Managing RA with DMARDs

This is the lay version of the 2019 update of the EULAR recommendations for the management of rheumatoid arthritis using synthetic and biologic disease-modifying antirheumatic drugs. The original publication can be downloaded from the EULAR website: www.eular.org.

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Introduction

EULAR recommendations give advice to doctors, nurses and patients about the best way to treat and manage diseases. In 2019, EULAR updated its recommendations on the management of people with rheumatoid arthritis (sometimes shortened to RA).

Doctors, nurses, other health professionals and patients worked together to develop this advice. The patients in the team ensured that the patient point of view was included. The authors looked at the evidence on three specific groups of drug treatments for people with rheumatoid arthritis.

What do we already know?

Rheumatoid arthritis is a condition where the joints become stiff, painful and damaged due to the immune system attacking the body's own tissues and causing inflammation. These recommendations include information on three types of disease modifying anti-rheumatic drugs (often shortened to DMARDs) that are used to treat rheumatoid arthritis. These drugs aim to change the course of the disease by reducing inflammation, and can prevent flares and disease worsening. They can also help to improve function and stop the progression of joint damage. The three different types are:

- **Conventional synthetic** DMARDs (sometimes shortened to csDMARDs).
- **Biologic** DMARDs (also called bDMARDs, biologics or biologicals)
- **Targeted synthetic** DMARDs (shortened to tsDMARDs).

EULAR recommendations published and updated since 2010 have now again been updated based on new evidence, and to include new treatments that have become available.

What do the recommendations say?

In total, there are 5 overarching principles and 12 recommendations. The principles stress the need for shared decision making between the patient and the doctor, including considerations of safety, cost and comorbidities. They also reinforce that rheumatologists should care for people with rheumatoid arthritis, in consultation with other medical specialists as needed. A new principle highlights that people may require multiple successive therapies throughout their life. Of the 12 recommendations, 9 remain unchanged, and the remainder are new or modified.

Each recommendation is based on the best current knowledge and studies of scientific evidence or expert opinion. The more stars a recommendation has the stronger the evidence is. However, recommendations with limited scientific evidence may be important, because the experts can have a strong opinion even when the published evidence may be lacking.

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One star (*) means it is a recommendation with limited scientific evidence.

Two stars (**) means it is a recommendation with some scientific evidence.

Three stars (***) means it is a recommendation with quite a lot of scientific evidence.

Four stars (****) means it is a recommendation supported with a lot of scientific evidence.

- **People should be prescribed a DMARD as soon as they are diagnosed with rheumatoid arthritis.******
  If you have symptoms, it is important to get a specific diagnosis of rheumatoid arthritis (if appropriate) quickly, so that treatment can be started as soon as possible. Early treatment can prevent irreversible joint damage.

- **For every person the treatment aim should be sustained remission or low disease activity.******
  Achieving remission or low disease activity are the main targets for therapy. If your disease activity is higher than this after trying a treatment for 6 months, then you do not have adequate disease control, and your doctor may change your treatment.

- **Your rheumatoid arthritis should be monitored every 1–3 months; treatment should be adjusted if there is no improvement after 3 months, or if your target has not been reached by 6 months.*****
  Your doctor should check your disease activity and examine your joints regularly to see how well your treatment is working. By measuring your disease activity the doctor can see if you are in remission (or low disease activity). If there has been no improvement in at least half of your complaints within 3 months of starting a new drug, then it probably will not work for you and your therapy should be adjusted. If there are such signs of improvement, you should carry on taking that drug for at least another 3 months to see if it can put you into remission. If the target has not been met by 6 months, your therapy should be adjusted. This might mean staying on the same drug but changing the dose, or you might need to switch to a different type of drug.

- **Methotrexate should be part of your first treatment strategy.******
  Methotrexate is a csDMARD. It is a good choice to try first for people with rheumatoid arthritis, because it is a well-known, effective and inexpensive drug. Your doctor may try different doses to find the right one for you, and may prescribe folic acid to be taken alongside, because this can reduce the side effects you might get. Methotrexate can be taken in combination with other drugs for rheumatoid arthritis, but this is normally saved for later stages of the disease.

- **Leflunomide or sulfasalazine should be considered instead of methotrexate for people who cannot take it, or who have side effects.******
  If you have kidney or liver disease, you may not be able to take methotrexate. A few people also find that they cannot tolerate methotrexate – it may cause sickness or other side effects. If this is the case, you may be prescribed leflunomide or sulfasalazine instead. Both are also csDMARDs. You may receive them alone or combined with other drugs.

- **You may need to take steroids when you start or change your csDMARDs, but they should be used for short periods of time.******
  Adding glucocorticoids, a type of steroid medicine, to csDMARDs can help them to work better. This can help to bridge the gap when starting a new treatment. Your doctor may give you a single steroid injection, or pills to take for up to 3 months. Using steroids for longer than this is not recommended because of the risk of side effects. The dose will be gradually reduced (sometimes called tapering) to

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help you come off the steroids as soon as possible.

- **If you do not reach your target with the first csDMARD, and there are no adverse prognostic factors, a different csDMARD should be tried.***
  Prognostic factors are aspects that can be used to predict how much your disease may damage your joints. Poor or adverse prognostic factors include having moderate or high disease activity after receiving csDMARDs, or if you have certain auto-antibodies or high levels of markers of inflammation in your blood. Antibodies are proteins produced by your immune system as part of your natural defence against infections. Some diseases cause the immune system to make auto-antibodies against the body's own tissues, and these can be detected in your blood. If none of these things apply to you, your doctor may replace your first csDMARD with another one if it is not working.

- **If you do not reach your target with the first csDMARD, and there are adverse prognostic factors affecting your disease, a bDMARD or tsDMARD should be added to your treatment.******
  If you have poor prognostic factors and your first csDMARD has not worked, a bDMARD or tsDMARD may be added instead of trying a second csDMARD.

- **bDMARDs and tsDMARDs should be combined with a csDMARD; if you cannot use csDMARDs, you may be offered IL-6 inhibitors or tsDMARDs.******
  All bDMARDs work better when combined with methotrextate than when taken on their own. If you cannot use methotrexate or other csDMARDs, you might be offered a type of biologic called an IL-6 inhibitor, or a group of tsDMARDs called JAK inhibitors. If these are not taken with csDMARDs they get better results than other drug types.

- **If a bDMARD**** or tsDMARD* does not work for you, you may receive a different bDMARD or tsDMARD.**
  If you try a bDMARD or tsDMARD and it does not work for you, you can swap to another bDMARD, including a drug of the same type, or to a tsDMARD (or JAK-inhibitor). For example, if one TNF inhibitor therapy has failed, patients may receive an agent with another mode of action or a second TNF inhibitor. However, if more than one of the same type of drug does not work for you, then your doctor should switch you to a drug that works in a different way.

- **If you achieve persistent remission after stopping steroids, you can also consider reducing your bDMARD or tsDMARD dose, especially if you are also taking a csDMARD.******
  You might be given a steroid called a glucocorticoid to help you switch between therapies. This will only be for a short time. If you achieve remission and stay there after the steroid has been withdrawn, you might also be able to lower your bDMARD or tsDMARD – either by taking a smaller dose, or taking it less often. It is very important that you do not change your dose yourself without talking to your doctor.

- **If your disease is in persistent remission, you might be able to reduce your csDMARD dose.*****
  If csDMARD treatment has worked and you have achieved remission without needing a bDMARD or tsDMARD, or if a bDMARD or tsDMARD has been stopped and you continue to be in remission on the csDMARD, then it may also be possible to lower the dose of your medicine – either by taking a smaller dose, or taking it less often. It is very important that you do not change your dose yourself without talking to your doctor.

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Summary

Overall, the recommendations highlight that there are many different treatments for people with rheumatoid arthritis. If you have rheumatoid arthritis, these recommendations will give you some guidance on what to expect from your doctor and what treatments you may be offered.

Recommendations with just one or two stars are based mainly on expert opinion and not backed up by studies, but these may be as important as those with three or four stars.

If you have any questions or concerns about your disease or your medication, you should speak to a health professional involved in your care.

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