

Use of Interferon- γ Release Assays (IGRAs) in TB control in low and middle-income settings

- EXPERT GROUP MEETING -

Date and time: 20-21 July 2010, 09:00 – 18:00
Venue: Salle B, WHO-HQ, Geneva, Switzerland

BACKGROUND

Latent tuberculosis infection (LTBI) is conventionally detected through the use of the tuberculin skin test (TST). Despite its widespread use as a proxy for LTBI, TST effectiveness is, however, limited due to various factors, including antigen cross-reactivity. There has been growing research investment and scientific interest in the possibility to measure the immunological response in humans following exposure to mycobacterial antigens to reflect LTBI. Interferon- γ release assays (IGRAs) for TB measure the amount of interferon-gamma released by sensitized T cells after exposure *in vitro* to specific *M. tuberculosis* antigens, mainly ESAT-6 and CFP10. Two interferon- γ release assays are currently commercially available: the QuantiFERON-TB Gold (Cellestis Ltd, Carnegie, Victoria, Australia) assay, and the T-SPOT.TB test (Oxford Immunotec, Oxford, UK). A huge number of studies have been carried out over the last ten years in order to evaluate the utility and role of IGRAs in detecting LTBI. Data are also now accruing on the potential of IGRAs to identify individuals with LTBI at high risk of progression to active TB, while IGRAs are also being used in some settings to diagnose active TB. A variety of guidelines have been issued on the use of IGRAs in replacement of - or in combination with – TST, especially in low-burden, high-income countries.

WORLD HEALTH ORGANIZATION: EVIDENCE-BASED PROCESS FOR POLICY GUIDANCE

In order to facilitate rapid policy guidance on the use of new diagnostic tools, new methods, and/or novel approaches using existing tools, WHO has developed a systematic, structured, evidence-based process: The first step involves a systematic review and meta-analysis of available data, using standard methods appropriate for diagnostic accuracy studies. The second step involves the convening of an Expert Group to evaluate the strength of the evidence base and recommend operational and logistical considerations for mainstreaming such tools/approaches into national TB control programmes, and/or identify gaps to be addressed in future research. The third and final step involves WHO policy guidance on the use of these tools/approaches, presented to the WHO Strategic and Technical Advisory Group for TB (STAG-TB) for endorsement and subsequent dissemination to Member States for implementation.

MEETING OBJECTIVES

- To review the evidence base and evaluate data from systematic reviews on the performance characteristics of IGRAs for the diagnosis of *active TB disease* in adults and children in low- and middle-income settings;
- To review the evidence base and evaluate data from systematic reviews on the performance characteristics of IGRA for the diagnosis of *latent TB Infection* in the following populations in low- and middle-income settings:
 - child contacts of confirmed TB cases
 - HIV infected individuals
 - health care workers
- To review the evidence base and evaluate data from systematic reviews on the *predictive value* of IGRAs in low- and middle-income settings;
- To evaluate the cost-effectiveness of IGRAs in high-burden TB and HIV settings;
- To outline potential issues to be addressed by WHO in subsequent policy recommendations for the use of IGRAs in low- and middle-income settings.

EXPECTED OUTCOMES

- Evidence-based recommendations on the use of IGRAs for the diagnosis of active TB disease in low- and middle-income settings;
- Evidence-based recommendations on the use of IGRAs for the diagnosis of latent TB infection in child contacts of confirmed TB cases, HIV infected individuals and health care workers;
- Evidence-based recommendations on the use of IGRAs to identify populations at high-risk of development of active TB;
- Assessment of the cost-effectiveness of IGRAs in high-burden TB and HIV settings.

PROVISIONAL AGENDA

Tuesday, 20 July 2010

Chair and co-chair: H. Schünemann and K. Weyer

Rapporteur: To be confirmed

09:00 – 09:10	Welcome	M. Raviglione, WHO R. Ridley, TDR
09:10 – 09:20	Meeting scope and objectives	K. Weyer
09:20 – 09:30	Declaration of Interest by Expert Group members	K. Weyer
09:30 – 10:00	Grading quality of evidence and strength of recommendations: Brief overview of GRADE	H. Schünemann
10:00 – 10:15	Questions	
10:15 – 10:45	BREAK	
10:45 – 11:15	<i>Systematic review and meta-analysis:</i> IGRAs for the diagnosis of active pulmonary TB in low- and middle-income countries	J. Metcalfe/K. Steingart
11:15 – 12:00	Discussion	All
12:00 – 12:30	Draft recommendations: Use of IGRAs in diagnosing active pulmonary TB in low- and middle-income countries	All
12:30 - 13:30	LUNCH	
13:30 - 14:00	<i>Systematic review and meta-analysis:</i> IGRAs for the detection of <i>M. tuberculosis</i> infection in children	A. Detjen
14:00 – 14:45	Discussion	
14:45 – 15:15	Draft recommendations: Use of IGRAs in detection of TB infection in children	All
15:15 - 15:30	BREAK	
15:30 – 16:00	<i>Systematic review and meta-analysis:</i> IGRAs for screening of contacts of TB cases and in outbreak investigations	A. Zwerling/M. Pai
16:00 – 16:30	Discussion	All
16:30 - 17:00	Draft recommendations: Use of IGRAs in contacts of TB cases and outbreak investigations	All
17:00 - 17:30	Field evaluation studies of Quantiferon-TB Gold In Tube in high-burden countries	R. O'Brien
17:30 - 18:00	Discussion	All

Wednesday, 21 July 2010

Chair and co-chair: H. Schünemann and C. Lienhardt

Rapporteur: To be confirmed

08:30 – 09:00	<i>Systematic review and meta-analysis:</i> IGRAs for the diagnosis of latent tuberculosis infection in HIV-infected individuals	A. Cattamanchi/K. Steingart
09:00 – 9:30	<i>Systematic review and meta-analysis:</i> IGRAs for screening of TB infection prior to isoniazid preventive therapy	A. Date
9:30 – 10:15	Discussion	All
10:15 – 10:45	Draft recommendations: Use of IGRAs in HIV-infected individuals	All
10:45 – 11:15	BREAK	
11:15 – 11:45	<i>Systematic review and meta-analysis:</i> IGRAs for tuberculosis screening of health care workers	A. Zwerling/M. Pai
11:45 – 12:30	Discussion	All
12:30 – 13:00	Draft recommendations: Use of IGRAs in health care workers screening	All
13:00 – 14:00	LUNCH	
14:00 – 14:30	<i>Systematic review:</i> Predictive value of IGRAs for incident active TB disease in low-, middle- and high-income countries	M. Rangaka/M. Pai
14:30 – 15:15	Discussion	All
15:15 – 15:30	BREAK	
15:30 – 16:30	Review of GRADE process and summaries	K. Weyer
16:30 – 17:00	Final recommendations	C. Lienhardt
17:00 – 17:30	Closing	M. Raviglione

