Clinical Outcomes in Persons Coinfected with HIV and HCV: Impact of HCV Treatment

L Peters¹, J Lundgren¹, J Rockstroh², J Gerstoft³, LD Rasmussen⁴, S Bhagani⁵, I Aho⁶, C Pradier⁷, J Bogner⁸, C Mussini⁹, A Castagna¹⁰, F Maltez¹¹, M Laguno¹², G Wandeler¹³, K Falconer¹⁴, T Trofimora¹⁵, E Borodulina¹⁶, D Jeytovic¹⁷, E Bakowska¹⁸, K Kase¹⁹, G Kyselyova²⁰, A Mocroft²¹ on behalf of the EuroSIDA Study

¹CHIP, Rigshospitalet, Copenhagen, Denmark. ²University of Bonn, Bonn, Germany. ³Rigshospitalet, Copenhagen, Denmark. ⁴Odense University Hospital, London, UK. ⁶Helsinki University Hospital, Helsinki, Finland. ⁷Centre Hospitalier Universitaire de Nice, Nice, France. ⁸Ludwig Maximilians University of Modena and Reggio Emilia, Modena, Italy. ¹⁰San Raffaele Scientific Institute, Milano, Italy. ¹¹Hospital de Curry Cabral, Lisbon, Portugal. ¹²Hospital Clinic, Barcelona, Spain. ¹³Bern University Hospital, Bern, Switzerland. ¹⁴Karolinska University Hospital, Stockholm, Sweden. ¹⁵Novgorod Centre for AIDS prevention and control, Novgorot the Great, Russia. ¹⁵Samara State Medical University, Samara, Russia. ¹⁵Horelous & Troical Diseases Hospital, Bellogical Diseases Hospital, Bellogical Spain. ²⁵Crimeael, Talkin, Estonia. ²⁵Crimeael, T

INTRODUCTION

- Chronic HCV infection causes hepatic and systemic inflammation which can lead to fibrosis and liver disease, but could potentially also have detrimental effect on extrahepatic organs¹.
- In contrast, chronic HCV infection is associated with lower levels of LDL cholesterol and levels have been shown to increase after HCV cure².
- Whereas HCV cure has been shown to reduce the risk of liver-related outcomes in HIV/HCV coinfected persons, there are few data on its impact on extra-hepatic clinical endpoints.

AIMS

 To investigate the impact of HCV coinfection and HCV treatment outcome on risk of cardiovascular disease (CVD), non-AIDS defining malignancies (NAMD) and end-stage liver disease (ESLD) in HIV-1 infected individuals.

METHODS

 Persons from the pan-European HIV cohort study EuroSIDA with known anti-HCV and HCV-RNA status after January 2001 were included and were divided into five groups based on time-updated HCV-RNA and HCV treatment status:

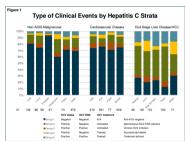
Group	Anti-HCV	HCV RNA	HCV treatment	HCV Group
1	Negative	Negative	N/A	Anti-HCV negative
2	Positive	Negative	Untreated	Spontaneous HCV-RNA clearers
3	Positive	Positive	Untreated	Chronic HCV infection
4	Positive	Negative	Treated	Successfully treated
5	Positive	Positive	Treated	Treatment failure

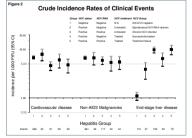
 Separate analyses were performed for three clinical events; ESLD (including hepatocellular carcinoma [HCC]), NADM (excluding HCC) and CVD (myocardial infarction, stroke, angioplasty, coronary bypass, carotid endarterectomy). Poisson regression was used to compare incidence rates between HCV groups.

RESULTS

- Of 22,826 persons enrolled in EuroSIDA, 18,736 persons had known anti-HCV and HCV-RNA status, and were eligible for inclusion into this analysis. The largest group was those anti-HCV negative (n=10433, 62.0%).
- Overall, most were male (74%), of white ethnic origin (85.2%), ever exposed to antiretroviral therapy (83.9%) and current smokers (54.3%) with a median age of 41 (interquartile range [IQR] 35 49) and CD4 cell count of 438 (IQR 281 630 cells/µl) but as expected, there was considerable heterogeneity between the 5 groups at baseline (Table).







RESULTS (CONTINUED)

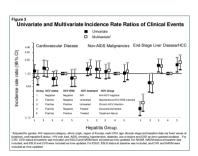
- During a median follow-up of 8.3 (IQR 3.1 13.7) years, there was a total of 887 CVD, 902 NADM and 436 ESLD events. Figure 1 shows a breakdown of the clinical events within each of these event categories. The crude incidence of NADM, ESLD and CVD are shown in Figure 2.
- Figure 3 shows the univariate and adjusted rate ratios of CVD, NADM and ESLD, using those who were successfully treated for HCV (group 4) as the reference group. Persons with chronic infection (group 3; adjusted incidence rate ratio [aIRR] 1.47; 95% CI 1.02 2.13; p=0.041) or treatment failure (group 5; aIRR 1.80; 95% CI 1.22 2.66; p=0.0033) had significantly increased incidence rates of ESLD compared to those successfully treated (group 4). Spontaneous clearers also had marginally significantly lower incidence rates of ESLD compared to those successfully treated (group 3; aIRR 0.61; 95% CI 0.36 1.02; p=0.058).
- There were no statistically significant differences in incidence of CVD or NADM across the five groups. There was also no evidence that the association between HCV strata and each of the clinical events differed according to age (above or below 50, all p-interaction >0.15).
- In sensitivity analyses there were no differences between the 5 groups and CVD and NADM when excluding persons from Central East and Eastern Europe who tend to be younger and therefore have been infected with HCV for a shorter period of time.
- Analysing myocardial infarctions and strokes separately also showed no differences between the HCV groups.

LIMITATIONS

- Measurement of HCV-RNA varies considerably across EuroSIDA countries, which means we
 had to define HCV treatment outcome on HCV-RNA measurements regardless of when they
 were measured after treatment.
- Grouping different types of NADM and CVD events together resulted in increased power, and
 while results were similar for AMI and stroke separately, the study was not sufficiently
 powered to investigate different types of malignancies.

CONCLUSIONS

- We found no evidence of any impact of HCV infection status or HCV treatment on incidence
 of both non-AIDS defining malignancies and cardiovascular disease in HIV coinfected
 persons while successful HCV treatment lowered the incidence of end-stage liver disease
 and hepatocellular carcinoma compared to those chronically infected or those failing HCV
 treatment
- Our results underline the importance of early and effective HCV treatment for reducing liverrelated complications in HIV/HCV infected persons.



REFERENCES

- Naggie et al; Hepatitis C Virus, Inflammation, and Cellular Aging: Turning Back Time. Topics in Antiviral Medicine 2017
- Carrero et al; Eradication of HCV: Effects on Cardiovascular Risk and Preclinical Atherosclerosis; Abstract 631, CROI 2018

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