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Study finds TNF inhibitor more effective with regular serum assessment to adjust dose

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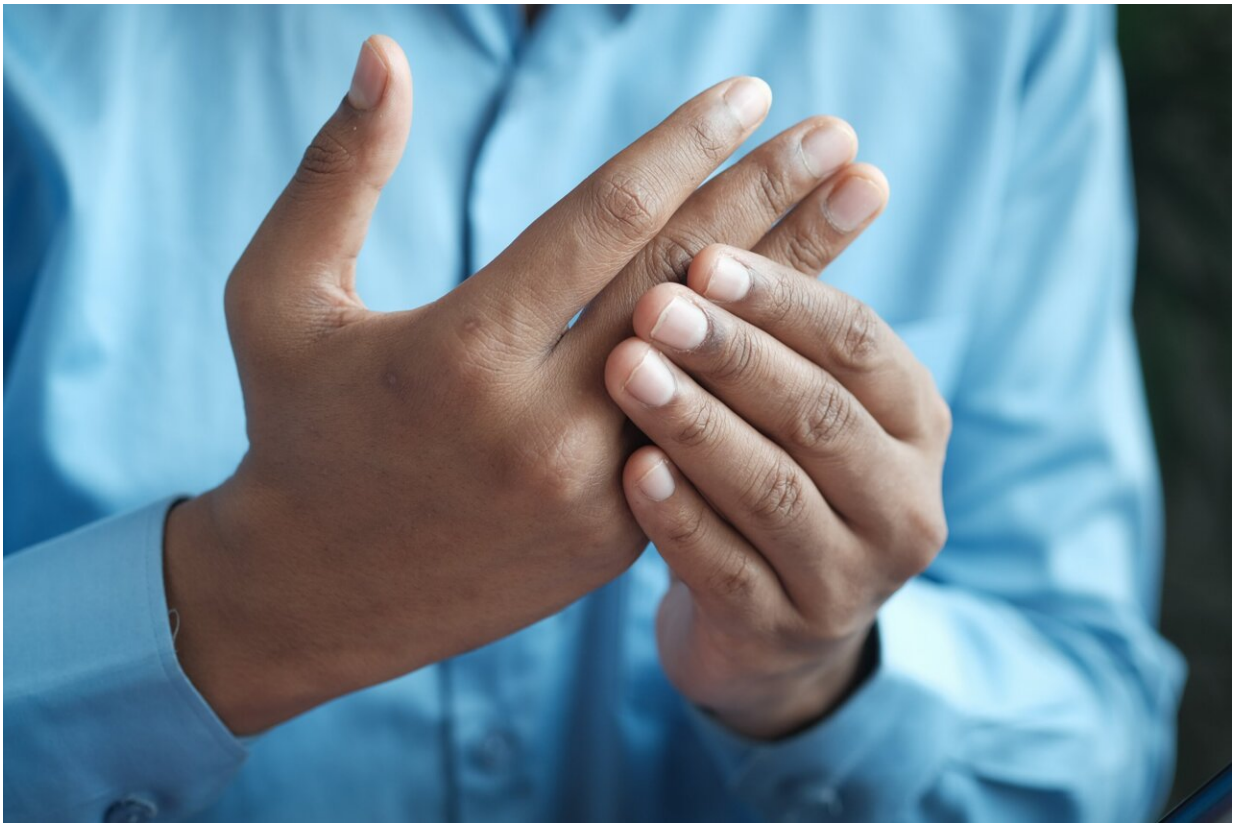

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New research presented this week at ACR Convergence, the American College of Rheumatology's annual meeting, shows that proactive therapeutic drug monitoring, a newer treatment strategy where a patient's

drug serum levels are regularly assessed to adjust the dose and intervals, controlled disease more effectively than standard therapy with infliximab, a tumor necrosis factor (TNF) inhibitor.

TNF inhibitors approved by the FDA include infliximab, adalimumab, etanercept, golimumab and certolizumab pegol. In healthy individuals, excess TNF in the blood is blocked naturally, but in those who have rheumatic conditions, higher levels of TNF in the blood lead to more inflammation and persistent symptoms. These medications can alter a disease's effect on the body by controlling inflammation in the joints, gastrointestinal tract, and skin.

Therapeutic drug monitoring has been proposed to improve safety and efficacy for patients taking these drugs regularly as maintenance therapy. Patients' blood samples are tested according to a schedule to check drug serum levels, then their medication dose and treatment intervals, or how often they receive infusions or injections, are adjusted according to an algorithm. Researchers conducted this 52-week, randomized, controlled, open-label multicenter trial to find out if therapeutic drug monitoring prevents disease flares compared to a standard approach.

"By optimizing drug concentrations and facilitating early detection of anti-drug antibodies, proactive therapeutic drug monitoring has the potential to prevent treatment failure and has been proposed to improve long-term efficacy of TNF inhibitors," says Silje Watterdal Syversen, MD, Ph.D., a rheumatologist at Diakonhjemmet Hospital in Oslo, Norway, and the study's author. "Treatment recommendations differ with respect to the use of proactive monitoring during maintenance therapy with TNF inhibitors within rheumatology as well as gastroenterology and dermatology, mainly due to lack of data from randomized controlled trials."

The trial randomized patients to be treated with infliximab, a TNF

inhibitor, with either therapeutic drug monitoring or standard therapy schedule for a minimum of 30 weeks between June 2017 and December 2019. Participants (458) had a variety of immune-mediated inflammatory diseases including rheumatic diseases: 79 with rheumatoid arthritis, 138 with spondyloarthritis, and 53 with psoriatic arthritis. Patients in the monitoring group had their infliximab dose and treatment intervals carefully adjusted to keep serum drug levels within the range of 3-7 mg/L. Infliximab dosing and intervals for patients in the standard therapy group were adjusted based on the doctor's clinical judgment. The primary outcome for the trial was sustained disease control without disease worsening based on specific scores or an agreement between the doctor and patient that prompted a major change in treatment.

During the one year of follow-up, 167 patients in the monitoring group achieved sustained disease control without disease worsening compared to 127 patients in the standard therapy group. These results remained consistent in sensitivity analyses. When investigators compared disease activity and patient-reported outcomes at week 52, they found no significant differences between the two groups. The mean infliximab dose that patients in both groups received during the trial was 4.8 mg/kg. In the monitoring group, 21 patients (9.2%) developed clinically relevant levels of anti-drug antibodies compared to 27 patients (15%) in the standard group. In addition, 137 patients in the monitoring group and 142 patients receiving standard therapy reported adverse events during the trial.

"The results of these trials support the implementation of proactive therapeutic drug monitoring during maintenance therapy with infliximab. Maintenance therapy with infliximab usually lasts for several years, and preventing disease worsening and its potential impact on quality of life and long-term outcome can make a great difference to a large number of patients with inflammatory joint diseases," says Dr. Syversen. "Using proactive monitoring in all patients on infliximab will

require feasibility with testing, availability of testing at a low cost, as well as education of health care providers. Due to the immunogenicity profile of infliximab, these data can not necessarily be extrapolated to other TNF inhibitors or biologics, but they encourage further therapeutic drug monitoring research within rheumatology."

More information: Silje Watterdal Syversen et al, Therapeutic Drug Monitoring Compared to Standard Infliximab Therapy in Patients with Immune-mediated Inflammatory Diseases: A Randomized Controlled Trial [abstract]. *Arthritis Rheumatology* (2021). Available at acrabstracts.org/abstract/ther … ed-controlled-trial/

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