Reviewer's report

Title: Use of a T cell interferon gamma release assay in the investigation for suspected active tuberculosis in a low prevalence area

Version: 1 Date: 23 January 2009

Reviewer: Jean-Pierre Zellweger

Reviewer's report:

This is a good paper, presenting the results of performing Interferon-Gamma Release Assays (IGRAs) in a group of patients with suspected TB, to assess if this test would have a sufficient positive and negative value to be of use for the diagnosis of TB. The results are disappointing (as could be expected from the existing literature) in that the IGRAs do not add a useful information for the diagnosis of tuberculosis, at least in the pulmonary forms. The results are clear, the paper is well written.

Three main comments:

First, do we need this information, as there are already several papers describing similar results - although in other settings. The only originality of the paper is the demonstration that IGRAs may be of use for supporting the diagnosis of extrapulmonary TB. The authors rightly conclude that IGRAs are not a standard diagnostic method for the diagnosis of TB, at least for pulmonary. For extrapulmonary, they omitted to mention studies comparing the yield of IGRAs in blood and body fluids (pleural fluid, CSF) (see Jafari ERJ 2008). The authors should also clearly state that the established place of IGRAs is for the detection of LTBI (for instance after exposure)

The second main comment is the fact that the authors do not discuss at all the problem of cut-off for the interpretation of IGRAs. This has been addressed in several papers, and proposals have been made for modifying the cutoffs for positivity, both for Quantiferon and T-SPOT (see Janssens ERJ 2007, Goletti PLoS One 2008, Soysal IJTLT 2008, Kang Chest 2007, Veerapathan PLoS One 2008). As the authors do not indicate the level of positivity of the individual tests, it is difficult to compare their data with data from other studies.

Furthermore, the high rate of indeterminate and (false-)negative in active TB is surprising. Although the authors give some immunological reasons for these results, they do not address the technical aspects which may be linked with indeterminate or negative results (see Doherty J Immunol Methods 2005 and Beffa ERJ 2008)

Minor comments:

Abstracts: Results: pulmonary TB disease... and extrapulmonary manifestations of TB.
Background: "Sweden has....the ability of new diagnostic methods to detect patients with TB or LTBI..."

Study population: did the authors record the risk factors for TB exposure among foreign-born patients in the control group (to assess the probability of LTBI)?

Results: among the "other parameters", it would be interesting to know if the clinical signs and the history of exposure was similar or different between the patients with positive and negative IGRAs

Negative results in patients with TB: 22/44 is one of the highest rate reported in the literature. Did the authors re-checked the patients with ELISPOT/T-SPOT.TB? or with the Qantiferon-In Tube assay?

In the sentence "Among 52 immigrants...", it is not clear if the "subjects" are patients or control

Factors associated with QFT-G results: were age and origin related to the results?

Discussion: the main objections are mentioned above

Tables: Tab 2a and 2b should indicate the N in both columns for TB and other clinical diagnosis. IN Tab 3a, the SS+ and SS- should be mentioned after the pulmonary TB (13 and 9 are subcategories of 22)

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I have received a travel fee from Oxfordimmunotec for attending a meeting at CDC in 2008