

Current Topics in HIV Care and Prevention

A publication of the ICAP Clinical Unit



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Director's Corner

Welcome to our inaugural issue of the ICAP Clinical Unit *Topics in HIV Care and Treatment*.

This monthly e-publication was created in response to your expressed need to have accessible, digestible clinical information. Key clinical issues and challenges identified by you during the course of your work will be explored. Each issue will summarize new scientific evidence and highlight recommendations in a user-friendly, "bite-sized" fashion. This is so important in the dynamic field of HIV medicine.

In our first issue, we address the question of when to start antiretroviral treatment (ART) in patients with TB/HIV co-infection. We highlight results from the SAPiT (Starting Antiretrovirals at three Points in Tuberculosis) study, the first randomized clinical trial to demonstrate that integrating TB and HIV treatment saves lives. We underscore the importance of understanding these results, and initiating discussions in-country regarding translating the study findings into national guidelines and clinical practice.

This is your publication. In this spirit, we encourage you to send along ideas, comments, questions and feedback – either on content or format. In fact, we plan to include a "Notes from the Field" section in future issues.

Respectfully,

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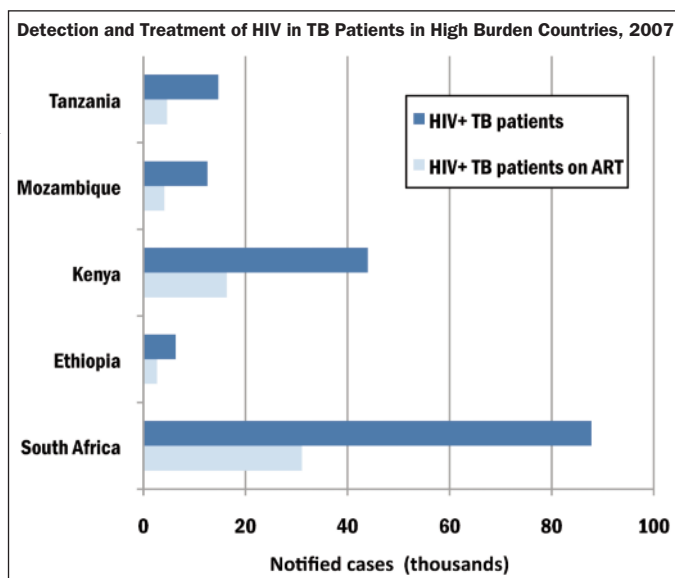
Send ideas, comments and questions to:
Kjersti Schmitz at kcs24@columbia.edu.
Please put "Clinical Topics" in the subject line.

SAPiT Trial Shows that Antiretroviral Therapy Should Be Initiated During TB Treatment in Co-infected Patients

Tuberculosis (TB) is the most common opportunistic disease reported worldwide in HIV-infected patients. A quarter of deaths in HIV-infected patients are estimated to be as a result of TB. TB/HIV co-infected patients are four times more likely to die during TB treatment compared to TB patients without HIV.

Prompt initiation of TB treatment in individuals with suspected or confirmed TB is a key priority. Knowledge of HIV status is also critical for all TB patients in order to ensure prompt linkage to HIV care and access to antiretroviral therapy (ART) programs. However, the optimal timing of ART initiation in patients with TB and HIV has remained unclear. Current guidelines recommend timing ART initiation in TB patients based on CD4 cell counts, with priority for earlier initiation in patients with lower counts. These guidelines are based largely on expert opinions and observational data.

Results from the SAPiT (Starting Antiretrovirals at three Points in Tuberculosis) trial, the first randomized clinical trial to study timing of ART initiation in patients with TB/HIV co-



Data from the World Health Organization.

infection, were presented at the 2009 Conference for Retroviruses and Opportunistic Infections (Karim SA, Naidoo K, Grobler A, et. al., Initiating ART during TB Treatment Significantly Increases Survival: Results from a Randomized Controlled Clinical Trial in TB/HIV-co-infected Patients in South Africa, Abstract #36a). The SAPiT trial demonstrated that initiating ART during TB treatment reduced the number of deaths by more than half, compared to waiting until completion of TB treatment before initiating ART.

Purpose of the study:

To determine the optimal timing of ART initiation in TB patients with HIV.

Coming next month...

Recommendations for a Tuberculosis Occupational Health Policy

Study Design:

- Inclusion criteria:
 - Patient with sputum smear-positive pulmonary TB;
 - HIV infected, ART naive;
 - CD4 count less than 500 cells/mm³;
 - For females: willing to use contraception.
- Eligible patients randomized to one of three arms:
 - A: ART initiation during intensive phase of TB treatment (months 1-2);
 - B: ART initiation during continuation phase of TB treatment (months 3-6);
 - C: ART initiation after completion of TB treatment (after month 6).
- Treatment regimens:
 - Standard TB regimen: four drugs (RHZE) during intensive phase followed by two drugs (RH) for continuation phase of TB treatment;
 - ART regimen: once-daily didanosine, lamivudine, and efavirenz.
- Endpoints:
 - Primary: all-cause mortality;
 - Secondary: tolerability, toxicity, HIV viral load, TB outcomes and immune reconstitution inflammatory syndrome (IRIS).

Results:

A total of 642 patients with TB/HIV were enrolled and followed in the study in Durban, South Africa. During study follow-up, an independent Data & Safety Monitoring Board reviewed the data and determined that TB/HIV patients who were in the study arms that initiated ART during TB treatment (arms A and B: average time to start ART 67 days) had significantly better survival when compared to those in the study arm that delayed ART until after TB treatment ended (arm C: average time to start ART 261 days). The mortality rate was 5.4 per 100 person-years in the patients who initiated ART during TB treatment (arms A and B) compared to 12.1 per 100 person-years in the group that initiated ART after completion of TB treatment (arm C). This translates into a decrease in mortality by more than half (56 percent) with initiation of ART during TB treatment (Hazard ratio 0.44, 95% CI: 0.25-0.79, p=0.003). These results held across CD4 counts.

Conclusions:

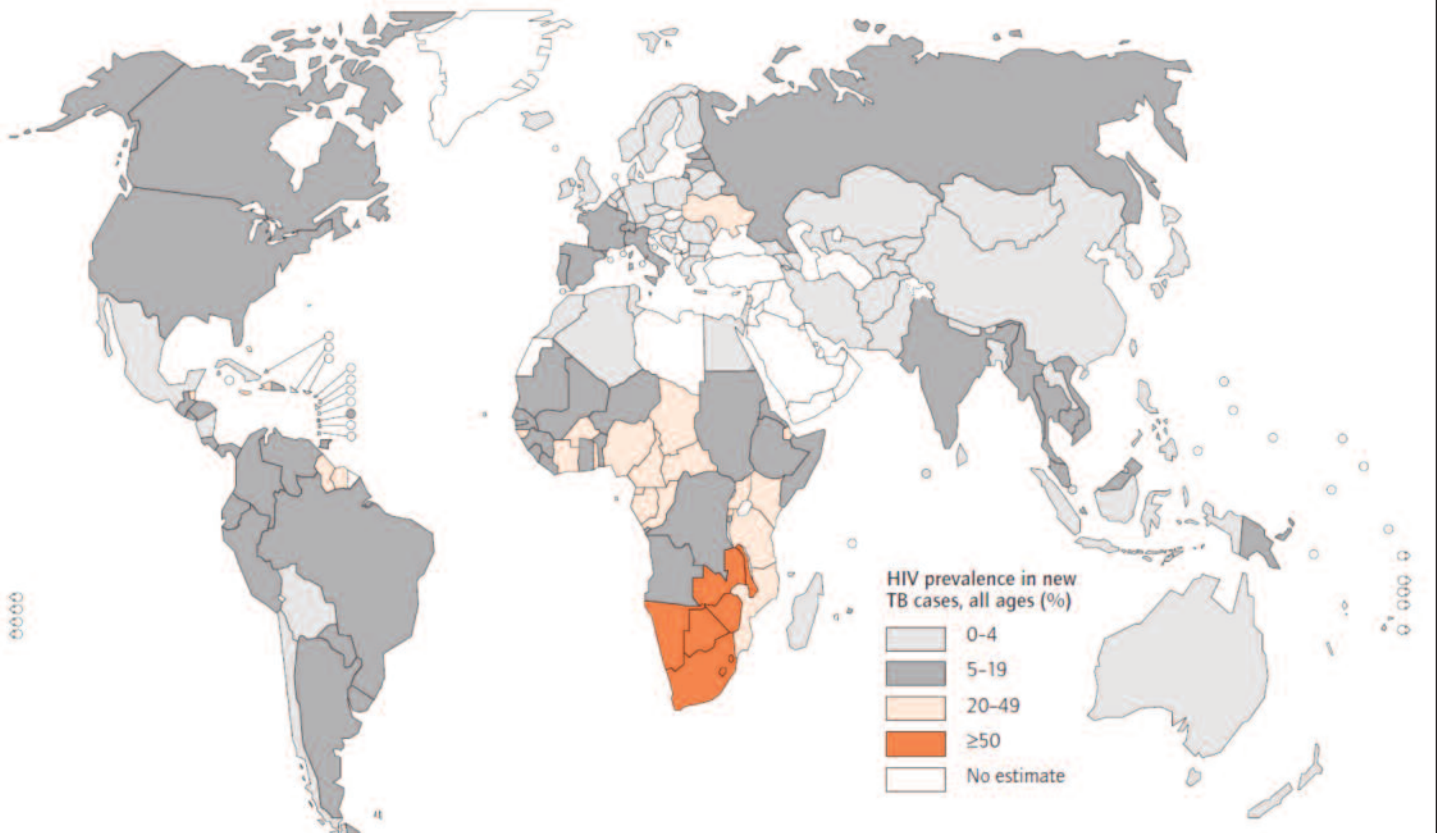
The findings from this study highlight the following:

- Knowledge of HIV status for all TB patients is important in order to provide those with HIV infection the needed interventions;
- TB/HIV patients should be promptly linked to HIV care and ART programs;
- TB/HIV patients should have CD4 testing;
- Patients with TB/HIV and counts <500 cells/mm³ should have ART initiated during TB treatment;
- Patients with TB/HIV should be closely monitored to ensure appropriate choices of ART, adherence to both TB and HIV treatment, and management of side effects and IRIS, both of which may occur more frequently when ART is started during TB treatment.

End Notes:

Arms A and B of the SAPiT trial are ongoing, with the aim to delineate more precisely the optimal time during TB treatment for initiation of ART. Of note is the average timing of ART initiation in arms A and B, which was 67 days after initiation of TB treatment. ■

Estimated HIV prevalence in new TB cases, 2007



Reprinted from the World Health Organization.