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Hepatitis C: Clinical aspects and therapy

OS001

Results of a ten year prospective observational study on acute hepatitis C in HCV-mono- and HIV/HCV-coinfected patients

Christiana Graf[1], Lara Fuhrmann[2,3], Lutz Thomas[4], Christoph Stephan[5], Gaby Knecht[4], Peter Gute[4], Markus Bickel[4], Kai-Henrik Peiffer[1], Fabian Finkelmeier[1], Georg Dultz[1], Nils Wetzstein[5], Natalie Filmann[6], Eva Herrmann[6], Stefan Zeuzem[1], Niko Beerenwinkel[2,3], Julia Dietz[1], Christoph Sarrazin[1,7]. *[1]Goethe University Hospital Frankfurt, Department of Internal Medicine I, Frankfurt, Germany; [2]ETH Zurich, Department of Biosystems Science and Engineering, Basel, Switzerland; [3]SIB Swiss Institute of Bioinformatics, Basel, Switzerland; [4]Infektiologikum, Frankfurt, Germany; [5]Goethe University Hospital, Department of Infectious Diseases, Frankfurt, Germany; [6]Goethe University Frankfurt, Institute of Biostatistics and Mathematical Modeling, Frankfurt, Germany; [7]St. Josefs-Hospital, Medizinische Klinik II, Wiesbaden, Germany*
Email: christiana.graf@kgu.de

Background and aims: Over the last two decades, a persistent epidemic of acute Hepatitis C virus (HCV) infections has been observed in HIV-positive men who have sex with men (MSM) in several metropolitan areas worldwide. In this study, epidemiological and clinical parameters as well as phylogenetic analyses were conducted to characterize HCV transmission among MSM.
Method: This prospective observational study analysed clinical and epidemiological parameters of patients with confirmed acute HCV infection between 2009 and 2019 from 3 centers in Frankfurt. NS5B population-based sequencing was performed at the time of diagnosis to determine HCV genotype (GT) and for phylogenetic analyses.
Results: A total of n = 161 patients diagnosed with acute HCV-infection were included in the study, of whom n = 140 (87%) were HIV-positive and n = 145 (90%) were MSM. We observed a different distribution of HCV genotypes over time. In the first eight years, HCV GT1a was most common (58–100%) but decreased to 30% in 2018. In contrast, the proportion of GT4d cases increased. While no GT4d cases were diagnosed in 2013, the proportion rose to 40% in 2019. There was a slight trend towards more GT3a cases in 2018 and 2019, while for GT1b and GT2 only individual cases were detected between 2009 and 2014. MSM were mainly infected with HCV GT1a (82%, 115/140) or GT4d (16%, 23/140 with sequencing data available). In contrast, HCV GT were almost equally distributed in non-MSM patients. Here, 36% were infected with HCV GT1a, 21% each with GT1b or GT3a and 16% had GT2. Phylogenetic analyses in NS5B showed a diverse sequence pattern in patients with HCV GT1b and GT3a. In contrast, HCV strains among MSM infected with HCV GT1a and 4d were more closely related. Based on the comparison of HCV GT or NS5B sequences, 24 patients (15%) were diagnosed with an HCV reinfection. The incidence rate in MSM for a first HCV infection declined in the period between 2017 and 2019 (3.6/1000PY) compared to the DAA era between 2013 and 2017 (6.8/1000 PY) and to the interferon era (2008–2013; 10.1/1000 PY). Conversely, the incidence of HCV reinfections among MSM increased slightly from 1.9/100PY to 2.8/100PY over time.
Conclusion: During the last 5 study years the prevalence of GT4 infections increased, while annual acute hepatitis C incidences decreased. HCV reinfection is an issue of major concern in HIV-positive MSM and may have implications for HCV elimination.

OS002

Multicenter prospective study for the use of shortened pre-emptive therapy with Glecaprevir/Pibrentasvir (G/P) and Ezetimibe in hepatitis C (HCV) seronegative non-liver solid organ transplant recipients of HCV viremic grafts

Bashar Aqel[1], Surakit Pungpapong[2], Adyr Moss[1], Rolland Dickson[1]. *[1]Mayo Clinic, Gastroenterology, Hepatology and Liver Transplant, Phoenix, United States; [2]Mayo Clinic, Jacksonville, United States*
Email: aqel.bashar@mayo.edu

Background and aims: Use of HCV viremic grafts has been associated with reduced waiting time and cost effectiveness analyses has been favorable. Preemptive treatment approach prevent delay in treatment initiation and will help eliminate risks of untreated HCV viremia. G/P is a highly effective direct acting antiviral agents with pangenotypic coverage and ezetimibe was found to help blocking the cholesterol receptor used by the HCV virus for cell entry.
Assess the efficacy and cost effectiveness of preemptive therapy with eight days of a combination of G/P and ezetimibe in recipients of non-liver HCV viremic solid organ transplant.
Method: This is a multicenter prospective, open label, internally funded study. Solid organ recipients who agreed to accept HCV viremic grafts were consented for the study. HCV pre-emptive therapy with G/P and ezetimibe was initiated upon call to the

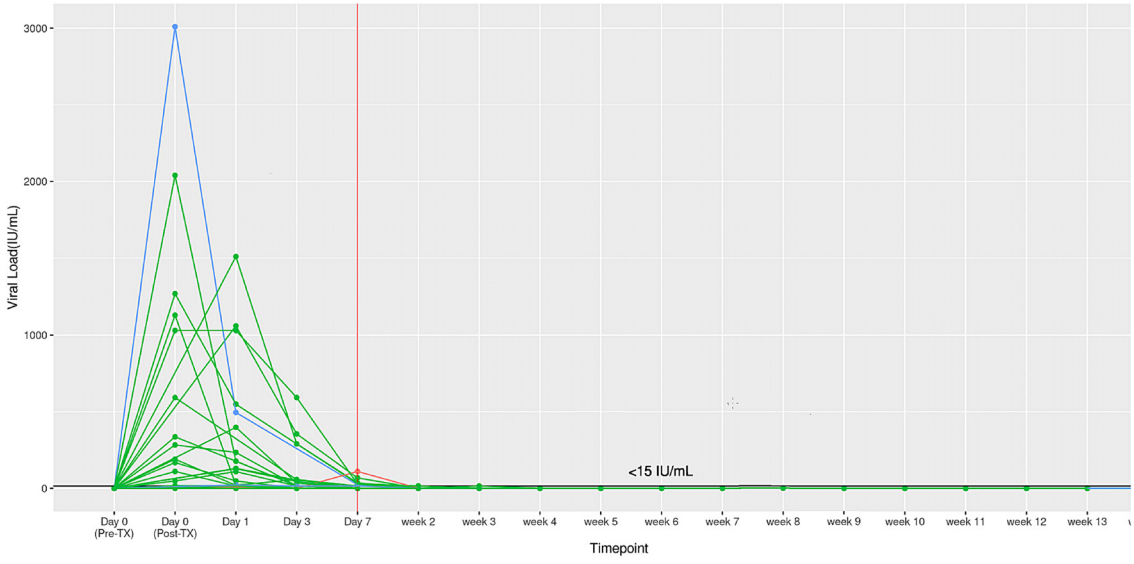

Figure: (abstract: OS002)

operative room. Combination therapy was continued for 7 days after transplant (total of 8 doses). HCV RNA was monitored up to 24 weeks post-transplant, and patients followed for 1 year to determine graft and patient survivals.
Results: 38 patients (32 kidney tx, 2 kidney/pancreas tx, 3 heart tx, 1 heart/kidney tx) have been enrolled to date. All patients completed treatment. Median age for patients was 60 years and 63% were males. Median time from list for HCV viremic grafts to tx was 32, 52, 71, and 151 days for heart, heart/kidney, kidney, and kidney/pancreas tx recipients respectively. Median donor age was 35 years. All donors had confirmed viremia. Transient viremia during the first 2 weeks post tx was detected in 28/38 (74%) patients (HCV RNA range 16–6870 IU/ml), and 12 patients had detectable viremia on post tx day 7 when treatment was completed (HCV RNA range of detectable but not measurable RNA-110 IU/ml). Four (4/38) patients continued to have detectable HCV RNA at week 2 post tx, and one of those patients remained detectable week 3 post tx. All patients achieved undetectable HCV RNA by week 4 post tx and all patients stayed negative 13 weeks post tx (SVR 12 of 100%) (Fig. 1). The cost of this preemptive approach was significantly lower when compared to the standard of care reactive treatment approach. Treatment was well tolerated, and all patients completed 8 days of combination therapy. One kidney transplant recipient died 65 days post-tx with acute subdural hematoma. This patient completed treatment per protocol and achieved viral clearance (undetectable HCV RNA at post tx week 8).
Conclusion: In the largest multicenter U.S. experience to date, G/P combined with ezetimibe was highly effective in preventing HCV infection in 100% of non-liver solid organ transplant recipients of HCV viremic grafts. Short-term graft and patient survivals are excellent. This approach appears to be cost effective and will potentially eliminate the risk of post-transplant complications from HCV transmission and enhance the use of HCV viremic grafts.

OS003
Effectiveness of voxilaprevir/velpatasvir/sofosbuvir in hepatitis C patients previously treated with direct-acting antiviral agents (DAA)

Christiana Graf[1], Julia Dietz[1], Beat Müllhaupt[2], Peter Buggisch[3], Jörn Schattenberg[4], Christoph Antoni[5], Stefan Mauss[6], Elena Durmashkina[7], Claus Niederau[8], Thomas Discher[9], Julian Schulze zur Wiesch[10], Tobias Müller[11], Thomas Berg[12], Christoph Neumann-Haefelin[13], Christoph Berg[14], Stefan Zeuzem[1], Christoph Sarrazin[1,7]. *[1]Goethe University Hospital, Department of Internal Medicine I, Frankfurt am Main, Germany; [2]University Hospital Zürich, Swiss-Hepato-Pancreato-Biliary Center and Department of Gastroenterology and Hepatology, Zürich, Switzerland; [3]Institute of Interdisziplinary Medicine IFI, Hamburg, Germany; [4]University Medical Center Mainz, I. Department of Medicine, Mainz, Germany; [5]University Hospital Mannheim, Department of Internal Medicine II, Mannheim, Germany; [6]Center of HIV and Hepatogastroenterology, Düsseldorf, Germany; [7]St. Josefs-Hospital, Wiesbaden, Germany; [8]St. Josefs-Hospital, Katholisches Klinikum Oberhausen, Oberhausen, Germany; [9]Justus Liebig University Gießen, Department of Medicine, Gießen, Germany; [10]University Medical Center Hamburg-Eppendorf, I. Department of Medicine, Infectious Disease Unit, Hamburg, Germany; [11]Charité Universitätsmedizin Berlin, Department of Hepatology and Gastroenterology, Berlin, Germany; [12]University Hospital Leipzig, Department of Gastroenterology and Rheumatology, Leipzig, Germany; [13]University Hospital Freiburg, Department of Medicine II, Freiburg, Germany; [14]University Hospital Tübingen, Department of Gastroenterology, Hepatology and Infectiology, Tübingen, Germany*
Email: christiana.graf@kgu.de

Background and aims: Voxilaprevir/velpatasvir/sofosbuvir (VOX/VEL/SOF) is approved for HCV retreatment of direct-acting antiviral agents (DAA)-experienced patients. However, real-life data are still limited. The aim of the study was to analyse the effectiveness of VOX/VEL/SOF in a real-world setting.
Method: All consecutive patients with HCV retreated with VOX/VEL/SOF after DAA failure were enrolled in 153 centers in Germany, Austria, Switzerland and Belgium between May 2015 and November 2020. Sustained virological response (SVR) was defined as undetectable HCV RNA 4 (SVR 4) or 12 (SVR12) weeks after the end-of-treatment.
Results: A total of 416 patients were included: median age was 55 (21–84) years, 79% were male, median HCV RNA was 383, 000 (10–58, 300, 000) IU/ml. HCV genotype (GT) was 1 in 54% (1a in 26%, 1b in 28%), 2 in 1%, 3 in 39% and 4 in 6%. Patients received VOX/VEL/SOF for 12 weeks, ribavirin was added in 4% of treatment schedules. Overall, 365/416 (87.7%) patients by intention to treat analysis and 401/416 (96.4%) by per protocol analysis achieved SVR12, respectively. Genotype 3a ($p = 0.008$) and hepatocellular carcinoma ($p = 0.0034$) were the only predictors of a treatment failure. Treatment effectiveness was not significantly affected by the type of previous DAA regimen, by liver cirrhosis, HCV GT 1a and baseline HCV-RNA viral load. Virologic relapse was observed in 20 patients (10% GT1a, 15% GT1b, 75% in GT3a). The presence of resistance-associated substitutions within NS3, NS5A, and NS5B genes did not impact SVR12 ($p = 0.06$).
Conclusion: VOX/VEL/SOF is an effective retreatment for patients with HCV who have failed on a previous DAA course in a real-life setting. We identified HCV GT 3a and HCC as the main predictors of VOX/VEL/SOF failure.

OS004
Glecaprevir/pibrentasvir and sofosbuvir for 16 weeks without ribavirin is safe and highly effective retreatment for patients who have failed an NS5A inhibitor containing antiviral regimen

Edward J. Gane[1], Bridget Faire[2], Sherine Helmy[3], James Freeman[4]. *[1]University of Auckland, Grafton Campus, Liver Unit, Auckland, New Zealand; [2]New Zealand Liver Transplant Unit-Ward 71, Auckland, New Zealand; [3]Pharco Corporation, Cairo, Egypt; [4]GP2U, Australia*
Email: edgane@adhb.govt.nz

Background and aims: Oral DAA therapy has been available in New Zealand since mid-2016 for treatment of chronic hepatitis C. Over the last 5 years, more than 10,000 New Zealanders have been treated with NS5A inhibitor- based DAA therapy, of whom more than 300 have had virologic failure. Retreatment of patients with confirmed antiviral resistance requires a triple DAA combination of a polymerase, a protease and an NS5A inhibitor.
Method: In an open-labelled, ethics-approved study, 100 New Zealanders who had failed DAA therapy with confirmed NS5A resistance will be retreated with glecaprevir/pibrentasvir (GLE/PIB) from Feb 2019) plus sofosbuvir for 16 weeks. Patients with decompensated cirrhosis or hepatocellular carcinoma or post-transplant are excluded.
Results: To-date, 57 patients have been enrolled in the study. Median age was 56 years (38–80), 78% were male and 44% had established cirrhosis. Thirty-five patients had previously failed GLE/PIB, 19 failed ombitasvir, paritaprevir, dasabuvir, and ritonavir (PrOD) and 1 each failed grazoprevir/elbasvir (GRZ/ELB), ledipasvir/sofosbuvir (LDV/SOF) and sofosbuvir/velpatasvir (SOF/VEL). Six patients had failed multiple regimens. Most frequently detected NS5A resistance-associated substitutions (RASs) were Y93H (57%), A30 K (26%), Q30 K/H (26%, M28 T/F/V (11%). Multiple NS5A RASs were detected in 39% patients. Resistance profiles were similar in PrOD and GLE/PIB failures.
One patient died from opioid overdose during treatment. There were no other SAEs or AE-related treatment discontinuations. Two other patients stopped treatment within 4 weeks because of psychosocial issues, one of whom has started retreatment.
45 patients have completed therapy and 37 have reached the SVR12 timepoint, of whom 36 (98%) are cured (complete SVR results will be available in early 2022). The only treatment failure to-date was a 53-year-old noncirrhotic female, previously treated with PrOD.