patients in the acute setting of acute myocardial infarction, and the majority of patients (88%) had not been taking any statin therapy at the time of enrollment. When designing our study, we were concerned that initiating a triple lipid-lowering therapy with the highest dose of rosuvastatin combined with a second oral medication (ezetimibe) and alirocumab might have created tolerability issues in a study population largely consisting of statin-naive patients. Although statin intolerance is relatively rare, it is dose dependent and may affect adherence to treatment. The PACMAN-AMI trial was a mechanistic imaging study aiming to compare the effects of standardized, guideline-recommended high-intensity statin therapy (ideally unchanged during the study) alone vs in combination with alirocumab. Notably, the control group in our study received higher doses of lipid-lowering therapy and had lower median LDL-C levels than in other recent studies of patients with acute myocardial infarction. For example, only 48% of patients in the SWEDHEART registry were treated with a high-intensity statin and had a median LDL-C level of 77 mg/dL, and only 59% of patients in the placebo group of the GLAGOV trial used a high-intensity statin and had a median LDL-C level of 93 mg/dL.

We disagree with Benson’s assumption that the comparison group in our study may have introduced bias in favor of alirocumab. If ezetimibe or a higher rosuvastatin dose had been initiated at study enrollment, these medications would have been added in both treatment groups and would have resulted in a similar degree of incremental LDL-C lowering and atheroma regression without differential effects in the alirocumab and placebo groups. On the other hand, if up titration of statin dose and/or addition of ezetimibe had been allowed during the course of the trial, the treating physicians and patients would have been unblinded, which would have deprived our study of the highest possible methodology standards of randomization with double blinding.

Dr Calderón and colleagues suggest that the degree of percent atheroma volume reduction stratified according to baseline percent atheroma volume should be reported. This is a prespecified subgroup analysis that will be reported in a separate article. They also raise the question about the mechanistic basis of macrophage reduction in the alirocumab group. Inflammatory cell infiltration is considered to correlate with lipid accumulation in the atheroma; preclinical studies have indeed shown that plaque delipidation in response to statin and PCSK9 inhibitor therapy reduces macrophage infiltration in atherosclerotic plaques. We therefore believe that the reduction of optical coherence tomography–defined macrophages following treatment with alirocumab plus statin in our study is a biologically plausible finding that extends previous evidence with statin treatment alone, although more research is needed to further elucidate the underlying mechanisms.

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CORRECTION

Error in Table: In the Review article titled “Diagnosis and Treatment of Pulmonary Arterial Hypertension: A Review,” published in the April 12, 2022, issue of JAMA, there was an error in the labeling of statistical data in Table 2. In the “Outcome Difference” column for the row containing data on the SERAPHIN study by Pulido et al, the confidence interval for the HR should have been labeled as “97.3% CI” instead of “95% CI.” This article was corrected online.