Managing difficult-to-treat arthritis

This is the lay version of the EULAR points to consider on the management of people with difficult-to-treat rheumatoid arthritis. 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. These are the first EULAR-endorsed points on the best way to treat people with difficult-to-treat rheumatoid arthritis. Based on the low level of evidence available for this topic, it was not possible to develop full recommendations, and the work has been presented instead as 'points to consider'.

Doctors, 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 difficult-to-treat rheumatoid arthritis, and the use of different pharmacological and non-pharmacological management options in people with this type of disease.

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. Although there are many treatment options for rheumatoid arthritis, some people do not reach low disease activity or remission and may still have symptoms after several cycles of treatment. These people are referred to as having "difficult-to-treat" disease. Managing difficult-to-treat disease can be very challenging, and until now there has not been any specific guidance for people with this kind of rheumatoid arthritis.

These points include information on different 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 used in rheumatoid arthritis are:

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

What do the points say?

In total, there are two overarching principles and 11 points to consider. The principles stress that this guidance is specifically for people who meet the official definition of difficult-to-treat. The points are underpinned by the EULAR recommendations for the general management of rheumatoid arthritis. The second principle states that it should be established whether a person has inflammation or not. This information guides the choice of pharmacological and non-pharmacological interventions.

The 11 points to consider cover confirming the diagnosis of difficult-to-treat rheumatoid arthritis, evaluation of inflammatory disease activity, pharmacological and non-pharmacological interventions, treatment adherence, functional disability, pain, fatigue, goal setting and self-efficacy, and the impact of comorbidities.

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

One star (*) means it is a point with limited scientific evidence.
Two stars (**) means it is a point with some scientific evidence.
Three stars (***) means it is a point with quite a lot of scientific evidence.
Four stars (****) means it is a point supported with a lot of scientific evidence.

- **If a person is thought to have difficult-to-treat rheumatoid arthritis, the possibility of misdiagnosis or multiple co-existing diseases should be considered as a first step. ***
  Rheumatoid arthritis can be confused with other diseases with similar symptoms. People may also have more than one disease at the same time. Diseases that can be misdiagnosed as rheumatoid arthritis include other types of arthritis, Still's disease, lupus, inflammatory myopathies, vasculitis, or fibromyalgia. Getting an accurate diagnosis is important to help choose the best treatment.

- **Where there is doubt on the presence of inflammatory activity based on clinical assessment and composites, health professionals should consider using ultrasound. ****
  In clinical practice, doctors use physical examinations and *composite measures* to decide if there is inflammation present in a joint. Composites are a way of using a number of different measures to get an overall score. However, in people with difficult-to-treat disease these can be hard to interpret. When traditional techniques are challenging, ultrasound may be the best way to see if there is inflammation present.

- **Composite indices and clinical evaluation should be interpreted with caution in the presence of comorbidities, as these may overestimate disease activity. ***
  Other conditions such as obesity and fibromyalgia may coexist with rheumatoid arthritis. When this is the case clinical measures and composites should be interpreted with caution. This is because comorbidities can directly intensify inflammatory activity. This may affect estimates of disease activity.

- **Your treatment adherence will be discussed and optimised within the process of shared decision-making.***
  Between 30% and 80% of people with rheumatoid arthritis do not take their treatment as prescribed. The rates are thought to be even higher in people with difficult-to-treat disease. This can result in higher disease activity levels and may contribute to inappropriate treatment choices and poor quality of life. Shared-decision making with your healthcare team can help you to improve your adherence. This should be discussed as part of your treatment plan.

- **After failure of a second or subsequent b/tsDMARD a different target should be considered.****
  If you have tried two or more b/tsDMARD therapies – and especially if you have tried two different medicines in the TNFi class (Tumour Necrosis Factor inhibitor) – a medicine with a different target should be considered. Biologic and targeted synthetic DMARDs act on many different molecules and processes in the body. Switching to a different mechanism might be helpful.

- **If a third or subsequent b/tsDMARD is being considered, the maximum dose should be used.****

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For people who have not responded to two b/tsDMARDs already, a third can be tried. This should be started at the maximum approved dose.

- **Comorbidities that impact quality of life should be carefully considered and managed.***
  People with rheumatoid arthritis may have other diseases at the same time. These are called comorbidities. These can have an impact on quality of life – either directly, or indirectly by limiting treatment options for the arthritis. For example, people with herpes zoster infection cannot use JAK inhibitors, and people with a digestive disease called diverticulitis cannot use tocilizumab. Comorbidities should be carefully managed and treated to limit their impact on treatment choices for people with difficult-to-treat rheumatoid arthritis.

- **In people with hepatitis B or C infection, b/tsDMARDs can be used;** antiviral treatment should be considered in close collaboration with a hepatologist.***
  If you have hepatitis B or C (often shortened to HBV or HCV), you can still use b/tsDMARDs for your rheumatoid arthritis. You may need to have treatment for the hepatitis before you can start the rheumatoid arthritis treatment. This will be managed by your healthcare team.

- **In addition to pharmacological treatment, non-pharmacological interventions should be considered to optimise management of functional disability, pain, and fatigue.****
  A number of factors can contribute to the signs and symptoms of rheumatoid arthritis, and not all of these can be fixed with medicines. Non-pharmacological interventions include recommendations on exercise, psychological wellbeing, education, and self-management. These should be considered to help you managed if you have disability caused by your rheumatic arthritis, or if you experience pain and fatigue (extreme tiredness).

- **You should be offered education and support to directly inform you about your choices for treatment goals and management.****
  Setting treatment goals is important in the management of rheumatoid arthritis. These are usually clinical remission or low disease activity after 3 or 6 months of a particular treatment. However, these goals may not be appropriate for people with difficult-to-treat disease. If you have difficult-to-treat rheumatoid arthritis, your goals should be tailored to your particular circumstances. Being informed about your disease will help you understand your goals. You should be offered education and support to help you make informed choices, and to participate in your management.

- **You should be offered self-management programmes, education or psychological interventions to optimise your ability to manage your disease confidently.****
  Self-efficacy is important in rheumatoid arthritis. This refers to your ability to control or manage various aspects of your disease. People with low self-efficacy are more likely to give up on their goals, and may be more likely to have pain, fatigue, depression, or stress. There are programmes that can help you to improve your self-efficacy. These may focus on educating you about your disease so that you are armed with the right knowledge. Or they may give you strategies for coping with pain, or improving relaxation. These are optional, but if you are interested in improving your self-efficacy you should speak to your healthcare team.

Summary

Overall, the points highlight how much more evidence is needed to make recommendations. In the meantime, EULAR hopes these will be a useful roadmap for health professionals involved in the care of people with

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difficult-to-treat rheumatoid arthritis. They should be used alongside the main recommendations for rheumatoid arthritis.

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

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