in women receiving HAART for more than one year, in comparison with those who did not receive treatment or less of its duration.

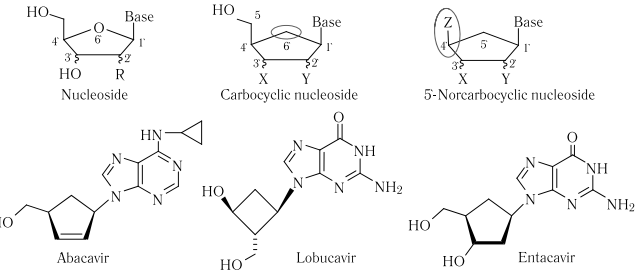
5'-Norcarbocyclic Nucleoside Derivatives: Synthesis and Spectrum of Biological Activity

E.S.Matyugina, S.N.Kochetkov, A.L.Khandazhinskaya
Moscow, Russia

In the last several decades, AIDS has become one of the major threats to human health. Many years of research efforts resulted in a variety of substances with an anti — HIV activity. Currently, the best treatment for HIV is highly active antiretroviral therapy (HAART), which includes several drugs with different mechanisms of action. Among clinically approved anti-HIV therapeutics more then 25 are modified nucleosides.

A class of nucleoside analogues, known as carbocyclic nucleosides, where a furanose oxygen in the sugar moiety replaced with a methylene group, have provided a wealth of drug candidates. Potent anti-HIV agent Abacavir, anti-HSV and anti-HBV drugs Lobucavir and Entecavir are important members of this class of compound in the field of medicinal chemistry.

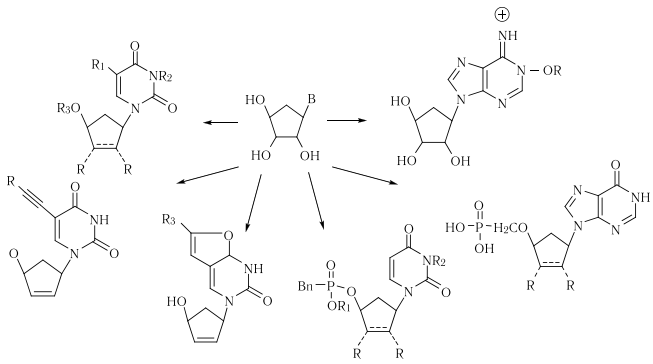
The field of our interests is a group of carbocyclic nucleosides — 5'-norcarbocycles. This type of compounds possesses interesting characteristics due to their increased stability toward cellular enzymes and lack of 5'-phosphorylation. This latter feature is responsible for a decrease in cytotoxicity of 5'-norcarbocycles.



Recent years we have designed and synthesized more then 80 new 5'-norcarbocyclic nucleosides belong to different groups, modified on heterocyclic base and/or carbocyclic fragment.

Purine-containing derivatives, being inhibitors of SAH-hydrolase, demonstrate wide spectrum of antiviral activity.

Pyrimidine-bearing compounds of this class act as non-nucleoside inhibitors of HIV reverse transcriptase; can suppress growth of *M. Tuberculosis* (including multi drug resistance strain). We also have preliminary results that 5'-norcarbocyclic nucleosides possess antiproliferative activity.



Hence 5'-norcarbocyclic nucleosides are very promising in search of new chemotherapeutic agents against HIV and opportunistic infections which are major cause of morbidity and mortality of AIDS patients.

Kisk of overdose and HIV progression in opioid dependent individuals receiving antiretroviral therapy and preventive naltrexone treatment

V.Palatkin, E.Blokhina, T.Yaroslavtseva, M.Vetrova, E.Zvartau, E.M.Krupitsky
St.-Petersburg, Russia

Introduction: Drug overdose is one of common cause of death among people living with HIV and the leading cause of death for people who inject drugs. It's well known that detoxification and relief of opioid withdrawal syndrome increase the chance of opioid overdose. It happens due to the loss of opioid tolerance and use of habitual high drug dose if relapse occurs. HIV disease progression can lead to cognitive deficit and by that also provoke overdose. Our study is aimed to evaluate the relationship of HIV disease progression and overdose frequency among opioid dependent patients receiving antiretroviral treatment and completed 12 months course of naltrexone pharmacotherapy.

Methods: we plan to enroll 200 HIV-positive opioid dependent patients who get antiretroviral treatment (ART) and completed 12 months course of oral or implantable naltrexone during their participation in the HAART study («Adherence to HIV Therapy in Heroin Addicts: Oral vs. Extended Release Naltrexone»). Patients will complete interview in12 months after enrollment and completion of naltrexone treatment. The interview contains questions about overdoses, adherence to ART, narcology care, symptoms of anxiety and depression, HIV stigma. For assessment of HIV disease progression, we are going to draw blood for CD4 count and viral load. We plan to do the participants' medical charts review to get additional information about ART. The primary outcomes are opioid overdoses, viral load, CD4 count, ART adherence.

Preliminary results: the proportion of men in the study was 68%. Mean age was (M±SD) 34,2±4,2 years, mean

duration of opioid dependence was (M±SD) — 8,0±3,9 years. At baseline 34 (17%) reported about overdose during last 3 months, during the lifetime overall number of overdoses was (M±SD) 4±1,9. At 12 months time point 2 deaths due to drug overdose were registered in the HAART project

Hypothesis: We suggest that patient adherent to ART will have better CD4 count, less viral load and less number of opioid overdoses compare to nonadherent participants. The new knowledge of the relationship of HIV disease progression and overdose frequency among patients receiving ART and naltrexone will inform the implementation of prevention interventions for those at risk.

Current status of the epidemiology and outcome of lymphomas in HIV infected patients: a multicenter retrospective study

M.Popova, E.Zinina, N.Popova, Y.Zhurba, T.Shneyder, I.Karaygin, I.Zuyzgin, O.Ryabykina, O.Ruzhinskaya, O.Uspenskaya, N.Medvedeva, A.Klimovich, V.Potapenko, N.Kotova, A.Myasnikov, S.Moshnina, A.Evseev, E.Karyagina, Zh.Stolypina, S.Dzola, A.Levanov, E.Borzenkova, N.Mikhaylova, L.Zubarovskay, B.Afanasyev

St.-Petersburg, Surgut, Petrozavodsk, Saratov, Russia

Background: HIV infected patients are at risk of cancer including lymphomas despite the widespread accessibility of highly active antiretroviral therapy (HAART). In parallel with increasing number of patients living with HIV, the number of patients suffering from HIV-associated malignancies of hematopoietic and lymphoid tissues has increased. In the early days of the HIV epidemic, treatment of HIV-positive patients diagnosed with Hodgkin lymphoma (HL) and non-Hodgkin lymphomas (NHL) was mainly palliative. Despite these remarkable advances in outcomes recent years, there are few controversial issues in an optimal approach for the treatment of HIV-associated lymphomas. The role of the concurrent use of HAART and rituximab in CD20 B-cell lymphomas are still subjects of dispute.

Aim. This study focuses on current status of the epidemiological characteristics and the outcome of lymphomas in HIV infected patients in Russian Federation.

Methods. We performed first in Russian Federation a retrospective multicenter study. An inclusion criterion was diagnosis of lymphoma in HIV infected patients. Seventy-three patients were enrolled with the period of observation from May 2006 to Dec 2015. The data of medical history, test results and treatment in hematological hospitals and «AIDS-centers» based on the established practice were analyzed. The median follow-up of patients was 30 (15–106) months. Primary end-points were overall survival (OS) and time to progression (TTP) at 2 years in patients with HIV and lymphomas. Secondary end-points were factors associated with OS and TTP at 2 years in patients with HIV and lymphomas. Separate analyze for CD20+ B-cell lymphomas was done.

Results. Mainly study group consisted of NHL 83,5%. HL was diagnosed in 13,7%, and two patients with multiple myeloma (MM) were enrolled. Median age was 32 (19–65). HIV status: HIV was detected before the diagnosis of lymphoma in 50% of patients. In 40% of patients the level of CD4+ cell count and viral load at the diagnosis of lymphoma were assessed. The level of CD4+ cell count was less than 200 cells/mm (50–420) in 4 pts and 50% of patients the viral load were less than 1000 RNA copies in 1 mm (0–800 thousand copies/ml). Only 25% of patient was on HAART at the moment of lymphoma diagnosis. Co-infection with hepatitis C or B virus was in 42% of patients. Aggressive lymphomas more often were diagnosed. Diffuse large B-cell lymphoma (DLBCL), Burkitt's lymphoma (BL) and «gray zone» lymphoma, intermediate between DLBCL and BL amounted 70% of study group. Most of patients had advanced stages of the disease with extra nodular involvements (78%) and B-symptoms (55%), Ann Arbor 3–4 stage — 78%, ECOG 3–4–17%, IPI (3>) — 51%. Patients received from 1 to 8 cycles of chemotherapy (CT) with median — 4 cycles. CT included for HL — BEACOPP 60%, ABVD 40%; for NHL: CHOP 40%, Hyper-CVAD/BFM 26%, EPOCH 34%). CT with HAART received 89% of patients. Overall survival in 2 years in patients with HIV and lymphomas was 67%. Overall survival at 2 years in HIV-infected patients with HL was 80%, NHL — 64%, two patients with MM still alive. TTP at 2 years of all patients was 12%. Non-relapse mortality was 9%. Fifty-three patients with CD20 B-cell lymphomas were diagnosed. Chemotherapy with Rituximab was applied in 72% of patients. There was no extra toxicity in CT in combination with Rituximab and HAART. Overall survival at 2 years in HIV-infected patients with CD20+ B-cell lymphomas was 60%: BL — 75%, DLBCL — 63,6%, intermediate lymphoma between BL and DLBCL — 50 %, undifferentiated B-cell aggressive lymphoma 33,3%, two patients with follicular lymphoma are alive. CT in combination with HAART and adequate CT to type and stage of lymphoma improves overall survival rate ($p<0,0001$). Usage of CT +rituximab improves overall survival (72,7% vs 44,4%, $p=0,1$) and reduces the probability of progression of CD20 B-cell lymphoma (9% vs 44,4%, $p=0,028$). LDH level greater than 500 U/l and the level of CD4 + cells is at least 100 are adverse prognostic factors. Conclusions. In HIV infected patients more often were diagnosed with DLBCL which characterized by aggressive course. Overall survival in 2 years in patients with HIV and lymphomas was 67%. CT