Rheumatoid arthritis – Treatment guidelines

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Learning objectives:

By the end of this screencast, you should be able to:

- Describe and apply appropriate guidelines for the management of RA

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- Aims of treatment –
  - Minimising joint pain and swelling
  - Preventing deformity and radiological damage (i.e. erosion)
  - Maintaining QoL
  - Controlling extra-articular manifestations

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Guidelines

National Institute for Health and Clinical Excellence (NICE) 2018 – Rheumatoid Arthritis in Adults: management. (Updated Oct 2020)

EULAR – European League Against Rheumatism

EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2022 update (https://ard.bmj.com/content/82/1/3.long - accessed 29/9/23

- Smolen JS, et al. *Annals of the Rheumatic Diseases* 2023;**82:**3-18.

Treatments

- Analgesia – NSAIDs
- Glucocorticoids
- DMARDs – Disease Modifying Anti-rheumatic Drugs
  - Main goal of DMARD treatment = remission.

Conventional DMARDs (cDMARD) – methotrexate, sulfasalazine, leflunomide
[hydroxychloroquine, azathioprine, penicillamine, gold, ciclosporin]

Biologic (bDMARD) - **Anti-TNF** - (Adalimumab, Etanercept, certolizumab, golimumab, infliximab)

Other biologics – Tocilizumab / sarilumab – IL-6 receptor inhibitor
Rituximab – Anti-B cell (anti-CD20 antibody)
Abatacept – Antibody blocking T-cell (lymphocyte) activation (costimulation modulator CD80/86)
Anakinra – IL-1 receptor inhibitor

Targeted (tDMARD) – **JAK inhibitors** – tofacitinib / baricitinib /upadacitinib / filgotinib

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NICE – NG 100

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Guidelines – NICE - Treatment

- **'Treat to target'** – a strategy which should include frequent review, formal assessment of joints and escalation of therapy if inflammation is still present until good control is reached.
  - Patients have an individual target (remission DAS 28 < 2.6 or low activity DAS 28 <3.2)
  - Requiring tight control

  The target should be remission if there is increased risk of radiological progression (i.e. anti-CCP positive or erosion at baseline).

  - CRP and disease activity (i.e. with DAS 28) monthly in specialist care until target reached.

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Guidelines – NICE - Treatment

Initial treatment (newly diagnosed active RA)

- **First line** – conventional Disease Modifying Anti-Rheumatic Drug (cDMARD) as MONOTHERAPY. As soon as possible (ideally within 3 months of onset of symptoms).
  - Methotrexate (oral) [sc may be used in practice]
  - Leflunomide
  - Sulfasalazine
  - [Consider as an alternative hydroxychloroquine (for mild or palindromic disease)]
- **Escalate dose** as tolerated.
- Consider short term **bridging** with glucocorticoid therapy when starting a new DMARD.

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Guidelines – NICE - Treatment

Step-up strategy

- When the treatment target has not been achieve (despite dose escalation)
- Offer ADDITIONAL cDMARD (oral methotrexate, leflunamide, sulfasalazine or hydroxychloroquine)

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Guidelines – NICE – Treatment

Further pharmacological management:

Biologics and targeted DMARDs

Moderate disease (DAS 28 3.2 – 5.1)	Severe disease (DAS 28 >5.1)
• **Anti-TNF**	• **Anti-TNF**
Adalimumab +/- MTX (TA 715)	Adalimumab +/- MTX (TA 375)
Etanercept +/- MTX (TA 715)	Etanercept +/- MTX (TA 375)
Infliximab + MTX (TA 715)	Infliximab + MTX (TA 375)
	Certolizumab + MTX (TA 375)
	Golimumab + MTX (TA 375)
• **Targeted DMARDs (Jak inhibitors)**	• **Targeted DMARDs (Jak inhibitors)**
Filgotinib +/- MTX (TA 676)	Filgotinib +/- MTX (TA 676)
Upadacitinib +/- MTX (TA 744)	Upadacitinib +/- MTX (TA 744)
-	Baricitinib +/- MTX (TA 466)
-	Tofacitinib +/- MTX (TA 480)
• **Anti – IL-6**	• **Anti – IL-6**
-	Sarilumab + MTX (TA 485)
-	Tocilizumab + MTX (TA 375)
• **Antibody blocking T-cell activation (CD8-/86)**	• **Antibody blocking T-cell activation (CD8-/86)**
Abatacept + MTX (TA 715)	Abatacept + MTX (TA 375)
• **Anti-B cell (anti-CD20 antibody)**	**Anti-B cell (anti-CD20 antibody)**
-	Rituximab +/- MTX

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Guidelines – NICE - Treatment

- For those with moderate disease – they must have a moderate response (DAS 28 improvement of ≥ 0.6 and ≤ 1.2) at 6 months to continue.
- For those with severe disease – they must have a moderate response (DAS 28 improvement of ≥ 1.2) at 6 months to continue.

Treatment options after failure of a biological or targeted DMARD are not considered here

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Guidelines – NICE - Treatment

- If maintained for at least 1 year (without corticosteroids (used for a flare)) consider **step-down strategy**
  - Consider cautiously reducing drug doses or stopping drugs
  - Return to previous DMARD regime if target no longer met

- **Symptom control**
  - Consider NSAID (traditional and COXII inhibitors) when control of pain and stiffness is inadequate.
    - Consider drug toxicities and patients risk factors
    - Use the lowest affective dose for shortest time
    - Offer a PPI
    - Review risk factors regularly

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Guidelines – NICE - Treatment

- Flare management
  - For patients with recent onset or established RA - short term glucocorticoids can rapidly reduce inflammation.
  - These should be – STOPPED
  - The only reason these may continue is – when ALL other treatment options have been offered.

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Guidelines – NICE – Monitoring

- Patients should be provided with information on how and when to access specialist care
  - Have rapid access during a flare
  - Ongoing drug monitoring
- Review 6 months after achieving target to ensure maintenance
- Annual review
  - Assess disease activity, damage and functional ability (i.e. with HAQ)
  - Check for development of comorbidities
  - Organise cross referral in the MDT
  - Assess the effect on personal life

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EULAR – European League Against Rheumatism

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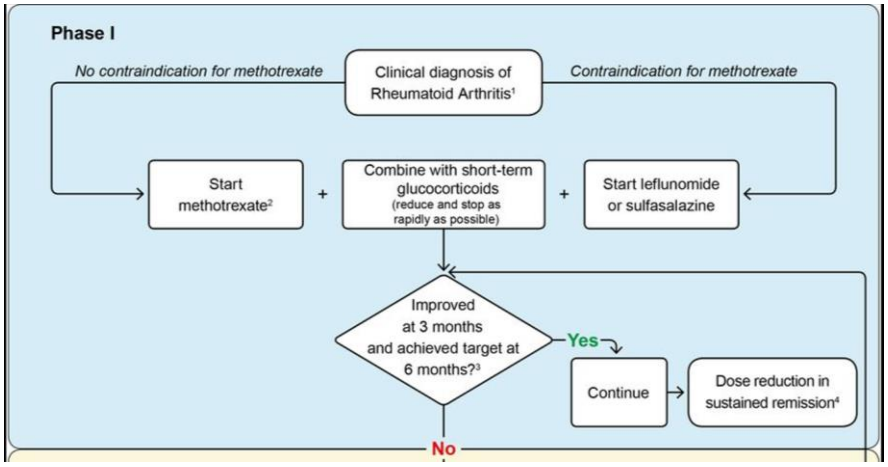
Guidance – EULAR (European League Against Rheumatism)



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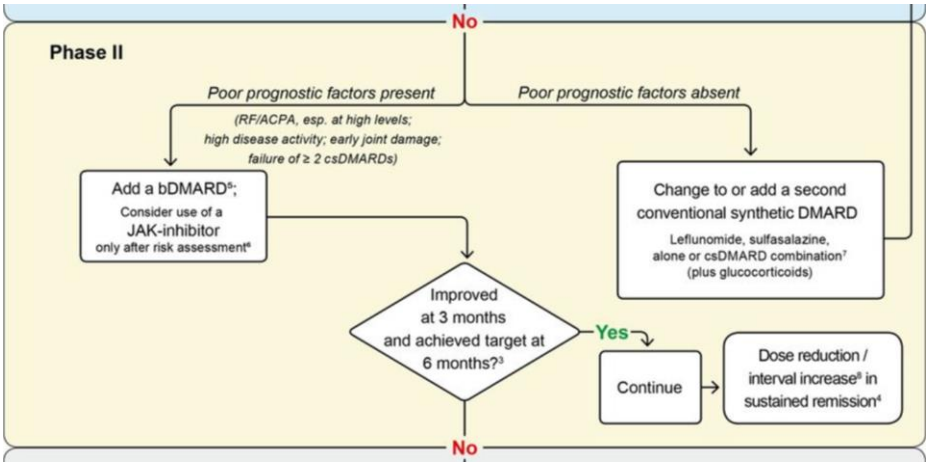
Guidance – EULAR (European League Against Rheumatism)



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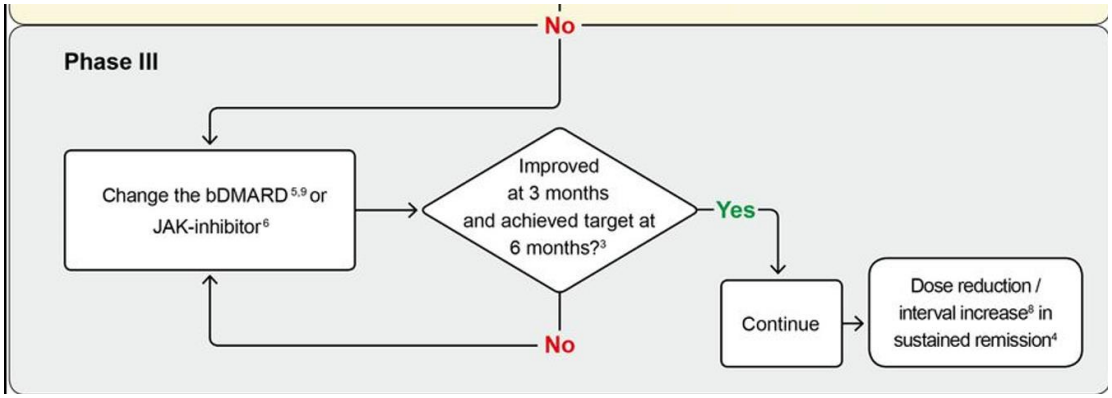
Guidance – EULAR (European League Against Rheumatism)



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Initial therapy – Decision making

- Drug choice is dependent on:
  - Patient preference
  - Patient characteristics
    - Co-morbidities, risk factors
  - Treatment characteristics
    - cautions / contraindications / side effects / dosing / interactions / monitoring requirements etc.

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