Biologic Therapy for Psoriatic Arthritis

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KEYWORDS

• Psoriatic arthritis • Psoriasis • Biologics • TNF inhibition • IL-12–23 inhibition • IL-17 inhibition • IL-23 inhibition

KEY POINTS

- Biologic medicines target specific cells and cytokines in the immunologic pathway of inflammation, inhibiting and modulating proinflammatory processes.
- Tumor necrosis factor (TNF) alpha is a key proinflammatory cytokine that drives inflammation and tissue destruction in autoimmune diseases, including psoriatic arthritis (PsA). Medicines that target and diminish the activity of this cytokine show significant benefit in curtailing arthritis, enthesitis, dactylitis, spondylitis, and skin and nail disease; inhibiting progressive structural damage; and improving function and quality of life.
- TNF inhibitors may not work in all patients and may lose effectiveness over time, partly because of immunogenicity. Agents with different mechanisms of action, including the interleukin (IL)-12/23 inhibitor ustekinumab, IL-17 inhibitors such as secukinumab, ixekizumab, and brodalumab, and potentially other emerging therapies such as abatacept and IL-23 inhibitors, show effectiveness in clinical domains of PsA.
- Adoption of treatment strategies such as treatment early in the course of disease, tight control, and treating to target, and the emerging use of biosimilars to reduce cost of therapy may improve outcomes and broaden availability of these medicines for patients.
- Serious safety issues can arise with biologic therapy, so cost-benefit risk must be weighed in decision making about use of biologic medications.

INTRODUCTION

Biologic therapies are parenteral (administered subcutaneously or intravenously) complex proteins biologically manufactured in mammalian or yeast cell lines that typically function by binding to proinflammatory cytokines or cell receptor sites to diminish

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immunologic cell function. Before the introduction of biologic therapy in the late 1990s, therapy for psoriatic arthritis (PsA) consisted primarily of synthetic medicinals such as methotrexate, sulfasalazine, nonsteroidal antiinflammatory medications, along with adjunctive approaches, including physical and occupational therapy.[1,2] Although partially effective, these medicines were not able to achieve low disease activity or remission states and often were not well tolerated. The first biologic therapies approved for the treatment of PsA were the tumor necrosis factor alpha (TNFα) inhibitors.[1,2] These agents have revolutionized the ability to effectively treat all of the clinical manifestations of PsA, including arthritis, enthesitis, dactylitis, spondylitis, skin and nail disease, as well as associated inflammatory bowel disease and uveitis. PsA treatment recommendations developed by international groups such as the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) and the European League Against Rheumatism (EULAR) recommend biologic agents as therapy for patients with moderate to severe disease, noting that the biologics are highly effective in all disease domains of PsA, including arthritis, enthesitis, dactylitis, spondylitis, and skin and nail disease.[3,4] Sustained remission or a low disease activity state is now achievable with these agents. With time, effectiveness may diminish and be lost, necessitating cycling between TNFα inhibitors or switching to agents with a different mechanism of action. This article addresses all biologic therapies for PsA, albeit with a greater emphasis on newer therapies.

TUMOR NECROSIS FACTOR INHIBITION

TNFα was one of the first proinflammatory cytokines implicated in the pathogenesis of numerous inflammatory/autoimmune diseases. It is produced by several types of immune cells and activates several key effector cells involved in tissue inflammation and destruction in psoriasis and PsA, including lymphocytes, macrophages, chondroctyes, osteoclasts, and keratinoctyes. Five agents that inhibit TNFα are now US Food and Drug Administration (FDA) approved, including etanercept, infliximab, adalimumab, golimumab, and certolizumab. These agents were first shown to be effective in the treatment of rheumatoid arthritis, and subsequently showed effectiveness in PsA and ankylosing spondylitis (AS). With the exception of etanercept, these agents are monoclonal antibodies with demonstrated effectiveness in inflammatory bowel disease, whereas etanercept has not. Etanercept, infliximab, and adalimumab are approved for the treatment of psoriasis. The effects of these agents in PsA are reviewed later and American College of Rheumatology (ACR) 20/50/70 responses are summarized in **Table 1**.

Table 1
Anti-TNF therapies in PsA: ACR responses

		ACR20%		ACR50%		ACR70%	
Trial	n	Rx	P	Rx	P	Rx	P
Adalimumab[a,10]	315	58	14	36	4	20	1
Certolizumab[a,16]	409	58	24	36	11	25	3
Etanercept[a,6]	205	59	15	38	4	11	0
Golimumab[b,13]	405	52	8	32	3.5	18	0.9
Infliximab[b,9]	200	58	11	36	3	15	1

Abbreviations: Rx, Treatment Arm; P, placebo.
[a] 12 weeks.
[b] 14 weeks.