Can Plaque Evaporate with Icosapent and Does it Matter?

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Disclosures

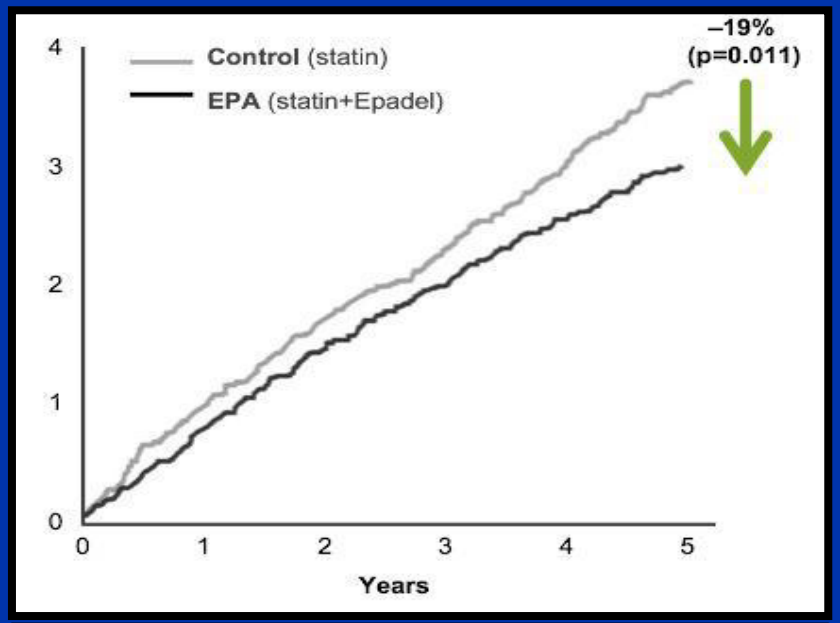
- Research support: AstraZeneca, Amgen, Anthera, Eli Lilly, Esperion, Novartis, Cerenis, The Medicines Company, Resverlogix, InfraReDx, Roche, Sanofi-Regeneron and LipoScience

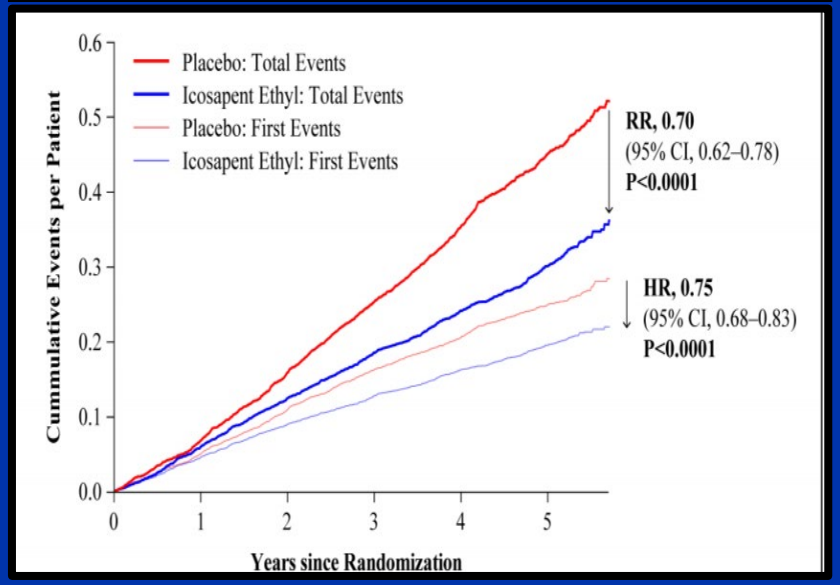
- Consulting and honoraria: AstraZeneca, Akcea, Eli Lilly, Anthera, Omthera, Merck, Takeda, Resverlogix, Sanofi-Regeneron, CSL Behring, Esperion, Boehringer Ingelheim

- Principal investigator of an ongoing trial of Epanova

Despair and Hope of Omega-3 Fatty Acids

- Population studies: dietary fish oil may protect against CVD
- GISSI: CV benefit with OM-3 FA
- Subsequent studies: no benefit
- Meta-analyses: no benefit
- VITAL and ASCEND: no benefit





Yokoyama M, et al. *Lancet.* 2007;370:215; Bhatt *N Engl J Med* 2018; Bhatt *J Amer Coll Cardiol* 2019

Why Did JELIS and REDUCE-IT Demonstrate CV Benefit?

- Right patients?
  - high CV risk, high TG levels
- Right dose?
  - Substantial elevation of tissue EPA levels
- Right omega-3 fatty acid?
  - Both involved purified EPA

How Does EPA Reduce CV Events?

- EPA has favorable effects on multiple CV factors
  - TG rich lipoproteins
  - Inflammation
  - Oxidative stress
  - Thrombosis
  - Arrhythmia
- Event curve separation in timeline consistent with an anti-atherosclerotic effect
- No clear evidence to suggest the benefit is due to lowering of TG rich lipoproteins

EVAPORATE

- 80 statin-treated patients with obstructive disease on CTCA and modest hypertriglyceridemia
- 84% underwent interim CTCA imaging at 9 months
- Observed differences in plaque parameters at baseline, although low statistical power
- No difference in the prespecified primary endpoint, change in low attenuated plaque volume
- Differences in the change in a number of additional CTCA derived plaque measures
- Similar progression with placebo in other studies

How Should We Interpret EVAPORATE?

- Icosapent failed to significantly modify the primary endpoint: change in low attenuated plaque
- Beneficial effects were observed on a number of secondary endpoints, which one is right?
- No adverse effect was observed with the mineral oil placebo when compared with historical controls
- Do the results reflect the intervention or the imaging?

How Should We Interpret EVAPORATE?

- This was a small study, performed at 2 sites, in a time period that may be too short to demonstrate an effect
- The effect on total plaque volume is promising
- It will be critical to insure maximal retention of patients on study drug until final imaging
- All plaque features progressed, emphasizing the importance of high TG levels and progressive CV risk

Next Steps?

- Will alternative high dose omega-3 fatty acid preparations have CV benefit?
- Will other patient groups derive benefit from administration of high dose EPA?
- Will imaging guide use of omega-3 fatty acids in clinical practice?
- More clinical trials will be required!