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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии
საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

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GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებშიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman (Кириллица)**, для текста на грузинском языке следует использовать **AcadNusx**. Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - <http://www.spinesurgery.ru/files/publish.pdf> и http://www.nlm.nih.gov/bsd/uniform_requirements.html В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректур авторам не высылаются, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or computer-printed on a single side of standard typing paper, with the left margin of 3 centimeters width, and 1.5 spacing between the lines, typeface - **Times New Roman (Cyrillic)**, print size - 12 (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf

In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

**Articles that Fail to Meet the Aforementioned
Requirements are not Assigned to be Reviewed.**

ავტორთა საქურაღებოლ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დაიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx**. შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შედეგის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფხიხლებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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SPECIFICS OF PRESCRIBING ANTIRETROVIRAL DRUGS IN THE TREATMENT OF HIV INFECTION

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Abstract.

HIV infection is one of the most acute problems of our time, characterized by slow development, prolonged course, and numerous clinical manifestations. Currently, there is a large number of drugs acting on different processes of human immunodeficiency virus replication, which constitute the group of highly active antiretroviral therapy (HAART). This article shows a theoretical review of modern HAART and analyzes the prescribed treatment regimens for patients with HIV infection. The study revealed two most common combinations: nucleoside reverse transcriptase inhibitors + protease inhibitors; nucleoside + non-nucleoside reverse transcriptase inhibitors.

Key words. Antiretroviral therapy, HIV infection, human immunodeficiency virus, lamivudine, abacavir, zidovudine, efavirenz.

Introduction.

As of December 31, 2020 (according to preliminary data), there were 1,492,998 people with an immune blot confirmed diagnosis of HIV infection among citizens of the Russian Federation, including: 1,104,768 Russians living with HIV and 388,230 deaths. The incidence of HIV infection as of December 31, 2020, was 752.8 per 100,000 of the Russian population. Cases of HIV infection have been detected in all constituent entities of the Russian Federation. The number of regions with high HIV prevalence (more than 0.5% of the total population) is constantly growing: from 22 in 2014 to 38 in 2020. Among the global level of officially registered HIV-infected patients, which amounts to 36.7 million people, Russia accounts for 1,168 million people [1-8]. The epidemic in the Russian Federation has recently been characterized by heterogeneity in the incidence and prevalence of HIV infection by region. Confirmation of the trend towards worsening of the epidemic situation is the fact that from 2005 to 2016, the number of patients increased more than 3-fold and mortality more than 31.5-fold [1]. The negative dynamics of HIV incidence indicates the need to develop, improve and select the optimal and most effective antiretroviral therapy (HAART).

The aim of the study is to investigate drug therapy regimens for HIV infection in real clinical practice.

Materials and Methods.

The study was conducted through retrospective analysis of 98 medical records of HIV-infected patients for the period 2022 (the criterion for selection of records was the presence of two treatment regimens).

Results.

HIV infection is an anthroponotic retroviral infection with slow development, long course, and diverse clinical manifestations, which ends with the development of acquired immunodeficiency

syndrome (AIDS). Human immunodeficiency virus (HIV) is an RNA-genomic virus characterized by the ability to transfer information from DNA to RNA. The main target cells of the virus are various CD4⁺ cells (T-helper cells, monocytes, dendritic cells, and some others). Adsorbed on the cells, the virus penetrates them, a complementary DNA strand is synthesized on the matrix of genomic RNA (+) (reverse transcriptase enzyme, or revertase), followed by a second DNA strand. With the help of the integrase enzyme, the double-stranded molecule is incorporated into the DNA of the host cell. In the process of transcription and subsequent translation, proviral proteins are "sliced" by viral protease into mature infectious agents [2]. Currently, drugs targeting each stage of virus reproduction in the host organism have been created, namely [3,5,8]:

1. Penetration inhibitors:
 - Fusion inhibitors
 - CCR5 coreceptor blockers
2. Nucleotide and nucleoside reverse transcriptase inhibitors (NRTIs)
3. Non-nucleotide reverse transcriptase inhibitors (NNRTIs)
4. Integrase Strand Transfer Inhibitor (INSTI)
5. Protease inhibitors (PIs).

Data on the drugs used and their mechanism of action are presented in Table 1 [3].

Inhibitors of penetration depending on the mechanism of action are subdivided into 2 groups. The first group is CCR5 chemokine receptor blockers, of which maraviroc is a representative. By binding to the co-receptor, which is necessary for the fusion of the virus envelope and the cytoplasmic membrane (CPM) of the host cell, the drug prevents HIV penetration into the cell. The most common adverse reactions when taking maraviroc are dyspeptic disorders, headache, anemia, possible increase in AST and ALT activity. The drug is contraindicated in people with hypersensitivity. The second group of penetration inhibitors - fusion inhibitors (enfuvirtide). The mechanism of action of the drug is based on binding to a section of the HIV supercapsid glycoprotein and changing its conformation. This prevents the fusion of the virus with CPM and its penetration into the cell. After 48 weeks of therapy with this drug, 30% of patients have undetectable HIV RNA level (less than 400 copies/mL). Enfuvirtide is administered only in combination with other antiretroviral drugs. Side effects of enfuvirtide include increased incidence of bacterial pneumonia, dyspeptic phenomena, local reactions during subcutaneous administration (allergic reactions), various nervous system disorders (headache, dizziness, nightmares). Contraindications are lactation and hypersensitivity.

Nucleoside reverse transcriptase inhibitors (NRTIs) include drugs containing one of the analogs of natural nucleosides:

Table 1. Classification of antiretroviral drugs.

Mechanism of action	Antiretroviral drug groups	Drugs
Penetration inhibitors	CCR5 coreceptor blockers	Maraviroc (MVC)
	Fusion inhibitors	Enfuvirtide (T-20)
Reverse transcriptase inhibitors	Nucleoside reverse transcriptase inhibitors (NRTIs)	Zidovudine (ZDV)
		Lamivudine (3TC)
		Didanosine (ddI)
Reverse transcriptase inhibitors	Nucleotide reverse transcriptase inhibitors (NtRTIs)	Stavudine (d4T)
		Abacavir (ABC)
		Emtricitabine (FTC)
Reverse transcriptase inhibitors	Non-nucleoside reverse transcriptase inhibitors (NNRTIs)	Tenofovir (TAF/TDF)
		Nevirapine (NVP)
		Efavirenz (EFV)
Integrase inhibitors	Integrase Strand Transfer Inhibitor (INSTI)	Etravirine (ETV)
		Raltegravir (MK518)
Integrase inhibitors	Integrase Strand Transfer Inhibitor (INSTI)	Elvitegravir (EVG)
		Lopinavir (LPV)
Protease inhibitors	Protease inhibitors	Ritonavir (RTV)
		Fosamprenavir (FOS, FPV)
		Darunavir (DRV)
		Atazanavir (ATZ, ATV)
		Saquinavir (SQV)
		Indinavir (IDV)
		Tipranavir (TPV)

1. thymidine analogs: Zidovudine; Stavudine; Phosphazide
2. adenine analogs: Didanosine
3. cytidine analogs: Lamivudine; Zalcitabine
4. guanine analogs: Abacavir

The mechanism of antiretroviral effect of the drugs is based on competitive inhibition of HIV reverse transcriptase and cessation of viral DNA replication. The ability of drugs to inhibit viral revertase is hundreds of times higher than the ability to inhibit human DNA polymerase [3]. Zidovudine is the first antiretroviral drug approved for use. It is highly active especially in combination with other antiretroviral drugs in treatment regimens. Characteristic side effects of all NRTIs are GI disorders (dyspepsia), they have mitochondrial toxicity, which leads to the development of lactoacidosis, myelosuppression, cardiomyopathy, peripheral neuropathy, hepatitis, and lipodystrophy. On this basis, contraindications to use are: neutro- and leukopenia (neutrophil count less than $0.75 \times 10^9/L$), anemia (hemoglobin level less than 70 g/L), folic acid and cyanocobalamin deficiency, hepatitis, obesity, lactation period.

HIV nucleotide reverse transcriptase inhibitors (NtRTIs) are nucleotide analogs. Tenofovir, a nucleoside monophosphate analog, belongs to this group of drugs. Its mechanism of action is inhibition of HIV reverse transcriptase by competing with the natural substrate deoxyribonucleotide for direct binding to the active site of the enzyme and breaking the DNA chain after incorporation into it. Associated with the administration of tenofovir is such as lactoacidosis, hepatomegaly with fatty dystrophy and lipodystrophy. Contraindications to the use of tenofovir are severe renal insufficiency, lactation period.

Non-nucleoside inhibitors of HIV reverse transcriptase (NNRTIs) inhibit early stages of the virus life cycle, so they are active against acutely infected cells. The representatives

of this group of drugs are efavirenz, nevirapine, etravirine. Efavirenz non-competitively inhibits HIV revertase, thus preventing intracellular multiplication of the virus. Efavirenz is highly toxic for CNS cells, causing dizziness, amnesia, hallucinations in patients, but these effects pass within 2-3 weeks from the beginning of administration. Often patients have allergic reactions against the background of taking this drug. In addition, efavirenz is teratogenic and embryotoxic. Hence there are contraindications: women of reproductive age, hypersensitivity. The mechanism of the antiretroviral effect of nevirapine is the destruction of the active center of revertase and the termination of the life cycle of the virus. The drug has pronounced hepatotoxicity (up to the development of acute liver necrosis). In addition, in 15-35% of cases nevirapine causes allergic reactions of varying severity [5]. Contraindications to nevirapine administration are hypersensitivity to the drug components, acute and chronic liver diseases.

The integrase inhibitors raltegravir and elvitegravir block HIV integrase and prevent covalent incorporation (integration) of viral DNA into the host cell DNA. Disassociation of the virus life cycle at this stage reduces the number of viral particles in the body. Side effects are expressed mainly from the digestive system and metabolism: decreased appetite; mental disorders: unusual dreams, behavioral disorders, CNS disorders: headache, dizziness.

Protease inhibitors bind to the specific protease of the virus and block the synthesis of mature viral proteins, preventing further spread of the virus. Currently, 4 HIV protease inhibitors are used in the world practice - saquinavir (Invirase), indinavir (Crixivan), nelfinavir (Virasept), ritonavir (Norvir). Side effects of these drugs are from the digestive system: nausea, vomiting, decreased appetite, diarrhea; nervous system: dizziness, headache, peripheral neuropathy. The most serious side effects

are acquired lipodystrophy (saquinavir), nephrolithiasis in 10-20% of cases (indinavir). Contraindications to use are hypersensitivity to drug components (possible development of Steven-Johnson syndrome, bullous dermatitis), pregnancy and lactation (proven embryotoxic effect; no reliable studies), childhood, in combination with drugs of different pharmacological groups.

Modern HAART is applied in the form of treatment regimens, which, in turn, are combinations of drugs (at least 3) with optimal effect of action and minimal side effects [8].

1. Preferred regimens are those with proven virologic efficacy, favorable tolerability, cost-effective and prescribed to the majority of patients.

2. Alternative regimens - regimens with proven virological efficacy, good tolerability, prescribed to special categories of patients or patients with contraindications to the use of preferred regimens.

Alternative regimens are preferred for so-called "special categories of patients".

These categories include:

1. Patients with anemia or granulocytopenia.
2. Women of childbearing age who cannot exclude childbirth on HAART.
3. Pregnant women.
4. Patients with low CD4+-lymphocyte count.
5. Older patients (over 50 years old) or patients with lipid and carbohydrate metabolism disorders.
6. Patients with chronic viral hepatitis or elevated aminotransferase levels.
7. Patients with tuberculosis.
8. Patients with very low CD4+-lymphocyte counts (<50cl/ μ L).
9. Patients infected with HIV-2.
10. Patients with cognitive impairment.
11. Patients with chronic kidney disease.

There is first, second, third, etc. line schemes and reserve schemes.

1. First-line regimens - administered to patients who have not previously received therapy.

2. Second-line regimens - prescribed when first-line regimens are ineffective.

3. Reserve (rescue) regimens - non-standardized regimens that are prescribed in case of ineffectiveness of the previous ones. Selection is prescribed individually depending on the patient's tests and virus resistance.

International experience in HIV treatment has been summarized to date in the international recommendations of the following major medical communities: European HIV/AIDS Clinical Society (EACS), the Expert Commission of the US Department of Health and Human Services (DHHS) and recommendations of the World Health Organization (WHO). In Russia, clinical recommendations on the treatment of HIV infection are developed and approved by the International Society for Infectious Diseases. The recommendations of EACS and DHHS, on the one hand, and WHO, on the other hand, are differently oriented and are focused on economically developed countries in the first case and on low-income countries with

epidemicly unfavorable HIV incidence rates in the second case. Nevertheless, national recommendations of different countries tend to be oriented towards these two extreme types [6].

As a result, EACS recommends as priority schemes:

1. NNRTIs + 2NRTIs/NtRTIs
 - RPV/TAF/FTC or RPV/TDF/FTC - both combinations are administered as a fixed dose combination, 1 tablet per day.
2. PIs + 2NRTIs/NtRTIs
 - DRV/c or DRV/r + TAF/FTC or TDF/FTC
3. INSTI + 2NRTIs/NtRTIs
 - DTG/ABC/3TC - fixed combination, 1 tablet per day.
 - DTG + TAF/FTC or TDF/FTC
 - EVG/c/TAF/FTC or EVG/c/TDF/FTC
 - RAL + TAF/FTC or TDF/FTC

Alternative Schemes:

1. NNRTIs + 2NRTIs/NtRTIs
 - EFV + ABC/3TC
 - EFV/TDF/FTC - fixed combination, once a day
2. PIs + 2NRTIs/NtRTIs
 - ATV/c or ATV/r + ABC/3TC
 - ATV/c or ATV/r + TAF/FTC or + TDF/FTC
 - DRV/c or DRV/r + ABC/3TC
 - LPV/r + TAF/FTC or TDF/FTC
3. INSTI + 2NRTIs
 - RAL + ABC/3TC - fixed combination, once a day
4. Non-standard schemes as alternative schemes
 - LPV/r + 3TC
 - RAL + DRV/c or DRV/r

DHHS guidelines suggest the following preferred regimens using TAF [6,7].

1. PIs + 2NRTIs/NtRTIs
 - DRV/r + TAF/FTC или TDF/FTC
2. INSTI + 2NRTIs/ NtRTIs
 - DTG/ABC/3TC
 - DTG + TAF/FTC or TDF/FTC
 - EVG/c/TAF/FTC or EVG/c/TDF/FTC
 - RAL + TAF/FTC or TDF/FTC

The major difference in the recommendations of DHHS priority regimens from EACS is the absence of NNRTIs.

DHHS recommends as alternative schemes:

1. NNRTIs + 2NRTIs/NtRTIs
 - EFV/TDF/FTC
 - EFV + TAF/FTC
 - RPV + TAF/FTC or RPV/TDF/FTC
2. PIs + 2NRTIs/NtRTIs
 - ATV/c или ATV/r + TAF/FTC or + TDF/FTC
 - DRV/c или DRV/r + TAF/FTC or TDF/FTC
 - DRV/c или DRV/r + ABC/3TC

Indications for initiation of HAART in adults and adolescents are multifaceted and based on:

1. the presence of clinical symptoms of secondary diseases that indicate the presence of immunodeficiency.
2. decrease in the number of CD4+ lymphocytes in the blood.
3. the presence and severity of HIV replication, as measured by plasma HIV RNA levels [8,9].

For clinical and immunologic indications, HAART should be administered:

1. Patients with disease stages 2B, 4 and 5 (patients with secondary disease).

2. Patients with CD4+-lymphocyte count <350 cells/ μ L regardless of the stage and phase of the disease.

3. The following categories of patients with CD4+-lymphocyte counts of 350-499 cells/ μ L:

- Patients with HIV>100,000 copies/mL.
- Patients over 50 years of age.
- Patients with chronic hepatitis C.
- Patients with chronic kidney disease, etc.

According to epidemiologic indications, it is recommended to prescribe HAART:

1. an HIV-infected partner who has a regular HIV-negative partner, subject to prior counselling of both.

2. When preparing an HIV-infected patient for the use of assisted reproductive technologies.

In addition, given the recommendations to expand the indications for HAART as a preventive measure, it can be administered to any patient willing and ready to receive it.

The efficacy of HAART is a key point indicating the correct selection of drugs and appropriate therapy based on clinical and laboratory criteria [8].

1. clinical criteria - assessment of HIV infection progression and secondary diseases.

2. laboratory criteria - assessment of treatment efficacy by determining CD4+-lymphocyte count and viral load (VL).

The most reliable and informative indicator of ART efficacy is the determination of VL. If this method cannot be used, the clinical picture and CD4+ level is assessed.

During the study, a comparative analysis of medical records of HIV-infected patients was conducted. It was found that in two treatment regimens there were drugs included in all 4 pharmacological groups of HAART drugs, in these regimens there were no drugs from the SSR5 co-receptor inhibitors subgroup. A total of 13 international generic names of drugs in Scheme 1 and 15 in Scheme 2 were encountered in medical prescriptions for these patients (Table 2).

Table 2. Pharmacologic groups of HAART and their prescriptions in medical records of patients with HIV infection.

№	Group/Group Combinations	Scheme 1		Scheme 2	
		abs.	%	abs.	%
1	NRTIs/NtRTIs	4	3,15	5	3,94
2	PIs	0	0,00	2	1,57
3	NNRTIs	0	0,00	2	1,57
4	NRTIs/NtRTIs + PIs	82	64,57	89	70,08
5	NRTIs/NtRTIs + NNRTIs	38	29,92	21	16,54
6	NRTIs/NtRTIs + NNRTIs + PIs	2	1,57	5	3,94
7	NRTIs/NtRTIs + NNRTIs + fusion inhibitors	1	0,79	3	2,36
Total medical records:		127		127	

Analysing the scheme data, the most prescribed drugs were noted:

1. from the group of integrase inhibitors - lamivudine (86.4% of prescriptions), zidovudine (51.8% of prescriptions), abacavir (29.8% of prescriptions), efavirenz (21.3% of prescriptions).

2. from the group of protease inhibitors - ritonavir (46.15% of prescriptions) and lopinavir (31.04% of prescriptions).

Drug therapy consisting of two groups of drugs is the most used in the practice of treatment of patients in both Scheme 1 and Scheme 2 (94.6% and 92.8%, respectively). Only 5 combinations of two groups of drugs in Scheme 1 and 3 - in Scheme 2 – were encountered in the studied sample of drugs.

The highest frequency of prescribing in these regimens occurs in combinations:

- nucleoside reverse transcriptase inhibitor + protease inhibitor (NNRTI + PI)

- nucleoside + non-nucleoside reverse transcriptase inhibitors (NRTI + NRTI) (87.53% of prescriptions in Scheme 1 and 92.3% of prescriptions in Scheme 2).

Analyzing the "NRTIs+PIs" group, the 2 most prescribed drug combinations were identified:

1. lamivudine+zidovudine+ritonavir (12.45% and 19.7% of prescriptions in Schemes 1 and 2, respectively).

2. lamivudine+abacavir+ritonavir (8.15% and 17.62% of prescriptions in Schemes 1 and 2, respectively).

In the "NRTIs+NNRTIs" group, the most prescribed combinations were as follows:

1. lamivudine+zidovudine+efavirenz (13.4% and 7.8% of prescriptions of the corresponding in Schemes 1 and 2).

2. lamivudine+abacavir+efavirenz (3.7% and 2.63% of prescriptions in Schemes 1 and 2, respectively).

Conclusion.

The results of the study showed that the most common combinations in the treatment of HIV infection are two:

1. nucleoside reverse transcriptase inhibitors + protease inhibitor.

2. nucleoside + non-nucleoside reverse transcriptase inhibitors.

These regimens are preferable, as they have proven virological efficacy, favorable tolerability by patients, and are economically feasible.

REFERENCES

1. Kovalenko V.S, Bogatova V.E, Kuharchuk A.E. Zabolevaemost' naseleniya RF VICH-infekciej - mediko-social'naya problema. Nauchno-prakticheskij elektronnyj zhurnal «Alleya Nauki». 2018;1:1-3.
2. Olejnik A.F, Fazylov V.H. Antiretrovirusnaya terapiya kak metod profilaktiki VICH-infekcii. Infekcionnye bolezni: Novosti. Mneniya. Obuchenie. 2016;3:113-117.
3. SHaldina M.V, Pirogova I.A. Antiretrovirusnaya terapiya kak osnovnoj metod lecheniya VICH-infekcii. Vestnik molodyh uchyonyh i specialistov CHelyabinskoy oblasti. 2017;4:71-74.
4. Docenko M, Karpov I, Il'enkova V, et al. Antiretrovirusnaya terapiya: naibolee chastye pobochnye efekty. Recept. 2007;4:104-110.
5. YUrin O.G, Efremova O.S. Evropejskie i Amerikanskije rekomendacii po lecheniyu VICH-infekcii. Medicinskij sovet. 2017;4:67-72.
6. A.V. Kravchenko. Primenenie NIOT – Tenofovira dizoproksila fumarata v skhemah ARVT pervoj linii. VICH-infekciya i immunosupressiya. 2010;2:65-72.

7. V.V. Pokrovskij, O.G. YUrin, A.V. Kravchenko i dr. Protokoly lecheniya bol'nyh VICH-infekciej. INFEKSIONNYE BOLEZNI: novosti, mneniya, obucheniya. 2012;1:1-15.

8. V.V. Pokrovskij, O.G. YUrin, A.V. Kravchenko i dr. Nacional'nye rekomendacii po dispansernomu nablyudeniyu i lecheniyu bol'nyh VICH-infekciej (proekt). 2015:47-61.