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Press release

The ANRS-sponsored STATIS trial concludes that systematic treatment of tuberculosis in advanced HIV infection is not superior to test-guided treatment

STATIS, a clinical trial comparing the benefits and risks of two strategies of fighting tuberculosis in severely immunosuppressed people living with HIV/AIDS in resource-limited countries, has just delivered its conclusions.

In an [article published today in the *New England Journal of Medicine \(NEJM\)*](#), the team of the ANRS-sponsored trial observes that after 24 and 48 weeks of follow-up of adults at an advanced stage of HIV infection who were not suspected to have tuberculosis and who had not previously received antiretroviral treatment, systematic treatment for tuberculosis is not superior to treatment guided by the results of various diagnostic tests. Furthermore, Prof. François-Xavier Blanc (Department of Respiratory Medicine, L'Institut du Thorax, Nantes University Hospital and University of Nantes) and the STATIS trial team note the more frequent occurrence of severe adverse events in those patients having received systematic treatment.

HIV and tuberculosis coinfection is very deadly. According to World Health Organization (WHO) estimations in 2019, 251,000 deaths per year are attributed to tuberculosis in the population of people affected by HIV, especially in Sub-Saharan Africa and Asia. In these regions, many people living with HIV only access antiretroviral therapy when they are already severely immunosuppressed. Mortality following the initiation of treatment is therefore high in these patients, with tuberculosis being a common cause of death. It is in this context that the STATIS clinical trial studied two innovative strategies aimed at reducing this mortality.

To conduct STATIS (*Systematic empirical vs. Test-guided Anti-tuberculosis Treatment Impact in Severely immunosuppressed HIV-infected adults initiating antiretroviral therapy with CD4 cell counts <math><100/mm^3</math>*), the authors enrolled 1,047 HIV-infected and severely immunosuppressed adults (CD4+ T-cell counts below 100 cells per cubic millimetre) in four countries across two continents: Ivory Coast, Uganda, Cambodia, and Vietnam. Following enrolment, which took place between 2014 and 2017, the patients were randomly assigned between:

- a group that systematically received treatment for tuberculosis (with a combination of 4 molecules to take daily for 2 months, then 2 molecules to take for 4 months).
- and a group that was only treated for tuberculosis when various diagnostic tests were positive. This group was regularly screened using a questionnaire to evaluate symptoms and then, if tuberculosis was suspected, patients underwent a urine test, a molecular test (also to detect potential resistance to one of the antituberculosis molecules), and a chest X-ray.

Medical visits were scheduled for all patients at weeks 2, 4, 8, 12, 16, 20, 24, 36 and 48 after the enrolment visit.

After 24 and 48 weeks, the results were evaluated according to various criteria (death, occurrence of an invasive bacterial disease, development of adverse events, success of the antiretroviral therapy, compliance with the antituberculosis and antiretroviral therapies...). The rate of death or invasive bacterial disease in the group receiving systematic antituberculosis treatment was 19.4 per 100 patient-years versus 20.3 in the other group, with no significant difference between the two groups. Interestingly, tuberculosis was diagnosed in 93 patients (17.7%) within the first 24 weeks of the trial thanks to the repeat-test strategy, demonstrating the extent of this disease in a population initially not suspected of having it. In spite of the strategies used, tuberculosis remains the most common cause of death in this study. A total of 495 serious adverse events

occurred in 322 patients (179 in the systematic treatment group and 143 in the other group). The probability of serious adverse events associated with the medications was higher in the group having received systematic antituberculosis treatment (17.4%) than in the group having received test-guided treatment (7.2%).

The authors conclude that "*the results of the STATIS trial show that, among severely immunosuppressed adults who had not previously received antiretroviral therapy, systematic treatment for tuberculosis is not superior to a strategy involving repeated testing for tuberculosis and targeted treatment, and is associated with a higher number of serious adverse events*".

However, the researchers reiterate that "*both strategies were associated with a lower than expected rate of death or invasive bacterial infection in comparison with previous studies*". These findings should logically encourage those doctors with access to tuberculosis screening tests to no longer prescribe empirical antituberculosis therapy for their HIV-infected immunosuppressed patients, in order to limit the risk of serious adverse events. "*These significant findings should be taken into account in the international guidelines*", commented ANRS Director, Prof. François Dabis.

For further information

Source

Systematic or Test-Guided Treatment for Tuberculosis in HIV-Infected Adults

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