REDUCE-IT Topline: A Tectonic Paradigm Shift in Atheroprevention!

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REDUCE-IT was a cardiovascular outcomes trial (CVOT) of patients with a baseline TG 150-499 mg/dL (median 216) and an LDL-C 41-100 mg/dL (median 75) while taking statin monotherapy. Among 8,179 participants, 70% had had a prior ASCVD event, and 30% had diabetes with at least one other major ASCVD risk factor. They received either added icosapent ethyl (IPE or pure EPA, brand name Vascepa) or placebo, 2g twice daily with food. After 4.9 years median follow-up, occurrence of its 5-point MACE (nonfatal myocardial infarction, nonfatal stroke, cardiovascular death, coronary revascularization or unstable angina requiring hospitalization) composite primary endpoint was reduced by about 25% ($p < 0.001$). This finding was supported by robust demonstrations of efficacy across several secondary endpoints. Safety and tolerability were consistent with FDA-approved labeling for IPE and other omega-3 fatty acids.

REDUCE-IT is a paradigm shift in atheroprevention in many ways.

1. It is the first CVOT to study patients selected for hypertriglyceridemia,
2. It is the first CVOT to test the full-dose of any prescription omega-3 agent.
3. It is the first CVOT to show benefit with any “TG-lowering agent” on top of standard-of-care statin therapy
4. It shows the greatest reduction in cardiovascular events among the 7 contemporary CVOTs which have shown event reductions with any agent added to background statin therapy (in all subjects).
5. It is the only CVOT to confirm event reduction seen with the same agent in a prior CVOT.

REDUCE-It is a “grand-slam homerun”, likely to change the clinical paradigm for treating patients at high risk of ASCVD with mild to moderate hypertriglyceridemia. REDUCE-IT confirms the safety and cardiovascular event reduction of IPE, shown in a prior large cardiovascular outcomes trial (JELIS). Interestingly REDUCE-IT and JELIS, have shown the largest ASCVD relative risk reduction (25% and 19% respectively), far greater than the other 5 recent positive CVOTs of statin adjunct therapy (IMPROVE-IT, FOURIER, CANTOS, REVEAL and ODYSSEY Outcomes, which showed much smaller 6-15% reductions in events). Thus, IPE appears to beat ezetimibe, evolocumab, canakinumab, anacetrapib and alirocumab handily in cardiovascular event reduction on top of statin therapy (although these comparisons are all indirect and only approximate due to differences in study population and design).