APEX Trial Results: Pexelizumab Shows No Effect on Mortality and Morbidity

It is common knowledge that there is room for improvement in outcomes for patients that have had a heart attack and reperfusion therapy. Despite successful epicardial coronary reperfusion, microvascular and myocardial tissue perfusion often remains compromised due to reperfusion injury. Pexelizumab is a complement C5 inhibitor that had shown promise in reducing damage caused by heart attack and reperfusion injury. Paul W. Armstrong, MD, Professor of Medicine in the Division of Cardiology at the University of Alberta, Edmonton, Alberta, presented the results from the Assessment of Pexelizumab in Acute Myocardial Infarction (APEX) trial that was conducted to determine whether treatment with pexelizumab would have an effect on all-cause mortality in this population.

Patients were randomized within six hours of heart attack onset to either pexelizumab 2 mg/kg bolus prior to PCI plus 0.05 mg/kg/hour for 24 hours or placebo. The trial did not meet its primary endpoint: there was no reduction in 30-day or 90 day cumulative risk of death after treatment with pexelizumab. There were 113 deaths (3.92%) out of 2,885 placebo patients and 116 deaths (4.06%) out of 2,860 pexelizumab-treated patients (HR=1.04; 95% CI[0.80-1.35]). There was also no difference between groups in 30-day cumulative risk of death, shock, re-infarction or congestive heart failure (HR=0.98; 95% CI [0.83-1.16]).

Outcomes at 30 days in APEX-AMI (revised end points and time frame)

End point	Pexelizumab, n= 2,860 (%)	Placebo, n=2,885 (%)
All-cause mortality*	4.06	3.92
Death, shock, or HF	8.99	9.19

*Primary end point, revised from 90-day all-cause mortality in original protocol.
No significant differences.

"The result was not what we expected", commented Dr. Armstrong. The projected mortality in the placebo group was 6.5 %, but turned out to be much lower (3.92%), which was very surprising to the investigators. "There was no effect of pexelizumab on mortality or morbidity despite earlier evidence to the contrary" said Dr. Armstrong.

He concluded by saying that Phase 2 data are sometimes overly optimistic in predicting what will occur. The therapies for reperfusion injury, especially those aimed at decreasing the degree of inflammation, have been disappointing possibly because of the multiple pathways involved in the reperfusion injury cascade.

Results of the TOSCA-2 Trial: PCI Maintains Patency but has no Effect on LVEF

Vladimir Dzavík, MD
Photo courtesy of the American Heart Association

Vladimir Dzavík, MD, presented the results of the Total Occlusion Study of Canada (TOSCA)-2, which was a mechanistic sub-study of the Occluded Artery Trial (OAT) funded by the National Institutes of Health. Observational studies have suggested beneficial effects of opening a persistently occluded infarct related artery so called "open artery hypothesis", and the TOSCA-2 study set out to determine the effects of stent-based interventions 3 to 28 days post-myocardial infarction. The co-primary endpoints were the change in the heart's pumping ability as measured by left ventricular ejection fraction (LVEF) and the number of arteries which were still open after one year (patency). Secondary endpoints included the changes in left