

When precision is required

QuantiFERON[®]-TB Gold | TNF- α inhibitor



Trusted Partner



www.QuantiFERON.com

Increased risk of active TB

- Tuberculosis (TB) exists as active disease or latent infection (LTBI)
 - Compared to the general population, patients on tumor necrosis factor-alpha (TNF- α) inhibitor therapy are at 4- to 8-fold increased relative risk of developing active TB^{1,2}
 - Patients on steroid hormone therapy have a >5-fold increased risk of progressing to active TB³

TNF- α inhibitor therapies can increase the risk of LTBI progressing to active TB^{1,2}

Improved testing for TB infection is now available

- QuantiFERON-TB Gold is a modern alternative to the tuberculin skin test (TST or Mantoux)⁴
- QuantiFERON-TB Gold is a blood test for TB infection. It measures the cell-mediated immune response (cytokines) to very specific TB antigens. It is an interferon-gamma (IFN- γ) release assay, commonly known as an IGRA⁴

IGRAs are emerging as standard practice in LTBI diagnosis across the world⁴



International guidelines and recommendations indicate IGRA for screening patients on TNF- α inhibitors for LTBI

IGRAs are an aid to the diagnosis of *Mycobacterium tuberculosis* infection and should be used in conjunction with detailed medical history and chest X-ray.^{4,6}

International Guidelines and recommendations

| | Guideline or position statement |
|--|--|
| Use of an IGRA alone | Germany Switzerland Japan Bulgaria Poland Austria |
| Use either an IGRA or TST | Australia (Australian Rheumatology Association) Denmark (IGRA favoured) France (IGRA preferred) USA (US CDC) ^{28*} Bosnia & Herzegovina ²⁹ |
| Use both an IGRA and TST | European Centre for Disease Prevention and Control (ECDC) UK (alternatively IGRA alone) USA (may be considered if either initial test negative; US CDC) ^{4**} Portugal Czech Republic Croatia Slovakia South Korea The Netherlands Ireland (TST preferred) |
| TST followed by an IGRA if TST negative | Canada Italy Spain Saudi Arabia |
| TST followed by an IGRA if TST positive | Spain Norway |
| TST alone | Brazil |
| No recommendations | Finland Australia (National TB Advisory Committee) |

Table adapted from Denkinger CM et al. 2011.⁷ IGRA: interferon-gamma release assay; TST: tuberculin skin test. Some countries are listed multiple times because recommendations vary across risk groups. *Guidance for immune-suppressed patients; no specific guidance for TNF- α inhibitor therapy. **Situation 1, p11

QuantiFERON-TB Gold detects TB-specific immune response⁸

Designed for specificity and unaffected by BCG vaccination status

| | ESAT-6 | CFP-10 | TB-7.7 |
|--------------------------------|--------|--------|--------|
| QuantiFERON-TB Gold | ✓ | ✓ | ✓ |
| <i>M. tuberculosis</i> complex | ✓ | ✓ | ✓ |
| Environmental strains* | - | - | - |
| All 8 BCG substrains | - | - | - |

*Except *M. kansasii*, *M. marinum*, *M. szulgai*.

More accurate than TST in immune-suppressed patients^{9,10}

Moderate-to-severe psoriasis¹¹



9 out of 50 patients were TST positive and QuantiFERON-TB Gold negative prior to TNF- α inhibitor

None developed active TB over 12 months

Rheumatic disease¹²

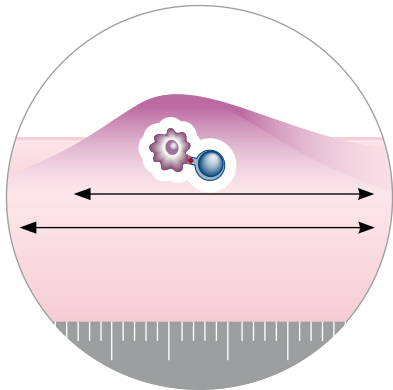
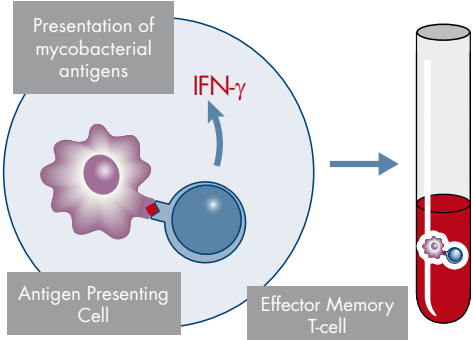


16 out of 107 patients were TST positive and QuantiFERON-TB Gold negative prior to TNF- α inhibitor

None developed active TB over 24.5 months

Meaningful results you can use in patients with rheumatic disease

Reduces unnecessary treatment of false-positives due to TST ^{11,13}

| | TST ⁴ | QuantiFERON®-TB Gold ⁸ |
|-------------------------------------|--|---|
| |  |  |
| | General response to tuberculin PPD mix | Tests for effector memory T-cell response to TB using specific proteins only found in TB |
| Cross reactivity with BCG | Possible/likely | No |
| Cross reactivity with non-TB | Possible/likely | No* |
| Controlled test | No | Yes (positive and negative controls included in the assay design) |
| Objectivity | Measures skin induration, highly subjective, high inter/intra-observer variability | Quantitative detection of IFN-γ |

*Except *M. kansasii*, *M. marinum*, *M. szulgai*. BCG: Bacillus Calmette-Guérin; PPD: purified protein derivative; TB: *M. tuberculosis*.

Reliable results in immune suppressed patients




| Patient Group | QuantiFERON-TB Gold Differentiator | QuantiFERON-TB Gold Benefit |
|--|--|---|
| Patients with prior BCG vaccination | Unlike TST, results are unaffected by prior BCG vaccination ^{12,14,15} | Eliminates false-positive results associated with BCG ^{12,15} |
| <p>Patients with rheumatic disease</p> <ul style="list-style-type: none"> ■ Rheumatoid arthritis ■ Ankylosing spondylitis ■ Juvenile rheumatoid arthritis <p>Patients on immune suppressive therapies</p> <ul style="list-style-type: none"> ■ Methotrexate ■ Prednisolone ■ 5-ASA ■ Azathioprine ■ Intramuscular injections of betamethasone, triamcicolon or methyl-prednisolone | <ul style="list-style-type: none"> ■ Less affected than TST by immune suppressive therapies in patients with rheumatic diseases^{9,16} ■ Identifies false-negative TST results^{9,17} ■ Positive control provides indication of a patient's ability to respond to an immune challenge⁸ | More accurately identifies those patients who have TB infection and are at greater risk of developing active TB ^{9,11,16,17} |
| Patients with prior QuantiFERON-TB Gold test | Unlike TST, no boosting of results created by prior testing ¹⁸ | Ideal for serial screening |
| Patients with history of TST* | Unlike TST, no boosting of results in LTBI-negative patients ¹⁸ | Ideal for serial screening |

*Defined as TST administered more than 28 days prior to QuantiFERON-TB Gold¹⁸

Reliable, meaningful results

Changing the way the world looks at TB

The test is performed by collecting whole blood (1 mL) into each of three blood collection tubes. Tubes are incubated at 37°C for 16 to 24 hours. The IFN- γ concentration in the plasma is determined using a sensitive ELISA.⁸

| | |
|--|--|
| <p>TB Antigen tube Assesses IFN-γ response to highly-specific TB antigens.</p> |  |
| <p>Mitogen tube (Positive control) Can be useful to indicate</p> <ul style="list-style-type: none"> ■ Patient's immune status ■ Correct blood handling and incubation <p>Note: a low-mitogen result, in conjunction with a negative TB result, is classified as an "indeterminate".</p> |  |
| <p>Nil tube (Negative control) Adjusts for background noise.</p> |  |

Interpretation criteria for QuantiFERON-TB Gold

| Interpretation | TB specific antigen response (IU/mL)* | Nil control (IU/mL) | Mitogen control (IU/mL)* |
|----------------------|---|------------------------|--------------------------|
| Positive | ≥ 0.35 (and $\geq 25\%$ of Nil) | ≤ 8.0 | any |
| Negative | < 0.35 (and $< 25\%$ of Nil) | ≤ 8.0 | ≥ 0.5 |
| Indeterminate | < 0.35 (and $< 25\%$ of Nil) | ≤ 8.0 second line | < 0.5 |
| | any | > 8.0 | any |

*Corrected for Nil response.

Changing the way the world looks at TB

- Unaffected by prior BCG vaccination^{12,15}
- High sensitivity in patients with rheumatic disease^{11,13,14}
- High specificity, virtually eliminating false-positive results seen with TST^{11,19}
- Proven performance in patients on immune suppression therapies (methotrexate, corticosteroids, TNF- α inhibitors)^{11,16,17}
- Does not boost subsequent test results, ideal for serial testing¹⁸
- Provides an objective, reproducible result unaffected by subjective interpretation^{8,15}

QuantIFERON®-TB Gold (QFT®) is CE marked. QFT is approved by the US FDA.

QFT is approved by the FDA as an *in vitro* diagnostic aid for detection of *Mycobacterium tuberculosis* infection. It uses a peptide cocktail simulating ESAT-6, CFP-10 and TB7.7(p4) proteins to stimulate cells in heparinized whole blood. Detection of IFN- γ by ELISA is used to identify *in vitro* responses to these peptide antigens that are associated with *M. tuberculosis* infection. FDA approval notes that QFT is an indirect test for *M. tuberculosis* infection (including disease) and is intended for use in conjunction with risk assessment, radiography and other medical and diagnostic evaluations. QFT Package Inserts, available in up to 25 different languages, can be found at www.cellestis.com.

References: 1. Winthrop KL *et al. Arthritis Rheum* 2005; 52:2968–2974. 2. Gardam MA *et al. Lancet Infect Dis* 2003; 3:148-155. 3. Cisneros JR and Murray KM. *Ann Pharmacother* 1996; 30:1298–1303. 4. Mazurek GH *et al. Centers for Disease Control and Prevention. Updated Guidelines for Using Interferon Gamma Release Assays to Detect Mycobacterium tuberculosis Infection. MMWR* 2010; 5:1-28. 5. Diel R *et al. Pneumologie* 2009; 63:329-334. 6. Beglinger C *et al. Swiss Med Wkly* 2007; 137:621-622. 7. Denkinge CM *et al. Clin Microbiol Infect* 2011; 17:806-814. 8. QuantIFERON®-TB Gold Package Insert, July 2011. 9. Matulis G *et al. Ann Rheum Dis* 2008; 67:84-90. 10. Ponce de Leon D *et al. J Rheumatol* 2008; 35:776-781. 11. Garcovich S *et al. J Eur Acad Derm Venereol* 2011; article accepted in press; DOI: 10.1111/j.1468-3083.2011.04220.x. 12. Chang B *et al. Clin Rheumatol* 2011; article accepted in press; DOI: 10.1007/s10067-011-1771-9. 13. Kwakernaak AJ *et al. Clin Rheumatol* 2011; 30:505-510. 14. Pratt A *et al. Rheumatology* 2007; 46:1035–1036. 15. Chiu H-Y *et al. Br J Dermatol* 2011; 164:553-559. 16. Inanc N *et al. J Rheumatol* 2009; 36:2675-2681. 17. Sauzullo I *et al. Int J Tuberc Lung Dis* 2010; 14(7):834-840. 18. van Zyl-Smit R *et al. Am J Respir Crit Care Med* 2009; 180(1):49-58. 19. Cobanoglu N *et al. Int J Tuberc Lung Dis* 2007; 11:1177–1182.

© QIAGEN 2012 M05995314B

Cellestis, a QIAGEN Company

World Headquarters ▪ Cellestis International ▪ +61 3 8527 3500 ▪ info@cellestis.com

Asia/Pacific ▪ QIAGEN Singapore PTE Ltd ▪ +65 6854 8100 ▪ asiapac@cellestis.com

Australia/New Zealand ▪ Cellestis International ▪ +61 3 8527 3500 ▪ anz@cellestis.com

Europe/Middle East ▪ Cellestis GmbH ▪ +49 6151 428 590 ▪ europe@cellestis.com

Japan/Korea ▪ QIAGEN KK ▪ +81 3 6890 7300 ▪ jp.kr@cellestis.com

North America/South America ▪ Cellestis Inc ▪ +1 661775 7480 ▪ customer.service@cellestis.com

