

The Current Guidelines in Practice: Rheumatoid Arthritis

In May 2012, the American College of Rheumatology updated their recommendations for the use of disease-modifying anti-rheumatic drugs (DMARDs) and biologic agents in the treatment of rheumatoid arthritis. Guidelines begin with some very important terms and definitions:

DMARDs: Hydroxychloroquine, Leflunamide, Methotrexate, Minocycline, and Sulfasalazine

DMARD combination therapy: Methotrexate + Hydroxychloroquine, Methotrexate + Leflunamide, Methotrexate + Sulfasalazine, Sulfasalazine + Hydroxychloroquine, Methotrexate + Hydroxychloroquine + Sulfasalazine

Anti-TNF biologics: Adalimumab, Certolizumab pegol, Etanercept, Infliximab, Golimumab

Non-TNF biologics: Abatacept, Rituximab, Tocilizumab

Early RA: RA disease duration < 6 months from diagnosis

Established RA: RA disease duration ≥ 6 months

Disease Activity: Categorized as low, moderate, and high as per validated common scales or the treating clinician's formal assessment

RA remission: A tender joint count, swollen joint count, C-reactive protein level, and patient global assessment of ≤ 1 each or a simplified Disease Activity Score of ≤ 3.3

Poor Prognosis: Presence of ≥ 1 of the following features: functional limitation, extra-articular disease, positive rheumatoid factor or anti-cyclic citrullinated peptide antibodies, and/or bony erosions by radiograph

The ACR recommends targeting remission or low disease activity in RA. Below are their recommendations of step-therapy to best achieve decreased disease activity balanced with lower probability of adverse events based on severity of disease. Therapies that were approved after the original literature review are not included in these recommendations.

Recommendations and indications for starting, resuming, adding, or switching DMARDs or biologic agents

Early Rheumatoid Arthritis

- For low disease activity and for moderate to high disease activity without the presence of poor prognostic features, DMARD monotherapy is recommended.
- For moderate or high disease activity with the presence of poor prognostic features, DMARD combination therapy is recommended.
- Also for high disease activity with the presence of poor prognostic features, anti-TNF biologic agents (with or without methotrexate) can be used. The only exception is infliximab; it should be used in combination with methotrexate, and not as monotherapy.

Established Rheumatoid Arthritis

Initiating and switching among DMARDs:

- If after 3 months of DMARD monotherapy, a patient deteriorates, DMARD combination therapy should be implemented.
- If after another 3 months of DMARD combination therapy, a patient still has moderate or high disease activity, add another non-methotrexate DMARD or switch to a different non-methotrexate DMARD.

Switching from DMARDs to biologic agents:

- If after 3 months of DMARD or DMARD combination therapy, the patient still has moderate or high disease activity, adding or switching to an anti-TNF biologic, abatacept, or rituximab is recommended.

Recommendations and indications for starting, resuming, adding, or switching DMARDs or biologic agents (cont'd)

Switching among biologic agents due to lack of benefit or loss of benefit:

- If after 3 months of anti-TNF biologic therapy, a patient still has moderate to high disease activity, switching to another anti-TNF biologic or non-TNF biologic is recommended.
- If after an additional 6 months on a non-TNF agent, switching to another non-TNF biologic or an anti-TNF biologic is recommended.

Switching among biologic agents due to harms/adverse events:

- If a patient has high disease activity after failing an anti-TNF biologic because of a serious adverse event, switch to a non-TNF biologic.
- If a patient has moderate or high disease activity after failing an anti-TNF biologic because of non-serious adverse events, switch to another anti-TNF biologic or a non-TNF biologic.
- If a patient has moderate or high disease activity after failing a non-TNF biologic because of an adverse event (serious or non-serious), switch to another non-TNF biologic or an anti-TNF biologic.

Use of biologic agents in RA patients with hepatitis, malignancy, or CHF, qualifying for more aggressive treatment

Hepatitis B or C:

- Hepatitis B: ACR recommends not using biologic agents in RA patients with untreated chronic hepatitis B and in RA patients with treated Hepatitis B with Child-Pugh class B and higher
- Hepatitis C: Etanercept could potentially be used in RA patients with hepatitis C requiring RA treatment

Malignancy:

- For patients who have been treated for solid malignancies or nonmelanoma skin cancer > 5 years ago, ACR recommends starting or resuming any biologic agent if those patients would otherwise qualify for this RA management.
- Rituximab can be used in those patients treated for solid malignancies or nonmelanoma skin cancer within the past 5 years

CHF:

- ACR recommends against using any anti-TNF biologic in RA patients with CHF that is NYHA class III or IV and who have an ejection fraction of $\leq 50\%$.

In summary, in patients with early RA, DMARD monotherapy and combination therapy should be utilized initially, then can be adapted to accommodate increasing severity of disease. In patients with established RA and either not currently on medication, DMARD combination therapy or biologic agents can be considered. Certain comorbid diseases, TB infections, and vaccinations can be greatly influenced by the type of anti-rheumatic treatment initiated.

References:

- Saag KG, Teng GG, Patkar NM, Anuntiyo J, et al. American college of rheumatology 2008 recommendations for the use of nonbiologic and biologic disease-modifying antirheumatic drugs in rheumatoid arthritis. American College of Rheumatology. 2008 June;59(6):762-784.
- Singh JA, Furst De, Bharat A, Curtis JR, et al. 2012 update of the 2008 American college of rheumatology recommendations for the use of disease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis. American College of Rheumatology. 2012 May;64(5):625-639.



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