Autoimmunity Reviews xxx (2015) xxx–xxx

Contents lists available at ScienceDirect

Autoimmunity Reviews

journal homepage: www.elsevier.com/locate/autrev

Review

Guidance for the management of patients with latent tuberculosis infection requiring biologic therapy in rheumatology and dermatology clinical practice

Fabrizio Cantini [a,*], Carlotta Nannini [a], Laura Niccoli [a], Florenzo Iannone [b], Giovanni Delogu [c], Giacomo Garlaschi [d], Alessandro Sanduzzi Zamparelli [e], Andrea Matucci [f], Francesca Prignano [g], Michele Conversano [h], Delia Goletti [i],
on behalf of SAFEBIO (Italian multidisciplinary task force for screening of tuberculosis before and during biologic therapy)

[a] Division of Rheumatology, Hospital of Prato, Italy
[b] Interdisciplinary Department of Medicine, Rheumatology Unit, University of Bari, Italy
[c] Institute of Microbiology, Università Cattolica del Sacro Cuore, Rome, Italy
[d] Department of Health Science (DISSAL), Section of Radiology, IRCCS Azienda Ospedaliera Universitaria San Martino, Genova, Italy
[e] Respiratory and Rheumatology Research Units, Department of Clinical and Experimental Medicine, University Federico II, Naples, Italy
[f] Immunoallergology Unit, Azienda Ospedaliero Universitaria Careggi, Florence, Italy
[g] Division of Clinical, Preventive and Oncology Dermatology, Department of Surgery and Translational Medicine, Florence University, Italy
[h] Department for Prevention, Local Health, Taranto, Italy
[i] Translational Research Unit, Department of Epidemiology and Preclinical Research, "L. Spallanzani" National Institute for Infectious Diseases (INMI), IRCCS, Italy

ARTICLE INFO

Available online xxxx

Keywords:
Tuberculosis
Biologics
Rheumatoid arthritis
Psoriatic arthritis
Ankylosing spondylitis
Psoriasis

ABSTRACT

Since the introduction of biologics for the treatment of rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis (AS), and psoriasis (Pso) an increased risk of tuberculosis (TB) reactivation in patients with latent tuberculosis infection (LTBI) has been recorded for anti-TNF agents, while a low or absent risk is associated with the non-anti-TNF targeted biologics. To reduce this risk several recommendation sets have been published over time, but in most of them the host-related risk, and the predisposing role to TB reactivation exerted by corticosteroids and by the traditional disease-modifying anti-rheumatic drugs has not been adequately addressed. Moreover, the management of the underlying disease, and the timing of biologic restarting in patients with TB occurrence have been rarely indicated. A multidisciplinary expert panel, the Italian multidisciplinary task force for screening of tuberculosis before and during biologic therapy (SAFEBIO), was constituted, and through a review of the literature, an evidence-based guidance for LTBI detection, identification of the individualized level of risk of TB reactivation, and practical management of patients with TB occurrence was formulated. The literature review confirmed a higher TB risk associated with monoclonal anti-TNF agents, a low risk for soluble receptor etanercept, and a low or absent risk for non-anti-TNF targeted biologics. Considering the TB reactivation risk associated with host demographic and clinical features, and previous or current non-biologic therapies, a low, intermediate, or high TB reactivation risk in the single patient was identified, thus driving the safest biologic choice. Moreover, based on the underlying disease activity measurement and the different TB risk associated with non-biologic and biologic therapies, practical indications for the treatment of RA, PsA, AS, and Pso in patients with TB occurrence, as well as the safest timing of biologic restarting, were provided.

* Corresponding author at: Rheumatology Division, Hospital of Prato, Piazza Ospedale, 1, 59100 Prato, Italy. Tel.: +39 0574 807578.
E-mail address: fbrzcantini@gmail.com (F. Cantini).

http://dx.doi.org/10.1016/j.autrev.2015.01.011
1568-9972/© 2015 Published by Elsevier B.V.

Contents

1. Introduction

Over the last 15 years biologic drugs have ensured relevant advantages in rheumatology and dermatology for the treatment of rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA), and psoriasis (Pso). To date, several agents with pharmacological activity targeted on different levels of immune response are available in clinical practice, including interleukin-6 inhibitor tocilizumab (TCZ), anti-CD20 rituximab (RTX), anti-interleukin-1 anakinra (ANK), anti-CD28 abatacept (ABA), anti-IL12-23 ustekinumab (UTK), and anti-tumor necrosis factor alpha agents (anti-TNFα) including adalimumab (ADA), etanercept (ETN), infliximab (IFX), golimumab (GOL), and certolizumab (CTP).

However, data from clinical trials and from real-life clinical practice have shown that currently used biologics, namely the anti-TNFα and to a lesser extent the non-anti-TNFα targeted agents, may constitute a risk factor for tuberculosis (TB) reactivation in subjects with latent TB infection (LTBI) [1,2]. Hence, LTBI screening and prevention of active TB represent a current worldwide challenge for biologic prescribers.

To reduce the risk of TB reactivation several sets of recommendations and guidelines have been proposed, but none of them may be appropriate for the single country due to the different social and economic conditions and the variable prevalence of TB [3]. The majority of recommendations/guidelines have been prompted for patients to be treated with the oldest anti-TNFα, namely IFX, ETN and ADA, while no policy document is available for the more recently marketed biologics such as GOL, CTP, TCZ, RTX, ABA, and UTK.

In addition, most of the current recommendations raise some concerns because they do not take in account the specific risk related to the host and to the previous or current treatments, and only two sets have been formulated through a multidisciplinary approach [4,5]. Furthermore, although biologics are loaded by a different TB risk, none of the recommendations provide indications for choosing the proper biologic treatment in function of the specific risk associated with the single patient. Finally, details concerning the management of the underlying rheumatic disease or Pso in case of active TB occurrence have been rarely indicated [6].

2. Objective

To provide an evidence-based algorithm for the detection of LTBI and prevention of TB reactivation, to examine the clinical variables, including the host-related, the traditional disease modifying anti-rheumatic drug (DMARD)-related, and the single biologic agent-related TB risk, that may influence the therapeutic choice in LTBI positive patients with RA, PsA, AS, and Pso requiring biologic therapy, and to suggest practical indications for the management of the patients with active TB complicating the clinical disease course.

3. Methods

3.1. SAFEBIO expert panel purpose

A multidisciplinary expert panel, the Italian multidisciplinary task force for screening of tuberculosis before and during biologic therapy (SAFEBIO), including specialists in rheumatology (FC, CN, LN, FI), microbiology (GD), radiology (GG), pneumology (ASZ), immunology (AM), dermatology (FP), epidemiology (MC), and infectious diseases (DG), was constituted to perform a systematic literature review on the existing recommendations for LTBI screening before biologic starting and overtime follow-up, the TB risk related to different biologics, the host-related risk, the previous therapy-related risk, and to formulate evidence-based practical guidelines for the management of LTBI positive patients with inflammatory rheumatic disorders and Pso.

3.2. Literature search

The literature review was made using PubMed database to identify English-language articles related to the previously mentioned topics. Regarding the TB risk associated with the specific biologic agent, all published clinical trials, data from post-marketing surveillance, and from national registries of currently used biologics for the treatment of RA, AS, and PsA, and Pso were reviewed to identify all cases of TB complicating the underlying rheumatic or dermatologic disease course. Data were extracted from phase III randomized controlled trials (RCTs), their open-label extension phase studies, and from open-label, prospective studies of at least 12-week duration focused on the efficacy and safety of each drug. As an additional selection criterion, we included only the studies published after October 2001, when the recommendations for LTBI detection and TB reactivation prevention where introduced. In addition, available data from biologic national registries, national healthcare databases, and post-marketing surveillance surveys were included. Reviews and meta-analyses were excluded.

The following drugs were investigated: IFX, ETN, ADA, GOL, CTP, RTX, TCZ, ANK, ABA, and UTK. The research was performed by crossing the single drug name with the following key terms: TB, infections,

Please cite this article as: Cantini F, et al, Guidance for the management of patients with latent tuberculosis infection requiring biologic therapy in rheumatology and dermatol..., Autoimmun Rev (2015), http://dx.doi.org/10.1016/j.autrev.2015.01.011