Seminars in Arthritis and Rheumatism 47 (2017) 29–37

Contents lists available at ScienceDirect

Seminars in Arthritis and Rheumatism

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

Switching biologics in the treatment of psoriatic arthritis

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ARTICLE INFO

Keywords:
Psoriatic arthritis
Biologic therapy
Treatment failure
Treatment switching

ABSTRACT

Objective: Psoriatic arthritis (PsA) is a heterogeneous inflammatory disorder that requires targeted treatment based on clinical manifestations, symptom severity, comorbidities, and other factors. Moderate or severe peripheral arthritis symptoms are typically treated with disease-modifying antirheumatic drugs (DMARDs) or biologic DMARDs (bDMARDs), and early and aggressive treatment is recommended in order to prevent permanent damage. Although rheumatologists are now able to choose between several bDMARDs for PsA that have different chemical structures, pharmacokinetic properties, dosing regimens, immunogenicity, safety profiles, and mechanisms of action, there is a lack of typical patient profiles or detailed treatment algorithms that can be followed when patients require alterations in their therapeutic regimens.

Methods: PsA treatment recommendations were evaluated to identify consensus guidelines on switching between bDMARD therapies. PubMed literature searches were then conducted using the terms psoriatic arthritis, switch/switching, biologic, and TNF/tumor necrosis factor. Articles were deemed relevant if they presented data on switching between different bDMARDs in patients with PsA.

Results: Data from the clinical literature on switching bDMARD therapies in PsA are limited. Evidence suggests that response to adalimumab, etanercept, and ustekinumab is lower after previous tumor necrosis factor inhibitor (TNFi) therapy and the efficacy of infliximab is independent of previous bDMARD treatment. Trials of ustekinumab and secukinumab showed efficacy responses were greater compared with placebo in patients who failed to respond to ≥ 1 TNFi.

Conclusion: Switching bDMARD therapies is a recommended strategy for patients who experience treatment failure. Many factors must be considered for determining which agent to switch to including PsA disease characteristics, comorbidities, cardiometabolic risk factors, treatment history, and patient preference. Switching between TNFis can be effective for many patients, but bDMARDs with different mechanisms of action may be superior alternatives.

Introduction

Psoriatic arthritis (PsA) is a complex, heterogeneous, and chronic inflammatory condition that affects roughly 25% of patients with psoriasis [1]. Individuals with PsA typically experience stiffness, pain, swelling, and tenderness of the joints as well as the surrounding ligaments and tendons [1,2]. Disease presentation can range from mild, nondestructive arthritis to severe and debilitating arthropathy [1].

Abbreviations: ACR, American College of Rheumatology; bDMARDs, biologic disease-modifying antirheumatic drugs; DMARDs, disease-modifying antirheumatic drugs; EULAR, European League Against Rheumatism; GRAPPA, Group for Research and Assessment of Psoriasis and Psoriatic Arthritis; IBD, inflammatory bowel disease; JAK, Janus kinase; IL, interleukin; MDA, minimal disease activity; MRI, magnetic resonance imaging; OMERACT, outcome measures in rheumatoid arthritis clinical trials; OTIS, Organization of Teratology Information Specialists; PASI, Psoriasis Area and Severity Index; PIANO, pregnancy in IBD and neonatal outcomes; PsA, psoriatic arthritis; SLE, systemic lupus erythematosus; SPIRIT, Study of Ixekizumab in Participants With Active Psoriatic Arthritis; TICOPA, tight control of inflammation in early psoriatic arthritis; TNF, tumor necrosis factor; TNFi, tumor necrosis factor inhibitor.

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Dr. Mody has no disclosures.

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http://dx.doi.org/10.1016/j.semarthrit.2017.02.001

Initial treatment considerations should be based on discrete clinical manifestations and symptom severity [3]. The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) treatment guidelines provide recommendations for treatment based on the involvement of the following 6 domains: peripheral arthritis, axial disease, enthesitis, dactylitis, skin, and nail [4]. The choice of initial treatment should also take into account comorbidities commonly associated with PsA, and the GRAPPA guidelines provide considerations for treatment based on the presence of concomitant comorbidities [4]. When making treatment decisions, it is important to consider that early and aggressive treatment of some patients can result in significant improvements in joint and skin symptoms, thus preventing permanent damage [5,6].

Biologic disease-modifying antirheumatic drugs (bDMARDs) have transformed the PsA treatment landscape and their use has steadily increased over the last decade [7]. These agents are recommended for patients requiring rapid control of skin and joint symptoms, and those who have failed to respond to non-biologic DMARDs after 3–6 months of treatment [8,9]. Numerous bDMARDs have demonstrated efficacy in PsA, including the tumor necrosis factor inhibitors (TNFis) adalimumab, certolizumab pegol, etanercept, golimumab, infliximab, the interleukin (IL)-12/23 inhibitor ustekinumab, and the IL-17A inhibitor secukinumab [10–12]. The small-molecule phosphodiesterase-4 inhibitor apremilast also has demonstrated efficacy and safety in patients with PsA [13,14]. However, other bDMARDs that are approved for the treatment of rheumatoid arthritis (such as abatacept, anakinra, and rituximab) have either demonstrated limited evidence of efficacy or failed to demonstrate consistent improvements in PsA [15]. In addition, updated GRAPPA guidelines for the management of axial disease in PsA noted that abatacept, rituximab, and the IL-6 inhibitors sarilumab and tocilizumab have failed to show efficacy in ankylosing spondylitis [16], making it unlikely that these agents would benefit patients with axial PsA. The key clinical trials assessing apremilast did not analyze axial disease outcomes [17], thus the updated GRAPPA guidelines were unable to make a recommendation for this therapy in axial PsA [16].

Rheumatologists are now able to choose between bDMARDs for PsA that have different chemical structures, pharmacokinetic properties, dosing regimens, immunogenicity, safety profiles, and mechanisms of action [18]. When a patient fails to respond or no longer responds to one bDMARD due to lack of efficacy or poor tolerability, evidence suggests that switching to another bDMARD can be a safe and effective treatment strategy [10]. However, data to guide clinicians on switching between different bDMARDs are limited [10]. This review discusses factors to consider when switching between bDMARD therapies for patients with PsA in the context of efficacy, safety, and evidence-based treatment guidelines, with a particular focus on extra-articular manifestations and comorbid conditions.

Methods

PsA treatment recommendations from organizations including the European League Against Rheumatism (EULAR) [9], Outcome Measures in Rheumatology (OMERACT) panels [19], GRAPPA [3,4,16,20,21], and other national rheumatology societies [22,23] were evaluated to identify consensus guidelines on switching between bDMARD therapies. PubMed literature searches were then conducted to identify more detailed information on the efficacy and safety of switching bDMARDs in randomized controlled trials or real-world settings. Searches were conducted using combinations of search terms including psoriatic arthritis, switch/switching, biologic, and TNF/tumor necrosis factor. Search results were supplemented based on the reference citations in articles identified in initial searches and based on the authors' familiarity with the published literature. Articles were deemed relevant if they presented data on switching between different bDMARDs in patients with PsA.

Considerations for switching

PsA is a heterogeneous disease, and there is a paucity of data from controlled clinical trials to guide decisions related to therapy changes in this disease area [9]. First, it should be understood that there are no “typical” patient profiles or detailed algorithms that can be followed when patients require alterations in their treatment regimens. Treatment of PsA is complicated by the need to manage both skin and joint disease, along with the increased incidence of comorbid disorders such as inflammatory bowel disease (IBD) [4], all of which may collectively drive therapeutic decisions. Further, skin, joint, and some other systemic manifestations of PsA may have common or differing pathophysiology, such that various treatments may differentially affect articular and extra-articular symptoms [9].

To better guide therapeutic decisions, the outcome measures in rheumatoid arthritis clinical trials (OMERACT) group has defined core PsA domains that should be measured to assess the effects of treatment [19]. These include peripheral joint activity, skin activity, pain, patient global assessment, physical function, and health-related quality of life [19]. With these domains in mind, criteria were developed to define minimal disease activity (MDA), which can serve as a target for treatment in clinical practice [24]. Subsequently, the tight control of inflammation in early psoriatic arthritis (TICOPA) study showed that patients assessed every 4 weeks to determine whether they had achieved MDA targets had better joint and skin outcomes than patients who were followed according to the current standard of care [5,6,25]. According to this tight control protocol, if a patient did not achieve MDA criteria at any visit, their treatment regimen was modified, either by increasing therapeutic doses or by adding or switching therapies [25]. Findings from the TICOPA study suggest that an aggressive treatment strategy that assesses and potentially modifies treatment every 4 weeks is a better approach to PsA management than making changes every 3–6 months, as needed, according to current guidelines [6,9]. Although TICOPA favors a tight control approach, extensive use of sulfasalazine is typically avoided in clinical practice. We recommend not changing biologic medications within 3 months of initiation unless there are serious safety concerns or virtually no response. The current MDA criteria for PsA are compromised by the fact that it is not a composite measure, and does not recognize that patients with significant skin activity may still meet MDA criteria. Therefore, an MDA strategy that addresses these limitations and accounts for skin, joint, and related disease activity in patients on systemic therapy is being developed.

When tracking patients' improvements, even when utilizing tight control strategies such as those in TICOPA, it is important for dermatologists to understand that expected improvements in joint symptoms are typically far less substantial than improvements in skin symptoms. For example, the American College of Rheumatology (ACR) 20 response is the standard benchmark for improvement in joint symptoms [25], whereas Psoriasis Area and Severity Index (PASI) 75 is the minimum benchmark for improvement in skin symptoms [26]. Despite improvements in measuring MDA, clear guidance is not yet available on how to best use imaging [magnetic resonance imaging (MRI) and ultrasonography] to measure radiographic progression in PsA. It is also important to