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Abstract Editor: **Ken Milne, MD**

Cardiovascular risk reduction with icosapent ethyl for hypertriglyceridemia

Bhatt DL, Steg PG, Miller M, et al. New Engl J Med. 2019;380:11-22. doi: 10.1056/NEJMoa1812792..

SUMMARY

This trial looked at whether icosapent ethyl was superior to placebo for treating patients with high triglyceride levels.

- This was a multi-center, randomized, double-blind, placebo-controlled trial.
- Patients with existing cardiovascular disease or diabetes with other risk factors who were on a statin and had a fasting triglyceride level of 125-499 mg/dL (1.52 to 5.63 mmol/L) and a low-density lipoprotein (LDL) of 41-100 mg/dL (10.6-2.59 mmol/L) were included; 20 exclusions were listed in the supplemental index.
- Patients were randomized to icosapent ethyl 2 g BID or placebo
- Primary outcome was a composite of cardiovascular deaths, nonfatal myocardial infarction, nonfatal stroke, coronary revascularization, or unstable angina.
- N=8,179, median age of 64 years, more than two-thirds male, and 58% had type 2 diabetes. Participants were followed for almost 5 years and lived in the United States, Canada, Netherlands, Australia, New Zealand, and South Africa.
- Primary outcome result was 17.2% intervention group vs. 22.0% in the placebo group (hazard ratio, 0.75; 95% confidence interval [CI], 0.68 to 0.83; P < 0.001).
- More atrial fibrillation/flutter and serious bleeds in the treatment group compared with placebo (3.1% vs. 2.1%, *P* = 0.004) and (2.7% vs. 2.1%, *P* = 0.06) respectively.

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EDITOR'S COMMENTARY: This was an industry-sponsored trial. The sponsor had representation on the steering committee. They helped develop the protocol, interpret the data and were solely responsible for the collection and analysis of the data. This does not make the conclusions wrong but should make us more skeptical. The primary composite outcome was mainly driven by re-hospitalizations and revascularizations (not necessarily objective outcomes). Cardiovascular death (more objective) had a large 95% CI that almost crossed 1.0 (line of no difference). I also could not find any results for all-cause mortality, even when searching the supplemental index. There was an increase in harm, and we know that harm is systematically under-reported in randomized controlled trials (RCTs). The study also had a very narrow inclusion and extensive exclusion criteria. The cost of icosapent ethyl on GoodRx is about $240/month.

BOTTOM LINE: We cannot recommend the routine use of icosapent ethyl at this time.