Table 2 Multivariate analysis

Age, years	$P < .001$	OR 1.2 (95% CI 1.14−1.26)
Active smoking	$P < .003$	OR 3.81 (95% CI 1.58−9.17)
NAFLD	$P < .022$	OR 2.94 (95% CI 1.17−7.41)
Severe NAFLD	$P < .024$	OR 5.27 (95% CI 1.24−22)

CI, confidence interval; NAFLD, nonalcoholic fatty liver disease; OR, odds ratio.

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AMR101, a Pure-EPA Omega-3 Fatty Acid, Lowers Triglycerides in Patients with Very High Triglycerides Without Raising LDL-C: The MARINE Study

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Synopsis: AMR101 is a >96% pure ethyl eicosapentaenoic acid (EPA) investigational agent that contains no docosahexaenoic acid (DHA). Previous studies in patients with very high triglycerides (TG) treated with either omega 3 fatty acids (OM-3) containing EPA and DHA or fibrates demonstrated significant TG lowering along with substantial LDL-C elevation.

Purpose: MARINE was a phase 3, multicenter, placebo-controlled, randomized, double-blind, 12-week study that evaluated the efficacy and safety of AMR101 in patients with very high TG.

Methods: A total of 229 patients with fasting TG ≥500 and ≤2000 mg/dL on stable diets with or without statin therapy were randomized with placebo, AMR101 2 g/day or AMR101 4 g/day. The primary end point was the median percent change in TG from baseline compared with placebo at 12 weeks.

Results: Median baseline TG levels were 703, 680, and 657 mg/dL for placebo, AMR101 4 g/day, and 2 g/day. Placebo-corrected median TG levels were reduced 33% ($P < .0001$) with AMR101 4 g and 20% ($P = .0051$) with AMR101 2 g. In patients with baseline TG >750 mg/dL (39%), AMR101 reduced median placebo-corrected TG levels by 45% (4 g; $P = .0001$) and by 33% (2 g; $P = .0016$). AMR101 reduced TG levels in both statin-treated patients (25% of patients) and nonstatin-treated patients versus placebo, with greater median reductions in statin-treated patients. AMR101 did not significantly increase placebo-corrected median LDL-C levels at 4 g (−2.3%) or 2 g (+5.2%) (both P = NS). AMR101 also significantly reduced placebo-corrected median non-HDL-C levels by 18% (4 g; $P < .0001$) and 8% (2 g; $P < .05$) and significantly reduced ApoB, lipoprotein-associated phospholipase A2 very–LDL-C TG, and total cholesterol. AMR101 was generally well tolerated, with a safety profile similar to placebo.

Conclusions: In the largest OM-3 trial conducted in patients with very high TG, AMR101, a novel pure-EPA OM-3 therapy (at 4 g and 2 g/day) significantly reduced placebo-corrected median TG levels and significantly improved other lipid parameters. In contrast to previous studies of OM-3 and fibrate treatments in patients with very high TG levels, AMR101 is the first TG-lowering therapy to demonstrate reduced TG without significant increases in LDL-C.

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Dissociation of Apolipoprotein B, Low-Density Lipoprotein Cholesterol, and Non-High-Density Lipoprotein Cholesterol Targets in Patients Receiving Lipid

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Synopsis: Treatment guidelines for hypercholesterolemic patients identify low-density lipoprotein cholesterol (LDL-C) as the primary treatment target with non-high-density lipoprotein cholesterol (non-HDL-C) and apolipoprotein (apo) B as secondary targets of therapy.

Purpose: To determine the extent to which statin monotherapy lowers LDL-C and non-HDL-C more than ApoB, and thus to gauge residual coronary risk caused by elevated levels of ApoB-containing particles in the circulation.

Methods: This post-hoc analysis evaluated the relationships between ApoB:LDL-C and ApoB:non-HDL-C using a pooled data set of 27 randomized, double-blind, active- or placebo-controlled clinical trials conducted in 21794 adult hypercholesterolemic patients receiving treatment with ezetimibe/statin (EZE/statin) or statin alone, administered as either first- (ie, in patients washed off of lipid-modifying drugs at baseline) or second-line therapy (ie, in patients treated with statin monotherapy at baseline), for up to 4 to 24 weeks. Simple linear regression analyses were employed to calculate LDL-C and non-HDL-C levels corresponding to ApoB values of 90 mg/dL at baseline (i.e., in drug-naive or statin-treated patients) and following treatment with EZE/statin or statin alone.

Results: At baseline in the first line therapy group, ApoB = 90 mg/dL corresponded to LDL-C and non-HDL-C values that were close to the usual LDL-C and non-HDL-C goals for high-risk patients (ie, 100 and 130 mg/dL, respectively). At baseline in the second line therapy group and following treatment with EZE/Statin or statin alone in both the first and second line therapy groups, the LDL-C and non-HDL-C values corresponding to ApoB = 90 mg/dL were closer to the very high risk LDL-C and non-HDL-C goals (ie, 70 and 100 mg/dL, respectively).

Conclusions: Compared with drug-naive patients, more aggressive LDL-C and non-HDL-C targets should be achieved in patients receiving lipid-lowering therapy to normalize the concentration of ApoB-containing lipoproteins. ApoB provides a more rigorous goal than does LDL-C or non-HDL-C for monitoring efficacy of LDL-lowering therapy.