ORIGINAL ARTICLE

To test or not to test? An updated evidence-based assessment of the value of screening and monitoring tests when using systemic biologic agents to treat psoriasis and psoriatic arthritis

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Background: Safety profiles of systemic biologic agents for the treatment of psoriasis and psoriatic arthritis (PsA) encompass a wide spectrum of adverse events. To date, no uniform evidence-based guidelines exist regarding screening and monitoring patients who are undergoing biologic therapy.

Objective: We sought to identify studies evaluating screening and monitoring tests in the treatment of psoriasis and PsA with systemic biologic agents, and to propose evidence-based practical guidelines.

Methods: The MEDLINE database was searched to identify data on risks associated with adalimumab, etanercept, infliximab, and ustekinumab. Articles were reviewed and graded according to methods developed by the US Preventative Services Task Force.

Results: Evidence was strongest (grade B) for tuberculosis screening. Interferon-gamma release assay was preferable to tuberculin skin testing. Among known hepatitis B virus carriers, the evidence grade was C for monitoring liver function tests and viral load.

Limitations: This study was limited by the lack of high-quality controlled trials evaluating screening and monitoring tests in patients treated with biologic agents.

Conclusions: Baseline tuberculosis testing remains the only screening test with strong evidence to support its practice. Other screening and monitoring tests commonly performed in patients who are taking biologic agents are supported only in certain clinical settings or lack evidence to support or recommend against their practice. (J Am Acad Dermatol http://dx.doi.org/10.1016/j.jaad.2015.06.004.)

Key words: adalimumab; biologics; etanercept; infliximab; monitoring; psoriasis; psoriatic arthritis; safety; screening; ustekinumab.

Since the introduction of biologic agents in dermatology in 2002, they have become one of the most frequently used systemic treatments for moderate to severe plaque psoriasis and psoriatic arthritis (PsA).[1] As clinicians have gained experience using biologics, the knowledge

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of potential adverse effects has expanded. Safety profiles of biologics include a wide spectrum of events, including opportunistic infections, the reactivation of infections, malignancy, hepatotoxicity, and the exacerbation of comorbidities.

Anti–tumor necrosis factor-alfa (TNF-α) agents that have been approved by the US Food and Drug Administration (FDA) for the treatment of psoriasis and PsA include infliximab, etanercept, and adalimumab. Ustekinumab, an interleukin-12/23 monoclonal antibody, was approved by the FDA in 2009. Based on trials conducted for registration, the FDA recommends screening and monitoring in patients treated with systemic biologic agents.[2] As new adverse effects have emerged, professional dermatologic associations, like the American Academy of Dermatology (AAD), the Japanese Dermatology Association (JDA), the British Association of Dermatologists (BAD), and the European Academy of Dermatology and Venereology (EADV) have attempted to provide guidance for screening and monitoring tests (Table I).[3-10]

CAPSULE SUMMARY

- There are no evidence-based guidelines for screening and monitoring patients who are receiving biologic therapy for psoriasis and psoriatic arthritis.
- We found that evidence was strongest (grade B) for tuberculosis screening in patients treated with biologic agents.
- High-grade evidence is lacking to support other routine testing; therefore, physicians should use their clinical judgement when screening and monitoring patients who are taking biologic agents.

In 2006, a previous systematic literature review sought to develop evidence-based guidelines for screening tests in the use of biologics.[11] Alefacept and efalizumab were discontinued in the United States and European Union in 2006, and ustekinumab has been introduced. The purpose of this study is to review the literature supporting the current recommendations for screening and monitoring with the use of currently available biologics. This study will highlight changes in screening and monitoring guidelines that have been recommended since our previous report and synthesize evidence-based guidelines for clinicians using biologics for the treatment of plaque psoriasis and PsA.

METHODS

The MEDLINE database was searched for studies pertaining to systemic biologic treatments and screening tests in the context of psoriasis and PsA. Additional articles not contained in the MEDLINE database were identified from citations within reviewed articles.[11] Search terms included: psoriasis or psoriatic arthritis, safety, screening tests, and biologic treatments (etanercept OR Enbrel OR adalimumab OR Humira OR infliximab OR Remicade OR ustekinumab OR Stelara). The search was limited to English articles published between July 1, 2006 and June 1, 2014. Case reports, data from animal studies, and studies involving multiple systemic agents used simultaneously or biologics used for indications other than psoriasis or PsA were excluded. Screening and monitoring tests in otherwise healthy patients without known comorbidities were distinguished from testing in patients with preexisting comorbidities.

Articles were reviewed and graded according to standardized methods developed by the US Preventative Services Task Force (USPSTF). Grades of evidence were determined using current guidelines of the USPSTF and correlated to practice suggestions (Appendices A and B, available at http://www.jaad.org).

RESULTS

A total of 1039 articles were identified. Screening for relevant articles yielded 145 records. After articles were assessed for content and eligibility, 26 were included in the qualitative analysis (Fig 1). Among these, 16 studied screening tests in patients without comorbidities[3,12-26] and 13 studied monitoring tests in patients with hepatitis C virus (HCV) infection, hepatitis B virus (HBV) infection, and congestive heart failure (CHF).[3,17,19,27-36]

Screening and monitoring tests

Anti–TNF-α agents were studied in HBV and HCV, tuberculosis, and human immunodeficiency virus (HIV) screening, skin cancer screening, renal, hepatocellular, and biliary liver function, complete blood cell counts (CBCs), urine studies, pregnancy tests, antinuclear antibody (ANA) and double-stranded DNA (dsDNA), and C-reactive protein (CRP). Ustekinumab was studied with regard to tuberculosis and skin cancer screening (Table II).

The highest evidence grade for screening studies was B, seen in the use of tuberculin skin testing (TST) and interferon-gamma release assay (IGRA; Table II). Based on the USPSTF grading system, it is