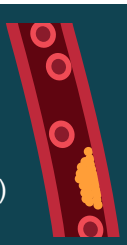
Efficacy and Safety of Alirocumab in Individuals with Diabetes Mellitus: Pooled Analyses from Five Placebo-Controlled Phase 3 Studies

Ginsberg HN et al. *Diabetes Ther*. 2018;9:1317–1334

What is the problem?

High cholesterol puts people at risk of heart disease, especially those with diabetes mellitus (DM)

Individuals with DM are, on average, at **double the risk** of atherosclerotic cardiovascular disease (ASCVD) in comparison to those without DM



What are the current treatment options?

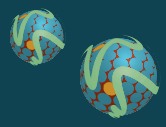
Physicians set individualized cholesterol treatment goals for each patient

Statins, prescribed to reduce high cholesterol levels, may not lower cholesterol enough in all people

The American Diabetes Association recently stated that therapy with a proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor may be considered for individuals with DM and ASCVD

Alirocumab is a PCSK9 inhibitor – a potential treatment option for individuals with elevated cholesterol levels including those with DM

Alirocumab is a medication for lowering low-density lipoprotein (LDL) cholesterol levels by inhibiting PCSK9



Alirocumab is intended for use in combination with maximally tolerated statin therapy

Previously, alirocumab significantly reduced LDL cholesterol levels in individuals with DM; however, its effect has yet to be compared in a larger pool of individuals with and without DM treated for longer treatment duration

Aim of our analysis

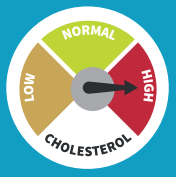
We compared the effects of alirocumab in people:

1054 with DM **versus** **2445** without DM

What data were included and how?

All patients at study entry had:

- Hypercholesterolemia
- Maximally tolerated, stable background statin therapy ± other lipid-lowering therapies



We combined data from five double-blind, randomized, placebo-controlled ODYSSEY Phase 3 studies with 52–78 weeks' treatment duration

ALIROCUMAB

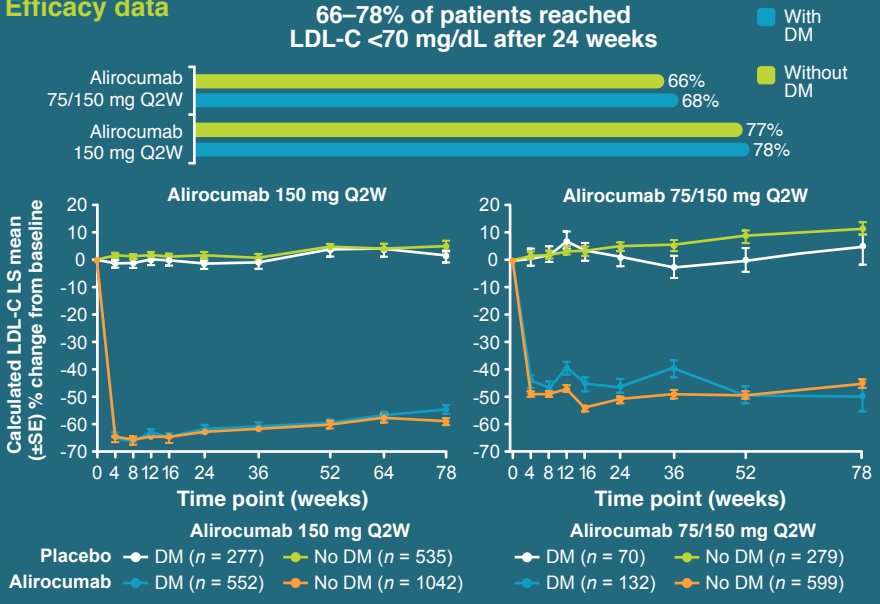
150 mg Q2W **OR**

75 mg Q2W → 150 mg Q2W

Dose adjustment per study protocol

What were the findings of this analysis?

Efficacy data



Alirocumab treatment was also associated with reduced levels of apolipoprotein B, lipoprotein (a), non-high-density lipoprotein cholesterol (non-HDL-C) and triglycerides, and increased levels of HDL-C.

Safety data

Overall, the incidence of treatment-emergent adverse events (TEAEs) was similar regardless of DM status in alirocumab-treated individuals versus in the corresponding placebo groups. In total, **20% (alirocumab)** and **24% (placebo) of individuals with DM**, and **15% (alirocumab)** and **14% (placebo) of those without DM** experienced treatment-emergent serious adverse events.

Regardless of DM status, the most common TEAEs were nasopharyngitis and upper-respiratory tract infection.

Conclusions

DM status does not appear to meaningfully affect the efficacy or safety of alirocumab treatment in individuals with or without DM

Alirocumab consistently lowered LDL cholesterol in people who had not reached cholesterol goals even with maximally tolerated statin dose, regardless of the DM status