

# ORION-10

Inclisiran for subjects with ACSVD and elevated low-density lipoprotein cholesterol

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# What we learned from ORION-10

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- Inclisiran is a long-acting small interfering RNA that inhibits the synthesis of PCSK9
- Inclisiran lowers LDL cholesterol impressively and durably
- One subcutaneous administration of inclisiran at a 300 mg dose led to over a 50% reduction in LDL-C, and four inclisiran injections over 18 months led to sustained LDL-C lowering
- Inclisiran was safe and well tolerated with an adverse event profile similar to placebo

# What we still don't know...

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- What effect does inclisiran have on other lipid parameters?
  - HDL-C, triglycerides, Lp(a)
- Will inclisiran be safe and effective over longer term follow up?
- Are there any important inter-individual differences in inclisiran response?
- What will be the impact of infrequent dosing on patient adherence?

# What we still don't know...

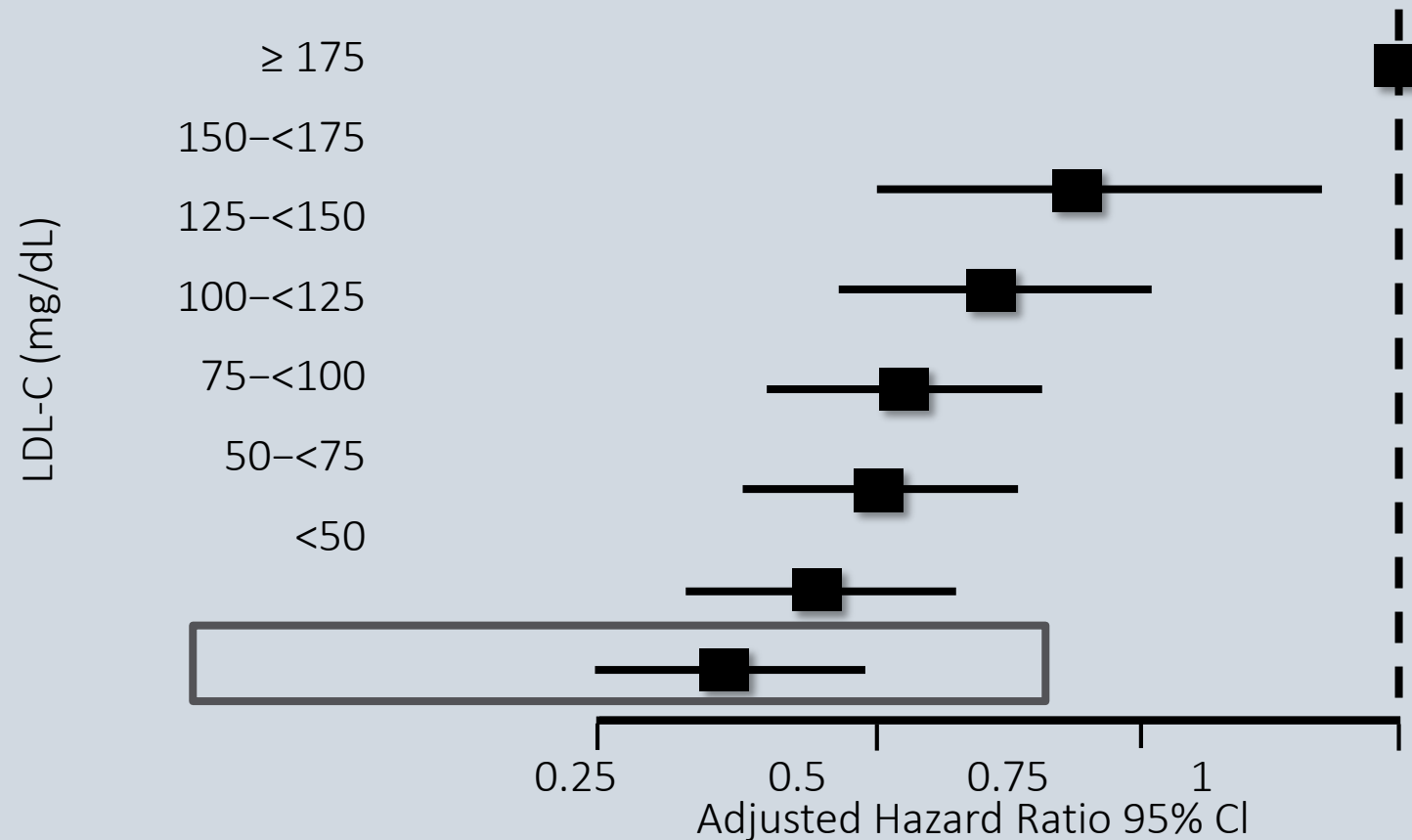
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- Will treatment with inclisiran lead to improved clinical outcomes?
  - above statin benefits
- How does LDL-C lowering with inclisiran compare to LDL-C lowering with statins in terms of clinical outcomes?

# Rationale for Pushing LDL-C Even Lower

Meta-analysis of 38,153 patients from 8 randomized statin trials

*LDL-C Levels  
and Risk of  
CV Events*



# Take home points

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- The effectiveness of statins and other cholesterol-lowering agents relies on patients taking them correctly and consistently
- Finding medications that are both effective and that can enhance patient adherence will improve outcomes
- Inclisiran is this first cholesterol-lowering agent in the siRNA class, opening up new and exciting possibilities
- Increasing the number of effective therapeutic options available will be good for our patients