

# Tuberculosis in rheumatic patients treated with biological therapies – is screening enough?



Romão VC<sup>1,2</sup>; Saavedra MJ<sup>2</sup>;Vieira-Sousa E<sup>1,2</sup>; Costa M<sup>2</sup>; Polido-Pereira J<sup>1,2</sup>; Rodrigues AM<sup>1,2</sup>; Ramos F<sup>2</sup>; Macieira C<sup>2</sup>; Capela S<sup>2</sup>; Resende C<sup>2</sup>; Madruga-Dias J<sup>1,2</sup>; Ponte C<sup>1,2</sup>; Campanilho-Marques R<sup>1,2</sup>; Castro A<sup>1,2</sup>; Furtado C<sup>1,2</sup>; Fernandes S<sup>1,2</sup>; Gonçalves MJ<sup>1,2</sup>; Pereira da Silva JA<sup>2</sup>; Canhão H<sup>1,2</sup>; Fonseca JE<sup>1,2</sup>  
<sup>1</sup> Rheumatology Research Unit, Instituto de Medicina Molecular – Faculdade de Medicina da Universidade de Lisboa; <sup>2</sup> Rheumatology Department, Lisbon Academic Medical Centre, Lisbon, Portugal

## Introduction

An increased risk of active tuberculosis (TB) has been reported in patients with rheumatic diseases treated with biological therapies, especially TNF inhibitors. Most TB cases result from an activation of a previous latent infection (LTB). In Portugal, stringent screening guidelines for detection of LTB have been issued and regularly updated since 2003. The aim of this study was to analyze TB cases in biological-treated patients from a single center.

## Methods

We included patients from Hospital Santa Maria treated with biological therapy and registered in Reuma.pt that had a diagnosis of TB after starting treatment. Data were obtained through Reuma.pt and clinical files.

## Results

We identified 736 treatments with biological therapies, 627 of which with TNF inhibitors, corresponding to 510 patients. There were 3 cases of TB after the start of biological treatment (0.59% of patients, 0.41% of treatments) - **Table 1**.

**Table 1** - Characteristics of the 3 patients diagnosed with TB after the start of a biological.

	Patient 1	Patient 2	Patient 3
Age (years)	27	48	17
Sex	Male	Female	Female
Rheumatic disease	Psoriatic Arthritis	Psoriatic Arthritis	juvenile-onset Spondyloarthritis
Biological	Infliximab	Infliximab	Adalimumab
Year of biological start	2009	2003	2010
Disease duration (years)	5	18	4
Screening <sup>§</sup>	Negative	Positive (TST 20mm)	Negative
Previous TB (year)	No	Yes, treated (1960)	No
LTB Treatment	No	Yes, INH 9m	No
Time on biological to TB (months)	5.1	18	14.5
TB site	Miliary	Pulmonary	Miliary
Contact with active case	No	Yes	Yes
TB diagnosis	Clinical*, sputum, imaging <sup>⌘</sup>	Clinical*, lymph node pathology, imaging <sup>⌘</sup>	Clinical*, BAL, imaging <sup>⌘</sup>
Treatment	HRZE	HRZE	HRZE
Evolution	Resolution	Resolution	Resolution
Biological reintroduction	No	No	No

<sup>§</sup>including epidemiological risk factors, two-step tuberculin skin test (TST), IGRA and chest X-ray (CXR); \*clinical signs and symptoms; <sup>⌘</sup>CXR and/or CT-scan. BAL, bronchoalveolar lavage; HRZE, quadruple therapy with isoniazid, rifampin, pyrazinamide and ethambutol; INH, isoniazid; LTB, latent tuberculosis; TB, tuberculosis.

## Conclusions

In biological-treated rheumatic patients TB occurred even after appropriate screening measures. No particular pattern could be seen in positive cases, except that all three patients were treated with anti-TNF monoclonal antibodies and two of them had contact with active TB cases. TB occurred between 5 and 18 months after starting treatment, in patients with positive and negative screening tests, with and without previous LTB treatment. **This highlights that even with thorough screening for LTB, there is still a risk of developing active TB at any time after the start of biological therapies, especially with TNF inhibitors. Thus, close vigilance is mandatory and patients should be clearly aware of the continuous increased risk of TB.**

## References

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