

**Annual European Congress of Rheumatology  
(EULAR 2018)**

Amsterdam, The Netherlands, 13-16 June 2018

**CANAKINUMAB SHOWN TO REDUCE RATES OF GOUT IN ATHEROSCLEROSIS  
PATIENTS BY MORE THAN HALF**

Serum urate confirmed as risk marker for gout although levels not affected by canakinumab

**Amsterdam, The Netherlands, 13 June 2018:** The results of a study presented today at the Annual European Congress of Rheumatology (EULAR 2018) demonstrate that canakinumab significantly reduced the rate of gout by more than half compared to placebo, regardless of baseline serum urate level.<sup>1</sup>

“These are significant results as they add to the evidence base demonstrating a potential preventative role for canakinumab in patients with gout,” said Professor Robert Landewé, Chairperson of the Scientific Programme Committee, EULAR. “They will also contribute to our understanding of the interaction between gout, uric acid and cardiovascular disease.”

Gout is a very common condition. It is caused by deposits of crystals of a substance called uric acid (also known as urate) in the joints, which leads to inflammation. Periods of time when gout symptoms occur are called flares. Flares can be unpredictable and debilitating, developing over a few hours and causing severe pain in the joints.

Canakinumab is a monoclonal antibody that blocks an inflammatory pathway mediated by interleukin-1 $\beta$ . It is licenced for the treatment of several rare auto-inflammatory disorders although it can also be used to treat flares in certain patients with gout who have contraindications to standard therapies.<sup>2</sup> There have been some reports to date of efficacy in preventing flares, however canakinumab is currently not approved for this indication.

“Our results demonstrate a striking effect of canakinumab on reducing the risk of gout attacks in atherosclerosis patients,” said Daniel Solomon, Professor of Medicine, Harvard Medical School and Brigham and Women’s Hospital. “Moreover, these data illustrate serum urate as a risk marker for both gout and cardiovascular events, though canakinumab has no effect on serum urate levels due to its mechanism of action.”

This report is a secondary analysis of the CANTOS (Canakinumab Anti-inflammatory Thrombosis Outcomes Study) trial which studied the impact of canakinumab in the secondary prevention of cardiovascular (CV) events.<sup>3</sup> For this analysis,<sup>1</sup> all participants were divided into three groups based on their serum urate level at baseline; low (<6.9mg/dl), medium (6.9-8.9mg/dl), and high ( $\geq$ 9.0 mg/dL). Canakinumab (pooled doses) significantly reduced the rate of flares of gout by more than half compared to placebo, across all baseline serum urate groups. The hazard ratio (95% confidence interval) was 0.40 (0.22-0.73), 0.48 (0.31-0.74), and 0.45 (0.28-0.72) for the low, medium and high baseline serum urate groups respectively.

The serum urate levels were not affected by canakinumab over time, although it did reduce high sensitivity C-reactive protein (hsCRP).<sup>1</sup>

By studying the rates of flares of gout and major CV events between the baseline serum urate groups, investigators demonstrated a correlation confirming it as a risk marker for both these conditions. Rates per 100-person years for the low, medium, and high baseline serum urate groups were 0.28, 1.36, and 5.94 respectively for gout-flares, and 4.1, 5.3, 5.6 respectively for major adverse CV events.<sup>1</sup>

The study included 10,061 patients with stable atherosclerosis (prior heart attack) and a hsCRP $\geq$ 2mg/L which indicates an increased risk of CV disease. Patients were randomly assigned to receive placebo or one of three doses of canakinumab (50mg, 150mg, or 300mg) once every three months. The groups were well balanced with respect to their baseline characteristics with a median follow-up time of 3.7 years. Median age was 61 years, 74% were male, median BMI was 29.8kg/m<sup>2</sup>, median serum urate level at baseline was 6.1 mg/dl.<sup>1</sup>

Serum urate and hsCRP were tested at baseline and every three months for the first year and then annually. A physician diagnosed history of gout was ascertained at baseline and subsequent attacks were assessed during follow-up as part of the systematic adverse event reporting. The rates of gout attacks and major adverse CV events (heart attack, stroke, re-vascularisation, and CV death) were compared across different baseline serum urate levels and by randomised treatment assignment.<sup>1</sup>

In the results from the original trial,<sup>3</sup> neutropenia was more common among patients who were assigned to receive canakinumab than among those in the placebo group, and significantly more deaths were attributed to infection or sepsis in the pooled canakinumab groups than in the placebo group (incidence rate 0.31 vs. 0.18 events per 100 person-years; P=0.02). Thrombocytopenia was more common among patients who were assigned to receive canakinumab than among those in the placebo group, but no significant difference in the incidence of haemorrhage was observed.

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**-ENDS-**

#### **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 affect any organ of the body. 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.<sup>4</sup>

## About 'Don't Delay, Connect Today!'

'Don't Delay, Connect Today!' is a EULAR initiative that unites the voices of its three pillars, patient (PARE) organisations, scientific member societies and health professional associations - as well as its international network - with the goal of highlighting the importance of early diagnosis and access to treatment. In the European Union alone, over 120 million people are currently living with a rheumatic disease (RMD), with many cases undetected.<sup>5</sup> The 'Don't Delay, Connect Today!' campaign aims to highlight that early diagnosis of RMDs and access to treatment can prevent further damage, and also reduce the burden on individual life and society as a whole.

## 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](http://www.eular.org).

## References

- <sup>1</sup> Solomon DH, Glynn RJ, MacFadyen JG, *et al.* Serum urate, gout, and cardiovascular disease in a randomized controlled trial of canakinumab: A CANTOS secondary analysis. EULAR 2018; Amsterdam: Abstract OP0014.
- <sup>2</sup> Richette P, Doherty M, Pascual E, *et al.* 2016 updated EULAR evidence-based recommendations for the management of gout. *Ann Rheum Dis.* 2017;76:29-42.
- <sup>3</sup> Ridker PM, Everett BM, Thuren T, *et al.* Anti-inflammatory Therapy with Canakinumab for Atherosclerotic Disease. *N Engl J Med.* 2017;377(12):1119-1131.
- <sup>4</sup> van der Heijde D, *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). *Annals of the Rheumatic Diseases.* 2018;doi:10.1136/annrheumdis-2017-212565. [Epub ahead of print].
- <sup>5</sup> EULAR. 10 things you should know about rheumatic diseases fact sheet. Available at: <https://www.eular.org/myUploadData/files/10%20things%20on%20RD.pdf> [Last accessed April 2018].