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LETTER TO THE EDITOR

Improvement in arterial stiffness after short-term treatment with PCSK9 inhibitors

Dear Editor,

Alirocumab and evolocumab are fully human monoclonal antibodies that inhibit proprotein convertase subtilisin–kexin type 9 [iPCSK9]. These agents reduce the risk of cardiovascular and limb events in statin-treated subjects [1,2]. However, the effect of iPCSK9 on arterial stiffness has not yet been reported. In this report, we present data from two patients who experienced an impressive improvement in carotid-femoral pulse wave velocity [cfPWV] after short-term treatment with iPCSK9.

Patient #1 is a 46-year-old man with heterozygous familial hypercholesterolemia (Dutch Lipid Clinic Network Score = 11) who had experienced a myocardial infarction at the age of 41 years. He presented with bilateral arcus cornealis and high LDL-cholesterol levels (LDL-C = 121 mg/dL) despite being treated with 40 mg rosuvastatin and ezetimibe for more than six months. To optimize the ongoing lipid-lowering therapy, he was started on alirocumab 75 mg every 14 days. After 3 months of therapy, lipid parameters improved (TC = −37%, non-HDL-C = −48%, LDL-C = −56%, Lp (a) = −26%) and the cfPWV – noninvasively assessed using the Vicorder® apparatus, which guarantees a very good intra- and interoperator reliability [3] – normalized, decreasing from 15.4 to 8.9 m/s (−42% vs. baseline). Of great interest, the patient experienced a further decrease in cfPWV (5.6 m/s at 6-month follow-up visit) with time despite having decided to stop taking rosuvastatin against medical advice and having experienced an increase in LDL-C (+48.7%) (Fig. 1).

Patient #2 is a 52-year-old man who had undergone a percutaneous transluminal coronary angioplasty 2 years previously. At the time of hospital discharge, the patient was prescribed 20 mg rosuvastatin with ezetimibe added at a subsequent follow-up visit. After one year of high-dose lipid-lowering combination treatment, the patient was referred to our lipid clinic because LDL-cholesterol remained persistently above 100 mg/dL (LDL-C = 111 mg/dL). To optimize the patient's cardiovascular risk profile, we prescribed a subcutaneous injection of 140 mg evolocumab every 14 days, in addition to the pre-existing therapy.

At 3-month follow-up, lipid parameters improved compared to baseline (TC = −33%, non-HDL-C = −51%, LDL-C = −67%) and the cfPWV decreased from 19.2 to 9.2 m/s (−52%).

A further improvement in cfPWV occurred after another three months of iPCSK9 treatment (cfPWV = 8.7 m/s) despite a simultaneous extraordinary increase in LDL-C secondary to the patient's poor adherence to statin therapy (LDL-C = +217.6%) (Fig. 1).

The improvement in arterial stiffness in these two patients after initiating iPCSK9 treatment is impressive, especially because it occurred very rapidly and largely independent of the comorbidities. Our patients were neither diabetic nor smokers, and their blood pressure levels were under control, as recommended in the most recent guidelines [4]. It remains to be established whether iPCSK9 has a direct effect on endothelial function and vasodilatory capacity.

Recently, Maulucci and co-workers showed that two months of treatment with 140 mg evolocumab is enough to improve endothelial function in subjects with increased cardiovascular risk, considering the improvement proportional to LDL-C reduction [5]. On the other hand, the cfPWV improvement despite the increase in LDL-C suggests that the iPCSK9s could independently exert a beneficial impact on vasomotor function. This may contribute to cardiovascular disease risk reduction independent of changes in serum lipoprotein concentrations [6].

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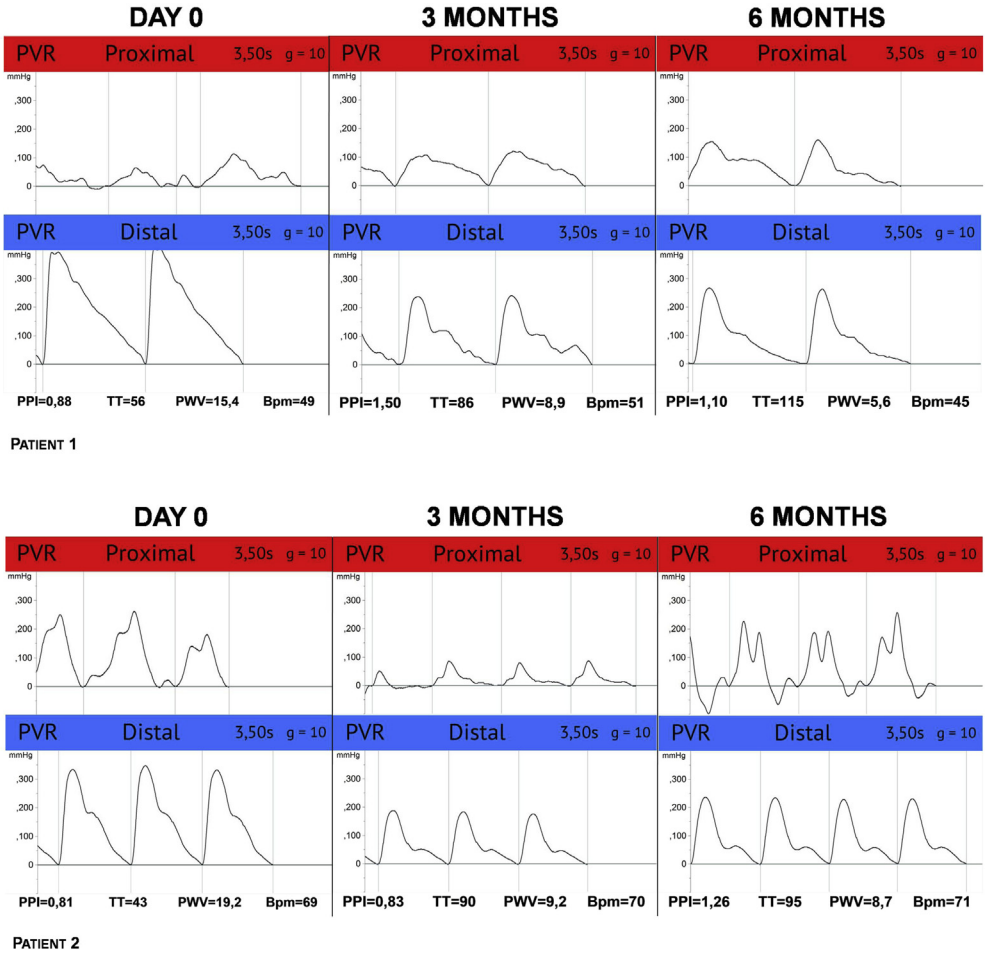

Figure 1 Changes in our patients' carotid-femoral pulse wave velocity with time.

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