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

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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

in combination with HAART, adequate CT to type and stage of lymphoma, and Rituximab in CD20 B-cell lymphomas improved overall survival rate. Usage of Rituximab reduced the probability of progression of CD20 B-cell lymphoma in HIV infected individuals.

Epstein–Barr virus and HIV-associated lymphomas

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Three main factors of the development of lymphomas in immunosuppressed patients are recognized: immune dysfunctions, oncogenic viruses (Epstein-Barr virus and type 8 herpesvirus), and molecular and cytogenetic anomalies associated with HIV infection (Besson et al., 2003; Martinez, 2011). EBV is oncogenic: it is able to transform B-cells *in vitro* into immortal lymphoblastoid cell lines. EBV genome is found in 30–70% of HIV-associated non-Hodgkin lymphomas, depending on their histological types, and in virtually all Hodgkin lymphomas. HIV influences the development of lymphomas indirectly, since it does not infect tumor cells (Besson et al., 2003; Pivnik et al., 2014). Nevertheless, HIV compromises viral setpoint by suppressing the cellular immunity (Rickinson et al., 1997; Harty et al., 2000) and thus promoting EBV reactivation. In the course of advancing of HIV infection, the initial drastic increase in VEB replication is followed by a slow increase in EBV load in the course of chronic HIV infection (Piriou et al.,2004). The loss of control over EBV results in the expansion of the population of infected lymphocytes and in the development of a lymphoproliferative state (Moses et al., 1998). In patients having HIV-associated lymphomas, EBV loads are higher (>2500 copies per 1 mL) than in controls (Fan et al., 2005), and this is associated with the presence of a lymphoma. High EBV loads found several months before a lymphoma has developed are associated with that the risk of the development of HIV-associated lymphomas, including systemic B-lymphomas, increases (Leruez-Ville et al., 2012). Also, a negative correlation is found between EBV load and CD4 cell counts (Bonnet et al., 2006; Amiel et al., 2009). In their turn, the titers of VCA and EBNA-1 IgG antibodies increase. These serological parameters and EBV load may serve as indirect prognostic markers, albeit week, for managing HIV patients.

Some aspects of the HIV replication inhibitors design: depot forms and new acyclic nucleotide analogues

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There are about 30 currently used drugs against HIV. Since the approval of the first-in-class anti-HIV drug 3'-azido-3'-deoxythymidine (AZT), nucleoside and nucleotide analogues have gained much attention, even now, with new classes of antivirals found. This conservative therapy is the most affordable; currently used drugs offer such pharmaceutical benefits as good water solubility, inexpensive synthesis, thoroughly studied mechanisms of action and resistance. Nevertheless, 30 years on, the topic remains: to make nucleosides and nucleotides less toxic in the long-term treatment. Therefore, prodrug and depot-form approaches have been developed.

We have synthesized two types of prodrugs based on phosphonate and carbamate derivatives that allowed us to lower the toxicity of AZT and L-2',3'-dideoxy-3'-thiacytidine (3TC) and tested them in cell cultures and animal models. We consider that 5'-O-AZT morpholinocarbamate, 5'-O,O'-bis-AZT fluoromethylphosphonate and 5'-O-3TC H-phosphonate are most potent prodrugs of these series.

More of ten than not, several viruses occur in a HIV-infected patient simultaneously, e.g., over 80% of patients suffer from herpes and other virus-induced infections. Search for substances with combined activity against different types of viruses is inevitable. Herein, we report synthesis of new acyclic nucleoside phosphonate analogues bearing unsaturated fragments in the chain. Phosphonate moiety is a useful bypass of the limiting first phosphorylation step, besides, it does not undergo enzymatic hydrolysis as natural phosphates do. The problem of a selective phosphonate attachment may be solved by the «click»-reaction with carbonyl group forming the oximes. Oximes are rarely used in drug design and yet their conformational rigidness and their stability in hydrolytic tests may be useful for nucleoside side chain drug design. One of the synthesized series is oxime-containing nucleoside phosphonates with activity against several types of viruses: 9-{2-[(phosphonomethyl)oximino]ethyl}adenine, -guanine and 9-{2-[(phosphonomethyl)oximino]propyl}adenine.

FOF1 ATP synthase, a Therapeutic Target for AIDS Associated Lymphoma: Design of New Inhibitors

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AIDS is associated with a plethora of diseases among which an aggressive lymphoma is a major cause of lethality. In particular, the frequency of Hodgkin's lymphoma increases sixfold in AIDS patients compared to general cohort. About 1% of total newly diagnosed cancer cases, or one per 25 000 individuals, has been reported to be due to Hodgkin's lymphoma. Treatment of this form is complicated by immunodeficiency.

We propose to develop a drug candidate that inhibits energy metabolism in malignant cells, thereby causing their death. Two targets will be blocked, that is, the serine-threo-