ONLINE SUPPLEMENT

The 2005 British Thoracic Society recommendations for TB screening in patients schedule for anti-TNF treatment

The BTS guidance document was published in 2005 and outlines an algorithm to provide guidance for screening of patients prior to commencement of TNF-α antagonist therapy.

The first consideration is whether the patient has symptoms of active TB, previous history of TB or abnormal chest radiograph consistent with prior or active TB. In such cases, a full work-up for active TB is recommended and the following recommendations are made:

- If the patient is confirmed to have active TB, it is recommended that they receive 6 months duration of standard quadruple therapy and start TNF-α antagonist therapy after at least 2 months

- If active TB is excluded, but the patients still has a history of previous TB or abnormal chest radiograph consistent with previous TB, an enquiry should be made about whether adequate chemotherapy was received. If adequate chemotherapy was received, it is recommended to monitor the patient during TNF-α antagonist therapy and reassess if symptoms develop. If adequate chemotherapy was not received, it is recommended to exclude activity with 6 months treatment if evidence of active disease or chemoprophylaxis for inactive disease.

If the patient has no symptoms of active TB/previous history of TB/abnormal chest radiograph, the next consideration is whether they are on immunosuppressant treatment. If this is the case, the algorithm states that the TST is unreliable, should not be performed and patients should be stratified for TB risk (see below)

In patients who are not on immunosuppressant treatment, a TST is recommended with interpretation based on presence or absence of prior BCG.

Tables to guide risks of TB and drug-induced hepatitis from chemoprophylaxis

In patients who require stratification for TB risk, it is recommended to consult tables contained within the guideline that allow calculation of the annual risk of TB disease/100,000 in England and Wales. These tables are based on the premise that the incidence of TB varies markedly within the UK, according to several factors: age, ethnic group and, for those not born in the UK, length of time since first entry. These tables can be consulted to calculate risk of TB for a particular patient and a separate table within the guideline can then be consulted to determine whether this risk exceeds the hepatotoxic risk of chemoprophylaxis /100,000. Chemoprophylaxis is advocated if the risk of TB exceeds the risk of hepatotoxicity. In general, Black Africans aged over 15 years and all South Asians born outside of the UK should receive chemoprophylaxis.
Comparison between patients on Immunosuppressants and those not on immunosuppressants

There were 157 patients taking immunosuppressants at the time of screening. eTable 1 shows characteristics in patients on immunosuppressants and those not on immunosuppressants.

<table>
<thead>
<tr>
<th></th>
<th>Patients on immunosuppressants (n=157)</th>
<th>Patients not on immunosuppressants (n=30)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>56 (45-66)</td>
<td>42 (34-54)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Male sex</td>
<td>69 (43.9%)</td>
<td>13 (43.3%)</td>
<td>1.0</td>
</tr>
<tr>
<td>BCG vaccinated</td>
<td>53 (33.8%)</td>
<td>12 (40%)</td>
<td>0.53</td>
</tr>
<tr>
<td>CXR features of previous TB</td>
<td>14 (8.9%)</td>
<td>2 (6.7%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Previous treated TB</td>
<td>10 (6.4%)</td>
<td>2 (6.7%)</td>
<td>1.0</td>
</tr>
<tr>
<td>High risk according to BTS</td>
<td>34 (21.7%)</td>
<td>6 (20.0%)</td>
<td>1.0</td>
</tr>
<tr>
<td>T Spot positive</td>
<td>35 (22.3%)</td>
<td>7 (23.3%)</td>
<td>1.0</td>
</tr>
<tr>
<td>T spot indeterminate</td>
<td>1 (1.2%)</td>
<td>0 (0%)</td>
<td>1.0</td>
</tr>
<tr>
<td>TST positive</td>
<td>36 (22.9%)</td>
<td>12 (40.0%)</td>
<td>0.07</td>
</tr>
<tr>
<td>T spot and TST both positive</td>
<td>14 (8.9%)</td>
<td>4 (13.3%)</td>
<td>0.50</td>
</tr>
<tr>
<td>Tspot or TST positive</td>
<td>57 (36.3%)</td>
<td>15 (50%)</td>
<td>0.21</td>
</tr>
<tr>
<td>Active TB</td>
<td>2 (1.2%)</td>
<td>0 (0%)</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Data presented as n (% of group) or median (IQR)

Proposed modified algorithm

eFigure 1 shows the current BTS screening algorithm and a proposed modified algorithm based on the findings of the current study.
**Figure 1:** BTS Algorithm and Proposed modified algorithm

**Current BTS Algorithm:**
- On Immunosuppressants at time of screening
- Consult risk tables to determine risk of TB versus risk of hepatotoxicity
  - LOW RISK
    - Treatment not required
  - HIGH RISK
    - Treat with chemoprophylaxis

**Proposed Alternate Algorithm:**
- On Immunosuppressants at time of screening
- Consult risk tables to determine risk of TB versus risk of hepatotoxicity
  - LOW RISK
    - Perform T.Spot and TST
      - Both negative
        - Treatment not required
      - Either test positive
        - Treat with chemoprophylaxis
  - HIGH RISK