ORION-10

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

KAROL E. WATSON, MD, PHD, FACC
PROFESSOR OF MEDICINE/CARDIOLOGY
DAVID GEFFEN SCHOOL OF MEDICINE AT UCLA
CO-DIRECTOR, UCLA PROGRAM IN PREVENTIVE CARDIOLOGY
What we learned from ORION-10

• 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...

• 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...

• 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**

LDL-C (mg/dL)

- ≥ 175
- 150−<175
- 125−<150
- 100−<125
- 75−<100
- 50−<75
- <50

Adjusted Hazard Ratio 95% CI
Take home points

• 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.