Icosapent Ethyl (Eicosapentaenoic Acid Ethyl Ester) in Women With Very High Triglyceride Levels: Results From the MARINE Study

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ABSTRACT

METHODS

The MARINE study was a phase 3, multicenter, double-blind, placebo-controlled, 12-week trial that randomized adult patients with triglyceride (TG) levels ≥500 and ≤2000 mg/dL to either placebo or icosapent ethyl 4 g/day (n = 229). Placebo was matched in all respects to icosapent ethyl and was matched to baseline TG levels. The primary analysis was based on intention to treat and included all randomized patients. This post-hoc analysis showed that icosapent ethyl 4 g/day significantly reduced TG, non-HDL-C, and TC levels without increasing LDL-C levels versus placebo among women in MARINE. The effect of icosapent ethyl on the risk of CV mortality and cardiovascular events was not determined in this study.

RESULTS

Appropriate patient populations for efficacy analyses were the subset of women from MARINE for TG and non-HDL-C in the subgroup of women from MARINE. The significance of lowering TG levels with icosapent ethyl 4 g/day was evaluated using LSCC in women from MARINE compared with placebo. Significant increases were documented in both placebo and RBC EPA concentrations in the placebo treatment group. The analysis was conducted non-parametrically in the median difference in percent change from baseline to week 12 in lipids, lipoproteins, RBC EPA concentrations, and lipoprotein-related inflammatory markers in women with TG levels ≥500 and ≤2000 mg/dL. The analysis was based on intention to treat and included all randomized women. The analysis was conducted non-parametrically in the median difference in percent change from baseline to week 12 in lipids, lipoproteins, RBC EPA concentrations, and lipoprotein-related inflammatory markers in women with TG levels ≥500 and ≤2000 mg/dL. The analysis was based on intention to treat and included all randomized women. The analysis was conducted non-parametrically in the median difference in percent change from baseline to week 12 in lipids, lipoproteins, RBC EPA concentrations, and lipoprotein-related inflammatory markers in women with TG levels ≥500 and ≤2000 mg/dL. The analysis was based on intention to treat and included all randomized women. The analysis was conducted non-parametrically in the median difference in percent change from baseline to week 12 in lipids, lipoproteins, RBC EPA concentrations, and lipoprotein-related inflammatory markers in women with TG levels ≥500 and ≤2000 mg/dL. The analysis was based on intention to treat and included all randomized women. The analysis was conducted non-parametrically in the median difference in percent change from baseline to week 12 in lipids, lipoproteins, RBC EPA concentrations, and lipoprotein-related inflammatory markers in women with TG levels ≥500 and ≤2000 mg/dL. The analysis was based on intention to treat and included all randomized women.

Objective

The objective of this analysis was to evaluate the efficacy of icosapent ethyl 4 g/day on TG levels, other atherogenic parameters, and EPA concentrations in the subgroup of women who participated in MARINE.

BACKGROUND

There are limited data on the treatment of women with severe hypertriglyceridemia; nonetheless, elevated TG levels have been shown to be a stronger predictor of CV disease in women than in men. Icosapent ethyl, a high-purity prescription formulation of EPA ethyl ester, was chosen to have beneficial effects on TG and other atherogenic parameters of the TG-rich plasma-rich moiety (TMRM) that was not consistent in LDL-C observed with other TG-lowering agents among patients with very high TG levels.

Objectives/Purpose

To evaluate the efficacy of icosapent ethyl 4 g/day in reducing TG and other atherogenic parameters and EPA concentrations in the subgroup of women who participated in MARINE.

METHODS

The overall MARINE study was a phase 3, multicenter, double-blind, placebo-controlled, 12-week trial that randomized adult patients with TG levels ≥500 and ≤2000 mg/dL to receive either icosapent ethyl 4 g/day or matching placebo (n = 229). Placebo was matched in all respects to icosapent ethyl and was matched to baseline TG levels. The primary analysis was based on intention to treat and included all randomized patients. This post-hoc analysis showed that icosapent ethyl 4 g/day significantly reduced TG, non-HDL-C, and TC levels without increasing LDL-C levels versus placebo among women in MARINE. The effect of icosapent ethyl on the risk of CV mortality and cardiovascular events was not determined in this study.

RESULTS

Appropriate patient populations for efficacy analyses were the subset of women from MARINE for TG and non-HDL-C in the subgroup of women from MARINE. The significance of lowering TG levels with icosapent ethyl 4 g/day was evaluated using LSCC in women from MARINE compared with placebo. Significant increases were documented in both placebo and RBC EPA concentrations in the placebo treatment group. The analysis was conducted non-parametrically in the median difference in percent change from baseline to week 12 in lipids, lipoproteins, RBC EPA concentrations, and lipoprotein-related inflammatory markers in women with TG levels ≥500 and ≤2000 mg/dL. The analysis was based on intention to treat and included all randomized women. The analysis was conducted non-parametrically in the median difference in percent change from baseline to week 12 in lipids, lipoproteins, RBC EPA concentrations, and lipoprotein-related inflammatory markers in women with TG levels ≥500 and ≤2000 mg/dL. The analysis was based on intention to treat and included all randomized women. The analysis was conducted non-parametrically in the median difference in percent change from baseline to week 12 in lipids, lipoproteins, RBC EPA concentrations, and lipoprotein-related inflammatory markers in women with TG levels ≥500 and ≤2000 mg/dL.

CONCLUSIONS

Icosapent ethyl 4 g/day significantly reduced TG, non-HDL-C, and TC levels without increasing LDL-C levels versus placebo among women in MARINE. The effect of lowering TG levels with icosapent ethyl 4 g/day was considered to be consistent with the overall MARINE result.

LIMITATIONS/SIGNIFICANCE

The primary analysis was powered to detect the benefit of lowering TG levels in women. MARINE was not powered to determine the potential benefit of lowering TG levels in women.

The primary analysis was preplanned by gender; however, only the analysis of TG levels in women was preplanned. All other subgroup analyses were preplanned for men and women separately.

The analysis was not powered to determine the benefits of reducing TG levels among women in the REDUCE-IT study (NCT01492361) (icosapent ethyl 4 g/day vs. placebo) in men and women with more modestly elevated TG levels. This analysis was conducted using data from the subgroup of women in the REDUCE-IT study. This subgroup analysis was not preplanned.

The analysis was conducted non-parametrically and is not powered to detect the potential implications of this post-hoc analysis on the risk of CV mortality and cardiovascular events among women in MARINE.

CONCLUSIONS

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The analysis was conducted non-parametrically and is not powered to detect the potential implications of this post-hoc analysis on the risk of CV mortality and cardiovascular events among women in MARINE.

REFERENCE

1. Mosca L, Bays HE, Philip S, et al. Icosapent Ethyl 4 g/day Versus Placebo Among Women With Very High Triglyceride Levels: Results From the MARINE Study. Presented at the Annual Scientific Session of the National Lipid Association; May 19–20, 2016, New Orleans, Louisiana

AUTHOR DISCLOSURES

No disclosure information is available.

ABBREVIATIONS

CV=cardiovascular; HR=heart rate; LDL-C=low-density lipoprotein cholesterol; MARINE=Monkeys, Atherosclerosis, Reducing Inflammation with Eicosapentaenoic Acid; NLA=National Lipid Association; RBC=red blood cell; REDUCE-IT=Reduction of Cardiovascular Events with EPA-Intervention; RLP-C=remnant-like particle cholesterol; TG=triglyceride; U.S. FDA=US Food and Drug Administration; USCI=US Cardiovascular Institute

ADDITIONAL INFORMATION

This study was sponsored by Amarin Pharma Inc., Bedminster, NJ, USA. Assistance with poster preparation was provided by Peloton Advantage, LLC, Parsippany, NJ, USA, and funded by Amarin Pharma Inc.

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