

# Systematic and empirical treatment of tuberculosis in HIV advanced infected patients

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## Background

In late presenting HIV+ adults, mortality following ART initiation is high with tuberculosis (TB) or invasive bacterial diseases (IBD) being major causes of mortality. We report the results of the STATIS open-label randomized controlled trial (ANRS 12290) that compared the efficacy and safety of 2 strategies aiming to decrease mortality and IBD in late presenters.

## Methods

ART-naïve HIV-1 infected adults with CD4<100 cells/μl were randomly assigned to either ART + extensive TB screening (arm 1) or ART + systematic empirical TB treatment (arm 2). In arm 1, extensive TB screening included Xpert MTB/RIF on sputum, urine lipoarabinomannan (LAM) and chest X-ray at baseline and at any time during follow-up in case of TB symptoms. ART was initiated immediately in patients who did not start TB treatment at baseline (arm 1 patients with negative TB screening) and 2 weeks after starting TB treatment in others (arm 1 patients with positive TB screening and arm 2 patients). The primary outcome was the occurrence of death or IBD at week 24 (W24).

## Results

1047 participants were included (arm 1: 525; arm 2: 522). Baseline characteristics were: 58% male, mean age 36 years, body mass index 20.1 kg/m<sup>2</sup>, CD4 36 cells/μl, plasma HIV RNA 5.4 log<sub>10</sub> copies/ml. At W24,

39 patients (3.8%) were lost to follow-up (arm 1: 21; arm 2: 18), while there were 69 deaths (arm 1: 36; arm 2: 33) and 29 IBD (arm 1: 14; arm 2: 15). The W24 hazard ratio of events between arm 2 vs. arm 1 was 0.93 (95%CI 0.61-1.42) for death or IBD, 0.92 (0.57-1.48) for death alone, 1.14 (0.54-2.40) for IBD alone and 2.70 (1.80-4.04) for grade 3-4 drug-related toxicity.

## Conclusions

We found that systematic TB treatment is not superior to extensive TB screening using Xpert MTB/RIF and urine LAM and targeted TB treatment to decrease the risk of mortality or IBD in ART-naïve adults with CD4<100/μl.

The STATIS trial compared the efficacy and safety of 2 strategies aiming to decrease mortality and invasive bacterial disease in late presenting HIV+ adults: initiation of TB treatment after extensive TB screening vs systematic empirical TB treatment. Systematic empirical TB treatment was not superior to extensive TB screening.