

Management of Lorlatinib-Induced Hyperlipidemia with PCSK9 Inhibitors: A Case Series

Andrea St Laurent¹ DO, Koosha Payday¹ MD, Tim Moriarty² MA MBA, Tochi M. Okwuosa³ MD, Jeffrey A. Borgia² PhD, Alexis Koon¹ PharmD, Kevin Cheng¹ PharmD, Salaheldin Abusin³ MD, Marta Batus¹ MD, Helen Ross¹ MD, Marina Chiara Garrassino⁴ MD, **Mary Jo Fidler¹ MD**

¹ Rush University Medical Center, Department of Medicine, Section of Hematology, Medical Oncology and Cell Therapy, Chicago, IL

² Rush University Medical Center, Departments of Anatomy, Cell Biology and Pathology, Chicago, IL

³ Rush University Medical Center, Department of Internal Medicine, Division of Cardiology

⁴ University of Chicago Medical Center, Department of Medicine, Chicago, IL

INTRODUCTION

- Lorlatinib is a preferred treatment for ALK-rearranged Non-small Cell Lung Cancer (NSCLC) and is associated with hyperlipidemia which is typically treated by statins, not always successfully.
- The role of PCSK9 inhibitors (PCSK9i) in resistant/severe cases is not well characterized. We present four patients with lorlatinib-induced, refractory mixed hyperlipidemia who had remarkable improvement with PCSK9i.

CASE 1

A 66-year-old male on second-line lorlatinib 75 mg daily had normal baseline lipid levels but progressed to mixed hyperlipidemia refractory to pravastatin 40 mg daily, and partially improved on rosuvastatin 40 mg daily and ezetimibe 10 mg daily. After prolonged lifestyle modification attempts over four and a half years, alirocumab 75 mg/mL every 2 weeks (Q2W) was added, achieving lipid control (figure 1).

CASE 2

A 74-year-old female with hypertension on dose-reduced second line lorlatinib (50 mg due to dizziness) had baseline mixed hyperlipidemia, which worsened on lorlatinib and was refractory to rosuvastatin 40 mg daily. One year later, evolucumab 140 mg/mL Q2W was added with excellent response.

CASE 3

A 59-year-old female with hypertension started lorlatinib 100 mg daily. Baseline labs showed mixed hyperlipidemia, which worsened on lorlatinib. Hyperlipidemia was refractory to rosuvastatin 40 mg daily. Seven months later, evolucumab 140 mg/mL Q2W was added improving all lipid parameters except triglycerides.

CASE 4

A 69-year-old female with moderate coronary calcification, started lorlatinib 75 mg daily. Baseline labs showed borderline LDL. She developed severe mixed hyperlipidemia, refractory to rosuvastatin 40 mg daily. Evolocumab 140 mg/mL Q2W added one year later achieved control. Statin was later stopped due to myalgia, causing rebound hyperlipidemia. Rosuvastatin 10 mg daily plus evolucumab 140 mg/mL Q2W triggered recurrent myalgia. Ezetimibe was not possible due to allergy. She transitioned to evolucumab 140 mg/mL Q2W with bempedoic acid 180 mg daily with mild improvement.

DISCUSSION

These findings suggest use of PCSK9i may be effective in statin-refractory cases. Early incorporation of PCSK9i in statin-refractory lorlatinib-associated hyperlipidemia warrants prospective clinical evaluation to determine whether it can improve lipid control and reduce long-term cardiometabolic risk.

CONCLUSION

These four case reports illustrate the benefit of addition of a PCSK9i in treatment-related, refractory hyperlipidemia. PCSK9i are effective in lowering total cholesterol and LDL in patients with lorlatinib-induced hyperlipidemia and may be considered early in severe and statin-refractory cases.

CONTACTS AND DISCLAIMERS

Correspondence: Mary Jo Fidler@rush.edu

References available upon request.

AI tool was not used in the generation of the poster.

Changes in Total Cholesterol (TC) and LDL Following Lorlatinib Initiation and Subsequent Lipid-Lowering Therapy

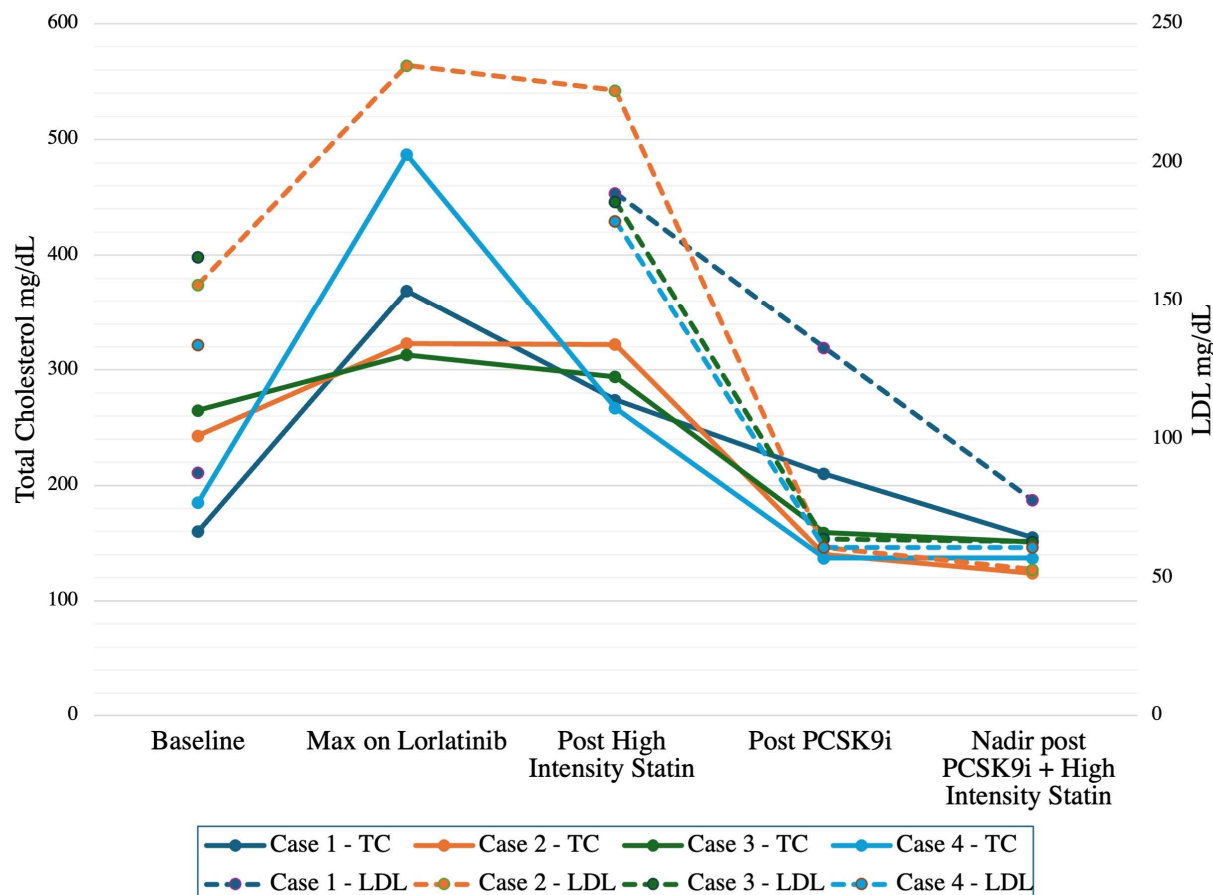


Figure 1. Change in total cholesterol (left y-axis) and LDL (right y-axis) following initiation of lorlatinib therapy followed by high intensity statin and subsequent PCSK9 inhibitor therapy.

* Max LDL on Lorlatinib could not be accurately estimated in Cases 1, 3, and 4 due to extremely elevated triglycerides