ORION-ll Long-term assessment of the efficacy and safety of inclisiran in patients with high risk of cardiovascular events

Ida Schram, MD, PhD, Minneapolis, MN

ORION-ll was a randomized, open-label extension trial of ORION-3/9/10/11 to assess the efficacy and safety of inclisiran when used over a long duration in patients with high risk of cardiovascular disease (ASCVD) who have elevated LDL-C levels despite taking maximum tolerated doses of statins or have ASCVD. The study was conducted as part of the ORION clinical trial program. ORION-ll is sponsored by Novartis.

Objectives of the study
- To assess the efficacy and safety of inclisiran in patients with high risk of cardiovascular disease (ASCVD) who have elevated LDL-C levels despite taking maximum tolerated doses of statins or have ASCVD.
- To extend the study duration from 2 years to up to 3 additional years after feeder studies.

What is inclisiran?
Inclisiran is a small interfering RNA (siRNA) that targets the gene encoding apolipoprotein B (apoB), which is involved in the production of very low density lipoprotein (VLDL). By reducing the production of apoB, inclisiran reduces the production of small, dense LDL particles, which are associated with an increased risk of cardiovascular events.

What was the inclusion criterion for patients?
- Patients with ASCVD or at increased risk of ASCVD were included in the study.

What were the key results?
- Inclisiran showed consistent LDL-C reduction of up to 52% over 4 years. When the level of LDL-C in the blood is high, it can accumulate in the artery walls creating what is known as atherosclerotic cardiovascular disease (ASCVD). When ASCVD occurs, it can lead to heart attacks, strokes, and other serious health issues.

What was the average age of participants at the beginning of the trial?
- The average age of participants at the beginning of the trial was 64.9 years.

Study design and population
The study was a randomized, open-label extension trial of ORION-3/9/10/11 to assess the efficacy and safety of inclisiran when used over a long duration in patients with high risk of cardiovascular disease (ASCVD) who have elevated LDL-C levels despite taking maximum tolerated doses of statins or have ASCVD. The study was conducted as part of the ORION clinical trial program. ORION-ll is sponsored by Novartis.

Why do the results matter?
- The results of ORION-ll further support the use of inclisiran as an additional therapy to reduce LDL-C and improve cardiovascular risk in patients with ASCVD.

Glossary
- **LDL-C**: Low-density lipoprotein cholesterol, which is a type of cholesterol that tends to stick to the walls of arteries, increasing the risk of heart attack and stroke.
- **ASCVD**: Atherosclerotic cardiovascular disease, a group of disorders that affects the heart and blood vessels.

Who sponsored this study?
Novartis Pharma AG, Basel, Switzerland sponsored both this study and the writing of this clinical summary.

References