The ACCELERATE Trial

Impact of the Cholesteryl Ester Transfer Protein Inhibitor Evacetrapib on Cardiovascular Outcome

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for the ACCELERATE investigators

Disclosure

Research support: AstraZeneca, Amgen, Anthera, Eli Lilly, Novartis, Cerenis The Medicines Company, Resverlogix, InfraReDx, Roche and LipoScience

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ACCELERATE was sponsored by Eli Lilly and Company

ACCELERATE Trial Design

12,092 patients at high vascular risk, defined as:

- ACS within 30-365 days
- Peripheral arterial disease
- Diabetes with coronary disease
- Cerebrovascular disease

1:1 randomization

Evacetrapib 130 mg

Placebo

- Event driven - Primary endpoint in 1670 patients (CV death, MI, stroke, coronary revascularization or hosp. for unstable angina)
- Minimum of 700 patients with hard events (CV death, MI or stroke), minimum of 1.5 years of follow-up per patient
- 84% power to detect a 13.5% reduction in the primary endpoint

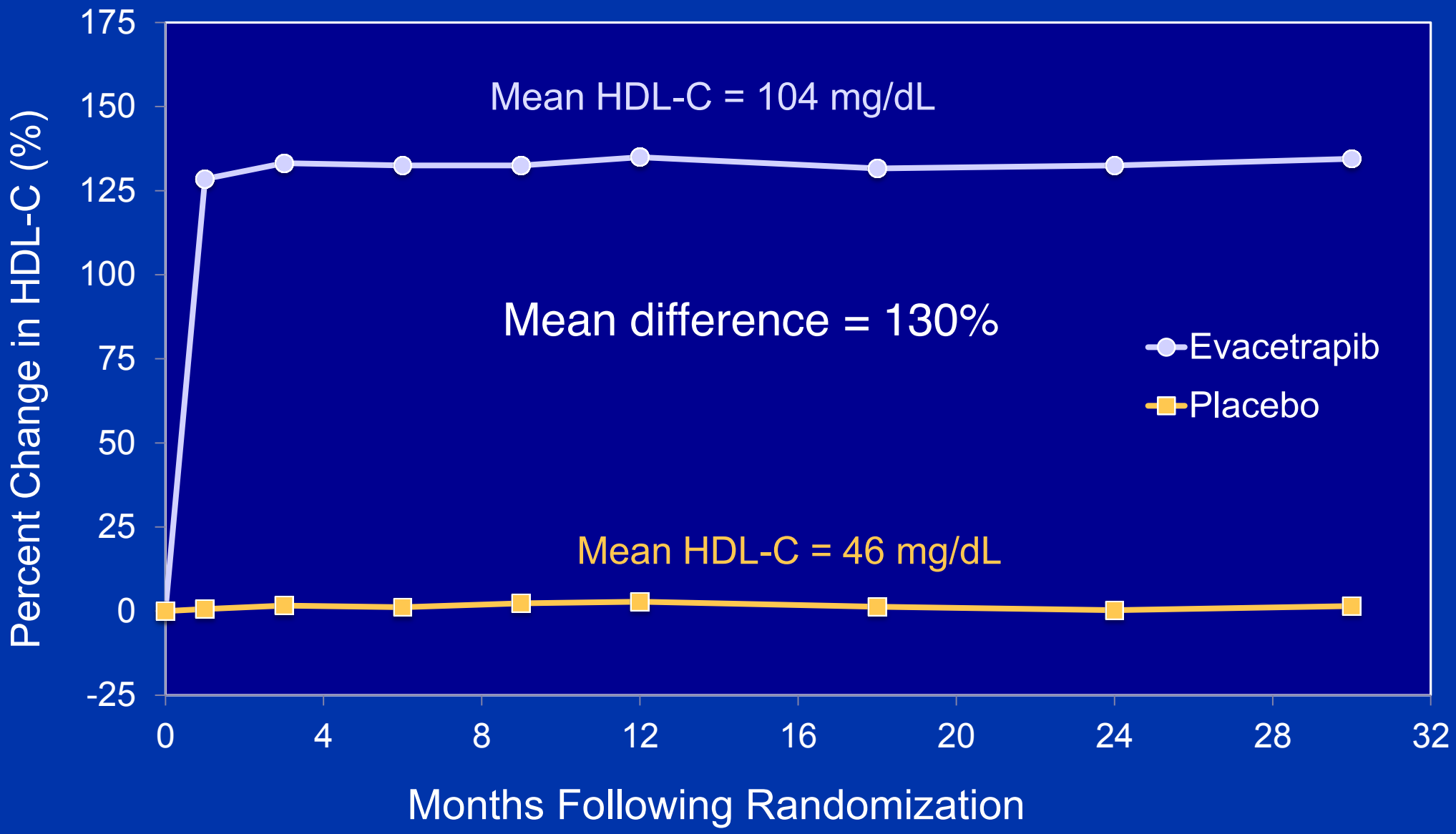
Baseline Clinical Characteristics

Parameter	Placebo (n=6054)	Evacetrapib (n=6038)
Age (years)	65	65
Males	77%	77%
Caucasian	83%	82%
Mean body mass index	30.2	30.3
History of hypertension	88%	87%
History of diabetes	68%	68%
Current smoker	16%	17%
Prior myocardial infarction	67%	67%
Prior PCI	72%	71%
Prior CABG	29%	30%

Additional Baseline Characteristics

Parameter	Placebo (n=6054)	Evacetrapib (n=6038)
Index diagnosis		
Acute coronary syndrome	31%	30%
Mean months from event	5.7	5.5
Cerebrovascular atherosclerotic disease	12%	12%
Peripheral arterial disease	14%	14%
Diabetes with coronary artery disease	64%	65%
Statin use	98%	97%
High intensity statin use	46%	46%
Lipid levels		
Mean LDL-cholesterol	81 mg/dL	82 mg/dL
Mean HDL-cholesterol	45 mg/dL	45 mg/dL

Percent Change in HDL-C Levels During the Trial



Preliminary analysis prior to formal database lock

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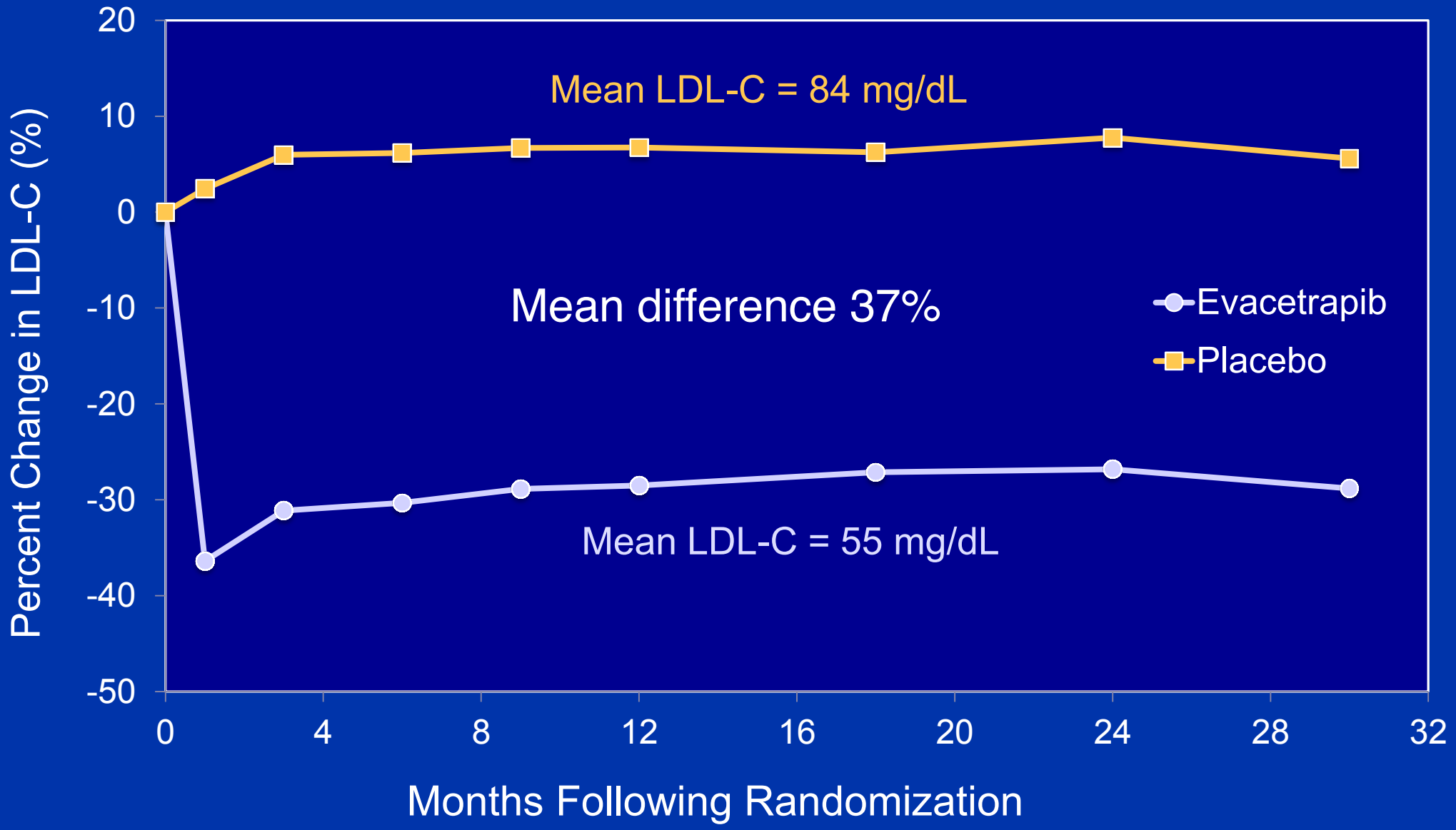

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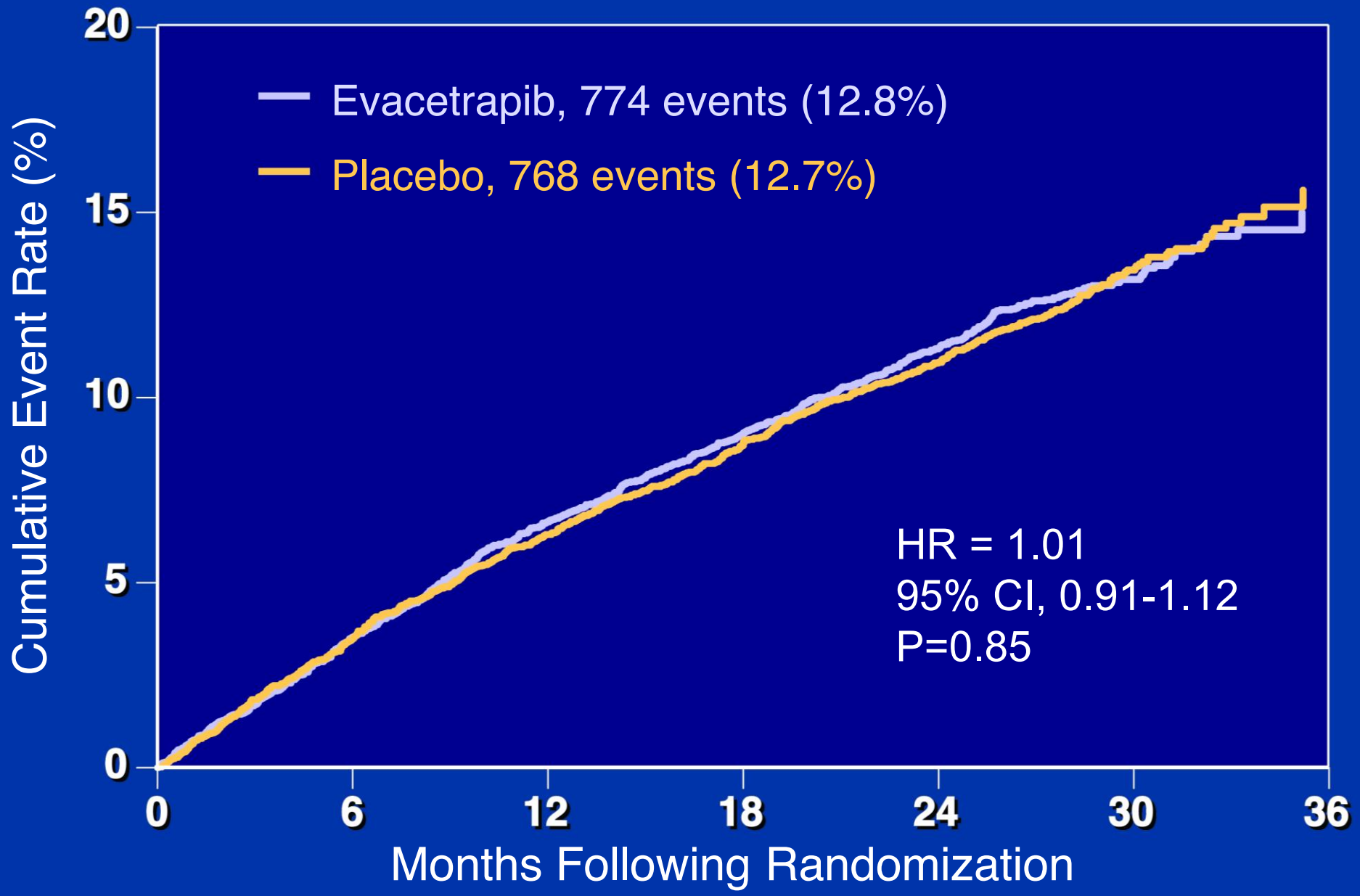
Cumulative Incidence of Primary Efficacy Endpoint



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Secondary Efficacy Endpoints

	Placebo (n=6054)	Evacetrapib (n=6038)	HR (95% CI)	P Value
CV death, MI, stroke	444 (7.3)	434 (7.2)	0.98 (0.86,1.12)	0.73
CV death	163 (2.7)	140 (2.3)	0.86 (0.68,1.08)	0.18
MI	255 (4.2)	256 (4.2)	1.00 (0.84,1.19)	0.97
Stroke	95 (1.6)	92 (1.5)	0.97 (0.73,1.29)	0.82
Hospitalization for unstable angina	143 (2.4)	155 (2.6)	1.08 (0.86,1.36)	0.48
Coronary revascularization	482 (8.0%)	485 (8.0%)	1.01 (0.89, 1.14)	0.92
All cause mortality	269 (4.1)	227 (3.8)	0.84 (0.71-1.01)	0.06

Preliminary analysis prior to formal database lock

Adverse Clinical and Biochemical Events

Parameter	Placebo	Evacetrapib	*P* Value
Discontinuation due to adverse events	8.7%	8.6%	0.86
ALT >3x ULN	0.7%	0.6%	0.31
Bilirubin >2x ULN	0.3%	0.1%	0.06
CK >3x ULN	3.1 %	2.3%	<0.01
Median change in hsCRP	-8%	+4.6%	<0.01
New onset diabetes	183 (3.0%)	149 (2.5%)	0.06
Investigator-reported hypertension	609 (10.1%)	686 (11.4%)	<0.05
Ventricular tachycardia	45 (0.7%)	28 (0.5%)	<0.05

Preliminary analysis prior to formal database lock

Conclusions

- Despite a 37% decrease in LDL-C and a 130% increase in HDL-C, evacetrapib did not reduce the primary composite endpoint of major adverse CV events.
- A borderline significant (p=0.06) reduction in all-cause mortality was observed in the evacetrapib group.
- The failure of decreases in LDL-C to result in an overall morbidity-mortality benefit emphasizes the limitations of surrogate endpoints.
- The findings continue to challenge the hope that CETP inhibition might successfully address residual CV risk.

ACCELERATE
Data Sharing Initiative

The study sponsor (Eli Lilly) and the academic leadership are pleased to announce that the trial database will be made available to independent investigators

- Proposals will be accepted beginning 12 months after the publication of the primary ACCELERATE manuscript
- Review of Proposals and Governance will be coordinated by the academic research organization at the Cleveland Clinic that led the trial (C5Research).
- Further information on submitting research proposals for review will be made available in the future at: http://c5research.clevelandclinic.org/Home.aspx