Early and delayed IL-1 beta antibody gevokizumab treatments prevent cardiac remodeling and reverse coronary endothelial dysfunction following myocardial infarction injury in Goto Kakizaki rats

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Aims: Cardiac interleukin-1 beta (IL1-β) production is enhanced acutely after myocardial infarction and is involved in myocardial damages. We tested if early and delayed IL-1β modulations by IL-1β antibody, gevokizumab, prevented left ventricular (LV) remodeling and endothelial dysfunction induced by LV ischemia/reperfusion (I/R) in diabetic rats.

Methods: Gevokizumab (Gev; 10 mg/kg) was administered 1 hour (early) or 7 days (delayed) following reperfusion, after a 20 min of transient ischemia induced by LV artery occlusion and continued every week for 90 days. Delayed perindopril (1 mg/kg) was used as a positive control. LV hemodynamics (Millar catheterization) and relaxation of isolated coronary arteries to acetylcholine (Mulvany wiregraph) were evaluated at 90 days. Collagen density and leukocytes infiltration were evaluated (Histology) at 90 days.

Results: At 7 days, early Gevo limited the early LV expansion and reduction of FS induced by I/R. At 90 days both of early and delayed Gevo as well as perindopril limited in a similar manner, the LV late dilatation, the reduction of FS and LV systolic and diastolic dysfunction induced by I/R. At 90 days, GK coronary endothelium-dependent relaxation to acetylcholine was impaired by I/R (59±13 vs.17±4%; p<0.05). Early, delayed Gevo and perindopril restored the (86±4, 92±2 and 98±1% respectively; p<0.05 vs GK+I/R) coronary relaxation to acetylcholine. Early, delayed Gevo and perindopril significantly reduced collagen density and leukocytes infiltration at 90 days.

Conclusions: In a clinically relevant model of acute myocardial infarction, the IL-1β antibody gevokizumab started early or late after myocardial reperfusion exerts immediate and late cardiovascular protection.