

**Icosapent Ethyl (eicosapentaenoic acid ethyl ester): Effects on Apolipoprotein C-III in Patients from the MARINE and ANCHOR Studies**

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**Background/Synopsis:** Apolipoprotein C-III (ApoC-III) is a small protein that resides on various lipoproteins, inhibits lipoprotein/hepatic lipases, impairs hepatic uptake of triglyceride (TG)-rich lipoproteins (such as lipoprotein remnants), and generally promotes hypertriglyceridemia. Its increased activity may also contribute to insulin resistance and atherosclerosis. Prior reports of the omega-3 fatty acid eicosapentaenoic acid (EPA) alone or in combination with the omega-3 fatty acid docosahexaenoic acid have suggested inconsistent effects on ApoC-III levels. Icosapent ethyl (IPE) is a high-purity prescription form of EPA ethyl ester approved to reduce TG levels in patients with severe hypertriglyceridemia (TG ≥500 mg/dL).

**Objective/Purpose:** To evaluate the effects of IPE on ApoC-III levels in patients from the MARINE and ANCHOR studies.

**Methods:** MARINE and ANCHOR were 12-week, phase 3, double-blind studies that randomized patients to IPE 4 g/day, 2 g/day, or placebo. MARINE randomized 229 patients with TG ≥500 and ≤2000 mg/dL while ANCHOR

randomized 702 patients at high risk for cardiovascular disease with TG ≥200 and <500 mg/dL despite low-density lipoprotein cholesterol (LDL-C) control while on statin therapy. This analysis assessed the median percent change from baseline to study end in ApoC-III levels compared with placebo.

**Results:** Total ApoC-III levels were assessed in 148 and 612 patients in MARINE and ANCHOR, respectively. In MARINE, IPE 4 g/day and 2 g/day statistically significantly reduced ApoC-III levels by 25.1% (p<0.0001) and 14.3% (p=0.0154) vs placebo, respectively. In ANCHOR, IPE 4 g/day and 2 g/day statistically significantly reduced ApoC-III levels by 19.2% (p<0.0001) and 8.5% (p=0.0008) vs placebo, respectively.

**Conclusion:** Compared to placebo, IPE significantly reduced ApoC-III levels in patients in the MARINE (TG ≥500 and ≤2000 mg/dL) and ANCHOR (TG ≥200 and <500 mg/dL) studies, in which IPE also significantly lowered TG and apolipoprotein B without increasing LDL-C.

**Table** ApoC-III levels in patients from the MARINE and ANCHOR Studies (IPE 4 g/day and placebo groups only)

ApoC-III	Median Baseline Value, mg/dL (IQR)	Median Final Value, mg/dL (IQR)	Median Change from Baseline, % (IQR)	Median Change from Baseline vs Placebo, % (p value)
MARINE IPE 4 g/day n=53	25.6 (11.6)	19.7 (10.5)	-10.1 (27.1)	-25.1 (<0.0001)
MARINE Placebo n=46	26.8 (17.3)	32.7 (14.6)	12.3 (41.5)	—
ANCHOR IPE 4 g/day n=208	15.2 (4.76)	13.7 (4.80)	-9.4 (25.9)	-19.2 (<0.0001)
ANCHOR Placebo n=201	14.8 (4.48)	16.2 (5.57)	10.9 (30.0)	—

ApoC-III = apolipoprotein C-III; IPE = icosapent ethyl; IQR = interquartile range.