



## LETTERS TO THE EDITOR

### Tuberculosis screening and compliance rate with guidelines among Northern Portuguese Hospitals prescribers of anti-TNF therapy



Dear Editor,

Tumor necrosis factor-alpha (TNF- $\alpha$ ) is a pleomorphic cytokine involved in the pathogenesis of many rheumatic diseases. Following anti-TNF therapy, the relative risk for tuberculosis is increased by up to 25 times, often as a rapidly progressive disease, extra-pulmonary or disseminated.<sup>1-4</sup> Aiming to evaluate compliance with guidelines for tuberculosis screening, the authors conducted an enquiry among northern Portuguese hospitals which prescribe anti-TNF therapy.

From all hospitals in northern Portugal the authors identified those that prescribed anti-TNF therapy, and from them randomly selected from among the Internal Medicine medical doctors (the specialty which most commonly prescribed biological therapy in these hospitals) those who had at least, one weekly consultation of autoimmune disease and were familiar with the hospital prescription procedures. One hospital which had only one doctor prescribing was excluded.

The enquiry was carried out in September 2012. The interview consisted of ten multiple-choice questions relating to each recommendation: TB screening, diagnostic exams, preventive treatment, when to start anti-TNF $\alpha$  therapy and TB monitoring through the course of anti-TNF $\alpha$  treatment. Compliance rates were determined for each clinical recommendation and each guideline [national, international or European consensus] (Table 1).<sup>5,1,6,7</sup>

Eleven hospitals were identified and ten were eligible. They performed TB screening in all patients treated with anti-TNF therapy. The screening method used by all hospitals was patient history and tuberculin skin test (TST), seven (70%) used interferon-gamma-release-assay (IGRA) and six (60%) used chest radiography (CRX). Compliance rate: 60% for UK guidelines and 50% for European consensus, USA and national guidelines (Table 2).

All hospitals performed TB screening prior to anti-TNF treatment (compliance rate of 100% with all guidelines); seven (70%) re-screened during anti-TNF treatment, due to

recent exposure to TB (compliance rate of 70% for USA, national guidelines and European consensus, UK guidelines do not give specific recommendations on this subject) and eight hospitals (80%) re-screened due to symptoms (compliance rate of 80% with all guidelines) (Table 2). Only one hospital (10%) re-tested asymptomatic patients with a previous negative screening, without recent exposure, during anti-TNF treatment (compliance rate 10% with national, American and European consensus, not applicable to UK guidelines) (Table 2).

Three hospitals (30%) screened in their own facilities, 4 (40%) in TB outpatient clinic, 1 (10%) in a primary care center and 2 (20%) in elsewhere.

Eight hospitals (80%) used TST cut-off of 5 mm, one (10%) 10 mm and one (10%) 15 mm. The compliance rate was 80% percent with national, UK and USA guidelines and 90% with European consensus (Table 2).

Seven hospitals (70%) initiated preventive therapy, if TST or IGRA were positive; one (10%) if both TST and IGRA were positive; two (20%) if TST was positive, without IGRA result. A compliance rate of 70% with European consensus, national and north-American guidelines was calculated. No compliance for UK guidelines (Table 2). All centers used isoniazid for preventive treatment. Eight hospitals (80%) treated their patients during nine months and two (20%) during 6 months. Compliance rates: 80% with national, American and European consensus and 20% with UK guidelines (Table 2). Eight hospitals (80%) initiated anti-TNF therapy 4 weeks after beginning LTBI treatment and two (20%) 3 months after. Compliance rate: 80% with national, American and European consensus; no compliance with UK guidelines (Table 2).

TB screening is performed routinely before anti-TNF treatment, according to the individual physician's awareness of TB risk. In our study, the European consensus was the guideline with highest percentage of compliance, presenting a medium rate of 69.4%, followed closely by National and American Guidelines (68.1%). UK recommendations had a lower adherence, with 64.3%. This rate is similar to the compliance rate observed by Smith et al. in the Gastroenterology and Dermatology G5 group (including the five foremost industrialized economies – Germany, France, Italy, Spain and the United Kingdom); it was lower than the one observed in the non-G5 Rheumatology group.<sup>8</sup>

Although this study has serious limitations, as TB screening performance was based on self-reported actions

**Table 1** Comparison between TB screening guidelines and the 2010 European consensus.

		European <sup>1</sup>	Portuguese <sup>5</sup>	UK <sup>7</sup>	USA <sup>8</sup>
How to screen?	Clinical history <sup>a</sup>	All	All	All	All
	Chest radiograph	All	All	All	TST+ or IGRA+
	TST	Without history of BCG vaccination	All	Not for patients on IS as unreliable <sup>b</sup>	All
TST "Cut-off" for treatment $\geq$	IGRA	Negative TST	All	Not used	All
		10 mm 5 mm if	5 mm if IS; 10 mm in others	Unvaccinated; 15 mm in vaccinated	5 mm if IS 10 mm if high risk <sup>c</sup> 15 mm in others
Who should receive prophylaxis?		TST+ and/or IGRA+	TST+ and/or IGRA+; Recent TB exposure; CXR sequelae of non-treated TB	TST+; Previous TB not treated; CXR sequelae of non-treated TB; IS and risk factors for TB exposure <sup>d</sup>	TST+ and/or IGRA+
LTBI treatment (months)		9–12 H or 3HR	9 H, 6 H, 3HR, 4 R	6 H or 3 HR	9 H
Time delay before TNF antagonist therapy	LTBI	4 weeks	4 weeks	Abnormal CXR or previous TB: complete prophylaxis; Others: no delay	4 weeks
	Active TB	Full treatment	6–8 weeks	2 months	Full treatment
Time to screening	Before TNF antagonist therapy	All	All <sup>e</sup>	All	All
	Re-testing	Annual	Annual	If symptoms of active TB; until 6 months stopping anti-TNF	Annual
	Close contact with active TB	All	All <sup>f</sup>	-	All

IS: immunosuppressive medication; H: isoniazid; R: rifampicin; CXR: chest radiograph.

<sup>a</sup> History of prior TB infection and treatment, close contacts of persons known or suspected to have active TB.

<sup>b</sup> TST will only become reliable once treatment has been stopped for 1 month in the case of steroids and for 3 months in the case of all other immunosuppressive drugs.

<sup>c</sup> New immigrant and drug users.

<sup>d</sup> Risk factors for TB exposure are defined based on a publication from the US Centres for Disease Control and Prevention as: close contacts of persons known or suspected to have active TB; foreign-born persons from areas that have a high incidence of active TB (e.g., Africa, Asia, Eastern Europe, Latin America, and Russia); persons who visit areas with a high prevalence of active TB, especially if the visits are frequent or prolonged; residents and employees of congregate settings whose clients are at an increased risk for active TB (e.g., correctional facilities, long-term care facilities, and homeless shelters); health care workers who serve clients who are at an increased risk for active TB; populations defined locally as having an increased incidence of latent *M. tuberculosis* infection or active TB, possibly including medically underserved, low-income populations, or persons who abuse drugs or alcohol; and infants, children, and adolescents exposed to adults who are at an increased risk for latent *M. tuberculosis* infection or active.

<sup>e</sup> Validated until 6 months prior initiation anti-TNF.

<sup>f</sup> Start chemoprophylaxis immediately, at the same time as TB screening.

**Table 2** Summary of results and compliance to recommendations (results in percentages).

	European	National	UK	American
Screen tools	50	50	60	50
Screen time	75	75	90	75
TST "cut-off"	90	80	80	80
Diagnosis methods of LTBI	70	70	0	70
LTBI treatment	80	80	20	80
Timing of initiation of anti-TNF if LTBI	80	80	0	80
TB re-testing	10	10	0	10

of the physicians concerned, we found that among the protocols followed by experienced anti-TNF prescribers, the rate of compliance with the guidelines is low and there is excessive confidence in the TST. Re-testing is neglected and is a something that needs to be improved. The availability of facilities in Portugal such as the TB outpatient clinic can be considered a real asset but they are not used to their full potential.

### Conflicts of interest

The authors have no conflicts of interest to declare.

### References

- Solovic I, Sester M, Gomez-Reino JJ, Rieder HL, Ehlers S, Milburn HJ, et al. The risk of tuberculosis related to tumour necrosis factor antagonist therapies: aTBNET consensus statement. *Eur Respir J.* 2010;36:1185–206.
- Askling J, Forede CM, Brandt L, Baecklund E, Bertilsson L, Coster L, et al. Risk and case characteristics of tuberculosis in rheumatoid arthritis associated with tumor necrosis factor antagonists in Sweden. *Arthritis Rheum.* 2005;52:1986–92.
- Gomez-Reino JJ, Carmona L, Valverde VR, Mola EM, Montero MD. Treatment of rheumatoid arthritis with tumor necrosis factor inhibitors may predispose to significant increase in tuberculosis risk: a multicenter active-surveillance report. *Arthritis Rheum.* 2003;48:2122–7.
- Wallis RS. Tumour necrosis factor antagonists: structure, function, and tuberculosis risks. *Lancet Infect Dis.* 2008;8:601–11.
- Duarte R, Campainha S, Cotter J, Rosa B, Varela P, Correia A, et al. Position paper on tuberculosis screening in patients with immune mediated inflammatory diseases candidates for biological therapy. *Acta Reumatol Port.* 2012;37:253–9.
- Thoracic Society (BTS) recommendations for assessing risk and managing tuberculosis in patients due to start anti-TNF-alpha treatments. *Thorax*, vol. 60. Joint Tuberculosis Committee of the British Thoracic Society; 2005. p. 800–5.
- Singh JA, Furst DE, Bharat A, Curtis JR, Kavanaugh AF, Kremer JM, et al. Update of the 2008 American College of Rheumatology recommendations for the use of disease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis. *Arthritis Care Res.* 2012;64:625–39.
- Smith MY, Attig B, McBamee L, Eagle T. Tuberculosis screening in prescribers of anti-tumor necrosis factor therapy in the European Union. *Int J Tuberc Lung Dis.* 2012;16(9):1168–73.

B.A. Ferreira\*, S. Ribeiro, J. Meireles, A. Correia, R. Duarte

*Centro Hospitalar Porto-Hospital Santo António, Internal Medicine, Largo Professor Abel Salazar, Porto, Portugal*

\*Corresponding author.

*E-mail address:* betania.ferreira82@hotmail.com (B.A. Ferreira).

## Oxygen therapy: a clinical audit in an Internal Medicine Department



Dear Editor,

Oxygen therapy, from prescription to administration, is still poorly handled,<sup>1–6</sup> and until the publication of "Guideline for emergency oxygen use in adult patients" by the British Thoracic Society<sup>1</sup> there were very little literature about oxygen therapy procedures.<sup>1,7</sup>

Recognizing the need to improve oxygen therapy procedures, the authors conducted an audit in 2008 to identify faulty practice and plan improvement measures. Three

years later, a second audit was performed in order to evaluate those measures.

A taskforce consisting of physicians and nurses was set up in 2007 to evaluate OT practice in Internal Medicine wards of Hospital de Santo António, Oporto, Portugal. Based on the BTS guidelines, and according to NICE principles for best practice in clinical audit,<sup>3</sup> an audit was designed to evaluate the different aspects of OT: prescription, transcription, administration and monitoring.

The audit was performed in two of the four wards of the department between January 1st and March 31st 2008. All patients to whom oxygen was administered or prescribed were included in the audit, except those with non-invasive ventilation during daytime. Assessments were performed two days per week. No assessments were performed at