QuantiFERON®-TB Gold In-Tube: 
A 7-year Experience at the Bellvitge University Hospital.

Dr. Miguel Santín 
Department of Infectious Diseases 
Bellvitge University Hospital 
University of Barcelona

2nd Symposium on IGRAs. 
Special Session World TB Day
Diagnosis and tx of TB

Contact-tracing and tx for infected people

Prevention of TB in patients at risk
  • Anti-TNF-treated patients
  • Transplant receptors
  • HIV (at the HIV Unit)

Diagnosis and tx of Non-TB Mycobacteria

Reference for MDR-TB
IGRAs in 2006

• Cross-sectional studies
  – IGRAs equal to greater sensitivity than TST
  – IGRAs higher specificity
  – High rates of discordant results
• High rates of indeterminate results in immunocompromised patients
• No longitudinal studies (no data on patient-important outcomes)
Detection of latent tuberculosis by the tuberculin skin test and a whole-blood interferon-γ release assay, and the development of active tuberculosis in HIV-seropositive persons

Miguel Santín, Susana Casas, Maria Saumoy, Ana Andreu, Raquel Moure, Fernando Alcaide, Elena Ferre, Daniel Podzamczer

Diagnostic Microbiology and Infectious Disease 69 (2011) 59–65

Diagnosis of tuberculosis infection by tuberculin skin test and a whole-blood interferon-γ release assay in patients considered for anti-tumor necrosis factor-α therapy

Susana Casas, Ana Andreu, Xavier Juanola, Xavier Bordas, Fernando Alcaide, Luis Anibarro, Eva Cuchi, Maria Esteve, Vera Ortiz, Maria Rosario Guerra, Jesus Rodríguez, Delia Reina, Georgina Salvador, Jordi Guardiola, Xavier Surís, Maria Angeles Pascual, Carmina Martín, Xavier Martínez-Lacasa, Jordi Cuquet, Lucia Gonzalez, Miguel Santín

Diagnostic Microbiology and Infectious Disease 71 (2011) 57–65

Comparison of the 2-Step Tuberculin Skin Test and the QuantiFERON-TB Gold In-Tube Test for the Screening of Tuberculosis Infection Before Liver Transplantation

Susana Casas, Laura Muñoz, Raquel Moure, Jose Castellote, Maria R. Guerra, Lucia Gonzalez, Ana Andreu, Antoni G. Rafecas, Fernando Alcaide, and Miguel Santín

1Department of Infectious Diseases, 2Department of Microbiology, 3Department of Gastroenterology, 4Liver Transplant Unit, and 5Department of General Surgery, Bellvitge University Hospital, Bellvitge Biomedical Research Institute, Barcelona, Spain; 6University of Barcelona, Barcelona, Spain; and 7Spanish Network for Research in Infectious Diseases (REIPI), Madrid, Spain

LIVER TRANSPLANTATION 17:1205-1211, 2011
QFT-GIT at BUH
Immunocompromised Patients

• Low rates of indeterminate results with QFT-GIT.
• QFT-GIT less affected by immunosuppression (CD4+, immunosuppressors and liver disease) than TST.
• High rates of discordance between TST and QFT-GIT
  – TST (+)/QFT-GIT (-) in less immunocompromised pts.
  – TST (-)/QFT-GIT (+) in more immunocompromised pts.
• Risk factors for TB infection associated with both TST and QFT-GIT.
• Very low risk of incident active TB in HIV-infected patients with either negative TST or QFT-GIT.

QFT for Screening Patients with Biologic Agents

QFT for Screening of HIV-infected Patients

QFT BCG-vacc. contacts

Nov. 2006 - Nov. 2007
Nov. 2006
Nov. 2006
Nov. 2006
Nov. 2006

2008-2009
2010-2011
2012

QFT Bios
QFT HIV
QFT LT

Bellvitge Hospital
Who are really infected?

Who will progress to active TB?

- TST (+)
- IGRA (+)
Predictive values of TST and IGRAs for Incident Active TB

• **Rangaka XM. Lancet Infect Dis 2012.**
  - TST (+) vs TST (-):* IRR 1.6 (0.9-2.7)
  - IGRA (+) vs IGRA (-): IRR 2.1 (1.3-3.5)

• **Diel R. Chest 2012.**

<table>
<thead>
<tr>
<th></th>
<th>PPV</th>
<th>NPV</th>
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<tbody>
<tr>
<td>TST</td>
<td>1.5%</td>
<td>99.4%</td>
</tr>
<tr>
<td>IGRAs</td>
<td>2.7%</td>
<td>99.7%</td>
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*10 mm
Interferon-γ release assays versus tuberculin skin test for targeting people for tuberculosis preventive treatment: An evidence-based review

Laura Muñoz a, Miguel Santin a,b,*

aDepartment of Infectious Diseases, Bellvitge University Hospital — IDIBELL, 08907 L'Hospitalet de Llobregat, Barcelona, Spain
bDepartment of Clinical Sciences, University of Barcelona, 08907 L'Hospitalet de Llobregat, Barcelona, Spain
### Interferon-γ release assays versus tuberculin skin test for targeting people for tuberculosis preventive treatment: An evidence-based review

Table 3  Incident TB in individuals considered not infected according to the TST and IGRA results. High-income countries.

| Reference (Year) | Population          | Follow-up   | Incident TB in individuals without TB infection n/N (Incidence)
|------------------|---------------------|-------------|---------------------------------------------------------------|
|                  |                     |             | TST (TST-ve) | IGRA (IGRA -ve) | TST/IGRA (TST-ve and TST+ve/IGRA-ve) | Increase in incidence
|                  |                     |             |               |               |                                          | IGRA vs TST | TST/IGRA vs TST |
| Song\(^{16}\) (2007) | TB case-contacts | 2 yrs | 10/1556 (0.6%) | N.A. | 10/1623 (0.6%) | N.A. | No |
| Kik\(^{17}\) (2009)\(^{c}\) | TB case-contacts | 2 yrs | 0/94 | N.A. | 2/212 (0.94%) | N.A. | Yes (0.94%) |
| Kik\(^{17}\) (2009)\(^{d}\) | TB case-contacts | 2 yrs | 0/94 | N.A. | 3/261 (1.1%) | N.A. | Yes (1.1%) |
| Diel\(^{18}\) (2010) | TB case-contacts | Up to 4 yrs | 2/346 (0.6%) | 0/750 | 2/756 (0.3%) | N.A. | No |
| Garcovich\(^{20}\) (2011) | Anti-TNF candidates | 1 yr | 0/39 | 0/44 | 0/42\(^{c}\) | No | No |
| Chang\(^{23}\) (2011) | Anti-TNF candidates | 2 yrs | 0/65 | 0/64 | 0/64 | No | No |
| Laffite\(^{19}\) (2009) | Anti-TNF candidates | 1.5 yrs | 0/28 | 0/38 | 0/38 | No | No |
| Harstad\(^{21}\) (2010) | Asylum seekers | 23–32 months | 0/394 | 0/562 | 0/601 | No | No |

*Note: TST = Tuberculin skin test, IGRA = interferon-γ release assay, TST-ve = TST negative, IGRA-ve = IGRA negative, TST+/IGRA-ve = TST positive/IGRA negative, Incidence = incidence rate.*
QFT for Screening Patients with Biologic Agents

QFT for Screening of HIV-infected Patients

QFT BCG-vacc. contacts

Nov. 2006 - Nov. 2007

Mar. 2007

Nov. 2006

QFT Bios

Mar. 2007

QFT HIV

Jul. 2008

QFT LT

QFT for Screening of HIV-infected Patients

Set. 2011

QFT BCG

Dec. 2012

QFT LT (f-up)
QuantiFERON®-TB Gold In-Tube in Contact-tracing

H.U. Bellvitge (2006-2010)
QuantiFERON®-TB Gold In-Tube in Contact-tracing
H.U. Bellvitge (2006-2010)

<table>
<thead>
<tr>
<th>BCG-vaccinated contacts (n=367)</th>
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<tbody>
<tr>
<td>Diagnosis</td>
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<tr>
<td>TST period</td>
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<tr>
<td>Treatment</td>
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<tr>
<td>TST period</td>
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- **Diagnosis**
  - TST period: 51%
  - QFT period: 83%

- **Treatment**
  - TST period: 47%
  - QFT period: 69%

Muñoz L, Santin M (ICAAC 2011)
### QuantiFERON®-TB Gold In-Tube in Contact-tracing

**H.U. Bellvitge (2006-2010)**

#### BCG-vaccinated contacts (n=367)

<table>
<thead>
<tr>
<th></th>
<th>TST period</th>
<th>QFT period</th>
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<tbody>
<tr>
<td>Diagnosis</td>
<td></td>
<td>51%</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
<td>47%</td>
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<td>69%</td>
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#### Complete cohort (n=759)

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<tr>
<th></th>
<th>TST period</th>
<th>QFT period</th>
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<tbody>
<tr>
<td>Diagnosis</td>
<td></td>
<td>52%</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
<td>49%</td>
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<tr>
<td></td>
<td></td>
<td>63%</td>
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Role of TST and QFT-GIT in Predicting Development of TB in Patients Undergoing Liver or HP Transplantation

• 48 LT patients
  – 22 (45.8%) TST or QFT-GIT (+)
  – No preventive treatment offered
  – Mean follow-up: 32 months

• TB:
  – One patient with TST and QFT-GIT positive.
  – PPV (TST or QFT-GIT): 4.5% (0.8-21.8)
  – NPV (TST or QFT-GIT): 100% (84-100)
Comparison of two strategies for therapeutic decision-making in tuberculosis contact tracing: a standard strategy based on tuberculin skin test (TST) alone vs TST combined with QuantiFERON®-TB Gold In-Tube. (OPTIMIST Study)

Protocol ID:
EUDRACT: 2009-017430-49
Clinical Trials Registration: NCT01223534

Promotor:
Dr. Miguel Santín
Objetives

• To demonstrate that the incidence of TB in subjects evaluated by TST combined with QFT will not higher than among subjects evaluated with TST alone.

• To demonstrate that the proportion of subjects with TB infection will be lower in subjects evaluated by TST combined with QFT than in subjects evaluated by TST alone.

Design

• Randomized, multicenter, non-inferiority clinical trial.
• Sample size: 435 subjects per arm.
• Follow-up: 2 years.
OPTIMIST Study Sites
Recruited (n=604)

Arm A: TST 301
- Non-assessable 54
- Definite diagnosis 247
  - Positive 169 (68%)
    - Preventive Tx 165 (68%)
  - Negative 78 (32%)

Arm B: TST/QFT 303
- Non-assessable 66
- Definite diagnosis 237
  - Positive 106 (45%)
    - Preventive Tx 101 (45%)
  - Negative 131 (55%)
Take-home messages

• QFT-GIT is an objective test, which has logistic advantages over the TST.

• QFT-GIT reduces the number of people considered for preventive treatment.

• Using a QFT-GIT in place of TST or as a confirmatory test does not increase the risk of subsequent TB.

• However...
  – Testing should be targeted to people at risk.
  – QFT-GIT should be used as a part of an overall clinical assessment.
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