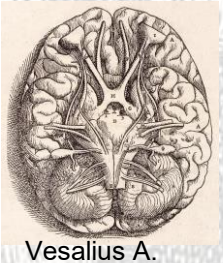
Evolocumab for Stroke Prevention in Patients at High CV Risk Without a Prior Stroke or MI in VESALIUS-CV

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On behalf of the VESALIUS-CV Investigators

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Vesalius A.
De humani corporis fabrica libri septem.
Basel: Johannes Oporinus; 1543. p. 607

vesalius-cv

TIMI

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Stroke Analysis

Disclosures

- Study Sponsor: Amgen, Inc
- TIMI Study Group receives grant support through Brigham and Women's Hospital
  - Abbott, Amgen, Anthos Therapeutics, ARCA Biopharma, Inc., AstraZeneca, Boehringer Ingelheim, Daiichi-Sankyo, Ionis Pharmaceuticals, Inc., Marea; Merck, Novartis, Pfizer, Regeneron Pharmaceuticals, Inc., Roche, Saghmos Therapeutics, Siemens Healthcare Diagnostics, Inc., Softcell Medical Limited, Verve Therapeutics, and Zora Biosciences.
- Consulting
  - Amgen, Merck, Novo Nordisk

Background

- Stroke is often a highly morbid event for patients.
- Furthermore, patients who experience a stroke are at a higher risk of subsequent adverse events, including a ~6-fold higher risk of non-CV death than those without a stroke[1]
- In the VESALIUS-CV study, intensive LDL-C lowering with the PCSK9 inhibitor evolocumab reduced the risk of MACE in patients with qualifying atherosclerosis or high-risk diabetes, but without a prior stroke or MI[2]
- In this pre-specified analysis, we focus on the efficacy of evolocumab for prevention of stroke in pts at high CV risk but without a prior stroke

[1]Bohula EA, et al. *NEJM.* 2026;394:117-127.
[2]Giugliano RP, et al. *Circulation.* 2026. In press.

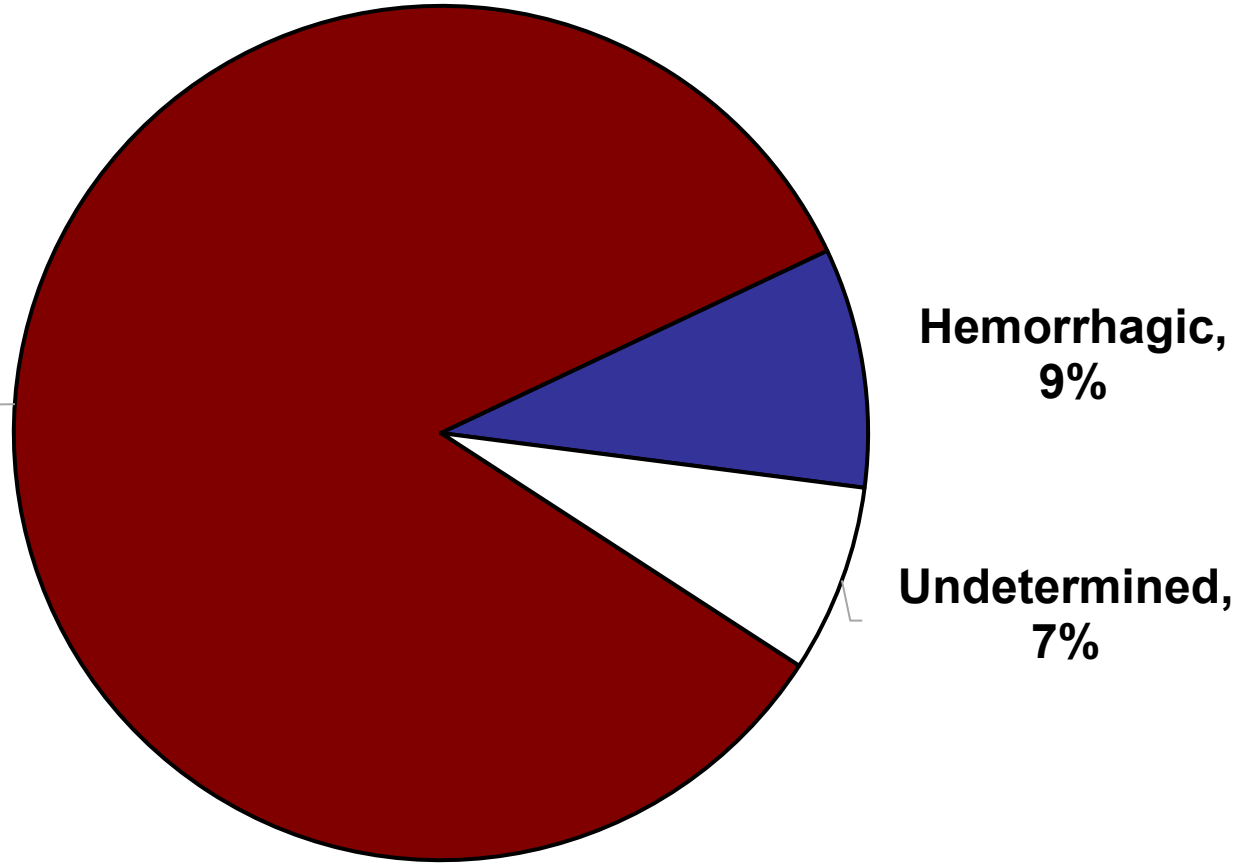
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Subcategorization of All Strokes

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Total # of First Strokes = 306 Participants (2.5% of 12,257)

Median follow up of 4.6 years (IQR, 4.0-5.2)



Stroke events adjudicated and subcategorized by a blinded clinical events committee

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Stroke Analysis

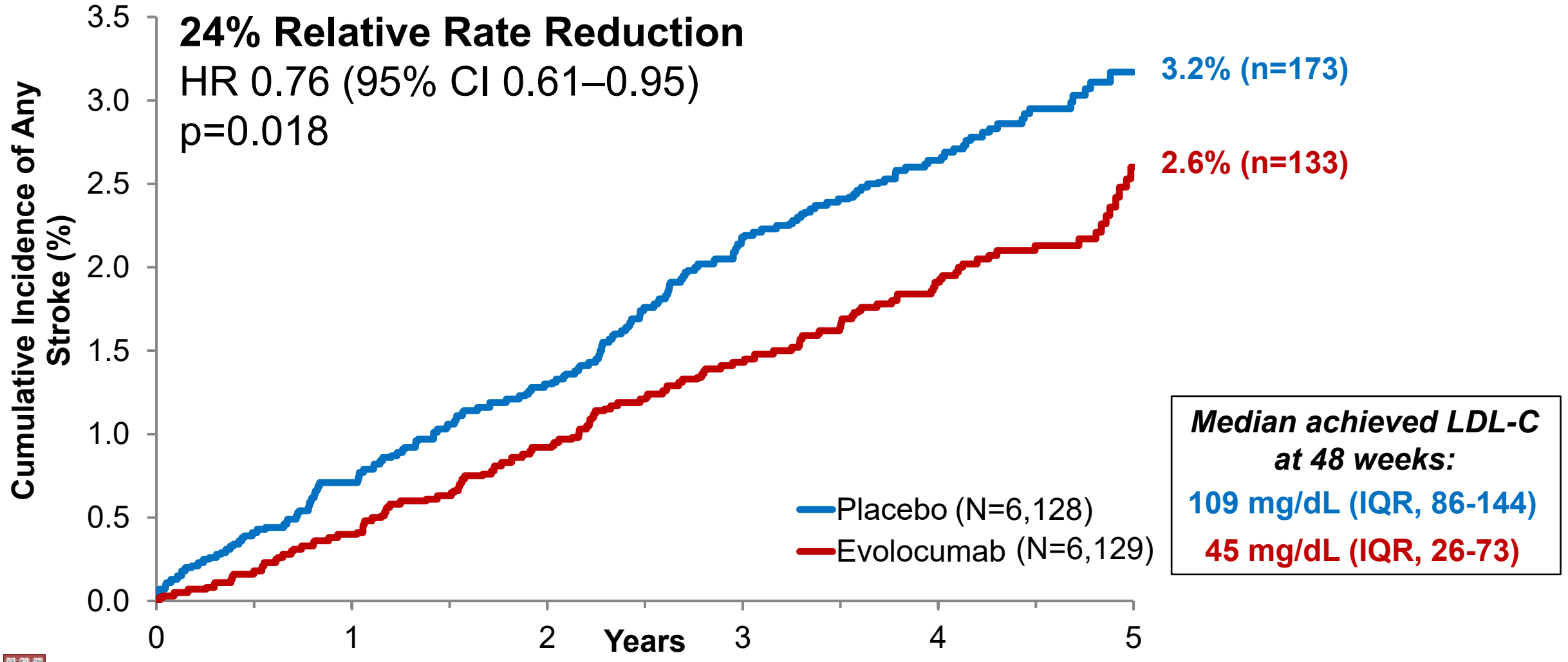
Baseline Characteristics

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% or median and interquartile range	**Stroke During Follow Up (N=306)**	**No Stroke During Follow Up (N=11,951)**	**P-value**
Age (years)	67 [62–73]	66 [60–71]	<0.0001
Female	38	43	0.10
Hypertension	91	87	0.045
Atrial fibrillation	24	9	<0.0001
Heart failure	28	21	0.0021
Qualifying Disease Categories*			
Any qualifying atherosclerosis	68	67	0.80
Cerebrovascular disease w/o stroke	10	10	0.89
High-risk diabetes	59	49	0.0003
Medications			
Any lipid lowering therapy	87	92	0.0017
High-intensity statin	62	68	0.0084
Aspirin	58	59	0.67
Anticoagulation	25	12	<0.0001
Lipid Values (mg/dL)			
LDL-C	122 [103-151]	122 [104-149]	0.96

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All Stroke



Median achieved LDL-C at 48 weeks:

109 mg/dL (IQR, 86-144)

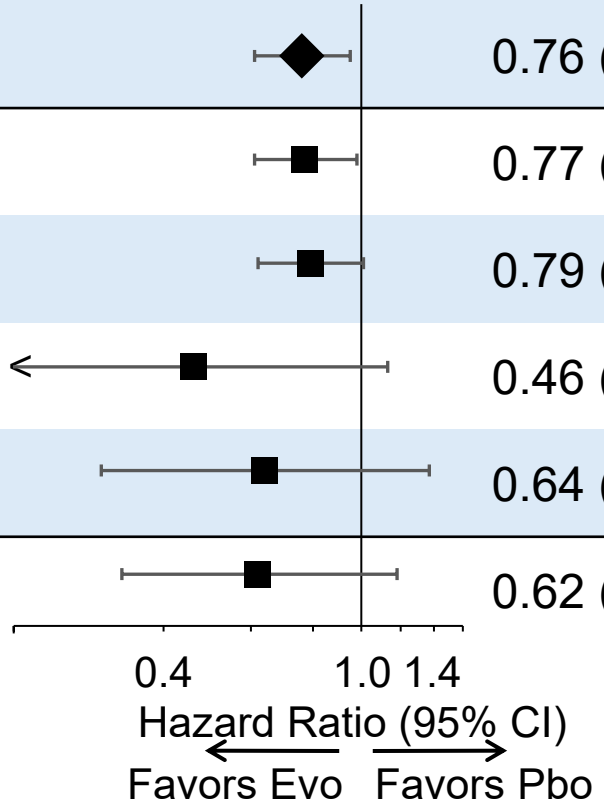
45 mg/dL (IQR, 26-73)

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Efficacy By Stroke Subtypes

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	Evolocumab n (5-Yr KM %)	Placebo n (5-Yr KM %)	HR (95% CI)	p-value
Any Stroke	133 (2.6)	173 (3.2)	0.76 (0.61, 0.95)	0.018
Non-hemorrhagic Stroke	122 (2.4)	157 (2.9)	0.77 (0.61, 0.98)	0.030
Ischemic Stroke	115 (2.3)	144 (2.7)	0.79 (0.62, 1.01)	0.062
Undetermined Stroke	7 (0.1)	15 (0.3)	0.46 (0.19, 1.13)	0.090
Hemorrhagic Stroke	11 (0.2)	17 (0.3)	0.64 (0.30, 1.37)	0.25
Fatal Stroke	15 (0.3)	24 (0.4)	0.62 (0.33, 1.18)	0.15

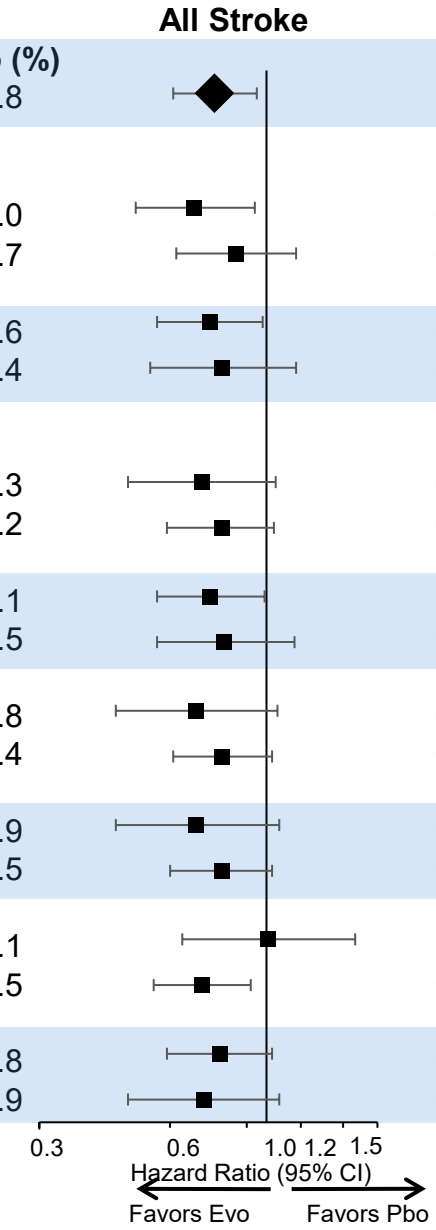


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Key Subgroups For All Stroke

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Subgroup	N	Evo (%)	Pbo (%)	HR	P-int
Overall	12257	2.2	2.8	0.76	-
Lipid Related					
Baseline LDL-C < median (<122 mg/dL)	6166	2.0	3.0	0.68	0.34
Baseline LDL-C ≥ median (≥122 mg/dL)	6090	2.3	2.7	0.85	
High intensity lipid lowering therapy (LLT)	8854	2.0	2.6	0.74	0.78
Not high intensity LLT	3403	2.7	3.4	0.79	
Other					
Age < 65	5389	1.7	2.3	0.71	0.69
Age ≥ 65	6868	2.6	3.2	0.79	
Male	7043	2.3	3.1	0.74	0.75
Female	5214	2.0	2.5	0.80	
eGFR 15-<60 ml/min/1.73m^2	2140	3.4	4.8	0.69	0.63
eGFR ≥60 ml/min/1.73m^2	10089	1.9	2.4	0.79	
History of heart failure	2542	2.8	3.9	0.69	0.65
No history of heart failure	9715	2.0	2.5	0.79	
History of atrial fibrillation/flutter	1193	6.1	6.1	1.01	0.22
No history of atrial fibrillation/flutter	11064	1.8	2.5	0.71	
Any qualifying atherosclerosis	8208	2.2	2.8	0.78	0.76
High-risk DM without qual athero	4001	2.1	2.9	0.72	



% is n/N

Summary

In patients with qualifying atherosclerosis or high-risk diabetes w/o prior MI or stroke, the addition of evolocumab to baseline LLRx resulted in:

- Median achieved LDL-C of ~45 mg/dL
- Lower rates of any stroke with consistency across all subtypes of stroke
- Consistency across subgroups, including by baseline LDL-C, intensity of lipid lowering therapy, and by presence or absence of qualifying atherosclerosis

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Conclusions

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Among patients with atherosclerosis or diabetes, but without a history of prior stroke, intensive LDL-C lowering with evolocumab down to ~45 mg/dL reduced the incidence of a first stroke.