

Issue 2: Current Therapies

Treating to target

The treatment of rheumatoid arthritis (RA) aims at maximizing long-term health-related quality of life through control of symptoms, prevention of structural damage, and normalization of function. The primary target for treatment should be to achieve a state of clinical remission, defined as the absence of signs and symptoms of significant inflammatory disease activity. Low disease activity may be an acceptable alternative goal if complete remission is not realistic or achievable, e.g., in long-standing disease. Treating to target by measuring disease activity and adjusting therapy as necessary can help in optimizing outcomes. ^[1]



Current therapies

Several biologic and non-biologic therapies are available for managing RA. Non-biologic agents include conventional disease modifying antirheumatic drugs (DMARDs) such as hydroxychloroquine, leflunomide, methotrexate, and sulfasalazine. Biologic therapies include abatacept, adalimumab, anakinra, certolizumab, etanercept, golimumab, infliximab, rituximab and tocilizumab.

Conventional DMARDs

Methotrexate (MTX) is the preferred and most frequently used first line therapy for RA, and despite the advent of effective biologic agents, it remains an anchor drug to enhance or maintain the efficacy of biologic agents. MTX therapy is rapidly escalated to 20-25 mg/week, or the highest tolerable dose, with a subsequent switch to subcutaneous administration in the case of an insufficient response or to minimize non-serious gastrointestinal side effects. Patients who respond inadequately to MTX may be treated sequentially with other DMARDs or with combinations of DMARDs (e.g., with hydroxychloroquine or sulphasalazine or both). Most drugs including non-steroidal antiinflammatory drugs (NSAIDs) can be used safely in combination with MTX. ^[2-5] An alternative DMARD with comparable efficacy to MTX is leflunomide. However, limitations of leflunomide include hepatic adverse effects and low retention rates. ^[6, 7]

Biologics



A major limitation of conventional DMARD therapy is that their use is frequently limited by inadequate efficacy and/or toxicity. The advent of biologic therapies has represented an important advance in RA management, targeting key cellular mediators and cytokines involved in the pathogenesis of RA.

Patients who do not adequately respond to MTX should be considered for therapy with a biologic agent.

Current practice involves starting with a TNF inhibitor (adalimumab, certolizumab, etanercept, golimumab, infliximab). These agents have comparable efficacy and tolerability. ^[8] Patients experiencing non-response, loss of efficacy, or toxicity with a first TNF inhibitor should be considered for treatment with an alternative agent. For primary non-response, changing to a drug of a different class rather than switching to

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Patient profile

Sarah is a 55-year old woman with RA. She is RF-positive and anti CCP-positive. She is a current smoker. Sarah received treatment with MTX, but had to discontinue this agent because of adverse effects. She was then treated with adalimumab, to which she responded initially, but later showed signs of secondary failure.

She is now receiving treatment with rituximab, but continues to have an unacceptably high tender and swollen joint count.

References

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In the next issue

Coming up in the next Rheumatoid Arthritis Newsletter, we will bring you the **breaking news** stories from the upcoming **American College of Rheumatology (ACR) Conference**.

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an alternative TNF inhibitor may be recommended. In the case of secondary non-response, either switching to another TNF inhibitor or changing to a drug of a different class may be appropriate. In the case of drug toxicity, switching to another TNF inhibitor or changing to a drug of a different class may be acceptable. ^[9]

The T-cell co-stimulatory blocker abatacept or the IL-6 inhibitor *tocilizumab* are alternatives to the TNF inhibitors; these agents may be employed either as first line therapies or after failure of TNF inhibitor therapy. Patients who do not respond to these agents can be considered for treatment with the anti-B cell agent rituximab. ^[8] All patients should be managed with intensive medication strategies, with patients who have poor prognostic factors having more to gain. Factors apart from disease activity, e.g., progression of structural damage, co-morbidities and safety concerns should be taken into account when adjusting treatment. ^[8]

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