Can Plaque Evaporate with Icosapent and Does it Matter?

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Disclosures

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• 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

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!