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Inhibition of Interleukin-1β and Reduction in Atherothrombotic Cardiovascular Events in the CANTOS Trial

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Abstract

Background:

Inflammation reduction with the interleukin (IL)-1β inhibitor canakinumab significantly reduces the first major adverse cardiovascular event in patients with prior myocardial infarction (MI) and residual inflammatory risk (high-sensitivity C-reactive protein ≥ 2 mg/l). However, the effect of canakinumab on the total number of cardiovascular events, including recurrent events collected after a first event, is unknown.

Objectives:

This study sought to determine whether randomly allocated canakinumab would reduce the total burden of serious cardiovascular events.

Methods:

We randomized 10,061 patients to placebo or canakinumab 50 mg, 150 mg, or 300 mg once every 3 months and compared the rates of the composite of all serious cardiovascular events (MI, stroke, coronary revascularization, and cardiovascular death) in active versus placebo groups. We used negative binomial regression to account for

correlations among repeated events in the same person and to estimate rate ratios and 95% confidence intervals.

Results:

During a median of 3.7 years of follow-up, 3,417 total serious cardiovascular events occurred in 2,003 individuals among the 10,061 unique patients randomized. Canakinumab reduced the rates of total serious cardiovascular events, with rates per 100 person-years in the placebo, 50 mg, 150 mg, and 300 mg canakinumab groups of 10.4, 8.4, 8.3, and 8.2, respectively. The corresponding rate ratios (95% confidence intervals) compared with placebo were 0.80 (0.69 to 0.93) for 50 mg, 0.79 (0.68 to 0.92) for 150 mg, and 0.78 (0.67 to 0.91) for 300 mg.

Conclusions:

Anti-inflammatory therapy with canakinumab significantly reduced the total number of cardiovascular events in patients with prior MI and evidence of residual inflammatory risk.

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Keywords:

NLRP3 inflammasome; canakinumab; coronary artery disease; inflammation; prevention.

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