RESUMEN

Approximately 40% of cases of myocardial infarction occur in patients with normal lipid concentrations. Type 2 diabetic patients are a paradigm of this situation since cardiovascular disease is their main cause of death being LDL cholesterol normal or only moderately elevated. Over the past few years, we and others have demonstrated that cardiovascular risk in these patients is better explained by other characteristics of lipoproteins such as particle abundance or particle diameter. Following this idea, we have been extending the list of lipoprotein characteristics that may be involved in cardiovascular risk in type 2 diabetic patients, such as electrical charge of lipoproteins, sialic acid proteoforms of apolipoprotein C-III and lipopolysaccharide content.

PCSK9 gene regulates cholesterol levels by accelerating low-density lipoprotein receptor (LDLR) degradation resulting in the decreased catabolism of LDL leading to hypercholesterolemia. The PCSK9 inhibitors (such as Alirocumab) have changed the paradigm for lipid-lowering therapy to prevent cardiovascular disease, showing the clinical benefit of lowering LDL cholesterol below the current goal. This therapy nowadays is only available for patients with severe hypercholesterolemia.

We have recently reported how PCSK9 concentration modulates lipoprotein features (others than LDL cholesterol) towards a more atherogenic profile in type 2 diabetic patients, and since PCSK9 inhibition also modifies lipoprotein kinetics, we hypothesize that treatment with Alirocumab (Praluent®) may also affect other atherogenic characteristics of lipoproteins. We propose to study the net electrical charge, the sialic acid proteoforms of apolipoprotein C-III and the lipopolysaccharide content, because they have been recently identified as potential risk factors for cardiovascular risk and diabetes, and they may promote the interaction of lipoproteins with the vascular wall or even worsen the inflammatory status.

Our objective is to study to what extend treatment with Praluent® modifies the following parameters:

- Particle number and diameter of 9 lipoprotein subclasses assessed by 2D-NMR.
- VLDL, IDL, LDL and HDL net electrical charge
- Total, VLDL, IDL, LDL and HDL apolipoprotein C-III content, plus relative amounts of apoC-III sialylated proteoforms (with none, 1 or 2 molecules of sialic acid)
- Total, VLDL, IDL, LDL and HDL content of lipopolysaccharide.