Pure Omega-3 prescription drug markedly reduces first, repeat and total CV events

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Taking a high dose of icosapent ethyl—a pure and stable prescription form of the omega-3 fatty acid known as EPA—significantly reduces the occurrence of first, subsequent and total ischemic events, including heart attacks, strokes and related deaths, among people at high cardiovascular risk despite already being on statin therapy, according to research presented at the American College of Cardiology's 68th Annual Scientific Session.

Compared with placebo, icosapent ethyl cut the combined rate of first and subsequent cardiovascular deaths, nonfatal heart attacks or strokes, procedures for coronary artery disease such as stenting, or hospitalizations for unstable angina (the study's primary endpoint) by 30 percent, demonstrating the drug may be more protective than previously reported. Earlier analyses of the Reduction of Cardiovascular Events with Icosapent Ethyl-Intervention Trial (REDUCE-IT), which were primarily focused on the first occurrence of a major adverse cardiovascular event, found a 25 percent reduction. This latest analysis aimed to determine the extent to which the drug reduced the total burden of (first and subsequent) cardiovascular events.

"In looking at the totality of events—not just the first ones, but subsequent ones too—we see that the drug provides even greater reductions in ischemic events. By looking only at first events, we underestimate the true underlying treatment benefit offered," said Deepak L. Bhatt, MD, MPH, executive director of interventional cardiovascular programs at Brigham and Women's Hospital, professor of

medicine at Harvard Medical School and the study's lead author. "From a patient's perspective certainly, and from a physician's point of view, icosapent ethyl's impact on total events is what matters most."

Bhatt said that patients with high triglycerides who also have atherosclerosis or diabetes are especially vulnerable to repeat cardiovascular complications, so finding ways to prevent subsequent events is important and potentially lifesaving. Over a median follow-up period of approximately five years, there were nearly 3,000 events; 1,606 first events and 1,303 subsequent events, which included 762 second events, 272 third events and 269 fourth or more events. For patients taking icosapent ethyl, first events were reduced by 25 percent, second events by 32 percent, third events by 31 percent and fourth or more events were cut nearly in half (48 percent). The drug also prevented 1 in 5 cardiovascular-related deaths, as previously reported.

"With this drug, we are not only preventing that first heart attack but potentially the second stroke and maybe that third fatal event," Bhatt said. "Prevention of such subsequent cardiovascular events could improve patient outcomes and quality of life and may lower the total cost burden of medical care."

REDUCE-IT included 8,179 patients with elevated cardiovascular risk who were already being treated with statins. Patients with well-controlled LDL-cholesterol (>40 and ?100 mg/dL) and with elevated triglycerides (135 to 499 mg/dL) and other cardiovascular risk factors were enrolled at 473 sites in 11 countries between 2011 and 2016. About 70 percent of patients in the study had established cardiovascular disease and the rest had diabetes without known cardiovascular disease but with at least one additional cardiovascular risk factor. At baseline, median triglyceride levels were 216 mg/dL and median LDL-cholesterol was 75 mg/dL.

Patients were randomized in double-blinded fashion to receive either 2

grams icosapent ethyl twice daily or a placebo and were followed for a median of 4.9 years. The main outcomes were total (first and subsequent) primary composite endpoint events (cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, coronary revascularization or hospitalization for chest pain related to blockages) and total key secondary composite endpoint events (cardiovascular death, nonfatal myocardial infarction or nonfatal stroke). Follow-up visits were at four months, 12 months and annually thereafter.

The primary endpoint occurred in 17.2 percent of patients taking icosapent ethyl versus 22 percent of patients taking the placebo—an absolute risk reduction of 4.8 percent. For every 1,000 patients treated for five years with icosapent ethyl vs. placebo, about 159 events could be prevented, including 12 cardiovascular-related deaths, 42 heart attacks, 14 strokes, 76 coronary revascularizations and 16 hospitalizations for unstable angina.

"That's a striking impact not only for that individual, but also if we consider the public health implications and potentially cost-effective ways to lower risk, this could be an appealing strategy," Bhatt said. "We were surprised by how large an effect size there is and how much of an impact the drug is having on these patients over time, especially in the context of patients who are already well treated with background therapy."

Baseline use of antiplatelet therapy, ACE-inhibitors/ARBs, beta blockers, aspirin and statins were all very high in REDUCE-IT, which Bhatt said provides reassurance that icosapent ethyl is providing separate and incremental benefits. "These are not undertreated patients, but they are really well treated and still remain at high cardiovascular risk," he said, adding that this drug could potentially benefit tens of millions of patients worldwide.

Researchers also reported consistent cardiovascular benefits across subgroups of patients, including across a range of triglycerides levels, such as those with baseline or achieved triglycerides above or below 150 mg/dL, which is considered the threshold for normal by current guidelines. Bhatt said this suggests there are likely additional cardioprotective effects unique to icosapent ethyl besides triglyceride-lowering, including anti-inflammatory properties, anti-thrombotic mechanisms and cell membrane stabilization. As previously reported, the drug had a good safety profile albeit with an increased incidence of atrial fibrillation and numerically more patients with serious bleeding episodes; however, Bhatt said the overall rates were low. He reported there was no increase in the risk of stroke, the most serious complication of atrial fibrillation, but rather a statistically significant 28 percent reduction with icosapent ethyl versus placebo, as well as significant reductions in heart attacks, cardiac arrest and sudden cardiac death.

Icosapent ethyl (Vascepa) is currently approved by the U.S. Food and Drug Administration (FDA) for people with triglycerides above 500 mg/dL. Bhatt said the study drug is a prescription medicine and that the results do not apply to dietary supplement formulations, which are not approved or strictly regulated by the FDA. The high dose of EPA, which in studies appears to be more cardiovascular protective than DHA, is comparable to what one would get after eating over 20 servings of fish a week but without the related saturated fat and other components of fish, he said.

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Provided by American College of Cardiology