

**Annual European Congress of Rheumatology
(EULAR 2019)**

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**VAGUS NERVE STIMULATION STUDY SHOWS SIGNIFICANT REDUCTION IN
RHEUMATOID ARTHRITIS SYMPTOMS**

Initial pilot data support the use of new neurostimulation treatment in a larger study in patients who have failed current standard of care¹

Madrid, Spain, 14 June 2019: The results of a pilot study presented today at the Annual European Congress of Rheumatology (EULAR 2019) suggest that electro stimulation of one of the nerves connecting the brain to the body (the vagus nerve), could provide a novel treatment approach for patients with rheumatoid arthritis.¹

“This is a really exciting development. For many patients suffering from rheumatoid arthritis, current treatments don’t work, or aren’t tolerated,” said Professor Thomas Dörner, Chairperson of the Scientific Programme Committee, EULAR. “These results open the door to a novel approach to treating not only rheumatoid arthritis, but other chronic inflammatory diseases. This is certainly an area for further study.”

The vagus nerve is the longest and the most complex of the 12 pairs of cranial nerves that originate from the brain. The name ‘vagus’ comes from the latin word for ‘wandering’. This is because the vagus nerve wanders from the brain into the organs of the neck, chest and abdomen.

Recent advances in neuroscience and immunology have mapped circuits in the brain that regulate immune responses. In one of the circuits, the ‘inflammatory reflex’, signals are transmitted in the vagus nerve that inhibit the production of cytokines including tumor necrosis factor (TNF), an inflammatory molecule that is a major therapeutic target in rheumatoid arthritis. It is thought that, by stimulating the activity of this inflammatory reflex, innate immune responses can be modulated without abolishing them or producing significant immunosuppression.²

In this pilot study, a novel miniaturised neurostimulator called a MicroRegulator was implanted into 14 patients with rheumatoid arthritis who had failed on at least two biologics or targeted oral therapies with different mechanisms of action. Patients were randomised to three groups who were either placebo, stimulated once daily, or stimulated four times a day for 12 weeks. At the end of the study, the patients who received once-daily stimulation were shown to have a better response than those on four-times-daily stimulation with two thirds meeting the EULAR good or moderate response criteria and a mean change in DAS28-CRP* of -1.24. The mean change in DAS28-CRP* in the placebo group was 0.16.¹

* Disease Activity Score 28-joint count C reactive protein

Cytokines (a broad and loose category of small proteins that are important in cell signalling) were also measured in the study with the actively stimulated groups showing a decrease of more than 30% in levels of Interleukin (IL) 1 β , IL-6, and TNF- α . Implantation and stimulation were generally well tolerated with no device or treatment-related SAEs and two surgery-related adverse events that resolved without clinically significant effects.¹

“Our pilot study suggests this novel MicroRegulator device is well tolerated and reduces signs and symptoms of rheumatoid arthritis,” said Mark Genovese, M.D., James W. Raitt Endowed Professor of Medicine, Stanford University, Stanford, California, USA. “These data support the study of this device in a larger placebo-controlled study as a novel treatment approach for rheumatoid arthritis and possibly other chronic inflammatory diseases.”

This study follows a proof-of-concept study which used reprogrammed epilepsy stimulators on the vagus nerve to demonstrate reduced systemic inflammation and improved disease activity in 17 patients with rheumatoid arthritis.³

The study included 14 patients with active rheumatoid arthritis who had had an insufficient response to more than two biological disease modifying anti-rheumatic drugs (bDMARDs) or JAK inhibitors with more than two modes of action. All patients remained on stable background of methotrexate. The first three patients were implanted and stimulated after three weeks, following safety review board approval, the remaining 11 patients were implanted and randomised to one minute of stimulation once-daily, one minute of stimulation four times daily, or one minute of placebo stimulation.¹



Illustration of miniaturised neurostimulator placed on left cervical vagus nerve to activate inflammatory reflex.

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NOTES TO EDITORS

For further information on this study, or to request an interview with the study lead, please do not hesitate to contact the EULAR Press Office:

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About Rheumatic and Musculoskeletal Diseases

Rheumatic and musculoskeletal diseases (RMDs) are a diverse group of diseases that commonly affect the joints, but can also affect the muscles, other tissues and internal organs. There are more than 200 different RMDs, affecting both children and adults. They are usually caused by problems of the immune system, inflammation, infections or gradual deterioration of joints, muscle and bones. Many of these diseases are long term and worsen over time. They are typically painful and limit function. In severe cases, RMDs can result in significant disability, having a major impact on both quality of life and life expectancy.⁴

About EULAR

The European League against Rheumatism (EULAR) is the European umbrella organisation representing scientific societies, health professional associations and organisations for people with RMDs. EULAR aims to reduce the burden of RMDs on individuals and society and to improve the treatment, prevention and rehabilitation of RMDs. To this end, EULAR fosters excellence in education and research in the field of rheumatology. It promotes the translation of research advances into daily care and fights for the recognition of the needs of people with RMDs by the EU institutions through advocacy action.

To find out more about the activities of EULAR, visit: www.eular.org

References

¹ Genovese MC, Gaylis N, Sikes D, *et al.* First-in-human study of novel implanted vagus nerve stimulation device to treat rheumatoid arthritis. EULAR 2019; Madrid: Abstract LB0009.

² Andersson U and Tracey KJ. Reflex Principles of Immunological Homeostasis. *Annu Rev Immunol.* 2012;30:313–335.

³ Koopman FA, Chavan SS, Miljko S, *et al.* Vagus nerve stimulation inhibits cytokine production and attenuates disease severity in rheumatoid arthritis. *Proc Natl Acad Sci U S A.* 2016;113(29):8284–8289.

⁴ van der Heijde D, Daikh DI, Betteridge N, *et al.* Common language description of the term rheumatic and musculoskeletal diseases (RMDs) for use in communication with the lay public, healthcare providers and other stakeholders endorsed by the European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR). *Ann Rheum Dis.* 2018 Jun;77(6):829-832.