EFFECTS OF INTERLEUKIN-1β INHIBITION WITH CANAKINUMAB ON IL-6, FIBRINOGEN, AND HSCRP: A RANDOMIZED PLACEBO CONTROLLED TRIAL

ACC Moderated Poster Contributions
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Background: Atherosclerosis is an inflammatory disease and biomarkers such as hsCRP, IL-6, and fibrinogen associate with increased vascular risk. The ongoing Canakinumab Anti-inflammatory Thrombosis Outcomes Study (CANTOS) is investigating whether interleukin-1β (IL-1β) inhibition with canakinumab will reduce rates of recurrent cardiovascular events. To assist in dose selection for CANTOS, a randomized placebo controlled trial was conducted to evaluate effects of canakinumab on inflammatory biomarkers and on lipid levels.

Methods: 551 diabetic patients were randomly allocated to SC placebo or to SC canakinumab at doses of 5, 15, 50, or 150 mg monthly and followed over 4 months to evaluate the median percent change in hsCRP, IL-6, fibrinogen, and lipid levels between baseline and end of study.

Results: Compared to placebo, significant reductions in hsCRP, IL-6, and fibrinogen were observed after the initial canakinumab injection and were maintained throughout the study period. The median reductions in hsCRP at 4 months were 36.4%, 53.0 %, 64.6%, and 58.7% for the 5, 15, 50, and 150 mg canakinumab doses, respectively, compared to 4.7% for placebo (all P-values <0.05). Similarly, the median reductions in IL-6 at 4 months across the canakinumab dose range tested were 23.9%, 32.5%, 47.9%, and 44.5%, respectively, compared to 2.9% for placebo (all P < 0.05) and the median reductions in fibrinogen at 4 months were 4.9%, 11.7%, 18.5%, 14.8%, respectively, compared to 0.4% for placebo (all P-values <0.05). Effects were similar in women and men. By contrast, when compared to placebo, no dose of canakinumab had a clinically relevant effect on LDLC or HDLC though a modest increase in TG level was observed in the 50 and 150 mg canakinumab groups.

Conclusions: Canakinumab significantly reduces hsCRP, IL-6, and fibrinogen without an apparent impact on LDLC or HDLC and thus provides a method to test the inflammatory hypothesis of atherosclerosis without confounding effects on plasma cholesterol. These phase II data support the dose range selected for the ongoing, multi-national CANTOS trial which is evaluating the role of canakinumab as a novel therapeutic agent in the secondary prevention of cardiovascular disease.