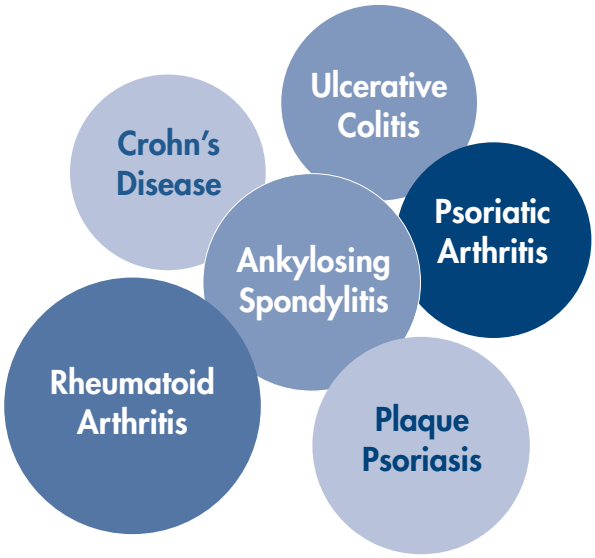
Modern TB testing is critical prior to receiving TNF inhibitors



Biologic recipients face an increased risk of 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-α inhibitors also increase the likelihood that patients carrying latent TB infection will progress to active TB (1–3).

- More than 13 million people in the U.S. are believed to carry latent TB infection (4).
- Patients receiving TNF-α inhibitor therapy are at 9-fold increased relative risk of developing active TB (5).
- TB reactivation risk should be evaluated in all patients prior to biologic therapy (6, 7).

The American College of Rheumatology recommends TB testing with an IGRA (6)

The American College of Rheumatology recommends TB testing of rheumatoid arthritis (RA) patients with either an Interferon Gamma Release Assay (IGRA) or Tuberculosis Skin Test (TST) before starting biologic agents. IGRAs are preferred for patients who have received prior BCG vaccination (6).

The CDC, ATS and IDSA preferentially recommend IGRA testing for the majority of the U.S. testing population (7)

- IGRA testing is preferred over the TST for individuals unlikely to be infected but for whom testing is required, and for those who are likely to be infected with low to moderate risk of disease progression.
- IGRA testing recommendations apply to all risk groups, regardless of BCG vaccination status or nationality of birth.
- For those likely to be infected and at high risk of progression, dual testing with IGRA and TST should be considered, with a positive result from either test as evidence of infection.

QuantiFERON®-TB Gold Plus is an IGRA to detect TB infection

QuantiFERON-TB Gold Plus (QFT®-Plus) is one IGRA available to detect TB infection. QFT-Plus requires only one patient visit, is not affected by BCG vaccination and is optimized to detect both CD4 and CD8 T cell responses. Published studies describe the use of QuantiFERON technology to detect tuberculosis infection in patients with autoimmune disorders.

Table 1. Peer reviewed publications using QuantiFERON technology in patients with autoimmune disorders

Publication	Results
Matulis, G., et. al. (2008) Ann. Rheum. Dis. **67**, 84–90.	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).
Hsia, E.B., et al. (2012) Arthritis Rheum. **64**, 2068–2077.	In a retrospective study of 2282 RA patients pooling data from 5 large randomly controlled trials, the rate of indeterminates with QFT upon retesting was only 1.8%. A large discordance between QFT and TST was found, with TST displaying significantly higher positivity in BCG-vaccinated patients.
Mariette, X., et al. (2012) Ann. Rheum. Dis. **71**, 1783–1790.	In a study of 429 RA patients spanning 15 hospitals, antibiotics were required for 177 patients (45.2%) when a positive TST result was included in the LTBI definition, but only 84 patients (21.4%) if TST results were replaced with QFT results.
Swaminath, A., et al. Inflamm. Bowel Dis. **19**, 2444–2449.	In a cost-effectiveness study among immunosuppressed 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.
Matsumura, R., et al. (2016) Int. J. Tuberc. Lung Dis. **20**, 1546–1553.	In a prospective study of 230 RA patients, 8.3% were QFT-positive. Age >60 years and suspicion of TB based on chest X-ray were selected as independent factors for QFT positivity with adjusted odds ratios of 4.73 and 3.25.
Gabriele, F., et al. (2017) World J. Pediatr. **13**, 472–478.	Among 79 children screened with TST and QFT prior to TNF-a treatment, a positive QFT result was 27.6 times more likely among patients with risk factors for TB, while the TST showed no positive correlation.
Sargin, G., et al. (2018) Tuberk Toraks **66**, 136–143.	In a study of 109 BCG-vaccinated patients diagnosted with RA and AS, QFT displayed 86% specificity and 74% sensitivity. QFT performed better than both T-SPOT.TB (74%/67%) and the TST (60%/48%) in the same patient population.
Jeong, D.H., et al. (2018) PLoS One **13**, e0198756.	In a study of 266 RA and 210 AS patients, the percentage of patients requiring LTBI treatment dropped from 43.8% to 32.6% when testing with QFT alone compared to dual testing with both TST and QFT – with no increase in adverse outcomes.
Vortia, E. et al. (2018) Inflamm Bowel Dis. **24**, 877–883.	In a prospective study of 93 children with IBD receiving infliximab treatment, QFT was indeterminate for 1 patient (1.1%), positive for 2 and negative for 90. The authors conclude that the robust IFN-gamma responses in these patients may support further use of QFT for periodic LTBI screening.

References:

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2. 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
3. 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.
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7. Lewinsohn, D.M. et al. (2017) Official American Thoracic Society/Infectious Diseases Society of America/Centers for Disease Control and Prevention Clinical Practice Guidelines: Diagnosis of Tuberculosis in Adults and Children. Clin. Infect. Dis. **64**, 111-115.

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