. 2024;154(5):1333–8.e4. DOI: 10.1016/j.jaci.2024.06.023
30. Boguniewicz M, Sher LD, Paller AS, Arkwright PD, Yoshihara S, Chen Z, Shah P, Marco AR. Dupilumab is Efficacious in Young Children with Atopic Dermatitis Regardless of Type 2 Comorbidities. Advances in Therapy. 2024;41(12):4601–16. DOI: 10.1007/s12325-024-02998-4
31. Domínguez-Sosa MS, Cabrera-Ramírez MS, Marrero-Ramos MDC, Dávila-Quintana D, Cabrera-López C, González Cuervo H, Benítez Del Rosario JJ, Carrillo-Díaz T. Efficacy of dupilumab on chronic rhinosinusitis with nasal polyps and concomitant asthma in biologic-naive and biologic-pretreated patients. Ann Int Med. 2024;56(1):2411018. DOI: 10.1080/07853890.2024.2411018
32. Szefler SJ, Roberts G, Rubin AS, Zielen S, Kuna P, Alpan O, Anzures-Cabrera J, Chen Q, Holweg CTJ, Kaminski J, Putnam WS, Matthews JG, Kamath N. Efficacy, safety, and tolerability of lebrikizumab in adolescent patients with uncontrolled asthma (ACOUSTICS). Clin Transl Allergy. 2022;12(7):e12176. DOI: 10.1002/clt2.12176

33. Hanania NA, Korenblat P, Chapman KR, Bateman ED, Kopecky P, Paggiaro P, Yokoyama A, Olsson J, Gray S, Holweg CT, Eisner M, Asare C, Fischer SK, Peng K, Putnam WS, Matthews JG. Efficacy and safety of lebrikizumab in patients with uncontrolled asthma (LAVOLTA I and LAVOLTA II): replicate, phase 3, randomised, double-blind, placebo-controlled trials. Lancet Resp Med. 2016;4(10):781–96. DOI: 10.1016/S2213-2600(16)30265-X

34. Brightling CE, Chanez P, Leigh R, O'Byrne PM, Korn S, She D, May RD, Streicher K, Ranade K, Piper E. Efficacy and safety of tralokinumab in patients with severe uncontrolled asthma: a randomised, double-blind, placebo-controlled, phase 2b trial. Lancet Resp Med. 2015;3(9):692–701. DOI: 10.1016/S2213-2600(15)00197-6

35. Abrams EM, Becker AB, Szefler SJ. Current State and Future of Biologic Therapies in the Treatment of Asthma in Children. Pediatr Allergy Immunol Pulmonol. 2018;31(3):119–31. DOI: 10.1089/ped.2018.0901

36. Castro M, Zangrilli J, Wechsler ME, Bateman ED, Brusselle GG, Bardin P, Murphy K, Maspero JF, O'Brien C, Korn S. Reslizumab for inadequately controlled asthma with elevated blood eosinophil counts: results from two multicentre, parallel, double-blind, randomised, placebo-controlled, phase 3 trials. Lancet Resp Med. 2015;3(5):355–66. DOI: 10.1016/S2213-2600(15)00042-9

37. Hom S, Pisano M. Reslizumab (Cinqair): An Interleukin-5 Antagonist for Severe Asthma of the Eosinophilic Phenotype. P T. 2017;42(9):564–8.

38. FitzGerald JM, Bleecker ER, Nair P, Korn S, Ohta K, Lommatzsch M, Ferguson GT, Busse WW, Barker P, Sproule S, Gilmartin G, Werkström V, Aurivillius M, Goldman M; CALIMA study investigators. 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):2128–41. DOI: 10.1016/S0140-6736(16)31322-8

39. Gupta A, Pouliquen I, Austin D, Price RG, Kempsford R, Steinfeld J, Bradford ES, Yancey SW. Subcutaneous mepolizumab in children aged 6 to 11 years with severe eosinophilic asthma. Pediatr Pulmonol. 2019;54(12):1957–67. DOI: 10.1002/ppul.24508

40. Lim YT, Williams TC, Langley RJ, Weir E. Mepolizumab in children and adolescents with severe eosinophilic asthma not eligible for omalizumab: a single Center experience. J Asthma. 2024;61(8):793–800. DOI: 10.1080/02770903.2024.2303767

41. Pavord I, Chan R, Brown N, Howarth P, Gilson M, Price RG, Maspero J. Long-term safety of mepolizumab for up to 10 years in patients with severe asthma: open-label extension study. Ann Int Med. 2024;56(1):2417184. DOI: 10.1080/07853890.2024.2417184

42. Golebski K, van Tongeren J, van Egmond D, de Groot EJ, Fokkens WJ, van Drunen CM. Specific Induction of TSLP by the Viral RNA Analogue Poly(I:C) in Primary Epithelial Cells Derived from Nasal Polyps. PLOS One. 2016;11(4):e0152808. DOI: 10.1371/journal.pone.0152808

43. Ebina-Shibuya R, Leonard WJ. Role of thymic stromal lymphopoietin in allergy and beyond. Nature Rev Immunol. 2023;23(1):24–37. DOI: 10.1038/s41577-022-00735-y

44. Krabbendam L, Bal SM, Spits H, Golebski K. New insights into the function, development, and plasticity of type 2 innate lymphoid cells. Immunol Rev. 2018;286(1):74–85. DOI: 10.1111/imr.12708

45. Menzies-Gow A, Ponnarambil S, Downie J, Bowen K, Hellqvist Å, Colice G. DESTINATION: a phase 3, multicentre, randomized, double-blind, placebo-controlled, parallel-group trial to evaluate the long-term safety and tolerability of tezepelumab in adults and adolescents with severe, uncontrolled asthma. Resp Res. 2020;21(1):279. DOI: 10.1186/s12931-020-01541-7

46. Corren J, Parnes JR, Wang L, Mo M, Roseti SL, Griffiths JM, van der Merwe R. Tezepelumab in Adults with Uncontrolled Asthma. New Eng J Med. 2017;377(10):936–46. DOI: 10.1056/NEJMoa1704064

47. Menzies-Gow A, Corren J, Bourdin A, Chupp G, Israel E, Wechsler ME, Brightling CE, Griffiths JM, Hellqvist Å, Bowen K, Kaur P, Almqvist G, Ponnarambil S, Colice G. Tezepelumab in Adults and Adolescents with Severe, Uncontrolled Asthma. New Eng J Med. 2021;384(19):1800–9. DOI: 10.1056/NEJMoa2034975

48. Shinkai M, Ebisawa M, Fukushima Y, Takeuchi S, Okada H, Tokiyo T, Hayashi N, Takikawa M, Colice G, Almqvist G. One-year safety and tolerability of tezepelumab in Japanese patients with severe uncontrolled asthma: results of the NOZOMI study. J Asthma. 2023;60(3):616–24. DOI: 10.1080/02770903.2022.2082309

49. O'Byrne PM, Panettieri RA Jr, Taube C, Brindicci C, Fleming M, Altman P. Development of an inhaled anti-TSLP therapy for asthma. Pulm Pharmacol Ther. 2023;78:102184. DOI: 10.1016/j.pupt.2022.102184

50. Gauvreau GM, Hohlfeld JM, FitzGerald JM, Boulet LP, Cockcroft DW, Davis BE, Korn S, Kornmann O, Leigh R, Mayers I, Watz H, Grant SS, Jain M, Cabanski M, Pertel PE, Jones I, Lecot JR, Cao H, O'Byrne PM. Inhaled anti-TSLP antibody fragment, ecleralimab, blocks responses to allergen in mild asthma. Eur Resp J. 2023;61(3):2201193. DOI: 10.1183/13993003.01193-2022

51. Clark VL, Gibson PG, McDonald VM. The Patients' Experience of Severe Asthma Add-On Pharmacotherapies: A Qualitative Descriptive Study. J Asthma Allergy. 2021;14:245–58. DOI: 10.2147/JAA.S296147

52. de Graaff MB, Bendien SA, van de Bovenkamp HM. 'Like a fish on dry land': an explorative qualitative study into severe asthma and the impact of biologicals on patients' everyday life. J Asthma. 2022;59(5):980–8. DOI: 10.1080/02770903.2021.1888976

53. Plank PM, Hinze CA, Campbell V, Konwert S, Welte T, Drick N, Kayser MZ, Suhling H, Fuge J. Relationship Between the Response to Antibody Therapy and Symptoms of Depression and Anxiety Disorders in Patients with Severe Asthma. J Asthma Allergy. 2023;16:421–31. DOI: 10.2147/JAA.S403296

DOI: 10.19163/2307-9266-2024-12-5-362-373

AUTHORS

Milana S. Matevosova – student of the Faculty of Medicine of Pyatigorsk Medical and Pharmaceutical Institute – branch of Volgograd State Medical University. ORCID ID: 0009-0002-0324-7933. E-mail: milalean2001@gmail.com

Leonid I. Agapitov – Doctor of Sciences (Medicine), Professor of the Department of Therapeutic Disciplines of Pyatigorsk Medical and Pharmaceutical Institute – branch of Volgograd State Medical University. ORCID ID: 0000-0001-5562-6594. E-mail: lagapitov@rambler.ru

Irina A. Averina – Candidate of Sciences (Medicine), senior lecturer of the Department of Therapeutic Disciplines of Pyatigorsk Medical and Pharmaceutical Institute – branch of Volgograd State Medical University; Head of the Pediatric Department of Clinical Hospital No. 10 – branch of North Caucasus Federal Scientific and Clinical Center (Lermontov, Russia). ORCID ID: 0000-0002-8713-5017. E-mail: iradoc77@mail.ru

Irina V. Sokolova – Deputy Head of the Medical Department of Clinical Hospital No. 10 – branch of North Caucasus Federal Scientific and Clinical Center (Lermontov, Russia). ORCID ID: 0009-0001-9461-8199. E-mail: irina.sokir@yandex.ru

Svetlana V. Zotova – Head of the children's clinic of Clinical Hospital No. 10 – branch of North Caucasus Federal Scientific and Clinical Center (Lermontov, Russia). ORCID ID: 0009-0001-0905-1627. E-mail: zotovasv77@gmail.com

Roman A. Chernigovsky – teacher of the Department of Therapeutic Disciplines of Pyatigorsk Medical and Pharmaceutical Institute – branch of Volgograd State Medical University; Pediatrician of the pediatric department of Clinical Hospital No. 10 – branch of North Caucasus Federal Scientific and Clinical Center (Lermontov, Russia). ORCID ID: 0009-0003-3828-5670. E-mail: gjgjgj26gjgjgj@gmail.com