Effective Health Care Program

Muscle, Bone, and Joint Conditions
Arthritis

Drug Therapy for Psoriatic Arthritis in Adults: Comparative Effectiveness

Research Focus for Clinicians

In response to a request from the public to AHRQ concerning the expanding use of DMARDs in treatment of inflammatory arthritis, a systematic review was undertaken to review the effectiveness and safety of the DMARDs, both oral and biologic, used to treat psoriatic arthritis (PsA). The review does not cover dermatological treatments specifically targeted to PsA skin disease. This summary is based on a systematic review that included 16 studies published before January 2011. The full report, listing all studies, is available at www.effectivehealthcare.ahrq.gov/dmardspsa.cfm. This summary, based on the full report of research evidence, is provided to clinicians to inform discussions of options with patients and to assist in decisionmaking along with consideration of a patient's values and preferences. However, reviews of evidence should not be construed to represent clinical recommendations or guidelines.

Background

PsA is one of the most disabling presentations of inflammatory arthritis. In addition to the characteristic pain, inflammation, joint damage, and loss of function that worsen over time, this form of arthritis is associated with the skin disease psoriasis. Along with the skin condition, PsA presents with small-joint polyarthritis and/or axial arthritis that involves the spinal, sacroiliac, and large joints. The prevalence of arthritis in the population of patients with psoriasis varies from 6 to 42 percent. In the general population, the prevalence is 0.3 to 1.0 percent, and it appears most often between 30 to 50 years of age.*

Treatment of PsA is aimed at controlling pain and inflammation, usually starting with NSAIDs. With disease modifying anti-rheumatic drugs (DMARDs) as treatment options, slowing or blocking progression of the disease may be possible. The oral DMARDs, particularly methotrexate (MTX), are widely used in treatment strategies for PsA, although their targets are not well defined. The biologic DMARDs approved by the U.S. Food and Drug Administration (FDA) for marketing as PsA treatment target tumor necrosis factor-alpha (TNF-α) signaling. A synthesis of the clinical evidence from studies of DMARDs used to treat PsA is needed to support decisionmaking that balances the benefits of controlling progressive disease against the risks of adverse effects.

Conclusion

Clinical study evidence about DMARDs as PsA treatment is limited. Low- to moderate-strength evidence indicates that anti–TNF-α biologic DMARDs improve psoriatic arthritis, assessed by multiple rating indices. Oral DMARDs may also be beneficial. However, sparse evidence from head-to-head comparisons (both within and between classes) does not permit conclusions about which DMARDs and treatment strategies are superior for minimizing joint damage and optimizing quality of life. Other than the reported infection risks associated with the TNF-α inhibitors, the evidence about adverse events associated with treatment of PsA using DMARDs of either class is insufficient to inform decisionmaking.

Clinical Bottom Line

Benefits

Oral DMARDs:

- **Sulfasalazine** (●●○) and **MTX** (●○○) treatment achieved greater improvement than placebo in a pooled index score† of disease activity, but the minimal clinically important difference (MCID) is not known. Functional capacity and health-related quality of life scores were not reported.
- **Leflunomide:**
  - Improved disease activity more than placebo (36% more patients achieved 20% improvement from baseline [ACR20]). ●○○
  - Led to a statistically but not clinically significant improvement in functional capacity (difference in HAQ was not greater than 0.22 when compared with placebo). ●○○
  - Achieved a statistically but not clinically significant improvement in physical components of health-related quality of life (SF-36 physical component score outside the range of 2.2 to 4.7 points greater than with placebo). ●○○
- Two retrospective cohort studies found that combination therapy with an anti–TNF-α DMARD and MTX provides no additional improvement in disease activity over TNF-α blocker monotherapy. ●○○

Biologic DMARDs *(See Table 1 on the next page.)*

†OMERACT (outcomes measures in rheumatoid arthritis clinical trials): a pooled index of scores on disability, pain, physician and patient global assessment, swollen and tender joint count, and radiographic change indices.

Strength of Evidence Scale

High:	●●●	High confidence that the evidence reflects the true effect. Further research is very unlikely to change our confidence in the estimate of effect.
Moderate:	●●○	Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of effect and may change the estimate.
Low:	●○○	Low confidence that the evidence reflects the true effect. Further research is likely to change our confidence in the estimate of effect and is likely to change the estimate.
Insufficient:	○○○	Evidence is either unavailable or does not permit a conclusion.

*Gladman DD, Antoni C, Mease P, et al. Ann Rheum Dis 2005;64 Suppl 2:ii4-7. PMID: 15708927. | Gelfand JM, Gladman DD, Mease PJ, et al. J Am Acad Dermatol 2005;53(4):573. PMID: 16198775.

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Table 1. Effects of Anti–TNF-α Biologic DMARDs on PsA Outcomes

The range of the effect sizes from individual studies (difference between drug and placebo) are shown.

	Improvement in Disease Activity	Functional Capacity (Mean Improvement)	HRQoL (Mean Improvement)
Biologic DMARDs	***Percentage Achieving ACR20****	***HAQ; MCID ≥ 0.22****	***SF-36 PCS; MCID = 2.2 to 4.7****
Adalimumab	39 to 57 ●●○	0.2 to 0.3 ●●○	2.9 to 7.9 ●○○
Etanercept	59 to 65 ●●○	0.5 to 1.1 ●●○	8.6 ●○○
Golimumab	45 to 51 ●○○	0.34 to 0.4 ●○○	5.9 to 7.2 ●○○
Infliximab	58 to 62 ●●○	0.4 to 0.6 ●●○	6.4 to 8 ●○○

*The range of results from studies, from lowest to highest.

ACR20 = American College of Rheumatology 20-percent improvement from baseline to end point; DMARDs = disease-modifying anti-rheumatic drugs; HAQ = Health Assessment Questionnaire; HRQoL = health-related quality of life; MCID = minimum clinically important difference; PCS = physical component score; SF-36 = Medical Outcomes Study Short Form 36

Adverse Effects

- TNF-α inhibitors are generally associated with increased risk of infections. The FDA has warned that cancer risk may be elevated with their use, but the actual risk to patients with PsA is not known.
- Some adverse effects have been reported with the use of DMARDs to treat PsA, when compared with placebo.
  - Rates of injection site reactions are increased with adalimumab and etanercept. ●○○
  - Etanercept has a lower risk of discontinuation due to adverse events when compared with infliximab. ●○○
  - Adding MTX to treatment with etanercept reduced the rate of withdrawals from treatment. ●○○

Gaps in Knowledge

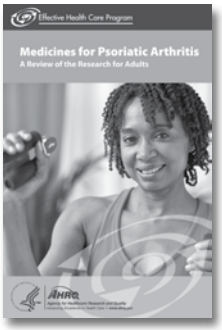
- Randomized controlled trials that examine DMARD effectiveness for treating PsA in head-to-head comparisons are needed.
- Studies that investigate combination therapies and specific treatment strategies are needed.
- Outcomes evaluated in future studies should include axial disease, enthesitis, and dactylitis along with joint counts and should specify the pattern of joint involvement in study patients.
- There are no data about how effectiveness and safety are modified by patient characteristics, subpopulations, and use in typical clinical settings.
- The evidence about the harms, tolerability, adverse effects, and adherence to treatment in studies of DMARD treatment for PsA is very limited and is insufficient to permit conclusions about specific risks for patients with PsA.

What To Discuss With Your Patients

- The role of DMARDs for reducing symptoms and improving disease control
- The limited research about the potential benefits and adverse effects of DMARDs for treating PsA
- Patient and caregiver preferences and values regarding treatment

Resource for Patients

Medicines for Psoriatic Arthritis, A Review of the Research for Adults is a free companion to this clinician research summary. It covers:



- A description of PsA
- The types of DMARDs that are used
- The evidence about the short- and long-term benefits and adverse effects associated with DMARDs used for patients with PsA
- Costs related to biologic and nonbiologic DMARDs

Ordering Information

For electronic copies of *Medicines for Psoriatic Arthritis, A Review of the Research for Adults*, this clinician research summary, and the full systematic review, visit www.effectivehealthcare.ahrq.gov/dmardspsa.cfm. To order free print copies, call the AHRQ Publications Clearinghouse at 800-358-9295.

Source

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