Anti-TNF- $\alpha$  therapy:

## Have you tested for TB?



Sample to Insight

# Published data indicate that TB blood tests, like QuantiFERON-TB Gold Plus, may provide more accurate detection of TB infection prior to anti-TNF- $\alpha$ therapy.

#### Testing for TB is critical prior to anti-TNF- $\alpha$ therapy

TNF- $\alpha$  inhibitor recipients face an increased risk of developing active TB

Autoimmune disorders such as rheumatoid arthritis, inflammatory bowel disease and Crohn's disease are commonly treated with biologics to slow progression of the disease. Unfortunately, biologics such as TNF- $\alpha$  inhibitors can also increase the likelihood that patients carrying latent TB infection will progress to active TB (1–3). As a result, many biologic treatments carry a warning stating that TB infection should be investigated and treated prior to initiating therapy.

- More than one third of the world's population is believed to carry latent TB infection (4)
- Patients receiving TNF-α inhibitor therapy face up to a 9-fold increased relative risk of developing active TB (5)
- TB reactivation risk should be evaluated in all patients prior to biologic therapy (2, 6)



### Published data indicate that QuantiFERON technology may provide more accurate detection of TB infection prior to start anti-TNF- $\alpha$ treatment

Studies performed among patients with chronic immune diseases have reported improved performance by detecting TB infection with QuantiFERON technology compared to the tuberculin skin test (TST) (1, 2, 7–10).

"In a TB-endemic population, the QuantiFeron-TB Gold In-Tube assay seemed to be a more accurate test for detection of LTBI in RA patients compared with the TST, and may potentially improve the targeting of prophylactic therapy before treatment with anti-TNF agents." – Ponce de Leon (2008) Published studies identify potential benefits of testing with QuantiFERON technology prior to  $TNF-\alpha$  inhibitor therapy:



- In a prospective study 142 Rheumatoid Arthritis (RA) patients, QuantiFERON-TB Gold results were more strongly associated with TB risk factors (odds ratio 23.8) than the TST (odds ratio 2.8) (1).
- In a cross-sectional study of 101 RA patients and 93 controls, the rate of TST positivity in RA patients was only 41% of that for the controls significantly lower than for QFT, where positivity was 75% of that for controls. (7).
- Among 79 children screened with TST and QFT prior to TNF-a treatment, the odds of a
  positive QFT result increased by a factor of 27.6 among patients with risk factors for TB,
  whereas the TST showed no positive correlation (8).

"[Our] findings suggest that the sensitivity of the QFT for the diagnosis of LTBI could be higher than that of the TST in patients with RA, even in cases of RA immunosuppression." -Ponce de Leon (2008)



 In a retrospective study of 2282 RA patients pooling data from 5 large randomly controlled trials, the rate of indeterminates with IGRAs upon retesting was only 1.8%. This study described a large discordance between QFT and TST, with TST displaying significantly higher positivity in BCG-vaccinated patients compared to QFT (9).

"In the absence of a true gold standard for latent TB infection, results of this comparison of IGRA and TST in a large cohort of patients with rheumatic diseases suggest that the IGRA provides greater specificity and possibly greater sensitivity than the TST" -Hsia (2012)



In a cost-effectiveness study among immunosuppressed inflammatory bowel disease (IBD) patients in a low incidence setting, testing with QFT resulted in 1.85 TB reactivations per 1000 patients vs. 6.7 with the TST (3).

"Under a broad range of parameter values, the QFT-G strategy dominates the TST strategy in cost-effectiveness. Consideration should be given to QFT-G as the preferred method of identifying latent TB in all immunosuppressed IBD patients." -Swaminath (2013)



 In a study of 429 RA patients spanning 15 hospitals, antibiotics were required for 177 patients (45.2%) if positive TST results were included in the LTBI definition, but only 84 patients (21.4%) if TST results were replaced with QTF-Gold IT results (10).

"Replacing TST with IGRA for determining LTBI allowed the proportion of patients with immune mediated inflammatory diseases needing prophylactic anti-TB antibiotics before beginning anti-TNF agents to be reduced by half" -Mariette (2012)

#### QuantiFERON-TB Gold Plus – four tubes, one clear result

- Highest accuracy of any test for TB infection
- Single patient visit and unaffected by prior BCG vaccination
- Automatable and scalable for high-throughput testing laboratories



Before you initiate TNF- $\alpha$  inhibitor therapy, trust QuantiFERON-TB Gold Plus for accurate TB detection. For more information, contact your QIAGEN sales representative or visit **www.QuantiFERON.com**.

#### **References:**

- Matulis, G., Juni, P., Villiger, P.M., and Gadola, S.D. (2008) Detection of latent tuberculosis in immunosuppressed patients with autoimmune diseases: performance of a Mycobacterium tuberculosis antigen-specific interferon gamma assay. Ann. Rheum. Dis. 67, 84–90.
- Cantini, F., et al. (2017) Risk of tuberculosis reactivation in patients with Rheumatoid Arthritis, Ankylosing Spondylitis, and Psoriatic Arthritis receiving non-anti-TNF-targeted biologics. Mediators Inflamm. 2017:8909834
- Swaminath, A. Bhadelia, N., and Wang, Y.C. (2013) Cost-effectiveness of QuantiFERON testing before initiation of biological therapy in inflammatory bowel disease. Inflamm. Bowel Dis. 19, 2444–2449.
- World Health Organization. Tuberculosis Fact Sheet. http://www.who. int/mediacentre/factsheets/fs104/en/. Accessed Sept 18 2017.
- Lobue, P. and Menzies, D. (2010) Treatment of latent tuberculosis infection: An update. Respirology. 15, 603.
- World Health Organization. (2015) Guidelines on the management of latent tuberculosis infection. WHO/HTM/TB/2015.01.

- Ponce de Leon, D., et al. (2008) Comparison of an interferon-gamma assay with tuberculin skin testing for detection of tuberculosis (TB) infection in patients with rheumatoid arthritis in a TB-endemic population. J. Rheumatol. 35, 776–781.
- Gabriele, F., et al. (2017) Performance of QuantiFERON®TB Gold In-Tube assay in children receiving disease modifying anti-rheumatic drugs. World J. Pediatr. doi: 10.1007/s12519-017-0050-5. [Epub ahead of print].
- Hsia, E.B., et al. (2012) Interferon- release assay versus tuberculin skin test prior to treatment with golimumab, a human anti-tumor necrosis factor antibody, in patients with rheumatoid arthritis, psoriatic arthritis, or ankylosing spondylitis. Arthritis Rheum. 64, 2068–2077.
- Mariette, X., et al. (2012) Influence of replacing tuberculin skin test with ex vivo interferon release assays on decision to administer prophylactic antituberculosis antibiotics before anti-TNF therapy. Ann. Rheum. Dis. **71**, 1783–1790.

QuantiFERON-TB Gold Plus (QFT.Plus) is an in vitro diagnostic aid for detection of infection (including disease) and is intended for use in conjunction with risk assessment, radiography and other medical and diagnostic evaluations. QFT.Plus results alone cannot distinguish active TB disease from latent infection. QFT.Plus Package Inserts, available in multiple languages, as well as up-to-date licensing information and product-specific disclaimers can be found at www.QuantiFERON.com.

Trademarks: QIAGEN®, Sample to Insight®, QuantiFERON®, QFT® (QIAGEN Group). Registered names, trademarks, etc., used in this document, even when not specifically marked as such, are not to be considered unprotected by law. PROM-11448-001 09/2017 1108404 © 2017 QIAGEN, all rights reserved.

Ordering www.qiagen.com/shop | Technical Support support.qiagen.com | Website www.QuantiFERON.com