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Original Contribution

Effects of MAT9001 containing eicosapentaenoic acid and docosapentaenoic acid, compared to eicosapentaenoic acid ethyl esters, on triglycerides, lipoprotein cholesterol, and related variables

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BACKGROUND: Long-chain omega-3 fatty acid concentrate pharmaceuticals are used in the United States for treatment of severe hypertriglyceridemia (≥500 mg/dL) and are under investigation as adjuncts to statins for lowering cardiovascular risk in patients with high triglycerides (TGs; 200–499 mg/dL).

OBJECTIVE: To evaluate MAT9001, an investigational prescription-only omega-3 fatty acid agent containing predominantly eicosapentaenoic acid (EPA) and docosapentaenoic acid, in 42 men and women with fasting TG 200 to 400 mg/dL.

METHODS: In this open-label, crossover trial, subjects received MAT9001 and EPA ethyl esters (EPA-EE) in random order. They were housed in a clinical research unit for 2 14-day treatment periods, separated by a ≥35-day washout. Lipoprotein lipids, apolipoproteins (Apos) and proprotein convertase subtilisin kexin type 9 levels were measured before and at the end of each treatment period.

RESULTS: MAT9001, compared with EPA-EE, resulted in significantly ($P < .05$) larger reductions from pretreatment levels for TG (−33.2% vs −10.5%), total cholesterol (−9.0% vs −6.2%), non–high-density lipoprotein cholesterol (−8.8% vs −4.6%), very low–density lipoprotein cholesterol (−32.5% vs −8.1%), Apo C3 (−25.5% vs −5.0%), and proprotein convertase subtilisin kexin type 9 (−12.3% vs +8.8%). MAT9001 also produced a significantly ($P = .003$) larger reduction in Apo A1 (−15.3% vs −10.2%), but responses for high-density lipoprotein cholesterol (−11.3% vs −11.1%), low-density lipoprotein cholesterol (−2.4% vs −4.3%), and Apo B (−3.8% vs −0.7%), respectively, were not significantly different relative to EPA-EE.

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CONCLUSIONS: MAT9001 produced significantly larger reductions than EPA-EE in several lipoprotein-related variables that would be expected to favorably alter cardiovascular disease risk in men and women with hypertriglyceridemia.

Introduction

Fasting and postprandial hypertriglyceridemia are associated with increased risk for cardiovascular disease and, when severe, pancreatitis.[1–5] Long-chain omega-3 fatty acid intake has been shown to lower triglyceride (TG) levels.[6–8] Currently in the United States, prescription forms of eicosapentaenoic acid (EPA) and EPA plus docosahexaenoic acid (DHA) concentrates have approved indications for the treatment of very high TG (≥500 mg/dL) to reduce the risk of pancreatitis. Although all lower TG levels, results from prior studies suggest that products with varying proportions and different chemical forms of these omega-3 fatty acids have differential effects on coronary artery disease and lipid responses.[9–14] This is likely due, at least in part, to the bioavailability of the omega-3 fatty acids in these products, for example, acid ethyl esters vs carboxylic acid forms.[11,15–17] In addition, some products, particularly those containing DHA, appear to raise low-density lipoprotein cholesterol (LDL-C) levels, whereas products with EPA alone do not.[9,10]

MAT9001 (Matinas BioPharma Holdings, Inc) is an omega-3 fatty acid formulation comprised of EPA and another long-chain omega-3 fatty acid with 5 double bonds, docosapentaenoic acid (DPA) but only trace amounts of DHA. In contrast to EPA and DHA, little is known about the effects of DPA on lipid levels in humans. In this clinical trial, MAT9001 was compared with icosapent ethyl, the ethyl ester of EPA (EPA-EE; Vascepa), a lipid-lowering agent approved by the Food and Drug Administration for use in adults with severe hypertriglyceridemia. The effects of MAT9001 and EPA-EE on lipoprotein lipids, apolipoproteins (Apos), and proprotein convertase subtilisin kexin type 9 (PCSK9) were evaluated and compared in men and women with hypertriglyceridemia while free of other lipid-altering drug therapy or while on stable-dose statin monotherapy.

Methods

Study design and treatments

This was a randomized, open-label, crossover trial with 2 14-day treatment periods, separated by at least a 35-day washout period (Fig. 1). Each treatment period had its own baseline. A sample of 42 subjects (31 men and 11 women) was randomized to 2 treatment sequences with 4 g/d MAT9001 or EPA-EE first, and crossover to the opposite treatment for the second period. MAT9001 is a long-chain omega-3 free fatty acid concentrate in a delayed release 1 g capsule, containing a proprietary and patented mixture of EPA and DPA predominantly, with trace levels of DHA and certain other omega-3 fatty acids (Matinas BioPharma, Inc, Bedminster, NJ).[18] The EPA-EE comparator was formulated and administered as 1 g capsules (Vascepa, icosapent ethyl, Amarin Pharma, Inc, Bedminster, NJ).[19] Four 1-g capsules were administered once daily, 30 minutes after consumption of a standard low-fat breakfast meal, along with 240 mL of water. The breakfast consisted of corn flakes, skim milk, honeydew melon, raisins, and toast, and provided 502 kcal (4% of energy from fat, 82% from carbohydrates, and 14% from protein).

Subjects were housed in a clinical research unit (Pharma Medica Research, Inc, Mississauga, Ontario, Canada) for the duration of each treatment period. Treatment compliance was ensured by the presence of study staff during study drug

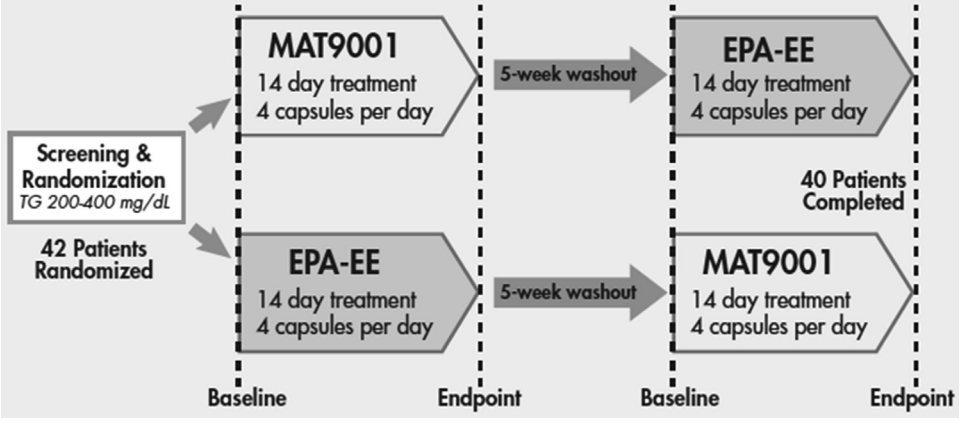

Figure 1 Study flow diagram. EPA-EE, eicosapentaenoic acid ethyl esters; TG, triglycerides.