A Comparison of Risk of Treatment Limiting Adverse Events in HCV-co-infected vs Non-co-infected Persons with HIV in EuroSIDA

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ABSTRACT

Background: Liver damage associated with hepatitis C (HCV) may adversely affect the likelihood of experiencing discontinuation due to toxicities or patient/physician choice (TOX) in patients taking combination antiretroviral therapy (cART). Limited information is available from clinical trials as patients with HIV are often excluded.

Aims: To compare incidence rates of discontinuation due to TOX associated with specific drugs in patients with or without HCV.

Methods: 2,121 patients from 23 countries were followed after initiation of a specific nucleoside pair (zidovudine/lamivudine, stavudine/lamivudine, or efavirenz/lamivudine) or third drug (abacavir, nelfinavir, indinavir, lopinavir, nevirapine, or other dual PI-containing regimen) and 15,323 patients with unknown HCV serostatus were studied by the EuroSIDA study. The incidence of any nucleoside pair or third drug due to TOX or other events requiring cessation of any nucleoside pair or third drug was calculated. Incidence rate ratios (IRR) were derived from Poisson regression models.

Results: In patients with HCV (n=1,074), during 8,474 person-years there were 292 discontinuations due to TOX for nucleoside pairs and 232 for third drugs. The incidence of discontinuation due to TOX was consistently higher in patients with HCV after stratification to nucleoside pair or third drug. After adjustment for CD4 count, gender, exposure group, time since starting HAART, time on HAART, region, treatment regimen, there were few differences in the rate of discontinuation in those with HCV compared to those without for any nucleoside pairs or third drugs when comparing those with or without HCV. When comparing nucleoside pairs or third drugs in patients with or without HCV, when adjusting for patient-physician choice of HCV positive patients to influence the choice between antiretrovirals used as part of a cART regimen.

In contrast, with nucleoside pairs or third drugs, the incidence of discontinuation due to TOX was considerably higher in IDU compared to non-IDU in both patients with and without HCV. There was no evidence to suggest that this was associated with any specific nucleoside-pair or third drug used as part of cART. Our results do not suggest that any specific component of cART is more poorly tolerated in patients with HCV or that the presence of HCV should influence the choice between antiretrovirals used as part of a cART regimen.

INTRODUCTION

Recently, we reported an excess risk of drug-related discontinuations of cART in HCV infected compared with HCV uninfected HIV positive individuals (Mocroft et al, 7th International Congress on Drug therapy in HIV infection. Amsterdam, 2001). We also showed that the incidence of discontinuation due to nefazodone was higher among patients with HCV than those without. This could change the treatment benefit for nefazodone and HCV infection, or may influence the use of nefazodone in future trials.

The aim of this study was to describe the reasons for stopping cART regimens according to HCV status and to determine whether the increased incidence of discontinuation of any nucleoside pair due to toxicities and patient/physician choice (TOX) seen in patients with HCV differs according to cART regimen.

METHODOLOGY

The EuroSIDA study is a prospective, European study of patients with HIV infection in 8 centres across Europe. At recruitment, in addition to demographic and clinical information, a complete antiretrovirals/therapy was collected together with the most recent CD4 counts and viral load measurements.

A total of 2,121 patients satisfied the inclusion criteria and are described in this study. At baseline, 1,075 patients were HCV negative (50.7%) and 1,046 were HCV positive (49.3%).

The incidence of discontinuation due to TOX after stratification by HCV status and nucleoside pair or third drug was calculated.

Poisson regression was used to determine the factors related to discontinuation due to TOX of either the nucleoside pair or the third drug, and was adjusted for factors found previously to be related to discontinuation due to TOX.

RESULTS

Figure 1: Shows the reasons for discontinuration. The most common reason for discontinuation was patient choice. There were significant differences in the reason for discontinuation when comparing those with and without HCV infection (p=0.002), and remained significant if discontinuation due to patient or physician choice were included (p=0.002).

Table 1: Shows the incidence of discontinuation due to TOX was significantly higher among patients with HCV compared to those without. After additional stratification for IDU transmission category, the incidence of discontinuation due to TOX was similar in patients with and without HCV, while the incidence of discontinuation due to TOX was considerably higher in 50% compared to non-IDU in both patients with and without HCV infection.

CONCLUSION

References:

For both nucleoside pairs and the third drug, the incidence of discontinuation due to TOX was significantly higher among patients with HCV compared to those without. After additional stratification for IDU transmission category, the incidence of discontinuation due to TOX was similar in patients with and without HCV, while the incidence of discontinuation due to TOX was considerably higher in 50% compared to non-IDU in both patients with and without HCV infection.