



**Universiteit  
Leiden**  
The Netherlands

## **REPLY: alirocumab in polyvascular atherosclerotic disease**

Zijlstra, L.E.; Schwartz, G.G.; Steg, P.G.; Jukema, J.W.

### **Citation**

Zijlstra, L. E., Schwartz, G. G., Steg, P. G., & Jukema, J. W. (2020). REPLY: alirocumab in polyvascular atherosclerotic disease, 75(2), 241-241. doi:10.1016/j.jacc.2019.10.053

Version: Publisher's Version  
License: [Creative Commons CC BY 4.0 license](https://creativecommons.org/licenses/by/4.0/)  
Downloaded from: <https://hdl.handle.net/1887/3232753>

**Note:** To cite this publication please use the final published version (if applicable).

4. Alkhalil M, Chai JT, Choudhury RP. Plaque imaging to refine indications for emerging lipid-lowering drugs. *Eur Heart J Cardiovasc Pharmacother* 2017;3:58-67.

5. Alkhalil M. Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors, reality or dream in managing patients with cardiovascular disease. *Curr Drug Metab* 2019;20:71.

### REPLY: Alirocumab in Polyvascular Atherosclerotic Disease



We appreciate the comments by Dr. Alkhalil on our paper (1). Measurement of plaque burden might provide information that would complement levels of circulating biomarkers, including low-density lipoprotein cholesterol (LDL-C), to identify subsets of patients who derive particular benefit from alirocumab treatment. Although LDL-C reduction and regression or slowed progression of coronary atheroma volume have been closely linked in prior investigations (e.g., REVERSAL [Reversal of Atherosclerosis with Aggressive Lipid Lowering], SATURN [Sequential Tarceva in Unresectable NSCLC], GLAGOV [Global Assessment of Plaque regression With a PCSK9 antibody as Measured by intravascular Ultrasound]) (2), it is not established whether vascular imaging should guide therapy with PCSK9 inhibitors.

Although most patients in ODYSSEY OUTCOMES (Evaluation of Cardiovascular Outcomes After an Acute Coronary Syndrome During Treatment With Alirocumab) underwent coronary angiography and 72% underwent percutaneous coronary intervention or coronary bypass surgery for the qualifying acute coronary syndrome, systematic collection of angiographic data accumulated before randomization was not possible in this large, multicenter, multinational trial. Therefore, we cannot determine whether the burden of coronary artery disease predicted the therapeutic benefit of alirocumab. It is possible that other imaging techniques that assess volume, virtual histology, or inflammatory characteristics of atherosclerotic plaque (3) might contribute in that regard, but such hypotheses remain to be tested. Moreover, application of vascular imaging techniques may be limited by invasiveness, sensitivity, cost, availability, or ease of implementation in daily clinical practice.

Risk stratification to guide optimal application of therapies in atherosclerosis is most often based on levels of lipid and inflammatory biomarkers and readily identified clinical features. The latter include diabetes, a history of coronary bypass grafting, or in the case of our analysis, polyvascular disease. Subanalyses of ODYSSEY OUTCOMES show that the presence of such high-risk characteristics is associated with absolute benefit of PCSK9 inhibition with

alirocumab, when added to high-intensity statin therapy (1,4,5).

An important future research objective would be to determine whether vascular imaging adds further prognostic information that helps to predict the clinical benefit of PCSK9 inhibitor treatment.

Laurien E. Zijlstra, MD  
Gregory G. Schwartz, MD, PhD  
Philippe Gabriel Steg, MD

\*J. Wouter Jukema, MD, PhD

\*Department of Cardiology  
Leiden University Medical Center  
PO Box 9600  
2300 RC Leiden  
the Netherlands

E-mail: [j.w.jukema@lumc.nl](mailto:j.w.jukema@lumc.nl)

<https://doi.org/10.1016/j.jacc.2019.10.053>

© 2020 by the American College of Cardiology Foundation. Published by Elsevier.

Please note: Dr. Schwartz has received research grants to the University of Colorado from Resverlogix, Sanofi, The Medicines Company, and Roche; and is coinventor of pending U.S. patent 14/657192 ("Methods of Reducing Cardiovascular Risk") assigned in full to the University of Colorado. Dr. Steg has received grants and nonfinancial support (cochair of the ODYSSEY OUTCOMES trial; as such he received no personal fees, but his institution has received funding for the time he has devoted to trial coordination, and he has received support for some travel related to trial meetings) from Sanofi; has received research grants and personal fees from Bayer (Steering Committee MARINER, grant for epidemiological study), Merck (speaker fees, grant for epidemiological studies), Sanofi (cochair of the ODYSSEY OUTCOMES trial; cochair of the SCORED trial; consulting, speaking), Servier (chair of the CLARIFY registry; grant for epidemiological research), and Amarin (executive steering committee of the REDUCE-IT trial [Disease Reduction of Cardiovascular Events With Icosapent Ethyl-Intervention Trial]; consulting); has received personal fees from Amgen, Bristol-Myers Squibb, Boehringer Ingelheim, Pfizer, Novartis, Regeneron Pharmaceuticals, Lilly, and AstraZeneca; and has a European application number/patent number, issued on October 26, 2016 (No. 15712241.7), for a method for reducing cardiovascular risk. Dr. Jukema has received research grants from the Netherlands Heart Foundation, the Interuniversity Cardiology Institute of the Netherlands, and the European Commission Seventh Framework Programme; and has received research support from Amgen, Astellas, AstraZeneca, Daiichi-Sankyo, Lilly, Merck-Schering-Plough, Pfizer, Roche, and Sanofi. Dr. Zijlstra has reported that she has no relationships relevant to the contents of this paper to disclose.

### REFERENCES

1. Jukema JW, Szarek M, Zijlstra LE, et al. Alirocumab in patients with polyvascular disease and recent acute coronary syndrome: ODYSSEY OUTCOMES Trial. *J Am Coll Cardiol* 2019;74:1167-76.
2. de Graaf MA, Jukema JW. High coronary plaque load: a heavy burden. *Eur Heart J* 2013;34:3168-70.
3. Alkhalil M, Chai JT, Choudhury RP. Plaque imaging to refine indications for emerging lipid-lowering drugs. *Eur Heart J Cardiovasc Pharmacother* 2017;3:58-67.
4. Goodman SG, Aylward PE, Szarek M, et al. Effects of alirocumab on cardiovascular events after coronary bypass surgery. *J Am Coll Cardiol* 2019;74:1177-86.
5. Ray KK, Colhoun HM, Szarek M, et al. Effects of alirocumab on cardiovascular and metabolic outcomes after acute coronary syndrome in patients with or without diabetes: a prespecified analysis of the ODYSSEY OUTCOMES randomised controlled trial. *Lancet Diabetes Endocrinol* 2019;7:618-28.