THE SENSITIVITY OF QUANTIFERON®-TB GOLD PLUS IS NOT AFFECTED BY HIV-STATUS (ID 711)

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Introduction

Current tests for latent TB infection (LTBI), the tuberculin skin test (TST) and interferon gamma release assays (IGRAs; QuantiFERON®-TB Gold In-Tube [QGIT; QIAGEN] and the T-Spot®.TB [Oxford Immunotec]) have poor sensitivity among people living with HIV (PLHIV). QGIT has been recently modified to include two antigen tubes, TB1 aimed at stimulating CD4 lymphocytes and TB2 aimed at stimulating CD4 and CD8 lymphocytes; now called QuantiFERON®-TB Gold Plus (QFT®-Plus). By combining CD4 and CD8 immune responses, QFT®-Plus may perform better among PLHIV. Therefore we investigated QFT®-Plus sensitivity for pulmonary TB (used as a surrogate for LTBI) in a Zambian TB clinic.

Methods

Between 06/2015-03/2016, consecutive smear or Xpert MTB/RIF positive adult (≥18 years) pulmonary TB patients, ≤2 days from starting TB treatment were recruited. Information on demographics, TB/HIV diagnosis and physical measurements were obtained. Body mass index (BMI) was defined as weight in Kg divided by height in m^2 and categorised as <18.5 underweight and ≥18.5 normal/overweight. Venous blood was collected for QFT®-Plus testing according to the manufacturer's specification. Positive results were defined using the manufacturer's thresholds (≥0.35 IU/ml); a positive result on either antigen tube (TB1 or TB2) was considered positive. Blood was collected for CD4 cell count estimation if TB/HIV co-infected. Sensitivity was defined as the number of positive QFT®-Plus results over the total number tested; the denominator included indeterminate results. To explore factors associated with positive QFT®-Plus results using logistic regression, negative and indeterminate QFT®-Plus categories were combined giving a binary variable. Due to the small number of negative/indeterminate results, individual factors were adjusted for age alone.





Results

Overall QFT®-Plus sensitivity among N=108 pulmonary TB patients was 83% (95% confidence interval [CI] 75-90%; Figure 1 and Table 1). 6/24 (25%) negative/indeterminate results by TB1 were positive on TB2.

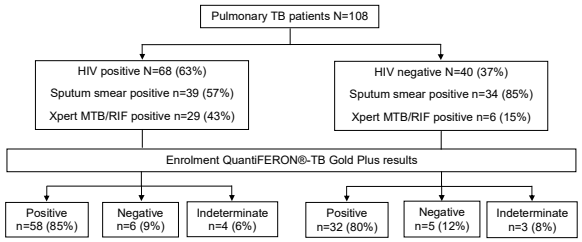


Figure 1: Patients with pulmonary TB enrolled to the study: HIV-status, microbiology results and QFT®-Plus results

Characteristics		n (%)
Age in years[n=104]	Median (IQR)	32 (27-38)
Gender[n=104]	Male	76 (73)
Any one of cough, fever, night sweats or weight loss[n=104]	Yes	104 (100)
Body mass index[n=104]	<18.5 Kg/m²	55 (53)
HIV-status	Positive	68 (63)
CD4 cell count category[n=52/68]	<100 cells/µl	8 (15)
QFT®-Plus result	Positive	90 (83)
	Negative	11 (10)
	Indeterminate	7 (7)

Table 1: Characteristics and QFT®-Plus results of N=108 pulmonary TB patients

There was no difference in sensitivity by HIV-status (HIV positive 85% [95%CI 75-93%; n=68] and HIV negative 80% [95%CI 64-91%; n=40]; p=0.59). The median interferon gamma concentration was significantly higher in TB2 compared to TB1 irrespective of HIV-status (Figure 2). Among those HIV negative, 2/10 (20%) negative/indeterminate results on TB1 were positive on TB2. Among PLHIV, 4/14 (29%) negative/indeterminate results on TB1 were positive on TB2. Among PLHIV, sensitivity was lower when CD4 cell counts were <100 cells/µl (50% [95%CI 16-84%]; n=8) compared with ≥100 cells/µl (89% [95%CI 75-96%]; n=44) (p=0.02).

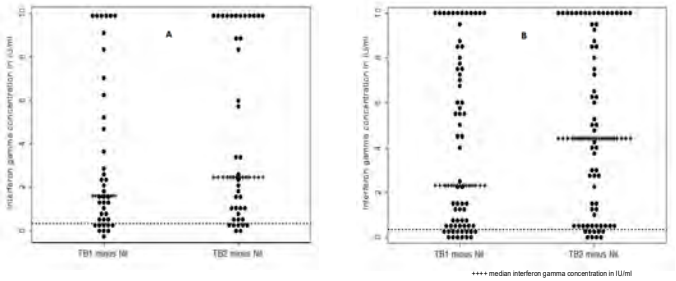


Figure 2: Dot plot of TB1 and TB2, minus the nil background interferon gamma concentration - A = HIV negative (n=40); B = PLHIV (n=68).

In models adjusted for age, CD4 cell count <100 cells/µl (odds ratio [OR] 0.15 [95%CI 0.02-0.96]; p=0.05), and, BMI <18.5 Kg/m^2 (OR 0.27 [95%CI 0.08-0.91]; p=0.02), were associated with decreased odds of positive QFT®-Plus results.

Comparison with QGIT and TST

A study conducted at the same clinic in 2007 using the same methods estimated QGIT and TST sensitivity in a similar population (Table 2). Overall QFT®-Plus, QGIT and TST sensitivity was similar. Compared to QGIT and TST, overall QFT®-Plus sensitivity was higher among PLHIV. While point estimates suggest QFT®-Plus sensitivity maybe higher than QGIT sensitivity in PLHIV with CD4 counts <100 cell/µl, the very small number in the stratum prevents firm conclusions.

Study features	Study in 2007		Study in 2015/16
	QGIT (n=112)	TST (n=92)	QFT-Plus (n=108)
Case definition	smear positive; ≤1 month of treatment		smear or Xpert positive; ≤2 days of treatment
TB-HIV co-infection	61%		63%
Median CD4 cell count among PLHIV	212 cells/µl		246 cells/µl
Sensitivity (%; 95% confidence interval)			
Overall	74 (66-82)	67 (58-77)	83 (75-90)
HIV positive	63 (50-74)	55 (40-70)	85 (75-93)
HIV negative	84 (71-96)	81 (62-92)	80 (64-91)
CD4 cell count <100 cells/µl	23 (5-54)	-	50 (16-84)
CD4 cell count 100-199 cells/µl	70 (46-88)	-	91 (59-99)
CD4 cell count 200-349 cells/µl	74 (52-90)	-	85 (62-97)
CD4 cell count ≥350 cells/µl	88 (75-95)	-	92 (64-99)

Table 2: The performance of QGIT, TST and QFT®-Plus among adults (≥18 years)

Conclusions

QFT®-Plus sensitivity was similar to QGIT and TST sensitivity for pulmonary TB, used as a surrogate for LTBI, but in contrast to these, overall sensitivity was not affected by HIV-status. However, QFT®-Plus sensitivity was lower among PLHIV with severe immunosuppression.

Disclosure

QIAGEN provided the QFT®-Plus kits free of charge for use in this study. They had no role in the study design, collection, analysis or interpretation of data or decision to publish findings. The views expressed are solely those of the study authors.