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2nd Central and Eastern European Meeting on Viral Hepatitis and Co-Infection with HIV

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Abstracts
Oral Presentations
Abstract: O_01

Treatment Issues - Hepatitis _ HIV coinfection

The effect of lamivudine-versus tenofovir-containing antiretroviral regimen on hepatitis B infection in a cohort of HIV infected long term survivors

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Background: HIV accelerates progression of HBV disease, HIV/hepatitis B virus (HBV)-coinfected patients having an increased risk of cirrhosis and liver-disease-related death. This study evaluates the prevalence and on treatment evolution of hepatitis B infection and the efficacy of lamivudine- versus tenofovir-containing antiretroviral regimen in a cohort of heavily-treated HIV infected long term survivors patients.

Material & Methods: 200 HIV-infected subjects (median age: 23 years) on combined antiretroviral therapy (median duration: 12 years), were evaluated for serologic markers of HBV infection (HBsAg, total anti-HBc and anti-HBsAg antibodies). Markers of HBV infectivity (HBeAg and HBV DNA) were evaluated in all HBsAg carriers. HBV resistance mutations were analyzed in the cases with HBV DNA > 10^3 IU/ml. Liver fibrosis was assessed using the AST to Platelet Ratio Index (APRI) and necroinflammatory activity by transaminase levels.

Results: 52.6% of the studied subjects were chronic HBsAg carriers, while 31% had resolved HBV infection. Detectable HBV DNA levels are present in 78% of the HBsAg carriers, but only 17 with significant viremia (above 1000 IU/ml). None of the patients had clinical signs of hepatitis, 24.7% had elevated transaminase levels and only 2.9% of patients had severe liver fibrosis (APRI>1.5). 87% of the HIV/HBV coinfected subjects are currently receiving a dually active drug consisting of either TDF for a median time of 3 years or 3TC for a median time of 5 years. No significant differences were recorded between the groups receiving 3TC or TDF regarding CD4 cell count, HIV viral load, HBV viral load or hepatic fibrosis. Nevertheless, HBV resistance-associated mutations were found in 85.7% of lamivudine-treated participants vs. 25% of tenofovir-treated participants (p=0.04). Patients currently not receiving an HBV active drug had a significantly higher median HIV viral load (p=0.01) and a lower median CD4 count (p=0.02) compared with those receiving 3TC or TDF; the median HBV viral load (p=0.04) and the percentage of severe liver fibrosis (p=0.01) were significantly higher in this subset of subjects.

Conclusions: The addition of a dually active drug in the combined antiretroviral treatment-regardless of the drug type, provides protection for the degree of liver damage, explaining the high prevalence of asymptomatic HBV chronic carriage in our cohort of HIV infected long term survivors. Tenofovir-containing cART is preferred for HIV-HBV coinfection due to a better resistance profile relative to lamivudine therapy.

No conflict of interest
Abstract: O_02A

Monitoring and Diagnostic Tools

The prevalence of HBV, HCV and HIV infection in Romania - a nationwide screening program for surveillance of viral infections

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Background: Twenty years after the introduction of nationwide vaccination of newborns against hepatitis B virus (HBV) infection, we aimed to determine an updated prevalence of HBV infection in the general population. Our study also focused on other viruses such as HCV or HIV, for which no effective vaccine is yet available.

Materials & Methods: We implemented a nationwide screening program to ascertain the prevalence of HBV, HCV and HIV in the general population in Romania. The statistical analysis was performed with IBM SPSS Statistics v.22 (Armonk, USA).

Results: We performed 13412 tests for HBs Ag and HIV Ab, and 30328 tests for HCV Ab, identifying a prevalence of 6.9% (n=920) for HBV, 2.5% (n=764) for HCV and 0.3% (n=46) for HIV. The highest prevalence of HBV infection was recorded in the Bucharest-IIfov region (17.5%) and the lowest in the Central region (3.5%, z-score=14.8033, p<0.001). The highest prevalence of HCV infection was recorded in the Bucharest-IIfov county (40%), followed by Calarasi (24.2%), which were considered HBV 'hot-spots' while the lowest prevalence was found in Covasna (2.8%), Mures (2.8%) and Salaj (0%). The highest prevalence of HIV infection was recorded in Botosani (8.5%), followed by Bacau (5.8%), while Ilfov, Ialomita, Buzau and Bistrita-Nasaud were 'HCV-free' (0%). The highest prevalence of HIV infection was recorded in Vâlcea (6.5%) and in Olt (2.9%), while 26 counties in Romania were 'HIV-free'.

Conclusions: Our study identified certain 'hot-spots' for HBV, HCV and HIV infection on the Romanian map, along with 'infection-free' areas. These results can lead the way to the targeted implementation of awareness campaigns and educational activities for preventing the transmission of viral infections in areas of high prevalence.

This study is part of the RO 19.02. Project 'Strengthening the prevention and control of HIV/AIDS, HBV, HCV in Romania', financed by the Norway Financial Mechanism 2009-2014, 'Public Health Initiatives'.

No conflict of interest
Abstract: O_02B

Monitoring and Diagnostic Tools

Prevalence of risk factors for HBV and HCV infection in two young cohorts in Romania

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Background: In an era when infection with hepatitis B virus (HBV) is preventable by vaccination and infection with hepatitis C virus (HCV) is curable with access to new direct-acting antivirals, these two viruses still account for major morbidity in the patient population in Romania. We have performed a study to assess the prevalence of risk factors for HBV or HCV infection in two young cohorts: a study group made up of international students, currently performing their MD studies in Romania (Group 1), and a control group from the general Romanian population, matched for age and gender (Group 2).

Materials & Methods: We have performed a screening study to assess the prevalence of HBV and HCV infection, and their specific risk factors, in two specific young cohorts in Romania. The statistical analysis was performed with SPSS Statistics for Windows (version 22.0, IBM Corp, Armonk, NY, USA), using Pearson Chi-squared test for multi-group comparisons and the Z-test for evaluating differences in terms of categorical characteristics.

Results: Group 1 included 77 participants (of which 48% males) and Group 2 included 294 controls (of which 50% males), with median ages of 25 years (interquartile range [IQR]: 24, 26.5 years) in Group 1 and 24 years (IQR: 24, 26 years) in Group 2. The prevalence of HBV and HCV infection was low in both groups; HBV infection was diagnosed in 0/33 (0%) of patients in Group 1, and 12/272 (4.4%) in Group 2; p=0.892, \(\chi^2(1)=0.122\). An uncertain history of STIs or HIV significantly increased the risk for HBV infection: 33% in subjects who did not know their status vs. 3.6% in those with negative history of STIs (OR: 13.227, 95%CI: 1.113, 157.130). However, this correlation was not observed for HCV infection. An uncertain history of coagulopathy was significantly associated with HBV infection (p=0.030, \(\chi^2(2)=6.999\)), and a positive history was associated with HCV infection (p<0.001, \(\chi^2(2)=151.998\)). A positive history of intravenous drug use (even if it consisted of a single injection) was significantly associated with HCV infection (p=0.003, \(\chi^2(1)=305.000\)), but not with HBV infection (p=1.000, \(\chi^2(1)=0.041\)). The same was true for needle sharing and HCV infection (p<0.001, \(\chi^2(2)=305.000\)), but not HBV infection (p=0.960, \(\chi^2(2)=0.082\)).

Conclusions: An uncertain history of STIs, HIV or coagulopathy was significantly associated with an increased risk for HBV infection, suggesting that the highest risk for hepatitis B can be seen in patients with regular contact with the healthcare system or with risk behaviors such as unprotected sex. A positive history of coagulopathy, intravenous drug use, or needle sharing was significantly associated with HCV infection. These results suggest that risk minimization interventions are still needed, at least in the general population in Romania, where the prevalence of HBV is currently at 4.4% and the prevalence of HCV at 0.4%.

No conflict of interest
Abstract: O_03

Monitoring and Diagnostic Tools

Expression of NS4 HCV in liver cells of HIV/HCV co-infected patients

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Introduction: Structural protein NS4 HCV is component of HCV replicative complex in hepatocytes. Subunits NS4A acts like cofactor of NS2-NS3 protease and is a target point for some direct anti-HCV agents (DAA) – boceprevir, telaprevir, simeprevir. NS4B takes key role in HCV replication and membranous net formation on endoplasmic reticulum.

Aim of study: to evaluate correlation between expression of NS4 HCV and p24 HIV, HLA-DP, DQ, DR in liver cells of HIV/HCV co-infected patients.

Material & Methods: Monoclonal anti-HIV p24, anti-human HLA-DP, DQ, DR antigen, (Dako), anti-hepatitis C, NS4 HCV (AbDserotec) were used. Expression of markers were evaluated in hepatocytes (HC) and Kupffer cells (KC) by immunohistochemistry in paraffined liver tissue in 18 patients with HIV/HCV. Marker's expression evaluated in points: 0 - negative staining, 1 - weak intensity, 2 - moderate, 3 - pronounced intensity. Mean age of patients was 36,1±5,1, males - 7 (38,9%); AIDS -15 (83,3%), ART – 12 (66,7%). Liver cirrhosis was in 6 (33,3%), chronic hepatitis C (CHC) of mild activity – in 12 (66,7%) patients. None of patients received antiviral therapy of CHC. «Statistica» version 10 was used, data are presented as Me and interquartile range (IQRs).

Results: Expression of NS4 in HC has been detected in 9 (50%) of patients in studied group. Significantly higher expression of p24 HIV in KC among positive NS4 HCV expression in HC was 7, among negative NS4 HCV expression in HC was 1 (5,6%), p <0,02, Yates corrected Chi-square. Expression of HLA-DP,DQ,DR in KC also was significantly higher in patients with positive NS4 HCV expression in HC in comparison with patients without NS4 HCV expression in HC: 1 (0 – 1) and 0 (0 – 0) points, respectively (p<0,05: Mann-Whitney UTest). Expression of HLA-DP, DQ, DR in KC was presented in 6 (55,5%) patients with positive NS4 HCV expression in HC and was absent in NS4 HCV negative ones, p <0,02, Yates corrected Chi-square. Simultaneous p24 HIV expression in HC and KC was detected in 8 (44,4%) HIV/HCV co-infected patients. Among them 7 had NS4 HCV expression in HC - 1,0 (1,0 -2,0). In the same time among 10 patients with negative result on p24 HIV expression in HC and KC only 2 patients had mild NS4 HCV expression in HC - 0 (0,0 -0,0), p<0,05, Mann-Whitney UTest. NS4 HCV expression in HC was established in 5 (41,7%) with CHC and in 4(66,7%) with liver cirrhosis (p>0,05). The right Spearman correlation between NS4 HCV expression in HC and liver cirrhosis was calculated: R=0,37 (p=0,03).

Conclusions: Synergism in expression of replicative markers of HCV (NS4) and HIV (p24) in liver cells of HIV/HCV co-infected patients has been established. We can propose that effect of DAA in HIV/HCV co-infected patients may be enhanced by achievement of strong HIV suppression.

No conflict of interest
Abstract: O_04

Treatment Issues - Hepatitis _ HIV coinfection

HCV reinfection in HCV/HIV coinfected patients treated for VHC in AIDS Center Prague

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Background: There are 2738 persons living with HIV (human immunodeficiency virus) infection in the Czech Republic and the prevalence is 0.026%. The occurrence of HCV (hepatitis C virus) infection is relatively low in the Czech Republic as well. According to recent studies, the prevalence of anti-HCV positivity is 1.67% in common population and it is higher than was originally supposed. 10.9% HIV infected persons are anti-HCV positive in the Czech Republic. Limited access to IFN (interferon)-free treatment regimens still constitutes a problem in the Czech Republic. Only 4 (four) HIV/HCV co-infected patients started IFN-free regimen therapy in AIDS-Center Prague by June 2016. Generally, HCV reinfections are frequent in HIV-positive MSM (men having sex with men).

Material & Methods: More than 50% of all HIV-infected persons in the Czech Republic are followed in AIDS-Center Prague. Forty-six (46) anti-HCV treatment courses with known SVR (sustain virologic response) in total of 42 HIV+ patients were provided in Prague Center between 2003 and now. Seven (17%) out of 42 patients were women, 35 (83%) were men and in total 32 (76%) were MSM. All patients were treated by pegylated interferon+ribavirin. Three (3) of those patients were treated for acute HCV infection and four (4) were treated for HCV reinfection.

Results: Twenty-six (26) out of 46 (56.5%) therapeutic courses using pegylated interferon/ribavirin had SVR 24. Reinfection was documented in seven (7) out of 26 (27%) previously successfully treated patients. Six (6) of them were MSM. Two (2) out of four (4) patients treated for reinfection reached SVR.

Conclusions: The prevalence of HIV infection and HIV/HCV co-infection is still relatively low in the Czech Republic. IFN containing regimen is still most frequent option for HCV treatment in HIV infected persons. We have observed that the HCV reinfection is not uncommon in HIV infected MSM treated for the HCV infection in the AIDS-Center Prague. We may then conclude that the reinfection still complicates the availability of the HCV treatment by DAA (directly acting antivirals). However, our results are not significant because of the small sample of patients.

No conflict of interest
Abstract: O_05

Treatment Issues - Hepatitis _ HIV coinfection

Chronic Hepatitis C Treatment among HIV/HCV co-infected PWID in Ukraine: community-supported treatment model experience

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Background: Ukraine belongs to the region with moderate prevalence of HCV infection. WHO estimates 3% of HCV infection prevalence among general population of Ukraine. At the same time official Ministry of Health records of CHC reports 62 807 cases registered in period between 2010–2014 yrs. HIV prevalence is 0.59% among adult population. There are 29 890 HIV/HCV co-infected people who are registered in care at HIV/AIDS centers. About 29% (n=4532) of HCV and 7% (n=1047) of HBV registered among newly detected HIV cases in 2014. The estimated number of PWID is 310,000 with HCV prevalence of 55% according to the bio-behavioral study 2013.

Materials and methods: Within a pilot project of HCV treatment among key populations sofosbuvir-based treatment regimens were introduced in 2015. The project services include facilitation of the access to HCV diagnostics, treatment and social support. Prevention of HCV reinfection is addressed by 3 months intervention performed by social workers. Treatment efficacy monitoring was established which include demographic, diagnostics and clinical data collection.

Results: Cohort consists of 264 patients who initiated treatment within June-December 2015. 73% were male, mean age was 38 years old. 246 (96%) were co-infected HIV/HCV, 19 (7%) were co-infected HIV/HCV/HBV, 10 (4%) were HCV mono infected. 56 (23%) out of HIV/HCV co-infected had TB treatment history. Key populations were presented primarily by PWID 220 (86%), 14 (5%) OST, 22 (8%) - were represented by CSW, MSM and other risk populations. Fibrosis stages distribution: F1 - 60 (23%), F2 – 87 (34%), F3 – 52 (20%), F4 (A), (B) – 56 (22%). The prevalent genotype was G1 (48%), followed by G3 (42%), G2 (9%) and G4 (1%). SOF+PegIFN+RBV (12w) were prescribed in 82% of patients, SOF+RBV (12 w) – in 9% and SOF+RBV (24 w) in 8% of patients. Overall 240 patients achieved SVR 12 (91%), 16 (6%) had relapse and 8 (3%) dropped out (2 adverse events, 4 refused treatment, 2 death). Patients with G1 achieved 90% SVR12, with G2 80%, G3 95% and G4 100% SVR 12 rates. Treatment response in non-cirrhotic and cirrhotic patients is 93% (n=191) SVR12 versus 86% (n=51).

Conclusions: Sofosbuvir-based HCV treatment regimens showed high SVR 12 rates among hard-to-reach high risk populations; primary HIV/HCV co-infected PWID. Dropout rates due to discontinuation of treatment are very low. Role of social/peer support services during and after the treatment should be studied further as service model in a standard HCV care for hard-to-reach populations.

No conflict of interest
Abstract: O_06

Monitoring and Diagnostic Tools

Quality of life in patients with HCV/ HIV co-infection

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Background: Quality of life (QOL) assessment is an important tool for effective management of patients with progressive chronic diseases. It is well known that the QOL is diminished in both groups of patients; with chronic HCV and HIV, but impact of HCV/ HIV co-infection on QOL is still not quite clear.

Materials & Methods: We performed a comparative analysis of QOL in 3 groups of patients: Group 1 - 57 patients with chronic HCV infection (35 - male and 22 - female), Group 2 - 39 patients with co-infection of HCV / HIV (22 - male, 17 - female), Group 3 - the control group: 30 healthy people (20 - male, 10 - female). Diagnosis established by local clinical protocols. We used adapted QOL questionnaire SF-36 to survey health status of patients. SF-36 questionnaire contains 36 questions grouped in eight domains: 1-4 scales reflect the physical health, and 5-8 - psychological. 1 - Physical functioning (pf), 2 - Role-physical functioning (rp), 3 - Bodily pain (p), 4 - general health (gh), 5 - Vitality (vt), 6 - social functioning (sf), 7 - Role-emotional (re), and 8 - mental health (mh).

Results: Comparison of the results showed no difference in the quality of life data between group of patients with HCV and patients co-infected with HCV / HIV. The overall rate physical health component was respectively 54,9±2,7 (HCV) and 53,11±3,27 (HCV / HIV). However in comparison with control group (80,03 ± 1,65) the of quality of life was significantly reduced (p<0,05). The similar results were obtained when comparing the psychological health scales: 54,05 ± 2,64 (1st group) and 48,79± 3,35 (2nd group) (control - 74,22±1,98 (p<0,05)). We also found that QOL declines dramatically in both groups with chronic hepatitis C, regardless of HIV status with the progression of liver of fibrosis.

Conclusions: Chronic hepatitis C and HCV/ HIV co-infection is a serious problem for patients. We found that the degree of the diminishing of the physical health was more significant than those that characterized the psychological component of health, especially in the group of co-infection of HIV / hepatitis C (p<0,05). Progressive liver disease significantly diminished QOL in both groups patients: HCV and HCV/ HIV co-infection.

No conflict of interest
Abstract: O_07

Treatment Issues - Hepatitis _ HIV coinfection

Efficiency of sofosbuvir and peginterferon alfa-2b/ribavirin in the treatment of chronic hepatitis C with genotype 1b and 3 in HIV-infected injecting drug users

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Introduction: HIV and chronic viral hepatitis belong to the socially significant diseases that can affect not only the health of patients, but also the demographic situation in the country. In Ukraine about 70% of patients infected with HIV also have HCV. It is known that IDUs are rarely able to achieve an adequate level of adherence in the long-term treatment of socially dangerous diseases such as HIV, tuberculosis, viral hepatitis. Reducing the overall duration of treatment of HCV with the emergence of Sofosbuvir and other drugs of direct action can significantly increase the retention of patient under active supervision and the effectiveness of this therapy.

Material & method: The study included 19 IDUs with HIV/HCV coinfection who received antiretroviral therapy at least for 6 months and had a complete suppression of HIV (HIV-RNA <50 copies/ml). The average age of patients was 41 (from 27 to 58 years). The average term of drug use was 14 years (from 2 to 26 years). 4 (21.1%) patients were on substitution maintenance therapy with buprenorphine. 2 (10.5%) patients were found to have concomitant chronic hepatitis B. The median level of CD4-lymphocytes before the treatment was 470 (IQR 310-675) cells/ml.

Results: In the majority of patients (14 - 73.7%) the antiretroviral treatment scheme included TDF / FTC (3TC) in combination with EFV (4 - 21.1%) or LPV / rtv (10 - 52.6%). In 5 (26.3%) patients the scheme of ABC / 3TC + LPV / rtv was used. The scheme of antiretroviral therapy did not change in all patients during the whole study period. Among the patients included in the study 9 (47.4%) had the HCV genotype 1b, 10 (52.6%) - HCV genotype 3. The median viral load of HCV-RNA before enrollment in the study was 5.71 (IQR 5.51-6.06) lg copies in ml. The transient elastography (FibroScan ©) was used the most often combined with FibroTest ©, APRI-index (cut-off value for the F4> 2,0) or FIB-4 index (cut-off value for the F4> 3,25). In accordance to the assessments of the two methods the degree of liver fibrosis was considered to be determined. Among the patients that were included in the study 10 (52.6%) had a moderate fibrosis (F2), 9 (47.4%) - severe fibrosis and cirrhosis (F3-F4). Cirrhosis in 2 (10.5%) patients was Class A on a Child-Pugh scale, with no signs of decompensation.

All patients, regardless of HCV genotype and degree of liver fibrosis, received sofosbuvir (400 mg daily) in combination with peginterferon alfa 2b (1.5 mcg / kg per week) and ribavirin (1000-1200 mg daily) for 12 weeks. After 4 weeks of treatment the HCV-RNA in plasma of all patients was not determined. The neutropenia was revealed the most often among the side effects, which occurred in 16 (84.2%). The side effects of the 4 severity were not recorded.

Conclusions: Thus, the 12-week treatment regimen with sofosbuvir and peginterferon alfa-2b / ribavirin is very effective in the treatment of chronic hepatitis C with 1b and 3 genotypes in HIV-infected injecting drug users.

No conflict of interest
Abstract: O_08

Treatment Issues - Hepatitis _ HIV co-infection

Predictors of HIV co-infection in HCV infected patients in Serbia

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Background: Hepatitis C virus (HCV) infection and associated liver disease (cirrhosis, end stage liver disease, hepatocellular carcinoma) are among the leading causes of morbidity and mortality globally. The reported prevalence of HIV/HCV co-infection varies significantly among studies, ranging from 4% up to 90%, depending on the geographical region and studied population. In Serbia, about one quarter of human immunodeficiency virus (HIV) infected persons in Serbia have also been found to be HCV co-infected. Previously, we have shown that in Serbian HIV/HCV coinfected patients HCV genotypes 3 and 4 prevail, unlike general population where HCV genotype 1 is the most prevalent. Here, we further analyze clinical and demographic parameters associated to HIV/HCV coинфекtion in Serbia.

Materials & Methods: The study included 214 consenting HIV/HCV co-infected patients followed at the Infectious and Tropical Diseases University Hospital in Belgrade, according to inclusion criteria: ELISA determined and western blot confirmed seropositive status for HIV/HCV co-infection and adult age. The study included patients in the period 1998 – 2012. Epidemiological, clinical, and behavioral data were collected using a standardized questionnaire. Transmission risk was defined as intravenous drug use (IDU), sexual contact, history of transfusion of blood/blood products, vertical and other. HIV disease was classified in stages A-C according to the 1993 Centers for Disease Control case definition criteria. Aspiration liver biopsy was performed in order to assess severity of fibrosis and necroinflammatory activity, using Ishak modification for hepatic activity index. The diagnosis of cirrhosis was established using histological or a combination of clinical, endoscopic and laboratory findings.

Results: The patients presented in different stages of HIV disease: 29/214 patients were CDC A (13.6%), 72/214 patients were in the stage B (33.6%), whereas 113/214 patients presented with CDC C (52.8%). Majority of coinfected patients (151/214, 70.5%) were IDUs and male (58.0%). Non-1 HCV genotypes were more commonly found among IDUs compared to other transmission risks (p=0.03). HCV viral load did not differ significantly across different genotypes. Logistic regression analyses revealed that certain HCV genotypes were not associated with the higher incidence of liver cirrhosis, while the independent predictor of ESLD was age above 40 (OR 2.7, 95% CI 1.7-4.5 , P=0.01). Univariate logistic regression identified age under 40, IDU, infection with non-1 HCV genotype and HCV viral load over 5log to be associated with HIV co-infection, all of which except the age was also confirmed in multivariant logistic regression analysis.

Conclusions: In Serbian cohort of coinfected patients we found history of IDU, infection with non-1 HCV genotype and HCV viral load over 5 log to be predictors of HIV co-infection.

No conflict of interest
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Abstracts
Poster Presentations
Abstract: P_09

Liver Cancer

Alteration of the Total Nuclear DNA Ploidy in Different Histopathological Liver Tissues Negative and Positive for HCV RNA

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Background: Hepatitis C virus (HCV) infection is associated with the development of hepatocellular carcinoma (HCC). The molecular mechanisms of HCV-associated carcinogenesis are unknown. We aim to investigate the alteration of the total nuclear DNA content (ploidy) in different histopathological liver tissues infected with HCV and their relation to the seropositivity of HCV RNA.

Methods: Blood and liver tissues were collected from 26 patients. Diagnosis was carried out according to clinical and pathological examinations by specialized physicians. HCV RNA was detected in patients’ sera and tissue samples by RT-PCR. To examine nuclear DNA ploidy, liver tissues were stained with blue Fulgen using the image analysis techniques. Finally, the patients’ DNA content was examined by histochemical analysis depending on the optical density of DNA from liver biopsies using the grey image menu in each specimen.

Results: The HCV RT-PCR results demonstrated that 13/26 (50%) patients had detectable HCV RNA in their sera samples while 18/26 (69%) had detectable HCV RNA in liver tissues. The DNA content from those patients measured by image cytometry showed a high level of alteration of nuclear DNA ploidy and proliferation in liver tissues with HCC, less alteration of nuclear DNA ploidy in cirrhotic patients, and least proliferation nearly normal in liver fibrosis patients. Moreover, the results of histochemical analysis confirmed the DNA image cytometry results and showed that positive HCV RNA liver tissues had more DNA ploidy than negative HCV RNA liver tissues with statistical significance (p-value < 0.05).

Conclusions: HCV positive liver tissue had alterations in DNA content (ploidy) which may lead to liver disease progression, malignant transformation of the liver cells and development of hepatocellular carcinoma.

No conflict of interest

Abstract: P_10

Liver Cancer

HCV and HCC – finally a melody of life

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Introduction: We investigated a small group of hepatitis C virus (HCV) cirrhotic patients who underwent eradication of the virus with interferon-free regimens after hepatocellular carcinoma (HCC) treatment was performed.

Patients & Methods: For the period 01.2015-06.2016, 5 patients (2 males) with HCV cirrhosis (Child A/B, MELD 12-15) and previous HCC treatment were HCV eradicated using interferon-free regimens (Paritaprevir/r/Ombitasvir/Dasabuvir±RBV – 3 patients, Ledipasvir/Sofosbuvir+RBV – one patient, Sofosbuvir + RBV – one patient). Prior to the HCV treatment the patients were diagnosed with HCC (BCLC A – 3, BCLC B – 1, BCLC C – 1) with contrast-enhanced US/CT and biopsy. Each of the 5 patients underwent a percutaneous ablative procedure, one patient also had a TACE performed, and one had a hepatic resection. The patients were followed-up with CEUS/CEPT.

Results: The percutaneous ablation technique (radiofrequency, microwave) achieved complete tumor necrosis in 4 of the 5 patients (in the BCLC-C patient the aim was cytoreduction). In one patient two new HCC
nodules appeared 3 years after complete ablation and in another local recurrence was observed. Both patients were further treated using local ablation achieving complete necrosis. All these events (but one – the local recurrence) preceded the interferon-free HCV treatment which proved to be successful in all cases (SVR12 - 5/5) with good tolerability.

Conclusions: The presented clinical scenarios are an evidence of the better outcome for patients with the HCV and HCC co-morbidity.

No conflict of interest

Abstract: P_11

Monitoring and Diagnostic Tools

Impact of viral hepatitis in hemodialysis patients with chronic kidney disease

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Introduction: Infections with hepatitis viruses B and C are major causes of morbidity and mortality in hemodialysis patients and the risk is increasing with the number of years of hemodialysis. Chronic Kidney Disease (CKD) on one hand and dialysis procedure on the other hand produce numerous changes of nonspecific and specific defense that favor the acquisition of these infections and decrease the rate of viral spontaneous clearance.

Materials and methods: The study was conducted on 154 haemodialysis patients with CKD, divided into three groups: group A (control) - 97 patients without viral hepatitis; group B - 30 patients with viral hepatitis B (HVB); group C - 27 patients with viral hepatitis C (HCV). The patients were investigated biochemically, haematologically, immunologically; positive serology for viral hepatitis was confirmed by viral load.

Results: In haemodialysis patients HBV had a prevalence of 19.48% and HCV 17.53%. The inflammatory syndrome was present in 56.94% of patients (investigated by erythrocyte sedimentation rate (ESR)> 30 mm / h, C-reactive protein (CRP)> 6 mg / L) and the anaemic syndrome in 83.02% of patients, assessed by haemoglobin level (HB). Inflammatory syndrome was present in 67.39% of patients without viral hepatitis, compared to 38.46% in patients with viral hepatitis (Chi squared test = 5.67, *p* = 0.017). Also in group A patients the CRP level was 25.59 mg / L (17.44 to 33.75) and HB level - 9.42 g / L (8.90 to 9.96), versus patients in group B where CRP was 22.51 mg / L (2.72-42.29) and HB - 9.98 g / L (8.85-11.12), and group C where CRP was 8.72 mg / L (3.42-14.00) and HB - 10.76 g / L (10.09-11.44). CRP and ESR showed no significant differences between the three groups (ANOVA test: *F* = 2.09, *p* = 0.131) due to increased variance in patients with viral hepatitis. Haemoglobin levels were significantly different in the three groups (ANOVA test: *F* = 4.22, *p* = 0.020) and post-hoc test (Bonferroni) showed a significant difference between patients with HCV and those without viral hepatitis (*p* = 0.017).

Conclusions: Inflammatory syndrome is present in lower percent in patients with CKD and viral hepatitis, who follow immunomodulatory treatments for viral disease. CRP level is decreased in patients with hepatitis C who are likely in the chronic phase, compared to those with hepatitis B.

No conflict of interest
Abstract: P_12

Monitoring and Diagnostic Tools

Assessment contributing factors to accelerated fibrosis progression in HIV/HCV coinfected patients in Ukraine

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Introduction: Approximately 40-75% of PLHIV in Ukraine are coinfected with HCV, 20-30% have active form tuberculosis (TB), that impairs the course and treatment of HIV infection. Despite the free access of ART and TB treatment, the number of reported deaths due to TB and advanced liver diseases continue to rise in PLHIV.

Methods: In study were analyzed clinical data of 95 HIV/HCV coinfected patients aged 25-47 years admitted to Poltava (central region of Ukraine) HIV/AIDS clinic in 2003-2014. We included 98 patients with known genotype HCV and stages of fibrosis in retrospective cohort study. Stage of fibrosis is determined with transient elastography. We analyzed factors contributing to accelerate fibrosis progression including socio-demographic and clinical data, presence of active forms and MDR TB, relapses of TB, adherence to chemoprevention of TB. We used Cox proportional hazards regression model to outcome measure included time from the first positive HCV test to diagnosis advanced liver fibrosis (F2-F4).

Results: Accelerated fibrosis progression was associated with injection of intravenous drugs (HR= 1.4; 95% CI [0.6-2.1]), male sex (HR= 2.4; 95% CI [1.2-4.5]), lower level of CD4 (HR= 1.5; 95% CI [1.2-1.9]). At the time of their first visit to a health facility, 36% had active form TB with relapse in 22%. Presence of TB relapses was associated with accelerated fibrosis progression (HR= 1.1; 95% CI [0.8-1.3]).

Conclusions: This study suggests a greater risk of accelerated fibrosis progression in HIV/HCV coinfected patients with presence of relapses of TB. HIV/TB/HCV coinfections impair the treatment and prognosis for patients.

No conflict of interest

Abstract: P_13

Monitoring and Diagnostic Tools

The risk of infection with hepatitis viruses B and C in hemodialysis unit

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Introduction: The hemodialysis procedure is a risk factor for infections with hepatitis viruses B and C. Evaluating the prevalence of viral hepatitis B and C impact in patients with chronic kidney disease (BCR) on hemodialysis may help to prevent the transmission of these diseases and can improve the management of the hemodialyzed patient.

Material and methods: We studied 4642 people, aged 23-79 years, divided in two lots: group A - 4461 apparently healthy blood donors; group B - 181 BCR patients on hemodialysis. We detected the immunological markers of viral hepatitis B and C by ELISA tests and electrochemiluminescence performed on COBAS 600 – ROCHE DIAGNOSTICS. The hemodialysis patients were subjected also to routine biochemical, hematological and immunological tests, as stated in the management protocol of these patients.

Results: In blood donors hepatitis B prevalence was 3.07% and hepatitis C prevalence 0.65%. In BCR patients prevalence of viral hepatitis was 17.13%: 7.18% - hepatitis B (OR = 2.65), 8.84% - hepatitis C (OR = 15.88) and 0.55% had hepatitis B and C co-infection. Hepatitis prevalence in BCR patients was 36.36% in 23-45 years age group.
Hepatitis B prevailed in men (12.36%) compared to women (3.49%), while hepatitis C prevailed in women (10.47%) compared with men (7.87%). There were no significant differences in serum transaminase levels in BCR patients with and without viral hepatitis. The risk of viral hepatitis increased with the number of hemodialysis sessions. Anemic syndrome was present in 80% of BCR patients and inflammatory syndrome in 52.00%.

**Conclusions:** Hemodialysis is a risk factor for acquisition of hepatitis viruses B and C. The viral hepatitis B and C can be considered as nosocomial infections in the hemodialysis unit.

*No conflict of interest*

**Abstract: P_14**

**Monitoring and Diagnostic Tools**

**Immunological status, antiretroviral treatment and serological pattern of EBV in HIV infected population – preliminary observations**

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**Background:** HIV-infected individuals are at the higher risk of EBV-related lymphoma development. Reactivation and lytic phase of EBV infection is associated with the oncogenic process. EBV serology can help to determine the lytic phase and reactivation. The aim of the study was to determine the correlation between immunological status, HIV replication and serological markers of EBV-reactivation.

**Materials and methods:** Serological EBV tests were performed in the serum samples of 79 HIV-infected individuals divided by the four groups (group A n=20: CD4<300 cells/mcl, antiretroviral-treatment naive; group B n=20: CD4<300 cells/mcl on suppressive cART (HIV-RNA <50 copies/ml); group C n=20: CD4<300 cells/mcl, antiretroviral-treatment naive; group D n=19: CD4>300 cells/mcl on suppressive cART (HIV-RNA <50 copies/ml). Patients with clinical symptoms of EBV infection and history of cancer were excluded from the study. EBV serology status was tested by recomLine EBV Microgen Diagnostic. Kruskal-Wallis and Chi² tests were used for statistical analysis.

**Results:** All patients were previous infected by EBV, there were no individuals with new acquired infection. Only in two cases (2.53%) the VCA-IgM were detected; one from group B, and one from group C. There were strong reaction with EA antigens in 17 cases (21.52%), what may suggest reactivation of EBV. There were no difference between the groups; p=0.66.

**Conclusion:** EBV coinfection is common among HIV-coinfected individuals, while the reactivation seems infrequent. As EBV remains vital in lymphoma-associated oncogenesis high prevalence of EBV antibodies may reflect the increased risk of this disease in HIV infected patients.

*No conflict of interest*

**Abstract: P_15**

**Monitoring and Diagnostic Tools**

**Assessment of Primary Care Doctors’ Linkages with Community Resources in the Management of Chronic Hepatitis in Constanta County, Romania**

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**Background:** Community linkages and civil society resources are key in improving the quality of care provided to patients with chronic diseases. In Constanta County hepatitis B and C prevalence rates are as high as 6%. A total
number of 438 family doctors are registered in the county. Baylor Foundation set to assess what is the current level of awareness of family physicians in Constanta region regarding the existing community resources, as well as their level of interest to refer patients for support and self-management interventions.

**Materials & Methods:** 250 randomly selected doctors from the total pool of 438 were invited to be part of the assessment. 102 accepted the face to face interview, 147 did not respond and 1 refused. The semi-structured interview assessed awareness regarding community resources, referral rates and preferred referral routes, as well as needs for services for patients with viral hepatitis.

**Results:** Family physicians’ knowledge on the existence of complementary services that community organizations offer to patients increases the likelihood for referral (49% of the physicians knew about the existence of support organizations in their area and two thirds of them actually recommended their patients to access community services). Service awareness and motives to refer patients to a community organization were limited to one or two services (usually, rapid testing and informative materials), although there were many other services available (mental health, legislative support, adherence, life-style, social support etc). Most (88%) referral routes are informal, such as verbal recommendation or phone intervention on behalf of the patient; about 10% of doctors actually implemented formal collaborations with the community organizations, mainly due to lack of system incentives. The following needs were ranked as priorities for patients with chronic viral hepatitis in Constanta: counselling and orientation regarding living with a chronic disease (75%), practical support for medical monitoring for uninsured patients or patients with low income (60%) and interventions for depression and associated mental health issues (48%).

**Conclusions:** There are untapped care strengthening opportunities available at the community level that can complement the primary care services for patients with chronic viral hepatitis in Constanta region. There is individual willingness from family physicians to increase the quality of care provided to their patients, but the current healthcare organization system does not stimulate, nor clarify how these partnerships are to be put into practice. National strategies for hepatitis should include aspects regarding strengthening linkages between primary physicians and community resources, to address the needs of patients with hepatitis.

*No conflict of interest*

**Abstract: P_16**

**Monitoring and Diagnostic Tools**

**Outcomes of an Eight Year Long, Opt-In, HIV, HBV & HCV Voluntary Counseling and Testing Program in Dobrogea Region, Romania – A Community Case Study of Baylor Foundation**

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**Background:** Across European countries, there are still low screening rates due to insufficient access to testing programs or to low adherence to guidelines’ recommendations. Baylor Black Sea Foundation (BBSF) has initiated a free of charge, rapid, voluntary counselling and testing program for HIV, HBV & HCV (3HVCT), by setting up 2 testing facilities in public county clinics, another private testing facility and one mobile laboratory, especially for testing in rural sites. The program is unfolded since 2007 exclusively through charity funding in Dobrogea region in Romania.

**Materials & Methods:** Through sensitization campaigns, people from the general population received information about how to access the 3HVCT services. Approximately 55K persons received pre and posttest individual counseling, including a detailed assessment of risk factors, alongside the rapid testing. Clients with negative results received reinforcements on how to stay negative; reactive cases were linked with existing healthcare system for confirmation of diagnosis. Targeted follow up of all confirmed cases ensured successful uptake and access to care of referred patients.
Abstract: The recorded prevalence rates in the group tested are of 0.37 for HIV, 2.82 for HCV and 3.98 for HBV. The mean age of the program beneficiaries during the entire period of the study was 43.2±17.2 years (limits: 0–94 years); 53.5% of the subjects were women, 67% had medical insurance and 67.9% had urban residence. 76% of the subjects were tested for the first time for any of the three infections. The acceptance of testing for all three infections was high (95% average, variation from 82% to 99%); the retesting rate was of 24%. The seroprevalence of HIV infection was highest in young persons, while significantly higher prevalence for hepatitis in patients older than 50 years compared with other age groups was recorded. 78% of all those seeking testing identified themselves as having a history of medium or high risk exposure situations. Regarding the distribution of risks among positive cases, the declared risk factors show that sexual transmission risk have the highest rates in the HIV positive patients, parenteral transmission (including dentistry, surgery etc) was most prevalent among those reactive to HCV, while HBV positive cases had either unknown risk factors or risk of contamination through medical procedures and unsterilized equipment.

Conclusions: Every year, the 3H VCT program was able to steadily increase the number of community members served, as the population interest for this free of charge screening opportunity was observed (high self-referral rates, high percentage of first-time testers), thus indicating that the program was responding to a community need. Our findings also confirm that the availability of a screening program increases the probability of seeking care in a community. In addition, testing for these infectious diseases provide opportunities for other preventive interventions, such as counseling and drawing people into care, which may result in reduced risk of transmission.

No conflict of interest

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Abstract: P_17

Monitoring and Diagnostic Tools

Evaluation of thyroid stiffness in patients with chronic HCV infection

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Background: Chronic infection with hepatitis C virus (HCV) leads to progressive fibrosis and liver scarring. However, fibrosis has recently been shown to be a dynamic and systemic process, involving other organs apart from the liver. The spleen is the most studied organ in terms of stiffness in chronic viral infection, while the thyroid has been explored more from an oncology perspective (i.e., stiffness of malignant nodules) than from an infectious diseases one. Therefore, we have conducted a study to determine the degree of thyroid fibrosis in patients with chronic hepatitis C.

Materials & Methods: Thyroid and liver stiffness were determined through shear-waves elastography Aixplorer (SuperSonic Imagine, France) in patients with chronic HCV infection. The statistical analysis was performed with IBM SPSS Statistics v.22 (Armonk, USA).

Results: Our study included 119 patients divided into two groups: patients with chronic genotype 1b HCV infection (n=99, 83.2%) and a control group matched for age and gender. The median (IQR) age was 56 (46, 62) years, and 78 (65.5%) of the patients were female. Most of the patients (n=110, 93.2%) did not have localized intrahepatic lesions. Some of the patients (n=21, 17.6%) had a preexisting underlying thyroid disorder, 27 patients (22.7%) had thyroid nodules, and 11 of them were receiving specific endocrinology treatment. The prevalence of thyroid disorders in general (but
not of thyroid nodules in particular – \( \chi^2(2)=3.056, p=0.217 \) was significantly higher in the HCV group compared with the control group (n=20, 27% vs. n=1, 5%, \( \chi^2(1)=4.403, p=0.028 \)). The median (IQR) stiffnesses were: 8.5 (6.2, 12.2) kPa for the liver, and 20.3 (15.5, 28.4) kPa for the thyroid. Liver stiffness was unsurprisingly higher in the HCV group (8.8 vs. 5.75 kPa, \( Z=-4.236, p<0.001 \)), while the differences in terms of thyroid stiffness were unremarkable (20.3 vs. 20.1 kPa, \( z=-0.668, p=0.504 \)). Thyroid stiffness was significantly higher in patients with underlying thyroid disorders (30.3 vs. 18.9 kPa, \( Z=-2.578, p=0.010 \)) and in those with thyroid nodules (29.4 vs. 18.8 kPa, \( Z=-3.097, p=0.002 \)). Most of the patients (86.8%) had received prior treatment for chronic HCV infection, 15 (12.6%) with peg-interferon and ribavirin and 12 (10.1%) with direct-acting antivirals with or without interferon, but thyroid stiffness was not influenced by previous anti-HCV treatment (\( Z=-0.331, p=0.741 \)) nor by the type of response (\( Z=-1.575, p=0.121 \)). We identified no direct correlation between liver and thyroid stiffness (\( r_s=1, p=0.344 \)).

**Conclusions:** Shear waves elastography can play an important role in identifying thyroid disorders or thyroid nodules, particularly among patients with HCV infection who routinely undergo shear waves assessment of liver stiffness. However, thyroid stiffness does not appear to be significantly increased in HCV-positive patients compared with controls, suggesting that this organ might not be as prone to HCV-induced fibrosis as the liver.

Given the significantly higher prevalence of thyroid disorders in patients with HCV infection, endocrinology screening and management is mandatory, even in the new era of interferon-free treatment.

*No conflict of interest*

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**Abstract:**

**New anti-HCV agents**

**Discovery of Novel 1,3,5-triazine-thiourea based dual inhibitor of HIV and HCV infection**

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**Background:** According to recent data of WHO, an estimated 2.3 million people living with HIV are coinfected with hepatitis C virus (HCV) globally. HIV and HCV infections are major global public health problems, with overlapping modes of transmission and affected populations. The study also reported that, HIV-infected people are on average six times more prone to HCV infection than HIV-uninfected people, which warrants need to improve integrated HIV/HCV services together with affordable newer medications. Therefore, present study was intended to discover novel 1,3,5-triazine-thiourea based dual inhibitor of HIV and HCV infection.

**Method:** The compounds were developed via facile synthetic route in excellent yield. These molecules have been subsequently tested for anti-HIV activity using TZM-bl cell lines along with Luciferase expression profile of the TZM-bl cells after infecting with NL4.3 virus and MTT assay for the cytotoxicity determination. The anti-HCV activity was also determined by capability to obstruct the HCV replicase (HCV NS5B) activity in vitro and HCV replication in a cell culture system carrying replicating HCV subgenomic RNA replicon.

**Results:** It has been found that compound 8a showed utmost 97 % inhibition of HIV with \( K_i = 523.45 \) nM against HIV-RT. Rest of the molecules showed also showed significant inhibition pattern. The target molecules also found to exhibit potent inhibition of RNA dependent RNA polymerase (RdRp) activity of HCV replicase in vitro with \( IC_{50} = 15.21 \) µg/ml. Compound 8c, significantly inhibited HCV replication in culture system which leads to...
reduction in HCV RNA titer and translation level of viral proteins in concentration-dependent manner.

**Conclusion:** As a concluding remark, we have developed novel 1,3,5-triazine-thiourea based dual inhibitor of HIV and HCV infection, while presenting no considerable toxicity at the test dosages.

*No conflict of interest*

**Abstract:**

New anti-HCV agents

**Discovery of Novel 1,3,5-triazine-pyrazole as inhibitor of HIV and HCV infection with favourable metabolic profile**

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**Background:** The HIV and HCV co-infection poses greatest threat to the clinical fraternity for its management because of similar mode of transmission. According to an estimate, nearly two million people infected with HIV are co-infected with hepatitis C virus (HCV) globally. Therefore, the current situation warrant the discovery of newer drugs or therapeutic modalities which can able to act on both HIV and HCV concomitantly. Thus, the present study aimed at the development of novel hybrid derivatives of 1,3,5-triazine-pyrazole as a inhibitor of HIV and HCV infection.

**Method:** The target compounds were developed via series of nucleophilic reaction with basic amine and pyrazole. These molecules have been subsequently tested for anti-HIV activity using TZM-bl cell lines along with Luciferase expression profile of the TZM-bl cells after infecting with NL4.3 virus and MTT assay for the cytotoxicity determination. The anti-HCV activity was also determined by capability to obstruct the HCV replicase (HCV NS5B) activity in vitro and HCV replication in a cell culture system carrying replicating HCV subgenomic RNA replicon. The metabolic profiling of the active compound was also carried out to define the formation of metabolites by the oral route.

**Results:** Among the tested derivatives, compound 6d found to exhibit 98% of inhibition of HIV with Ki of 245.12 nM against HIV-RT with more than 50% inhibition of HIV replication. Moreover, compound 6e showed significant inhibition of RNA dependent RNA polymerase (RdRp) activity of HCV replicase in vitro with IC50 7.8 µg/ml. It also showed significant inhibition of HCV replication in culture system which leads to reduction in HCV RNA titer and translation level of viral proteins in concentration-dependent manner. In metabolic analysis, it has been found that, the skeleton of the hybrid compound remained intact for the longer duration to exert its effect.

**Conclusion:** Together with excellent bioactivities against HIV and HCV infection and favorable metabolic profile, the derivatives of 1,3,5-triazine-pyrazole showed promising option to develop newer therapeutics against the HIV and HCV co-infection.

*No conflict of interest*
Abstract: P_20

New anti-HCV agents

The management of drug-drug interactions in patients undergoing interferon-free direct-acting antiviral treatment for chronic hepatitis C

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Background: After the introduction of interferon-free direct-acting antiviral (DAA) agents, the treatment of chronic infection with hepatitis C virus (HCV) has been redesigned, and it now associates high rates of sustained virological response (SVR) with minimal adverse events. However, in Romania DAA treatment is currently available only to a selected patient population, those with advanced fibrosis (F4 or F3 plus contraindication to interferon). These patients often present multiple comorbidities, and require administration of concomitant medication, which can potentially associate drug-drug interactions (DDIs) with DAAs.

Materials & Methods: We used the HEP-Drug Interaction Charts (University of Liverpool, UK) to check for DDIs between ombitasvir/paritaprevir/ritonavir plus dasabuvir (AbbVie, USA) and the real-life concomitant medication administered to patients with chronic HCV infection and advanced fibrosis.

Results: Our analysis included 67 patients, of which 35 (52.2%) were males. Their median (interquartile range) was 58 (49, 64) years and they had a mean±standard deviation duration of HCV infection of 9±4.9 years. Most of the patients (n=51, 76.1%) had comorbidities, cumulating 131 pathologies, with a median (IQR) number of 2 (1, 5) comorbidities per patient (range: 0-14 comorbidities per patient).

Most of the patients (n=45, 67.2%) were also on concomitant medication at the time of DAA treatment initiation, cumulating 131 drugs, with a median (IQR) number of 2 (1, 5) drugs per patient (range: 0-9 drugs per patient). We identified DDIs in 24 patients (35.8%), and the actions taken ranged from: no change (n=17) to dose change (n=10), drug change (n=3), or stopping the concomitant drug altogether (n=10). Follow-up data is available for 51 patients (76.1%) and all of them obtained SVR by 12 weeks post-treatment. The median (IQR) liver stiffness as measured by shear-waves elastography on Aixplorer (SuperSonic Imagine, France) was 14.8 (9.8, 21.8) kPa at baseline, and it decreased significantly by post-treatment week 12, to 12 (6.8, 16.5) kPa (z=-5.122, p<0.001) and by post-treatment week 24, to 12.85 (6.3, 20.3) kPa (Z=-2.864, p=0.004). The median (IQR) decrease in kPa was -4 (-5, -3) kPa by post-treatment week 12 and -4 (-5, -3) kPa by post-treatment week 24. The presence of comorbidities did not influence response to treatment but it did influence the decrease in liver stiffness at 24 weeks post-treatment (p=0.019). However, if managed correctly and followed up closely, the presence or management of DDIs did not impact the response to treatment or the decrease in liver stiffness at 12 weeks post-treatment (p=0.062) or 24 weeks post-treatment (p=0.909).

Conclusions: Treatment with DAAs of Romanian patients with chronic HCV infection and advanced fibrosis was efficient, with 100% SVR at 12 weeks post treatment. The identification and correct management of potential DDIs did not influence the rate of SVR or the decrease in liver stiffness post-SVR. However, the presence of comorbidities significantly impaired liver regeneration and was associated with a lower decrease in liver stiffness by post-treatment week 24. Therefore, the indication of DAA treatment should be extended to patients with less advanced liver diseases, to ensure optimal responses and the best long term prognosis.

Conflict of interest financial relationship(s): Subinvestigator in clinical trials by AbbVie, Allos Bipharma Inc, Boehringer Ingelheim, Bristol-Myers Squibb, Gilead Sciences Inc, Janssen, Merck, Sharp and Dohme Corp.
Abstract: P_21

Hepatitis C Drug Resistance

Treatment of hepatitis C in pediatric cancer patients: a single centre Ukraine experience

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Background: According to the WHO statistic, prevalence of viral hepatitis C (HCV) in Ukraine reaches above 5%. Children with cancer have higher risk of infection due to high frequency of transfusion and invasive manipulation, immune suppression after anticancer therapy. Also these children more often have progressive course of the disease.

Materials & Methods: A total of 35 pediatric cancer survivors patients with chronic viral hepatitis C (CHC) were treated for 10 years in the infectious diseases clinic of Kyiv O.Bogomolets National Medical University. Treatment regime was 48 weeks for genotype 1 or 24 weeks for genotype 2/3 of weight-based ribavirin and interferon α2a/b or pegylated interferon α2b.

Results: Of 35 patients 11 (31,4%) had HCV genotype 1 (HCV-1), and 24 (68,6%) – genotype 2 or 3 (HCV-2/3). Of HCV-1 patients 9 (81,8%) had high level of baseline viral load (>10⁵IU/mL) and low level (<10⁵IU/mL) – 2 (8,2%). High viral load at baseline had 9 (37,5%) of HCV-2/3 subjects and low level – 15 (62,5%). High baseline ALT level (>2 ULN) had 10 (90,9%) of HCV-2/3 subjects and no one of HCV-1 patients and no one of HCV-2/3 subjects had high level of ALT. Seventeen (48.6%) achieved SVR and 18 (51.4%) failed to achieve SVR. Among genotype 1 subjects achievement of SVR was detected in 5 (45,5%) children and genotype 2/3 – 12 (50%). HCV treatment started in term 24-36 weeks after end of cancer therapy associated with 40% SVR achievement, if started >36 weeks – 50% SVR.

Conclusions: Our data shows good treatment outcomes for CHC in pediatric cancer patients with an SVR rate of 48.6%. No significant differences of SVR rates between genotype 1 and 2/3 was revealed.

No conflict of interest

Abstract: P_22

Hepatitis B Drug Resistance

Identification of occult hepatitis B virus infection and viral antigens in healthcare workers who presented low to moderate levels of anti-HBV after HBV vaccination

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Introduction: Worldwide, healthcare workers (HCWs) show different levels of response to hepatitis B virus (HBV) vaccine. One of the factors associated with vaccine unresponsiveness may be the existence of current or past HBV infection. Regardless of the presence of hepatitis B surface antigens (HBsAg) (overt infection), occult HBV infection (OBI, defined as presence of HBV DNA in the absence of HBsAg) might also account for some non- or hypo-response cases.

Methods: Sera from 120 HBsAg-negative HCWs with low and moderate levels of anti-HBs, <10 IU/mL (group I) and <100 IU/mL (group II) respectively, were selected and were examined for OBI by sensitive real-time PCR regardless of HBV serological profiles. Direct sequencing on surface genes was carried out in OBI-positive cases.

Results: Four (3.3%) were positive for OBI. All were negative for anti-HBc. Two of the positive cases had moderate levels of anti-HBs (>10 to <100 IU/mL). No significant differences were found between the two groups in terms of risk.
factors or serological data. No mutations were found in surface proteins of OBI cases.

**Conclusion:** OBI in these subjects might be due to other factors rather than presence of ‘a’ determinant mutations. Healthcare workers with inadequate to moderate levels of anti-HBs (<100 IU/mL) following vaccination, regardless of their serological profile for HBV, should be tested for the presence of HBV DNA by sensitive molecular tests. Anti-HBc is not a reliable marker for suspicion of OBI, especially in high-risk group individuals.

No conflict of interest

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**Abstract: P_23**

**Hepatitis B Drug Resistance**

**Interleukin 17 and Interleukin 22 genetic polymorphisms in hepatitis B virus vaccine non- and low-responders among healthcare workers**

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**Introduction:** Healthcare workers constitute a population at high risk for hepatitis b virus (HBV) infection. Efficient vaccination options are available; however, the individual response to HBV vaccination may vary widely between subjects, potentially due to cytokine profiles and genetic variations. In the present study, we investigated the relationship between interleukin (IL) -17 and IL-22 gene polymorphisms versus non- and low-responsiveness to HBV vaccination in healthcare workers.

**Methods:** We selected the following IL-17 and IL-22 polymorphisms: rs4711998 (A/G) from IL-17 and rs2227501 (A/T), rs2227503 (A/G), rs1026786 (A/G) from IL-22 sequences genes. These were determined by polymerase chain reaction restriction fragment length polymorphisms.

**Results:** The IL-17 rs4711998 GG genotype had a significantly lower frequency in non-responders compared to low-responders (p=0.025). However, we did not identify a relationship between IL-22 rs1026780, rs2227501 and rs2227503 genotypes and the anti-HBs response following HBV vaccination.

**Conclusion:** These data suggest that genetic variation in rs4711998 polymorphisms in the IL-17 cytokine may influence vaccine-induced immune responses to HBV vaccine in healthcare workers.

No conflict of interest

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**Abstract: P_24**

**Treatment Issues - Hepatitis _ HIV coinfection**

**Quality of Life of patients living with Human Immunodeficiency Virus Infection – Evidence from South India**

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**Introduction:** With anti-retroviral therapy (ART) for human immunodeficiency virus infection (HIV) coming into picture, quality of life (QOL) has gained importance. Knowledge on the factors affecting QOL would be helpful in making important policy decisions and health care interventions.

**Aims:** The aim of this study is to assess the quality of life of people living with HIV (PLWH) and to identify the factors influencing their QOL.

**Materials and Methods:** The study was done among 100 PLWH attending a tertiary care hospital, and three Non-Governmental Organizations at Calicut, Kerala, India, from June 2011 to May 2014. QOL was assessed using HIV specific World Health Organization Quality Of Life scale (WHOQOL-HIV) – BREF questionnaire which has six domains (physical, psychological, level of independence, social...
Abstract

Relatives, environment and spirituality/religiousness/personal belief. Social support and stigma were measured using 'Multidimensional Scale of Perceived Social Support' and 'HIV Stigma Scale,' respectively, using Likert Scale. Factors influencing QOL were identified using backward stepwise multiple linear regression with the six domain scores as the dependent variables.

Results: Male: Female ratio was 1:1 and 58% were in early stage of the disease (stage I/II). Psychological and SRPB (Spirituality Religiousness and Personal Beliefs) domains were the most affected domains. All the regression models were statistically significant \((P<0.05)\). The determination coefficient was highest for the social relationship domain (57%) followed by the psychological domain (51%). Disease stage and perceived social support significantly influenced all the domains of WHOQOL. Younger age, female gender, rural background, shorter duration of HIV, non-intake of ART and greater HIV related stigma were the high risk factors of poor QOL.

Conclusion: Interventions such as ART, family, vocational and peer counselling would address these modifiable factors influencing QOL, thereby improving the QOL of PLWH.

No conflict of interest

Abstract: P_25

Treatment Issues - Hepatitis - HIV coinfection

HBV and HCV co-infection in HIV infected patients attending a tertiary hospital

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Introduction: Co-infection with hepatitis B virus (HBV) and hepatitis C virus (HCV) in human immunodeficiency virus (HIV) infected individuals results in increased hepatic complications. We undertook this study to evaluate the presence of HBV and HCV in HIV infected individuals attending a tertiary hospital.

Material and Methods: A total of 100 cases with HIV infection and 100 healthy adult control subjects were included in the study. Samples were tested for hepatitis B surface antigen (HBsAg) and anti-HCV antibodies by enzyme linked immunosorbent assay (ELISA) method. HBsAg and anti-HCV positive serum samples were further tested for the presence of hepatitis B e antigen (HBeAg), anti-HBe antibodies, HBV-DNA and HCV-RNA.

Results: The most common mode of transmission was sexual promiscuity (79%), followed by spouse positivity (15%) and history of blood transfusion (6%). Among HIV infected patients, presence of HBeAg and anti-HBe antibodies was seen in 33.3 and 55.5 per cent, respectively; both HBeAg and anti-HBe antibodies were negative in 11.1 per cent. HBV DNA and HCV RNA were positive in 10 of 15 and in all anti-HCV positive samples. Triple infection with HBV, HCV and HIV was seen in five patients. CD4+ T-lymphocyte count less than 200/\(\mu l\) was seen in 11 of 24 co-infected cases.

Conclusion: The findings of our study showed presence of HBV (15%) and HCV (8.3%) co-infections in HIV positive patients which was higher than that seen in HIV negative controls. Co-infection with HBV and HCV is a common problem in HIV infected patients in India. Hence, all HIV patients need to be routinely tested for markers of HBV and HCV infection.

No conflict of interest
Abstract: P_26

Treatment Issues - Hepatitis _ HIV coinfection

Therapeutic aspect of HIV/primary liver tropism viruses co-infection-analysis of supervised cases in Iasi regional centre (poster presentation)

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Background: The infection with primary liver tropism viruses is a reality in HIV-infected patients; Due to the antiretroviral therapy which can slow down the progression of liver disease by maintaining or restoring immune function and decrease the viremia of the hepatitis virus involved, it is vital achieving a screening test on liver function and markers of hepatitis virus infection in HIV-infected patients.

Objectives: achieving a study considering the medical charts of HIV-infected from the North-Eastern part of Romania, in order to reveal the therapy for HIV-infected patients which are co-infected with primary liver hepatic tropism viruses.

Materials and methods: we assayed the HIV-infected patients charts database from the region of Moldova and we extracted the co-infected cases with primary liver tropism viruses.

Results: in Iasi Regional Centre, we are actively tracking 1,444 HIV-infected patients, of which 296 are co-infected patients with primary liver tropism viruses, which represents 20.5% of all HIV-infected patients. 275 patients have hepatitis B infection, accounting for 92.9%, 16 patients have hepatitis C infection, accounting for 5.4%, and a small sample of patients was diagnosed with hepatitis B + C infection-4 cases (1, 35%) and, finally, 1 case of B + C + D virus infection (0.33%). Of these, 55.74% are males, 44.25% females, and the majority come from the rural areas. The counties distribution shows the highest percentage is found in Neamt county. For infected and co-infected HIV patients with hepatitis viruses, the therapy was carried out from the beginning with products containing Lamivudine in all schemes, namely ABC + 3TC / AZT + 3TC. Currently, about 12% of these patients are receiving Raltegravir and none of the patients are receiving Tenofovir / free Interferon / pegylated Interferon. Patients received all the support from the medical team, doctors, nurses, social worker and psychologist, through psychotherapy sessions.

Conclusions: In the North-Eastern part of Romania there is a relatively high incidence of co-infection with primary liver tropism viruses, representing 20.5% of all HIV-infected patients. This requires a careful evaluation of the liver function and treatment options oriented towards molecules which have activity against the hepatic viruses.

No conflict of interest

Abstract: P_27

Treatment Issues - Hepatitis _ HIV coinfection

Influence of L-arginine Additory Use on Endothelium Functional State in Patients with Chronic Hepatitis with Mixed Cryoglobulinemia

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Introduction: The peculiarity of the chronic hepatitis C (CHC) is a frequent formation of extrahepatic manifestations. The role of the virus as an etiologic causative agent is proved in the development of mixed cryoglobulinemia, in the presence of which fixation on the minute vessels of the immune complexes takes place. The main component in this case is cryoglobulin, which provides conditions for
endothelium dysfunction formation. In the pathogenetic treatment of the patients with HCV-associated mixed cryoglobulinemia there are no consistent approaches, in addition endothelium function state is ignored in current methods of treatment.

Material and methods: 67 patients with CHC with mixed cryoglobulinemia were observed. Depending on performed pathogenetic treatment patients were divided into groups: the I group – 30 patients, who were treated with L-arginine in addition to the basic treatment; the II group – 37 patients, who were treated only with the basic methods. Patients were included to the study process by random selection.

For the evaluation of endothelium function, identification of endothelium-depend vasodilatation of brachial artery (ultrasonic examination), quantitative content of nitrites in blood serum (spectrophotometric method), endothelin-1 (immunoenzymometric analysis), L-arginine (chromatographic method) was conducted.

Results: During the course of treatment in the patients from the I group the decrease of astenovegetativ signs, which were noted in 76,7% patients before the treatment, was distinguished, and at the time of the end of therapy – in 40,0% patients (?<0,01); along with the frequency of arthralgic syndrome reduction almost in 2 times (?<0,05). In the patients from the I group duration decrease (?<0,05) of haemorrhagic cryobulinemic vasculitis skin manifestations was noted till (8,3±1,5) days versus (12,8±1,6) days in the patients from the II group. Regress of clinical implications of mixed cryoglobulinemia in patients from the I group took place during the reduce (?=0,002) of mixed cryoglobulins quantitative content, in contrast to the II group (?>0,05). Pathogenetic treatment patients of the I group caused 38,2% (?=0,04) increase of quantity content of nitrites in blood serum, 37,9% (?=0,02) decrease of endothelin-1 amount, and also the increase of reactive hyperemia rate in 2,8 times (?=0,04). Using only standard pathogenetic treatment, aforementioned parameters in patients with CHC with mixed cryoglobulinemia did not demonstrate statistically significant changes (?>0,05). It should be emphasized that rates improvement of endothelium-depend function of endothelium took place under the conditions when patients’ blood serum was oxygenated with L-arginine, the amount of which was increasing (?=0,009) only in case of proper treatment in patients from the I group.

In patients from the I group, after treatment, the activity of alanineaminotransferase in the blood serum decreased by 43,5% (?<0,05).

Conclusions: Usage of L-arginine during the basic pathogenetic treatment of patients with CHC with mixed cryoglobulinemia assists endothelium functional recovery, duration decrease of haemorrhagic cryobulinemic vasculitis skin manifestations, occurrence reduce of astenovegetativ and arthralgic symptoms, duration decrease activity of alanineaminotransferase.

No conflict of interest

Abstract: P_28

Treatment Issues - Hepatitis _ HIV coinfection

Adverse effects of antituberculous and antiretroviral therapy in patients with co-infection of HIV, tuberculosis and chronic hepatitis C

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Introduction: According to the literature data 40-65% of HIV-positive people suffer from active pulmonary and extrapulmonary tuberculosis (TB), which remains the cause of death in the majority of patients with HIV. Antituberculous treatment requires a large number of hepatotoxic drugs. Its efficiency and tolerability is significantly worse in the case of co-infection with chronic viral hepatitis C, that accompanies HIV/TB-coinfection in 43-51% of cases.

Objectives: to study the frequency of adverse reactions of antituberculous therapy in patients coinfected with HIV, tuberculosis and hepatitis C virus (HCV) depending on the use of antiretroviral therapy (ART).
**Material & Methods:** The study included 68 patients co-infected with HIV, tuberculosis and chronic hepatitis C: 50 (73.5%) males and 18 (26.5%) females with average age 36.5±3.8 years. All patients underwent complex laboratory and instrumental studies that included: complete blood count, urinalysis, blood chemistry (alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), gammaglutamatintranspeptidase (GGTP), bilirubin, total protein), ultrasound of the abdomen, X-ray or computer tomography (CT) scan of the chest. Enzyme-linked immunosorbent assay (ELISA) and polymerase chain reaction (PCR) were used in diagnosis of HIV and HCV infection. Diagnosis of pulmonary and extra-pulmonary TB included medical history, clinical data, results of X-ray or CT scan of the chest, ultrasound and CT of the abdomen, pleural sinuses, laboratory tests (sputum smear microscopy, sputum culture for M. tuberculosis), study of cerebrospinal fluid, histological examination of biopsy lymph nodes.

**Results:** All patients were divided into 2 groups. The main group consisted of 35 patients who started antiretroviral therapy (ART) during the maintenance phase of antimycobacterial therapy. 33 patients of control group underwent TB treatment only. During the treatment in patients of both groups the development of side effects of anti-TB drugs was observed, such as dyspeptic disorders (anorexia, nausea), jaundice and biochemical signs of acute inflammation in the liver (increased activity of ALT and AST, alkaline phosphatase, GGTP, bilirubin). Adverse events occurred in 20 patients (57.1%) of the main group and in 17 patients (51.5%) of the control group, but significant difference in the frequency of adverse reactions wasn’t found (p>0.05). Side effects did not require discontinuation of therapy.

**Conclusion:** In the treatment of tuberculosis in patients coinfected with HIV, tuberculosis and chronic hepatitis C adverse reactions to TB drugs are observed with high frequency (51.5%), primarily due to their hepatotoxic effects, that leads to clinical and laboratory exacerbations of chronic hepatitis C. ART appointment after the intensive phase of tuberculostatic treatment slightly increased the frequency of adverse reactions (57.1%), that does not require therapy discontinuation.

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**Abstract:** P_29

**Treatment Issues - Hepatitis _ HIV coinfecion**

**Peer Support Intervention for increasing effectiveness of Georgian HCV Elimination Program**

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**Objective:** HCV prevalence among PWIDs (49,700) in Georgia is the highest compared to other key affected populations and varies between 50-92% according to different sources of data. For many years, access to hepatitis C treatment in Georgia was restricted because of the high cost of treatment. Since 2015 the government of Georgia started the HCV elimination program which aims to reduce HCV-related morbidity, mortality and prevalence in the country. However, criminalization and systematic discrimination, health authorities’ and providers’ concerns regarding their adherence to treatment and risk of reinfection, and non-supportive national policies represent the main obstacles to HCV treatment for PWIDs in the framework of the program. The study (implemented collaboratively by New Vector and Medicines du Monde France) aims to improve the uptake, linkage to and retention in HCV treatment as well as to improve behaviors to lower risk of reinfection after treatment.

**Methods:** a special care model based on peer-support intervention has been developed to facilitate access and retention of PWIDs in the National HCV treatment program, and to prevent reinfection after treatment. A research part of the project assesses the effectiveness of the intervention in terms of improving durably the behaviors at risk of reinfection among PWIDs.

**Results:** Overall, 244 New Vector beneficiaries were involved in the program. 229 have already finished their treatment, 158 already received SVR158, out of which 15 could be considered to have relapses while 143 have got positive SVR 12 results. The PWIDs adherence in the treatment was very
high: 95% of those screened, involved in the program. In terms of retention, 90% did not miss any doses and 83% did not miss any appointments with a doctor. Assessment of their risky behavior showed that, using each other's needles and syringes decreased considerably. However, problems remain with sharing container and paraphernalia during group injection as well as wiping and being assisted during injections.

Conclusion: The analysis showed, the peer-based intervention provides very positive results in assisting HCV infected PWIDs to improves their adherence and retention in the HCV treatment, while HCV related counseling helps them to acquire necessary knowledge for safer injection. However, other problematic issues in terms of shared paraphernalia still remains. Further research and interventions are needed for the development of new strategy that will reduce risky injecting practice among PWIDs in Georgia in order to avoid reinfection.

No conflict of interest

Abstract: P_30

Treatment Issues - Hepatitis _ HIV coinfection

HCV-infected people who inject drugs (PWID): engagement in care and treatment, and prevention of reinfection

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Background: People who inject drugs (PWID) are disproportionately represented within the HCV-infected population of Canada. Unsafe injection practices and sharing of paraphernalia favor viral infection and increase the risk of recurrent viremia after successful HCV therapy. Engagement of this vulnerable population within a multidisciplinary care program with enhanced long-term follow-up post-cure of HCV (achievement of a sustained virologic response, or SVR) is critical to reducing the prevalence and incidence of HCV infection in the population. This study seeks to assess the efficacy of such a model in clinical practice.

Methods: An observational, retrospective cohort study was conducted among HCV-infected patients (mostly current or recent PWID) attending a tertiary clinic in Downtown Vancouver, Canada. HCV treatment was offered to all who qualified for it on medical grounds. This analysis attempts to elucidate the efficacy of all-oral (vs. older) regimens and rates of recurrent viremia in high risk populations. All individuals had access to multidisciplinary care to address medical, psychiatric, addiction-related, and social needs prior to, during and after HCV therapy, with maintenance in long-term follow-up at our centre. Endpoints were achievement of SVR and occurrence of recurrent viremia, based on systematic twice yearly evaluation post-SVR.
Results: Among 339 HCV-infected PWID, 95 actively injected drugs during HCV treatment, and 42 received all-oral HCV regimens. Key demographics included: mean age 53 years, 85% male, 60% genotype 1, 57% HIV co-infected, 22% cirrhotic, 83% treatment-naïve, 63%/70% using heroin/stimulants, 58% on opiate substitution therapy. In the general PWID population, the SVR rate was 78%, 74% among active/recent PWID, 86% among those receiving all-oral regimens. With a mean follow-up period of 5.5 years, there were 5 cases of recurrent viremia, all in the active PWID cohort, giving a rate of 12.9 cases/1000 person years of follow-up (95% CI, 0.031 - 0.157%) within that group. No individuals that experienced recurrent viremia were on all-oral HCV treatment regimens. Among the five cases of recurrent viremia, we note: mean age 52 years, 100% male, 80% genotype 1, 60% cirrhotic, 100% HIV co-infected, 100%/80% using amphetamines/heroin.

Conclusion: A multidisciplinary care model addressing medical, psychiatric, addiction-related, and social needs allows for high rates of HCV treatment and cure in a vulnerable PWID population, and rates of recurrent viremia post-SVR 66% lower than reported in recent meta-analysis of this issue. Highly effective all-oral regimens paired with a model of care such as ours will be a powerful tool in the control of the HCV epidemic, expanding HCV treatment programs among PWID by promoting engagement in care and minimizing the risk of post-treatment reinfection.

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