Do you treat patients with unmanaged hypertriglyceridemia?

CORE a hypertriglyceridemia study

CORE$_2$ a hypertriglyceridemia study

Help advance research for patients suffering from severe hypertriglyceridemia (sHTG).

CORE and CORE$_2$ are now open for enrollment.[1,2]

What are the CORE trials?

Phase III, multicenter, double-blind, placebo-controlled studies evaluating the efficacy and safety of olezarsen administered subcutaneously for patients with sHTG (triglyceride [TG] levels ≥500 mg/dL).

What is the purpose of the CORE trials?

Determine the safety and efficacy of olezarsen in reducing TG levels in patients with **baseline TG levels ≥500 mg/dL.**[1,2]

What is goal of the CORE trials?

Bring patients a new **RNA-targeted therapy** that is **designed to reduce excessive TG levels** in the blood.

The urgency behind sHTG research

Hypertriglyceridemia (HTG) is a common condition, which is defined as having a high level (>150 mg/dL) of TGs, a type of fat, in the bloodstream.[3] There are >3 million adults in the United States with sHTG,[4] which is defined as having a TG level >500 mg/dL.[4,5]

Unmanaged sHTG is associated with a high risk for **atherosclerotic cardiovascular disease** and **acute pancreatitis**. sHTG can also complicate the management of **obesity**, **diabetes and insulin resistance**.[3,6]

An unmet need exists for effective and well-tolerated treatments for patients suffering from sHTG.[6]

What is olezarsen?

Olezarsen is an investigational ligand-conjugated antisense (LICA) medicine designed to inhibit the production of apolipoprotein C-III (apoC-III), a protein that regulates TG metabolism in the blood.[7]

What is an antisense medicine?

Antisense therapies, also known as antisense oligonucleotides, or ASOs, are designed to bind precisely with RNA, halting the process of creating a disease-causing protein.[8,9]

What is LICA technology?

LICA is a chemical technology developed by Ionis that involves the attachment of a molecule called a ligand that binds with receptors on the surfaces of cells in a highly specific manner.[9,10]

Olezarsen is an investigational drug that is not approved by the U.S. Food & Drug Administration.

Why are the CORE trials important?

Early-stage clinical studies support once-monthly administration of olezarsen to significantly reduce and sustain TG levels with a well-tolerated safety profile.[11] Further studies are needed to evaluate the safety and efficacy of olezarsen for this use.*

What would enrolling mean for patients? [1,2]

Participants will be randomized to receive olezarsen or placebo in a 53-week treatment period. The length of participation in the study will be ~74 weeks, including screening, treatment and post-treatment evaluation.

Any symptoms and experiences will be closely monitored and discussed with a study doctor throughout the trial.

There is no cost to participate. All study-related visits, tests, and study drug will be covered by the study sponsor.

What patients will qualify?

Patients may be eligible to participate in CORE or CORE$_2$ if they:[2]

- Are over 18 years old
- Are on lipid-lowering therapy that should adhere to standard-of-care per local guidelines
    - Have fasting TG levels ≥500 mg/dL despite ongoing use of standard-of-care lipid-lowering medications

Patients with glycated hemoglobin (HbA1C) levels ≥9.5% and/or estimated glomerular filtration rates (eGFRs) of <30 mL/min/m^2 at screening are not eligible and other inclusion and exclusion criteria will be evaluated before enrollment.

Help advance research for patients with elevated triglycerides and enroll eligible participants today!

Please contact us at ionisSHTGtrials@clinicaltrialmedia.com or call (844) 691-2147.

Where are the clinical trial locations?

The CORE trials are currently recruiting participants at over 60 locations globally. Visit **clinicaltrials.gov** for full study details (NCT05079919 and NCT05552326) and locations.

CORE
a hypertriglyceridemia study

CORE2
a hypertriglyceridemia study

References

1. ClinicalTrials.gov. A Study of Olezarsen Administered Subcutaneously to Participants With Severe Hypertriglyceridemia. ClinicalTrials.gov identifier: NCT05552326. Updated September 26, 2022. Accessed September 30, 2022. https://clinicaltrials.gov/ct2/show/NCT05552326
2. ClinicalTrials.gov. A Study of Olezarsen (ISIS 678354) Administered to Participants With Severe Hypertriglyceridemia. ClinicalTrials.gov identifier: NCT05079919. Updated June 30, 2022. Accessed July 26, 2022. https://clinicaltrials.gov/ct2/show/NCT05079919
3. Santos-Baez LS, Ginsberg HN. Hypertriglyceridemia-Causes, Significance, and Approaches to Therapy. *Front Endocrinol (Lausanne)*. 2020;11:6-16.
4. Christian JB, et al. Prevalence of severe (500 to 2,000 mg/dl) hypertriglyceridemia in United States adults. *Am J Cardiol*. 2011;107(6):891–897.
5. Grundy SM, et al. 2018 Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation 2019;139:e1082-143.
6. Laufs U, Parhofer KG, Ginsberg HN, et al. Clinical review on triglycerides. *Eur Heart J*. 2020;41(1):99-109c.
7. Tardif JC, Karwatowska-Prokopczuk E, et al. Apolipoprotein C-III reduction in subjects with moderate hypertriglyceridaemia and at high cardiovascular risk. *Eur Heart J*. 2022;43(14):1401-1412.
8. Moumné L, Marie A, Crouvezier N. Oligonucleotide Therapeutics: From Discovery and Development to Patentability. *Pharmaceutics*. 2022;14:260.
9. Crooke S. RNA-directed therapeutics at Ionis. *Nature*. October 16, 2019. Accessed July 28, 2022. https://www.nature.com/articles/d42473-019-00296-0
10. Ämmälä C, et al. Targeted delivery of antisense oligonucleotides to pancreatic b-cells. *Sci Adv*. 2018;4:eaat3386.
11. Alexander VJ, et al. N-acetyl galactosamine-conjugated antisense drug to APOC3 mRNA, triglycerides and atherogenic lipoprotein levels. *Eur Heart J*. 2019;40:2785–96

*Patients completed treatment with comparable rates of treatment discontinuation between the active and placebo groups. TEAEs were also balanced between groups.

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MED-US-OLZ-2300009

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This document is intended for healthcare providers only to support discussions with patients regarding enrollment. Direct distribution to patients is prohibited.