Hot News

New Antiretroviral Treatment Guidelines from the IAS-USA Panel

The International Antiviral Society-USA Panel (formerly International AIDS Society-USA Panel) issued this summer a new edition of the antiretroviral treatment guidelines (Thompson, et al. JAMA. 2012;308:387-402). Certainly, the most outstanding and innovative proposal concludes that in established HIV infection, antiretroviral therapy should be offered to all individuals regardless of CD4 cell counts. This statement is mainly based on extensive data from large cohort studies demonstrating that antiretroviral therapy protects from non-AIDS-related complications and reduces the risk of sexual transmission of HIV. The new guidelines also extend treatment to all individuals in the acute phase of primary HIV infection, regardless of the presence of symptoms. The only subset of HIV individuals for whom antiretroviral therapy may be deferred is represented by elite controllers and long-term nonprogressors.

No major changes are recorded in the guidelines with respect to combinations preferred for antiretroviral-naive individuals. However, the dual NRTI combination abacavir/lamivudine, together with efavirenz or atazanavir/ribinavir, is now indicated as a first-line option instead of as an alternative regimen for HLA-B*5701-negative patients with baseline plasma HIV RNA < 100,000 copies/ml. On the other hand, nevirapine (now available as a 400 mg once-daily pill) or rilpivirine, any in combination with tenofovir/emtricitabine or abacavir/lamivudine, are now considered as alternative regimens. Finally, the QUAD coformulation (elvitegravir/cobicistat/tenofovir/emtricitabine) is recorded as an initial antiretroviral option, subject to regulatory approval. In all situations, the presence of viral load values between 50 and 200 HIV RNA copies/ml should prompt evaluation of factors leading to failure and consideration of changing the antiretroviral regimen.

The panel tackles as well some particular situations in certain groups of HIV patients, such as postmenopausal women. Given the increased risk of bone fractures in this population, when possible it may be cautious to avoid tenofovir as part of initial therapy. Comorbidities and opportunistic infections are also dealt with. Initiation of antiretroviral therapy should not be deferred in patients presenting for the time with opportunistic diseases other than cryptococcal or tuberculous meningitis. In all circumstances, however, attention must be paid to drug interactions and potential immune reconstitution inflammatory syndrome. In HIV-infected patients with tuberculosis, antiretroviral therapy should be given preferably within two weeks of tuberculosis treatment when CD4 counts are < 50 cells/µl, and by 8-12 weeks when CD4 counts are higher.

Pablo Labarga and Francisco Blanco
Department of Infectious Diseases
Hospital Carlos III
Madrid, Spain

Unveiling Extrahepatic Consequences of Chronic Hepatitis C – The REVEAL-HCV Study

There is growing evidence indicating that chronic viral infections may produce harm by direct organ-specific damage as well as by indirect systemic inflammatory phenomena derived from continuous viral replication. This has been well established for HIV infection, whose uncontrolled replication leads to increased risk of cardiovascular events and accelerated ageing. For hepatitis C there is no similar evidence so far, although extrahepatic manifestations of chronic HCV infection are well known, including cutaneous, rheumatic and neurologic complications.

The first results of the REVEAL-HCV study have recently been released (Lee, et al. J Infect Dis. 2012;206:469-77). A total of 19,636 adults were enrolled in Taiwan in 1991-1992 and followed for an average of 16.2 years. There were 1,095 HCV-seropositive patients (4% of total), of whom 69.4% were viremic. During the study period there were 2,394 deaths. The HCV-seropositive subjects had greater liver mortality, mostly related to complications of cirrhosis and liver cancer, as compared with HCV-seronegative individuals (multivariate adjusted hazard ratios [MAHR] of 12.5 [9.3-16.7] and 21.6 [14.8-31.5], respectively). Unexpectedly, non-liver-related causes of death were also more frequent in HCV-antibody positive individuals than in HCV-seronegative subjects. Mortality was increased as result of a greater incidence of cardiovascular events, kidney disease, and some cancers (esophagus, prostate and thyroid) (Fig. 1).

In a second step, mortality rates were examined in HCV-seropositive individuals according to the presence or absence of HCV RNA, given that around 20% of individuals exposed to HCV may clear the virus spontaneously. It was striking to find that the excess mortality for both liver and non-liver etiologies seen in HCV-seropositive subjects was driven by HCV viremia (Fig. 2). As compared with HCV RNA-negative/HCV-antibody positive, viremic seropositive patients had MAHR of 1.5 (1.1-2.2) and 3.0 (1.4-6.2) for deaths due to cardiovascular events and renal disease, respectively. These figures were

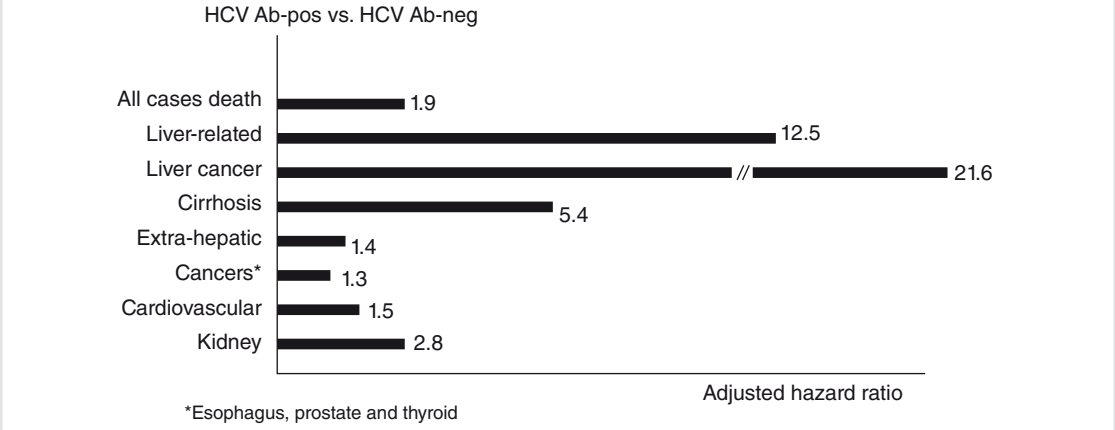

Figure 1. *Risk of death in the REVEAL-HCV study.*

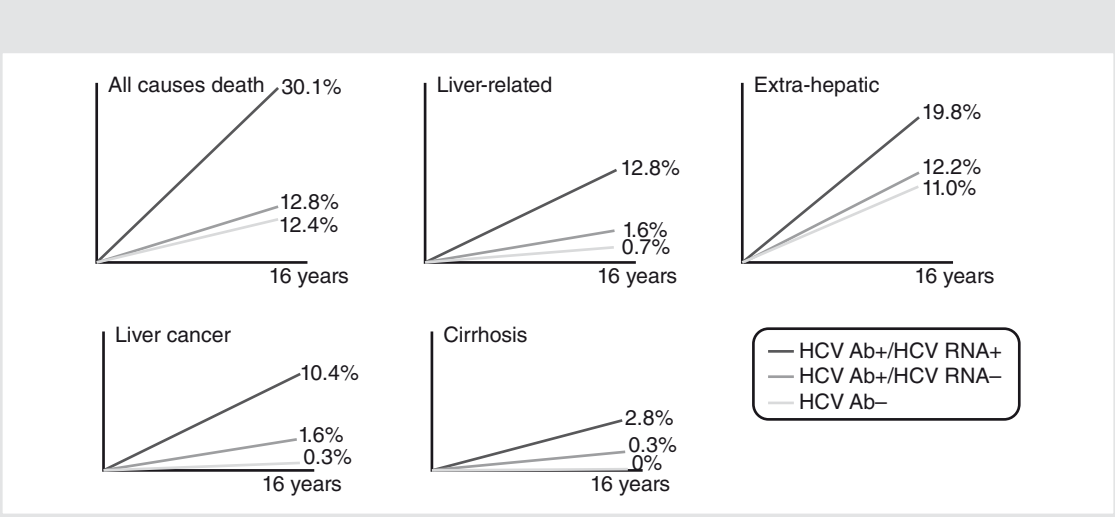

Figure 2. *Cumulative mortality in the REVEAL-HCV study.*

5.9 (2.0-17.3) and 5.8 (1.6-20.8) for esophagus and prostate cancers.

Altogether, these findings strongly indicate that persistent HCV replication, besides having the well known deleterious effect on the liver, may also be harmful for the whole body, increasing the risk of heart and kidney disease, as well as favoring neoplasms. The mechanisms involved in these indirect effects of uncontrolled HCV replication are so far unclear, but systemic inflammation processes may trigger atherosclerosis and thrombosis phenomena. Kidney dysfunction might additionally result from deposition of immune complexes.

Similarly to what has occurred in the HIV field, where antiretroviral therapy has moved to be recommended to almost all infected individuals, the advent of direct-acting antivirals for hepatitis C should push the prescription of therapy to all chronic hepatitis C patients. Besides removal of liver damage, the benefit will extend to protect chronic hepatitis C patients from extrahepatic harmful effects of uncontrolled, persistent HCV replication.

Pablo Barreiro
Department of Infectious Diseases
Hospital Carlos III
Madrid, Spain