Reviewer’s report

Title: T-SPOT.TB responses during treatment of pulmonary tuberculosis

Version: 1 Date: 26 October 2008

Reviewer: Charles von Reyn

Reviewer’s report:

The authors have performed the commercial T spot test on frozen PBMCs from a population of HIV-negative patients treated for TB in Brazil. They conclude that although responses generally diminish with treatment there is marked variability in the patterns of change and that this test does not appear to have clinical utility for assessing response to treatment.

Major compulsory revision:

1. There is insufficient attention given in the methods, results and discussion to the fact that the commercial test is designed to be tested on fresh cells and that the authors used frozen cells. The critical controls are missing – performing the test on fresh cells and then on a separate aliquot from the same sample after the maximum duration of freezing. It is conceivable, for example, that the baseline samples (frozen for the longest time) gave falsely low SPCs and thereby reduced the chances of detecting a fall in response with treatment. Either these controls need to be added to show the results are equivalent or the conclusion needs to be that use of the T spot with frozen cells does not have clinical utility in this setting. That the test was performed on frozen cells should be mentioned in the title.

2. Results: The authors give eligibility but no consort diagram for the number of subjects screened to arrive at the final 58 subjects.

3. Were the isolates all drug sensitive? If not, T spot decreases would not be expected. Drug resistant cases would need to be analyzed separately.

Minor revisions

4. Abstract: Should clarify this was a study in HIV-negative subjects (with one HIV negative in parentheses); it would have been better to exclude this one patient since immunsuppression may affect T spot results. If the patient is retained the CD4 count should be given in the results.

5. Background: ‘correlate more closely...’. With what?

6. Methods: Why was there no T spot test at 8 weeks of treatment, which was the timing of the primary endpoint of the parent trial?

7. Methods: As with freezing the authors should clarify if their method of defining a reactive test followed manufacturer’s instructions or represents their own method.
8. Can the authors correlate quantitative microbiologic data (# AFB, # CFUs) with T spot responses? This would have been preferable to the radiologic surrogate of a presumed higher organism burden in cavitary TB.

9. Was overall treatment success equal with the 2 drug regimens? If not, T spot results should be stratified by regimen.

**Level of interest:** An article whose findings are important to those with closely related research interests

**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 modest direct research support from Oxford Immunotech for studies with the commercial T spot assay; I have not received salary support and have no financial interest in the company.