

EULAR COVID-19 Recommendations

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TREATING patients with autoimmune diseases, the rheumatology community is naturally concerned with the spread of COVID-19; as Prof Robert Landewé of the University of Amsterdam, Amsterdam, the Netherlands stated: “immunosuppression and infection do not go along very well.” On April 3rd 2020, EULAR President-Elect Prof Hans Bijlsma founded a task force to create a comprehensive set of guidelines for clinicians treating patients with rheumatic disease and COVID-19, though not in a typical manner. Using Microsoft Teams and teleconferences, the newly founded committee set out to create a comprehensive set of recommendations. Time was of the essence, as the virus continued to spread and rheumatologists looked to EULAR for guidance. Exactly 3 months later the guidelines were presented at the EULAR 2020 virtual congress on 3rd June 2020.

PROVISIONAL RECOMMENDATIONS

Musculoskeletal disease guidelines in the context of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), as outlined by EULAR, is “an unprecedented set of recommendations,” according to Prof Landewé. In a pandemic, EULAR’s usual methodical approach to finalising recommendations, which takes at least 12–18 months, had to be significantly shortened; the stages of consensual approach and systematic literature research were forgone as there was no literature or evidence to guide them.

The recommendations for patients with rheumatic disease and COVID-19 start with five overarching principles:

1. There is no evidence that these patients are more at risk of contracting SARS-CoV-2, nor do they have a worse prognosis if they are infected.

2. Diagnosis and treatment of patients is the primary responsibility of an expert in treating COVID-19 (e.g., a respiratory physician or infectious disease specialist).

3. Decisions based on immunosuppressive treatment (e.g., disease-modifying antirheumatic drugs [DMARD]), maintenance, or discontinuation should involve rheumatologists.

4. Rheumatologists should be involved in local, regional, or national guideline committees regarding use of DMARD, the use of which should be a multidisciplinary decision.

5. Off-label use of DMARD in COVID-19 outside the context of clinical trials should not be encouraged.

Prof Landewé concluded by highlighting “the current evidence is extremely sparse and fragmented” and that as a task force they are “flying blindly,” whilst also following many jurisdictions within Europe, with many conflicting opinions.



ACR RECOMMENDATIONS

The American College of Rheumatology (ACR) recommendations were subsequently presented by the Chair of the ACR COVID-19 Clinical Task Force Prof Ted Mikuls of the University of Nebraska Medical Center, Omaha, Nebraska, USA. To accommodate the changing literature and evidence landscape regarding the virus, the ACR task force has committed to a monthly update of the recommendations, compared to EULAR's quarterly pledge. Voting initially on 81 statements, of which 77 were approved, the team combined these into a list of 25 guidance statements, compared to EULAR's 13.

The ACR recommendations are divided into three groups, the first being guiding principles with a primary focus on the patient and provider level, based on the sparse but rapidly evolving evidence. The second grouping of ACR guidance concentrates on stabilising patients: "In the absence of known exposure and the absence of COVID-19 infection, our panel felt very strongly about the importance of continuing rheumatic disease treatments," conveyed Prof Mikuls. The overarching theme of this second group was the potential risk that unchecked inflammation and rheumatic disease posed to patients with COVID-19.

Finally, the third grouping provided guidance to physicians for patients with known exposure or presumed infection of SARS-CoV-2. Prof Mikuls was careful to point out that "our recommendations suggest at least temporary discontinuation of most immunosuppressive and biologic medications" while patients recover from infection.

Though tasked with describing the differences between the EULAR and ACR recommendations, Prof Mikuls found the similarities reassuring: "we're approaching the unknown from very different parts of the world, and arriving in a very similar place."

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MAPPING THE EVIDENCE OF A NEW DISEASE

Critical situations, such as the COVID-19 pandemic, spark many questions in need of answers, explained Dr Féline Kroon of Leiden University Medical Centre, Leiden, the Netherlands. Beginning with a discussion of the literature on COVID-19, Dr Kroon used the case of hydroxychloroquine for the treatment of COVID-19. *In vitro* studies initially showed that the drug may be beneficial to those infected with COVID-19, leading to its incorporation into many clinical protocols as some physicians embraced the opportunity of a potential treatment.

“Oversimplification and also quick dissemination of these publications was done in the lay press and social media,” leading to shortages of the drug to patients with rheumatic diseases, relayed Dr Kroon. Hydroxychloroquine has now been associated with risk of serious adverse events and the first controlled clinical trials have not been able to confirm its efficacy.

From January 1st–May 22nd 2020 there has been an exponential increase in publications on PubMed relating to the search terms “COVID-19 AND rheumatic diseases OR drugs used in rheumatic diseases”. Dr Kroon analysed the search results and found that most publications were

viewpoints or narrative reviews and contained no original data, and that the number of clinical trials was, in fact, negligible.

Of the 23 studies published between April 2nd and May 20th using the aforementioned search terms, 13 were cohort studies and 10 were case studies (including case reports and case series). Looking at the 10 case studies, the majority assessed hospitalised patients and the median number of patients was one, whereas in the 13 cohort studies the median number of patients was 165, most of whom were from the outpatient clinic. The type of rheumatic disease ranged from rheumatoid arthritis to vasculitis, systemic sclerosis, or psoriatic arthritis. Combining both sets of studies, the median percentage of positive COVID-19 patients was 3%.

Taking into account the available data up to this point, the key messages from Dr Kroon were that the publication landscape of patients with COVID-19 and rheumatic diseases is evolving at a rapid pace, and that there is no current, robust evidence strong enough to draw conclusions on the effects of the virus on patients with rheumatic disease.

“It is our responsibility to carefully interpret the study details that do emerge, especially in this digital era,” Dr Kroon emphasised in her concluding remarks.