Supplementary Online Content

Banach M, Duell PB, Gotto AM Jr, et al. Association of bempedoic acid administration with atherogenic lipid levels in phase 3 randomized clinical trials of patients with hypercholesterolemia. *JAMA Cardiol*. Published online July 1, 2020. doi:10.1001/jamacardio.2020.2314

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Randomized, Double-blind, Parallel-Group, Placebo-Controlled, Multicenter, Phase 3 Studies Included in the Pooled Analysis of Bempedoic Acid Efficacy

Study	Duration	Population	Results at 12 Weeks
CLEAR Wisdom[1]	52 weeks	Patients with ASCVD and/or HeFH and LDL-C ≥ 70 mg/dL while receiving maximally tolerated statin (with or without other LLT)	Bempedoic acid added to maximally tolerated statin (with or without other LLT) reduced LDL-C by 17.4% (95% CI, –21.0, –13.9) more than placebo (*P* < .001)
CLEAR Harmony[2]	52 weeks		Bempedoic acid added to different intensities of background statin treatment (low, moderate, or high) with or without additional LLT reduced LDL-C from baseline (difference vs placebo, –18.1% [95% CI, –20.0%, –16.1%]; *P* < .001)
CLEAR Tranquility[3]	12 weeks	Patients with hypercholesterolemia and a history of statin intolerance who required additional LDL-C lowering	Bempedoic acid added to stable LLT, including ezetimibe, reduces LDL-C up to 28.5% (95% CI, –34.4, –22.5) more than placebo (*P* < .001)
CLEAR Serenity[4]	24 weeks		Treatment with bempedoic acid reduced LDL-C 21.4% (95% CI, –25.1, –17.7) more than placebo (*P* < .001)

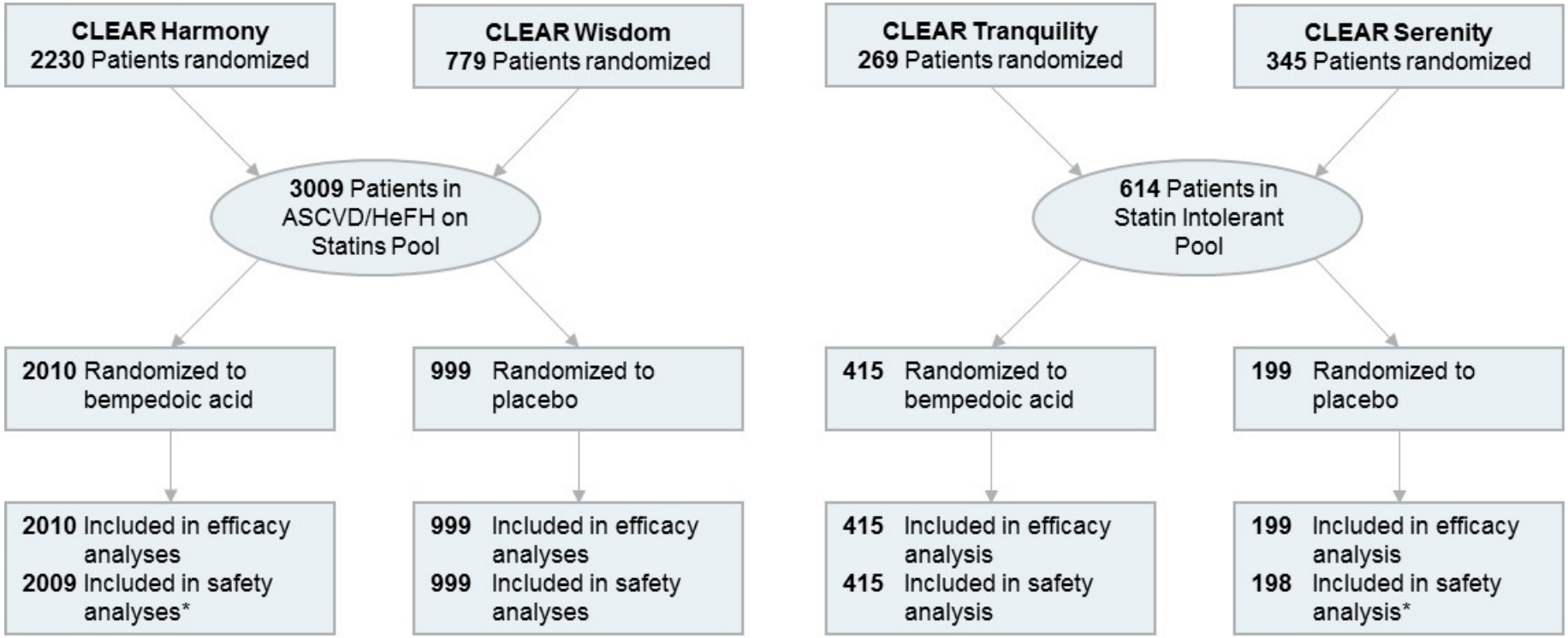
Abbreviations: ASCVD, atherosclerotic cardiovascular disease; CI, confidence interval; HeFH, heterozygous familial hypercholesterolemia; LDL-C, low-density lipoprotein cholesterol; and LLT, lipid lowering therapy.

eTable 2. Baseline Statin Intensity Categories (Daily Dose)

Study	High Intensity	Moderate Intensity	Low Intensity[a]
CLEAR Wisdom[1] and CLEAR Harmony[2]	Atorvastatin (40–80 mg) Rosuvastatin (20–40 mg)	Atorvastatin (10–20 mg) Rosuvastatin (5–10 mg) Simvastatin (20–40 mg) Pravastatin (40–80 mg) Lovastatin (40 mg) Fluvastatin XL (80 mg) Fluvastatin (40 mg BID) Pitavastatin (2–4 mg)	Simvastatin (10 mg) Pravastatin (10–20 mg) Lovastatin (20 mg) Fluvastatin (20–40 mg) Pitavastatin (1 mg)
	Very Low Dose	**Low Dose**	
CLEAR Tranquility[3] and CLEAR Serenity[4]	Rosuvastatin (< 5 mg) Atorvastatin (< 10 mg) Simvastatin (< 10 mg) Lovastatin (< 20 mg) Pravastatin (< 40 mg) Fluvastatin (< 40 mg) Pitavastatin (< 2 mg)	Rosuvastatin (5 mg) Atorvastatin (10 mg) Simvastatin (10 mg) Lovastatin (20 mg) Pravastatin (40 mg) Fluvastatin (40 mg) Pitavastatin (2 mg)	

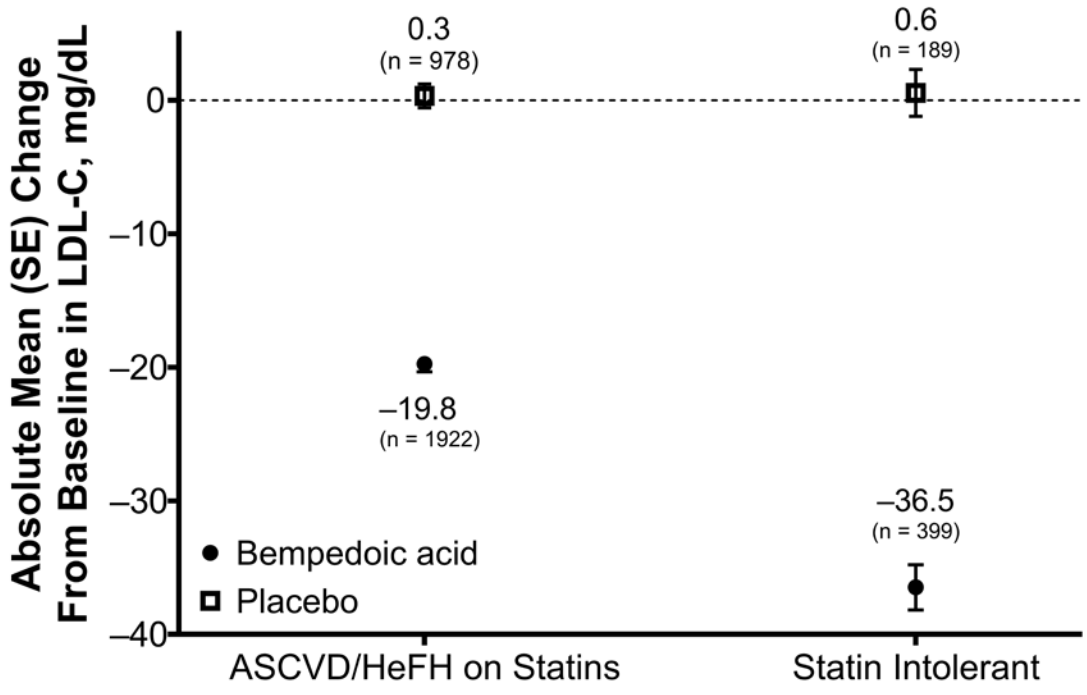
[a]Also includes alternate regimens (ie, every other day or a prespecified number of times/week). BID = twice daily.

eFigure 1. Patients Included in the Pooled Analysis by Study and Treatment Group



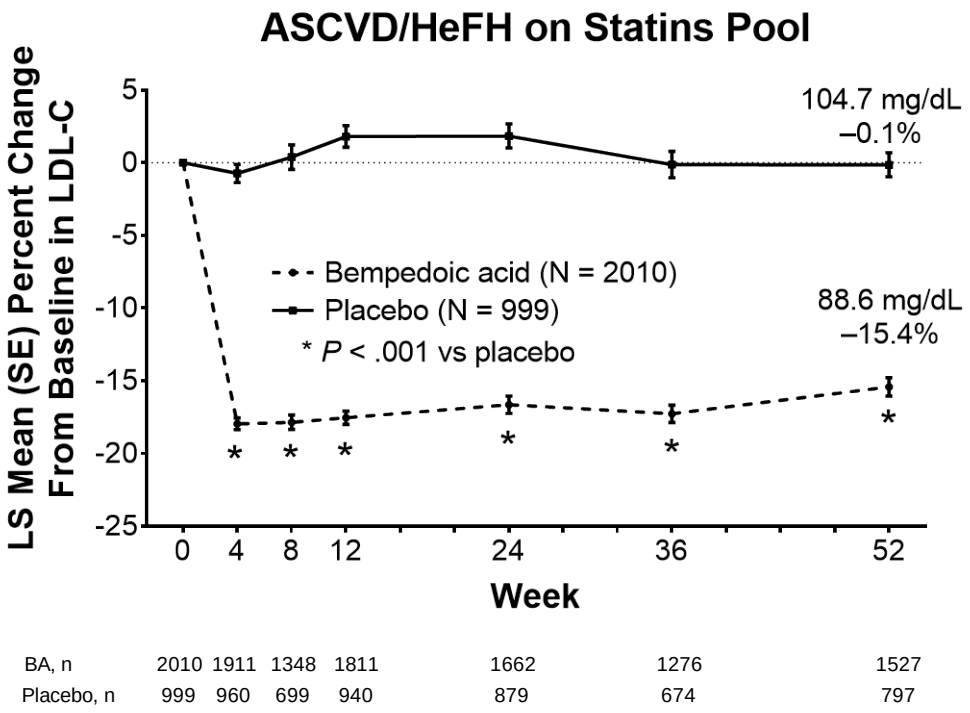
*Two patients (1 patient in the bempedoic acid treatment group and 1 patient in the placebo treatment group) did not receive any dose of study drug and were excluded from the safety analysis population. Abbreviations: ASCVD, atherosclerotic cardiovascular disease; HeFH, heterozygous familial hypercholesterolemia.

eFigure 2. Absolute Change in Low-Density Lipoprotein Cholesterol at Week 12



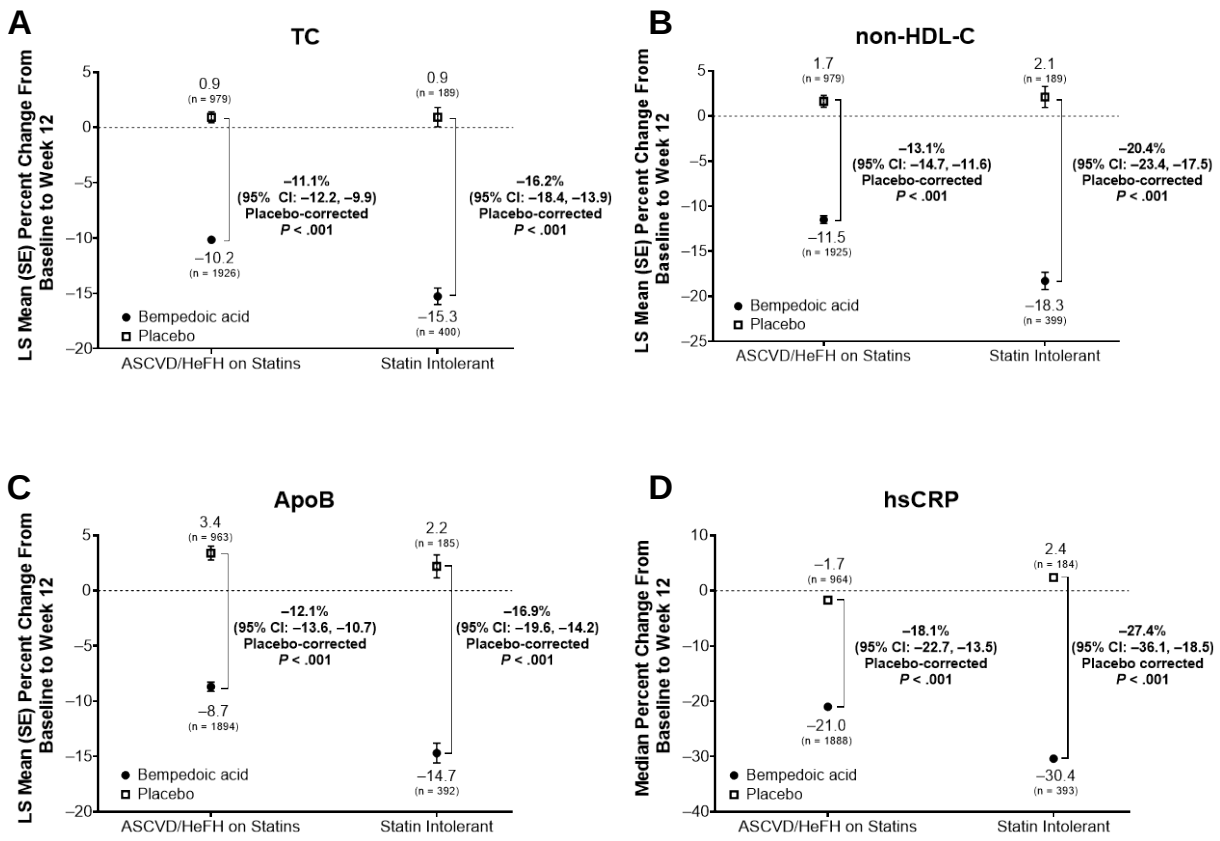
Abbreviations: ASCVD, atherosclerotic cardiovascular disease; HeFH, heterozygous familial hypercholesterolemia; SD, standard deviation.

eFigure 3. On-Treatment Analysis of Low-Density Lipoprotein Cholesterol (LDL-C) Over Time for Patients in the ASCVD/HeFH on Statins Pool



Data are LS means ± SEs. The on-treatment analysis included only those patients who were still receiving assigned study treatment within 7 days prior to LDL-C measurement. The difference between bempedoic acid and placebo was nominally significant at each time point ($P < .001$). Abbreviations: ASCVD, atherosclerotic cardiovascular disease; HeFH, heterozygous familial hypercholesterolemia; LS, least squares; SE, standard error.

eFigure 4. Percentage Changes in Secondary Efficacy Measures From Baseline to Week 12 Associated with Bempedoic Acid Administration



ASCVD indicates atherosclerotic cardiovascular disease; HeFH, heterozygous familial hypercholesterolemia; and LS, least-squares.

eReferences

1. Goldberg AC, Leiter LA, Stroes ESG, et al. Effect of bempedoic acid vs placebo added to maximally tolerated statins on low-density lipoprotein cholesterol in patients at high risk for cardiovascular disease: The CLEAR Wisdom randomized clinical trial. *JAMA.* 2019;322:1780-1788. doi:10.1001/jama.2019.16585.
2. Ray KK, Bays HE, Catapano AL, et al; for the CLEAR Harmony Trial. Safety and efficacy of bempedoic acid to reduce LDL cholesterol. *N Engl J Med*. 2019;380:1022-1032.10.1056/NEJMoa1803917.
3. Ballantyne CM, Banach M, Mancini GBJ, et al. Efficacy and safety of bempedoic acid added to ezetimibe in statin-intolerant patients with hypercholesterolemia: a randomized, placebo-controlled study. *Atherosclerosis*. 2018;277:195-203.10.1016/j.atherosclerosis.2018.06.002.
4. Laufs U, Banach M, Mancini GBJ, et al. Efficacy and safety of bempedoic acid in patients with hypercholesterolemia and statin intolerance. *JAHA*. 2019;8:e011662.10.1161/JAHA.118.011662.