in both FH I and II trials (−48.8% and −48.7% vs 9.1% and 2.8%, respectively; $P<.0001$). To reach a prespecified LDL-C level <1.81 mmol/L (70 mg/dL), an uptitration to 150 mg Q2W at week 12 was necessary in 43.4% and 38.6% of patients receiving alirocumab treatment in both trials.

Similarly, by week 24, significantly more alirocumab-treated patients compared to those on placebo had reached the LDL-C goal of a level <2.59 mmol/L (100 mg/dL) in high-risk patients or <1.81 mmol/L (70 mg/dL) in very high-risk patients (72.2% vs 2.4% in FH I, and 81.4% vs 11.3% in FH II; both $P<.0001$). Most patients receiving alirocumab achieved their LDL-C goals at week 24 in both trials (72.2% and 81.4% vs 2.4% and 11.3%; $P<.0001$), and this reduction was maintained to 52 weeks (1.7 mmol/L and 1.9 mmol/L [65.9 mg/dL and 74.3 mg/dL]).

In an analysis of pooled data from the 2 trials at week 52, alirocumab appeared to be well tolerated. Treatment-emergent adverse events (TEAEs) occurred in a similar proportion of patients treated with alirocumab and placebo (74.8% vs 75.4%) and led to discontinuation in 3.1% and 3.7% of patients, respectively. The most commonly reported TEAEs (occurring in ≥5% of patients in each treatment arm) were injection-site reactions, nasopharyngitis, influenza, and headaches.

With such a large proportion of patients achieving their target LDL-C levels, and the lack of major adverse safety signals compared with placebo, alirocumab represents a very promising treatment approach for this very high-risk patient population, concluded Prof Farnier.

IBIS-4: High-Dose Rosuvastatin Reduces Plaque Burden in Patients With STEMI

Written by Nicola Parry

Lorenz Räber, MD, Bern University Hospital, Bern, Switzerland, presented results from the Integrated Biomarker and Imaging Study-4 [IBIS-4; Räber L et al. *Eur Heart J*. 2014], a prospective substudy embedded in the COMFORTABLE trial [Räber L et al. *JAMA*. 2012] comparing biolimus-eluting stents vs bare-metal stents in patients with STEMI undergoing percutaneous coronary intervention (PCI). Data from IBIS-4 demonstrated that high-dose daily rosuvastatin was associated with a significant reduction in atherosclerotic burden in the non–infarct-related epicardial coronary arteries (non-IRAs) in patients with STEMI who underwent successful primary PCI.

For the past 2 decades, statins have been the mainstay of therapy in patients with high levels of low-density lipoprotein cholesterol (LDL-C), potently reducing cardiovascular events with acute coronary syndromes [Roth EM, Diller P. *Future Cardiol*. 2014]. According to Prof Räber, however, although statins are a key component of treatment for patients with acute STEMI, their long-term impact on coronary atherosclerosis is unknown. This study therefore aimed to investigate the effect of high-dose statin therapy on plaque burden, composition, and phenotype in the non-IRAs of patients with STEMI undergoing primary PCI.

IBIS-4 included 103 patients with STEMI who underwent intravascular ultrasonography (IVUS) and radiofrequency ultrasonography (RF-IVUS) of the 2 non-IRAs following successful primary PCI. Exclusion criteria included subjects with either non-IRA with >50% stenosis.

All patients received rosuvastatin 20 mg/d for the first 2 weeks, followed by a dose increase to 40 mg/d for the remainder of the study period. Atherosclerotic burden was evaluated in the proximal arterial segments at baseline and 13 months using IVUS and RF-IVUS.

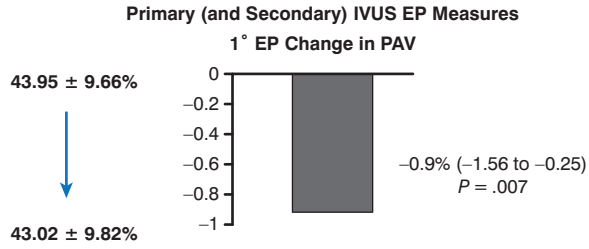
The primary IVUS end point was the change in percent atheroma volume (PAV), and the primary RF-IVUS end point was the change in percent necrotic core, both at 13 months. Successful serial imaging was available for 82 patients with 146 analyzed non-IRAs at both time points.

From baseline to 13 months, LDL-C had decreased from a median of 3.29 to 1.89 mmol/L ($P<.001$). With regard to the primary end point, IVUS demonstrated a significant reduction of atheroma volume (43.95% to 43.02%; 95% CI, −1.56 to −0.25, $P=.007$; Figure 1).

There was no significant change, however, in percent necrotic core with RF-IVUS (21.14% to 21.02%; 95% CI, −1.05 to 0.96; $P=.93$). Similarly, the proportions of plaques with necrotic core and different plaque phenotypes were unchanged.

Dr Räber noted that the proximal segments of non-IRAs in these patients contained a high atherosclerotic plaque

Figure 1. Effect of Rosuvastatin on Atheroma Volume



EP, end point; IVUS, intravascular ultrasonography; PAV, percent atheroma volume.
Source: Räber L et al. *Eur Heart J*. 2014.
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