The NEW ENGLAND JOURNAL of MEDICINE

Olezarsen for Familial Chylomicronemia Syndrome

A PLAIN LANGUAGE SUMMARY

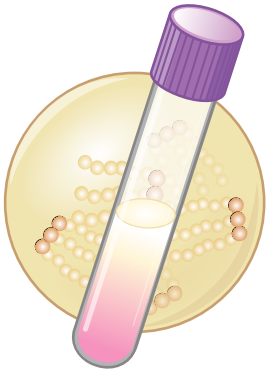
Based on the NEJM publication: Olezarsen, Acute Pancreatitis, and Familial Chylomicronemia Syndrome by E.S.G. Stroes et al. (published May 16, 2024)

In this trial, researchers assessed the efficacy and safety of olezarsen for lowering triglyceride levels in patients with familial chylomicronemia syndrome.

Familial chylomicronemia syndrome is a rare, inherited form of severe hypertriglyceridemia. Major complications include acute and recurrent episodes of pancreatitis.

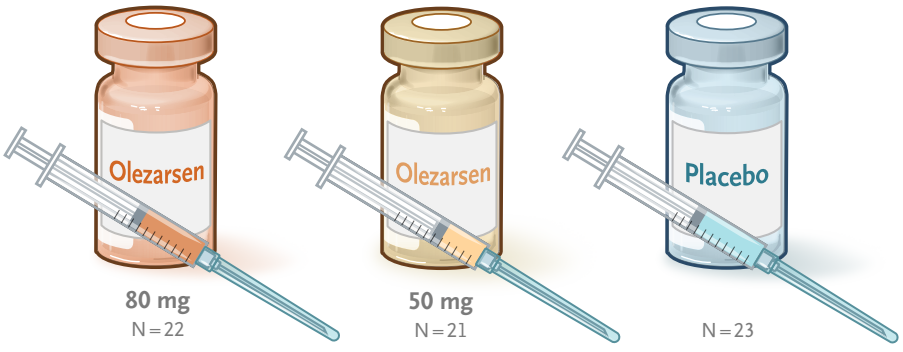
WHY WAS THE TRIAL DONE?

Patients with familial chylomicronemia syndrome have a minimal response to conventional triglyceride- and lipid-lowering therapies. Olezarsen is an investigational antisense oligonucleotide that has shown promise in reducing triglyceride levels.



HOW WAS THE TRIAL CONDUCTED?

66 patients were assigned to receive either olezarsen or placebo subcutaneously once every 4 weeks for 49 weeks. The primary end points were the differences between each olezarsen dose group and the placebo group in the percent change in the fasting triglyceride level at 6 months, assessed first in the 80-mg olezarsen group and then in the 50-mg olezarsen group.



PATIENTS

WHO	66 adults
	≥18 years of age
	Women: 58%; Men: 42%
CLINICAL STATUS	Fasting triglyceride level ≥880 mg/dl
	Genetically identified familial chylomicronemia syndrome

TRIAL DESIGN

- PHASE 3
- RANDOMIZED
- DOUBLE-BLIND
- PLACEBO-CONTROLLED
- LOCATION: 29 CENTERS IN 11 COUNTRIES

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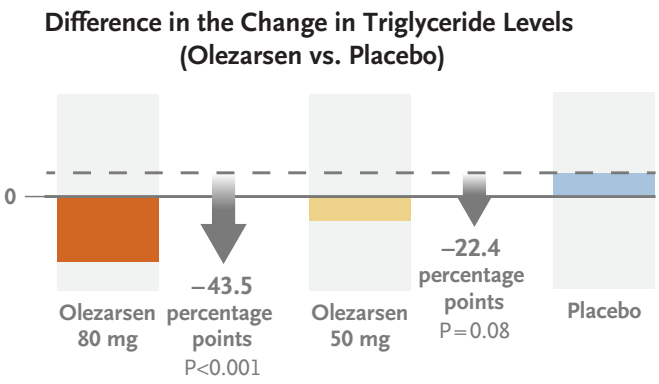
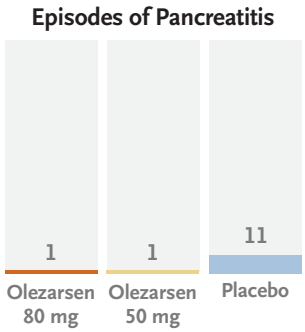
RESULTS

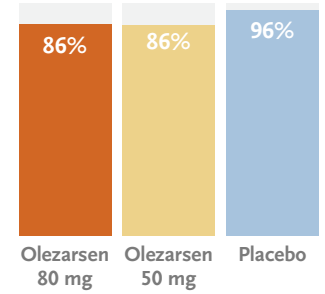
At 6 months, triglyceride levels were **reduced significantly** with 80 mg of olezarsen — but not with 50 mg of olezarsen — as compared with placebo.



One episode of acute pancreatitis (a secondary end point) occurred in each olezarsen group, and 11 episodes occurred in the placebo group.

Overall, **adverse events were less common with olezarsen than with placebo**. Adverse events of moderate severity that were considered related to olezarsen occurred in four patients in the 80-mg group.

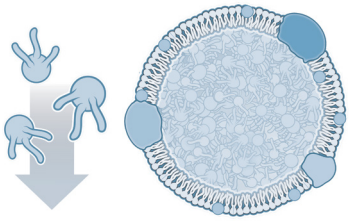




TRIGLYCERIDE CHANGES

Triglyceride levels decreased significantly with the higher dose of olezarsen.

80-mg dose decreased triglyceride levels



LIMITATIONS AND REMAINING QUESTIONS

- The number of trial patients was small.
- Patients were told to limit fat intake and avoid alcohol, but whether they followed this diet is uncertain.
- Most patients were White.

CONCLUSIONS

In adults with familial chylomicronemia syndrome, 80 mg of olezarsen given subcutaneously once every 4 weeks reduced fasting triglyceride levels at 6 months significantly more than placebo.

LINKS: FULL ARTICLE | NEJM QUICK TAKE

FURTHER INFORMATION

Trial registration: ClinicalTrials.gov number, NCT04568434

Funding: Ionis Pharmaceuticals

Full citation: Stroes ESG, Alexander VJ, Karwatowska-Prokopczuk E, et al. Olezarsen, Acute Pancreatitis, and Familial Chylomicronemia Syndrome. N Engl J Med 2024;390:1781-92. DOI: 10.1056/NEJMoa2400201.

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