



How to taper bDMARD therapy in RA course

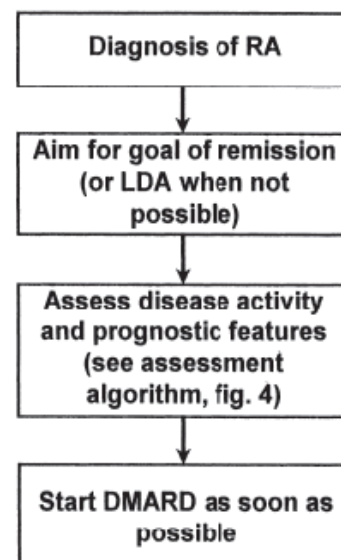
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بیاد و خاطره استاد بی تکرار و غیرقابل جایگزین گرامی

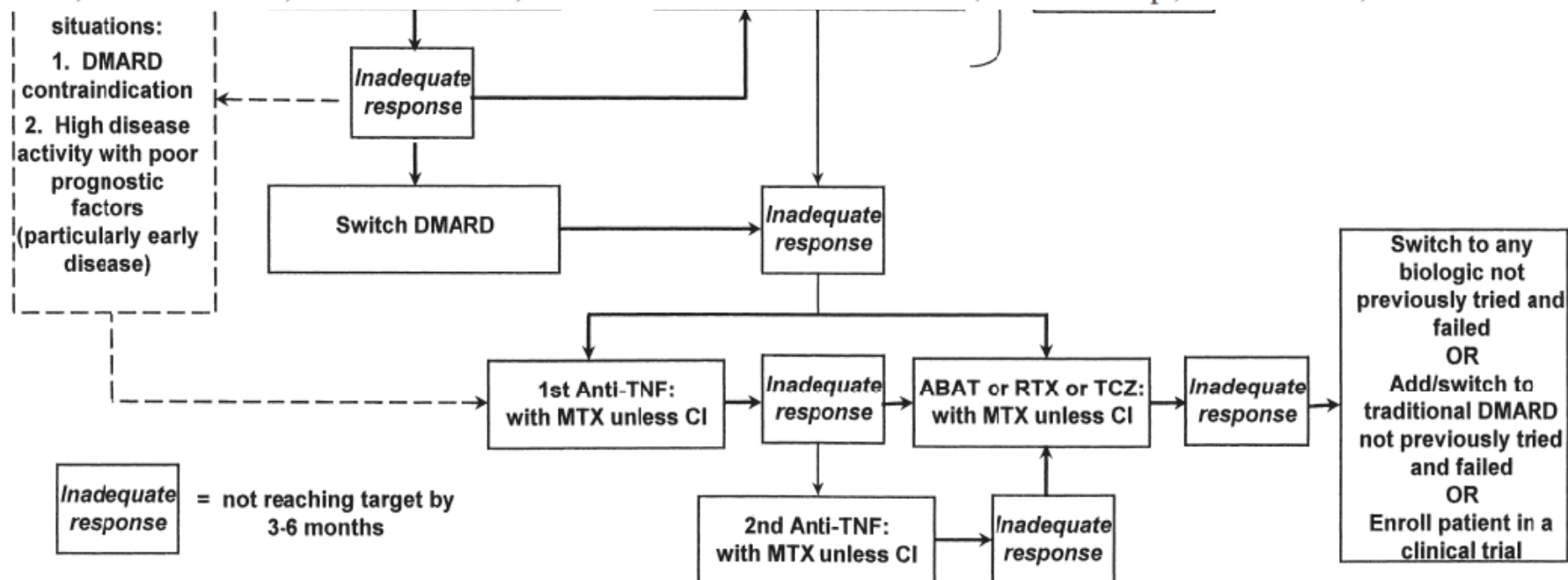




Diagnosis



2. Algorithm based on the Canadian Rheumatology Association (CRA) recommendations for the pharmacological treatment of rheumatoid arthritis (RA) with traditional and biologic disease-modifying antirheumatic drugs (DMARD). LDA: low disease activity; DMARD: disease-modifying antirheumatic drug; CI: contraindication; intraarticular; IM: intramuscular; MTX: methotrexate; anti-TNF: tumor necrosis factor inhibitor; ABAT: abatacept; RTX: rituximab; TCZ: tocilizumab.



1. After insufficient response to MTX, is step-up therapy using a combination of csDMARDs as efficacious as step-up therapy using a bDMARD? Such trials should be thoroughly performed by defining an appropriate end point, adhering to the a priori primary end point, and recruiting/evaluating sufficient numbers of patients in accordance with the original power calculation.
2. Can triple therapy with MTX, sulfasalazine and hydroxychloroquine be regarded as a treatment with 'three different DMARDs' or is it just a 'single DMARD strategy'?
3. What is the most successful tapering strategy of glucocorticoids after bridging or longer-term therapy?
4. What is the balance of benefit/harm of long-term (>6 months) treatment with glucocorticoids at doses up to 10 mg/day in established RA?
5. How long can low-dose glucocorticoids be applied with benefit and without causing harm?
6. How do biological agents plus MTX compare with MTX plus low-dose glucocorticoids in patients with early RA?
7. Is induction therapy with bDMARDs plus MTX as a first treatment strategy followed by withdrawal of the biological agent after 6–12 months as promising an option for abatacept and tocilizumab as it appears to be for TNF inhibitors, and can therefore an induction regimen with bDMARDs plus MTX become a new therapeutic paradigm?
8. With respect to the efficacy and safety of tofacitinib, can biological agents be safely used after tofacitinib (with or without a washout period) and can tofacitinib be safely and effectively used after abatacept, rituximab and tocilizumab?
9. How comparable are the different biological agents to each other and to tofacitinib?
10. Are there, aside from rituximab, differences in responsiveness to bDMARDs between seropositive and seronegative patients?
11. Is there a difference between reducing dose and increasing interval when tapering biological agents after the targeted state has been reached?
12. Is it correct that, when patients have not reached the target on MTX, those with risk factors for bad outcome benefit more from the addition of a biological agent than from switching to or addition of csDMARDs?
13. Is it correct that, when patients have not reached the target on MTX, those with no risk of bad outcome benefit equally from switching to or addition of csDMARDs as they would from addition of a biological agent?
14. Can we find common or specific predictors of response to the different biological agents, csDMARDs and tsDMARDs?
15. What are the risk factors that define patients who benefit from a more intensive initial treatment modality?
16. Which factors predict who will be able to successfully withdraw bDMARDs and who not?
17. How big is the difference in clinical, functional and structural efficacy when treatment strategies aiming to achieve remission are compared with those aiming to achieve low disease activity?
18. How can immunogenicity of bDMARDs explain the similarity of clinical trial data observed with both immunogenic and non-immunogenic compounds?
19. How good is patient adherence to biological agents and can lack of adherence be related to loss of efficacy?
20. Is measurement of serum drug and/or drug antibody levels useful in clinical practice?
21. Which degree of improvement is needed at 3 months to ensure reaching the treatment target at 6 months and beyond?
22. How long should we aim to use concomitant GC therapy in RA?
23. To understand more in detail how the molecular mechanisms of genomic and non-genomic GC actions (and their dose dependency!) mediate the clinically wanted benefits but also the known adverse effects.
24. To improve treatment with conventional GCs (eg, in respect of timing and circadian rhythms) and develop innovative GC or novel GC receptor ligands.
25. To evaluate further possibilities to reduce the (subjective) adverse events of MTX, the anchor drug in treating RA.
26. Long-term safety data in real life (registries) are needed for non-TNF inhibitor biological agents and tofacitinib.
27. Is tocilizumab monotherapy as efficacious and safe as other bDMARDs plus MTX?
28. Can bDMARDs and/or sDMARDs be safely withdrawn in patients with established disease who have long-standing (>6 months) remission according to the ACR–EULAR definition?

ACR, American College of Rheumatology; bDMARD, biological DMARD; csDMARD, conventional synthetic DMARD; DMARD, disease-modifying antirheumatic drug; EULAR, European League against Rheumatism; GC, ; MTX, methotrexate; RA, rheumatoid arthritis; TNF, tumour necrosis factor; tsDMARD, targeted synthetic DMARD.

Step I:
monotherapy

methotrexate (15mg/week) + glucocorticoids

4-6 weeks

Step II:
optimized
monotherapy

adjustment of methotrexate and glucocorticoids

4-6 weeks

Step III:
traditional DMARD
combination

methotrexate
+ leflunomide

methotrexate
+ sulfasalazine
+ hydroxychloroquine

3 months

Step IV:
1st biologic DMARD

abatacept, adalimumab*, certolizumab*, etanercept*,
golimumab, infliximab, tocilizumab**
+ methotrexate

3-6 months

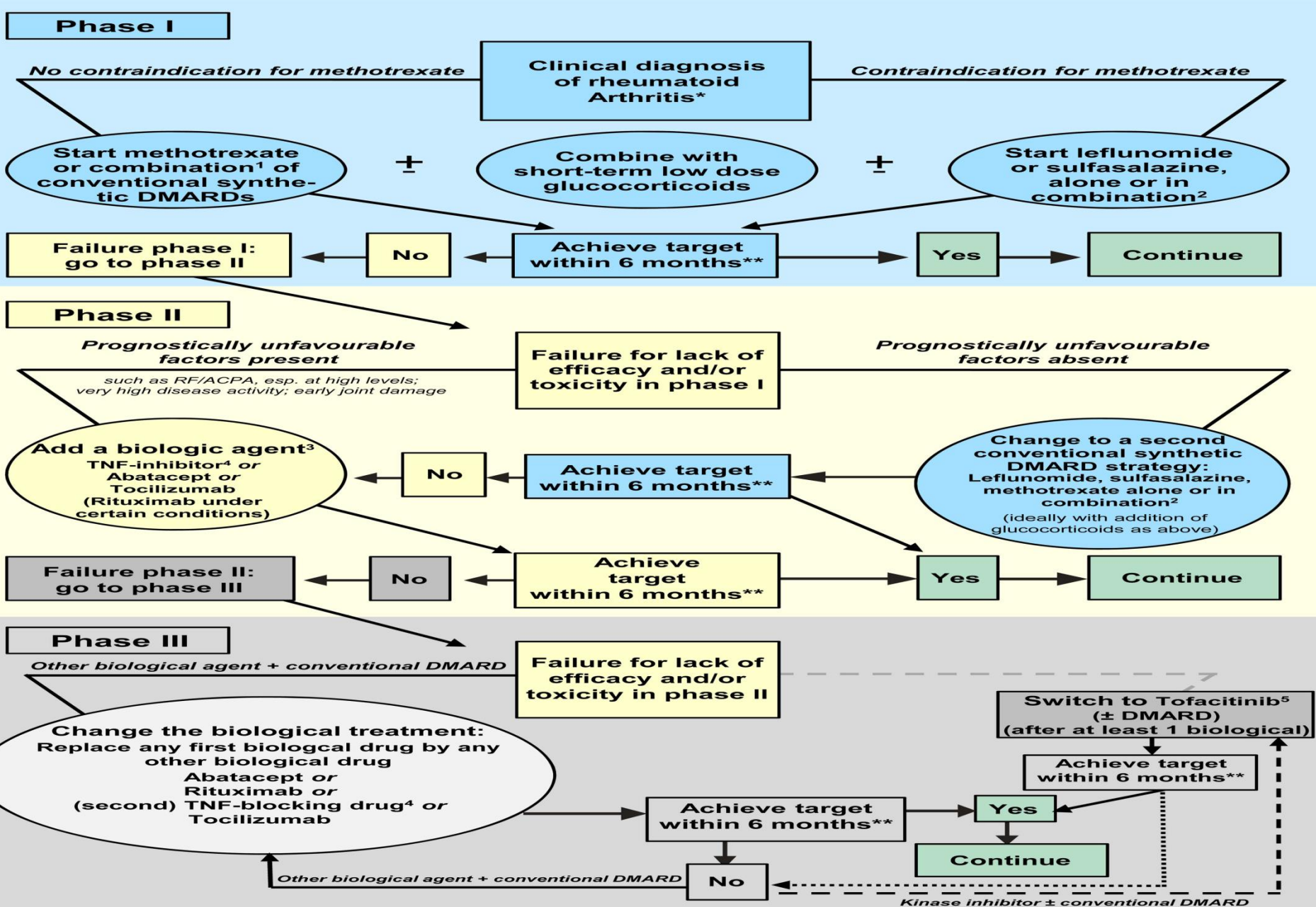
Step V:
2nd biologic DMARD

abatacept, rituximab, TNF-inhibitors*, tocilizumab**
+ methotrexate

Alternative:

- leflunomide
- sulfasalazine
- injectable gold
- (hydroxy)chloroquine
- cyclosporine A
- azathioprine
- methotrexate + cyclosporine A
- anakinra + methotrexate
- cyclophosphamide
- other immunotherapies

poor prognostic factors



*2010 ACR-EULAR classification criteria can support early diagnosis; **The treatment target is clinical remission according to ACR-EULAR definition or, if remission is unlikely to be achievable, at least low disease activity; the target should be reached after 6 months, but therapy should be adapted or changed, if no improvement is seen after 3 months. ¹The most frequently used combination comprises methotrexate, sulfasalazine and hydroxychloroquine; ²Combinations of sulfasalazine or leflunomide except with methotrexate have not been well studied, but may include combining these two and also with antimalarials; ³these circumstances are detailed in the text; ⁴Adalimumab, certolizumab, etanercept, golimumab, infliximab or respective well studied and FDA/EMA approved biosimilars; ⁵where licensed.

Lines: Full black line, recommended; as shown; grey interrupted line: recommended for use after biologics failure (ideally two failed biologics); interrupted black line: recommended after two biologics failed, but efficacy and safety after failure of abatacept, rituximab and tocilizumab not sufficiently studied; black dotted line: possibly recommended, but efficacy and safety of biological use after tofacitinib failure unknown at the time of developing the 2013 update of the recommendations.

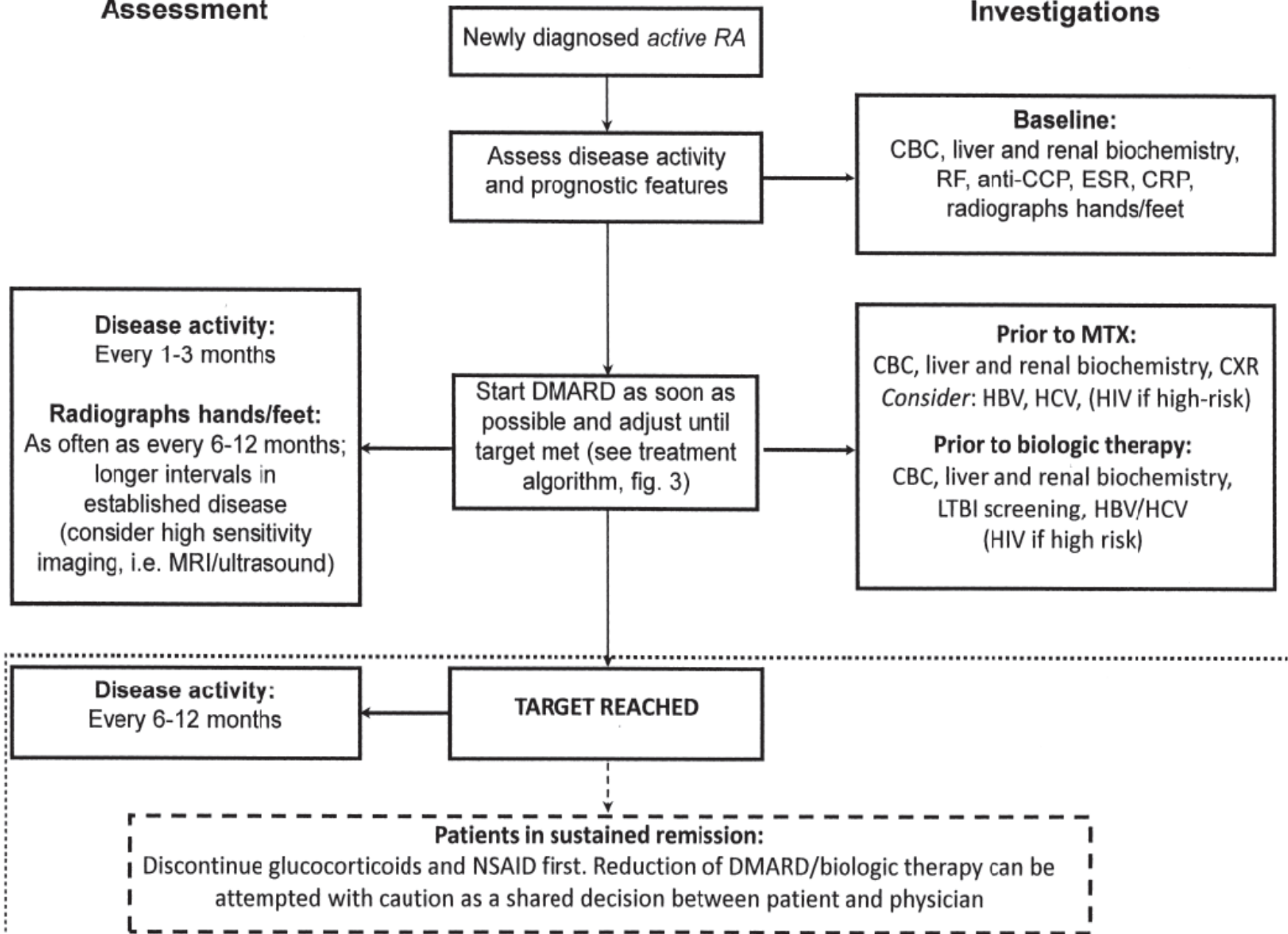
Recommendations	Level	Strength
General RA management strategies		
1. The goal of treatment is remission and, when not possible, minimal disease activity (I) while controlling symptoms, halting damage, preventing disability, and improving quality of life (IV)	I, IV	A
2. The presence of the following poor prognostic features should be assessed at baseline and considered when making treatment decisions: RF positivity, anti-CCP positivity, functional limitation, high number of swollen and tender joints, early erosions, extraarticular features, high ESR or CRP	II	B
3. RA care providers should monitor disease activity as frequently as every 1 to 3 months in patients with active RA (I). Patients with well controlled disease and patients in remission can be monitored at longer intervals (IV)	I, IV	A
4. Traditional and biologic DMARD therapy should be adjusted every 3-6 months, as long as the goal has not been achieved	I, IV	B
5. Radiographs of the hands and feet are recommended as frequently as every 6-12 months in patients with recent-onset disease (II). Radiographs can be performed at longer intervals in patients with established disease (IV)	II, IV	B
6. A change in therapy should be considered in patients with radiographic progression despite adequate clinical response	IV	D
Treatment with glucocorticoids		
7. Glucocorticoids (oral, intramuscular, or intraarticular) can be added to DMARD therapy as part of the initial treatment strategy of patients with RA (I), and may be an option for managing flares, as bridge therapy while waiting for DMARD to take effect, or for symptom control if no other options exist (IV). Glucocorticoids should be used in the lowest possible dose and tapered as rapidly as clinically feasible (IV)	I, IV	A/D
Treatment with MTX/DMARD		
8. In patients with persistent synovitis, DMARD should be introduced as soon as possible	I	A
9. MTX is the preferred DMARD with respect to efficacy and safety and should be the first DMARD used in patients with RA unless contraindicated	I	A
10. A complete blood count (II), liver (I) and renal biochemistry (II), and a chest radiograph (II) should be ordered prior to initiating MTX therapy. Screening for hepatitis B and C should be considered (III), and HIV testing is recommended in high-risk patients (IV)	I-IV	B/D
11. Dosing of MTX should be individualized to the patient (IV). MTX should be started oral or parenteral and titrated to a usual maximum dose of 25 mg/week by rapid dose escalation. In patients with an inadequate response or intolerance to oral MTX, parenteral administration should be considered (I)	I, IV	A
12. Initial combination therapy with traditional DMARD should be considered, particularly in patients with poor prognostic features, moderate-high disease activity, and in patients with recent-onset disease. Combination therapy should also be considered in patients who have an inadequate response to monotherapy	I	B

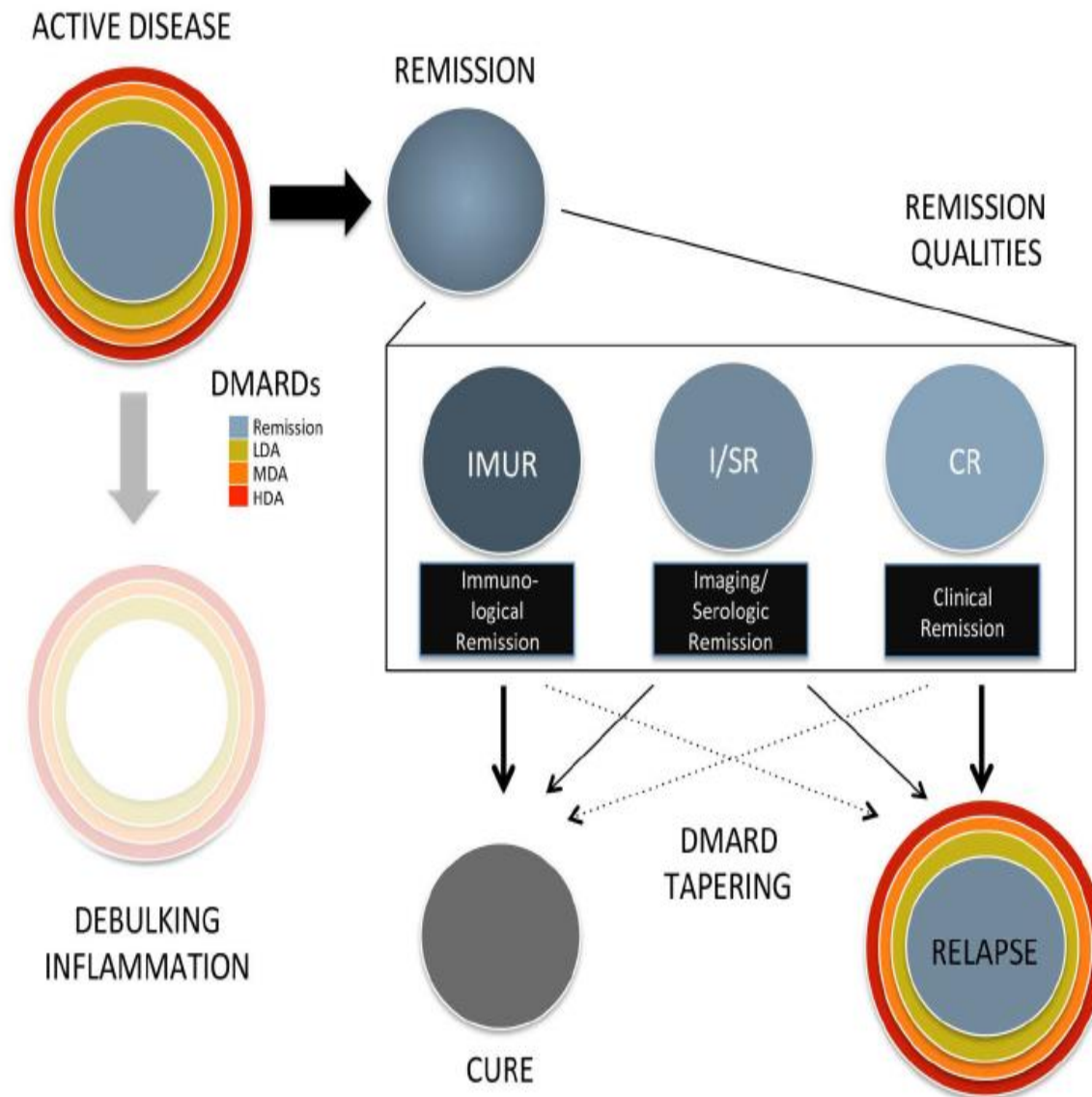
13. When treating with combination therapy, MTX should be used as the anchor drug unless contraindicated. Combinations not including MTX can be considered on a case-by-case basis	I	A
14. Combination therapy with leflunomide and MTX should be used with caution as it is associated with higher toxicity (gastrointestinal and liver) (I) and has no added benefit relative to other DMARD combinations (IV)	I, IV	A
Treatment with biologics		
15. In patients being considered for biologic therapy, an inadequate response to DMARD is defined as moderate to high disease activity despite treatment with at least 2 DMARD (including MTX unless contraindicated) in mono or combination therapy after 3 months at target dose	IV	D
16. Routine laboratory tests (complete blood count, liver and renal biochemistry) and screening for hepatitis B and C (and HIV in high-risk patients) are recommended prior to initiating all biologic therapy. Screening for latent tuberculosis is recommended prior to anti-TNF, abatacept, and tocilizumab. Baseline antinuclear antibody testing could be considered prior to starting anti-TNF	IV	D
17. MTX coprescription with biologics is recommended for improved efficacy	I	A
18. Anti-TNF therapy is recommended for treatment of patients with RA after an inadequate response to DMARD (I). In exceptional circumstances involving patients with DMARD contraindications or high disease activity and poor prognostic factors (particularly early disease), anti-TNF therapy may be an option after failure of DMARD monotherapy or in DMARD naive patients	I	A
19. Abatacept is recommended for the treatment of patients with RA after inadequate response to DMARD or anti-TNF therapy	I	A
20. Rituximab is recommended for the treatment of patients with RF-positive RA after an inadequate response to DMARD or anti-TNF therapy	I	A
21. Patients should not be expected to flare before they are retreated with rituximab (IV). Retreatment can occur as early as 6 months if the patient has had an initial response but has persistent synovitis (II)	II, IV	C
22. Tocilizumab is recommended for the treatment of patients with RA after inadequate response to DMARD or anti-TNF therapy	I	A
23. In patients who have failed treatment with 1 anti-TNF due to lack of efficacy or toxicity the following options are recommended: switch to another anti-TNF (I, II), switch to another biologic with a different mechanism of action (abatacept, rituximab, tocilizumab) (I), or add MTX (or other DMARD) if anti-TNF was used in monotherapy (II)	I, II	B
24. In patients who have failed treatment with 2 anti-TNF a switch to another biologic with a different mechanism of action (abatacept, rituximab, tocilizumab) is recommended	II/IV	C
25. In the absence of data on therapeutic strategies after failure of abatacept, rituximab, or tocilizumab the following options can be considered: switch to any biologic not previously tried and failed, add or switch to a traditional DMARD not previously tried and failed, or enroll the patient in a clinical trial with a new agent	IV	D
26. If a patient achieves sustained remission after discontinuation of NSAID and glucocorticoids, a reduction in traditional and biologic DMARD can be attempted with caution as a shared decision between the patient and physician	IV	D

RA: rheumatoid arthritis; DMARD: disease-modifying antirheumatic drug; anti-CCP: anti-cyclic citrullinated peptide antibody; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; HIV: human immunodeficiency virus; MTX: methotrexate; NSAID: nonsteroidal antiinflammatory drug; RF: rheumatoid factor.

Frequency of Assessment

Pre-treatment Investigations






Remission criteria



Disease Activity Measures	Remission	Low	Moderate	High	Formula
ACR/EULAR Boolean-based definition for remission	TJC28 \leq 1, SJC28 \leq 1, CRP \leq 1 mg/dl, PGA \leq 1	—	—	—	Each criterion must be satisfied
ACR/EULAR index-based definition for remission:					
Simple Disease Activity Index (SDAI)	\leq 3.3	—	—	—	See details for SDAI below
Disease Activity Score (DAS, range 0–10)	$<$ 1.6	1.6 to 2.4	$>$ 2.4 to 3.6	$>$ 3.6	$[0.54 \times \sqrt{(\text{RAI})}] + [0.065 \times 44 \text{SJC}] + [0.33 \times \ln(\text{ESR})] + [0.0072 \times \text{GH}]$ Calculator: http://www.das-score.nl
Disease Activity Score 28 (DAS28, range 0–9.4) ^{††}	$<$ 2.6	2.6 to 3.2	$>$ 3.2 to 5.1	$>$ 5.1	$0.56 \times \sqrt{(\text{TJC28})} + 0.28 \times \sqrt{(\text{SJC28})} + 0.36 \times \ln(\text{ESR}) + 0.014 \times \text{PGH} + 0.96^{\dagger}$
Simplified Disease Activity Index (SDAI, range 0.1–86)	\leq 3.3	$>$ 3.3 to 11	$>$ 11 to 26	$>$ 26	TJC28 + SJC28 + PGA + PhGA + CRP
Clinical Disease Activity Index (CDAI, range 0–76)	\leq 2.8	$>$ 2.8 to 10	$>$ 10 to 22	$>$ 22	TJC28 + SJC28 + PGA + PhGA
Patient-reported Rheumatoid Arthritis Disease Activity Index (RADAI, range 0–10); data are medians	—	$<$ 2.2	2.2 to 4.9	$>$ 4.9	(PGA + patient reported disease activity based on SJC and TJC + pain + morning stiffness + TJC48)/items answered
Patient Activity Scale (PAS or PASII, range 0–10)	—	\leq 1.9	$>$ 1.9 to 5.3	$>$ 5.3	$[(\text{HAQ}/\text{HAQ-II} \times 3.3) + \text{pain} + \text{PGA}]/3$
Routine Assessment Patient Index Data (RAPID3, range 0–30) \leq 3		3 to 6	$>$ 6 to \square 12	$>$ 12	MDHAQ functional score + pain + PGA

[†] Calculator: <http://www.das-score.nl>. ^{††} Alternative DAS/DAS28 formulas based on the use of CRP rather than ESR are available from <http://www.das-score.nl>. Other cut points for the DAS28 have also been proposed (remission \leq 2.4, low activity \leq 3.6, high activity $>$ 5.5)⁵. DAS: Disease Activity Score based on 44 joint counts; RAI: Ritchie Articular Index; DAS28: Disease Activity Score based on 28-joint counts; TJC28: tender joint count based on 28-joint count; SJC28: swollen joint count based on 28-joint count; ESR: erythrocyte sedimentation rate; PGH: patient global assessment of health [visual analog scale (VAS) 0–100 mm]; PGA: patient global assessment of disease activity (VAS 0–10 cm); PhGA: physician global assessment of disease activity (VAS 0–10 cm); CRP: C-reactive protein, mg/l; TJC48: tender joint count based on 48-joint count; HAQDI: Health Assessment Questionnaire Disability Index (0–3); HAQ-II: modified HAQ (0–3); MDHAQ: Multidimensional Health Assessment Questionnaire (0–10).



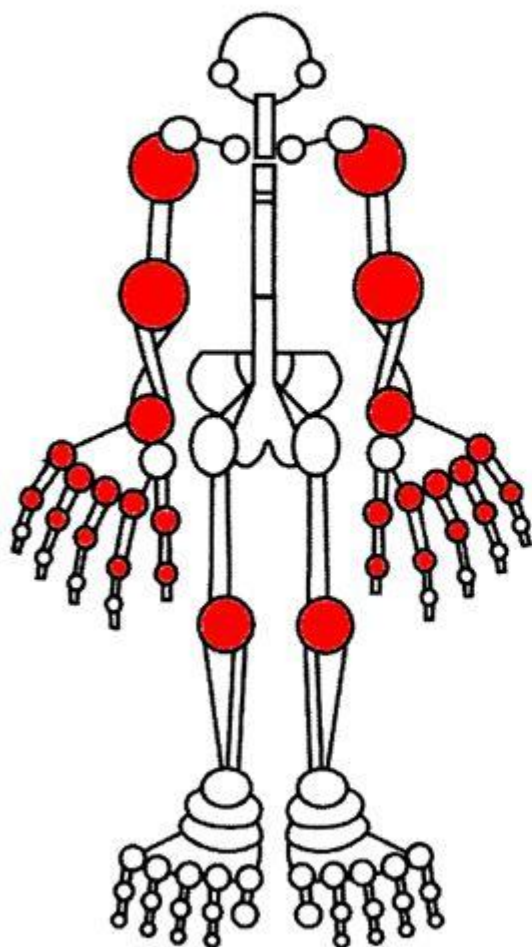
DAS/DAS 28 Threshold for Remission*

- DAS: Ritchie joint index and 44 swollen joint ct
- DAS28: 28 tender & swollen joint count
- ESR/CRP versions
- Both use a 'general health' VAS (0-100)
- DAS28 remission: < 2.6
- DAS remission: < 1.6

** Fransen J et al. Rheumatology 2004;43:1252-5.*

Components of DAS 28 score

JOINTS



- SJC

Number of Swollen Joints out of 28 joints: shoulders, elbows, wrists, MCP joints, PIP joints and knees

- TJC

Number of Tender Joints out of 28 joints



SDAI/CDAI Remission

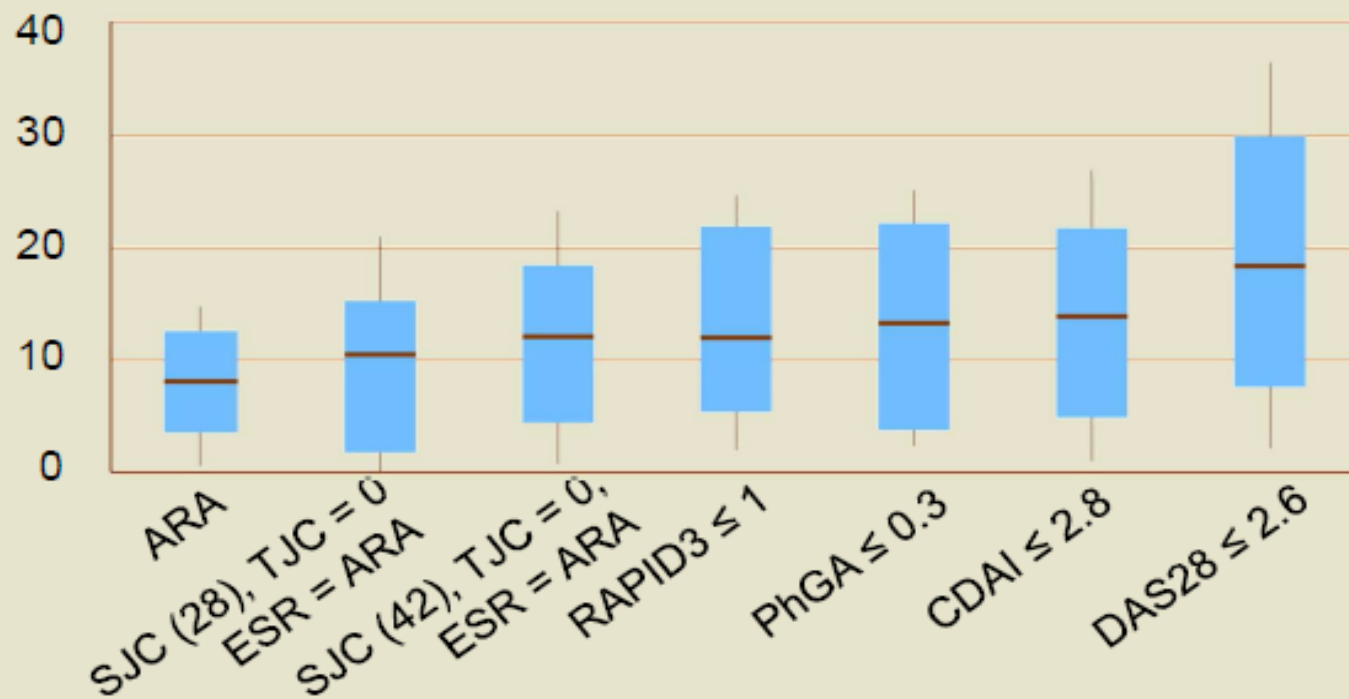
- $SDAI = (28TJC) + (28SJC) + MDGA + PtGA + CRP^*$
- $CDAI = (28TJC) + (28SJC) + MDGA + PtGA^*$
- SDAI remission $\leq 3.3^{**}$
- CDAI remission $\leq 2.8^{**}$
- Developed in patient profile exercise and validated in observational datasets

* *Smolen JS et al. Rheumatology. 2003;42:244*

* * *Aletaha D et al. Arthritis Rheum. 2005;52:2625*

How Strict Are Current Definitions? Prevalence of Remission in QUEST-RA*

- Survey of RA patients in 24 countries



Approach	Advantages	Limitations
Clinical perspective	<p>1- Offers a definition of remission according to validated thresholds</p> <p>2- applicable in routine clinical practice</p> <p>5- allows to measure disease activity according to a systemic perspective</p> <p>6- allows to define remission stability in longitudinal terms based on serial assessments</p>	<p>3- does not allow to measure sub-clinical inflammatory activity</p> <p>4- does not allow to measure synovial stroma pathology</p>
US and MRI perspective	<p>3- allows to measure sub-clinical inflammatory activity (according to surrogate markers)</p> <p>5- allows to measure inflammatory activity according to a multi-site perspective (US)</p> <p>6- allows to measure inflammation stability in longitudinal terms based on serial assessments</p>	<p>1- does not (yet) offer a definition of remission according to validated thresholds</p> <p>2- requires equipment and experienced operators</p> <p>4- does not allow to measure directly synovial stroma pathology</p>
Pathological perspective	<p>3- allows to measure sub-clinical inflammatory activity (according to direct markers)</p> <p>4- allows to measure synovial stroma pathology</p>	<p>1- does not (yet) offer a definition of remission according to validated thresholds</p> <p>2- limited applicability in routine clinical practice (requires <i>ad-hoc</i> facilities)</p> <p>5- does not allow to measure inflammatory activity according to a systemic or multi-site perspective</p> <p>6- does not (routinely) allow to measure inflammation stability in longitudinal terms based on serial assessments</p>

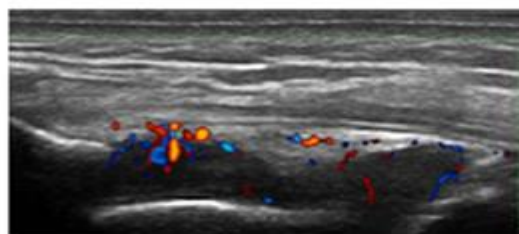
clinical remission



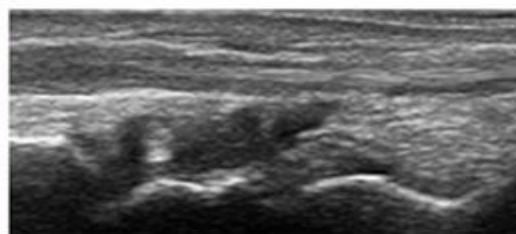
residual swollen joints



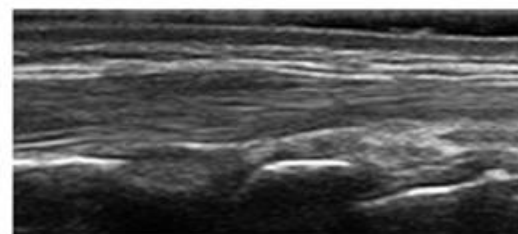
no residual swollen joints



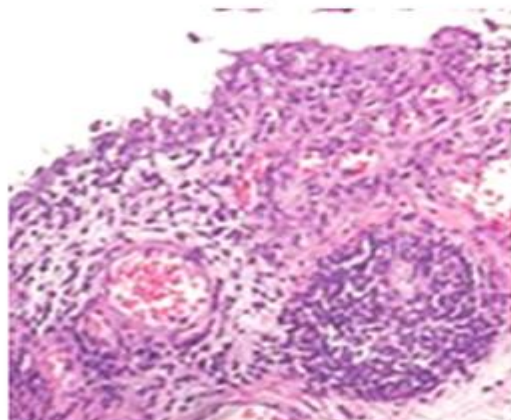
US-PD synovitis



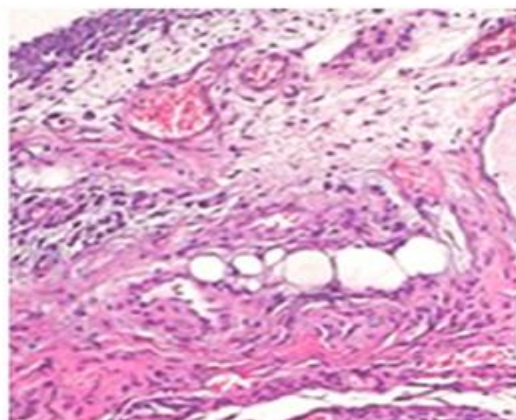
US-GS synovitis



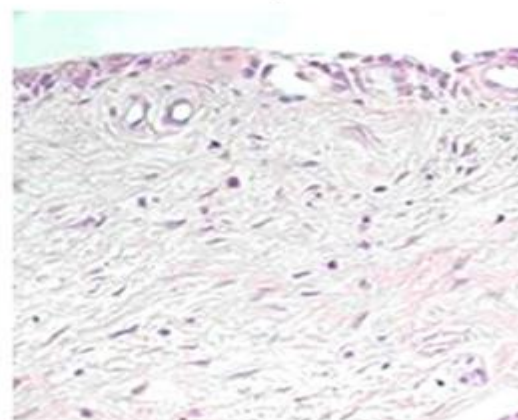
no US synovitis



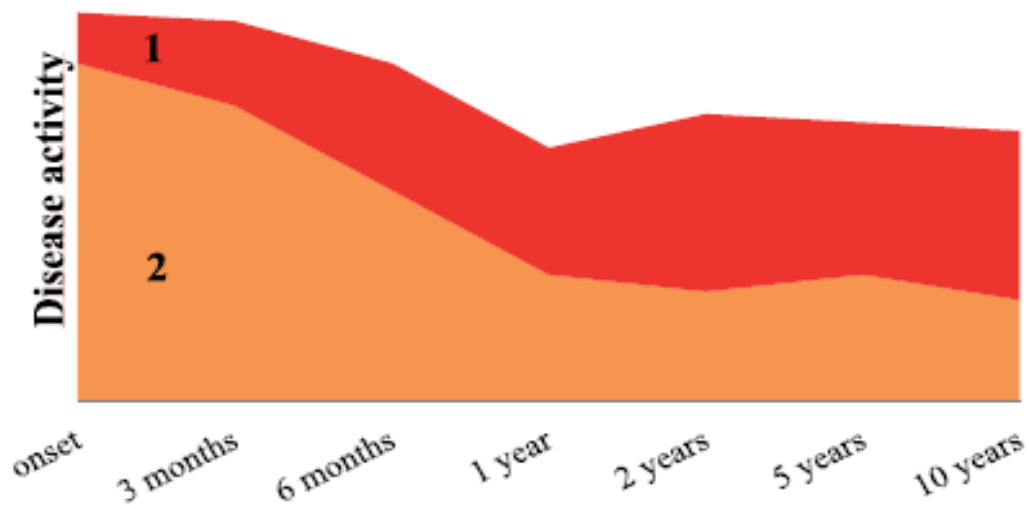
inflammatory infiltrate



sublining fibrosis



normal synovium

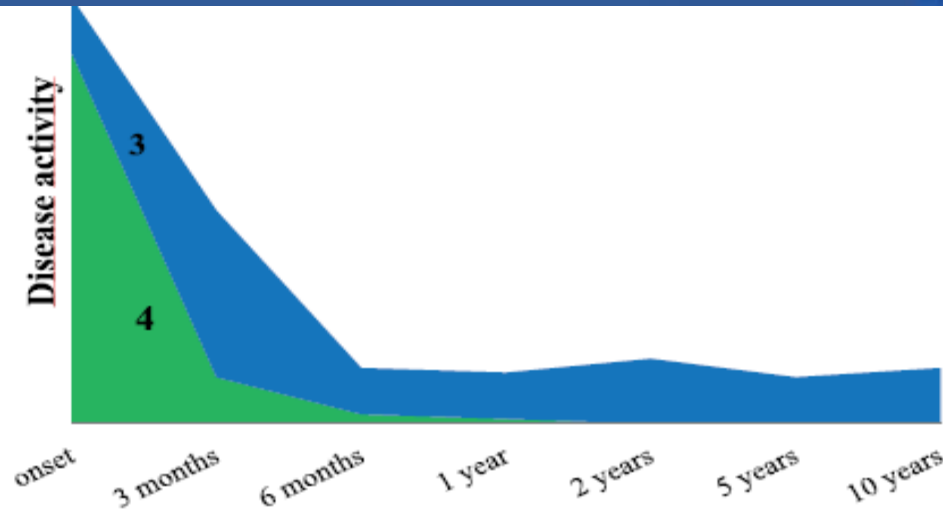


1 – ‘Historically’ chronic persistent disease course

- sustained disease activity
- sustained arthritis-related symptoms
- high risk of joint destruction
- high risk of loss of function
- accentuated premature mortality

2 – Treatment targeted at low disease activity

- low disease activity at some timepoint(s)
- sustained residual disease activity
- lower level of arthritis-related symptoms
- lower risk of joint destruction
- lower risk of loss of function
- lower risk of premature mortality



3 – Early treatment targeted at sustained low disease activity

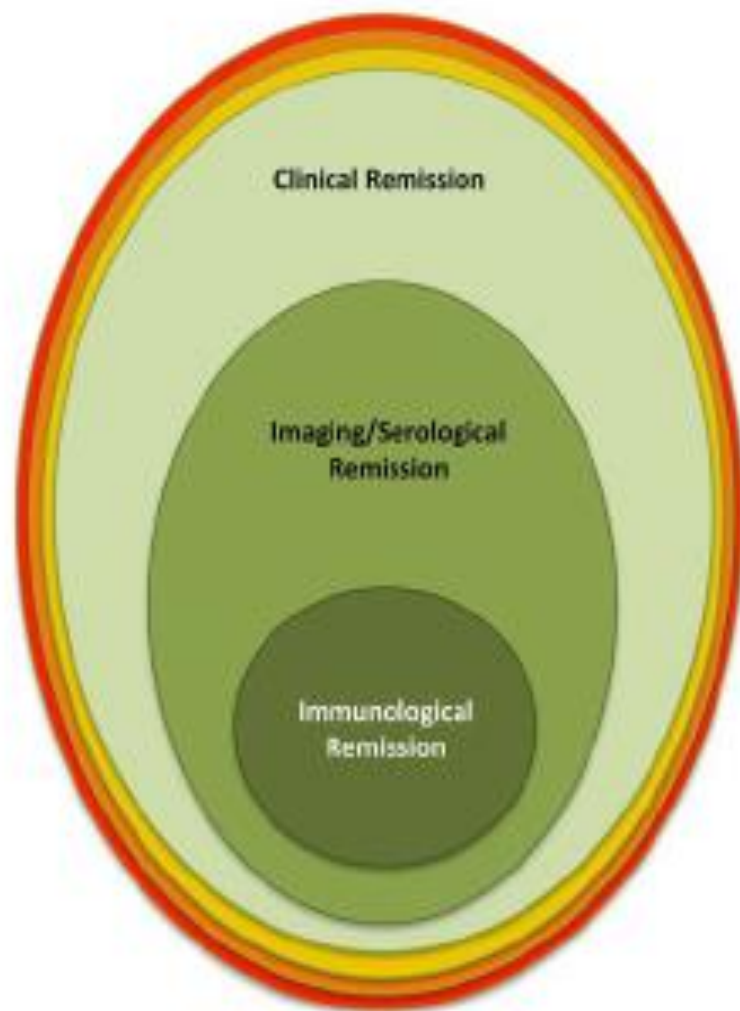
- early suppression of disease activity
- prolonged periods of low disease activity/remission
- possible therapy reduction
- sustained very low level of arthritis-related symptoms and improved health status
- absence/low risk of joint destruction
- absence/low risk of loss of function
- improved survival

4 – ‘Induction’ treatment targeted at sustained remission

- rapid resolution of disease
- prolonged periods of remission
- therapy reduction
- possible therapy discontinuation and sustained drug-free remission
- sustained absence of arthritis-related symptoms and normalized health status
- absence of joint destruction
- normalized function
- normalized survival

Validity of Candidate Remission Definitions: Predicting a Good Outcome for X-ray

	Percent in Remission with Good Outcome	Percent NOT in Remission with Good Outcome	Positive Likelihood Ratio	P Value
TJC28, SJC28, CRP ≤ 1	69%	50%	2.0	0.01
+ PtGA ≤ 1	77%	51%	2.9	0.006
+ Pain ≤ 1	74%	51%	2.6	0.01
+ PhGA and PtGA ≤ 1	77%	51%	2.9	0.01
+ PhGA and Pain ≤ 1	77%	51%	2.9	0.01
+ PtGA and Pain ≤ 1	76%	51%	2.8	0.001
+ PhGA, PtGA and Pain ≤ 1	76%	51%	2.8	0.02



Clinical remission

Absence or very low-level symptoms related to arthritis assessed by standardised scores and cut-offs (DAS28 <2.6, DAS44 <1.6, SDAI <3.3, CDAI <2.8, ACR/EULAR remission)



Imaging/Serological Remission

Clinical remission PLUS

- No signs of ultrasound synovitis
- No signs of MRI synovitis or osteitis
- No serologic signs of inflammation



Immunological Remission

Clinical and imaging/serological remission PLUS

- Rheumatoid factor and ACPA negative
- Rheumatoid factor and ACPA seroconversion is documented



Why to taper drugs of RA?

THE CONCEPT OF DMARD TAPERING



- (i) Taking chronic medication for a symptom-free disease state may provide more harms than benefits in certain individuals.**
- (ii) The costs of DMARDs, especially bDMARDs are high and healthcare resources are under growing economic pressure.**
- (iii) Finally and, most importantly, only de-escalation of therapy will allow distinction between mere suppression of inflammation by DMARDs from real cure of the disease.**



When we can taper the drugs of patients of RA

Discontinuation

Complete withdrawal of the biologic

Tapering by dose reduction

Tapering by injection/
infusion frequency
reduction

Progressive stepwise

Disease activity-
driven tapering

Flare

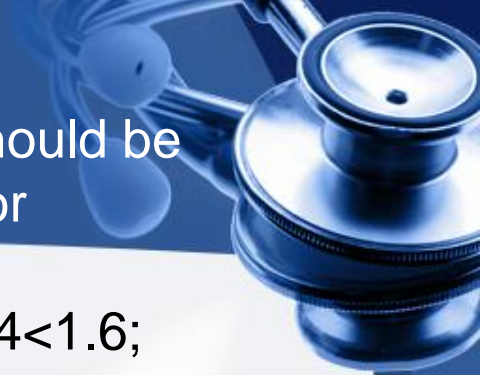
Maintaining the same frequency of dose, but reducing the quantity of the drug per administration

Maintaining the same quantity of drug per administration, but increasing the time in between injections/infusions

Initially tapering by dose reduction or tapering by injection/infusion frequency reduction, and then further tapering again by dose reduction or frequency reduction (i.e. initially 50 mg/7 days then 25 mg/7 days then 25 mg/14 days)

The decision is made whether or not to dose-down based on the patient's disease activity

Considered in the paper as synonymous with relapse or loss of remission/LDA or failure of the tapering strategy



Eligible patients

Disease-modifying antirheumatic drug (DMARD) tapering should be considered if patients (a) fulfil standardised clinical criteria for

remission state (disease activity score (DAS)28 <2.6 ; DAS44 <1.6 ; simplified disease activity index (SDAI) <3.3 ; Clinical Disease Activity Index <2.8 ; American Colleague of Rheumatology (ACR)/European League Against Rheumatism(EULAR) remission), (b) show sustained remission for at least 6 months documented by appropriate disease activity instruments at three sequential visits, (c) use stable DMARD treatment with respect to type and dose of DMARDs over the last 6 months and (d) do not use glucocorticoids to maintain their remission state

Risk and predictors for relapse

Some rheumatoid arthritis patients can successfully taper or even stop DMARD treatment. Anticitrullinated autoantibody negativity and presence of 'deep' remission such as absence of ultrasound synovitis and/or normal serum markers of inflammation are associated with higher chances to achieve drug-free remission

How to taper of RA drugs





Guideline	Method for reviewing and rating quality of evidence	Recommendation	Quality of evidence
2015 ACR Guideline for the Treatment of Rheumatoid Arthritis [3]	GRADE ^a methodology was used to evaluate the literature	For patients with established RA who are in remission: Taper DMARD therapy Taper TNF-I, non-TNF biologic or tofacitinib	Conditional recommendation Low Moderate to very low
EULAR recommendations for the management of RA: 2013 update [6]	Most evidence came from three SLRs; provides levels of evidence, grades of recommendations, and strengths of recommendations	If a patient persists in remission after tapering glucocorticoids, then the clinician can consider tapering bDMARDs, especially if combined with a csDMARD	LoE: ^b 2b GoR: B SoR: 8.7 ± 1.8 Votes: 100%
APLAR RA treatment recommendations [7]	The ADAPTE framework was used to identify and review international RA guidelines, and the AGREE II instrument was used to assess the quality of the guidelines	Tapering of bDMARDs can be considered for patients in extended remission (>12 months)	LoE: 2 Strength: B



Mode of DMARD tapering/withdrawal

Both direct DMARD withdrawal and dose tapering protocols were studied. Patients need to be informed about the mode and how to taper their DMARD. For practical reasons, gradual withdrawal with an initial dose tapering phase may be preferable over immediate withdrawal. This concept applies to both biological and synthetic DMARDs

Monitoring and relapse management

Particularly when starting DMARD tapering and/or withdrawal regular monitoring needs to be scheduled in order to early detect relapses. Patients need to be instructed about the risks of relapse as well as the way to manage them. Reintroduction of the former DMARD regimen has shown to recapture remission in virtually all patients relapsing

