Early HIV therapy in HIV–HCV-coinfected individuals appears advisable in order to not only improve HIV outcome but also delay the natural course of liver disease. Indeed, antiretroviral-therapy-induced control of HIV infection with undetectable plasma HIV RNA levels affects HIV–HCV viral interactions and decreases liver inflammation resulting in lower fibrosis progression rates. Although these findings have influenced current revised HIV guidelines, HIV therapy is still started too late in most HCV-coinfected individuals, suggesting that, particularly in special at-risk patient populations, such as intravenous drug users, barriers to treatment uptake are still existing.

As HCV is transmitted with high efficacy via direct blood-to-blood contact, the prevalence of hepatitis C coinfection within different countries, regions and populations is closely related to the prevalence of blood-borne (mainly through intravenous drug use) HIV-infection. Among all HIV-infected patients from Europe, Australia and the US, at least one out of four is infected with concomitant hepatitis C [1,2]. HCV-coinfection rates as high as 70% are observed in Eastern European countries, such as Ukraine and Russia, where intravenous drug use is the main route of HIV transmission [3]. Hepatitis C in HIV-coinfected individuals is characterized by a faster liver fibrosis progression and associated with significant liver-disease-associated morbidity and mortality [4,5]. Indeed large cohort analyses looking at non-AIDS death causes in HIV-infected adults show liver disease to be the main cause of mortality in HIV-coinfected adults from the post-HAART era [6]. Following the observation that liver disease was particularly pronounced in HIV–HCV-coinfected patients with more advanced immunodeficiency, the question arose whether the HIV-therapy-associated increase in CD4+ T-cell counts and prevention of developing more advanced immunodeficiency could ameliorate some of the faster fibrosis progression observed in HIV–HCV-coinfected patients [4]. In 2001 a first biopsy study found slower fibrosis progression in HIV protease-inhibitor-treated patients as well as higher CD4+ T-cell counts, suggesting an added benefit from more potent antiviral therapy [7]. Subsequently, various cohort studies demonstrated that with the introduction of HAART, not only was a great decline in HIV-associated morbidity and mortality achievable, but liver-disease-associated mortality also decreased in parallel [8]. This was particularly true for coinfected patients with undetectable HIV viraemia under HIV therapy and with higher CD4+ T-cell counts [9]. Furthermore, liver biopsy studies in HIV–HCV-coinfected patients achieving complete control of HIV replication demonstrated a decline in liver inflammation, which may account for these favourable changes in liver disease outcome [10]. Other studies exploring the viral interactions between HIV and HCV also demonstrated a decline in apoptosis markers in coinfected patients starting HIV therapy, however, Fas expression did not reach levels found in healthy controls [11].

As a consequence, HIV therapy is recommended earlier in the EACS HIV treatment guidelines for HIV–HCV-coinfected patients [12]. ART should be initiated in all HCV-coinfected patients with a CD4+ T-cell count <500 cells/µl. Some guidelines (such as the DHHS guidelines) even recommend considering HIV therapy for HIV–HCV-coinfected patients regardless of CD4+ T-cell count; however, for patients infected with HCV genotype 1, some clinicians may choose to defer ART in HIV treatment-naive patients with CD4+
T-cell counts >500 cells/mm³ until HCV treatment that includes the HCV NS3/4A protease inhibitors is completed [13]. In the current issue of Antiviral Therapy, Loko et al. [14] describe the first study on the evolution of liver stiffness measured by Fibroscan™ (Echosens, Paris, France), over ≥24 months of follow-up in HIV–HCV-coinfected patients in the prospective French ANRS CO 13 HEPAVIH cohort. Most interestingly, long-term antiretroviral therapy and sustained virological response under HCV therapy were the only significant factors associated with lack of increase in liver stiffness [14]. These data confirm other observational data from retrospective analyses of patients with HCV–HIV coinfection undergoing HCV therapy, demonstrating a decrease in the risk for developing liver disease relevant events in patients successfully cured of HCV, even when cirrhosis was present at baseline [15]. More importantly however, these data again underline the benefit associated with HIV therapy for further liver disease evolution when commenced in an HIV–HCV-coinfected individual. Nevertheless, despite the increasing evidence of delayed fibrosis progression under HIV therapy, CD4⁺ T-cell counts upon HIV treatment initiation in most cohorts remain relatively low. The median CD4⁺ T-cell count at HIV treatment initiation in the large German ClinSurv cohort according to HIV transmission risk groups shows that, in particular, intravenous drug users with clearly the highest prevalence of chronic HCV started HIV therapy relatively late and thereby possibly missed out on some of the positive effects of HIV therapy on further liver disease development (Figure 1; C Kollan, Robert Koch Institute, Berlin; personal communication). Although a clear increase in CD4⁺ T-cell count upon treatment initiation has been demonstrated in recent years, these data should remind us all to think about earlier HIV treatment in HCV-coinfected patients in order to delay further liver fibrosis progression. In view of the rapidly evolving HCV treatment armamentarium, and the potential for much better tolerated and more easily taken HCV therapies in the near future, the prevention of fibrosis progression through HIV therapy gains even more importance as it potentially allows patients to wait for the development of more successful interferon-free HCV treatment strategies.

Disclosure statement

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References


