

# Prospects of using the genetically engineered preparation dupilumab for the treatment of atopic dermatitis in the adult population

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## Abstract

**Background** Currently, the genetically engineered drug dupilumab, which was recently registered in Russia and is planned for use, is widely used in the world for the treatment of atopic dermatitis..

**Objective** Possibility of use of the genetically engineered drug dupilumab for the treatment of atopic dermatitis among adult population.

**Methods** To address the issues of treatment tactics in patients with atopic dermatitis, a 12-week placebo-controlled study of its effectiveness was carried out on two control groups of 45 people each, divided into three subgroups of 15 people (1 subgroup - placebo; subgroup 2 - dupilumab 300 mg subcutaneously 1 time in 2 weeks; subgroup 3 - dupilumab 200 mg subcutaneously 1 time per week). Evaluation of the effectiveness of the treatment of atopic dermatitis with the targeted drug dupilumab was carried out using the following scales: EASI, IGA, NRS, SCORAD, POEM, DLQI, HADS.

**Results** The results of the study show a significant improvement in the symptoms and manifestations of atopic dermatitis according to the SCORAD, EASI-70 and POEM scales. All patients taking dupilumab showed cleansing of the skin, a decrease in the intensity of pain and skin itching, which contributes to an improvement in the quality of life of patients with atopic dermatitis (a decrease in the DLQI value from 12-14 to 6-7), as well as a decrease in the level of anxiety and stress. At the same time, the number of side effects that occur in patients taking dupilumab and placebo is comparable.

**Conclusion** Based on the study and the results of earlier studies of the effectiveness of targeted therapy of atopic dermatitis with the genetically engineered drug dupilumab, it is possible to recommend a regimen for the use of this drug registered in the Russian Federation for the treatment of atopic dermatitis in the adult population: the initial dose of the drug is 600 mg, then 300 mg every 2 weeks with the regular use of moisturizers 2 times a day during the entire period of treatment. In the case of a protracted severe course of the disease, a weekly subcutaneous injection of the drug at a dose of 200-300 mg is possible.

## Key words

Atopic dermatitis, targeted therapy, genetically engineered drugs, dupilumab.

## Introduction

Atopic dermatitis is a chronic multifactorial

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inflammatory skin disease characterized by early manifestation, recurrent and progressive course (from atopic dermatitis to allergic rhinitis, bronchial asthma and food allergy) with a lifelong period. This disease has a worldwide prevalence that has increased from 1 to 12% among the adult population and from 10 to 24%

among children since 2019, so it is a problem of interest in the modern medicine worldwide.<sup>1,2</sup>

In the modern tactics of treating atopic dermatitis, the main goal is not only to eliminate the symptoms of this disease, but also to achieve its remission over a long period of time, taking into account the severity of the inflammatory process on the skin surface. Thus, in the treatment of mild, moderate and severe forms of atopic dermatitis, glucocorticosteroids of low, medium and high activity are used, respectively, as well as calcineurin blockers. In the absence of a positive effect from topical therapy, systemic drugs (for example, cyclosporin A) were prescribed until recently, which in most cases can cause various negative effects (for example, nephrotoxic and hepatotoxic effects), therefore they are used in rare cases and require regular monitoring of the condition patients.<sup>3,5</sup>

According to recent studies on the pathogenesis of atopic dermatitis, a correlation has been established between the level of interleukins (IL-4 and IL-13) and the stage of the disease, which became the basis for the development of targeted drugs that interact with interleukin receptors (IL-4Ra) and block their action, thereby preventing the onset, recurrence and progression of atopic dermatitis.<sup>6-8</sup> Dupilumab is one such drug used for the treatment of atopic dermatitis and bronchial asthma in most countries of the world.<sup>9</sup> However, in Russia this drug was registered quite recently (04.04.2019) and will soon be available for prescribing to patients. This raises questions about the tactics treatment of patients with atopic dermatitis with the genetically engineered drug dupilumab.

## **Methods**

Purpose of the study: development of practical recommendations for dermatologists for the use of the genetically engineered drug dupilumab for

the treatment of atopic dermatitis among adult population.

## **Research objectives**

- 1) To study the efficacy and safety of the use of the genetically engineered drug dupilumab for the treatment of atopic dermatitis among adult population, depending on the chosen treatment tactics;
- 2) To compare the obtained results of the study of the efficacy and safety of the use of the genetically engineered drug dupilumab for the treatment of atopic dermatitis among adult population with previous clinical international studies;
- 3) On the basis of the study, to offer practical recommendations for dermatologists for the use of the genetically engineered drug dupilumab for the treatment of atopic dermatitis among adult population.

The study of the efficacy and tactics of treating atopic dermatitis using the targeted drug dupilumab, which is a recombinant human-identical monoclonal antibody, was carried out at the Novgorod Regional Dermatovenerologic Dispensary in Veliky Novgorod.

In a double 12-week placebo-controlled study, 90 people with a confirmed diagnosis of atopic dermatitis took part. The main criteria for the inclusion of patients with atopic dermatitis in the study, in addition to the signed voluntary informed consent to participate in the study, were:

- Age over 18;
- The duration of the confirmed diagnosis of atopic dermatitis is more than 5 years;
- Absence of pregnancy and lactation;
- The value on the EASI scale is more than 15 points;

- The value on the IGA scale is not less than 3 points;
- The value on the NRS scale is more than 3 points;
- The affected area of the body surface is more than 10%;
- Ability to accurately follow the research protocol.

For the study, the patients were randomly divided into two control groups of 45 people, in each of which three subgroups of 15 people were randomly formed (1 subgroup - placebo; 2 subgroup - dupilumab 300 mg subcutaneously 1 time in 2 weeks; 3 subgroup - dupilumab 200 mg subcutaneously once a week). All patients applied moisturizers 2 times a day during the week before the start of the study and 2 times a day during the entire study period.

Evaluation of the effectiveness of the treatment of atopic dermatitis with the targeted drug dupilumab was carried out using the following scales: EASI, IGA, NRS, SCORAD, POEM, DLQI, HADS.

## Results

The average values of the indicators used to assess the effectiveness of the use of the drug

dupilumab in the treatment of atopic dermatitis in patients before the start of the study are presented in **Table 1**.

From the presented data, it can be seen that the majority of patients who took part in the study have a high severity of itching and the prevalence of the inflammatory process, which have a negative impact on their quality of life.

The dynamics of changes in the average values of the main indicators used to assess the effectiveness of the use of the genetically engineered drug dupilumab in the treatment of atopic dermatitis in patients during the entire period of the study is shown in **Figures 1-4**.

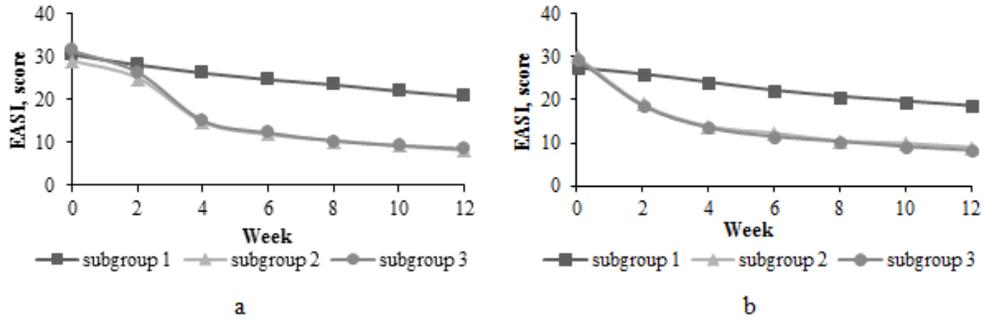
From the data presented it can be seen that in patients with atypical dermatitis during targeted therapy with dupilumab in both concentrations, there are comparable improvements on the EASI scale by 50% by 4 weeks of the study and by 70% by 12 weeks of the study compared with patients taking placebo (**Figure 1**).

On the IGA scale, patients with atypical dermatitis undergoing targeted therapy with dupilumab at both concentrations showed significant skin cleansing compared to patients taking placebo (**Figure 2**).

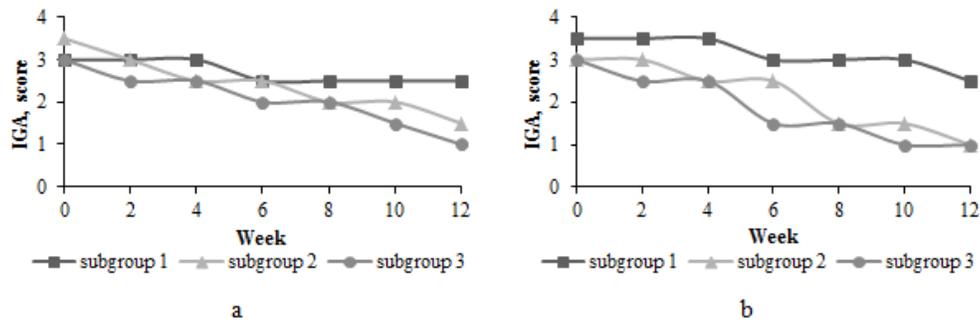
**Table 1** Average values of indicators before the start of the study.

Indicators	Control group 1 Subgroups			Control group 2 Subgroups		
	1	2	3	1	2	3
Duration of the disease, years	14.2	16.1	15.5	15.0	17.3	16.4
Affected body area,%	35.3	40.1	38.5	39.4	43.7	40.6
EASI, score	30.5	29.1	31.4	27.5	30.1	29.6
IGA, score	3.0	3.5	3.0	3.5	3.0	3.0
NRS, score	7.1	7.5	6.9	7.6	7.0	7.2
SCORAD, score	57.1	55.4	56.3	56.9	58.0	57.5
POEM, score	20.0	21.0	20.0	22.0	23.0	21.0
DLQI, score	12.0	14.0	13.0	11.0	13.0	12.0
HADS, score	15.0	13.0	13.0	14.0	12.0	13.0
More than 8 points on the HADS-A and / or HADS-D scale, %	46.7	40.0	46.7	53.3	40.0	46.7

Source: Compiled by the authors.



**Figure 1** Dynamics of changes in the average EASI values of control group 1 (a) and control group 2 (b) during the study period. *Source:* Compiled by the authors.



**Figure 2** Dynamics of changes in the average IGA values of control group 1 (a) and control group 2 (b) during the study period. *Source:* Compiled by the authors.

According to **Figure 3**, in patients with atypical dermatitis undergoing targeted therapy with dupilumab at both concentrations, there is a noticeable decrease in the intensity of pain and pruritus starting from week 2 of the study, reaching 50% by 12 weeks of the study compared with patients taking placebo.

Consequently, during targeted therapy with dupilumab in patients with atypical dermatitis, a

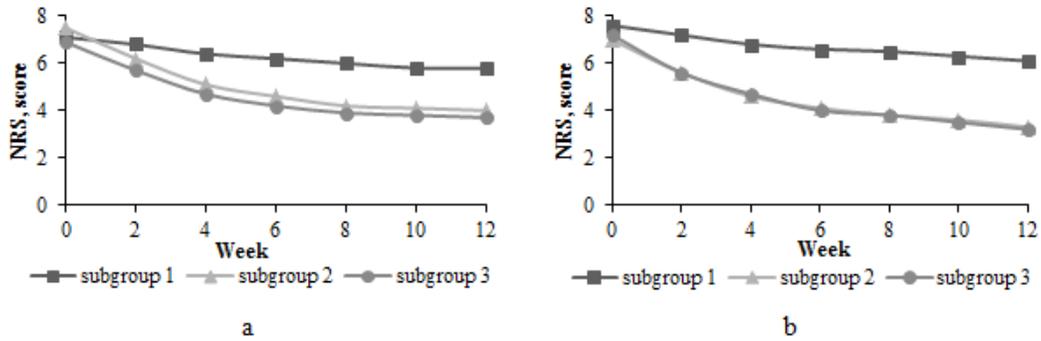
pronounced decrease in the symptoms of the disease is observed, which improves the quality of life of patients and helps to reduce their anxiety and depression (**Figure 4**).

The average values of the indicators used to assess the effectiveness of the use of the drug dupilumab in the treatment of atopic dermatitis in patients after 12 weeks of the study are presented in **Table 2**.

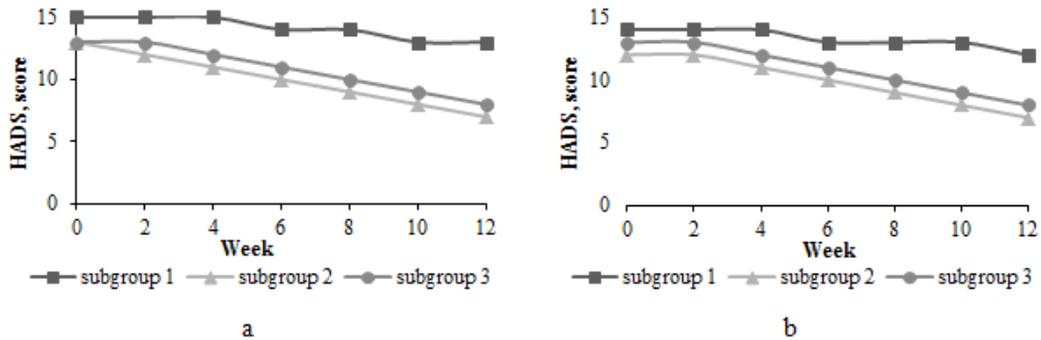
**Table 2** Average values of indicators after 12 weeks of the study.

Indicators	Control group no. 1 Subgroups			Control group no. 2 subgroups		
	1	2	3	1	2	3
EASI, score	20.7	8.2	8.6	18.7	9.0	8.3
IGA, score	2.5	1.5	1.0	2.5	1.0	1.0
NRS, score	5.8	4.0	3.7	6.1	3.3	3.2
SCORAD, score	51.3	35.1	36.0	50.7	38.7	37.2
POEM, score	17.0	8.0	7.0	18.0	9.0	8.0
DLQI, score	11.0	6.0	7.0	11.0	7.0	7.0
HADS, score	13.0	7.0	8.0	12.0	7.0	8.0
More than 8 points on the HADS-A and / or HADS-D scale, %	40.0	26.7	26.7	46.7	20.0	26.7

*Source:* Compiled by the authors.



**Figure 3** Dynamics of changes in the average NRS values of control group 1 (a) and control group 2 (b) during the study period. *Source:* Compiled by the authors.



**Figure 4** Dynamics of changes in the average HADS values of control group 1 (a) and control group 2 (b) during the study period. *Source:* Compiled by the authors.

From the results of a 12-week study of the effectiveness of the treatment of atopic dermatitis with the genetically engineered drug dupilumab, it can be seen that patients in both control groups showed a significant improvement in the symptoms and manifestations of atopic dermatitis on the SCORAD scale. The majority of patients (73.3% of patients taking 300 mg dupilumab once every two weeks and 60.0% of patients taking 200 mg dupilumab once a week) showed an improvement in the EASI-70 score. All patients taking dupilumab showed significant cleansing of the skin, a decrease in the intensity of pain and itching. The effectiveness of the targeted therapy of atopic dermatitis with dupilumab is also confirmed by a significant decrease in the values for the patient-oriented measure of eczema (POEM scale), regardless of the concentration of dupilumab administered subcutaneously.

The results of the study of the effectiveness of the treatment of atopic dermatitis with the genetically engineered drug dupilumab show a significant improvement in the quality of life of patients with atopic dermatitis, which is confirmed by a decrease in the values of the dermatological index of quality of life (DLQI scale) from 12-14 (a very large effect of the disease on the quality of life of patients) to 6-7 (moderate effect of the disease on the quality of life of patients), as well as a decrease in the level of anxiety and stress to the level of reliably absent symptoms on the HADS-A and HADS-D scales in most patients taking dupilumab. In both control groups of patients taking placebo, the above effects were not detected.

It should be noted that in both control groups and all subgroups, about a third of patients who took part in the study of the effectiveness of targeted therapy for atopic dermatitis with

dupilumab had bronchial asthma and other allergic diseases in history. At the same time, the number of side effects that occur in patients taking dupilumab and placebo is comparable.

## **Discussion**

The results of the study of the effectiveness of targeted therapy with dupilumab for atopic dermatitis are comparable to previous international clinical trials in the adult population. In all clinical studies of the effectiveness of the treatment of atopic dermatitis with the genetically engineered drug dupilumab, there is a significant cleansing of the skin, a decrease in the intensity of pain and itching, which have a significant effect on the quality of life of patients with atopic dermatitis.<sup>9-11</sup>

Comparable results of the effectiveness of targeted therapy with dupilumab for atopic dermatitis in subgroups 2 and 3 of each control group, taking dupilumab at a concentration of 300 mg subcutaneously 1 time in 2 weeks and 200 mg subcutaneously 1 time per week, respectively, indicate that there is no need to increase the dose of this drug. When using a higher dose of the drug, a higher efficiency of its action was observed in some indicators during the study, however, by the end of the study, there were no significant differences in the effectiveness of dupilumab in subgroups 2 and 3. The data obtained are in good agreement with earlier studies of the effect of the concentration and frequency of dupilumab administration on the effectiveness of the treatment of atopic dermatitis.<sup>12,13</sup>

The absence of pronounced side effects in patients taking the genetically engineered drug dupilumab compared with the control groups of patients taking placebo is confirmed by the data of a previous study of the clinical safety of

patients taking atopic dermatitis of the genetically engineered drug dupilumab CHRONOS, which lasted for a year. As a result of the study, there is a slightly higher manifestation of side effects, such as conjunctivitis, irritation at the injection site, upper respiratory tract disease in patients taking dupilumab compared to patients taking placebo. However, the incidence of recurrent dermatitis and skin infections was significantly lower in the dupilumab group than in the placebo group.<sup>14</sup>

Thus, based on the study and the results of earlier studies of the effectiveness of targeted therapy of atopic dermatitis with the genetically engineered drug dupilumab, it is possible to recommend a regimen for the use of this drug registered in the Russian Federation for the treatment of atopic dermatitis in the adult population: the initial dose of the drug is 600 mg, then every 2 weeks of 300 mg of the drug with regular use of moisturizers 2 times a day during the entire period of treatment. In the case of a protracted severe course of the disease, a weekly subcutaneous injection of the drug at a dose of 200-300 mg is possible.

## **Conclusion**

As a result of the study, the high efficiency of the genetically engineered drug dupilumab in the treatment of patients with atopic dermatitis was established. The results obtained, which are in good agreement and complement the previous international clinical studies of the efficacy and safety of this drug in the adult population, confirm the effectiveness of the dupilumab drug use regimen registered in the Russian Federation in the treatment of atopic dermatitis and allow an increase in the frequency of subcutaneous administration of the drug in the case of a torpid course of the disease in adults patients.

A prospect for further research may be to study the efficacy and safety of the use of the genetically engineered drug dupilumab for the treatment of atopic dermatitis in pediatric practice.

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