What is the Effect on the IGRA Response By Anti-inflammatory Treatment and Smoking

• Study 1:

The effect of anti-inflammatory treatment on TST and QFT-IT Performance

• Study 2:

The effect of smoking on QFT-IT performance

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Background: How Does Immunosuppression Influence the IGRA and TST?

Girndt, Kid Int 2001
Solovio, ERJ 2011
Cattamanchi, J Acquir Immune Defic Syndr. 2011
Ling, Paed Resp Rev 2011
Ferrara, Lancet 2006
Study 1: Effect of Anti-inflammatory Treatment on QFT-IT and TST Response

- **Aim**
  - Is QFT-IT and TST performance affected by treatment with:
    - DMARDs
    - Corticosteroids

- **Study Design**
  - A cross-sectional screening of 248 patients:
    - Rheumatological Diseases (RD)
      - Spondylo-arthritis (N=44)
      - Rheumatoid arthritis (N=111)
    - Inflammatory Bowel Disease (IBD)
      - Crohn’s disease (N=54)
      - Ulcerative colitis (N=39)

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**Method**

- **Patient history:**
  - Risk factors for TB acquisition
  - BCG vaccination
  - Current medication

- **All patients were tested with:**
  - QFT-IT
  - TST
## Results: Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>RD</th>
<th>IBD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N (%)</strong></td>
<td>248</td>
<td>155 (63)</td>
<td>93 (37)</td>
</tr>
<tr>
<td><strong>Age median, years (range)</strong></td>
<td>44 (18-84)</td>
<td>56 (27-84)</td>
<td>33 (18-65)</td>
</tr>
<tr>
<td><strong>Sex, N (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>83 (33)</td>
<td>43 (28)</td>
<td>40 (43)</td>
</tr>
<tr>
<td><strong>Treatment, N (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prednisolone</td>
<td>44 (18)</td>
<td>16 (10)</td>
<td>28 (30)</td>
</tr>
<tr>
<td>Long-acting corticosteroid</td>
<td>32 (12)</td>
<td>32 (21)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Other treatments:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methotrexate, Azathioprine, 5-ASA, Other</td>
<td>168 (68)</td>
<td>107 (69)</td>
<td>60 (65)</td>
</tr>
<tr>
<td>No treatment</td>
<td>74 (30)</td>
<td>43 (28)</td>
<td>31 (33)</td>
</tr>
</tbody>
</table>

*Percentages do not total 100 as some patients received more than one drug.

## Results: TST and QFT-IT Outcome

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>RD</th>
<th>IBD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TST, N (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>54 (23)</td>
<td>45 (29)</td>
<td>9 (10)</td>
</tr>
<tr>
<td>Negative</td>
<td>184 (77)</td>
<td>104 (67)</td>
<td>80 (86)</td>
</tr>
<tr>
<td>N/A</td>
<td>10</td>
<td>6 (4)</td>
<td>4 (4)</td>
</tr>
<tr>
<td><strong>QFT-IT, N (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>7 (3)</td>
<td>7 (5)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Negative</td>
<td>229 (92)</td>
<td>143 (92)</td>
<td>86 (92)</td>
</tr>
<tr>
<td>Indeterminate</td>
<td>12 (5)</td>
<td>5 (3)</td>
<td>7 (8)</td>
</tr>
</tbody>
</table>
Effect of Prednisolon on Mitogen Induced IFN-γ Responses

Logistic Regression Analyses with Various Outcomes and the Test Results as Explanatory Variables

<table>
<thead>
<tr>
<th>Positive TST</th>
<th>Positive QFT-IT</th>
<th>Indeterminate QFT-IT</th>
</tr>
</thead>
<tbody>
<tr>
<td>AOR</td>
<td>AOR (95%) P-value</td>
<td>N/N (%) (95%) P-value</td>
</tr>
<tr>
<td>All population</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prednisolone</td>
<td>3/42 (7) 0.22 (0.1-0.8) 0.018</td>
<td>0/44 (0) N/A N/A</td>
</tr>
<tr>
<td>No Prednisolone</td>
<td>51/196 (26) 1 -</td>
<td>7/204 (7) 1 -</td>
</tr>
</tbody>
</table>
Dose-dependent Risk of Indeterminate QFT-IT Results

Conclusions of Study 1

- Prednisolone treatment suppresses IFN-γ production
- Prednisolone treatment results in higher degree of indeterminate QFT-IT results
- Recommendation
  Screen for LTBI before initiation of immunosuppressive drugs
Study 2: Smoking is Associated with False Negative and Indeterminate IGRA Results

• Cigarette smoking is associated with tuberculosis disease

• Cigarette smoke is known to impair IFN-γ responses to Antigen stimulation both in vitro and in vivo
  (Feng, I&I 2011, Doyle, Mol immunol 2009, Modestou, Resp Res 2010)

Aim and Study Design

• Aim
  • Is QFT-IT performance affected by smoking in TB patients in a low and high TB prevalence setting

• Study Design
  • A cross-sectional screening of 206 patients with confirmed TB (positive culture/PCR for Mtb)
    • 34 patients from Denmark
      • 20 smokers (59%),
      • 4 HIV co-infected (8%)
    • 172 patients from Tanzania
      • 23 smokers (13%),
      • 75 HIV co-infected (44%)
Results: QFT-IT Results

Danish patients
- Positive QFT-IT: 50%
- False-negative QFT-IT: 25%
- Indeterminate QFT-IT: 25%

Tanzanian patients
- Positive QFT-IT: 50%
- False-negative QFT-IT: 25%
- Indeterminate QFT-IT: 25%

p=0.03, p=0.01, p=0.56

Aabye et al., preliminary data

Results: IFN-γ Responses to TB Specific Antigens

Danish patients
- p=0.04

Tanzanian patients
- p<0.01

No effect found on nil and mitogen IFN-γ levels
Results: Predictors of False Negative and Indeterminate QFT-IT Results

<table>
<thead>
<tr>
<th></th>
<th>False negative</th>
<th></th>
<th>Indeterminate</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AOR (95% CI)</td>
<td>p</td>
<td>AOR (95% CI)</td>
<td>p</td>
</tr>
<tr>
<td>Smoking</td>
<td>17.1 (3.0-99.1)</td>
<td>&lt;0.01</td>
<td>5.1 (1.2-21.3)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Adjusted for age, gender, HIV co-infection, alcohol consumption

Conclusions

- Cigarette smoking is associated with false negative and indeterminate QFT-IT results
- This was shown in both a high and a low TB prevalence setting
Overall summary

• We have shown that both treatment with prednisolone and smoking have an impact on QFT-IT test outcome

For more Information: Related Poster

• "Smoking is Associated with False Negative and Indeterminate Interferon Gamma Release Assay Results among Pulmonary Tuberculosis Patients"

• Poster 18

• Saturday, January 14, at 5:30 pm
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