

# Liver-related Deaths among HIV-infected Persons

## Data from the D:A:D Study

R Weber<sup>1</sup>, N Friis-Møller<sup>2</sup>, CA Sabin<sup>3</sup>, P Reiss<sup>4</sup>, A D'Arminio Monforte<sup>5</sup>, F Dabis<sup>6</sup>, W El-Sadr<sup>7</sup>, S De Wit<sup>8</sup>,  
L Morfeldt<sup>9</sup>, MG Law<sup>10</sup>, C Pradier<sup>11</sup>, G Calvo<sup>12</sup>, O Kirk<sup>13</sup>, AN Phillips<sup>3</sup>, JD Lundgren<sup>2</sup>  
on behalf of the D:A:D study group

<sup>1</sup>SHCS, University Hospital Zürich, Switzerland; <sup>2</sup>Copenhagen HIV Programme (CHIP), Hvidovre University Hospital, Denmark; <sup>3</sup>Royal Free Centre for HIV Medicine and Department of Primary Care and Population Sciences, Royal Free and University College, United Kingdom; <sup>4</sup>ATHENA, HIV Monitoring Foundation, Academic Medical Center, University of Amsterdam, The Netherlands; <sup>5</sup>ICONA, L Sacco Hospital, University of Milan, Italy; <sup>6</sup>Aquitaine Cohort, Bordeaux University Hospital, INSERM U593, France; <sup>7</sup>CPCRA, Columbia University/Harlem Hospital, USA; <sup>8</sup>Saint-Pierre Cohort, C.H.U. Saint-Pierre Hospital, Belgium; <sup>9</sup>HivBIVUS, Karolinska Hospital, Sweden; <sup>10</sup>AHOD, National Centre in HIV Epidemiology and Clinical Research, Australia; <sup>11</sup>Nice Cohort, CHU Nice Hospital de l'Arche, France; <sup>12</sup>BASS, Autonomous University of Barcelona, Spain; <sup>13</sup>EuroSIDA, CHIP, Hvidovre University Hospital, Denmark

### BACKGROUND

With the availability of combinations antiretroviral therapy (cART), the causes of deaths in HIV-infected patients have evolved. A substantial proportion of deaths in HIV-infected persons are due to liver failure. We aimed to assess the predictors of liver-related deaths (LRD).

### METHODS

D:A:D is a prospective observational study of 23,441 HIV-1 infected patients from 11 cohorts in Europe, Australia and the United States. Information on deaths occurring between the initiation of D:A:D in 2000 and February 2004 was collected; causes of death were coded centrally. Relative rates (RR) of factors associated with LRD were estimated using Poisson regression.

### RESULTS

A total of 1248 (5.3%) patients died (incidence:1.6 deaths/100 person-years).

The leading causes of death were AIDS (31%), liver-related (15%), cardiovascular disease (9%), and non-AIDS related malignancies (9%).

The rates of death from all causes and LRD remained stable over time (Figure 1).

Clinical reports showed that 76% of LRD were associated with viral hepatitis (66% HCV, 17% HBV), 9% occurred in the context of hepatocellular carcinoma, and alcohol abuse was reported in 14% of cases.

The univariable association of risk factors with LRD is illustrated in Figures 2-5. Univariable analyses showed no significant relationship between cumulative exposure to cART of up to 7 years and liver-related death (RR 1.00 [0.93-1.07] per year of exposure, p=0.93).

After adjusting for other factors (multivariable results shown in Figure 6), the predictors of LRD were:

- Age (1.3 [1.2-1.4] per 5 years older).
- HIV transmission group (2.0 [1.2-3.4] for intravenous drug use versus homosexual infection),
- CD4 cell count (adjusted RR per halving of the latest CD4 count : 1.23 [95% CI: 1.17-1.29], p<0.0001)
- HCV infection ( 6.7 [3.9-11.2])
- HBV antigenemia ( 3.7 [2.4-5.9])

The associations were unchanged after excluding 9 patients in whom an AIDS-defining illness was a contributing cause of death.

### CONCLUSIONS

Death from liver disease was the most frequent non-AIDS-related cause of death in the D:A:D study. Rates of LRD were stable over calendar time. Risks for LRD included age, transmission group, HCV and HBV infection. Furthermore, we found a strong association between immuno-deficiency (CD4 cell count) and increased risk of liver-related deaths that was independent of other factors including hepatitis.

In univariable analyses, there was no association between duration of cART exposure and the risk of LRD. However, because the CD4 count-raising effect of cART (which we would expect could reduce risk of LRD) might be masking a detrimental effect of cART, future analyses will focus on the association between years of exposure to cART and risk of LRD after adjusting for latest CD4 count.

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Cohort coordinators and data managers: S Zaheri, L Gras (ATHENA), R Thiébaud, E Balestre (Aquitaine), K Petoumenos (AHOD), S Mateu, F Torres (BASS), B Sommereijns, B Poll (Brussels), G Bartsch, G Thompsen (CPCRA), J Kjaer (EuroSIDA), P Pezzotti (ICONA), E Fontas, C Caissotti (Nice), A Sundström, G Thulin (HivBIVUS), M Rickenbach, O Keiser (SHCS)

Statisticians: CA Sabin, AN Phillips \*

Community representative: S Collins \*

DAD coordinating office: N Friis-Møller, S W Worm, A Sawitz, JD Lundgren \*†

Steering Committee: Members indicated w/\*; † chair;

Additional members: T Mertenskoetter\*, E Loeliger \*, R Tressler \*, I Weller \*

Rainer Weber, M.D.  
Division of Infectious Diseases  
University Hospital  
CH-8091 Zurich  
Switzerland  
Tel:+41-1-255 38 26  
Fax:+41-1-255 32 91  
E-mail:infweb@usz.unizh.ch

