Lower for Longer : Effective lipid lowering – Rising on Ezetimibe Therapy

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Disclosure

- None

Contents

- Relationship between LDL-C and CV disease
- “Lower is better” - evidence & safety
- Benefit of Ezetimibe combination

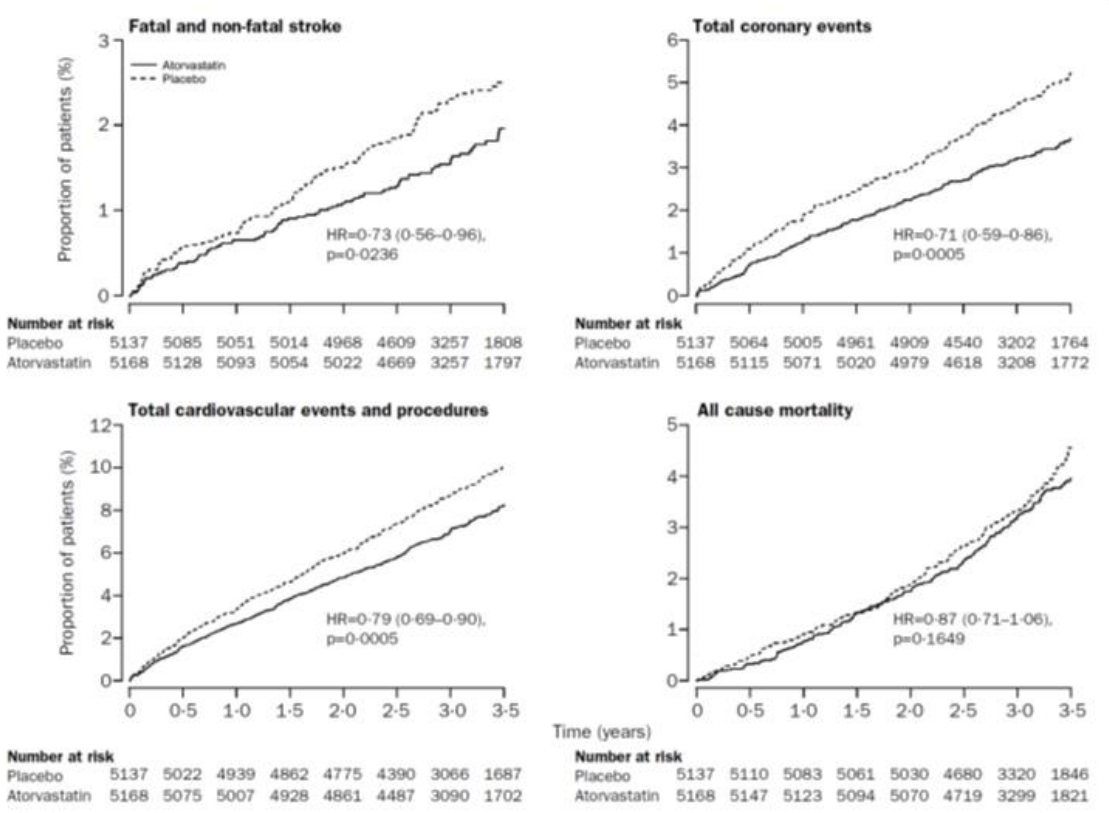
Contents

- **Relationship between LDL-C and CV disease**
- **“Lower is better” - evidence & safety**
- **Benefit of Ezetimibe combination**

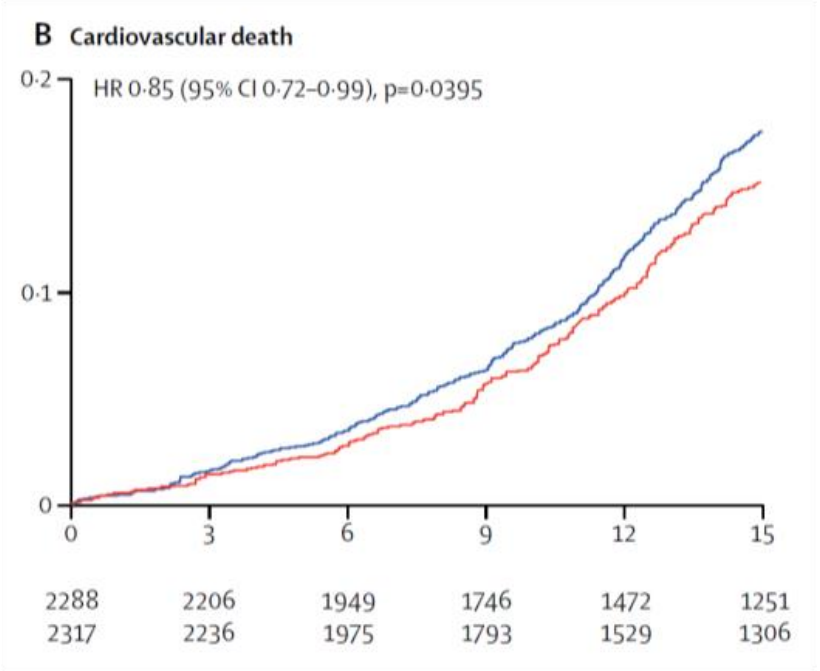
Statin therapy reduce future CV events

Atorvastatin 10mg vs. Placebo

Atorvastatin 10mg was associated with lower coronary and cerebral events in the ASCOT-LLA trial



Benefits of statins persisted in reducing CV death (ASCOT-Legacy)



Lancet 2003; 361: 1149–58 / Lancet 2018; 392: 1127–37

LDL-C lowering is correlated with CV risk reduction

- Mean absolute
  (Meta-analysis of 14

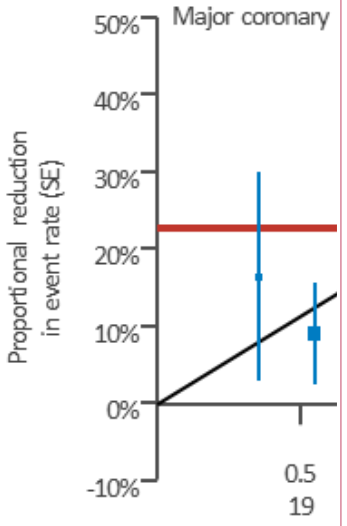
events.

1 mmc

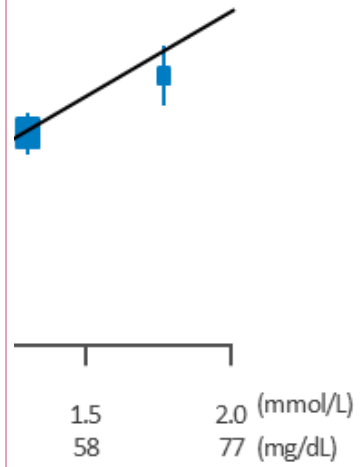
ears with:

23% re

or vascular events



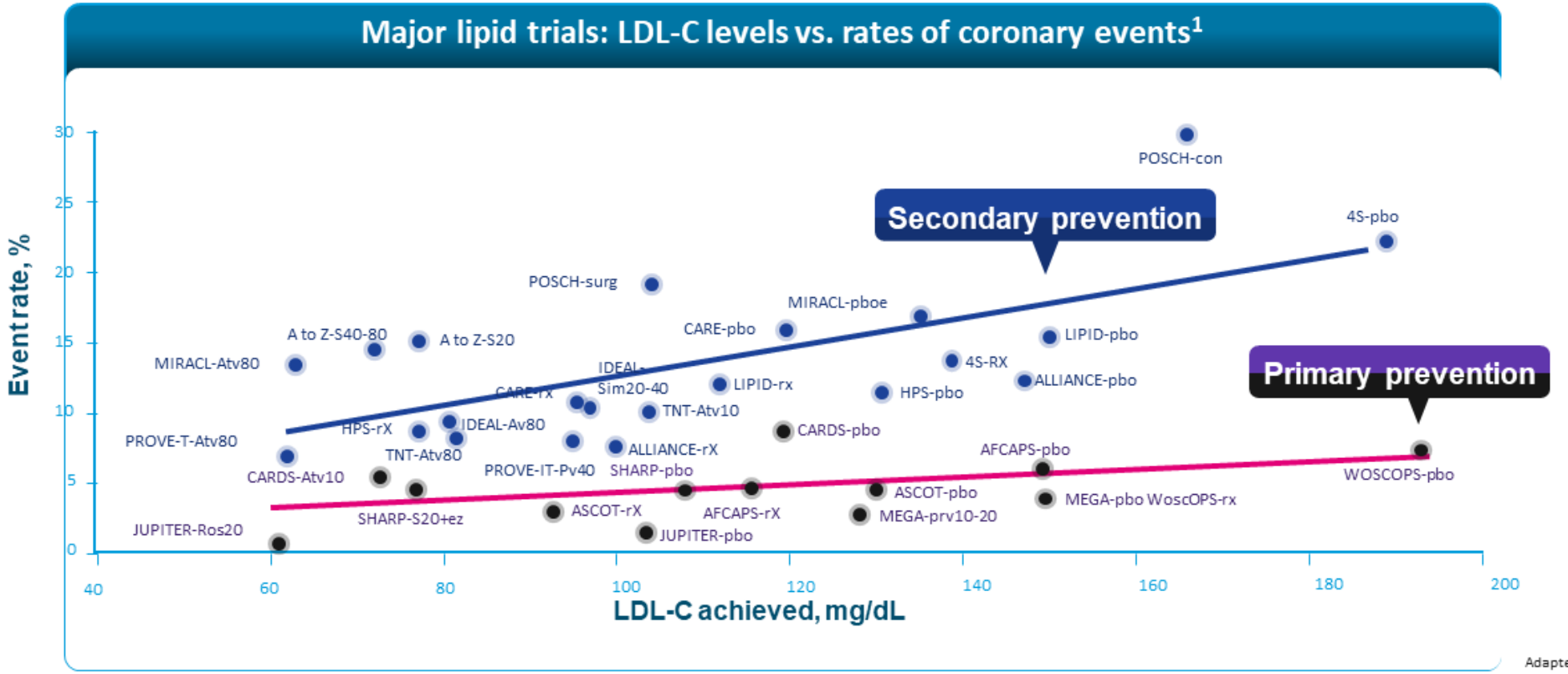
Cause of death	Events (%) Treatment (45 054)	Control (45 002)	RR (CI)
Vascular causes:			
CHD	**1548 (3·4%)**	**1960 (4·4%)**	**0·81 (0·76 –0·85)**
Stroke	265 (0·6%)	291 (0·6%)	0·91 (0·74 –1·11)
Other vascular	289 (0·6%)	302 (0·7%)	0·95 (0·78 –1·16)
Any non-CHD vascular	**554 (1·2%)**	**593 (1·3%)**	**0·93 (0·83 –1·03)**
Any vascular	**2102 (4·7%)**	**2553 (5·7%)**	**0·83 (0·79 –0·87)**
Non-vascular causes:			
Cancer	1094 (2·4%)	1069 (2·4%)	1·01 (0·91 –1·12)
Respiratory	98 (0·2%)	125 (0·3%)	0·82 (0·62 –1·08)
Trauma	51 (0·1%)	57 (0·1%)	0·89 (0·59 –1·34)
Other/unknown	487 (1·1%)	550 (1·2%)	0·87 (0·73 –1·03)
Any non-vascular	**1730 (3·8%)**	**1801 (4·0%)**	**0·95 (0·90 –1·01)**
Any death	**3832 (8·5%)**	**4354 (9·7%)**	**0·88 (0·84 –0·91)**



Lowering LDL-C saves lives!

Cholesterol Treatment Trialists' (CTT) Collaborators, et al. Lancet. 2005;366:1267-1278.

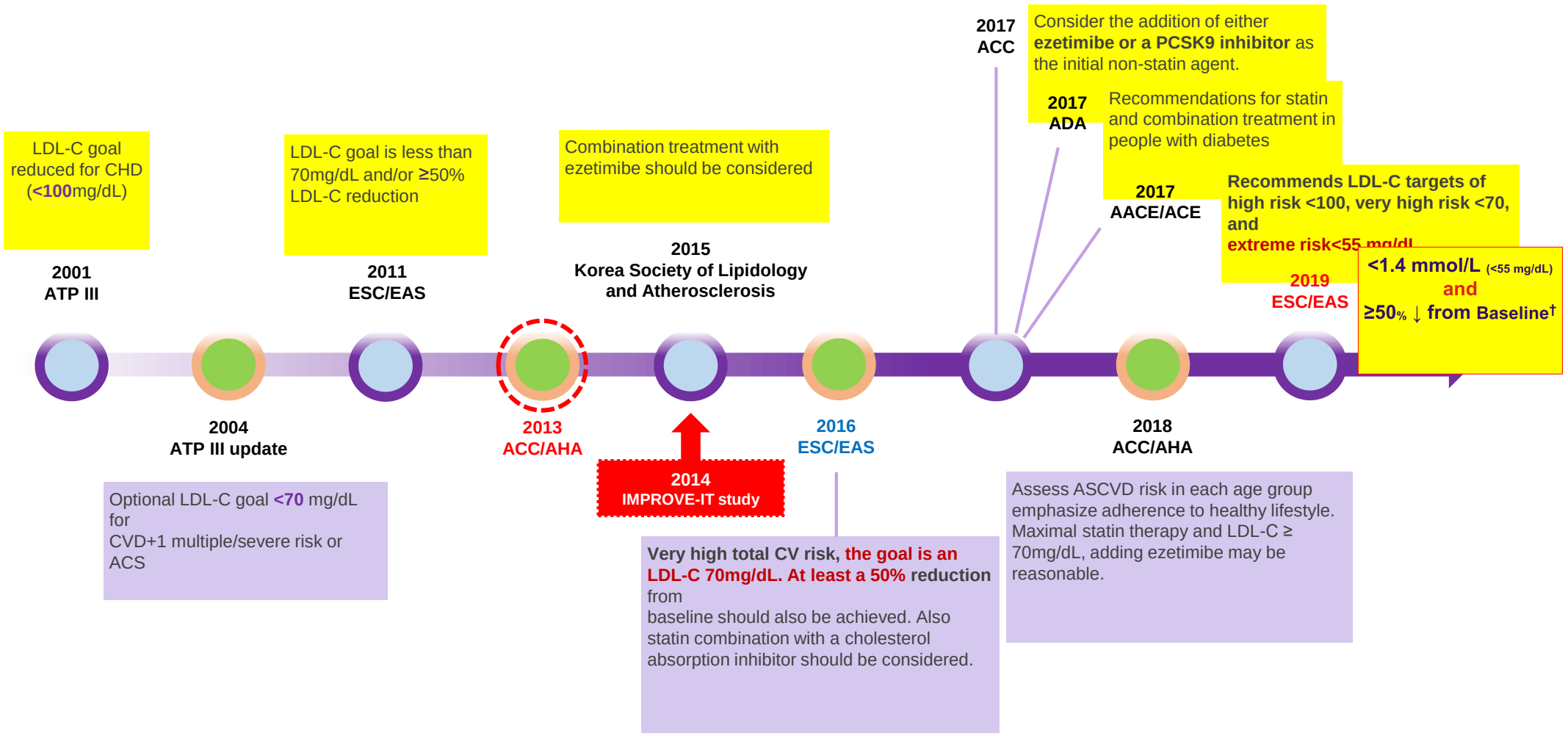
Relationship between achieved LDL-C levels and absolute risk[1]



Adapted from Raymond C, *et al*.[1]

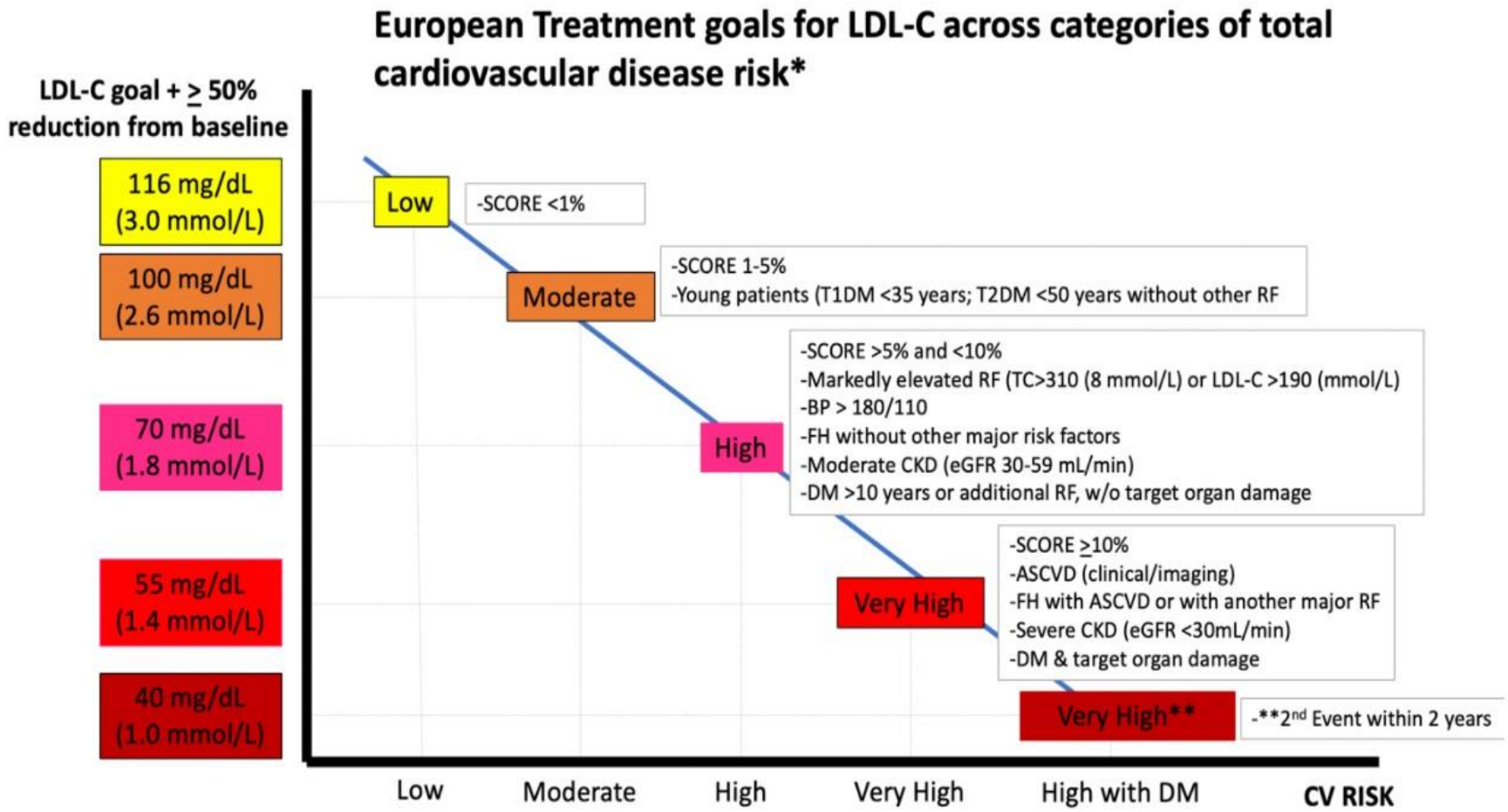
Raymond C, et al. New cholesterol guidelines: Worth the wait? Cleve Clin J Med. 2014;81(1):11-9.

Trends in guidelines for treatment of cholesterol



2019 ESC/EAS Dyslipidemia Guideline

Treatment goals for LDL-C



Eur Heart J. 2019:1-78

Three Key Concepts of Lipid-lowering Strategies

2019 ESC/EAS Guidelines

ESC European Society of Cardiology
European Heart Journal (2019) **00**, 1-78
doi:10.1093/eurheartj/ehz455
ESC/EAS GUIDELINES

2019 ESC/EAS Guidelines for the management of dyslipidaemias:
Lipid modification to reduce cardiovascular risk

- **Concept Change I: Start Early**
  - *Less "lipid-exposure" leads to prevention of lesion formation*
- **Concept Change II: Treat (Much More) Aggressively**
  - *From desirable target to "LDL-C elimination in the blood"*
- **Concept Change III: Use Combination Therapy**
  - *Statin + Ezetimibe (+/- PCSK9 Inhibitor) induced LDL-C lowering reduces CV risk*

Eur Heart J. 2019:1-78

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Addition of ezetimibe lowers LDL-C and CV events

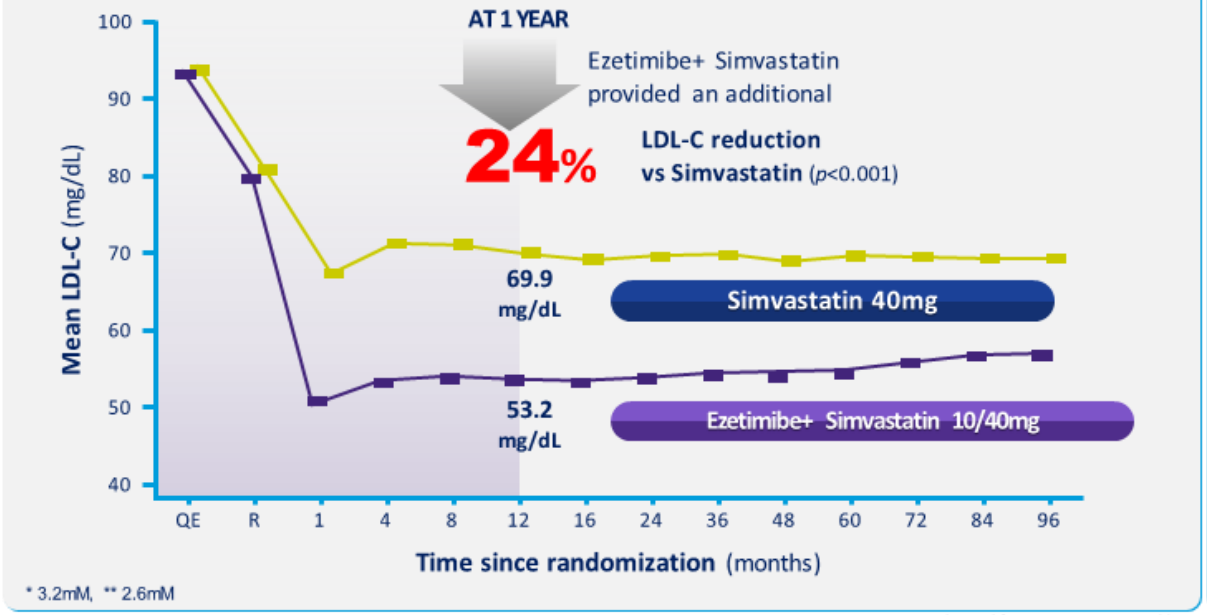
IMPROVE-IT

18,144 patients stabilized post ACS ≤ 10 days: LDL-C 50–125*mg/dL
(or 50–100**mg/dL if prior lipid-lowering Rx)

- **Ezitimibe/simvastatin 10/40 mg**
- **Simvastatin 40 mg**

Primary Endpoint:
CV death, MI, hospital admission for UA, coronary revascularization (≥ 30 days after randomization), **or stroke**
Duration: Minimum 2½--year follow-up (at least 5250 events)

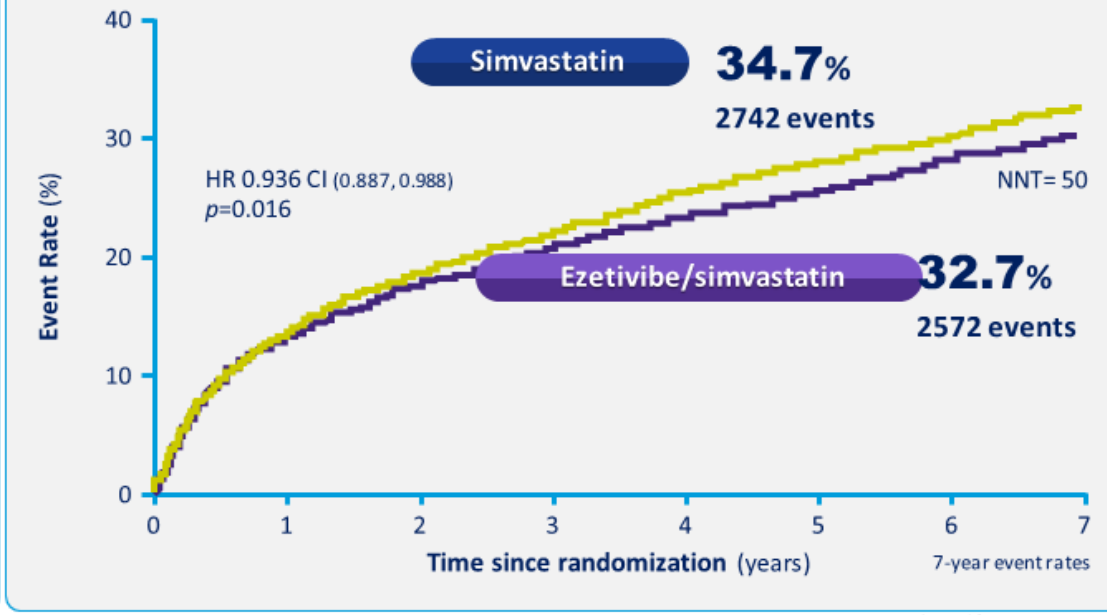
Change of LDL-cholesterol[4,5]



* 3.2mM, ** 2.6mM

Adapted from Cannon CP, *et al.*[4]

Primary Endpoint[4]



Adapted from Cannon CP, *et al.*[4]

N Engl J Med 2015; 372:2387-2397

Benefit of Targeting LDL-C <70mg/dL after an Ischemic Stroke

Treat Stroke to Target (TST)

Benefit of Targeting a LDL (Low-Density Lipoprotein) Cholesterol <70 mg/dL During 5 Years After Ischemic Stroke

Pierre Amarenco, MD; Jong S. Kim, MD; Julien Labreuche, BST; Hugo Charles, BST; Maurice Giroud, MD; Byung-Chul Lee, MD; Marie-Hélène Mahagne, MD; Norbert Nighoghossian, MD; Philippe Gabriel Steg, MD; Éric Vicaut, MD; Eric Bruckert, MD; on behalf of the Treat Stroke to Target Investigators*

Background and Purpose—The TST trial (Treat Stroke to Target) evaluated the benefit of targeting a LDL (low-density lipoprotein) cholesterol of <70 mg/dL to reduce the risk of cardiovascular events in 2860 patients with ischemic stroke with atherosclerotic stenosis of cerebral vasculature or aortic arch plaque >4 mm, in a French and Korean population. The follow-up lasted a median of 5.3 years in French patients (similar to the median follow-up time in the SPARCL trial [Stroke Prevention by Aggressive Reduction in Cholesterol Level]) and 2.0 years in Korean patients. Exposure duration to statin is a well-known driver for cardiovascular risk reduction. We report here the TST results in the French cohort.

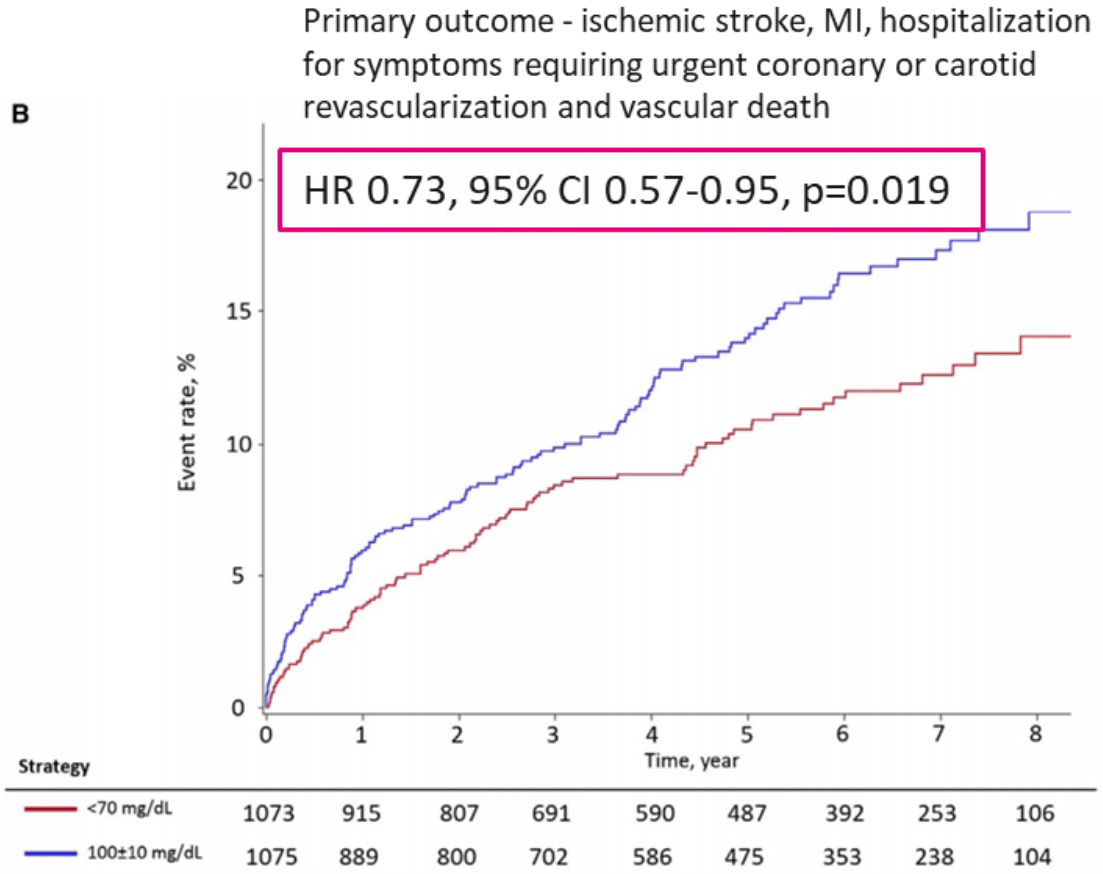
Methods—One thousand seventy-three French patients were assigned to <70 mg/dL (1.8 mmol/L) and 1075 to 100±10 mg/dL (90–110 mg/dL, 2.3–2.8 mmol/L). To achieve these goals, investigators used the statin and dosage of their choice and added ezetimibe on top if needed. The primary outcome was the composite of ischemic stroke, myocardial infarction, new symptoms requiring urgent coronary or carotid revascularization and vascular death.

Results—After a median follow-up of 5.3 years, the achieved LDL cholesterol was 66 (1.69 mmol/L) and 96 mg/dL (2.46 mmol/L) on average, respectively. The primary end point occurred in 9.6% and 12.9% of patients, respectively (HR, 0.74 [95% CI, 0.57–0.94]; *P*=0.019). Cerebral infarction or urgent carotid revascularization following transient ischemic attack was reduced by 27% (*P*=0.046). Cerebral infarction or intracranial hemorrhage was reduced by 28% (*P*=0.023). The primary outcome or intracranial hemorrhage was reduced by 25% (*P*=0.021). Intracranial hemorrhages occurred in 13 and 11 patients, respectively (HR, 1.17 [95% CI, 0.53–2.62]; *P*=0.70).

Conclusions—After an ischemic stroke of documented atherosclerotic origin, targeting a LDL cholesterol of <70 mg/dL during 5.3 years avoided 1 subsequent major vascular event in 4 (number needed to treat of 30) and no increase in intracranial hemorrhage.

Registration—URL: https://www.clinicaltrials.gov; Unique identifier: NCT01252875.

(*Stroke*. 2020;51:1231-1239. DOI: 10.1161/STROKEAHA.119.028718.)



Stroke. 2020;51:1231-1239.

Intensive lowering of LDL-C associated with lower CV & cerebral events

Outcomes	<70 mg/dL (N=1073)	100±10 mg/dL (N=1075)	Hazard Ratio (95% CI)	*P* Value
Primary outcome				
Major cardiovascular events	103/1073 (9.6)	139/1075 (12.9)	0.74 (0.57–0.95)*	0.019*
Death from cardiovascular causes	17/1073 (1.6)	22/1075 (2.0)		
Fatal cerebral infarction or undetermined stroke	3/1073 (0.3)	6/1075 (0.6)		
Fatal myocardial infarction	1/1073 (0.1)	1/1075 (0.1)		
Other vascular deaths	7/1073 (0.7)	5/1075 (0.5)		
Sudden death	6/1073 (0.6	10/1075 (0.9)		
Nonfatal cerebral infarction or undetermined stroke	65/1073 (6.1)	89/1075 (8.3)		
Nonfatal acute coronary syndrome	15/1073 (1.4)	22/1075 (2.0)		
Urgently required coronary revascularization	3/1073 (0.3)	3/1075 (0.3)		
Urgently required carotid revascularization	3/1073 (0.3)	3/1075 (0.3)		
Secondary outcomes				
Myocardial infarction or urgent coronary revascularization	18/1073 (1.7)	27/1075 (2.5)	0.66 (0.37–1.20)	0.18
Cerebral infarction or urgent carotid or cerebral artery revascularization	72/1073 (6.7)	98/1075 (9.1)	0.73 (0.54–0.99)	0.046
Cerebral infarction or TIA	103/1073 (9.6)	125/1075 (11.6)	0.83 (0.64–1.08)	0.16
Any revascularization procedure (both urgent and elective)	90/1073 (8.4)	87/1075 (8.0)	1.01 (0.75–1.36)	0.94
Carotid	17/90	22/87		
Coronary	41/90	41/87		
Peripheral	32/90	24/87		
Vascular death	22/1073 (2.1)	29/1075 (2.7)	0.76 (0.44–1.32)	0.32
All-cause death	86/1073 (8.0)	86/1075 (8.0)	1.0 (0.74–1.35)	0.99
Cerebral infarction or intracranial hemorrhage	80/1073 (7.5)	112/1075 (10.4)	0.72 (0.54–0.96)	0.023
Intracranial hemorrhage	13/1073 (1.2)	11/1075 (1.0)	1.17 (0.53–2.62)	0.70
Newly diagnosed diabetes mellitus†	87/1073 (8.1)	66/1075 (6.1)	1.33 (0.97–1.84)	0.076
Primary outcome or intracranial hemorrhage	111/1073 (10.3)	146/1075 (13.6)	0.75 (0.58–0.96)	0.021

26% reduction

27% reduction

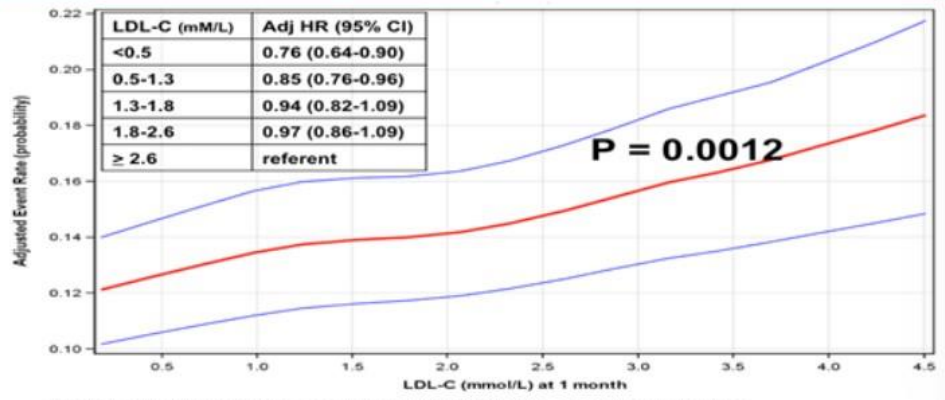
Stroke. 2020;51:1231-1239.

Benefit of intensive cholesterol-lowering therapy

Clinical efficacy and safety of achieving very low LDL-CLDL-cholesterol concentrations with the PCSK9 inhibitor evolocumab (FOURIER trial)

Robert P Giugliano, Terje R Pedersen, Jeong-Gun Park, Gaetano M De Ferrari, Zbigniew A Gaciong, Richard Ceska, Kalman Toth, Ioanna Gouni-Berthold, Jose Lopez-Miranda, François Schiele, François Mach, Brian Ott, Estella Kanevsky, Armando Lira Pineda, Ransi Somaratne, Scott M Wasserman, Anthony C Keech, Peter S Sever, Marc S Sabatine; on behalf of the FOURIER Investigators

Primary Efficacy Endpoint*



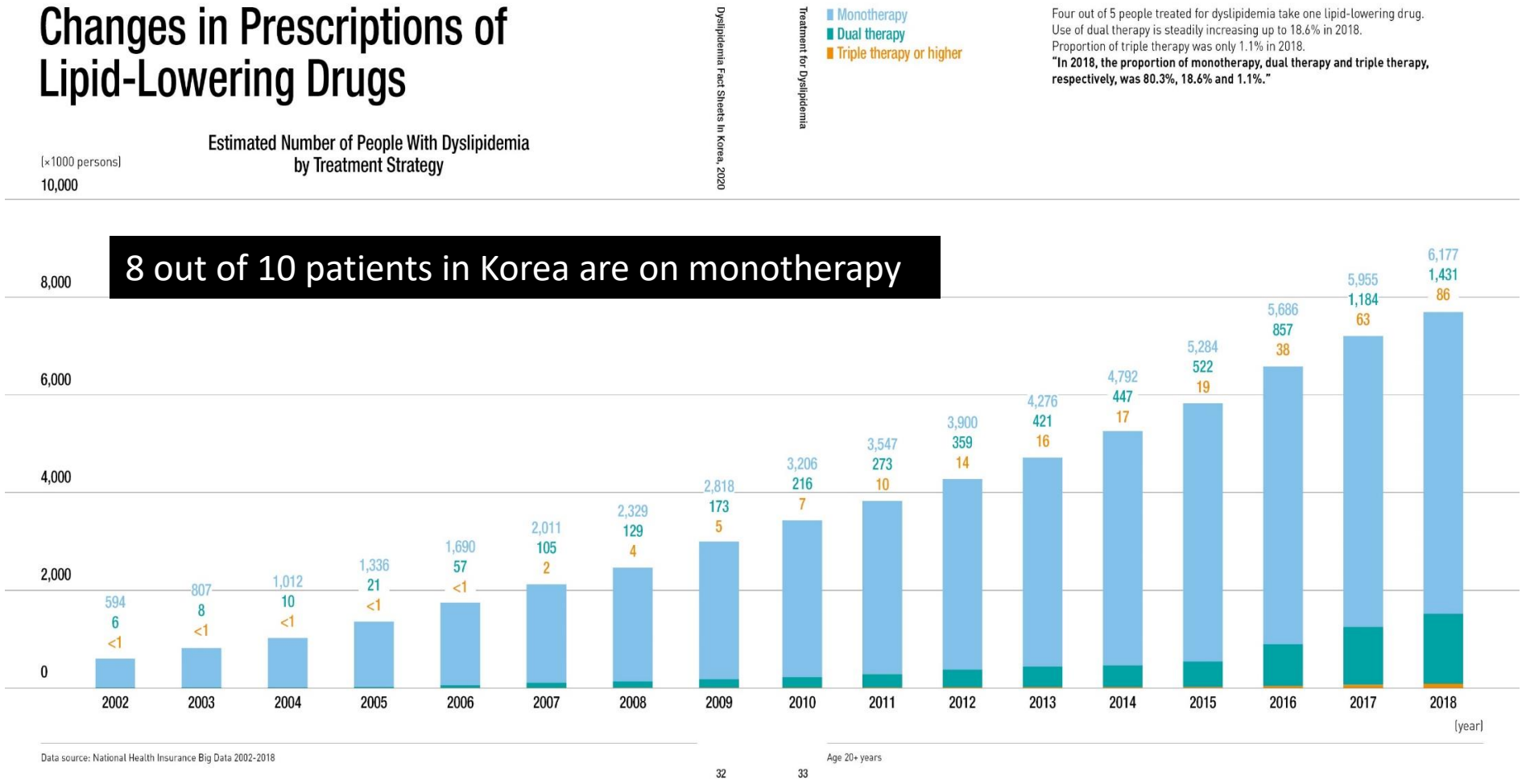
*CV death, MI, stroke, hospitalization for UA, coronary revasc

Exploratory Analysis – 1 Achieved LDL-C <0.4 mM/L*

	LDL-C at 4 Weeks			
	<0.4 (N=1335)	≥2.6 (N=4395)		
	n (%)	n (%)	Adjusted HR (95% CI)	P
Efficacy Endpoints				
CVD, MI, stroke, UA, cor revasc	105 (7·9)	521 (11·9)	0·71 (0·56-0·89)	0·003
CV death, MI, stroke	66 (4·9)	345 (7·8)	0·66 (0·50-0·88)	0·005
Safety Endpoints				
Serious AE	313 (23·4)	1022 (23·3)	0·96 (0·81-1·13)	0·63
AE -> drug DC	42 (3·1)	149 (3·4)	0·89 (0·60-1·32)	0·56

Lancet 2017;390:1962

Trends in lipid lowering therapy



The Korean Society of Lipid and Atherosclerosis. Dyslipidemia fact sheet in Korea 2018

LDL-C goal achievement and incidence of cardiovascular disease in South Korean patients

PLOS ONE

RESEARCH ARTICLE

Achievement of the low-density lipoprotein cholesterol goal among patients with dyslipidemia in South Korea

Siin Kim[1], Sola Han[1], Pratik P. Rane[2], Yi Qian[2], Zhongyun Zhao[2], Hae Sun Suh[1]*

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OPEN ACCESS

Citation: Kim S, Han S, Rane PP, Qian Y, Zhao Z, Suh HS (2020) Achievement of the low-density lipoprotein cholesterol goal among patients with dyslipidemia in South Korea. PLoS ONE 15(1): e0228472. https://doi.org/10.1371/journal.pone.0228472

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Peer Review History: PLOS recognizes the benefits of transparency in the peer review process; therefore, we enable the publication of

Abstract

Background

It is important to achieve the low-density lipoprotein cholesterol (LDL-C) goal recommended by clinical guidelines in managing the risk of cardiovascular (CV) events, however, the current management of LDL-C in actual clinical settings is suboptimal. We examined the LDL-C level among patients with dyslipidemia against the 2015 Korean guidelines, the crude rates of CV events based on LDL-C goal achievement, and the factors associated with LDL-C goal achievement.

Methods

This was a retrospective cohort study using the National Health Insurance Service–National Health Screening Cohort (NHIS-HEALS) database from 2006 to 2013. Patients who had a health examination with LDL-C measurement between January 1, 2007, and December 31, 2011 were identified. Patients were required to have at least one diagnosis of dyslipidemia during the 1 year before the index date, defined as the first date of LDL-C measurement. The 2015 Korean guidelines were used to measure LDL-C goal achievement based on the CV risk level. Crude CV event rates were calculated for total and individual CV events as the

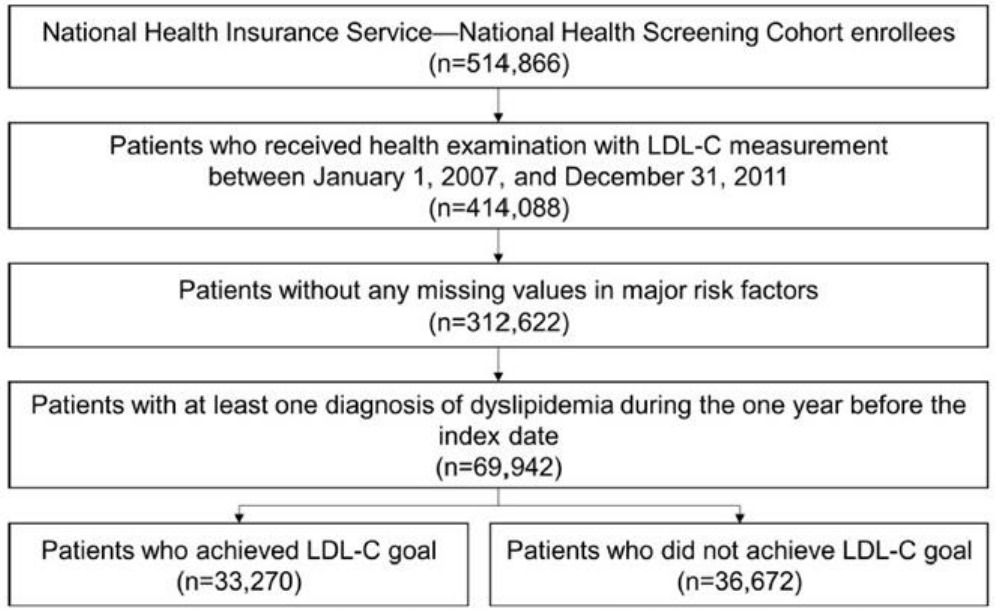


Fig 2. Sample selection process. The index date was defined as the first date of health examination with LDL-C measurement. LDL-C goals per CV risk level were defined by the 2015 Korean guidelines. LDL-C, low-density lipoprotein cholesterol.

https://doi.org/10.1371/journal.pone.0228472.g002

Conclusions

In South Korea, LDL-C goal achievement among patients with very high or high CV risk was suboptimal. Patients who did not achieve the goal showed a higher rate of CV events during the follow-up period than patients who achieved the goal. LDL-C management strategies should be highlighted in dyslipidemia patients who are less likely to achieve the goal, such as female, overweight or obese patients, patients not adherent to statin, or patients with very high or high CV risk.

PLoS One. 2020 Jan 30;15(1):e0228472

LDL-C goal achievement and incidence of cardiovascular disease in South Korean patients

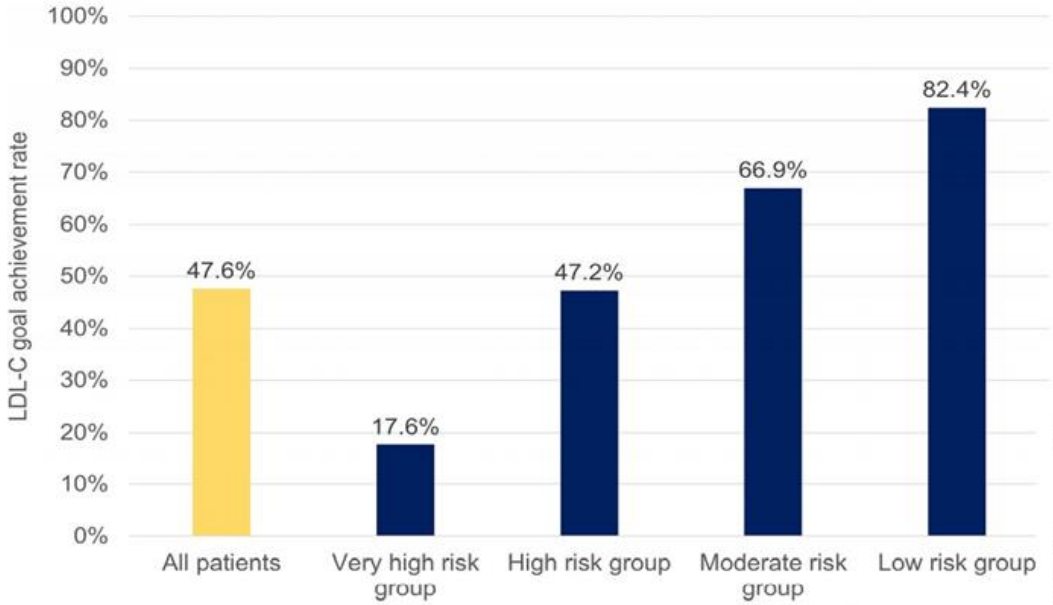


Fig 3. LDL-C goal achievement rates among patients with dyslipidemia (based on the 2015 Korean guidelines). LDL-C, low-density lipoprotein cholesterol.

https://doi.org/10.1371/journal.pone.0228472.g003

<70 mg/dL for very high risk

<100 mg/dL for high risk

<130 mg/dL for moderate risk

<160 mg/dL for low risk.

Table 2. Crude cardiovascular event rates based on LDL-C goal achievement.

CV events	LDL-C goal achievers		LDL-C goal non-achievers		*P*-value[a]
	Number of events	Rates per 100 PYs	Number of events	Rates per 100 PYs	
Total CV events[b]	11,560	11.93	19,890	24.35	<0.0001
All-cause death	539	0.56	718	0.88	<0.0001
CV death	39	0.04	73	0.09	<0.0001
Acute coronary syndrome[c]	1,764	1.82	3,021	3.70	<0.0001
Ischemic stroke	1,686	1.74	3,584	4.39	<0.0001
Peripheral artery disease	7,571	7.81	12,567	15.38	<0.0001

CV, cardiovascular; LDL-C, low-density lipoprotein cholesterol; PY, person-year.

[a]*P*-values for differences between rates of LDL-C goal achievers and non-achievers.

[b]Total CV events included all-cause death, acute coronary syndrome, ischemic stroke, and peripheral artery disease.

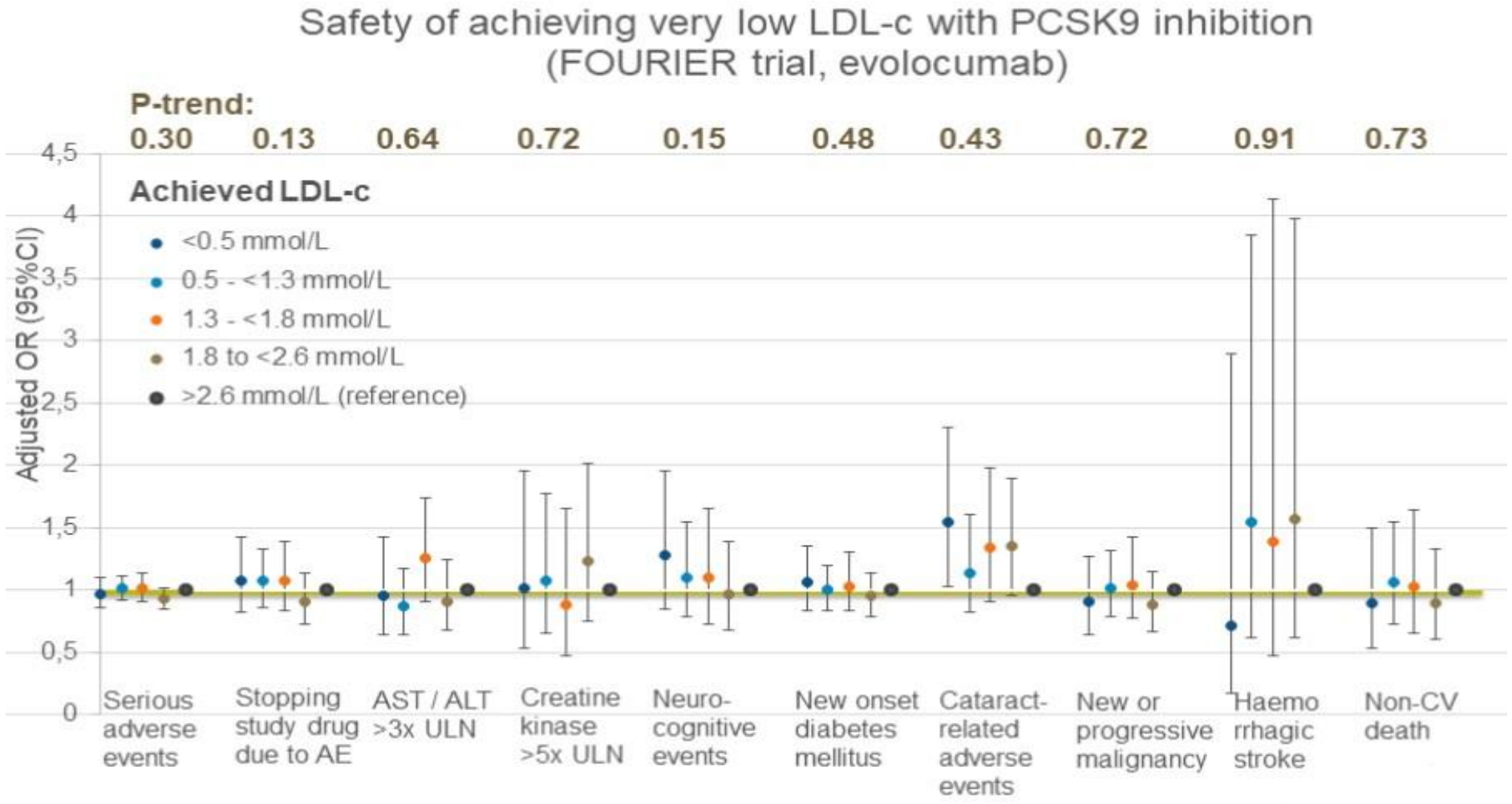
[c]Acute coronary syndrome is a composite of myocardial infarction and unstable angina.

https://doi.org/10.1371/journal.pone.0228472.t002

PLoS One. 2020 Jan 30;15(1):e0228472

Safety of very low LDL-C

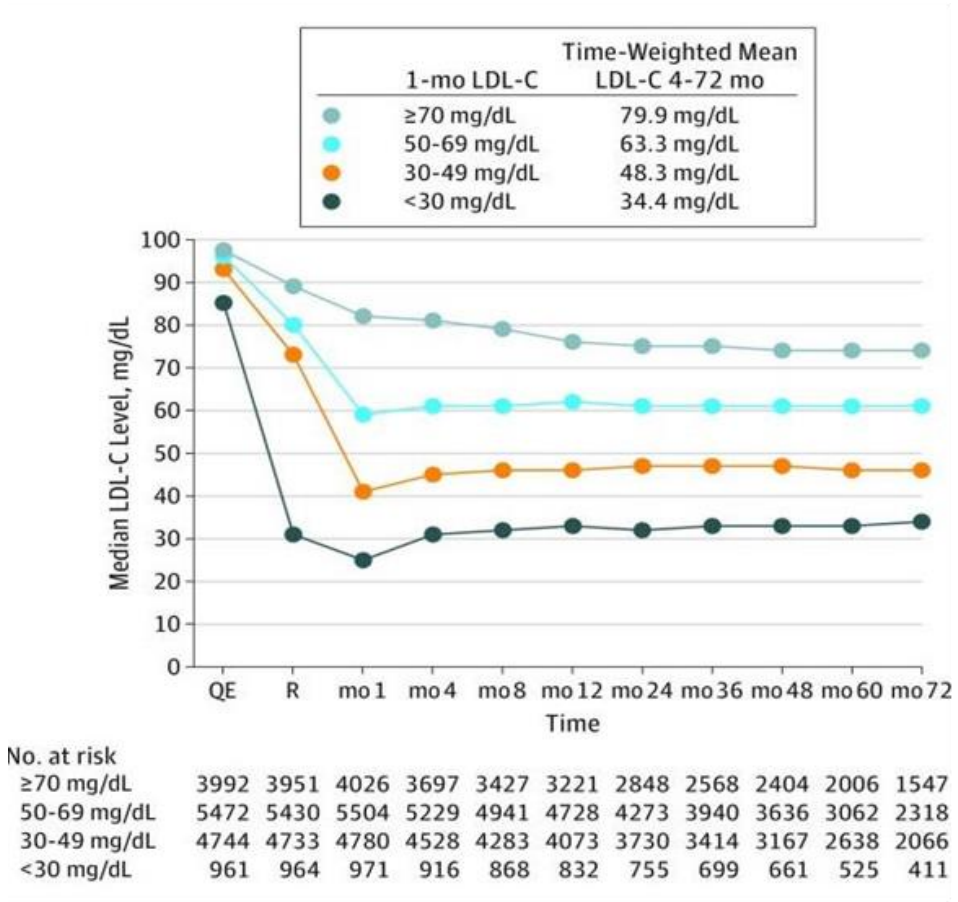
– Insights from the FOURIER trial

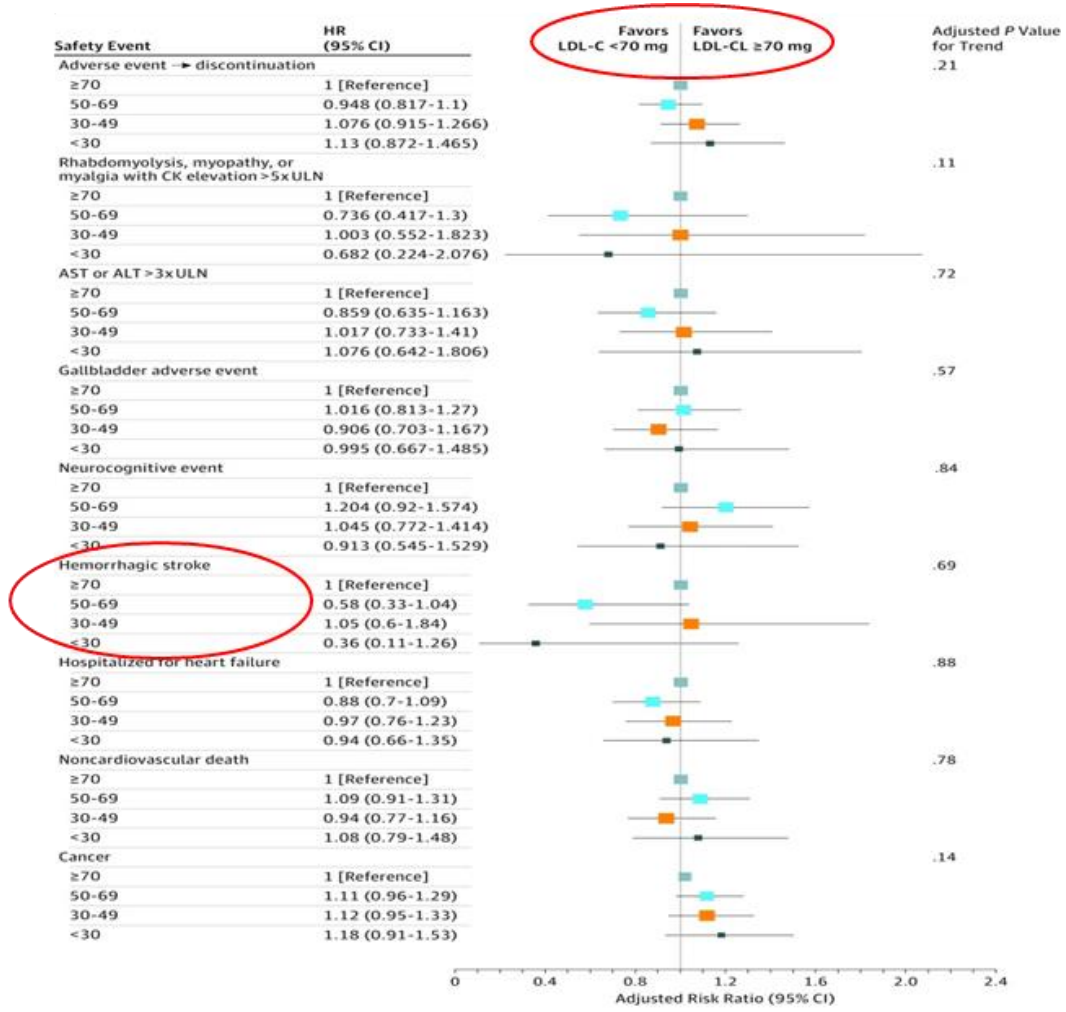


Lancet. 2017;390(10106):1962-1971

Safety of very low LDL-C

– Insights from IMPROVE-IT subanalysis





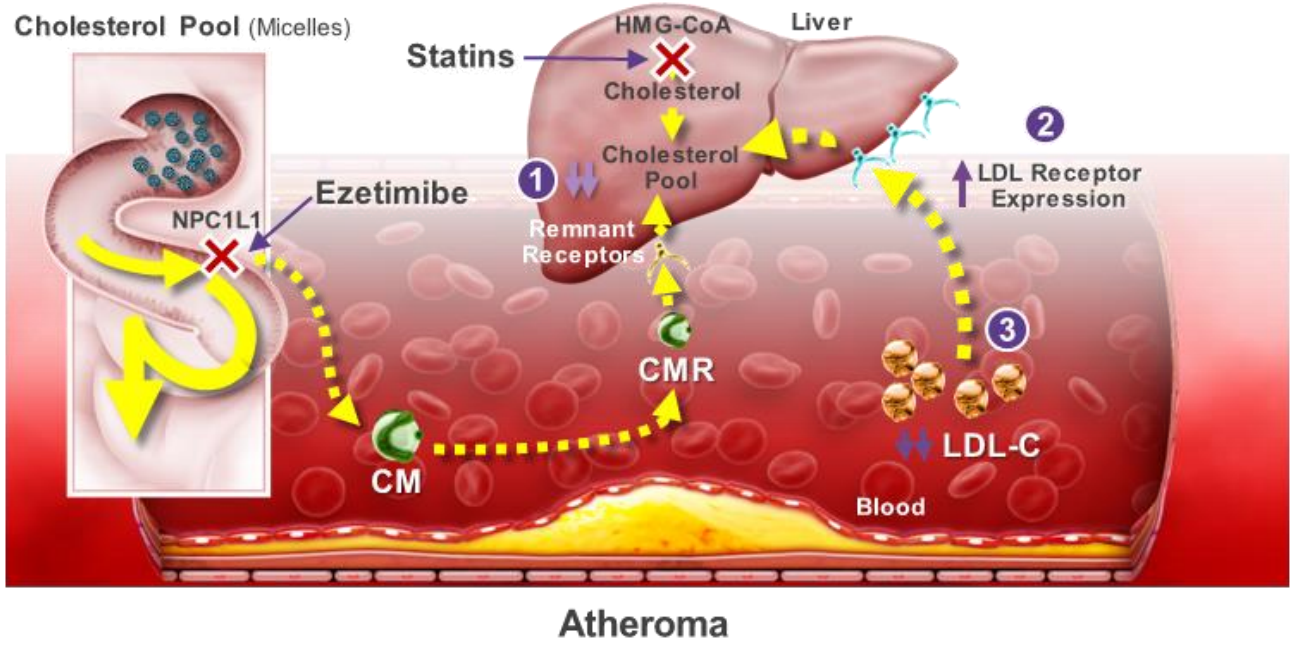
JAMA Cardiol. 2017 May 1;2(5):547-555.

Contents

- Relationship between LDL-C and CV disease
- “Lower is better” - evidence & safety
- **Benefit of Ezetimibe combination**

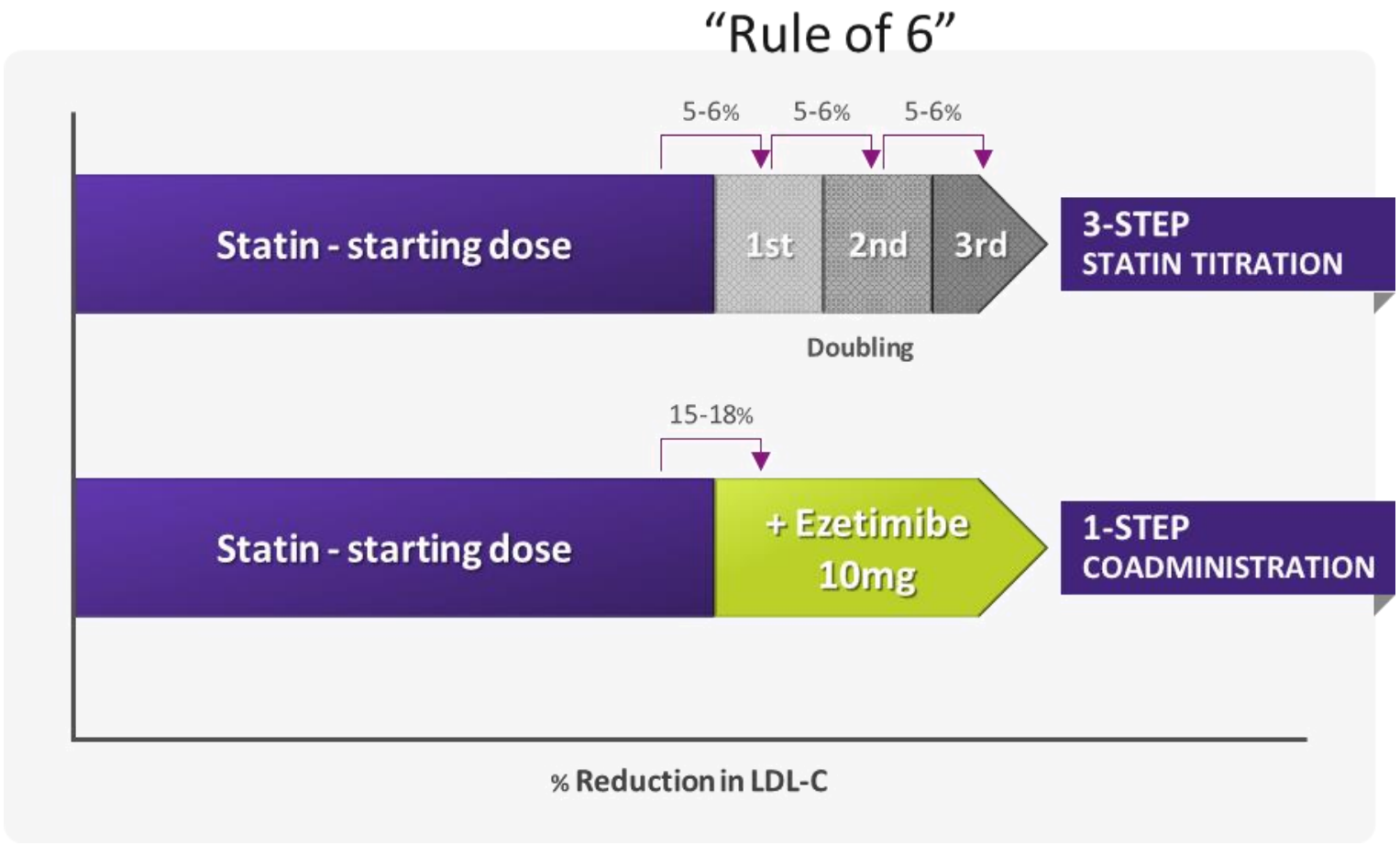
Ezetimibe and statins have complementary mechanisms of action

- **Together, ezetimibe in combination with a statin provides[1]:**
  1. Reduction of hepatic cholesterol
  2. Increased LDL receptor expression
  3. Increased clearance of plasma LDL-C



Vas Health Risk Manag. 2008;4:267-278.

Ezetimibe add-on therapy lowers LDL-C as much as 8x dose of statins

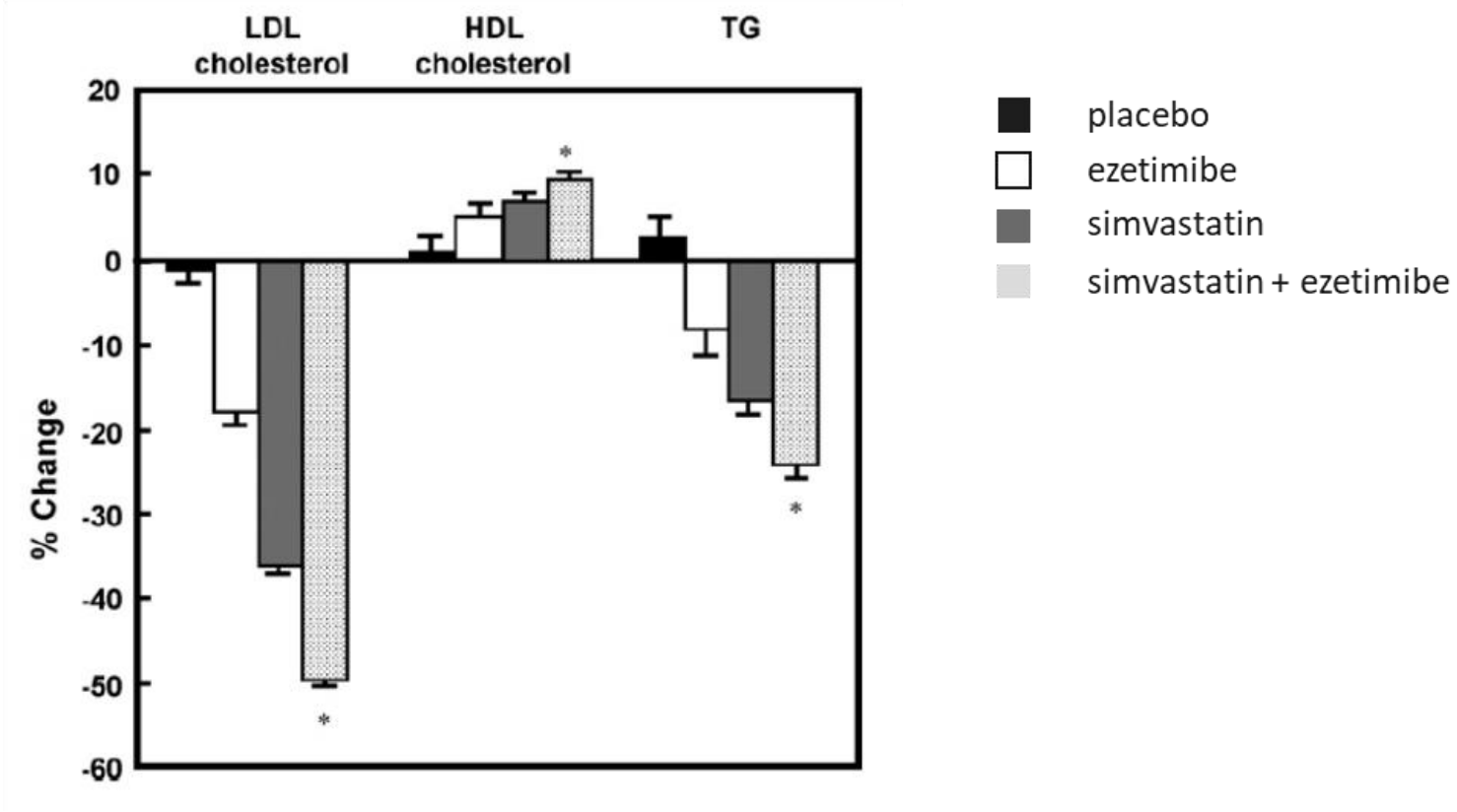


Clin Ther. 2004;26:1758-1773

Benefits of ezetimibe treatment

cholesterol improvement

- Addition of ezetimibe not only improved LDL cholesterol, but also HDL-C, TG



Journal of Cardiology (2008) 52, 1—6

Benefits of ezetimibe treatment

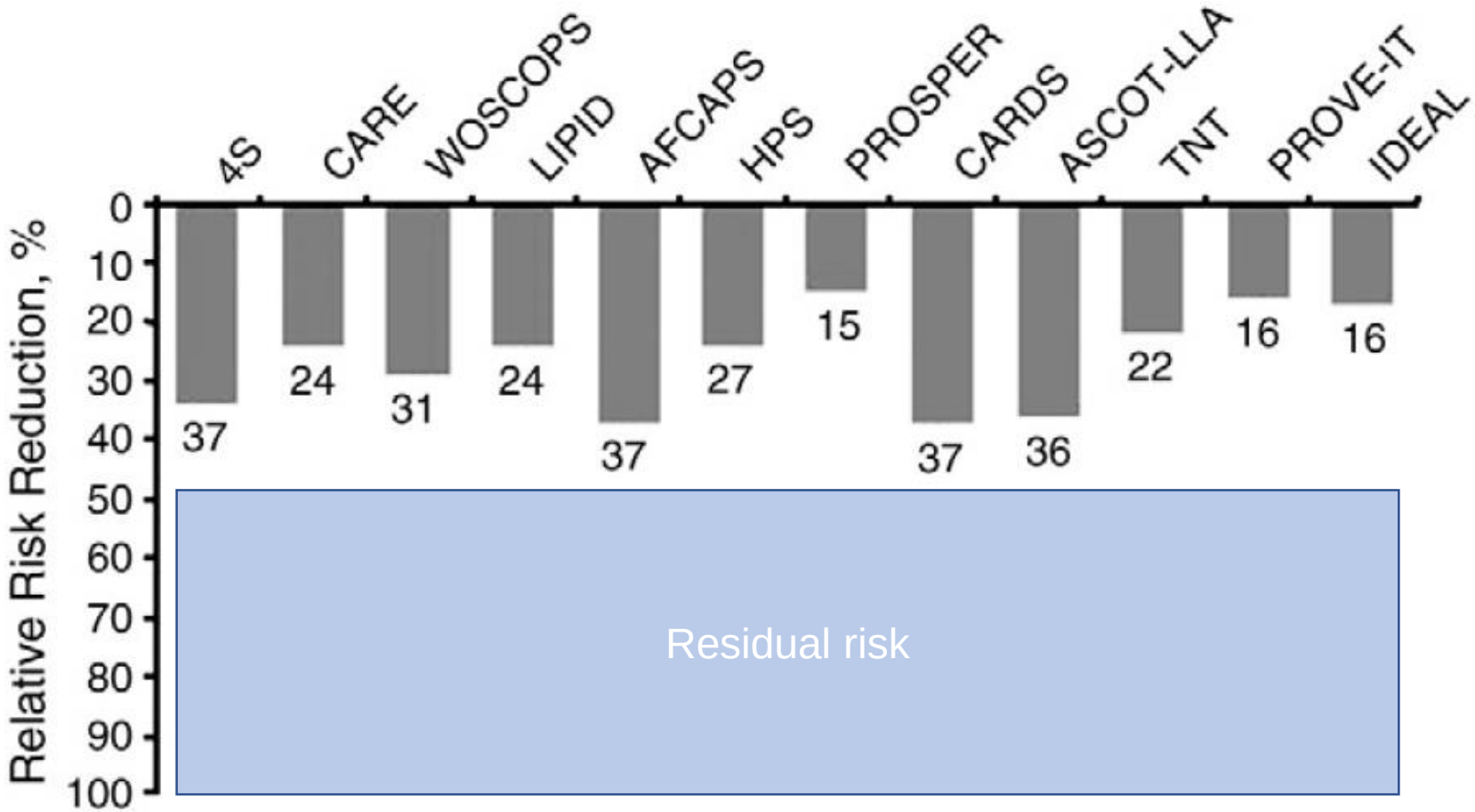
metabolic improvement

A 12-week treatment of additional ezetimibe in patients with dyslipidemia improved glucose metabolism and inflammatory markers

	n	Baseline	After treatment	% change	*p* value
Fasting Blood Glucose (mg/dL)	116	94.0 ± 23.8	94.3 ± 28.4	0.5 ± 14.7	NS
Fasting Insulin (μIU/mL)	102	12.7 ± 17.5	9.4 ± 8.2	− 12.8 ± 9.8	$p<0.05$
HbA1c (%)	35	6.2 ± 1.0	5.9 ± 1.0	− 3.4 ± 8.6	$p<0.05$
High sensitive C reactive protein (ng/mL)	76	601.8 ± 461.6	485.1 ± 366.9	− 10.8 ± 36.8	$p<0.01$
High molecular weight adiponectin (μg/mL)					
Total	102	10.8 ± 5.9	11.8 ± 6.8	13.4 ± 47.5	$p<0.01$
Male	42	8.6 ± 4.7	8.9 ± 4.8	5.4 ± 26.2	NS
Female	60	12.4 ± 6.2	13.8 ± 7.2	19.2 ± 57.6	$p<0.01$

J atheroscler thromb 2010;17:106-114.

Limitations of high-dose statin monotherapy



Int J Cardiol 2013;166:8-14.

Limitations of high-dose statins

Risk of diabetes mellitus

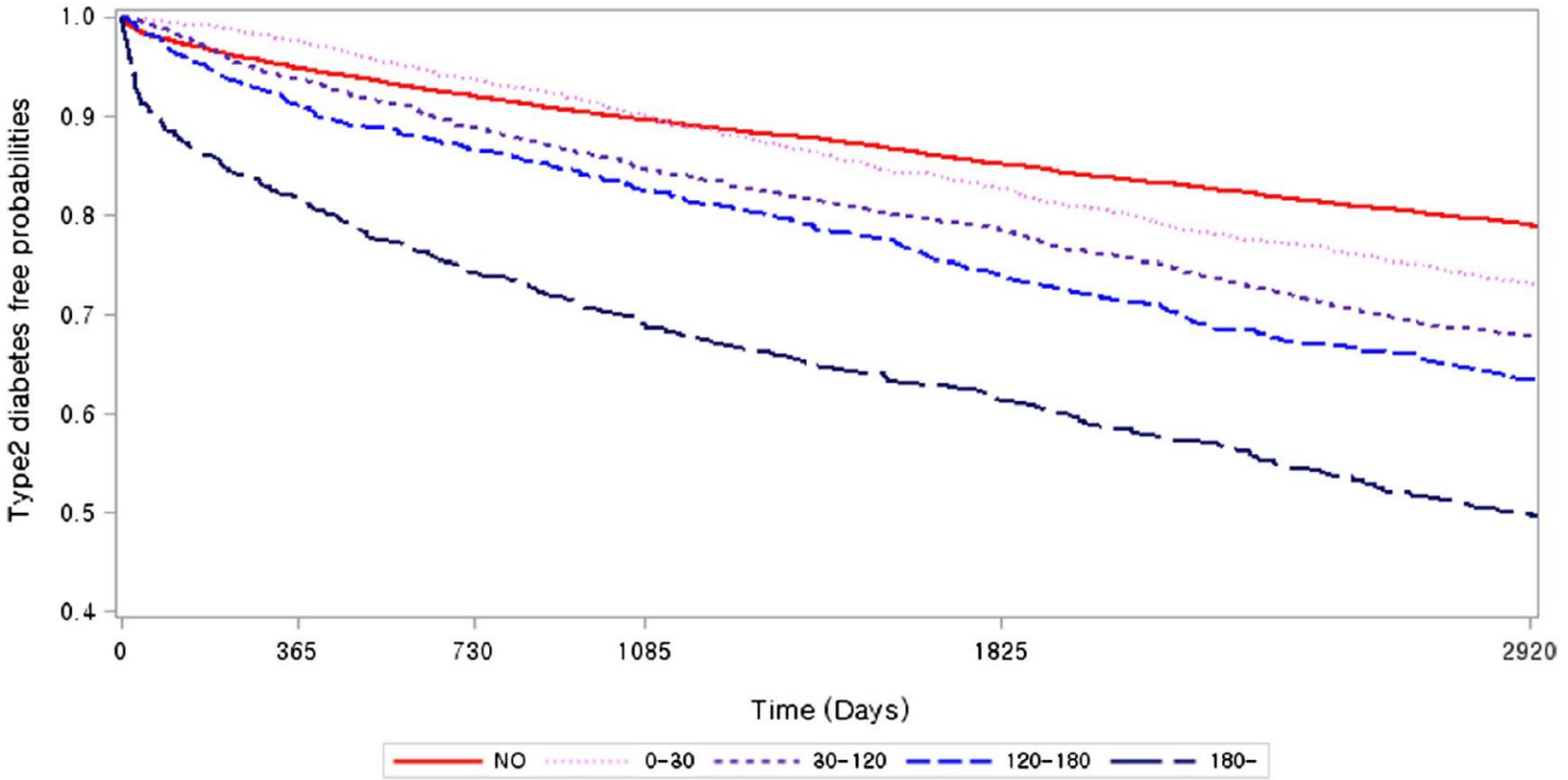
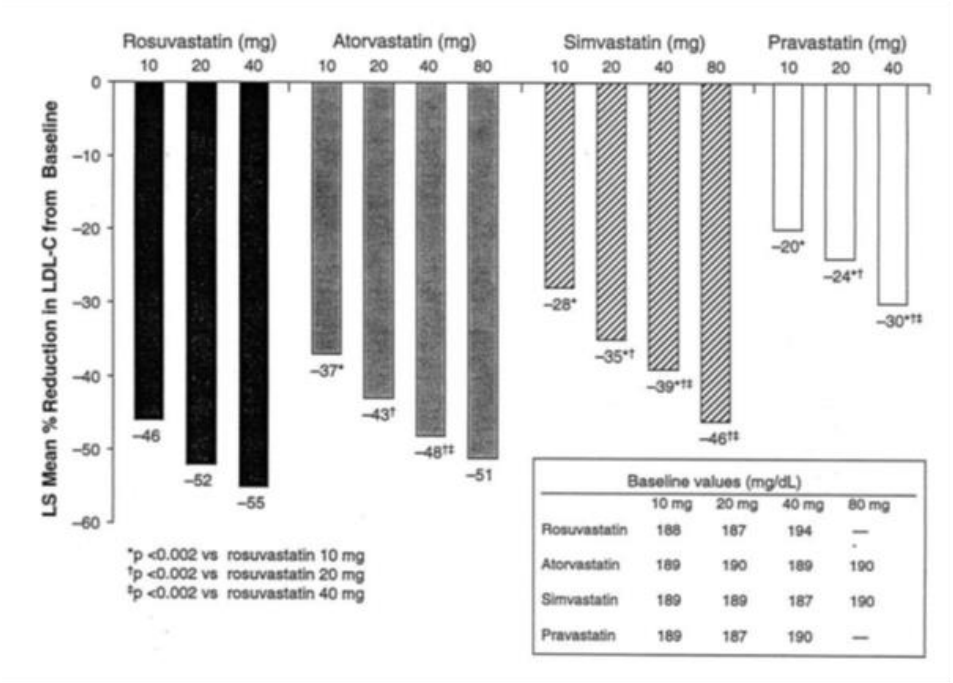


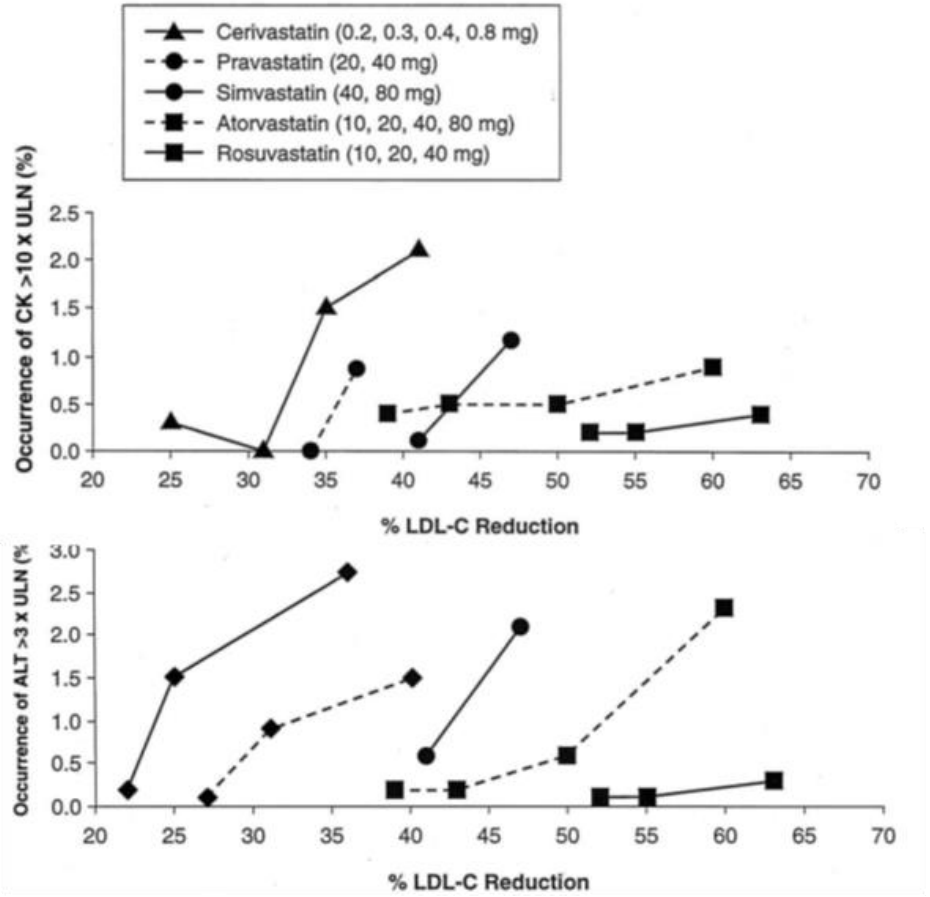
Fig. 3 Kaplan-Meier curves according to cumulative daily defined dose (cDDD) per year

Cardiovasc Diabetol. 2020;19(1):67.

Limitations of high-dose statins

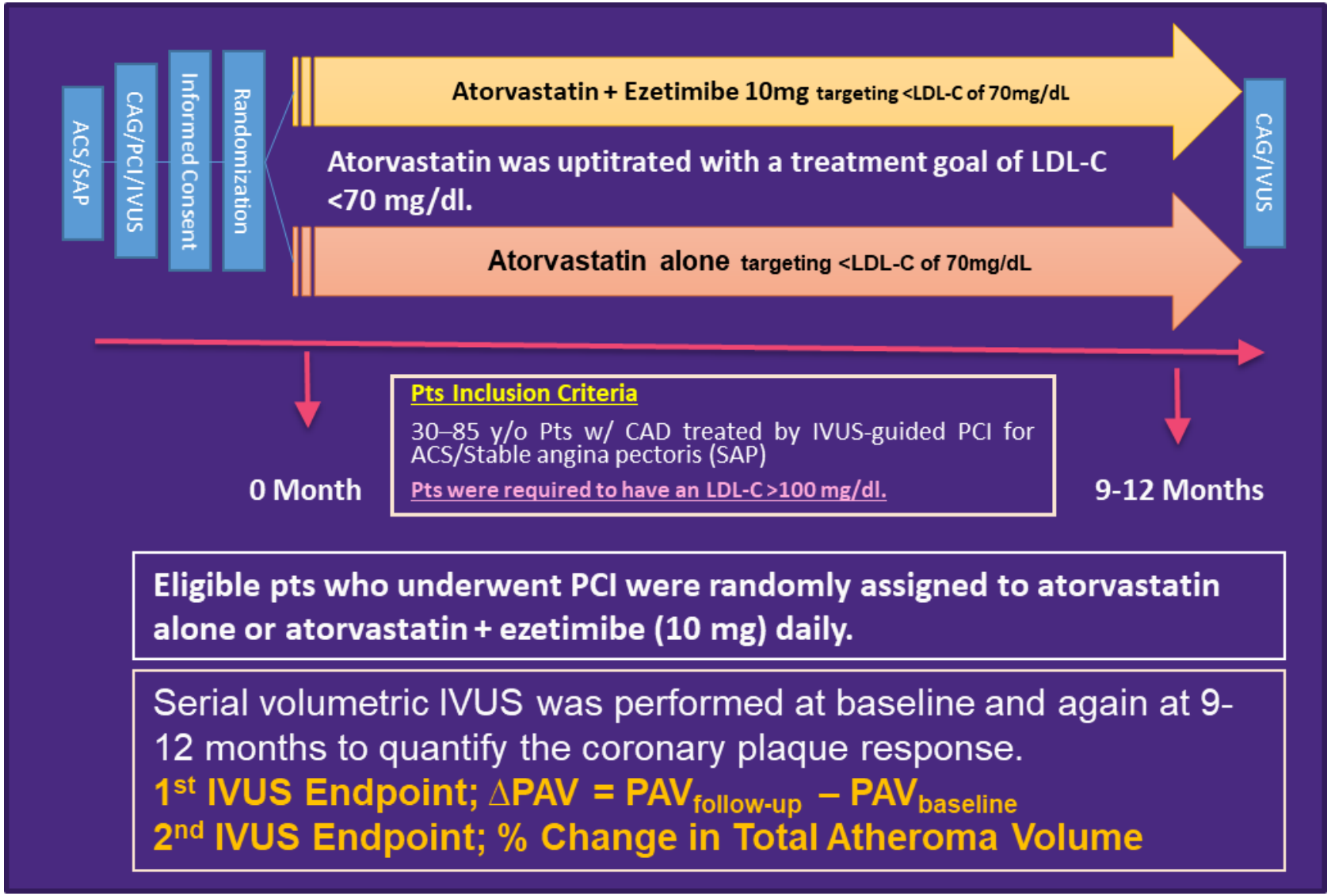
Risk of SAMS





Am J Cardiol 2003;92(suppl):23K-29K.

PRECISE-IVUS Study



Eligible pts who underwent PCI were randomly assigned to atorvastatin alone or atorvastatin + ezetimibe (10 mg) daily.

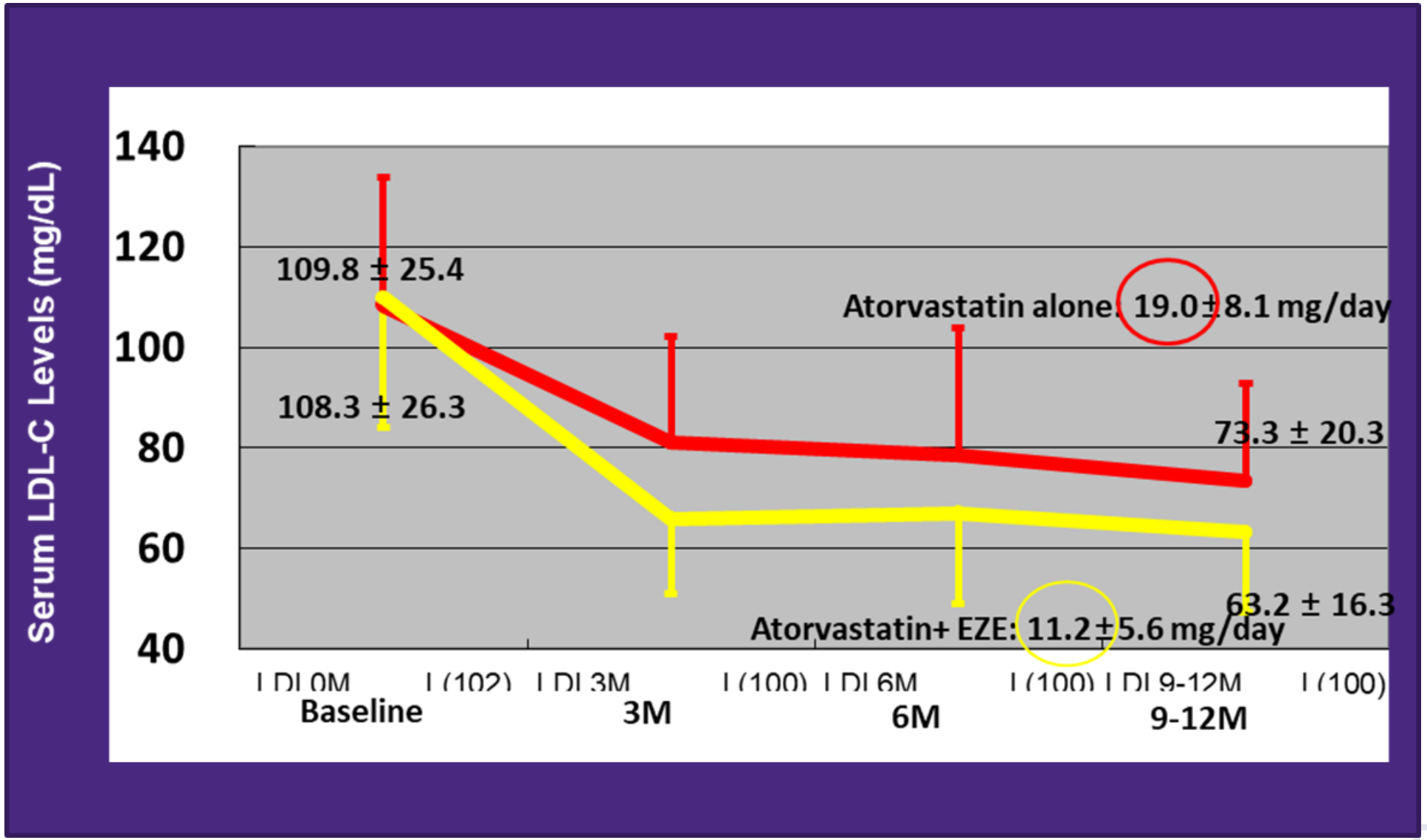
Serial volumetric IVUS was performed at baseline and again at 9-12 months to quantify the coronary plaque response.

1st IVUS Endpoint; ΔPAV = $PAV_{follow\text{-}up}$ – $PAV_{baseline}$

2nd IVUS Endpoint; % Change in Total Atheroma Volume

Tsujita K, Ogawa H, et al. J Am Coll Cardiol 2015;66:495–507

Changes in LDL-C



Tsujita K, Ogawa H, et al. J Am Coll Cardiol 2015;66:495–507

Coronary Plaque Regression

	Baseline			9–12 Months Follow-Up		
	LZ Group (n = 100)	L Group (n = 102)	p Value	LZ Group (n = 100)	L Group (n = 102)	p Value
Plaque volume (mm^3)	73 (38-117)	76 (46-128)	0.5	70 (35-107)	77 (45-126)	0.2

For superiority, the absolute change in PAV decreased by –1.4% in the Atorvastatin +EZE group and by –0.3% in the Atorvastatin group. A significantly greater percentage of pts in the Atorvastatin +EZE group showed coronary plaque regression (78% vs. 58%).

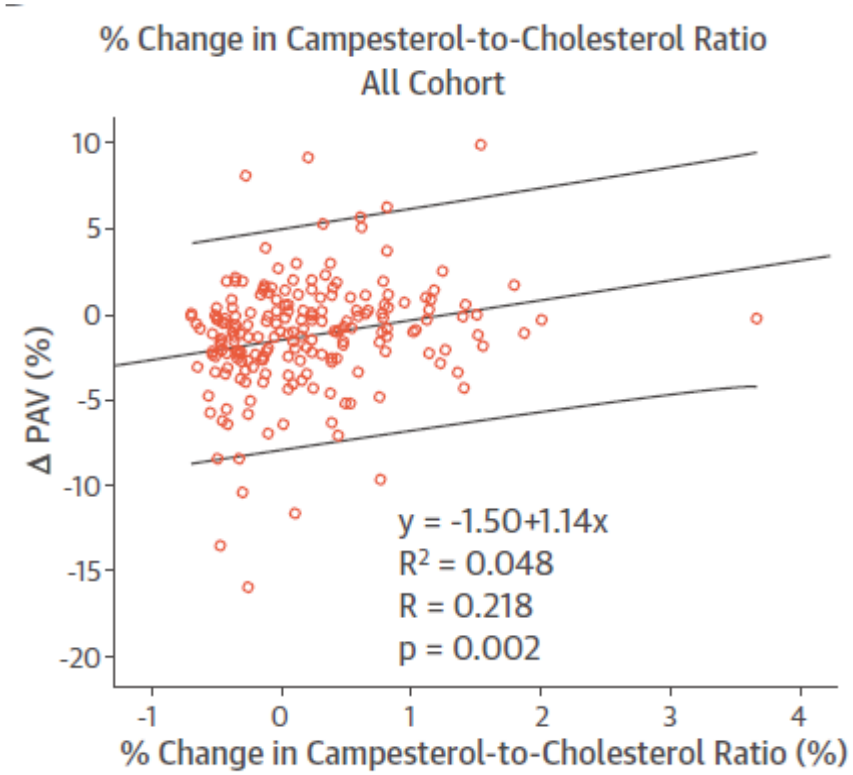
Lesion length (mm)	10.1 (5.6-14.6)	12.4 (7.5-16.0)	0.11	9.7 (5.8-14.5)	11.9 (7.2-15.9)	0.10

	Change				
	LZ Group (n = 100)	p Value With Baseline	L Group (n = 102)	p Value With Baseline	p Value Between Groups
Plaque volume (mm^3)	-3.9 (-10.6-0.0)	<0.001	-1.0 (-6.8-5.7)	0.4	0.001
PAV (%)	-1.4 (-3.4--0.1)	<0.001	-0.3 (-1.9-0.9)	0.03	0.001
ACS cohort	-2.3 (-3.7--0.5)	<0.001	-0.2 (-1.3-0.5)	0.2	<0.001
SAP cohort	-1.2 (-2.2--0.1)	0.001	-0.7 (-2.3-1.1)	0.08	0.2
TAV_{norm} (mm^3)	-5.3 (-12.4-0.1)	<0.001	-1.2 (-5.7-3.3)	0.1	<0.001
Vessel volume (mm^3)	-4.1 (-12.6-3.1)	0.001	-0.6 (-11.8-10.6)	0.9	0.04

Tsujita K, Ogawa H, et al. J Am Coll Cardiol 2015;66:495–507

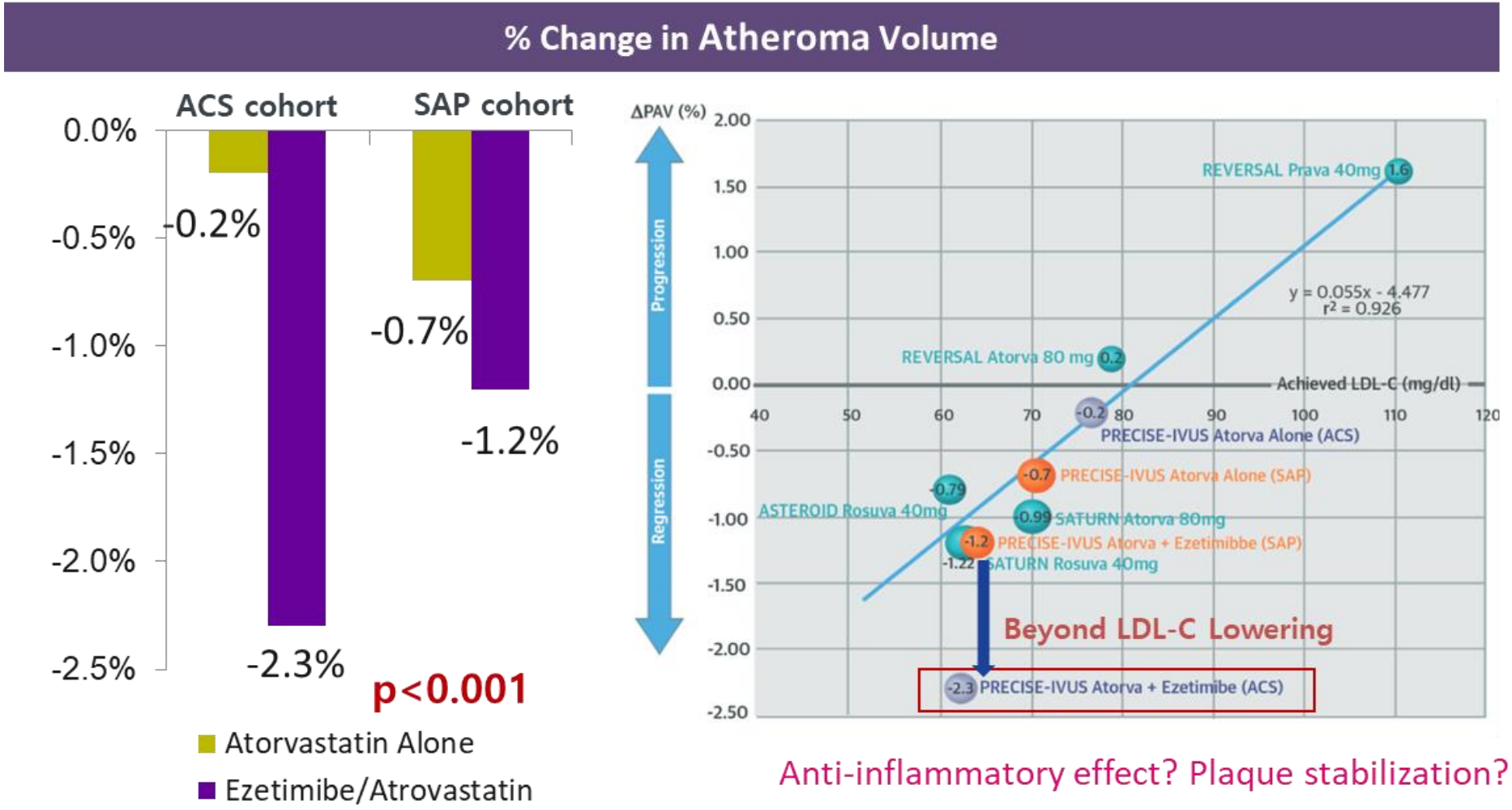
Changes in laboratory data

	Percent Change (%)		
	LZ Group (n = 100)	L Group (n = 102)	p Value
TC, mg/dl	-25 ± 17	-18 ± 18	0.006
HDL-C, mg/dl	14 ± 26	11 ± 25	0.5
LDL-C, mg/dl	-40 ± 18	-29 ± 24	<0.001
Triglycerides, mg/dl	-14 (-33 to 18)	-9 (-33 to 25)	0.3
Lipoprotein (a), mg/dl	-12 (-42 to 17)	-20 (-50 to 7)	0.1
Apolipoprotein A-I, mg/dl	15 ± 21	11 ± 17	0.2
Apolipoprotein B, mg/dl	-34 ± 16	-26 ± 20	0.001
Free fatty acid, μEq/l	-7 (-50 to 59)	-11 (-56 to 68)	0.8
MDA-LDL, U/l	-27.7 ± 27.0	-15.3 ± 38.5	0.1
RLP-C, mg/dl	-28 (-48 to 3)	-17 (-37 to 17)	0.02
sdLDL-C, mg/dl	-28.5 ± 33.5	-21.4 ± 35.0	0.2
Insulin, μIU/ml	15 (-33 to 73)	22 (-18 to 51)	0.99
HbA_{1c}, %	3 (-2 to 5)	2 (-4 to 4)	0.2
Total adiponectin, μg/ml	28 (-4 to 64)	19 (-5 to 63)	0.4
HMW adiponectin, μg/ml	24 (-25 to 74)	19 (-25 to 86)	0.9
Lathosterol, μg/ml	-15 (-53 to 45)	-53 (-71 to -22)	<0.001
Campesterol, μg/ml	-46 (-61 to -30)	22 (-5 to 61)	<0.001
Sitosterol, μg/ml	-39 (-53 to -20)	31 (-6 to 67)	<0.001
Lathosterol, μg/100 mg TC	14 (-28 to 68)	-36 (-57 to 2)	<0.001
Campesterol, μg/100 mg TC	-30 (-43 to -10)	53 (24 to 82)	<0.001
Sitosterol, μg/100 mg TC	-15 (-34 to 9)	60 (27 to 106)	<0.001
Campesterol/lathosterol	-40 (-66 to 10)	167 (48 to 267)	<0.001
hs-CRP, mg/l	-89 (-97 to -59)	-86 (-95 to -70)	0.9



Tsujita K, Ogawa H, et al. J Am Coll Cardiol 2015;66:495–507

Does ezetimibe help stabilize coronary plaque?



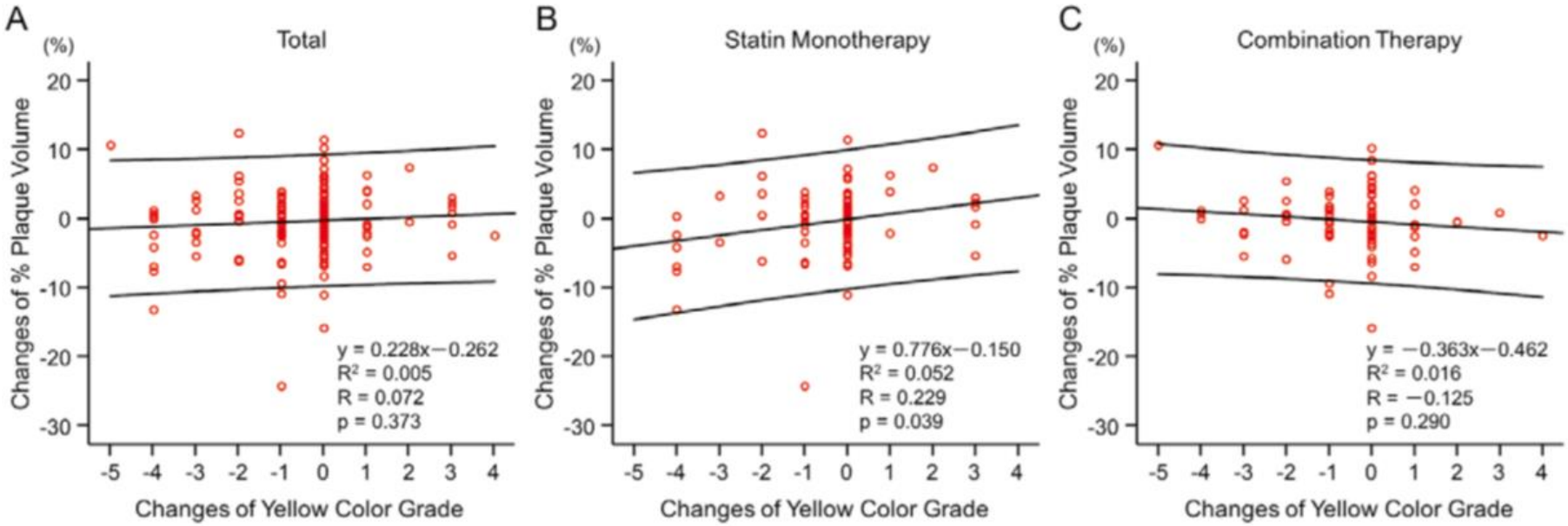
Anti-inflammatory effect? Plaque stabilization?

Tsujita K, Ogawa H, et al. J Am Coll Cardiol 2015;66:495–507

Effect of Ezetimibe on Stabilization and Regression of Intracoronary Plaque

The ZIPANGU Study

Conclusions: Compared with statin monotherapy, combination therapy with ezetimibe further reduced LDL-C levels. Significant plaque volume reduction was achieved by the combination therapy, but not statin monotherapy; however, plaque stabilization was similarly achieved by both therapies. Furthermore, reduction in plaque volume was dependent on reduction in LDL-C, regardless of whether it was achieved by statin alone or statin plus ezetimibe.



Circ J 2017; 81: 1611–1619 doi:10.1253/circj.CJ-17-0193

Effects of ezetimibe

- Additional lowering of LDL cholesterol
- Improvement of other cholesterols (HDL, ApoB, postprandial TG)
- Improves glucose metabolism, inflammation
- Plaque volume regression

- Statin dose-sparing effect

→ Lower adverse events

Conclusion

1 LDL-C is the first goal for preventing future CV events

The association between LDL-C and CVD has been confirmed through various clinical trials, and guidelines have called for lower LDL-C targets. Recent guidelines set LDL-C target at 55 mg/dl for very high-risk patients. In patients with recurrent events within 2 years, it is recommended to target a level of 40 mg/dL.

2 LDL-C – "The Lower, the Better" , and its also SAFE

Various clinical trials, such as IMPROVE-IT and TST, have shown that lower LDL-C can prevent occurrence of cardiovascular disease.

3 Combination therapy with Ezetimibe benefits patients

It has been shown in several clinical trials that use of ezetimibe helps reduce plaque, and LDL-C targets can be reached more easily, showing several advantages for high-risk patients.

Thank you