

Olezarsen for Hypertriglyceridaemia in High-Risk Patients



Elevated levels of lipids in the bloodstream (hypertriglyceridaemia) increase the risk of heart attack, stroke, and acute pancreatitis. Current medications, such as statins, ezetimibe, fibrates, and prescription omega-3 fatty acids, typically lower triglyceride levels by varying degrees, ranging from below 10% to up to 40%. While these treatments are beneficial, they may not be sufficient to prevent cardiovascular events in all individuals.

The BRIDGE-TIMI 73aA was a placebo-controlled, double-blind trial conducted by researchers at Brigham and Women's Hospital, a founding member of the Mass General Brigham healthcare system. Findings from the trial suggest that an experimental therapy could further reduce triglycerides in the blood. The results were presented at the 2024 American College of Cardiology's Annual Scientific Session & Expo and simultaneously published in the New England Journal of Medicine.

The trial was conducted at 24 locations across the United States and Canada. One hundred fifty-four patients were included, with a median age of 62 years, comprising 42% women and 92% White individuals. These patients had either moderate hypertriglyceridaemia (HTG) ranging from 150 to less than 500 mg/dL, coupled with high cardiovascular risk, or severe HTG of 500 mg/dL or more. They were divided into groups receiving either 50 mg or 80 mg doses of olezarsen, or a placebo. Treatment involved subcutaneous injections every four weeks for a maximum of 49 weeks, alongside standard-of-care lipid treatment. At the outset, the median triglyceride level among participants stood at 241.5 mg/dL.

Olezarsen is an antisense oligonucleotide designed to inhibit APOC3, a gene associated with elevated triglyceride levels, by targeting its mRNA.

Results showed that olezarsen significantly reduced triglyceride levels by 49% at the 50mg dose and 53% at the 80mg dose compared to placebo. Additionally, the experimental drug lowered levels of apolipoprotein B and non-HDL cholesterol, both crucial factors in plaque formation, by 18 to 18.5% and 23% to 25%, respectively.

While larger and longer-term studies are necessary to fully evaluate the efficacy and safety of olezarsen in preventing heart attacks and strokes, these findings offer promising insights into potential new avenues for improving the cardiovascular health of individuals at high risk. According to corresponding author Brian Bergmark from the Division of Cardiovascular Medicine at Brigham and Women's Hospital, targeting APOC3 mRNA represents a promising novel approach for reducing triglyceride levels and potentially lowering the risk of heart attack and stroke.

Source: Brigham and Women's Hospital
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