HIV/tuberculosis co-infection:
The CAMELIA trial paves the way for optimal management

How should patients co-infected with HIV and tuberculosis be treated? Specifically, when should patients be started on antiretrovirals during tuberculosis treatment, particularly when they are severely immunocompromised? In a randomized clinical trial, a team of Cambodian, French and American scientists have shown for the first time that HIV antiretrovirals should be started two weeks after antituberculosis treatment initiation. This is an important advance in the management of this common and deadly co-infection in resource-limited countries.

Tuberculosis is the most frequent co-infection in people living with HIV. According to WHO, 1.37 million people worldwide have HIV/tuberculosis, which kills 456 000 people every year, accounting for approximately one quarter of all deaths among HIV-infected patients.

The treatment of patients with simultaneous HIV and tuberculosis disease is very challenging. Each of the treatments can cause drug side effects, there are interactions between the different classes of drugs, and a large number of tablets must be taken. Moreover, simultaneous treatment of the two infections can lead to an exaggerated immune response (paradoxical reaction). In November 2009, WHO recommended treating patients with antiretrovirals “as soon as possible” within the first 2 months following the start of tuberculosis treatment.

The CAMELIA (CAMbodian Early versus Late Introduction of Antiretroviral drugs) trial sponsored by the French National Agency for Research on AIDS and viral hepatitis (ANRS) and the US National Institutes of Health (NIH) (ANRS 1295/12160 - CIPRA KH 001/10425) provides precise data on the optimal timing of treatment. The Principal Investigators of the study are Thim Sok (Cambodian Health Committee-CHC, Phnom Penh), François-Xavier Blanc (Kremlin-Bicêtre Hospital, Assistance Publique - Hôpitaux de Paris) and Anne Goldfeld (Immune Disease Institute, Harvard Medical School, Boston and CHC). The trial was coordinated by CHC with support from the NIH and by the Institut Pasteur in Cambodia, within the framework of ANRS Cambodian site support.

This randomized trial was conducted between 2006 and 2010 in five hospitals in Cambodia, recruiting 661 patients co-infected with HIV and tuberculosis, who were severely immunocompromised (72% had a CD4 cell count below 50/mm³ at inclusion). Standard tuberculosis treatment was started in all patients as soon as they were diagnosed. Patients were then randomly assigned to start identical triple-drug therapy against HIV 2 weeks (“early treatment” arm) or 8 weeks (“late treatment” arm) later. 332 patients were enrolled in the early arm and 329 patients in the late arm. Patients were then followed up for a mean duration of 26 months. The primary objective of the study was to determine whether early introduction of ARV reduced the high mortality in these patients.
The first results of the trial were presented as a late-breaker at the International AIDS Conference in Vienna on July 22nd, 2010. The data demonstrated that mortality among patients in the “early treatment” arm was significantly lower than in the “late treatment” arm. The risk of death was reduced by 34% in the “early treatment” arm (p = 0.007). Nevertheless, the patients in the early arm experienced more paradoxical reactions. In basic scientific studies associated with the CAMELIA trial, work is now underway to understand the mechanisms underlying these paradoxical reactions that occur more frequently when antiretroviral treatment is started early.

This randomized trial is the first to demonstrate that the introduction of antiretrovirals two weeks after initiation of tuberculosis treatment significantly reduces mortality in patients co-infected with HIV and tuberculosis. This is an important advance in improving patient care and enhancing survival.

Source

Significant enhancement in survival with early (2 weeks) vs. late (8 weeks) initiation of highly active antiretroviral treatment (HAART) in severely immunosuppressed HIV-infected adults with newly diagnosed tuberculosis.


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International Aids Society Conference, Vienna, Late Breaker presentation, July 22nd, 2010

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