

## Dual Testing Approach with TST and IGRAS for Detection of LTBI in HIV

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### Abstract

In a recent article, our team demonstrated that HIV infected people have a significantly lower response to TST for detection of LTBI and that a discordance between IGRAs and TST is evident mainly in patients with advanced immunosuppression. TST cannot be considered the optimal test to determinate LTBI mainly in immunosuppressed individuals, due to the high number of false negative results related to the energy of immune system. We showed a higher percentage of positive results of TST and IGRAs in HIV infected people with higher CD4 cell count but among TST negative individuals both T-SPOT TB and QFT IT were positive in 9.2% cases.

**Keywords:** HIV; latent tuberculosis infection; Interferon gamma release assays.

In a recent article published on "In vivo", our team report an interesting observation about the effectiveness of interferon gamma release assays (IGRAs) and tuberculin skin test (TST) for the detection of latent tuberculosis infection (LTBI) in HIV positive patients with different setting of immunodeficiency. Tuberculosis (TB) is a leading cause of morbidity and mortality worldwide accounting for about 9.6 million new cases and 1.5 million deaths annually. It is estimated that over 13 million people are coinfecting with HIV and Mycobacterium tuberculosis. In 2016 there were an estimated 10.4 million new tuberculosis cases, 90% adults, and 10% people living with HIV. In the same year, there were an estimated 1.3 million TB deaths among HIV negative people and an additional 374.000 deaths resulting from TB among people with HIV infection.

Countries of Sub-Saharan Africa account for around 70% of all TB deaths among people living with HIV [1]. LTBI infection is the presence of Mycobacterium tuberculosis in the body without signs and symptoms or radiographic or bacteriologic evidence of the disease. HIV infection is the most important risk factor for progression from latent tuberculosis infection to active TB and the annual risk of developing acute TB is approximately 10% per year compared to a lifetime risk of 5-10% in immunocompetent subjects. Thus, the risk of progression to TB disease is 10 times greater for those who are HIV infected [2]. Datas in literature report that isoniazid preventive treatment in LTBI may reduce the risk of progression to active TB, thus it is urgent to identify and to treat latent tuberculosis mainly in HIV positive population [3].



IGRAs are simple blood tests alternative to TST for detection of TB infection, that measure a person's immune reactivity to *Mycobacterium tuberculosis*. Quantiferon TB Gold in Tube (QFT IT and T-SPOT TB) are more specific than TST, have advantages over TST in sensitivity and a higher positive predictive value when applied in immunocompromised patients with risk factor for LTBI. Moreover, prior BCG vaccination does not cause a false positive IGRA test result, unlike TST. A positive test result suggests that TB infection is likely; a negative one suggests that infection is unlikely. As known, the two IGRAs can yield indeterminate test results (ITRs) which limit their clinical utility mainly in T-SPOT TB test [4]. In our recent study we observed a low proportion of indeterminate results in T-SPOT TB test and in QFT IT one that seemed prevalent in patients with a low CD4 cell count. In the article by Parrella et al, the authors demonstrated that HIV infected people have a significantly lower response to TST for detection of LTBI and that a discordance between IGRAs and TST is evident mainly in patients with advanced immunosuppression. TST cannot be considered the optimal test to determine LTBI mainly in immunosuppressed individuals, due to the high number of false negative results related to the energy of immune system. We showed a higher percentage of positive results of TST and IGRAs in HIV infected people with higher CD4 cell count but among TST negative individuals both T-SPOT TB and QFT IT were positive in 9.2% cases.

The poor agreement among all tests used to detect LTBI in HIV people makes difficult to validate a golden standard method. Dual testing with TST and IGRAs should be the optimal approach of LTBI screening in HIV infected population. Diagnosis and treatment of LTBI is the most effective strategy to control TB among patients with HIV infection. Further investigations in a larger number of cases and that compare IGRAs and TST for detection of LTBI in HIV people are needed, in order to confirm our results and to evaluate the clinical impact of dual testing.

## References

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