MaHTAS
Malaysian Health Technology Assessment Section

T.SPOT.TB ASSAY – AN UPDATE
Executive Summary
[Adapted from the report by NOORMAH MOHD DARUS]

Review Group Membership

MaHTAS Reviewer:
Noormah Mohd Darus
Datin Dr. Rugayah Bakri

External Reviewer:

For further information please contact:

Health Technology Assessment Section (MaHTAS)
Medical Development Division
Ministry of Health Malaysia
Level 4, Block E1, Precinct 1
Government Office Complex
62590 Putrajaya.

Tel: 603 8883 1246

Fax: 603 8883 1230

Available at the following website:
http://www.moh.gov.my

2014

Introduction
Tuberculosis (TB) is still the most common deadly infectious disease worldwide. Despite ongoing advances in medical prevention, detection, and treatment, the global prevalence of TB remains high, with an incidence at approximately 9.2 million cases in 2006. The current treatment strategy for active TB is not adequate for disease elimination, partially owing to latent TB infection (LTBI), which may not be identified initially but can develop into an active disease after a certain period of latency. It has been estimated that one third of the world population has LTBI. People with LTBI can serve as potential reservoirs for future acute infections if the host immune system is compromised due to aging, corticosteroid medications, and/or immunodeficiency conditions such as HIV infection. Therefore, identifying and treating people with LTBI are crucial for TB control, especially in low endemic geographic areas (eg, the United States) and high-risk populations (eg, health care workers).

Although the finding of tubercle bacilli is necessary for the diagnosis of active TB, there is no gold standard test for the diagnosis of LTBI. Until recently; it was the only available diagnostic method to screen for LTBI. Although traditionally widely accepted, Tuberculin skin test (TST) is not an ideal diagnostic tool. Because purified protein derivative (PPD) used in the TST is a mixture of more than 200 Mtb antigens, most of which are highly homologous to the antigens in bacillus Calmette-Guérin (BCG) vaccines and non–tuberculosis mycobacterium (NTM) species, TST response has been known to be affected by prior BCG vaccination and/or NTM infection. To overcome the relatively low specificity associated with TST, antigens encoded in the region of difference (RD1) of the Mycobacterium tuberculosis (Mtb) genome were studied to develop T lymphocyte–based interferon (IFN)-γ release assays (IGRAs), which became commercially available in 2005. Two IGRA systems using RD1-encoded antigens are currently commercially available for TB detection. One system includes QuantiFERON-TB Gold (QFT-G) and its variant QuantiFERON-TB Gold In-Tube (QFT-GIT) (Cellestis, Carnegie, Australia), both use whole blood specimen to measure IFN-γ released by antigen-activated T lymphocytes. In those QFT assays, enzyme-linked immunosorbent assay (ELISA) is used to measure the concentration of IFN-γ released into plasma supernatant. The other system, T-SPOT.TB (Oxford Immunotec, Oxford, England), uses the ELISpot method to measure INF-γ-secreting T cell counts (“spots”) on stimulation by Mtb-specific antigens in microplate wells.

This review was requested by Dr. Jiloris F. Dony from Disease Control Division, Ministry of Health Malaysia (MOH) to assess the usefulness of T.SPOT.TB for the diagnosis of latent tuberculosis to strengthen the control of tuberculosis program in the Public Health Division, MOH.

Objective/Aim
The objective of this systematic review was to assess the effectiveness and economic as well as organizational implication of T.SPOT.TB in the diagnosis of latent tuberculosis.

Results and Conclusions

A total of 905 titles were identified through the Ovid interface and PubMed. Fifteen articles related to the diagnosis of latent tuberculosis using T.SPOT.TB was included in this review consisting of one systematic review and fourteen cross sectional studies. The studies were conducted in Switzerland, United Kingdom, Spain, Iran, China, Saudi Arabia, Brazil, Uganda, Ireland, Korea, United States and Canada.

From the above review it was found that T.SPOT.TB has low agreement between TST and both IGRAs test (T.SPOT.TB and QFT-GIT). Both IGRAs tests have lower sensitivity but higher specificity for diagnosing latent TB infection.

There was moderate level of evidence to show that T-SPOT.TB, but not TST, was able to identify those individuals who had been occupationally exposed to smear-positive TB patients. This suggests that in a high TB burden health-care setting T-SPOT.TB may

provide an accurate, targeted method of diagnosing LTBI.

In patients with SLE, those receiving corticosteroids (irrespective of dose) and/or other immunosuppressive drugs, the result of the TST can be affected, increasing the number of false negatives. In these cases, T.SPOT.TB test may be the diagnostic technique of choice.

Methods

Electronic databases were searched through the Ovid interface: Ovid MEDLINE® In-process and other Non-indexed citations and Ovid MEDLINE® 1948 to present, EBM Reviews - Cochrane Central Register of Controlled Trials – August 2014, EBM Reviews - Cochrane Database of Systematic Reviews - 2009 to August 2014, EBM Reviews - Health Technology Assessment – 2nd Quarter 2014, EBM Reviews - Database of Abstracts of Reviews of Effects – 2nd Quarter 2014, EBM Reviews – NHS Economic Evaluation Database 2nd Quarter 2014, Embase – 1988 to 2014 week 35. Searches were also run in PubMed. Google was used to search for additional web-based materials and information. No limits were applied. Additional articles were identified from reviewing the references of retrieved articles. Last search was conducted on 1st September 2014.