©Copyright by Croatian Cardiac Society. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (https://creativecommons.org/licenses/by/4.0/) which permits users to read, download, copy, distribute, print, search, or link to the full texts of these articles in any medium or format and to remix, transform and build upon the material, provided the original work is properly cited and any changes properly indicated.

Marked Lipoprotein(a) Reduction with Pelacarsen in a Young Patient with Premature Coronary Artery Disease: What Next After Lp(a) HORIZON?

Ivica Bošnjak[1,2]*, Đorđe Pojatić[3,4], Aleksandar Kibel[2,4,5,6]

[1]Health Center of Osijek-Baranja County, Osijek, Croatia
[2]Josip Juraj Strossmayer University of Osijek, Faculty of Medicine Osijek, Osijek, Croatia
[3]Vinkovci General Hospital, Vinkovici, Croatia
[4]Josip Juraj Strossmayer University of Osijek, Faculty of Dental Medicine and Health, Osijek, Croatia
[5]International Medical Center Priora, Čepin, Croatia
[6]Josip Juraj Strossmayer University of Osijek, Scientific Centre of Excellence for Personalized Health Care, Osijek, Croatia

KEYWORDS: lipoprotein(a), pelacarsen, familial hypercholesterolemia, residual cardiovascular risk.

CITATION: Cardiol Croat. 2026;21(11-12):332. | https://doi.org/10.15836/ccar2026.332

***ADDRESS FOR CORRESPONDENCE:** Ivica Bošnjak, Dom zdravlja Osječko-baranjske županije, Park kralja Petra Krešimira IV, HR-31000 Osijek, Croatia. / Phone: +385-91-9227-756 / E-mail: dribosnjak79@gmail.com

ORCID: Ivica Bošnjak, https://orcid.org/0000-0002-0223-4287 • Đorđe Pojatić, https://orcid.org/0000-0001-9813-9008 Aleksandar Kibel, https://orcid.org/0000-0001-7843-1079

Introduction: Markedly elevated lipoprotein(a) [Lp(a)] is associated with premature atherosclerotic cardiovascular disease, particularly in patients with familial hypercholesterolemia. Although several therapies can substantially lower circulating Lp(a), whether this translates into fewer cardiovascular events remains an important clinical question.[1,2]

Case report: We present a 39-year-old man with heterozygous familial hypercholesterolemia who suffered an ST-elevation myocardial infarction in October 2022. Coronary revascularization included PCI of the left anterior descending artery and implantation of three drug-eluting stents in the right coronary artery. At presentation, left ventricular ejection fraction (LVEF) was 36%. Moderate aortic stenosis was also diagnosed. The patient was treated with guideline directed medical therapy that also included atorvastatin 80 mg, ezetimibe 10 mg and inclisiran, achieving LDL cholesterol concentrations below 0.3 mmol/L. However, baseline Lp(a) was markedly elevated at 560 nmol/L. Given his young age, extensive coronary disease and exceptionally high Lp(a), pelacarsen was introduced through a compassionate-use programme. After eight months of pelacarsen treatment, Lp(a) had decreased from 560 to 147 nmol/L, representing a 73.8% reduction. In parallel, guideline-directed medical therapy for heart failure was associated with improvement in LVEF from 36% to 45%. Despite the substantial reduction in Lp(a), pelacarsen was discontinued following the negative results of the Lp(a)HORIZON trial. This case raises a practical question: how should we manage a young patient with premature coronary artery disease, well-controlled LDL cholesterol and persistently elevated Lp(a) when a targeted treatment has demonstrated a marked biochemical effect but failed to improve cardiovascular outcomes in a large clinical trial? The neutral results of Lp(a)HORIZON and ZEUS, which investigated IL-6 inhibition, challenge the assumption that lowering an individual risk-related biomarker necessarily improves clinical outcomes. However, the findings of these trials should not be interpreted as evidence that Lp(a) or inflammation are irrelevant to atherosclerotic disease.

Conclusion: In this patient, intensive lipid-lowering treatment and eight months of pelacarsen therapy achieved exceptionally low LDL cholesterol and a substantial reduction in Lp(a). Nevertheless, the negative Lp(a)HORIZON results have left an important therapeutic gap. Whether alternative Lp(a)-lowering agents, earlier treatment or more profound and sustained reductions will improve outcomes remains to be established.

RECEIVED:
October 23, 2026
UPDATED:
November 4, 2026

LITERATURE

1. Sabouret P, Giamundo DM, Asher E, De Rosa S, Andò G, Gragnano F, et al. Pelacarsen and Lp(a)HORIZON: Interpreting the Disconnect Between Lipoprotein(a) Lowering and Cardiovascular Outcomes. Am J Med. 2026 Oct 15:S0002-9343(26)00749-7. https://doi.org/10.1016/j.amjmed.2026.10.005
2. Anderer S. Lipoprotein(a)-Lowering Agent Fails to Reduce Cardiovascular Events. JAMA. 2026;336(15):1300. https://doi.org/10.1001/jama.2026.14725