**INCIDENCE OF EXTRAHEPATIC COMPLICATIONS IN HIV/HCrimoniraces WHO ACHIEVED SVR**

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**SUMMARY**

There is increasing evidence that the achievement of sustained virologic response (SVR) after interferon plus ribavirin treatment reduces the incidence of liver-related events. Data on the effects of SVR on the outcome of extrahepatic complications are scarce. Therefore, we conducted this study to assess the impact of SVR on the incidence of chronic kidney disease (CKD), diabetes mellitus (DM), and cardiovascular disease (CVD) in a cohort of HIV/HCrimoniraces patients.

**Methods**

We analyzed cohorted HIV/HCrimoniraces patients in the MASTER center in order to evaluate the incidence of CKD, DM, and CVD. Only event-free patients with a serum HIV-RNA determination at the baseline were eligible for the study. Patients were divided into groups with: SVR, IFN-εxposed without SVR; INF-free without SVR; DM and both were defined as eGFR and fasting plasma levels ≥60 mL/min/1.73 m² and >106 g/dL in 2 consecutive time points, respectively. All major CVD, including coronary heart disease, cerebrovascular disease, chronic heart failure and peripheral vascular disease were evaluated. Cimrmonitrans was defined by a P<0.05 score >3.25. Kaplan-Meier curves and Cox regression analyses were used.

**Results**

Data of 2227 patients were analyzed (73.0% males; 46.12% IDU; 87.33%, cirrhosis 14.14%). Overall, the incidence of CKD, DM, and CVD and death were 5.14% (95% CI: 4.96-5.32), 6.40% (95% CI: 5.87-6.97), 12.14% (95% CI: 11.59-12.69) per 1000 PYFU, respectively. The Cox regression analysis for treated patients. SVR was not associated with a lower risk of CVD (HR 1.05 (0.95-1.15), DM (HR 0.95 (0.87-1.03)), CVD (HR 0.97 (0.86-1.10)) and death (HR 1.17 (0.97-1.39)) compared to non-SVR. Cimrmonitrans was significantly associated with the risk of CVD (HR 2.21(1.94-2.56)), death (HR 2.44(1.80-3.33), and composite outcome (HR 1.45(1.24-1.70), death (HR 1.48(1.16-1.88), death (HR 1.68(1.31-2.15)).

**Conclusions**

Our results suggest that the achievement of an SVR after anti-HCV treatment in patients coinfected with HIV does not reduce liver-related extrahepatic complications and mortality. However, people with cirrhosis have an increased risk of CKD, DM, and death. Thus, coinfected patients should early be treated to prevent the progression of liver fibrosis.

**INTRODUCTION**

The widespread use of combined antiretroviral therapy (ART) has substantially improved the prognosis of HIV-infected patients. As a consequence of the increase in survival, non-AIDS-related diseases now account for more than 50% of all deaths.

Liver disease is a leading cause of death among persons with HIV infection, especially in the south of Europe, where the prevalence of coinfected patients is high.

The risk for HCV, liver decompensation, and death in patients with liver cirrhosis related to HCrimoniraces is reduced after SVR (sustained virologic response). However, data on the effects of SVR on the outcome of extrahepatic complications are scarce.

Therefore, we conducted this study to assess the impact of SVR on the incidence of chronic kidney disease (CKD), diabetes mellitus (DM), and cardiovascular disease (CVD) in a cohort of HIV/HCrimoniraces patients.

**PATIENTS**

Patients were selected from the Italian MASTER (Management of Standardized Evaluation of Retrospectively HIV Infection) cohort, which is a prospective longitudinal multicentre cohort composed of the general HIV patient population in referral centres throughout Italy. The distinguishing characteristic of this cohort is that data are collected by a common electronic database (CertiCrea™ or HealthMate™) in use in 10 Italian centres for clinical purposes since 1999. The electronic database is implemented to manage everyday activity of the outpatient HIV clinics in each centre. The resulting cohort is, therefore, an open cohort with non-preselected patients, are continuously enrolled. Demographics, medication and disease history are recorded at enrolment and updated on a monthly basis. All event-free (without DM, CKD, and CVD at baseline) coinfected HCV/HCrimoniraces patients were evaluated. Of these, only the patients with a serum HIV-RNA determination at the baseline were eligible for the study. Patients were divided into 4 groups: a) INF-exposed with patients who achieved a SVR; b) INF-exposed without SVR; c) INF-free with patients who did not achieve a SVR; d) INF-free with patients who were uninfected (after the enrolment) patients with HIV/HCrimoniraces positive but positive baseline HIV-RNA.

**DEFINITIONS**

SVR was defined as an undetectable serum HIV-RNA level 24 weeks after discontinuation of therapy. Patients not fulfilling SVR criteria, including those who relapsed after achieving end-of-treatment response, were classified as non-SVR. CKD and DM definition were defined as eGFR and fasting plasma levels ≥60 mL/min/1.73 m² and >106 g/dL in 2 consecutive time points, respectively. All major CVD, including coronary heart disease, cerebrovascular disease, chronic heart failure and peripheral vascular disease were evaluated. Cimrmonitrans was defined by a P<0.05 score >3.25.

**STATISTICAL ANALYSIS**

Descriptive results are presented as medians with interquartile range (IQR) and percentages with 95% confidence intervals (CI). The person-years of follow-up (PYFU) were calculated for each participant as the time from the enrolment data either to the date of death or to 31 December 2012 for those who were still alive. Then, incidence of extrahepatic events and death was expressed per 1000 PYFU. The cumulative risk of events was estimated by the Kaplan-Meier method and the statistical significance of the difference was examined by log-rank test. Cox proportional hazard models were used to explore baseline factors predictive of extrahepatic outcomes. Statistical significance levels were determined by a 2-sided P<0.05.

**RESULTS**

There were 2227 anti-HCV seropositive in this study. Their baseline characteristics are shown in Table 1. In total, 73.01% were male, the median age was 46.6 years (IQR 36.0-56.5), 14.7% had a comorbid 82.8% had prior AIDS-defining conditions, 15.4% had a CD4+ cell count <200/mm³. Overall, the incidence of CKD, DM, and death were 5.14% (95% CI: 3.96-6.57), 6.40% (95% CI: 5.06-7.97), 12.14% (95% CI: 10.46-14.46) per 1000 PYFU, respectively. Kaplan-Meier curves showing the occurrence of extrahepatic events and deaths according to the study-groups are reported in Figure 1. The probability of events according to anti-HCV therapy status are shown in Figures 2. In the Cox regression analysis for treated patients, SVR was not associated with a lower risk of CVD (HR 1.05 (0.95-1.15)), DM (HR 0.95 (0.87-1.03)), and death (HR 1.17 (0.97-1.39)) compared to non-SVR. Cimrmonitrans was significantly associated with the risk of CVD (HR 2.21(1.94-2.56)), death (HR 2.44(1.80-3.33), and composite outcome (HR 1.45(1.24-1.70), death (HR 1.68(1.31-2.15)).

**DISCUSSION**

Our study showed that the achievement of an SVR after anti-HCV treatment in patients coinfected with HIV/HCrimoniraces does not reduce liver-related extrahepatic complications and mortality. However, the results are likely influenced by sample size. Overall, the use of antiviral therapy is associated with significantly lower death rate. Moreover, people with cirrhosis have an increased risk of DM. Our results suggest that HIV-infected patients should early be treated to prevent the progression of liver fibrosis.

**REFERENCES**