Perspectives on diabetes and dyslipidemia – Part 3

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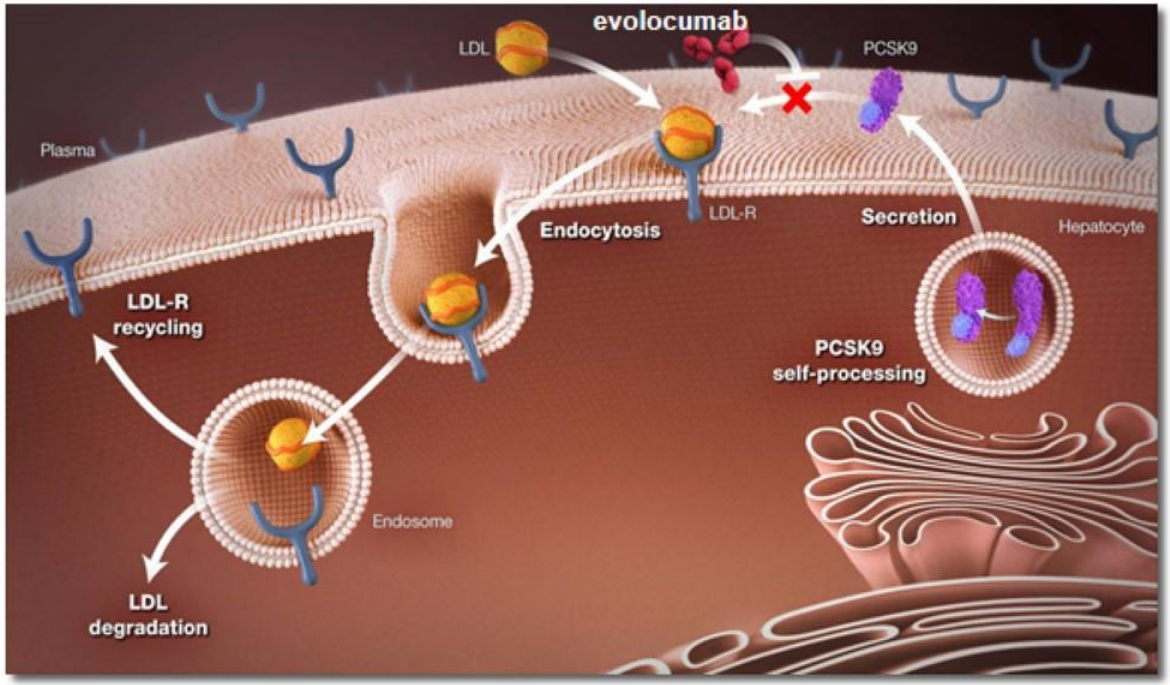
Multiplicities of interest

- The practice of medicine
- Consultant/advisor: Sanofi, Astra Zeneca, Janssen, Merck, Intarcia, Novartis
- Speaker: Amgen, Merck, Astra Zeneca, Janssen
- Stockholder: Allergan, Pfizer, Zimmer Biomet, Novartis

Background

Proprotein convertase subtilisin/kexin type 9 (PCSK9)

- Chaperones LDL-R to destruction → ↑ circulating LDL-C
- Loss-of-fxn genetic variants → ↑ LDL-R → ↓ LDL-C & ↓ risk of MI



Evolocumab

- Fully human anti-PCSK9 mAb
- ~60% ↓ LDL-C
- Safe & well-tolerated in Ph 2 & 3 studies
- Exploratory data suggested ↓ CV events

Sever P & Mackay J. *Br J Cardiol* 2014;21:91-3
Giugliano RP, et al. *Lancet* 2012;380:2007-17
Sabatine MS, et al. *NEJM* 2015;372:1500-9

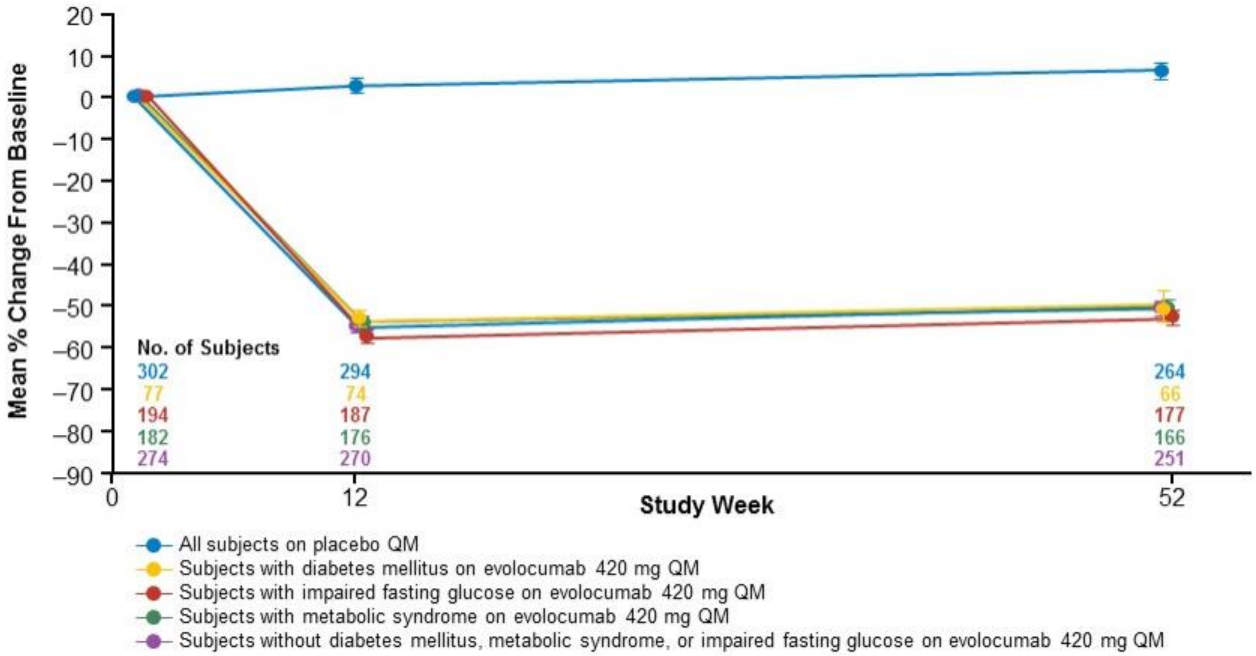
Evolocumab: Glycemic and Lipid effects vs diabetes status

TABLE 2 Week 52 results

Parameter	Type 2 diabetes Pbo (N = 43) vs EvoMab (N = 77)	IFG Pbo (N = 99) vs EvoMab (N = 194)	MetS Pbo (N = 107) vs EvoMab (N = 182)	No dysglycaemia or MetS Pbo (N = 119) vs EvoMab (N = 274)
Glycaemic parameters				
HbA1c Tx difference vs Pbo, median change from baseline (SE)[1]	0.10 (0.10)	0.00 (0.05)	0.00 (0.03)	0.00 (0.03)
FPG Tx difference vs Pbo, median change from baseline (SE)[1]	−0.11 (0.21)	0.00 (0.07)	−0.06 (0.06)	0.06 (0.06)
Insulin Tx difference vs Pbo, median change from baseline (SE)[1]	−7.2 (14.6)	0.0 (7.3)	0.0 (5.5)	−7.2 (5.5)
C-Peptide Tx difference vs Pbo, median change from baseline (SE)[1]	0.1 (0.1)	0.0 (0.04)	0.0 (0.04)	0.0 (0.03)
HOMA_%B Tx difference vs Pbo, median change from baseline (SE)[1]	5.5 (5.7)	−1.3 (3.5)	−1.7 (3.9)	−2.3 (4.2)
HOMA_IR Tx difference vs Pbo, median change from baseline (SE)[1]	−0.2 (0.3)	0.0 (0.1)	−0.1 (0.1)	−0.1 (0.1)
Lipid parameters				
Low-density lipoprotein cholesterol Tx difference vs Pbo, LS mean % change from baseline (SE)	−50.8 (6.0)[2]	−59.4 (3.4)[2]	−55.0 (3.5)[2]	−58.1 (3.5)[2]
Lipoprotein (a) Tx difference vs Pbo, LS mean % change from baseline (SE)	−18.5 (4.8)[2]	−23.6 (3.5)[2]	−21.9 (3.5)[2]	−24.6 (3.0)[2]
Triglycerides Tx difference vs Pbo, LS mean % change from baseline (SE)	−8.8 (9.0)	−9.4 (5.2)	−17.2 (5.2)[3]	−10.9 (4.3)[3]
High-density lipoprotein cholesterol Tx difference vs Pbo, LS mean % change from baseline (SE)	2.0 (2.3)	4.6 (2.0)[3]	5.5 (2.1)[3]	8.1 (1.7)[2]
Apolipoprotein B Tx difference vs Pbo, LS mean % change from baseline (SE)	−38.0 (5.2)[2]	−46.1 (2.8)[2]	−43.3 (2.8)[2]	−45.0 (2.8)[2]

Blom D et al, Diabetes Obes Metab 2017; 19:98–107

Evolocumab: LDL-lowering vs diabetes status



- In all glycemic subgroups, evolocumab reduced LDL-C by > 50% compared with placebo
- There was no loss of efficacy from week 12 to week 52
- Baseline glycemic category did not influence achieved LDL-C reduction

Error bars represent standard error of the mean.
LDL-C = low-density lipoprotein cholesterol; QM = once a month
Blom DJ, et al; [published online ahead of print September 13, 2016]. *Diabetes Obes Metab*. doi:10.1111/dom.12788.

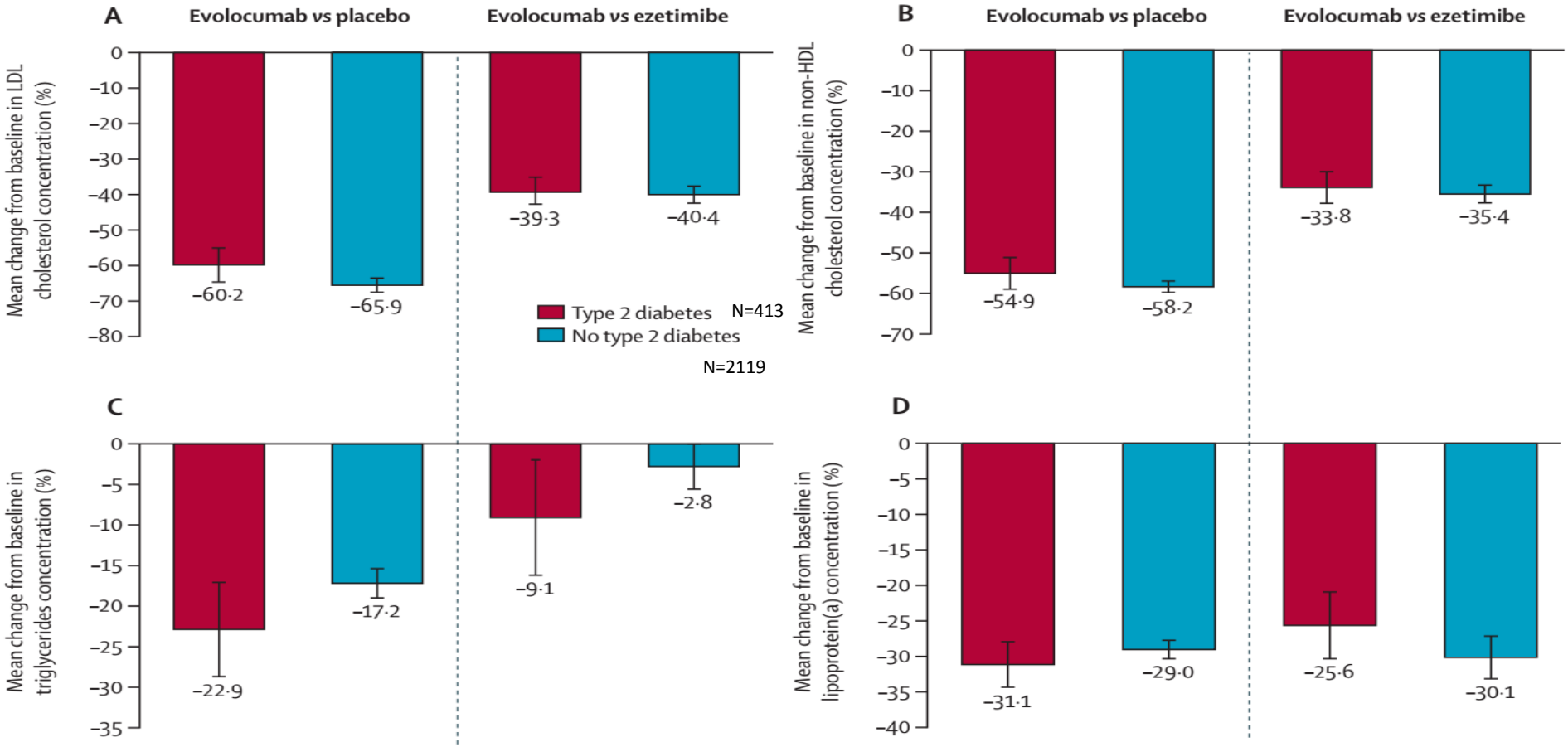
Evolocumab: Effect on glycemia vs diabetes status

	Type 2 Diabetes Placebo (n = 43) vs EVO (n = 77)	IFG Placebo (n = 99) vs EVO (n = 194)	MetS Placebo (n = 107) vs EVO (n = 182)	No Dysglycemia or MetS Placebo (n = 119) vs EVO (n = 274)
Glycemic parameters Treatment difference vs placebo, median change from baseline (SE)[a]				
HbA_{1c}	0.10 (0.10)	0.00 (0.05)	0.00 (0.03)	0.00 (0.03)
FPG	–0.11 (0.21)	0.00 (0.07)	–0.06 (0.06)	0.06 (0.06)
Insulin	–7.2 (14.6)	0.0 (7.3)	0.0 (5.5)	–7.2 (5.5)
C-peptide	0.1 (0.1)	0.0 (0.04)	0.0 (0.04)	0.0 (0.03)
HOMA_%B	5.5 (5.7)	–1.3 (3.5)	–1.7 (3.9)	–2.3 (4.2)
HOMA_IR	–0.2 (0.3)	0.0 (0.1)	–0.1 (0.1)	–0.1 (0.1)

- No significant differences were observed in glycemic parameters in the subgroups for EVO vs placebo treatment

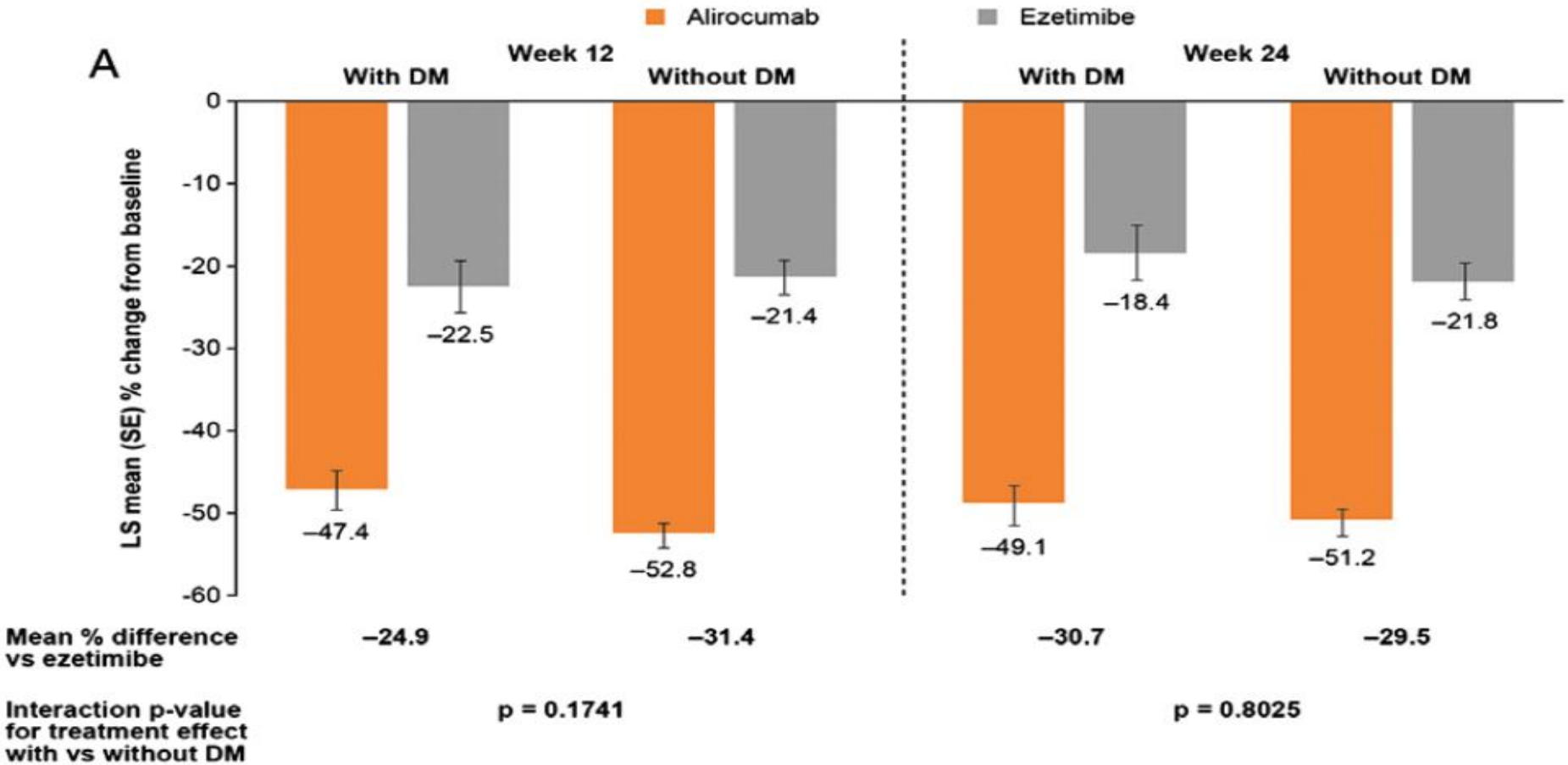
[a]Differences in median and SE were calculated using the Hodges-Lehmann method; *P* values were calculated using the Wilcoxon rank-sum test and found to be nonsignificant ($P > 0.05$) for all glycemic parameters.
EVO = evolocumab; FPG, fasting plasma glucose; HbA_{1c} = glycated hemoglobin; HOMA_%B = homeostasis model assessment β-cell function; HOMA_IR = homeostasis model assessment insulin resistance; IFG, impaired fasting glucose;
MetS = metabolic syndrome; SE = standard error
Blom DJ, et al; [published online ahead of print September 13, 2016]. *Diabetes Obes Metab*. doi:10.1111/dom.12788.

Evolocumab: Effect on lipids vs diabetes status



Sattar N et al, Lancet Diabetes Endocrinol 2016; 4: 403–10

Alirocumab vs ezetimibe add-on to statin: LDL-C Effect in DM vs nonDM



Leiter L et al, Diabetes Obes Metab. 2017;19:989-996

Alirocumab: Effect on LDL-C in insulin-treated T2D and in T1D

	Type 2 diabetes			Type 1 diabetes		
	Alirocumab (n = 287)	Placebo (n = 142)	Difference vs. placebo, % [95% CI], P-value	Alirocumab (n = 49)	Placebo (n = 25)	Difference vs. placebo, % [95% CI], P-value
Calculated LDL-C, mean (SD), mg/dL [mmol/L]						
Baseline	110.3 (35.9) [2.9 (0.9)]	109.5 (38.7) [2.8 (1.0)]		122.5 (47.8) [3.2 (1.2)]	110.2 (31.2) [2.9 (0.8)]	
Week 24	55.1 (33.7) [1.4 (0.9)]	107.3 (37.0) [2.8 (1.0)]		55.9 (33.5) [1.4 (0.9)]	101.8 (31.8) [2.6 (0.8)]	
Primary endpoint: % change from baseline to week 24, LS mean (SE)	–48.2 (1.6)	0.8 (2.2)	–49.0 (2.7) [–54.4 to –43.6], $P < .0001$	–51.8 (3.7)	–3.9 (5.3)	–47.8 (6.5) [–60.7 to –35.0], $P < .0001$

Leiter L et al, Diabetes Obes Metab. 2017;19:1781-1792.

GLAGOV: Key Inclusion Criteria

- Men or women aged > 18 years
- Clinically indicated coronary angiogram, evidence of coronary disease
- LDL-C criteria met within 4 weeks of screening visit or, if applicable, at the end of lipid-stabilization period:
  - LDL-C ≥ 80 mg/dL, **OR**
  - LDL-C ≥ 60 but < 80 mg/dL in the presence of risk factors as shown in the table below:

Major Risk Factors (One Required)	• Non-coronary atherosclerotic vascular disease • Documented myocardial infarction or hospitalization for unstable angina within the last 2 years • Documented type 2 diabetes mellitus

OR

Minor Risk Factors (Three Required)	• Age (men ≥ 50 years; women ≥ 55 years) • Hypertension (BP ≥ 140/90 mmHg or current use of antihypertensive medications) • Low HDL-C (men: < 40 mg/dL; women < 50 mg/dL) • Family history of premature coronary heart disease (first-degree male relative < 55 years of age or first-degree female relative < 65 years of age) • hs-CRP ≥ 2 mg/L • Cigarette smoking (current)

Nicholls SJ, et al. *JAMA*. [published online ahead of print November 15, 2016]. doi: 10.1001/jama.2016.16951.
Puri R, et al. *Am Heart J*. 2016;176:83-92.

GLAGOV: Baseline Characteristics of Randomized Patients

Parameter*	Placebo (N = 484)	Evolocumab (N = 484)
Age, years	59.8±8.8	59.8±9.6
Men, n (%)	350 (72.3)	349 (72.1)
White, n (%)	452 (93.4)	456 (94.2)
BMI	29.5±5.0	29.4±5.0
Hypertension, n (%)	405 (83.7)	398 (82.2)
Previous PCI, n (%)	188 (38.8)	189 (39.0)
Previous MI, n (%)	171 (35.3)	169 (34.9)
Smoking, n (%)	113 (23.3)	124 (25.6)
Diabetes, n (%)	104 (21.5)	98 (20.2)
Baseline statin use,* n (%)	476 (98.3)	478 (98.8)
High intensity†, n (%)	290 (59.9)	280 (57.9)
Moderate intensity, n (%)	185 (38.2)	196 (40.5)
Low intensity, n (%)	1 (0.2)	2 (0.4)
Baseline ezetimibe use,* n (%)	9 (2.1)	9 (2.1)
Baseline medications		
Anti-platelet therapy, n (%)	465 (96.1)	454 (93.8)
Beta-blocker, n (%)	370 (76.4)	362 (74.8)
ACE inhibitor, n (%)	264 (54.5)	260 (53.7)
ARB, n (%)	92 (19.0)	87 (18.0)

Age and BMI expressed as mean ± standard deviation. *Baseline statin and ezetimibe use is defined as subject treated with statin or ezetimibe therapy at the end of the lipid stabilization period at randomization. †High intensity statin as defined by ACC/AHA criteria

Nicholls SJ, et al. *JAMA*. [published online ahead of print November 15, 2016]. doi: 10.1001/jama.2016.16951.

GLAGOV: Biochemical Measures

Parameter	Baseline		On-treatment			Absolute Change (95% CI)		
	Placebo (n = 484)	Evolocumab (n = 484)	Placebo (n = 484)	Evolocumab (n = 484)	P-Value*	Placebo (n = 484)	Evolocumab (n = 484)	P-Value*
Total cholesterol, mg/dL mean (95%CI)	166.2 (163.1 to 169.2)	166.1 (163 to 169.2)	169.1 (166.3 to 172)	108.6 (160 to 111.3)	< 0.001	1.8 (-2.0 to 5.6)	-59.0 (-62.8 to -55.2)	< 0.001
LDL-C, mg/dL† mean (95%CI)	92.4 (90 to 94.8)	92.6 (90.1 to 95.0)	93.0 (90.5 to 95.4)	36.6 (34.5 to 38.8)	< 0.001	0.2 (-2.9 to 3.4)	-56.3 (-59.4 to -53.1)	< 0.001
Lp(a), mg/dL median (IQR)	10.9 (3.9 to 50.7)	12.1 (4.6 to 57.1)	8.9 (3.9 to 48.1)	7.1 (2.5 to 46.7)	0.07	-1.0 (-2.2 to 0.2)	-7.8 (-9.0 to -6.6)	< 0.001
hs-CRP (mg/L) median (IQR)‡	1.6 (0.8 to 3.4)	1.6 (0.8 to 3.4)	1.4 (0.7 to 3.0)	1.4 (0.7 to 3.0)	0.47	-0.3 (-1.3 to 0.6)	-0.4 (-1.3 to 0.6)	0.35

Note: On-treatment laboratory parameters are the time-weighted averages (95% CIs) of all post-baseline values, and estimates are derived from an analysis of variance model with factors for treatment group and region. Baseline and time-weighted average on-treatment values and absolute changes of laboratory measures and blood pressure of patients treated with placebo or evolocumab with evaluable imaging at baseline and follow-up. Results expressed as mean (95% CI) at baseline and least-squares mean (95% CI) for on-treatment values.

*P-value for between-treatment group comparison. †When the calculated LDL-C level is less than 40 mg/dL or triglyceride level is greater than 400 mg/dL, ultracentrifugation LDL-C was determined from the same blood sample. ‡Tested using Wilcoxon rank-sum test. Final measurements are used for on-treatment values. Absolute changes are presented as least-squares means (95% CIs).

LDL-C = low-density lipoprotein cholesterol; hs-CRP = high-sensitivity C-reactive protein; Lp(a) = lipoprotein(a)

Nicholls SJ, et al. *JAMA*. [published online ahead of print November 15, 2016]. doi: 10.1001/jama.2016.16951.

GLAGOV: Biochemical Measures *(continued)*

Parameter	Baseline		On-treatment			Absolute Change (95% CI)		
	Placebo (n = 484)	Evolocumab (n = 484)	Placebo (n = 484)	Evolocumab (n = 484)	P-Value*	Placebo (n = 484)	Evolocumab (n = 484)	P-Value*
HDL-C, mg/dL mean (95%CI)	45.4 (44.2 to 46.5)	46.7 (45.5 to 47.8)	47.1 (46.0 to 48.2)	51.0 (49.8 to 52.1)	< 0.001	0.7 (-0.1 to 1.6)	3.3 (2.4 to 4.1)	< 0.001
TG, mg/dL† median (IQR)	124.5 (90.0 to 173)	117.0 (88 to 155)	130.5 (100.3 to 177.2)	105.1 (82.5 to 141.6)	< 0.001	8.1 (-0.4 to 16.6)	-10.9 (-19.4 to -2.5)	< 0.001
ApoA, mg/dL mean (95%CI)	139.5 (137.2 to 141.9)	140.5 (138.3 to 142.8)	145.4 (143.4 to 147.4)	151.6 (149.5 to 153.7)	< 0.001	3.5 (1.5 to 5.5)	8.5 (6.5 to 10.5)	< 0.001
ApoB, mg/dL mean (95%CI)	81.9 (80.1 to 83.6)	81.1 (79.3 to 82.9)	83.5 (81.8 to 85.2)	42.4 (40.8 to 44.0)	< 0.001	0.3 (-2.0 to 2.6)	-40.3 (-42.6 to 38.0)	< 0.001

Note: On-treatment laboratory parameters are the time-weighted averages (95% CIs) of all post-baseline values, and estimates are derived from an analysis of variance model with factors for treatment group and region. Baseline and time-weighted average on-treatment values and absolute changes of laboratory measures and blood pressure of patients treated with placebo or evolocumab with evaluable imaging at baseline and follow-up. Results expressed as mean (95% CI) at baseline and least-squares mean (95% CI) for on-treatment values.

*P-value for between-treatment group comparison. †Tested using Wilcoxon rank-sum test.

HDL-C = high-density lipoprotein cholesterol; TG = triglycerides; Apo = Apolipoprotein

Nicholls SJ, et al. *JAMA*. [published online ahead of print November 15, 2016]. doi: 10.1001/jama.2016.16951.

GLAGOV: Biochemical Measurements for Diabetes and Blood Pressure

Parameter	Baseline		On-treatment			Absolute Change (95% CI)		
	Placebo (n = 484)	Evolocumab (n = 484)	Placebo (n = 484)	Evolocumab (n = 484)	P-Value*	Placebo (n = 484)	Evolocumab (n = 484)	P-Value*
Glucose, mg/dL†,‡ mean (95%CI)	107.3 (104.6 to 110.1)	104.0 (101.8 to 106.2)	109.4 (106.9 to 112.0)	110.1 (107.8 to 112.3)	0.72	3.9 (1.3 to 6.5)	7.8 (5.3 to 10.4)	0.02
HbA1c, %‡ mean (95%CI)	5.9 (5.8 to 6.0)	5.8 (5.8 to 5.9)	6.0 (5.9 to 6.1)	6.0 (5.9 to 6.1)	0.85	0.2 (0.1 to 0.2)	0.2 (0.15 to 0.25)	0.09
Systolic blood pressure, mmHg mean (95%CI)	129.6 (128.2 to 131.0	131.4 (130.1 to 132.7)	131.9 (130.8 to 133.1)	131.5 (130.4 to 132.5)	0.55	0.9 (-0.7 to 2.5)	-1.3 (-2.9 to 0.4)	0.007
Diastolic blood pressure, mmHg mean (95%CI)	76.7 (75.8 to 77.6)	78.0 (77.2 to 78.9)	78.5 (77.8 to 79.2)	78.6 (77.9 to 79.2)	0.94	2.2 (1.0 to 3.3)	0.9 -0.2 to 1.99)	0.01

Note: On-treatment laboratory parameters are the time-weighted averages (95% CIs) of all post-baseline values, and estimates are derived from an analysis of variance model with factors for treatment group and region. Baseline and time-weighted average on-treatment values and absolute changes of laboratory measures and blood pressure of patients treated with placebo or evolocumab with evaluable imaging at baseline and follow-up. Results expressed as mean (95% CI) at baseline and least-squares mean (95% CI) for on-treatment values.

*P-value for between-treatment group comparison. †Tested using Wilcoxon rank-sum test. ‡Final measurements are used for on-treatment values. Absolute changes are presented as least-squares means (95% CIs)

Hb = hemoglobin

Nicholls SJ, et al. *JAMA*. [published online ahead of print November 15, 2016]. doi: 10.1001/jama.2016.16951.

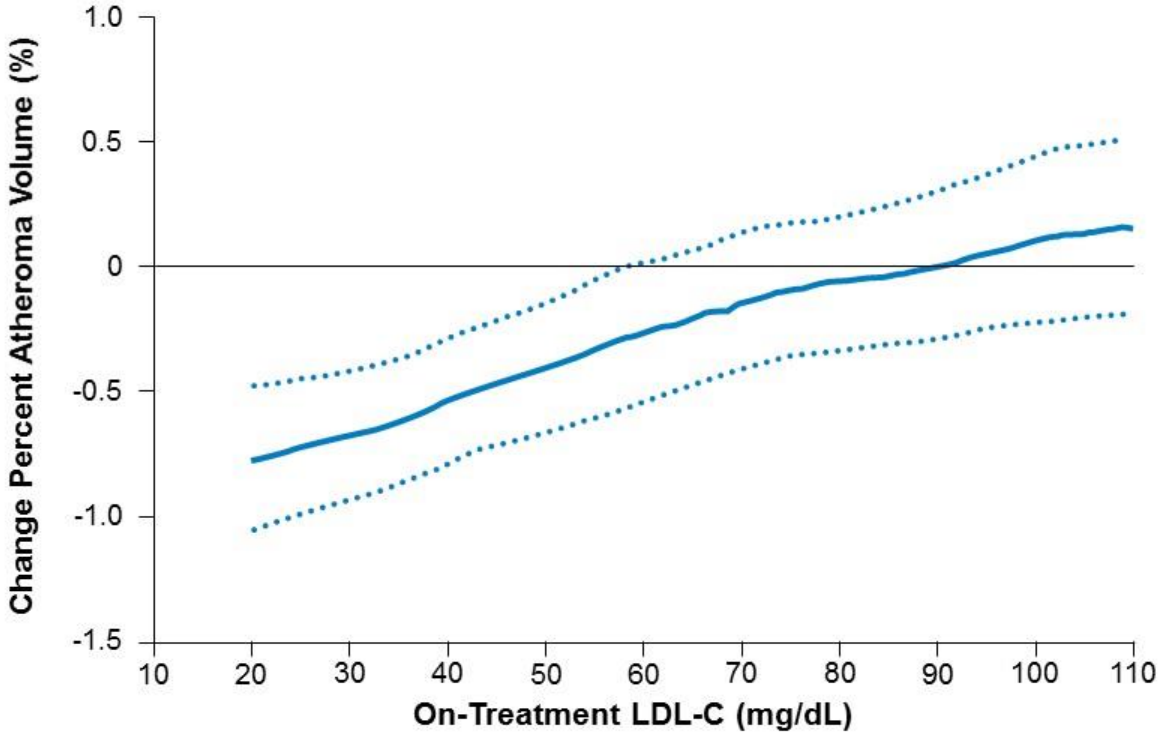
Evolocumab Effect on Coronary Disease in Statin-Treated Patients: GLAGOV Randomized Clinical Trial

Table 3. Primary and Secondary Study End Points as Evaluated on Intravascular Ultrasonography

Parameter	Placebo (n = 423)	Evolocumab (n = 423)	Between Group Differences, Least Squares Means (95% CI)	*P* Value
Baseline				
Percent atheroma volume				
Mean (95% CI)	37.2 (36.4 to 38.0)	36.4 (35.6 to 37.2)	−0.76 (−1.9 to 0.4)	.18
Median (95% CI)	37.1 (36.0 to 38.0)	36.4 (35.5 to 37.5)		
Total atheroma volume, mm^3				
Mean (95% CI)	191.4 (183.2 to 199.6)	187.0 (179.1 to 194.8)	−4.3 (−15.6 to 7.0)	.63
Median (95% CI)	175.8 (164.0 to 187.4)	174.6 (164.1 to 183.1)		
Follow-up at 78 wk				
Percent atheroma volume				
Mean (95% CI)	37.3 (36.5 to 38.1)	35.6 (34.8 to 36.4)	−1.7 (−2.8 to −0.6)	.002
Median (95% CI)	36.8 (35.7 to 37.8)	35.7 (34.8 to 36.5)		
Total atheroma volume, mm^3				
Mean (95% CI)	190.6 (182.5 to 198.7)	181.5 (174.1 to 188.9)	−8.9 (−19.9 to 2.0)	.23
Median (95% CI)	174.4 (164.3 to 186.6)	169.6 (160.9 to 180.7)		
Change From Baseline				*P* Value for Between Groups[a]
Percent atheroma volume				
Least squares mean (95% CI)	0.05 (−0.32 to 0.42)	−0.95 (−1.33 to −0.58)	−1.0 (−1.8 to −0.64)	<.001
P value for change from baseline	.78	<.001		
Total atheroma volume, mm^3				
Least squares mean (95% CI)	−0.91 (−3.29 to 1.47)	−5.80 (−8.19 to −3.41)	−4.9 (−7.3 to −2.5)	<.001
P value for change from baseline	.45	<.001		
Patients with regression, % (95% CI)				
Percent atheroma volume	47.3 (42.5 to 52.0)	64.3 (59.7 to 68.9)	17.0 (10.4 to 23.6)	<.001
Total atheroma volume	48.9 (44.2 to 53.7)	61.5 (56.8 to 66.1)	12.5 (5.9 to 19.2)	<.001

Nicholls et al. JAMA 2016;316:2373-84

Exploratory Analysis: Achieved LDL-C and Change in PAV in All Patients



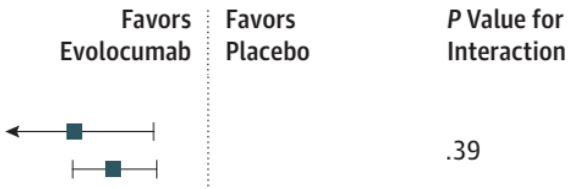
Local regression (LOESS) curve illustrating the association (with 95% CI) between achieved LDL-C levels and change in PAV in all patients undergoing serial IVUS evaluation. PAV = percentage atheroma volume; LDL-C = low-density lipoprotein cholesterol

Nicholls SJ, et al. *JAMA*. [published online ahead of print November 15, 2016]. doi: 10.1001/jama.2016.16951.

Evolocumab Effect on Atheroma Volume in Statin-Treated Patients: GLAGOV Randomized Clinical Trial

Figure 3. Prespecified Subgroup Analysis of Change in Percent Atheroma Volume From Baseline to Week-78 Follow-up

Subgroup	No.		Change in PAV, Mean (95% CI), %		Treatment Difference (95% CI)	*P* Value for Interaction
	Placebo	Evolocumab	Placebo	Evolocumab		
Type 2 diabetes mellitus						
Yes	87	88	0.43 (-4.90 to 5.77)	-0.85 (-5.70 to 3.99)	-1.32 (-2.10 to -0.54)	.39
No	336	335	0.04 (-5.66 to 5.75)	-0.78 (-6.54 to 4.97)	-0.93 (-1.34 to -0.51)	



Nicholls et al. JAMA 2016;316:2373-84

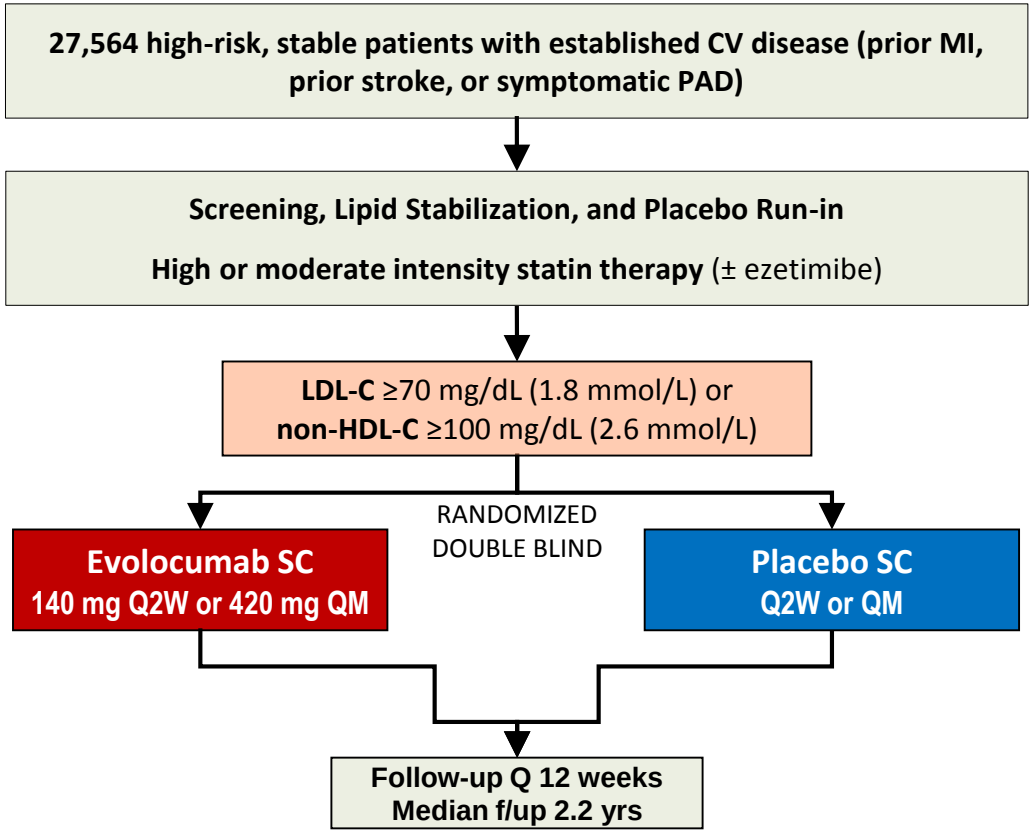
The NEW ENGLAND JOURNAL of MEDICINE
2017; 376:1713-22

ORIGINAL ARTICLE

Evolocumab and Clinical Outcomes in Patients with Cardiovascular Disease

Marc S. Sabatine, M.D., M.P.H., Robert P. Giugliano, M.D., Anthony C. Keech, M.D., Narimon Honarpour, M.D., Ph.D., Stephen D. Wiviott, M.D., Sabina A. Murphy, M.P.H., Julia F. Kuder, M.A., Huei Wang, Ph.D., Thomas Liu, Ph.D., Scott M. Wasserman, M.D., Peter S. Sever, Ph.D., F.R.C.P., and Terje R. Pedersen, M.D., for the FOURIER Steering Committee and Investigators*

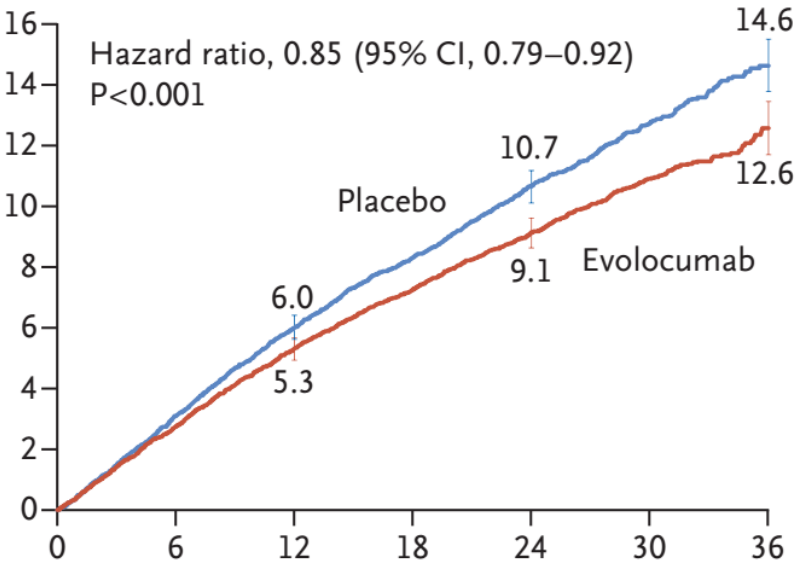
FOURIER - evolocumab vs placebo



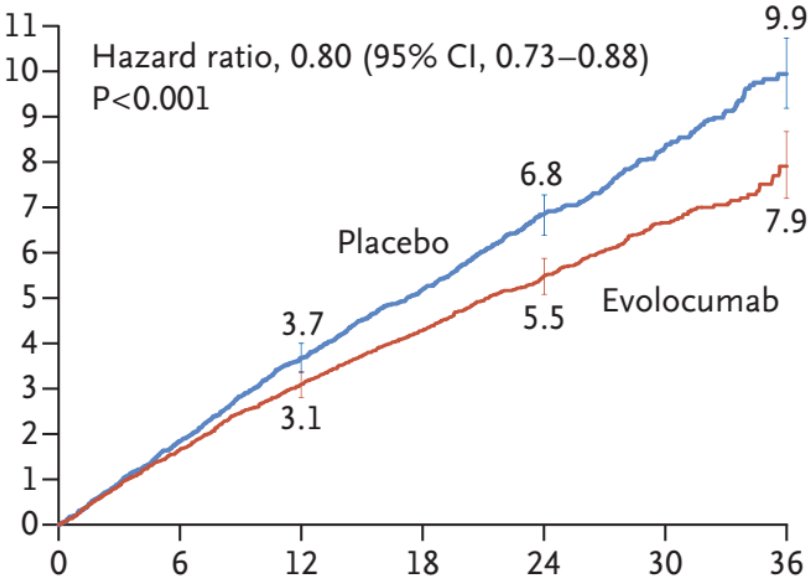
Sabatine MS et al. Am Heart J 2016;173:94-101

FOURIER - evolocumab vs placebo

1ary endpoint: CV death, MI, stroke, unstable angina hospitalization, coronary revascularization



2ary endpoint: CV death, MI, stroke

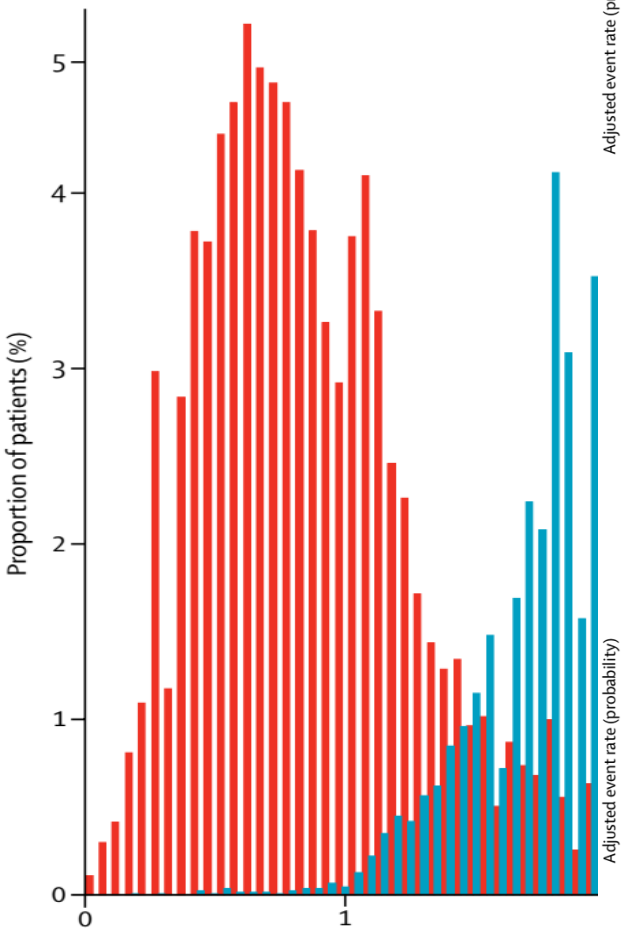


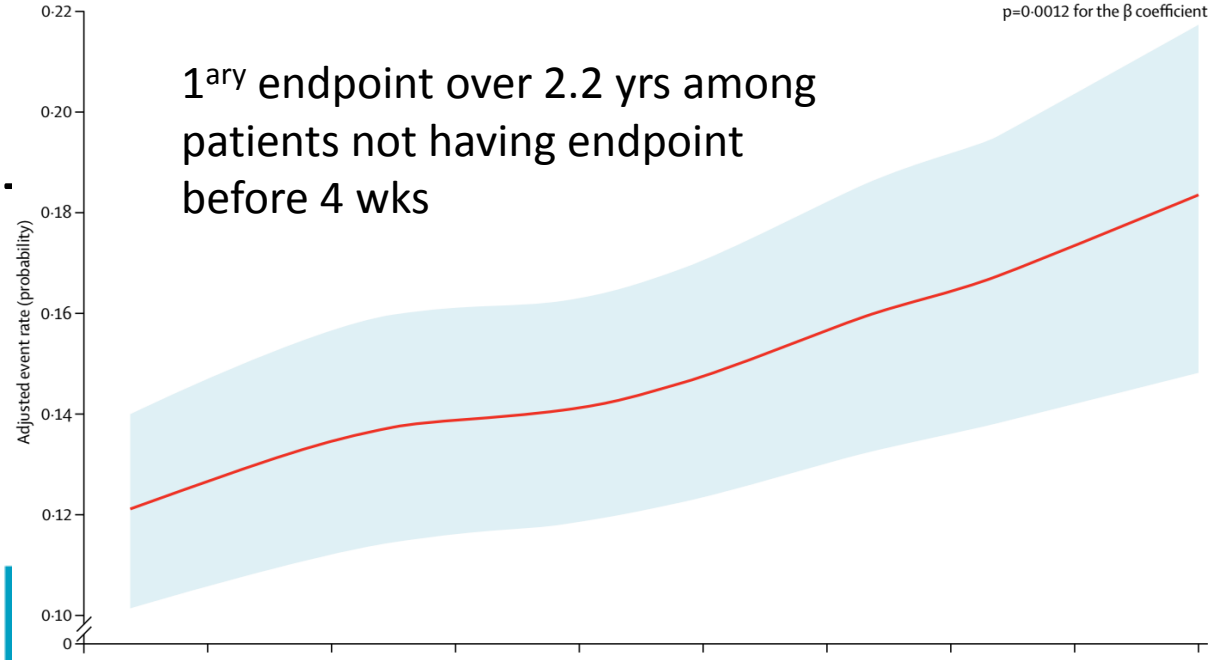
Sabatine et al. NEJM 2017; 376:1713-22

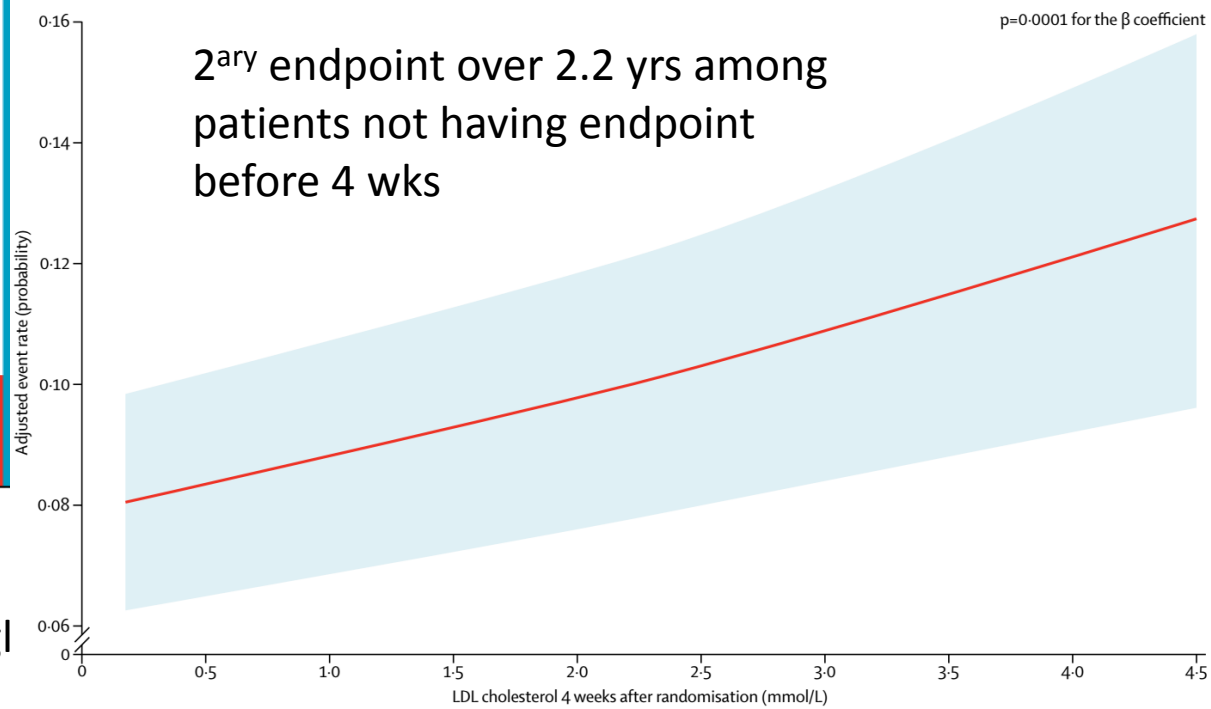
Outcome	Hazard Ratio (95% CI)	
	In first year	Beyond first year
Primary end point	0.88 (0.80-0.97)	0.81 (0.73-0.89)
Key secondary end point	0.84 (0.74-0.96)	0.75 (0.66-0.85)
Cardiovascular death	0.96 (0.74-1.25)	1.12 (0.88-1.42)
Myocardial infarction	0.80 (0.68-0.94)	0.65 (0.55-0.77)
Hospitalization for unstable angina	0.97 (0.77-1.22)	0.99 (0.75-1.30)
Stroke	0.83 (0.63-1.08)	0.76 (0.60-0.97)
Coronary revascularization	0.84 (0.74-0.96)	0.72 (0.63-0.82)
Urgent	0.84 (0.71-1.00)	0.63 (0.52-0.75)
Elective	0.86 (0.72-1.03)	0.81 (0.68-0.97)
CTTC composite endpoint	0.87 (0.79-0.97)	0.78 (0.71-0.86)
Coronary heart death, MI, ischemic stroke, or urgent revascularization	0.86 (0.76-0.97)	0.76 (0.68-0.86)
Coronary heart death, MI, or stroke	0.84 (0.73-0.95)	0.73 (0.65-0.83)
Fatal or nonfatal MI or stroke	0.81 (0.70-0.93)	0.67 (0.59-0.77)

Sabatine et al. NEJM 2017; 376:1713-22

FOURIER







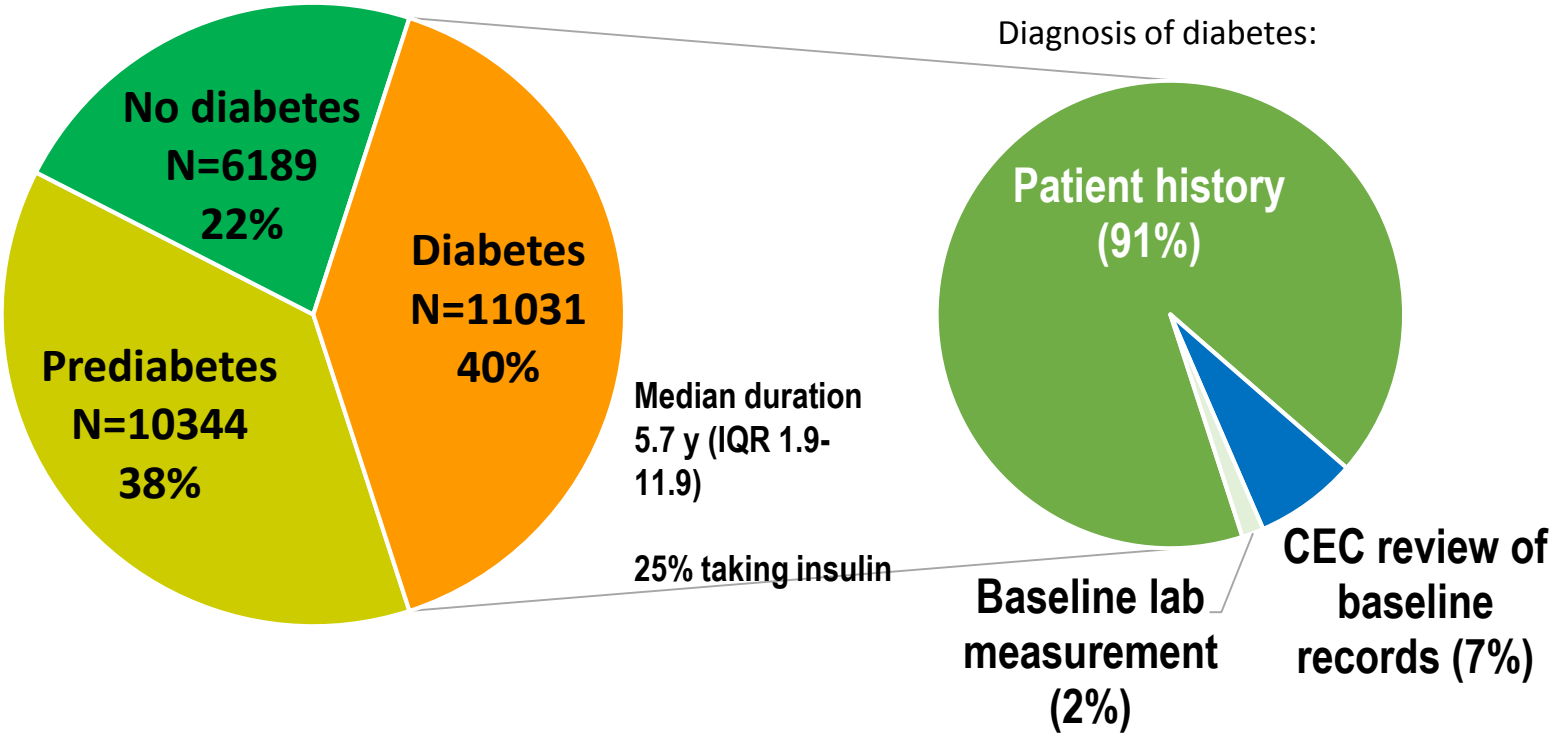
locumab
cebo

(%)
669 (10)
003 (31)
444 (13)
471 (29)
395 (17)

Giugl

FOURIER - evolocumab vs placebo

Diabetes at Baseline



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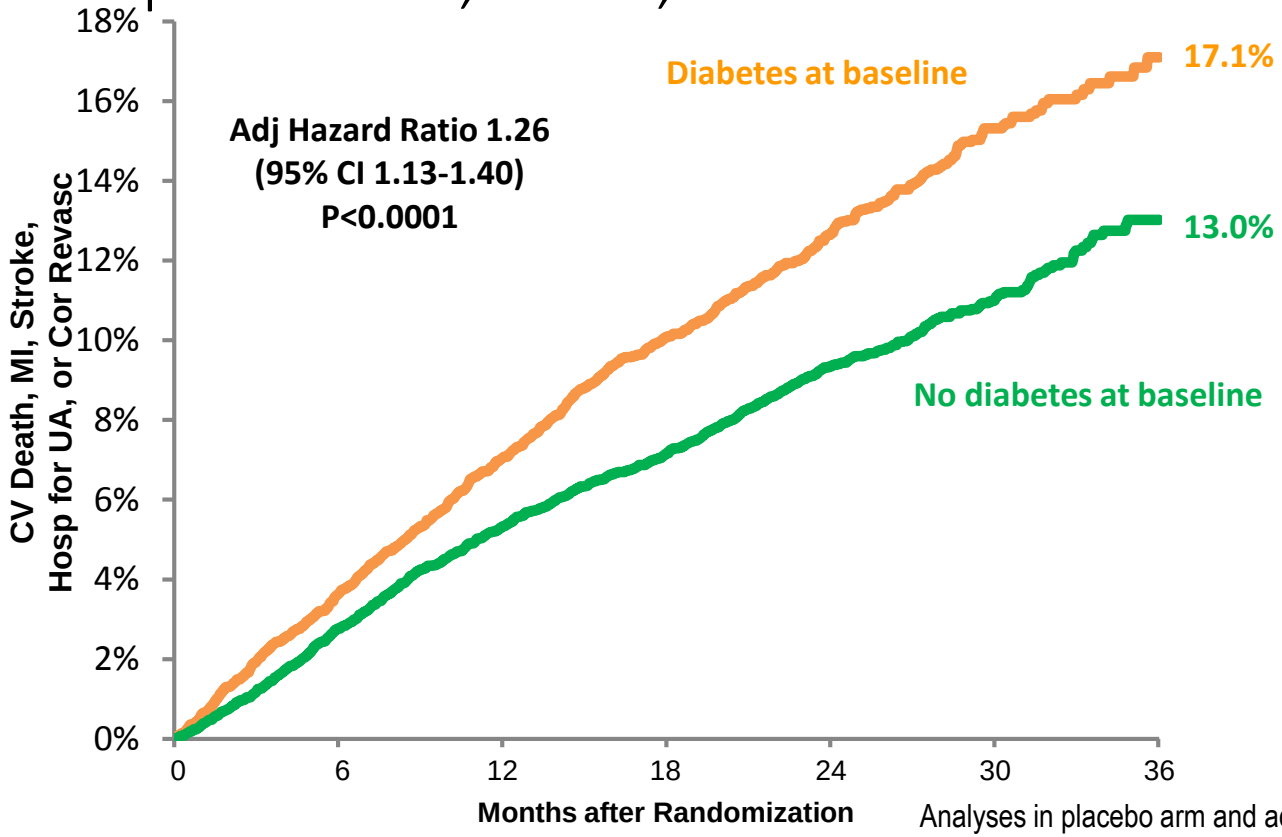
1ary Endpoint: MI, Stroke, CV Death, UA Hospitalization, CABG, PCI



Analyses in placebo arm and adj for age, sex, BMI, race, region, history of MI, stroke, PAD, HTN, smoking, HF, eGFR, lipids, statin.

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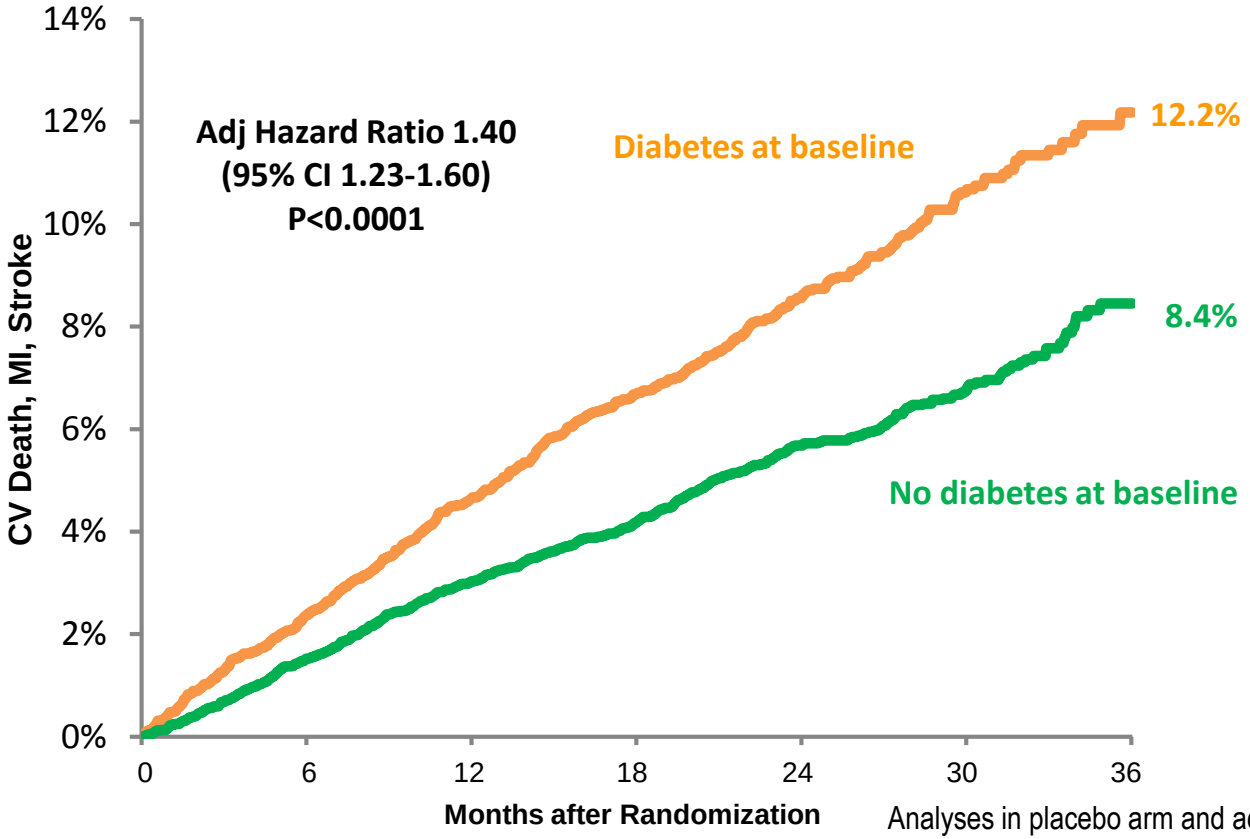
FOURIER - evolocumab vs placebo

2ary Endpoint: MI, Stroke, CV Death



Analyses in placebo arm and adj for age, sex, BMI, race, region, history of MI, stroke, PAD, HTN, smoking, HF, eGFR, lipids, statin.

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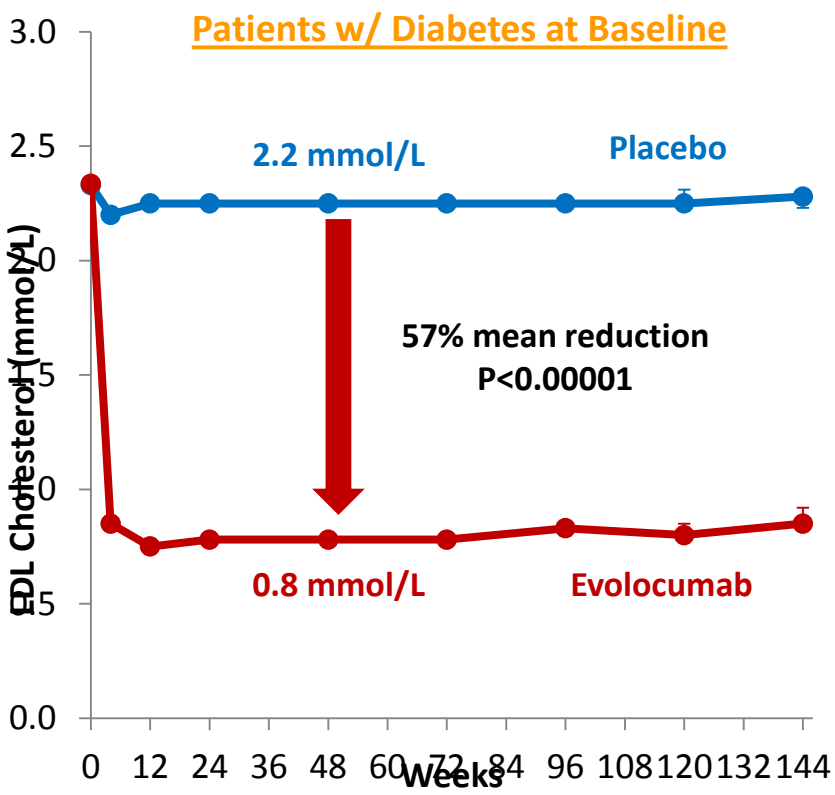
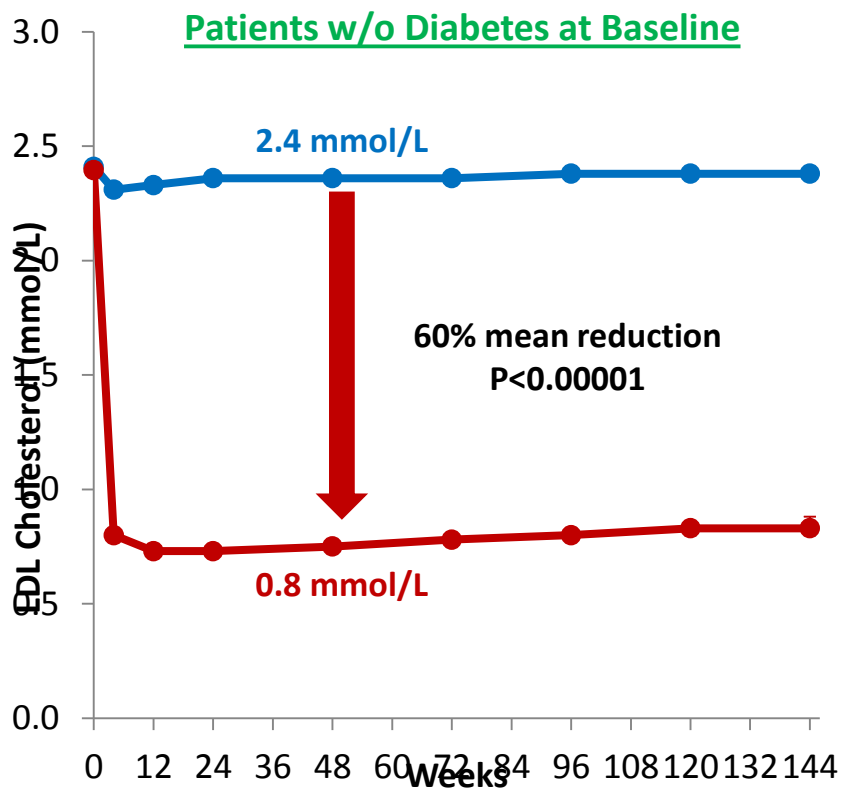
FOURIER - evolocumab vs placebo

LDL-C Reduction with Evolocumab





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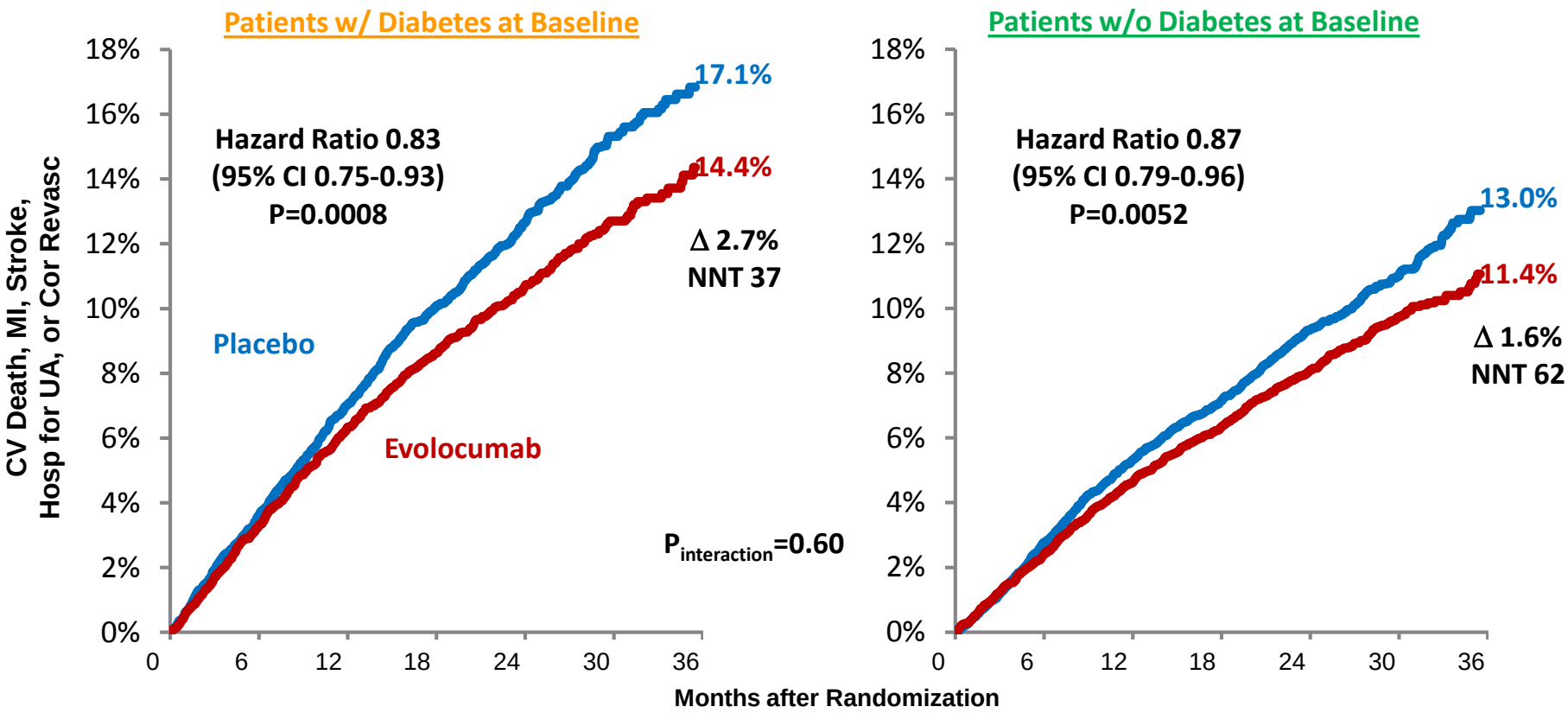
FOURIER - evolocumab vs placebo

1ary Endpoint



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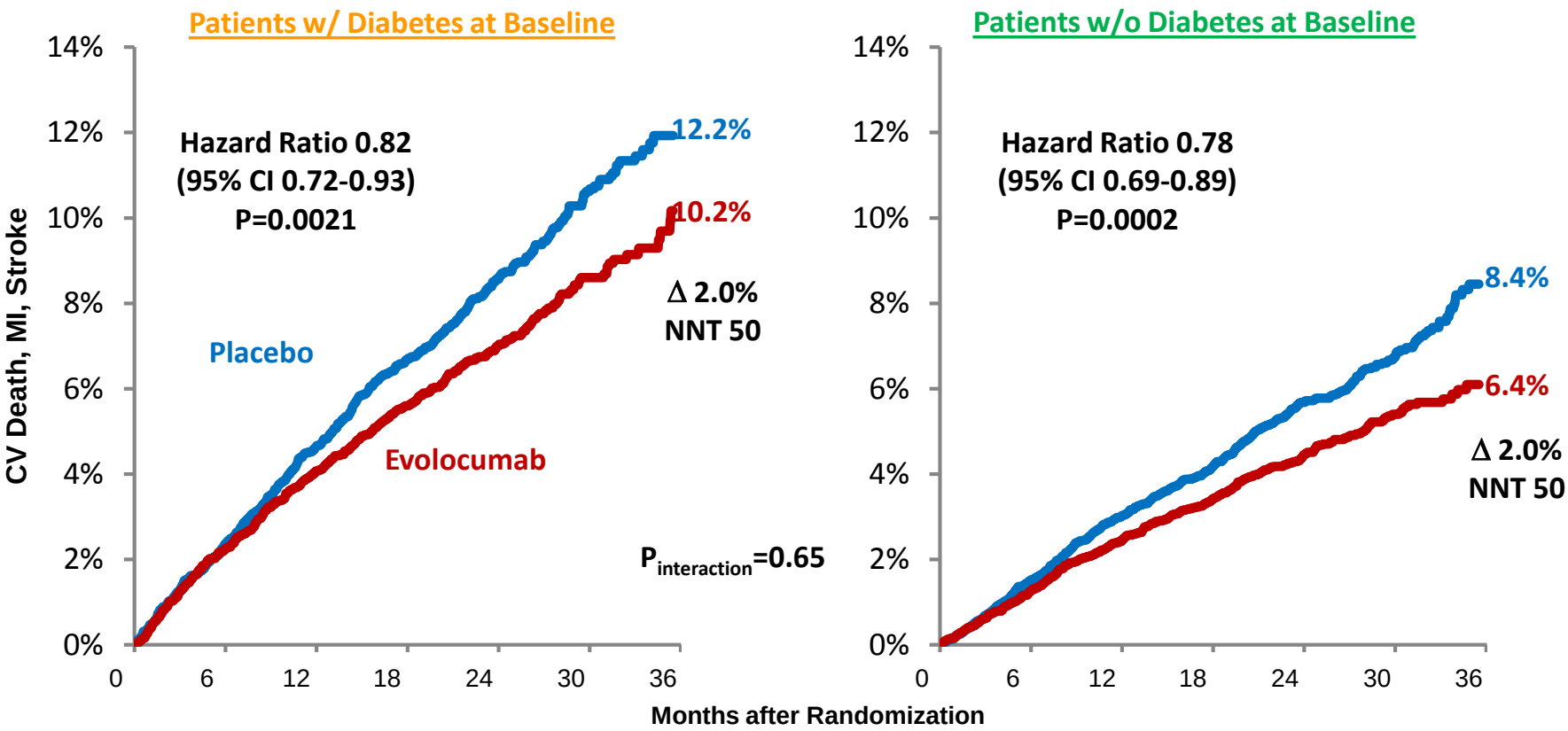
FOURIER - evolocumab vs placebo

2ary Endpoint



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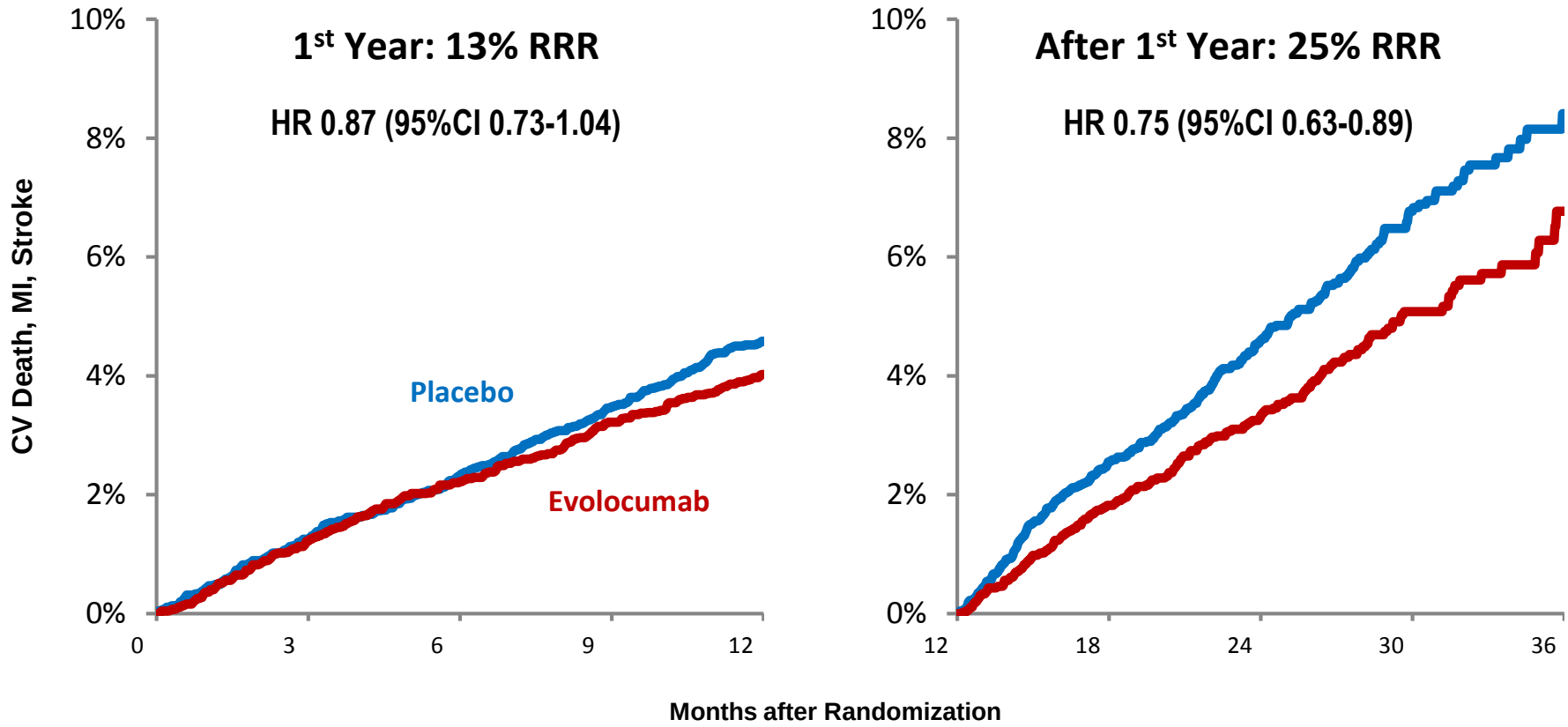
FOURIER - evolocumab vs placebo

2ary Endpoint with Diabetes at Baseline



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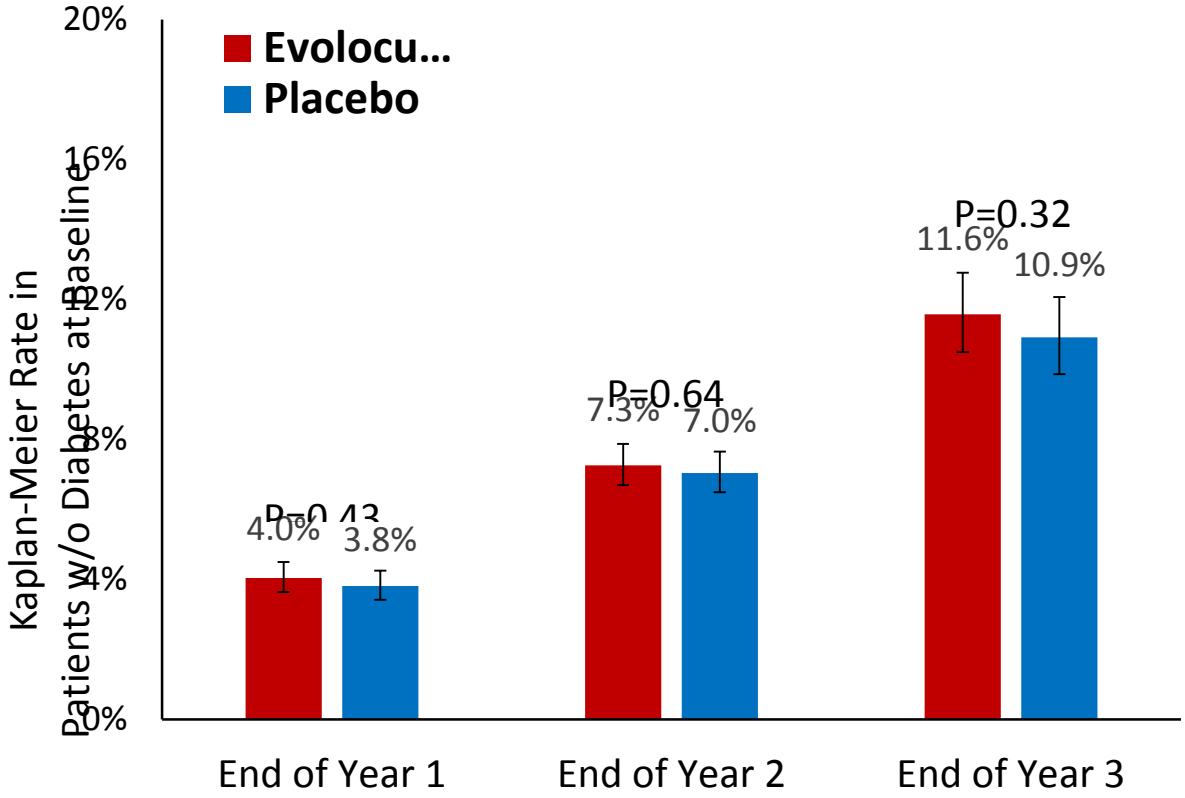
FOURIER - evolocumab vs placebo

New-Onset Diabetes



In all patients w/o diabetes at baseline (1294 incident cases in 16,510 patients):

HR 1.05 (95% CI 0.94-1.17)

In patients w/ prediabetes at baseline (1163 incident cases in 10,338 patients):

HR 1.00 (95% CI 0.89-1.13)

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Pushback on PCSK9i

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EDITORIAL

Proprotein Convertase Subtilisin/Kexin Type 9 Inhibitor Therapy—Breakthrough in Low-Density Lipoprotein Cholesterol Lowering, Breakdown in Value

oes PCSK9i therapy measure up? Using a good-value benchmark of $100 000 per QALY, the results of Fonarow et al ndicate that for every dollar invested in PCSK9i therapy, only $0.37 are returned. The model of Kazi et al [6] puts the rom PCSK9i therapy at $0.22. Investing money and getting less than equivalent value in return is not economically sustainable health policy. In light of the size of the patient population potentially eligible for PCSK9i therapy (around n the United States), routine use is not affordable for either health systems or health insurance plans. [12]

us far for unraveling this Gordian knot include a radical lowering of the price (which so far seems very unlikely) or a erapy to patients with a markedly elevated risk, the details of which have yet to be worked out. We must also not lose oney spent on PCSK9i therapy could be invested by health systems to make better use of the affordable drugs we roving adherence to statins and prescribing the most effective doses of statins). Finally, there are several other the pipeline that also target PCSK9. The opportunities are tremendous for a company that could produce a new drug ects of PCSK9i therapy at a more affordable price.