When is it best to start HAART?

Over the past 18 months, international treatment guidelines in high-income countries have suggested that HAART be started when CD4+ counts fall below the 350-cell mark. In these guidelines treatment can begin when the CD4+ count is higher, depending on special circumstances such as hepatitis co-infections, kidney disease, pregnancy and so on.

This is a major departure for the international guidelines, as for many years they had encouraged that treatment begin when the CD4+ count had fallen below the 200-cell mark. The reason for the change was that several studies had recently found an increased risk of death in people not taking HAART whose CD4+ counts were between 200 and 350 cells compared to people who were taking HAART (see TreatmentUpdate 170 and TreatmentUpdate 171 for further details). Moreover, there are trends from large database-centered studies suggesting increased survival when HAART is started at even higher CD4+ cell counts.

However, these trends are not definitive and need to be confirmed in prospective randomized clinical trials. Until such trials have been completed, currently available guidelines are meant to be used as a guide because there is as yet no answer to the question: When is the best time to begin HAART?

Massive databases

Research teams in many high-income countries have assembled large databases containing health information on HIV positive people. These data sets can be used to analyse trends in health. One collection of these databases is called the ART-Cohort Collaboration and includes information from several countries and regions as follows:

- United States
- European Union
- Switzerland
- Alberta
- British Columbia

The collaboration has amassed and analysed information from 24,444 HIV positive people, of whom 808 have died. Researchers affiliated with this database wondered about the risk of death in people who began therapy at different CD4+ counts. To explore the issue of when it is best to begin HAART, they used their database to mimic a randomized clinical trial with 21,247 participants. For this theoretical exercise they did not include HIV positive people who were injection drug users (IDUs) because, on average, there is an increased rate of death among HIV positive IDUs because of issues such as substance use, mental health and co-infections with liver-destroying viruses.

The study team found that people who began therapy when their CD4+ counts were less than 250 cells had the highest death rates. This was somewhat reduced when people began therapy at cell counts between 251 and 350 cells. The findings from this study suggest that starting HAART at CD4+ counts of 351 or higher is likely to reduce death rates.

These findings are based on an observational cohort study in selected people. Such studies cannot entirely rule out bias when interpreting their results, but they can serve as a guide to develop studies with a more robust study design. The findings from the ART-Cohort Collaboration confirm the recent decisions by treatment guideline committees to increase the threshold for initiating therapy to around the 350-cell mark. But the findings also raise the question about starting HAART at much higher counts.

REFERENCE:

1. Sterne J and the When to Start consortium. When should HIV-1-infected persons initiate ART? Collaborative
analysis of HIV cohort studies. In: Program and abstracts of the 16th Conference on Retroviruses and Opportunistic Infections, February 8-11, 2009, Montreal, Canada. Abstract 72 LB.
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