effect/suppressor population of T-lymphocytes. In the treatment of atopic dermatitis, the need for the use of antihistamines and topical GCS decreases (the frequency of administration and dose decreases till complete cancellation). The obtained results – treatment with thymogen had a positive effect on the state of local defense factors – immunocorrection of the cellular link of the immune system – skin in atopic dermatitis, an increase in secretory immunoglobulin A, normalization of immunoglobulin E, A, M, G

Conclusions.

It is recommended to prescribe thymogen (cream) as a basic therapy for AD. It is safe, applied to the skin, and reduces the frequency and intensity of exacerbation, restores the protective shield of the skin (cellular and humoral immunity).

1. Sepiashvili, R. I. (2003). Functional system of immune homeostasis. *Allergology and Immunology*, 2(4), 5-14.
2. Zheleznikova, G. F. (2002). Immunoglobulin E: a biological role in infectious diseases. *Medical Immunology*, 4(4-5), 515-530/
3. Herd R.M., Tidman M.J., Perscott R.G., Hunter J.A.A. *Br J Dermatol* 1996;135:20-3.
4. Gushchin, I. S. (2000). *Antihistamines: A guide for doctors*. Moscow.
5. Leung, D. (1995). Atopic dermatitis: the skin as a window into the pathogenesis of chronic allergic disease. *All Clin Immunol*, 96, 312-319.
6. Karaulova, A. V. (ed.) (2002). *Clinical immunology and allergology: Textbook manual*. Moscow: Med. inform. agency.
7. Latysheva, T. V., Poroshina, Y. A., Gushchin, I. S. (1987). *Acute toxic and allergic reactions to medications (clinic, treatment, prevention): Method, recommendations*. Moscow.
8. Pytsky, V. I., Andrianova, N. V., Artomasov, A. V. (1999). *Allergic diseases*. 3rd ed. Moscow: Triada-X.
9. Goryachkina, L. A., Pospelova, R. A., Khramtsova, N. N., Frolov, M.K. (1987). *Therapy of emergency conditions in allergology and their prevention: Textbook*. Moscow.

Moskalets O.V.

The incidence of anti-drug antibodies in patients with non-Hodgkin's lymphoma

*Moscow Regional Research Clinical Institute named after M.F.Vladimirskij
(Russia, Moscow)*

doi: 10.18411/scienceconf-06-2021-06

Introduction.

Monoclonal therapeutic antibodies are widely used to treat lymphoproliferative and rheumatologic disorders [1,2]. Because of their higher target specificity, monoclonal antibodies treatments are generally considered to pose a lower risk of adverse reactions than chemical drugs. Rituximab, a chimeric monoclonal antibody targeted against the pan-B-cell marker CD20, was the first monoclonal antibody to be approved for therapeutic use [2]. It is usually used in combination with chemotherapy. Treatment with rituximab at standard weekly dosing is effective in more than 50% of patients with relapsed or refractory CD20-positive follicular non-Hodgkin's lymphoma, but is not curative. It is less effective in other subtypes of CD20-positive lymphoma and for retreatment, even with CD20 still expressed [3]. Thus, binding of rituximab to CD20 is not sufficient to kill many lymphoma cells, indicating that there are mechanisms of resistance.

There are quite a lot of data in the literature that therapeutic antibodies occasionally elicit an antibody response in patients, which can result in loss of response or adverse effects [4-7]. However, antibodies that bind a drug are sometimes found in pre-treatment serum samples, with the amount depending on drug, assay, and patient population. The accurate prediction and assessment of (clinically relevant) immunogenicity remains a challenging endeavor [4].

Purpose of the study - to determine the incidence of anti-drug antibodies (ADA) in patients with non-Hodgkin's lymphoma (nHL) treated by rituximab.

Materials and methods.

The study involved 32 patients with nHL (11 newly diagnosed, 21 - resistant / recurrent form), aged from 36 to 70 years (average age 49,5 years), of which 18 women and 14 men and 13 practically healthy individuals, matched by age and sex.

In 55% of patients, stage 2 of the disease was detected, in 45% of patients - stages 3 and 4. Patients with refractory / relapsing forms have previously received 4-6 courses of R-FC therapy. Determination of anti-rituximab antibodies in peripheral blood serum was performed by enzyme-linked immunoassay using a test system manufactured by Bender Medsystems (Austria) (semi-quantitative analysis).

Results.

None of the patients with newly diagnosed disease have antibodies to rituximab. Positive results were recorded in 7 (33%) patients who received rituximab earlier. Of particular note is a patient with a very high antibody level (74,7 c.u.) who received 6 courses of combination therapy and showed pronounced progression of the disease. At the same, in the group of practically healthy persons, positive results were obtained in 2 (15,4%) cases, in particular, with a procedural nurse who regularly contacts the drug.

Conclusion.

Most recombinant engineered therapeutic proteins are administered to patients as repeated doses, over their lifetime. Generation of ADA is a potential outcome to almost all such therapeutics. The results of the study demonstrated that ADA are revealed in 1/3 patients with resistant forms of the disease treated by rituximab. Moreover, pre-existing ADA were detected in several healthy controls. Of course, it should be borne in mind that the effect of ADA on the therapeutic efficacy of the drug can be different: it could be targeting predominantly the idiotype and thus clinically relevant, or due to pre-dose antibodies that can bind the therapeutic antibody, but are often irrelevant. If we suppose that immunogenicity is an important factor that should be considered in the overall treatment strategy, we should take actions to reduce antidrug antibodies formation: modifying drug administration; increasing dose; decreasing immunogenicity by adding immunosuppressive agents to the regimen or using new drugs which are supposed to be less immunogenic such as humanized or fully human monoclonal antibodies.

1. Chan A.C., Carter R.T. Therapeutic antibodies for autoimmunity and inflammation. *Nat. Rev. Immunol.* 2009. Vol.10. P.301-316. Doi:10.1038/nri2761.
2. Smith M.R. Rituximab (monoclonal anti-CD20 antibody): mechanisms of action and resistance. *Oncogene.* 2003. Vol.22(47). p.7359-7368. Doi 10.1038/sjonc120639.
3. Maloney D.R. Anti-CD20 antibody therapy for B-cell lymphomas. *N Engl. J. Med.* 2012.Vol.316. P.2008-2018 DoI:10/1056/NEJMct1114348.
4. Rosenberg A.S., Sauna Z.E.Immunogenicity assesment during the development of protein therapeutics. *J. Pharm. Pharmacol.* 2018. Vol.70(5). P.584-594. Doi:10.1111/jphp12810.
5. Krishna M., Nadler S.G. Immunogenicity to biotherapeutics – the role of anti-drug immune complexes. *Front. Immunol.* 2016; 7:21 Doi: 10.3389/fimmu.2016.00021.
6. Tada M., Ishii-Watabe A., Suzuki T., Kawasaki N. Development and characterisation of an anti-rituximab monoclonal antibodies. *Mabs.* 2018. Vol.10(3). P.370-379. Doi: 10.1080/19420862.2018.1424610.
7. vanSchi K.A., Wolbink G.J., Respens T. Cross-reactive and pre-existing antibodies to therapeutic antibodies – Effects on treatment and immunogenicity. *Mabs.* 2015. Vol.7. 662-671. DoI:10.1080/19420862.2015.10481111.