

Dyslipidemia Management

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Disclosures:

Advisory for Aegerion, BASF, Kowa, Merck, Sanofi, and NHP.

Lipid Modulating Agents

- **Statins (LDL, TG)**
- **Niacin (HDL, TG, LDL)**
- **Fibrates (TG, HDL)**
- **Resins (LDL)**
- **Ezetimibe (LDL)**
- **Omega 3 fats (TG)**
- **PCSK9 inhibitors (LDL)**

2013: ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults

Identified four groups of patients with most extensive evidence of benefit of statin therapy for ASCVD prevention

1. Individuals with clinical ASCVD
2. Individuals with primary elevations of LDL-C ≥ 190 mg/dl
3. Individuals 40-75 years of age with diabetes and LDL-C 70-189 mg/dl
4. Individuals without ASCVD or diabetes, 40-75 years of age, with LDL-C 70-189 mg/dl and an estimated 10-year ASCVD risk of $\geq 7.5\%$ by the Pooled Risk Equations

ACC = American College of Cardiology; AHA = American Heart Association; ASCVD = atherosclerotic cardiovascular disease.

Stone NJ, et al. *Circulation*. 2014;129(25 Suppl 2):S1-45;
Goff DC, et al. *Circulation*. 2014;129(25 Suppl 2):S49-73.

High, Moderate, and Low-intensity Statin Therapy Used in Clinical Trials

High-Intensity Statin Therapy	Moderate-Intensity Statin Therapy	Low-Intensity Statin Therapy
Daily dose lowers LDL-C on average, by approximately $\geq 50\%$	Daily dose lowers LDL-C on average, by approximately 30 to $<50\%$	Daily dose lowers LDL-C on average, by approximately $<30\%$
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

*Statins demonstrated reduction in major CVD events.

**FDA approved doses not tested in clinical trials.

FDA = Food and Drug Administration.

Stone NJ, et al. *Circulation*. 2014;129(25 Suppl 2):S1-45;
Goff DC, et al. *Circulation*. 2014;129(25 Suppl 2):S49-73.

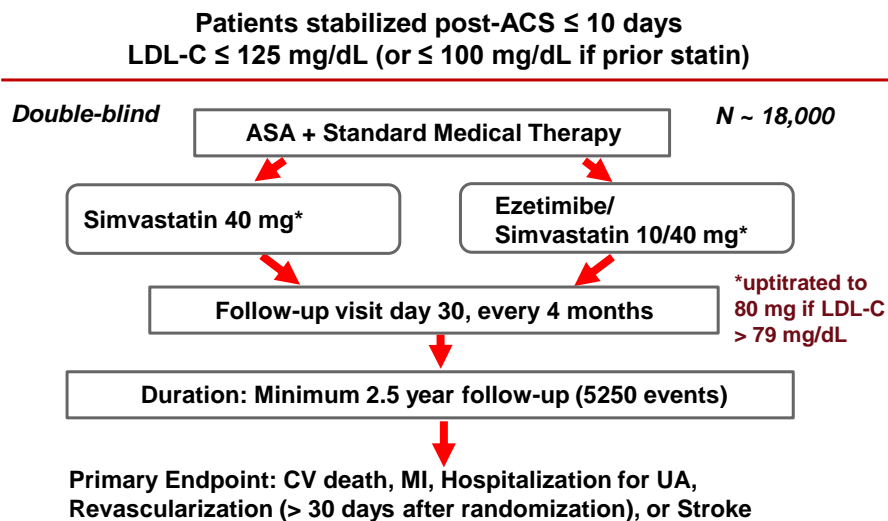
Criteria for ASCVD Risk Assessment, Treatment Goals, Levels at Which to Consider Drug Therapy

Risk Category	Criteria	Treatment Goal	Consider Drug Therapy
		Non-HDL-C mg/dL LDL-C mg/dL	
Low	<ul style="list-style-type: none"> 0-1 major ASCVD risk factors Consider other risk indicators, if known 	<130 <100	≥190 ≥160
Moderate	<ul style="list-style-type: none"> 2 major ASCVD risk factors Consider quantitative risk scoring Consider other risk indicators 	<130 <100	≥160 ≥130
High	<ul style="list-style-type: none"> ≥3 major ASCVD risk factors Diabetes mellitus* (Type 1 or 2) <ul style="list-style-type: none"> 0-1 other major ASCVD risk factors, and No evidence of end organ damage Chronic kidney disease Stage 3B or 4 LDL-C ≥190 mg/dL (severe hypercholesterolemia) Quantitative risk score reaching the high risk threshold 	<130 <100	≥130 ≥100
Very High	<ul style="list-style-type: none"> ASCVD* Diabetes mellitus* (Type 1 or 2) <ul style="list-style-type: none"> ≥2 other major ASCVD risk factors or Evidence of end organ damage 	<100 <70	≥100 ≥70

*For patients with ACVD or diabetes mellitus, consideration should be given to use of moderate or high intensity therapy, irrespective of baseline atherogenic cholesterol levels.

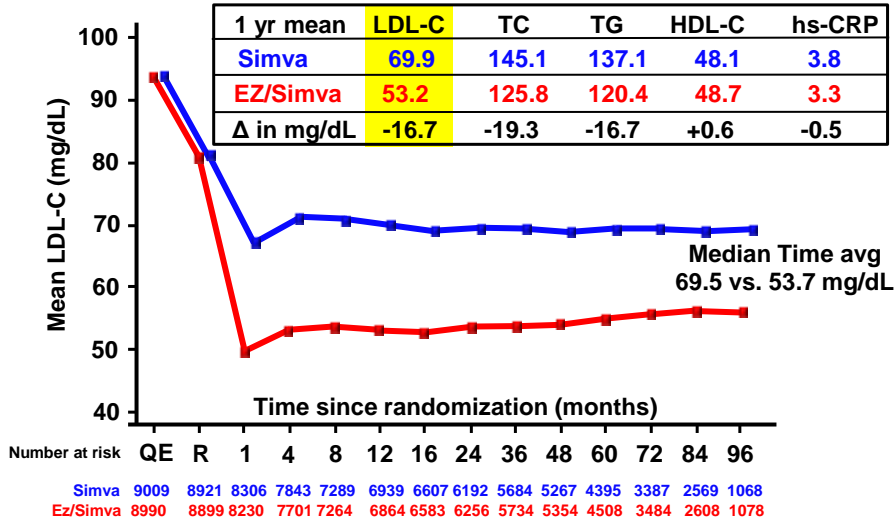
National Lipid Association. *Recommendations*. www.lipids.org/recommendations. September 11, 2014. Accessed December 2, 2014.

IMProved Reduction of Outcomes: Vytorin Efficacy International Trial (IMPROVE IT): Design



New Engl J Med, June 3, 2015DOI: 10.1056/NEJMoa1410489

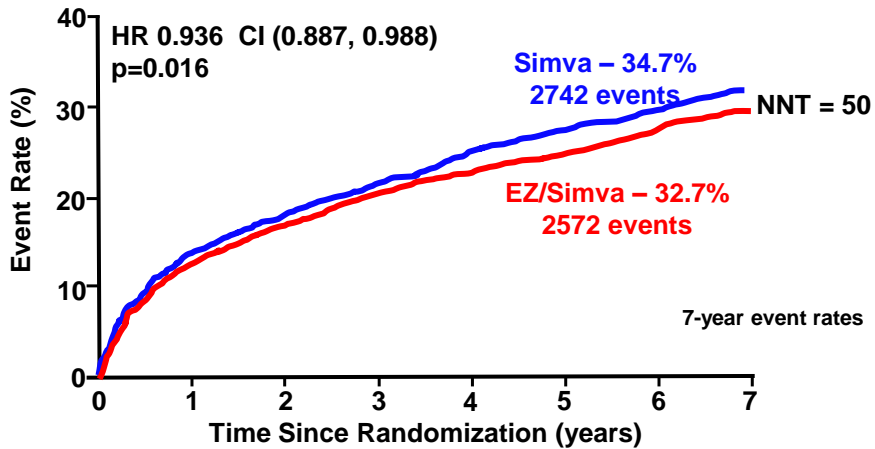
IMProved Reduction of Outcomes: Vytorin Efficacy International Trial (IMPROVE IT)



New Engl J Med, June 3, 2015DOI: 10.1056/NEJMoa1410489

IMProved Reduction of Outcomes: Vytorin Efficacy International Trial (IMPROVE IT)

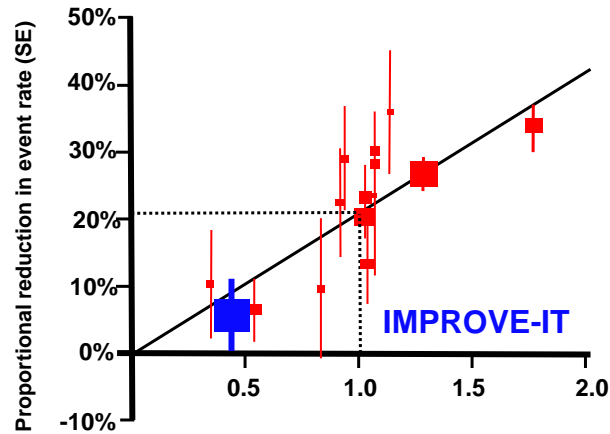
Primary Endpoint - ITT



New Engl J Med, June 3, 2015DOI: 10.1056/NEJMoa1410489

IMPROVED Reduction of Outcomes: International Trial (IMPROVE IT)

Ezetimibe vs Statin Benefit

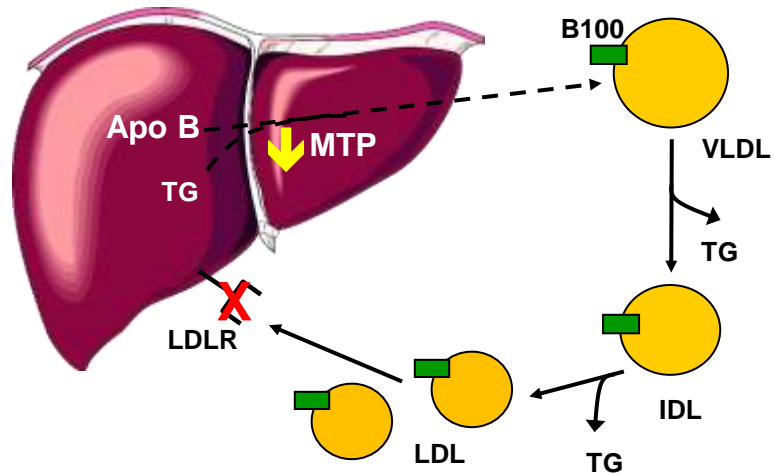


New Engl J Med, June 3, 2015;DOI: 10.1056/NEJMoa1410489

Lipid Lowering Agents for Orphan-status
Hypercholesterolemia:

Blocking Lipoprotein Production

Blocking ApoB Synthesis or the Delivery of the Lipid Droplet to ApoB Reduces Lipoprotein Output



TG = triglycerides; LDLR = low-density lipoprotein receptor; MTP = microsomal triglyceride transfer protein.

Cuchel M, et al. *Lancet*. 2013;381(9860):40-6.

A Case of Homozygous FH

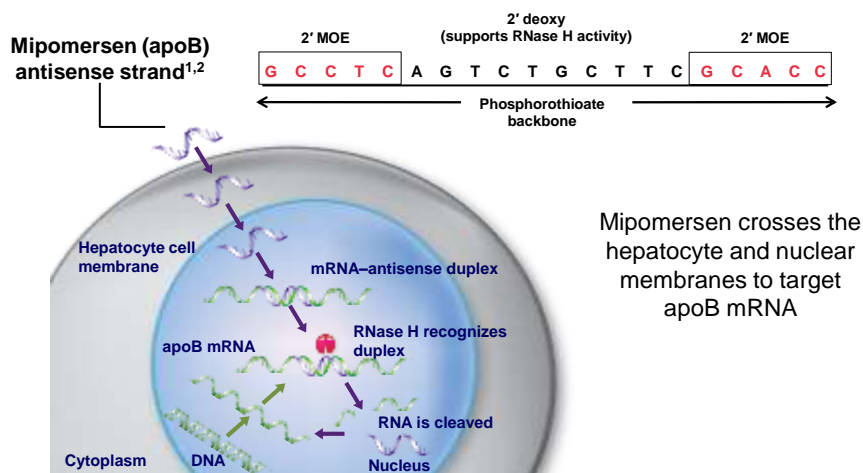
- 55 yo woman with history of multiple coronary stenting and two CABG surgeries
- On LDL apheresis for two years until AV fistula clogged
- On 3 medications, LDL around 650 mg/dl
- One affected child with a less severe hypercholesterolemia

ApoB Antisense

Microsomal Triglyceride Transfer Protein Inhibition

13

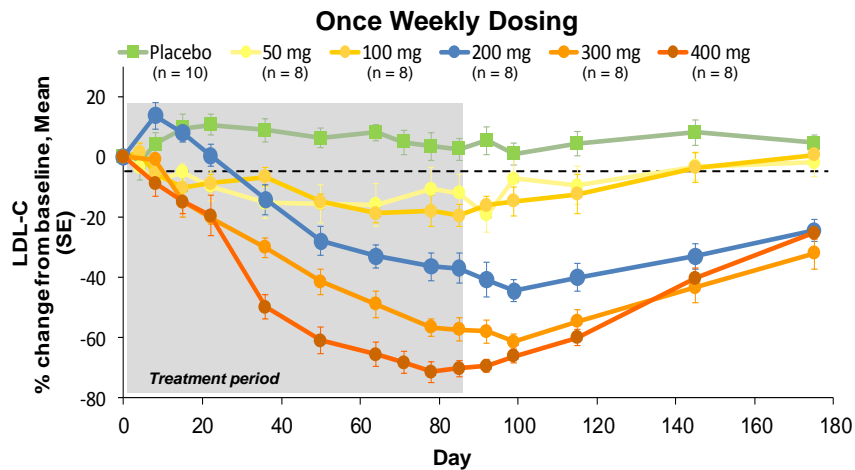
Mipomersen: Mechanism of Action



RnaseH = Ribonuclease H.

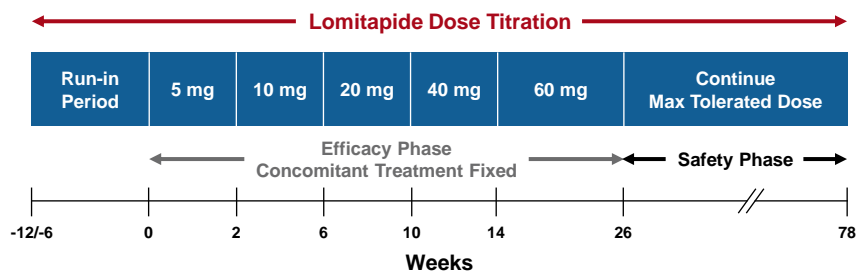
1. Kastelein JJ, et al. *Circulation*. 2006;114(16):1729-35; 2. Crooke ST, ed. *Antisense Drug Technology: Principles, Strategies and Applications*. 2nd ed. 2008:601-39; 3. Yu R, et al. *Drug Metab Dispos*. 2007;35(3):460-8.

Phase 2: Hypercholesterolemia, Monotherapy Dose-dependent Reduction of LDL-C



SE = standard error.
Akdim F, et al. *Eur Heart J*. 2011;32(11):2650-59.

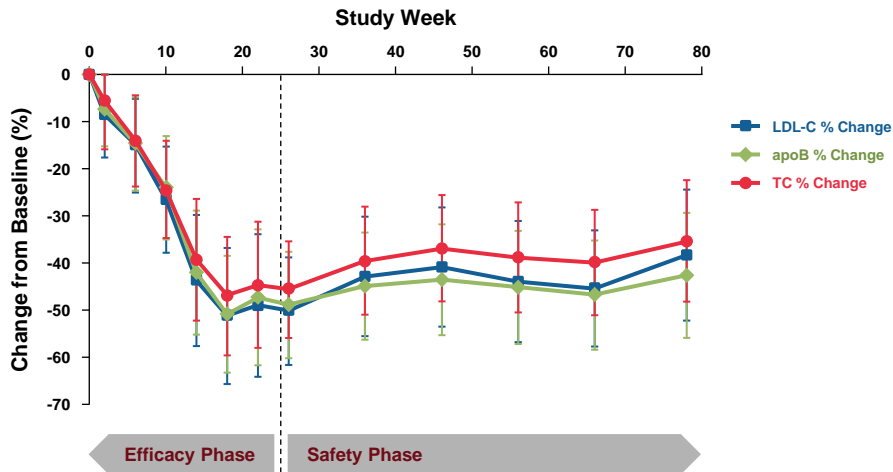
HoFH Phase 3 Study Design



- Open label, ascending dose of lomitapide
- Low fat diet
- Careful LFT monitoring
- Liver fat evaluation by MRI + spectroscopy

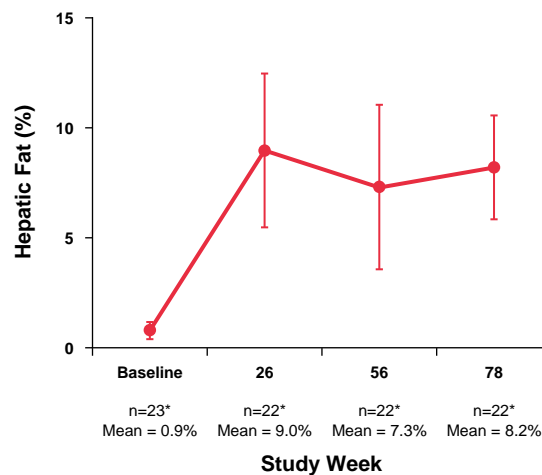
LFT = liver function test; MRI = magnetic resonance imaging.
Cuchel M, et al. *Lancet*. 2013;381(9860):40-6.

Pharmacologic MTP Inhibition Reduces LDL-C Levels in HoFH



Data are mean, 95%CI (n=23).
Cuchel M, et al. *Lancet*. 2013;381(9860):40-6.

HoFH Phase 3 Study: Hepatic Fat Content

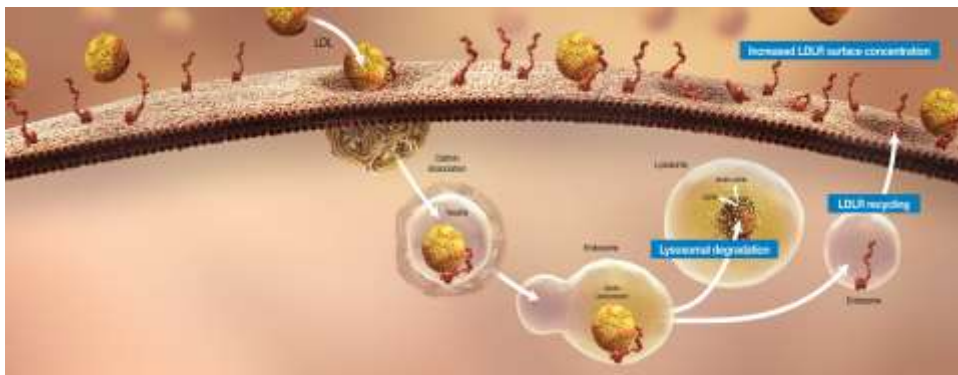


*Fewer number of MRS reads due to patients with contraindication for MRI.
Cuchel M, et al. *Lancet*. 2013;381(9860):40-6.

Newly approved PCSK9 Inhibitors

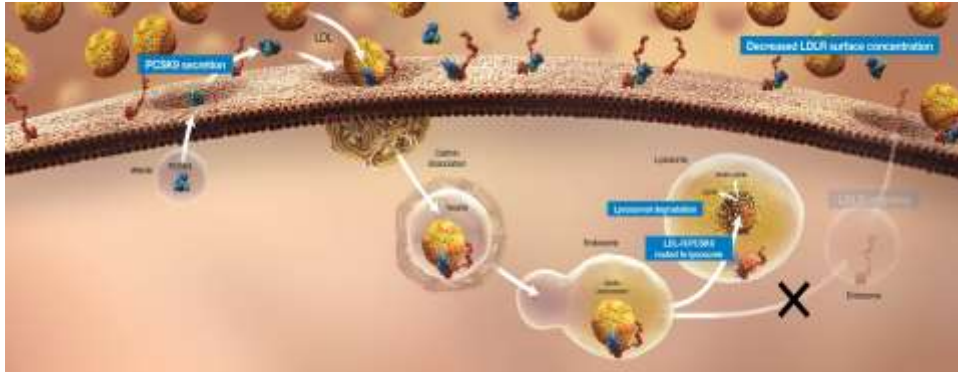
PCSK9 = Proprotein convertase subtilisin/kexin type 9.

Recycling of LDLRs Enables Efficient Clearance of LDL-C Particles



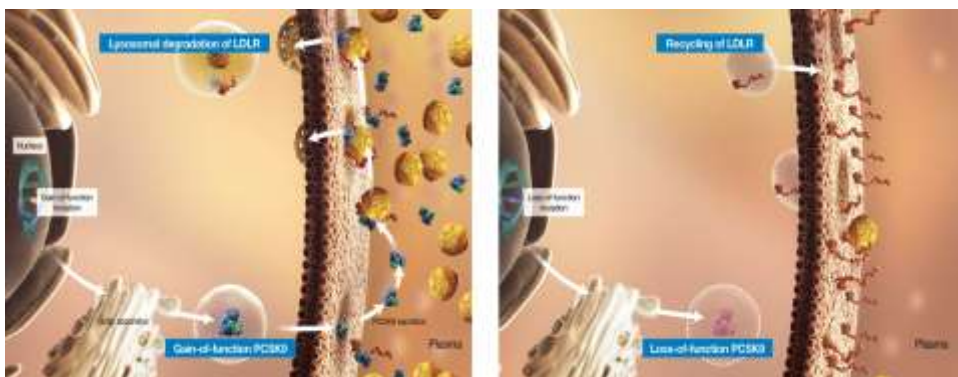
Brown MS, Goldstein JL. *Proc Natl Acad Sci USA*. 1979;76(7):3330-3337; Steinberg D, Witztum JL. *Proc Natl Acad Sci USA*. 2009;106(24):9546-9547; Goldstein JL, Brown MS. *Arterioscler Thromb Vasc Biol*. 2009;29(4):431-438.

PCSK9 Regulates the Surface Expression of LDLRs by Targeting for Lysosomal Degradation



Qian YW, et al. *J Lipid Res.* 2007;48(7):1488-1498; Horton JD, et al. *J Lipid Res.* 2009;50:S172-S177; Zhang DW, et al. *J Biol Chem.* 2007;282(55):18602-18612.

Genetic Variants of PCSK9 Demonstrate Its Importance in Regulating LDL Levels



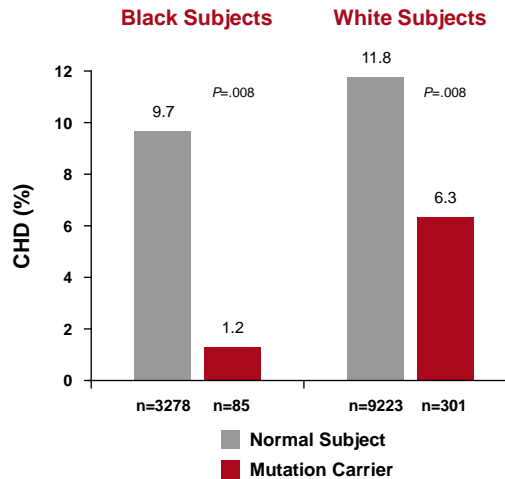
PCSK9 Gain of Function = Less LDLRs

PCSK9 Loss of Function = More LDLRs

Qian YW, et al. *J Lipid Res.* 2007;48(7):1488-1498; Horton JD, et al. *J Lipid Res.* 2009;50:S172-S177; Zhang DW, et al. *J Biol Chem.* 2007;282(55):18602-18612.

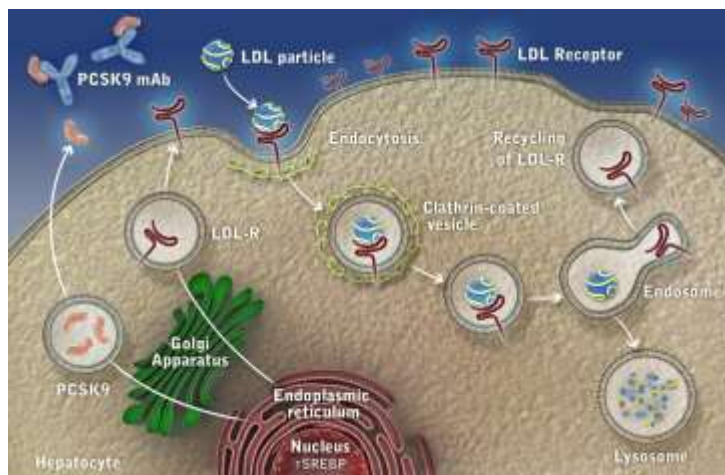
PCSK9 Loss-of-Function Mutations Resulted in Low LDL-C Levels and Reduced CHD Rates

- Wild-type PCSK9 degrades LDL receptors. 1,2
- Loss-of-function mutations increase hepatic LDL receptor expression, reducing LDL-C levels by 15%-40%. 2,3
- CHD was reduced 47% to 88% in PCSK9 loss-of-function mutation carriers compared with normal individuals. 3



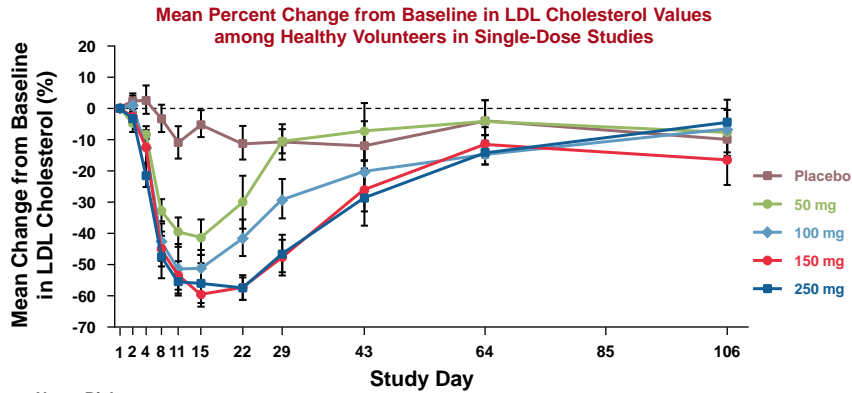
1. Peterson AS, Fong LG, Young SG. *J Lipid Res.* 2008;49(7):1595-1599. 2. Cohen J, et al. *Nature Genetics.* 2005;37(2):161-165. 3. Cohen JC, et al. *N Engl J Med.* 2006;354(12):1264-1272.

Impact of a PCSK9 mAb on LDL Receptor Expression



Qian YW, et al. *J Lipid Res.* 2007;48(7):1488-1498; Horton JD, et al. *J Lipid Res.* 2009;50:S172-S177; Zhang DW, et al. *J Biol Chem.* 2007;282(55):18602-18612.

Results: Single-Dose SQ Subcutaneous Administration

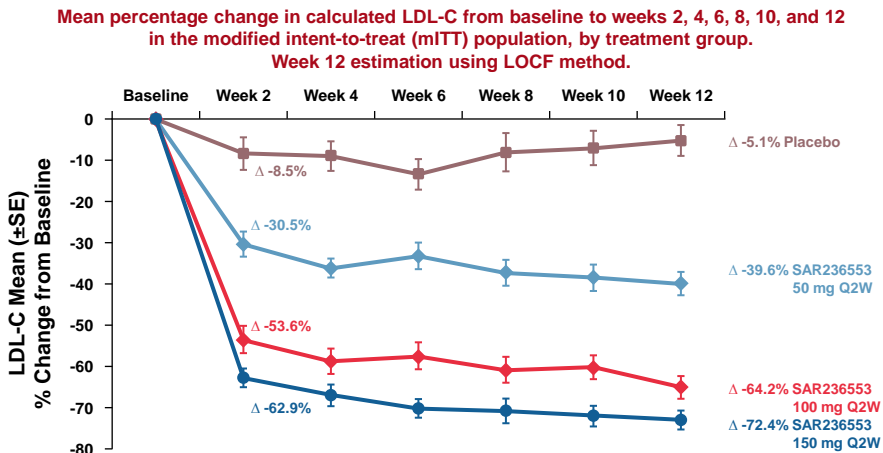


No. at Risk:

	1	2	4	8	11	15	22	29	43	64	85	106
Placebo	8	8	8	8	8	8	8	8	7	7		7
50 mg	6	6	6	6	6	6	6	6	5	6		5
100 mg	6	6	6	6	6	6	6	6	5	6		6
150 mg	6	6	5	5	5	5	5	5	5	4		5
250 mg	6	6	6	6	6	6	6	6	6	6		6

Among subjects receiving increasing single doses of REGN727, values are shown for subcutaneous administration. LDL cholesterol values were calculated with the use of the Friedwald formula. The I bars indicate standard errors. Stein EA, et al. *N Engl J Med.* 2012;366(12):1108-1118.

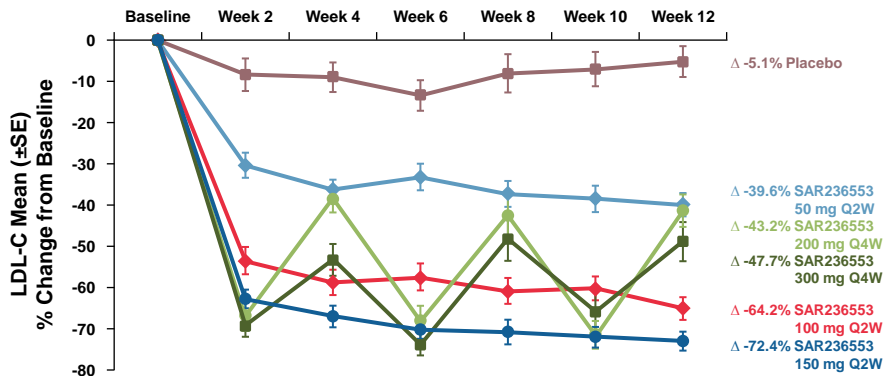
Change in Calculated LDL-C at 2 Weekly Intervals from Baseline to Week 12



LOCF = last observation carried forward. McKenney JM. *A Randomized, Double-blind, Placebo-controlled Trial of the Safety and Efficacy of a Monoclonal Antibody to Proprotein Convertase Subtilisin/Kexin Type 9 Serine Protease, REGN727/SAR236553, in Patients with Primary Hypercholesterolemia (NCT: 01288443).* American Cardiology Conference 2012, Chicago, IL.

Change in Calculated LDL-C at 2 Weekly Intervals from Baseline to Week 12

Mean percentage change in calculated LDL-C from baseline to weeks 2, 4, 6, 8, 10, and 12 in the modified intent-to-treat (mITT) population, by treatment group.
Week 12 estimation using LOCF method.



McKenney JM. A Randomized, Double-blind, Placebo-controlled Trial of the Safety and Efficacy of a Monoclonal Antibody to Proprotein Convertase Subtilisin/Kexin Type 9 Serine Protease, REGN727/SAR236553, in Patients with Primary Hypercholesterolemia (NCT: 01288443). American Cardiology Conference 2012, Chicago, IL.

Summary of TEAEs (Safety Population)

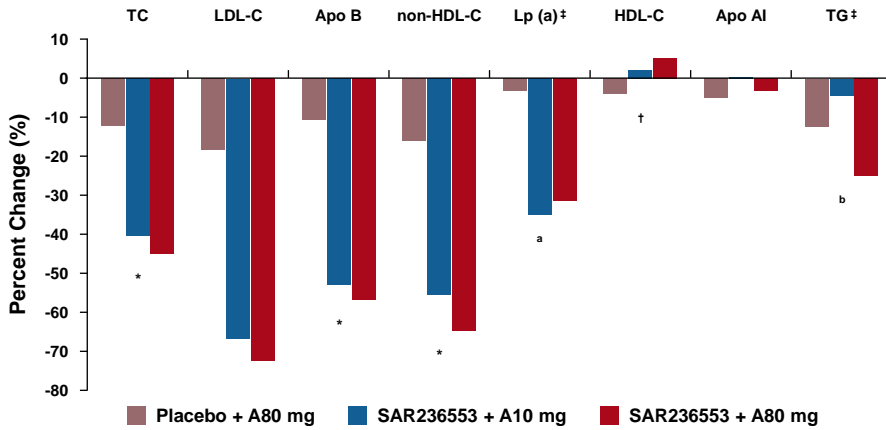
	Q2W Dosing				Q4W Dosing	
	Placebo (N=31)	50mg (N=30)	100mg (N=31)	150mg (N=31)	200mg (N=30)	300mg (N=30)
Overview of all TEAEs – no.						
Any TEAE	14	18	20	19	20	14
Any treatment-emergent SAE	1	0	1	0	1	1
Any TEAE leading to permanent treatment d/c	0	0	1	1	3	1
AEs of special interest — no.						
ALT or AST >3 x ULN	0	0	0	0	0	0
Muscle (including pain, weakness)	1	1	2	1	1	2
CK >10 x ULN	1	0	0	0	0	0

Injection-site reactions occurred in the SAR236553 groups only and were generally mild and non-progressive.

TEAE = treatment-emergent adverse events; SAE = serious adverse event; AST = aspartate aminotransferase.

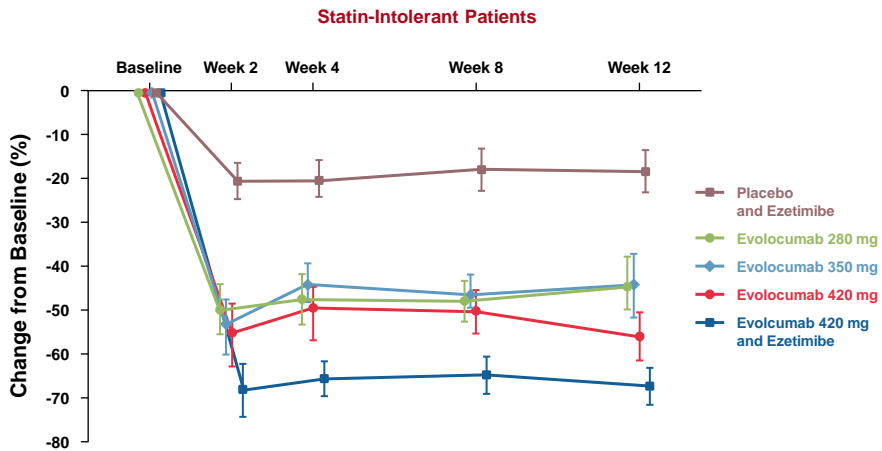
McKenney JM. A Randomized, Double-blind, Placebo-controlled Trial of the Safety and Efficacy of a Monoclonal Antibody to Proprotein Convertase Subtilisin/Kexin Type 9 Serine Protease, REGN727/SAR236553, in Patients with Primary Hypercholesterolemia (NCT: 01288443). American Cardiology Conference 2012, Chicago, IL.

Change in Lipids/Lipoproteins from Baseline to Week 8 LOCF



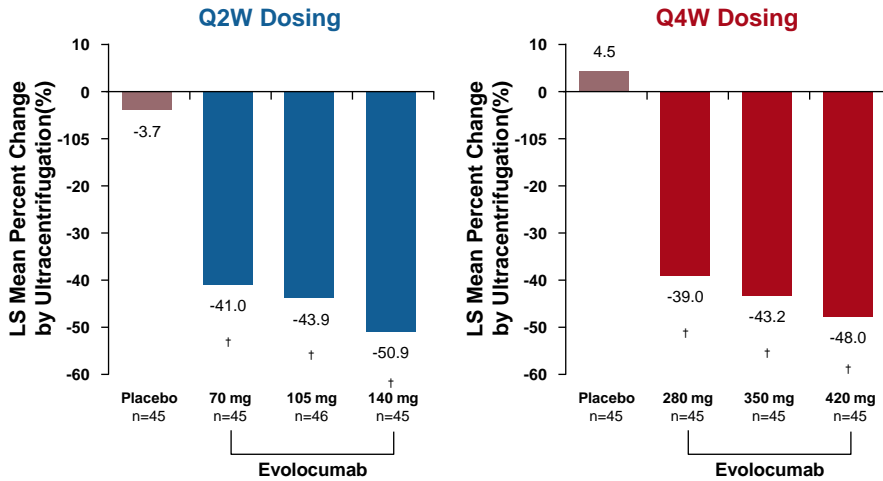
‡Percent change from baseline median data are reported. Clinicaltrials.gov no. NCT01288469.
^{*}P<.001 vs Placebo + A80mg; [†]P= .051 vs Placebo + A80mg; ^aP=.0003 vs Placebo + A80mg; ^bP<.05 vs Placebo + A80mg.
 McKenney JM. A Randomized, Double-blind, Placebo-controlled Trial of the Safety and Efficacy of a Monoclonal Antibody to Proprotein Convertase Subtilisin/Kexin Type 9 Serine Protease, REGN727/SAR236553, in Patients with Primary Hypercholesterolemia (NCT: 01288443). American Cardiology Conference 2012, Chicago, IL.

GAUSS: Effect of Evolocumab on Percentage Change in LDL-C From Baseline



GAUSS = Goal Achievement After Utilizing an Anti-PCSK9 Antibody in Statin Intolerant Subjects. Sullivan D, et al. JAMA. 2012;308(23):2497-506.

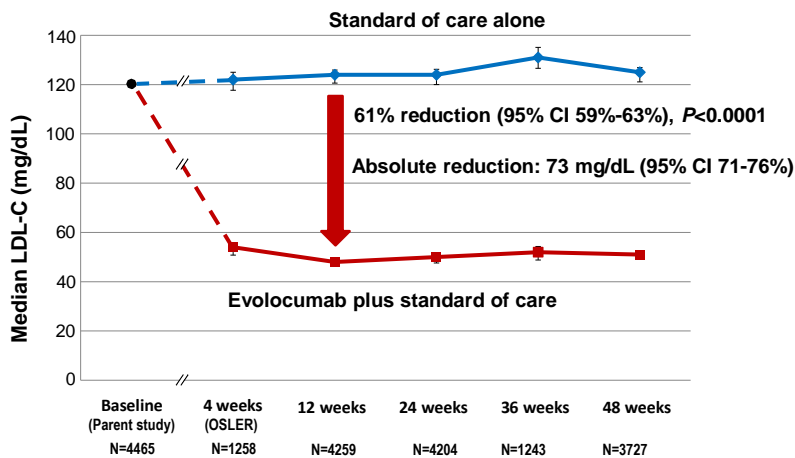
MENDEL: Effects of Evolocumab on LDL-C at Week 12 Relative Change in LDL-C from Baseline*



*Primary endpoint; †P<.001 vs placebo.

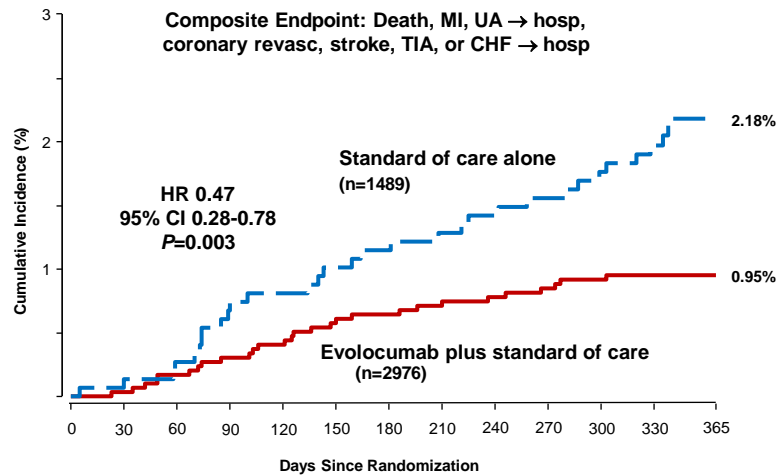
MENDEL = Monoclonal Antibody Against PCSK9 to Reduce Elevated LDL-C in Patients Currently Not Receiving Drug Therapy For Easing Lipid Levels-2; LS = least squares.
Koren MJ, et al. *Lancet*. 2012;380(9858):1995-2006.

OSLER Trial: Effect of Evolocumab on LDL Cholesterol



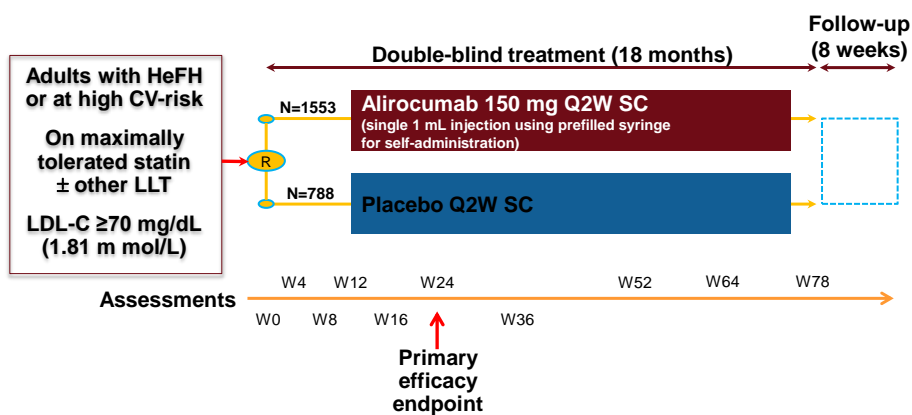
Sabatine MS, et al. *N Engl J Med*. 2015;372:1500-1509.

OSLER Trial: Effect of Evolocumab on Cardiovascular Outcomes



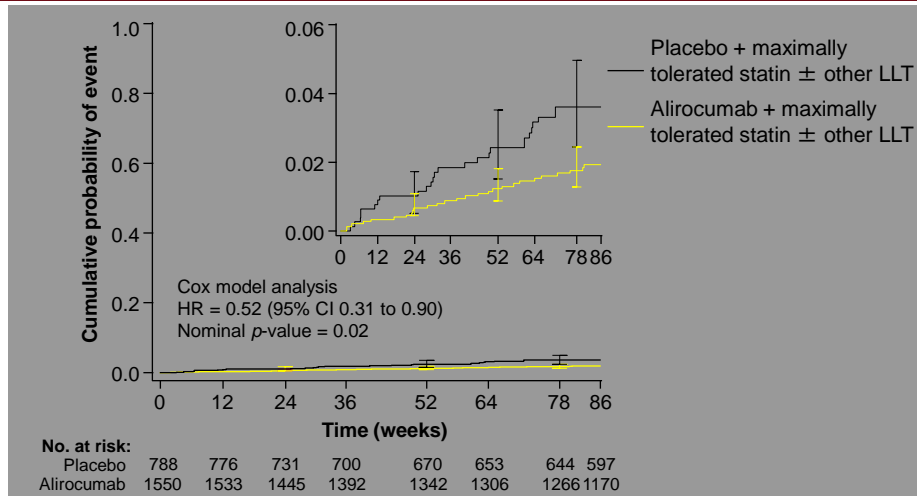
TIA = transient ischemic attack; CHF = congestive heart failure; MI = myocardial infarction; UA = unstable angina.
Sabatine MS, et al. *N Engl J Med.* 2015;372:1500-1509

ODYSSEY Long Term: Study Design



SC = subcutaneous; W = week.
Robinson JG, et al. *N Engl J Med.* 2015;372:1489-1499.

Post hoc Analysis of Adjudicated Major Adverse Cardiovascular Events*



*Based on primary endpoint for the ODYSSEY OUTCOMES trial, including CHD death, non-fatal MI, fatal and non-fatal ischemic stroke, and unstable angina requiring hospitalization. Unstable angina requiring hospitalization was considered based on strict criteria/clear progression of ischemia.

Robinson JG, et al. *N Eng J Med.* 2015;372:1489-99.

Treatment-Emergent General Allergic and Neurologic Serious Adverse Events

Number of patients (%)	Alirocumab (n=1550)	Placebo (n=788)
General Allergic custom MedDRA query serious AEs	8 (0.5)	3 (0.4)
Asthma	3 (0.2)	1 (0.1)
Angioedema	1 (<0.1)	0
Dermatitis allergic	1 (<0.1)	0
Drug hypersensitivity	1 (<0.1)	0
Hypersensitivity	1 (<0.1)	0
Hypersensitivity vasculitis	1 (<0.1)	0
Laryngeal oedema	1 (<0.1)	0
Rash	1 (<0.1)	0
Acute respiratory failure	0	1 (0.1)
Cytokine release syndrome	0	1 (0.1)
Neurologic custom MedDRA query serious AEs	5 (0.3)	2 (0.3)
Ataxia	1 (<0.1)	0
Demyelination	1 (<0.1)	0
Dysarthria	1 (<0.1)	0
Miller Fisher Syndrome	1 (<0.1)	0
Optic neuritis	1 (<0.1)	0
Hypoaesthesia	0	2 (0.3)

MedDRA = Medical Dictionary for Regulatory Activities.

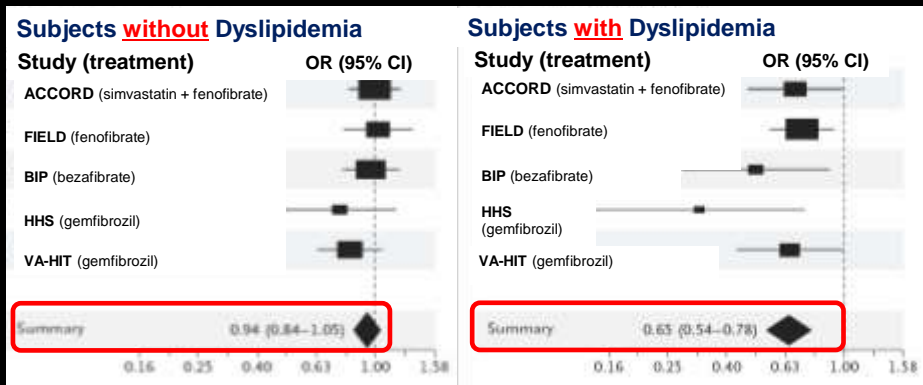
Robinson JG, et al. *N Eng J Med.* 2015;372:1489-1499.

Cardiovascular Outcomes Trials of PCSK9 Inhibitors

	Alirocumab	Evolocumab	Bococizumab	
Sponsor	Sanofi/Regeneron	Amgen	Pfizer	
Trial	ODYSSEY Outcomes	FOURIER	SPIRE I	SPIRE II
Sample Size	18,000	22,500	12,000	6300
Patients	4-16 weeks post-ACS	MI, stroke, or PAD	High risk of CV event	
Statin	Evidence-based Rx	Atorvastatin ≥ 20 mg or equivalent	Lipid-lowering Rx	
LDL-C	≥ 70 mg/dL	≥ 70 mg/dL	70-99 mg/dL	≥ 100 mg/dL
PCSK9i Dosing	Every 2 weeks	Every 2 or Every 4 weeks	Every 2 weeks	
Endpoint	CHD death, MI, ischemic stroke, or UA hospitalization	Primary: CV death, MI, stroke, UA hospitalization or coronary revascularization Key Secondary: CV death, MI, or stroke	CV death, MI, stroke, or urgent revascularization	
Completion	March 2018	December 2017	August 2017	

Fibrates Reduce CHD Risk in Patients with HTG and Low HDL-C

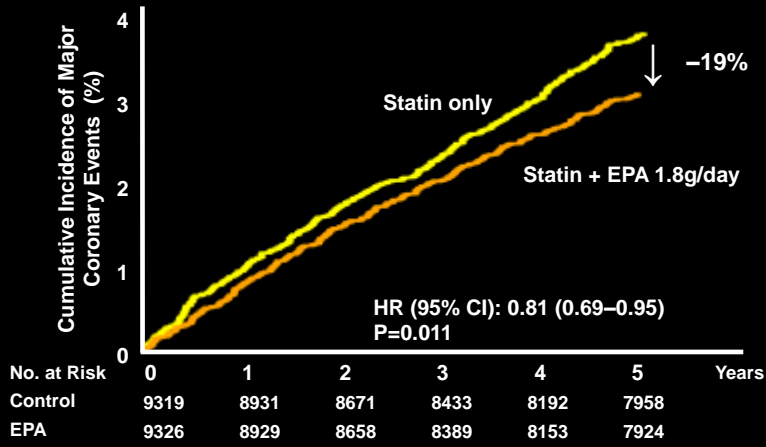
A meta-analysis of randomized fibrate trials



TG ≥ 204 mg/dL, HDL-C ≤ 34 mg/dL

Sacks FM et al. *N Engl J Med.* 2010;363:692-4.

JELIS: EPA Reduced Major Coronary Events* in Hypercholesterolemic Patients on Statins

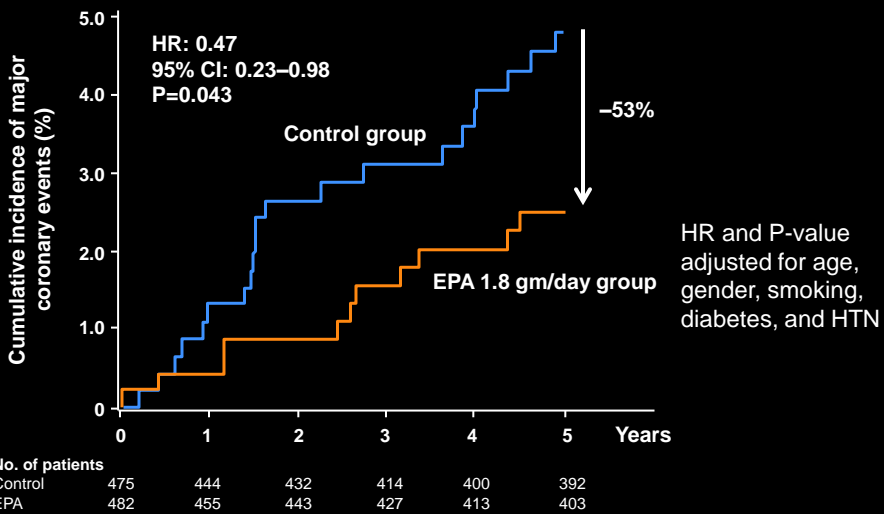


N=18,645 Japanese pts with TC ≥251 mg/dL prior to baseline statin Rx. Baseline TG=153 mg/dL. Statin up-titrated to 20 mg pravastatin or 10 mg simvastatin for LDL-C control.

*Primary endpoint: sudden cardiac death, fatal and non-fatal MI, unstable angina pectoris, angioplasty, stenting, or coronary artery bypass graft.

Yokoyama M et al. *Lancet*. 2007;369:1090-8.

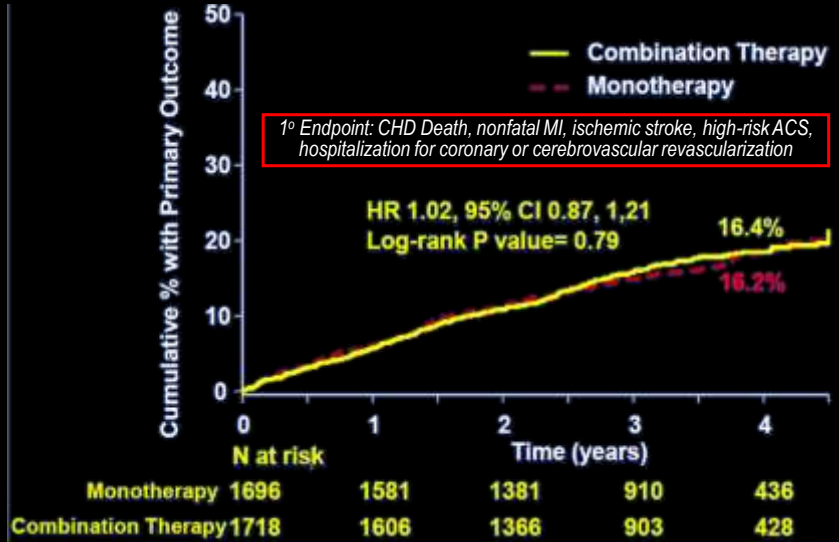
JELIS: Larger Decrease in MACE in those with TG >150 mg/dL & HDL-C <40 mg/dL*



*Pre-specified. MACE=major adverse CV event. Saito Y et al. *Atherosclerosis*. 2008;200:135-40.

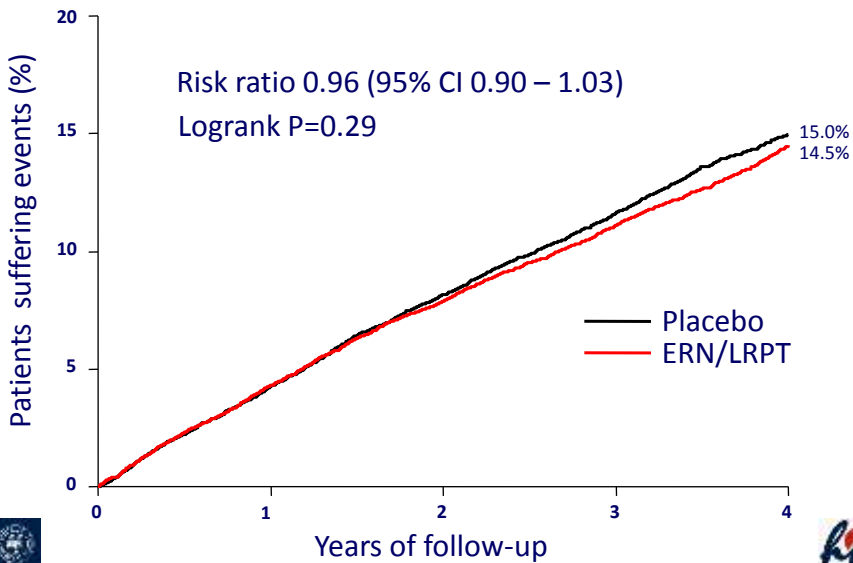
AIM-HIGH Study Results

Primary Outcome



Boden WE. *N Engl J Med*. epub 15 Nov 2011; doi:10.1056/NEJMoa1107579.

Extended Release Niacin and Major Vascular Events



NEJM 2014



Raising HDL via CETP Inhibition

CETP = cholesterylester transfer protein.

Mechanism of Action of CETP

- Two hypotheses have been proposed for the mechanism by which CETP transfers neutral lipids between plasma lipoproteins
- (i) a shuttle mechanism that involves CETP collecting cholesteryl esters from one lipoprotein and delivering them through the aqueous phase to another lipoprotein.
- (ii) a tunnel mechanism in which CETP bridges two lipoproteins to form a ternary complex, with lipids flowing from the donor to acceptor lipoprotein through the CETP molecule

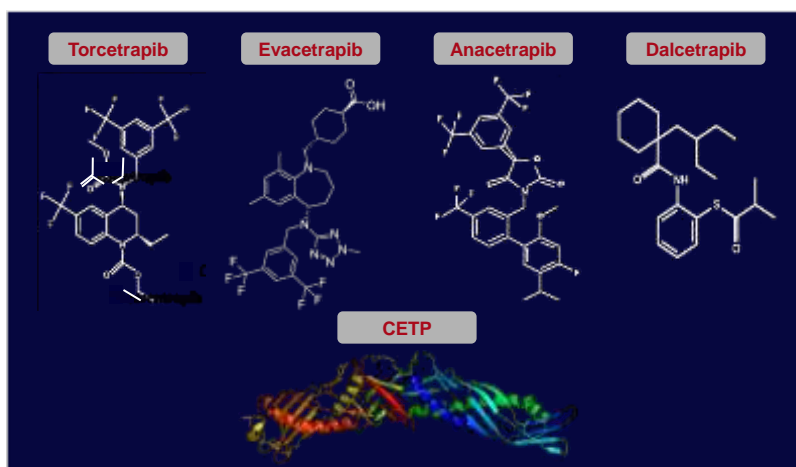
Barter PJ, et al. *Biochem J.* 1982;208(1):1-7; Ihm J, et al. *J Lipid Res.* 1982;23(9):1328-41; Swenson TL, et al. *J Biol Chem.* 1988;263(11):5150-7; Tall AR. *J Lipid Res.* 1993;34(8):1255-74; Zhang L, et al. *Nature Chem Biol.* 2012;8(4):342-9.

CETP Polymorphisms and Cardiovascular Risk in Humans

- A meta-analysis has been conducted of studies investigating relationships between CETP polymorphisms and cardiovascular disease in humans
- 46 studies had data on 27,196 coronary cases and 55,338 controls
- Those polymorphisms that were associated with lower CETP mass and lower CETP activity had higher levels of HDL-C and a significantly reduced coronary risk

Thompson A, et al. *JAMA*. 2008;299(23):2777-2788.

CETP Inhibitors and Modulators



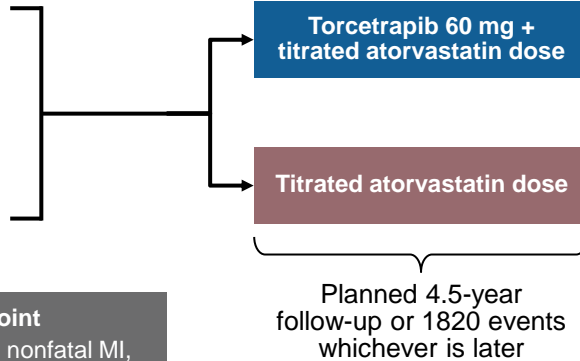
Barter PJ, et al. *N Engl J Med*. 2007;357(21):2109-2122;
 Qiu X, et al. *Nat Struct Mol Biol*. 2007;14(2):106-112.

ILLUMINATE

Investigation of Lipid Level Management to
Understand its Impact in Atherosclerotic Events

15,067 patients

- Men and women
- Aged 45-75 years
- 250 sites in 7 countries
- CHD or risk equivalent, any HDL-C level, statin eligible

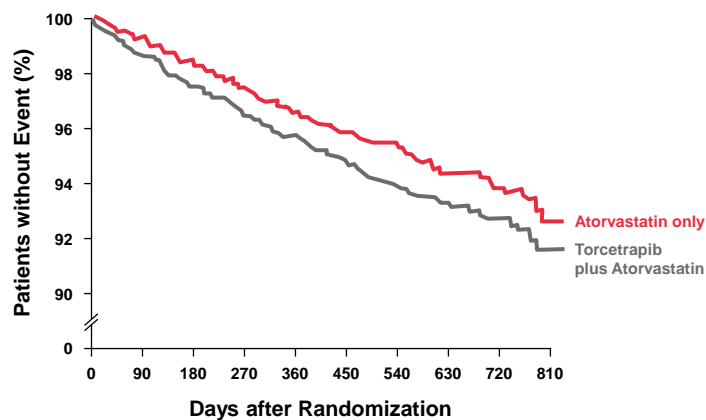


Primary End Point

Composite of fatal CHD, nonfatal MI, stroke (fatal and non-fatal and unstable angina requiring hospitalization)

Barter PJ, et al. *N Engl J Med.* 2007;357(21):2109-2122.

Torcetrapib: “Beneficial” Effects on Lipoproteins, but Increased Cardiovascular and Non-Cardiovascular Morbidity and Mortality



Was the toxicity of torcetrapib related to off-target effects specific to this molecule?

Barter PJ, et al. *N Engl J Med.* 2007;357(21):2109-2122.

dal-HEART Program

Dalcetrapib HDL Evaluation, Atherosclerosis, and Reverse Cholesterol Transport

The dal-HEART Program tests a novel hypothesis that raising HDL through CETP inhibition will attenuate cardiovascular risk.

dal-OUTCOMES¹

A double-blind, randomized, placebo-controlled study in 15,600 patients recently hospitalized for ACS

Goal: To evaluate the effect of dalcetrapib on CV outcomes

dal-VESSEL²

A double-blind, randomized, placebo-controlled study in 450 patients with CHD or CHD risk equivalent

Goal: To evaluate the effect of dalcetrapib on endothelial function and blood pressure, measured by FMD and ABPM

dal-PLAQUE³

A double-blind, randomized, placebo-controlled study in 130 patients with CHD

Goal: To evaluate the effect of dalcetrapib on inflammation, plaque size, and burden, measured by PET/CT and MRI

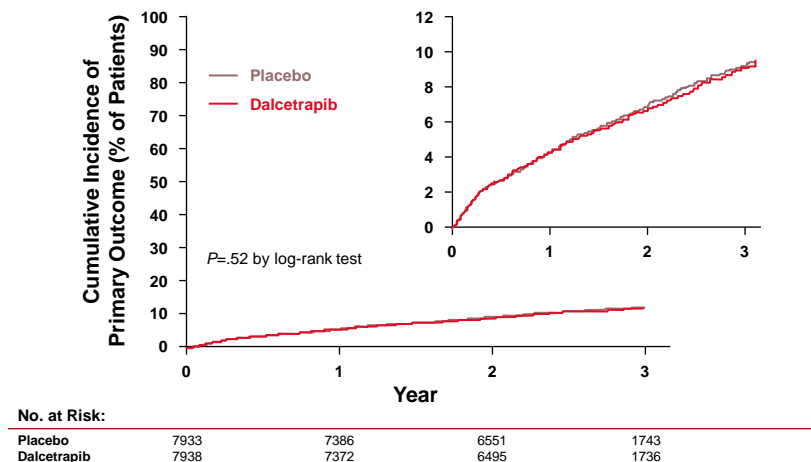
dal-PLAQUE 2⁴

A double-blind, randomized, placebo-controlled study in 900 patients with CAD

Goal: To evaluate the effect of dalcetrapib on atherosclerotic progression, assessed by IVUS and carotid B-mode ultrasound

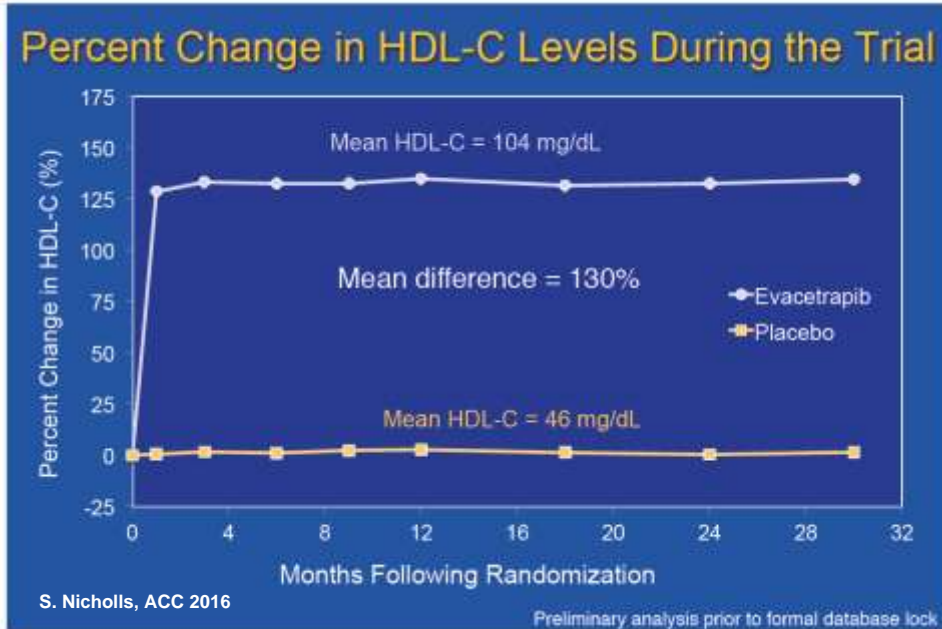
dal-OUTCOMES = Dalcetrapib in Stable Coronary Heart Disease Patients with Recent Acute Coronary Syndrome; dal-VESSEL = Vascular Effects and Safety of Dalcetrapib in Patients with or at Risk of CHD; dal-PLAQUE = Safety and efficacy of dalcetrapib on atherosclerotic disease using novel non-invasive multimodality imaging.
¹Schwartz GG, et al. *N Engl J Med.* 2012;367(22):2089-2099; ²Luscher TF, et al. *Eur Heart J.* 2012;33(7):857-865; ³Fayad ZA, et al. *Lancet.* 2011;378(9802):1547-1559; ⁴Not yet published.

dal-OUTCOMES Results: No ↓CVD

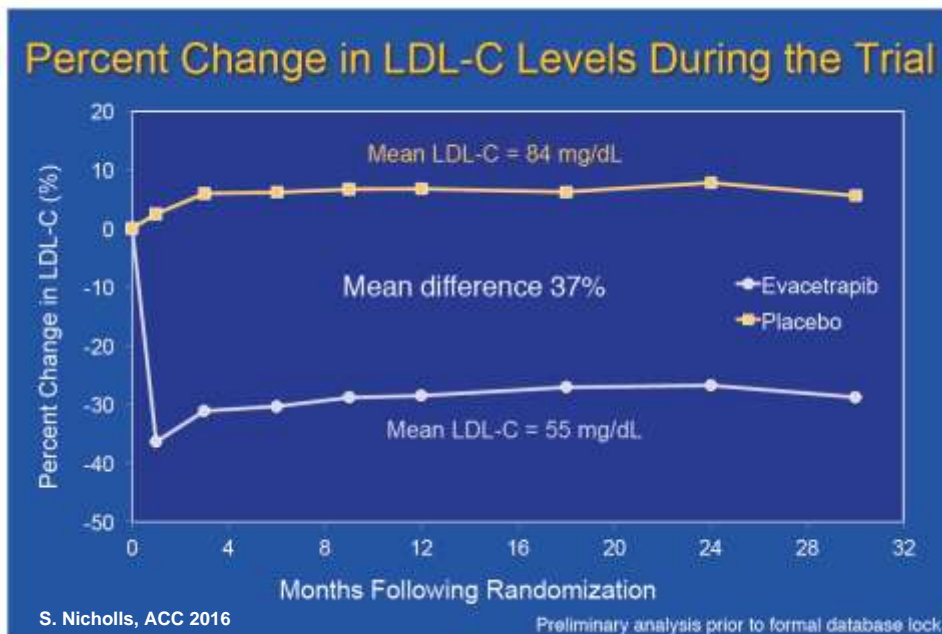


Schwartz GG, et al. *N Engl J Med.* 2012;367(22):2089-99.

ACCELERATE Trial of Evacetrapib



ACCELERATE Trial of Evacetrapib





➤ Valeant Severs
Ties With Holder



➤ Exxon Results
Slide Less Than
Expected



➤ Taxes Drive
Potential Pfizer,
Allergan Deal

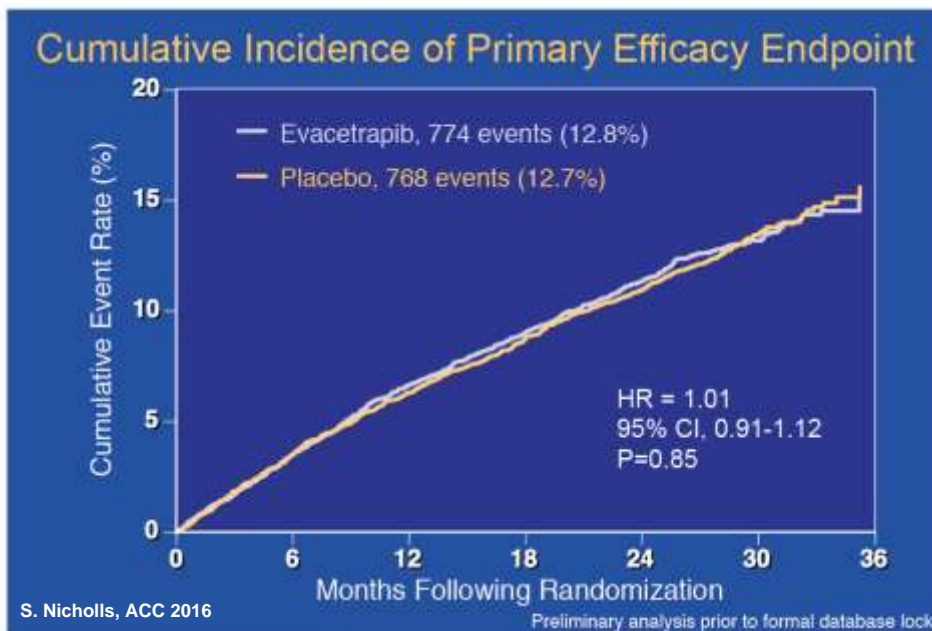


BUSINESS | HEALTH CARE | HEALTH

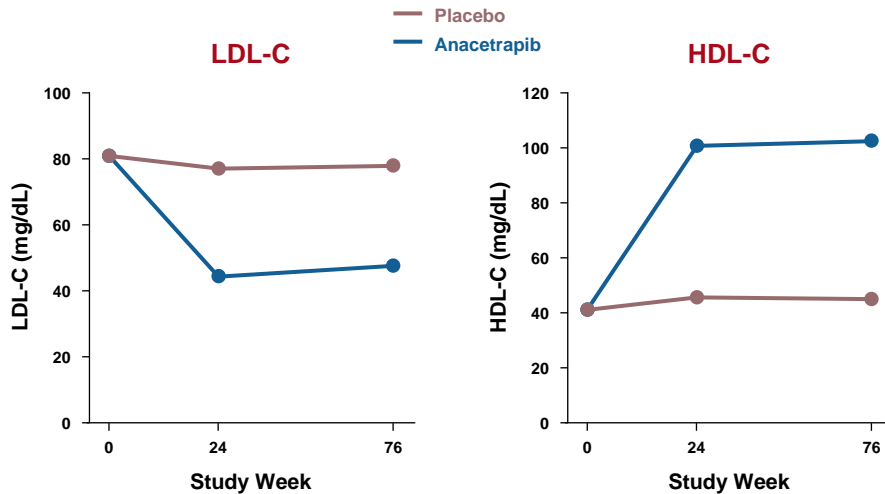
Lilly to Halt Development of Experimental Cholesterol Drug

Company anticipates \$90 million pretax charge for discontinuing evacetrapib development

ACCELERATE Trial of Evacetrapib



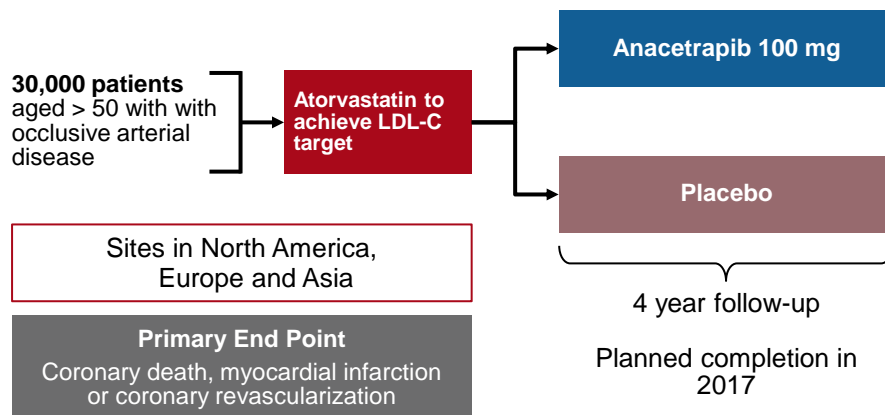
CETP Inhibitor Anacetrapib



Cannon CP, et al. *NEJM*. 2010;363(25):2406-15.

REVEAL Trial

Randomized Evaluation of the Effects of Anacetrapib through Lipid-Modification



University of Oxford. *Reveal*. www.revealtrial.org. Accessed November 2, 2014.

Summary and Conclusions

- Statins as mainstay of cholesterol control.
- Additional agents as adjuvants in statin intolerant subjects or to achieve LDL goal.
- For TG control, fibrates and omega 3 fats have yet to produce evidence of CVD benefits.
- For HDL control, niacin has failed to produce evidence of CVD benefits.
- New agents available for management of orphan-status HoFH.
- PCSK9 inhibitors for common FH and to help CAD subjects reach LDL goal.
- Raising HDL does not help.