ACC 22: PACMAN-AMI Shows Reduced Plaque Regression in AMI Patients Treated with Alirocumab

- My name is Lorenz Räber. I'm an interventional cardiologist working at Bern University Hospital in Bern, Switzerland.

Importance of this Trial

The trial is asking the question whether vulnerable plaques that are responsible for myocardial infarction, or sudden cardiac death in a large proportion, whether we can ameliorate those plaques by high-intensity lipid lowering with the use of alirocumab on top of high-intensity statin therapy.

Study Design and Patient Cohort

We enrolled a total of 300 patients presenting with either non-STEMI or STEMI. They were treated in their culprit lesion with a stent and, if they had non-obstructive disease in the two non-infarct related vessels, we imaged them using intracoronary imaging consisting of three techniques. First, with the combined catheter using intravascular ultrasound and near-infrared spectroscopy, those two catheters can assess the plaque burden and the lipid pool, both important vulnerability characteristics and the second catheter we used for intracoronary imaging is optical coherence tomography, which is a high-precision method that allows to measure the fibrous cap thickness, which is again an important vulnerability characteristic. Patients, after the imaging, were then randomly allocated to receive either alirocumab, 150 milligrams biweekly on top of high-intensity statin therapy consisting of Rosuvastatin, 20 milligrams daily or placebo biweekly on top of Rosuvastatin, 20 milligrams. After 52 weeks, patients underwent again, the same intracoronary imaging procedures using IVUS, NIRS and OCT at exactly the same localisation.

Outcomes of this Study

We have shown that alirocumab on top of high-intensity statin therapy, as compared to placebo on top of high-intensity statin therapy, reduces significantly percent atheroma volume, which is a measure of the plaque burden. It was reduced 2.1% in the alirocumab group and 0.9% in the placebo and statin group. On top of that, we provided data and evidence on a significant reduction in the lipid content of the plaques and of a significant fibrous cap thickening. Altogether, this provides evidence that alirocumab, initiated early in patients with acute coronary syndrome, can lead to plaque regression, delipification and stabilisation.

Take-home Messages for Clinicians

We also assessed a correlation between the on-treatment LDL and the reduction in the vulnerability markers like plaque burden, lipid content and fibrous cap thickness. And interestingly, when we achieved LDL levels below 50 milligrams per decilitre, the reduction in plaque volume and lipid content and the thickening of the fibrous cap was achieving the highest values. Therefore, the conclusion really is that the lower you get your LDL-C in this very high-risk population, the more regression, the more delipification and the more stabilisation you achieve in untreated non-obstructive lesions with vulnerability characteristics that potentially could lead, in the future, to myocardial infarction or coronary death.

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Further Study Needed

Well, this is a mechanistic study providing evidence for the benefit of an early administration of a PCSK9 inhibitor, alirocumab, the early setting of ACS and that with that regimen you achieve plaque regression and stabilisation. However, what the potential next step should be is a clinical trial that actually investigates to which degree clinical outcomes can be reduced by such a treatment regimen. I would like to make you aware of one specific design feature of the PACMAN-AMI trial and that is the entry criteria with respect of the LDL-C. Most patients did not receive a statin at entry and their LDL had to be above 125 milligrams per decilitre, which is rather low. So therefore, the PACMAN-AMI really provides the grounds for a more aggressive and early LDL lowering, initiated in patients with high-risk characteristics.