VEITH SYMPOSIUM Connecting The Vascular Community 51st

VEITH Vascular Endovascular Issues Techniques Horizons

Friday, November 22, 2024. Session 83 (Grand Ballroom East)

Lipid management for high-risk carotid lesions: Statins, Ezetimibe, PCSK9 and what else: Should LDL-C be monitored?

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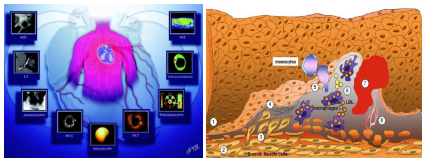
NO DISCLOSURES RELATED TO THE TOPIC

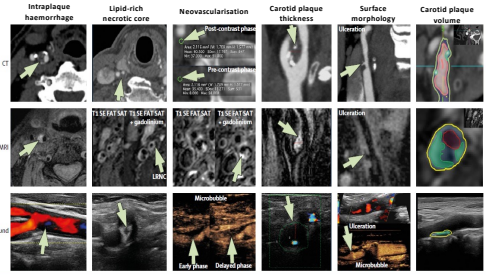
Identifying the high-risk carotid lesion

Clinical information, family history, genetics
+

Imaging **Biological Markers**

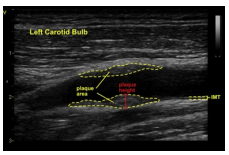


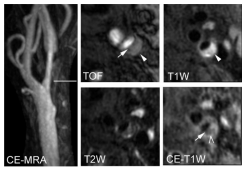
Imaging features of plaque vulnerability by CT, MRI, US



Saba L. et.al Lancet Neurol 2019

Carotid Plaque





Can we stop / reverse and deactivate this?

A positive correlation has been found between low-density lipoprotein cholesterol (LDL-C) levels and stroke risk

- Each **10% reduction** in LDL-C levels reduced the **risk** of all strokes by **15.6%**
- **Statin** treatment is associated with a significant **17-21%** proportional **reduction** in the incidence of first stroke of any type, per mmol/l lower LDL
- **Hemorrhagic stroke ?**

Proportional effects on major vascular events per mmol/L LDL cholesterol reduction

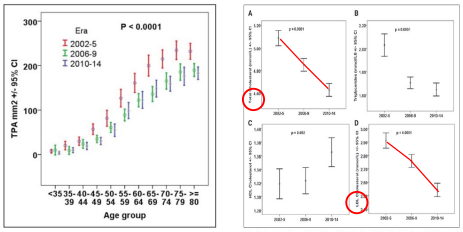
Endpoint	Events (%) Treatment (45 054)	Events (%) Control (45 002)	RR (CI)
Non-fatal MI	2001 (4·4%)	2769 (6·2%)	0·74 (0·70–0·79)
CHD death	1548 (3·4%)	1960 (4·4%)	0·81 (0·75–0·87)
Any major coronary event	3337 (7·4%)	4420 (9·8%)	0·77 (0·74–0·80)
CABG	713 (1·6%)	1006 (2·2%)	0·75 (0·69–0·82)
PTCA	510 (1·1%)	658 (1·5%)	0·79 (0·69–0·90)
Unspecified	1397 (3·1%)	1770 (3·9%)	0·76 (0·69–0·84)
Any coronary revascularisation	2620 (5·8%)	3434 (7·6%)	0·76 (0·73–0·80)
Haemorrhagic stroke	105 (0·2%)	99 (0·2%)	1·05 (0·78–1·41)
Presumed ischaemic stroke	1235 (2·8%)	1518 (3·4%)	0·81 (0·74–0·89)
Any stroke	1340 (3·0%)	1617 (3·7%)	0·83 (0·78–0·88)
Any major vascular event	6354 (14·1%)	7994 (17·8%)	0·79 (0·77–0·81)

0·5 1·0 1·5
Treatment better Control better
Effect p<0·0001

Baigent, C et al, CTT, Lancet 2005

"All vascular patients should be on statins"
Severity of carotid atherosclerosis is declining over time!!

Total plaque area n= 6039 Lipids



Hackam DG, Spence JD Stroke. 2018

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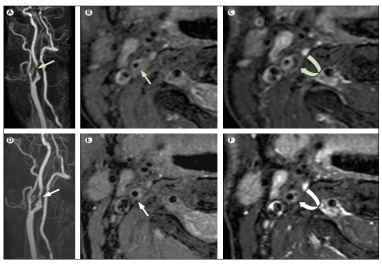
3 Tesla MRI Studies of plaque regression and statins



Saba L. et.al Lancet Neurol 2019

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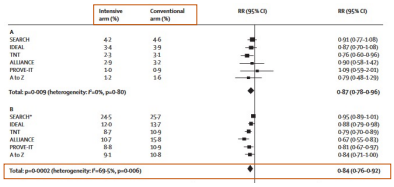
Intensive lipid-lowering therapy versus standard statin therapy in high CV risk patients



Lowering of cholesterol concentrations with intensive lipid-lowering therapy reduces the risk of stroke in high CV risk populations

Amarenco P. et al The Lancet Neurology 2009

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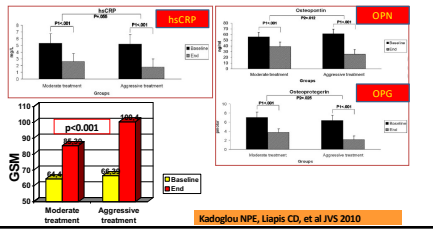
GSM, Biomarkers, Statins & Carotid Plaque stabilization

Superior benefits of aggressive vs moderate statin treatment on carotid plaque echolucency in patients with carotid stenosis

1-year follow up study of 140pts with carotid stenosis not indicated for intervention



Kadoglou NPE, Liapis CD, et al JVS 2010

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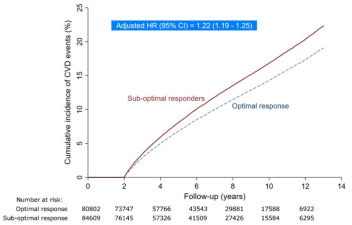
Statins and LDL-C cholesterol



Statins exhibit variations in the effectiveness on LDL-C cholesterol

Akyea R. et. al. Heart 2019

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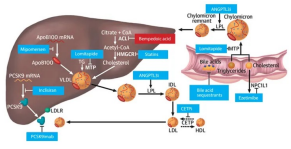
What about PCSK9 inhibitors?

- Monoclonal antibodies
- Decrease serum LDL-C
- Stabilize the vulnerable carotid atherosclerotic plaques
- Reduce arterial wall inflammation
- Reduce carotid stiffness and improve CIMT



The NEW ENGLAND JOURNAL of MEDICINE

Evolocumab and Clinical Outcomes in Patients with Cardiovascular Disease

Stroke 2020

Stroke Prevention With the PCSK9 (Proprotein Convertase Subtilisin-Kexin Type 9) Inhibitor Evolocumab Added to Statin in High-Risk Patients With Stable Atherosclerosis

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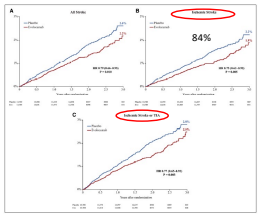
Are PCSK9s part of the optimal BMT for high-risk carotid lesions?

- Of the 27.564 pts, 469 (1.7%) strokes
- No subgroup analysis regarding degree of carotid stenosis
- Only 19% of participants had a prior stroke

Results significant for primary prevention?



Giugliano R. et al Stroke 2020 ..... FOURIER

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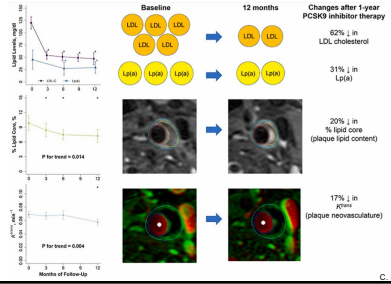
Carotid plaques and PCSK9

n = 27

Regression in plaque composition and neovasculature were observed under PCSK9 inhibition on carotid MRI



Lepor N. et al Atherosclerosis 2021

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Treating the patient with carotid stenosis ESVS Recommendations

Statin use is mandatory in both asymptomatic and symptomatic patients

Recommendation 13 — Changed

For patients with asymptomatic carotid stenosis, lipid lowering therapy with statins (with or without ezetimibe) is recommended for the long-term prevention of stroke, myocardial infarction, and other cardiovascular events.

Class	Level	References	ToE
I	B	Zhan *et al.* (2018)[111], Halliday *et al.* (2010)[228], Cholesterol Treatment Trialists Collaboration (2012)[229]	

Recommendation 35 — New

For symptomatic carotid stenosis patients who do not reach their lipid targets on maximum doses or maximum tolerated doses of statins, ezetimibe (10 mg daily) is recommended.

Class	Level	References	ToE
I	B	Amarenco *et al.* (2020)[7]	

Recommendation 36 — New

For symptomatic carotid stenosis patients who are intolerant of, or not achieving target low density lipoprotein levels on statins, with or without ezetimibe, additional or alternative treatment with PCSK9 inhibitors should be considered.

Class	Level	References	ToE
IIa	B	Giugliano *et al.* (2020)[18]	

Evidence is lacking to support specific LDL-C targets in ACS patients

Naylor R. et al. Eur J Vasc Endovasc Surg 2023

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How low LDL-C Levels for high-risk carotid lesions ?

Per Radiation Dose

As Low As Reasonably Achievable

ALARA Principle

Famous herbivores

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Conclusions

For high-risk carotid lesions
In order to:

- ✓ Prevent ischemic stroke
- ✓ Protect the patient from MACE
- ✓ Increase peri-op protection in case of intervention

- Statins + ezetimibe tick all the boxes
- The addition of PCSK9 inhibitors maybe considered if the target levels of LDL-C are not achievable.
- We should investigate further the appropriate lipid therapy for high-risk carotid lesions

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In the meantime…

- The Effect of Early Administration of PCSK9 Inhibitor to Acute Ischemic Stroke Patients Associated With Atherosclerosis on the Stroke Prognosis and Lipid Profile
- Study to Evaluate Changes in Cognitive Function in Patients Treated With PCSK9 Inhibitors (MEMOGAL)
- Efficacy and Safety of Bempedoic Acid in Association With Anti-PCSK9 and Ezetimibe in Statin-intolerant Patients: a Randomized Crossover Trial
- Trial of PCSK9 Inhibition in Patients With Acute Stroke and Symptomatic Intracranial Atherosclerosis - a Prospective, Randomized, Open-label, Blinded End-point Study With High-resolution MR Vessel Wall Imaging
- LAPLACE TIMI 57 - A Double-blind, Randomized, Placebo-controlled, Multicenter, Dose-ranging Study to Evaluate Tolerability and Efficacy of Evolocumab on LDL-C in Combination With Statins in Hypercholesterolemic Subjects

Prescription only

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- Phase 3 Randomized, Placebo-Controlled Clinical Study to Evaluate the Efficacy and Safety of MK-0616 in Reducing Major Adverse Cardiovascular Events in Participants at High Cardiovascular Risk (ORAL)
- A RaNdomized Double-blInd Placebo ConTrolled Study Characterizing THe Effects of PCSK9 Inhibition On Arterial Wall Inflammation in Patients With Elevated Lp(a) (ANITSCHKOW)
- A Phase 3, Randomized, Double-Blind Study to Evaluate the Efficacy and Safety of MK-0616 Compared With Ezetimibe or Bempedoic Acid or Ezetimibe and Bempedoic Acid in Adults With Hypercholesterolemia
- A Randomized, Multicenter, Open-label Trial Comparing the Effectiveness of Inclisiran (RNA inhibitor) to Bempedoic Acid on LDL Cholesterol (LDL-C) Lowering in Participants With Atherosclerotic Cardiovascular Disease (VICTORION-CHALLENGE)
- Impact of Evolocumab on the Effects of Clopidogrel in Patients With High On-Treatment Platelet Reactivity

And more to come…

Phase 3 trial

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