Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibition with evolocumab decreases myocardial inflammation in individuals with acute coronary syndrome (ACS)

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Background/Introduction: Although inflammation is commonly present and often beneficial in the period following tissue injury, prolonged inflammation may impair healing and repair following acute ischemic injury. In addition to its impact on cholesterol metabolism PCSK9 is elevated in patients with inflammatory diseases and is thought to be a pro-inflammatory mediator. The presence and early trajectory of myocardial inflammation, and the impact of PCSK9 inhibition on that trajectory, in patients with an acute myocardial infarction have not been characterized.

Purpose: Our goals were to assess myocardial inflammation in patients with an acute myocardial infarction using 18F-FDG-PET scans obtained at the time of hospitalization for the infarction and at 30-days following the infarction and the impact of PCSK9 inhibition with evolocumab on inflammation in a placebo-controlled, randomized trial.

Methods: Fifty-five participants from the Evolocumab in Acute Coronary Syndrome trials, with a NSTEMI and a troponin-I of > 5 ng/ml or with a STEMI were randomized to placebo (n=30) or to 420 mg SQ of evolocumab (n=25) within 24 hours of admission. 18F-FDG-PET scans were performed within five days (2 [1-4]) of randomization and at 30 days. The myocardial mean Standardized Uptake Value (SUV) in the two randomized groups at baseline and the changes from baseline to 30 days were compared. All participants received guideline-directed therapies for acute infarction.

Results: Mean±SD age of the cohort was 57±13 years, 22% were African American, and 36% were women. There were no significant differences in demographic or clinical characteristics between the two groups. Mean SUV at baseline did not differ between the placebo (2.4 ±0.5) and the evolocumab (2.7±0.7) groups, p=0.25 for the between groups comparison. Mean SUV decreased in both groups, from 2.4±0.5 to 2.1±0.7 in the placebo group (p=0.05) and from 2.7±0.7 to 1.9±0.5 in the evolocumab group (p <0.0001), and the decrease was less in the placebo group, p=0.039 for the between groups comparison. The percent-change in the placebo group (-10.4%±36%) was also less than the percent change in the evolocumab group (-26.7%±20%), p = 0.04 for the between groups comparison. In addition, the percent of participants in whom the mean SUV units decreased was lower in the placebo group (60%) than in the evolocumab group (88%), p=0.03 for the between groups comparison.

Conclusion: Myocardial inflammation assessed using 18F-FDG-PET decreases but is still present 30 days following an acute myocardial infarction. PCSK9 inhibition with evolocumab given within the first 24 hours of admission improves resolution of the inflammation. In addition to its marked impact on lipid levels, PCSK9 inhibition has significant anti-inflammatory effects in the early post-infarction setting.

Figure 1: Myocardial Inflammation in the Peri- and 30-Day Post-Infarction Settings. Representative ¹⁸F-FDG-PET images from a participant randomized to placebo and a participant randomized to evolocumab.