


Η λιποπρωτεΐνη Lp (a) ως παράγοντας κινδύνου της αθηρωματικής νόσου: Το παρόν και το μέλλον της θεραπευτικής αντιμετώπισης

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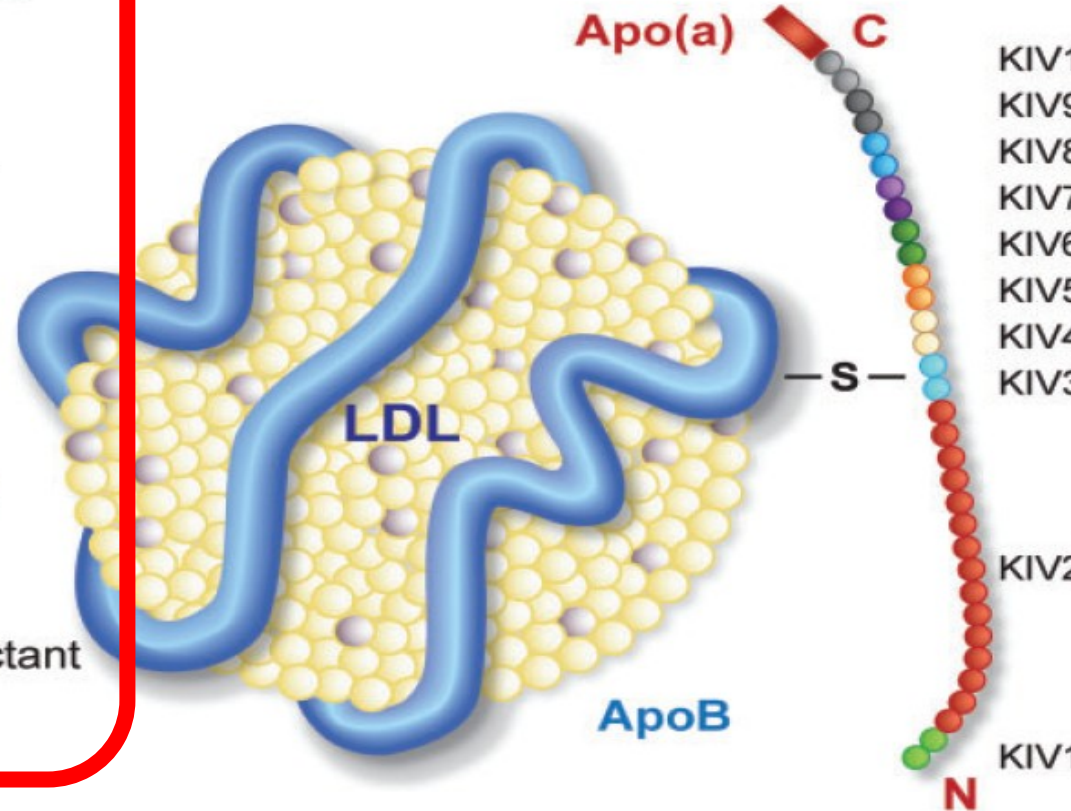
Περιστατικό

- **Γυναίκα 40 ετών**
- **LDL CHOL 165 mg/dL**
- **Lp(a) 190 mg/dL**
- **Hellenic risk SCORE II: 4%**  **Στόχος LDL-C <100 mg/dl**

Lipoprotein (a)

Proatherogenic

- ↑ Oxidized PL
- ↑ Foam cell Formation
- ↑ SMC proliferation
- ↑ Monocyte chemoattractant

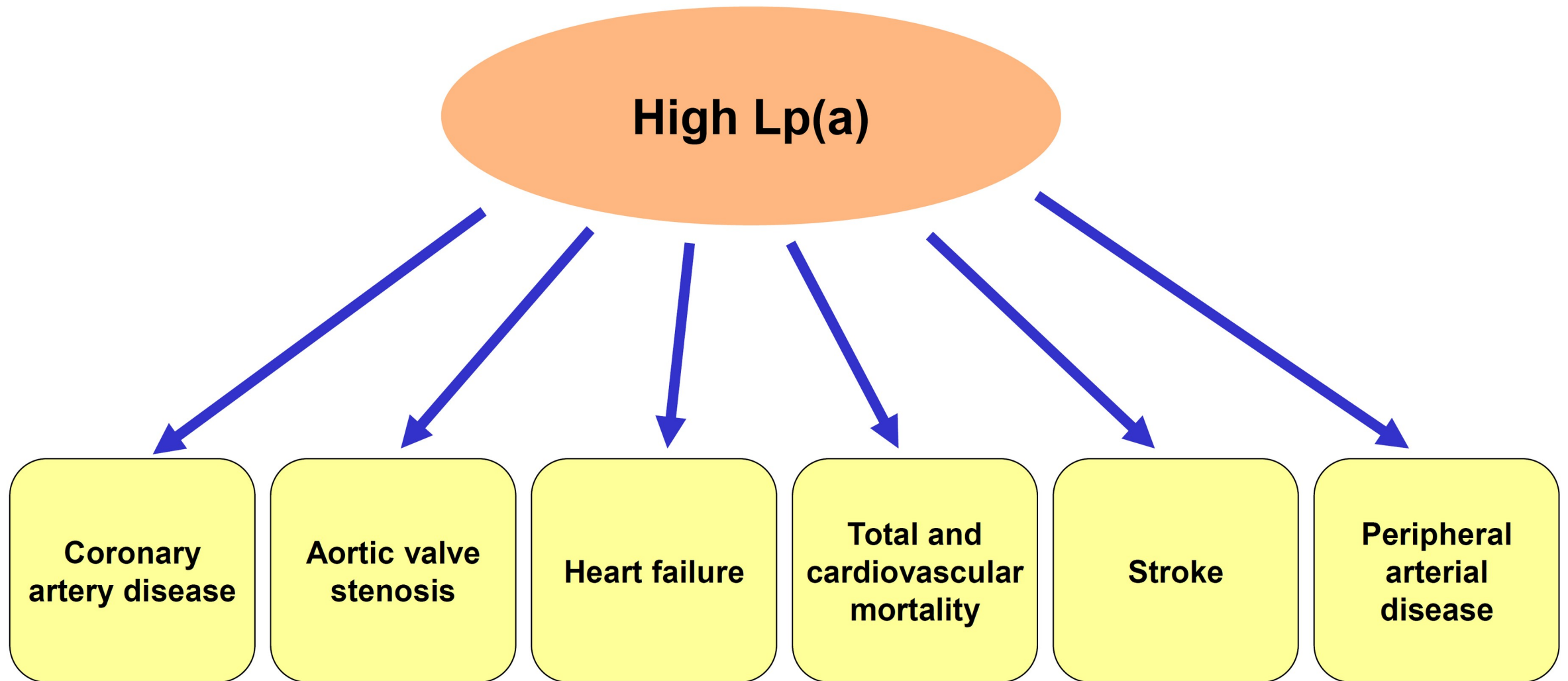


Prothrombotic

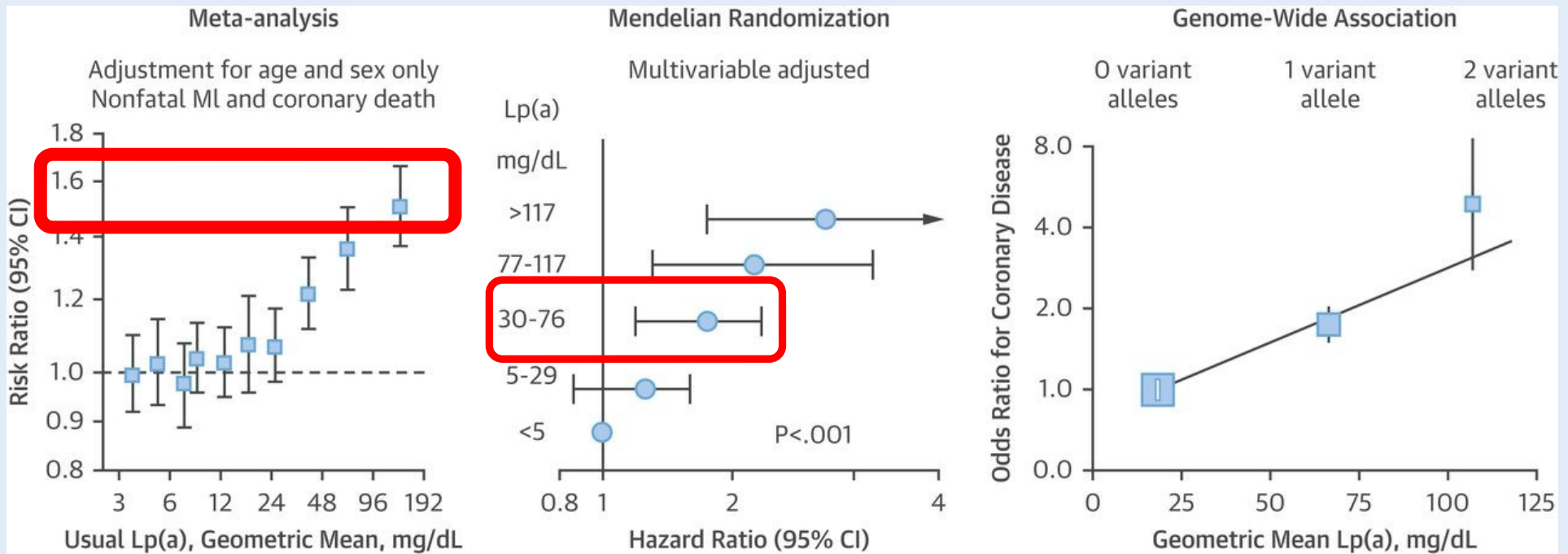
- ↓ Plasminogen Activation
- ↓ TFPI
- ↓ Clot permeability
- ↑ Platelet response

The number of KIV2 defines the size of Lp(a).

Lp(a) και άλλες εκδηλώσεις



Lp(a) και καρδιαγγειακός κίνδυνος



Hellenic Atherosclerosis Society Guidelines for the Diagnosis & Treatment of Dyslipidemias 2023



Guidelines

Hellenic Atherosclerosis Society Guidelines for the Diagnosis and Treatment of Dyslipidemias - 2023

**Katsiki N^{*1,2}, Filippatos TD^{*3}, Vlachopoulos C⁴, Panagiotakos D⁵, Milionis H⁶, Tselepis A⁷,
Garoufi A⁸, Rallidis L⁹, Richter D¹⁰, Nomikos T¹¹, Kolovou G¹², Kypreos KE^{2,13}, Chrysohoou C¹⁴,
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Kotsis V²¹, Pitsavos C²², Elisaf M²³, Tsioufis K²⁴, Liberopoulos E²⁵**

**Equal contribution*

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TABLE 9. Lp(a) determination for ASCVD risk stratification.

Recommendation	Class
Lp(a) levels are recommended to be measured at least once in each person's lifetime	I
Lp(a) assessment should be considered for the reclassification of patients having a borderline estimated 10-year ASCVD risk	IIa
Lp(a) levels are recommended to be measured in patients with a family history of premature ASCVD	I

ASCVD: atherosclerotic cardiovascular disease; Lp(a): lipoprotein(a)

**Lp(a) determination
for ASCVD risk stratification**

Περιστατικό

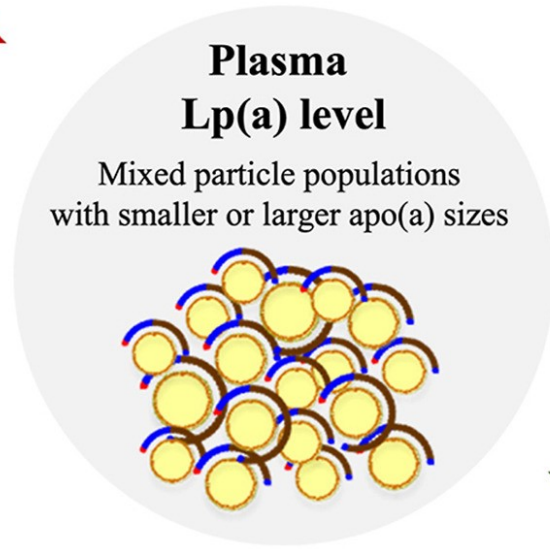
- Γυναίκα 40 ετών με κληρονομικότητα ΣΝ
- LDL CHOL 165 mg/dL
- Lp(a) 190 mg/dL
- Hellenic risk SCORE II: 4%  Στόχος LDL-C <100 mg/dl

Παράγοντες που επηρεάζουν την Lp(a)

Non-genetic influences on Lipoprotein(a) concentrations

Increasing:

- *Dietary saturated fat reduction*
- *Hypothyroidism*
- *Menopause, growth hormones*
- *Kidney disease:*
 - *Chronic kidney disease & hemodialysis (large isoforms only)*
 - *Peritoneal dialysis*
 - *Nephrotic syndrome*
 - *Kidney transplantation*



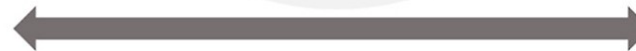
Decreasing:

- *Low-carb diet in high saturated fat*
- *Hyperthyroidism*
- *Hormone replacement therapy*
- *Liver disease, dependent on the cause*
 - *Mixed results for non-alcoholic fatty liver disease*



No appreciable influence:

- *Physical activity/exercise*
- *Endogenous sex hormones*

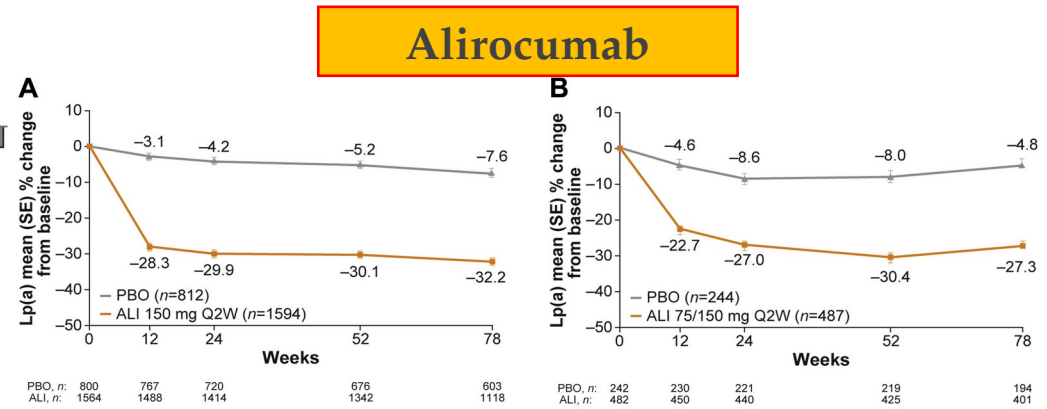
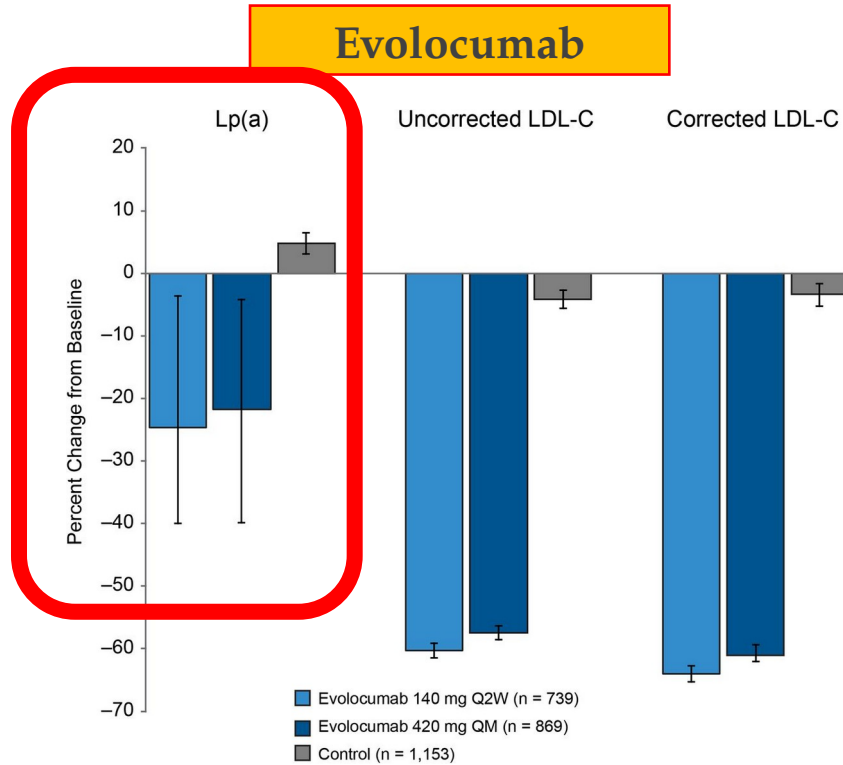


Θεραπευτικές παρεμβάσεις που μειώνουν την Lp(a)

Table 1. Lp(a) lowering strategies rated for the capacity to lower Lp(a)

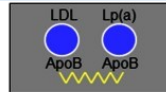
Strategy	Mechanism	Reduction in Lp(a)	Reduction in LDL-C
Statins	Increased LDLR expression	0 to +7%	50%
Niacin	Reduced apo(a) transcription, or reduced apoB secretion via inhibition of TG synthesis	20%	13%
CETP inhibitor	Attenuation of apoB lipidation due to inhibited transfer of TG and cholesterol esters between apoB lipoproteins and HDL	24-36%	36-42%

PCSK9 inh και Lp(a)

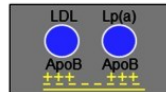


LDL και Lp(a) αφαίρεση

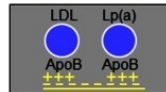
HELP: Heparin-induced extracorporeal LDL-precipitation
precipitation of a complex consisting of heparin, LDL, lipoprotein(a), and fibrinogen at pH 5.12



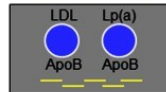
DALI: Direct adsorption of lipoproteins
Electrostatic interaction of negatively charged polyacrylate anions with positively charged apoB



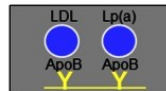
Lipoprotein apheresis with dextran sulfate
Electrostatic interaction of negatively charged dextran sulfate with positively charged apoB



Lipid filtration/membrane differential filtration
Series of filters eliminate LDL and lipoprotein(a) from plasma based on size properties



Immunoabsorption: Anti-apoB100 antibodies
Plasma is passed through columns containing polyclonal anti-apoB100 antibodies



Lipopac: Anti-apoprotein(a) antibodies
Plasma is passed through columns containing polyclonal anti-apo(a) antibodies

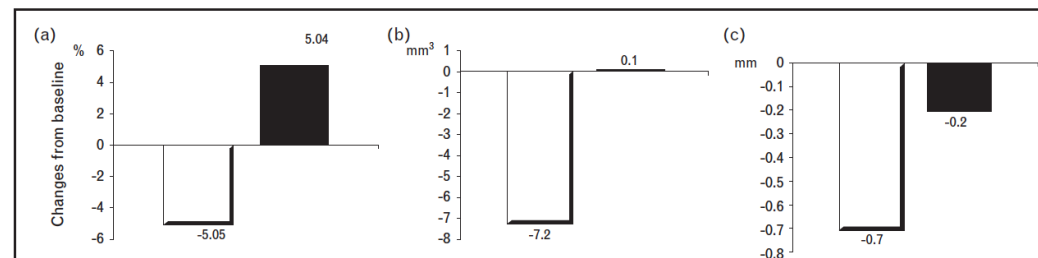
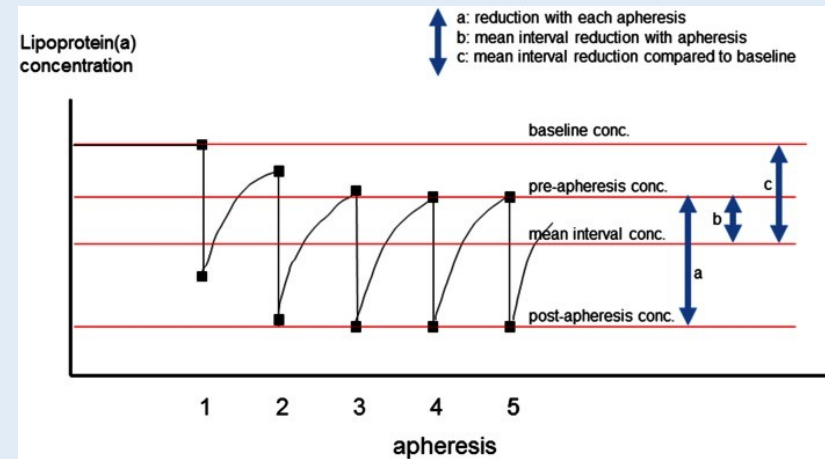
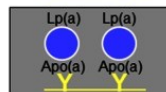
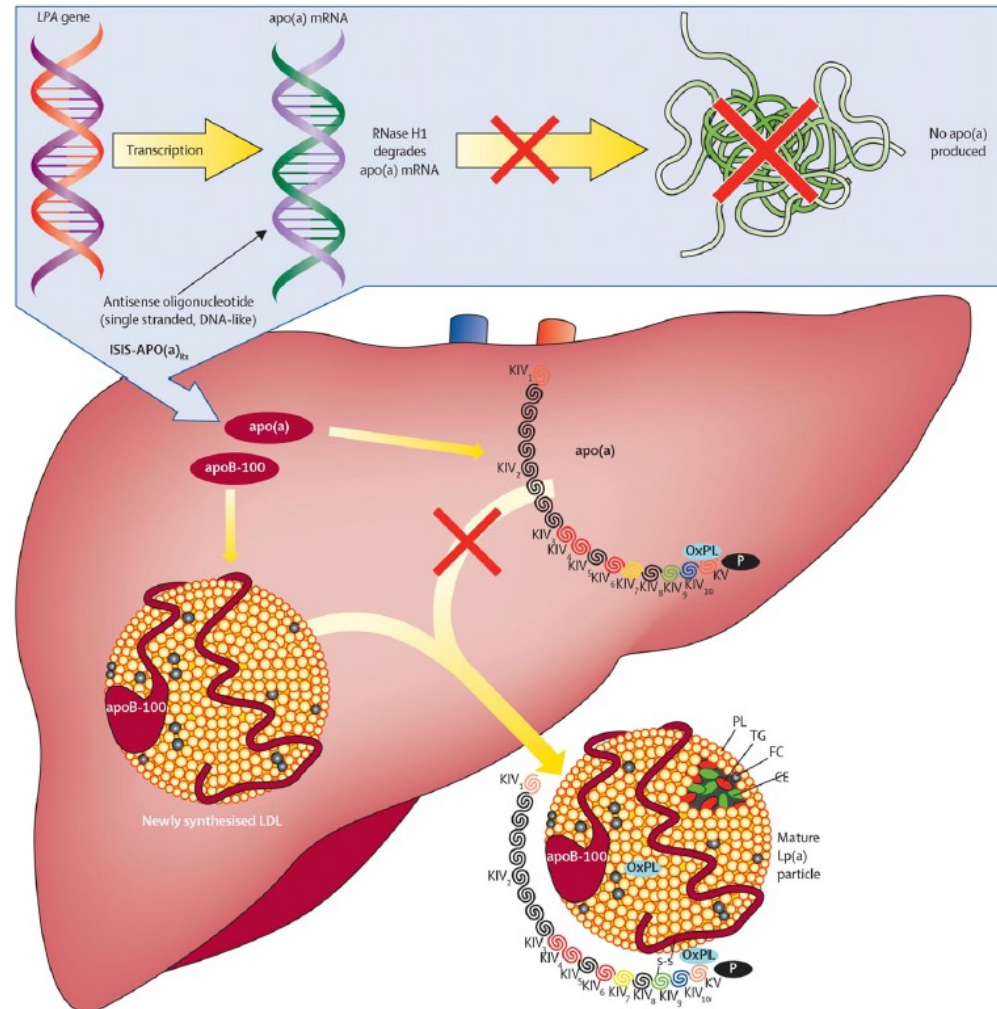


FIGURE 2. Changes in mean percentage diameter stenosis (a), mean total atheroma volume (b) of coronary arteries and mean carotid intima-media thickness (c) in patients from the specific Lp(a) apheresis (white bars) and control (black bars) groups.

Antisense oligonucleotides against apo(a)

• Pelacarsen

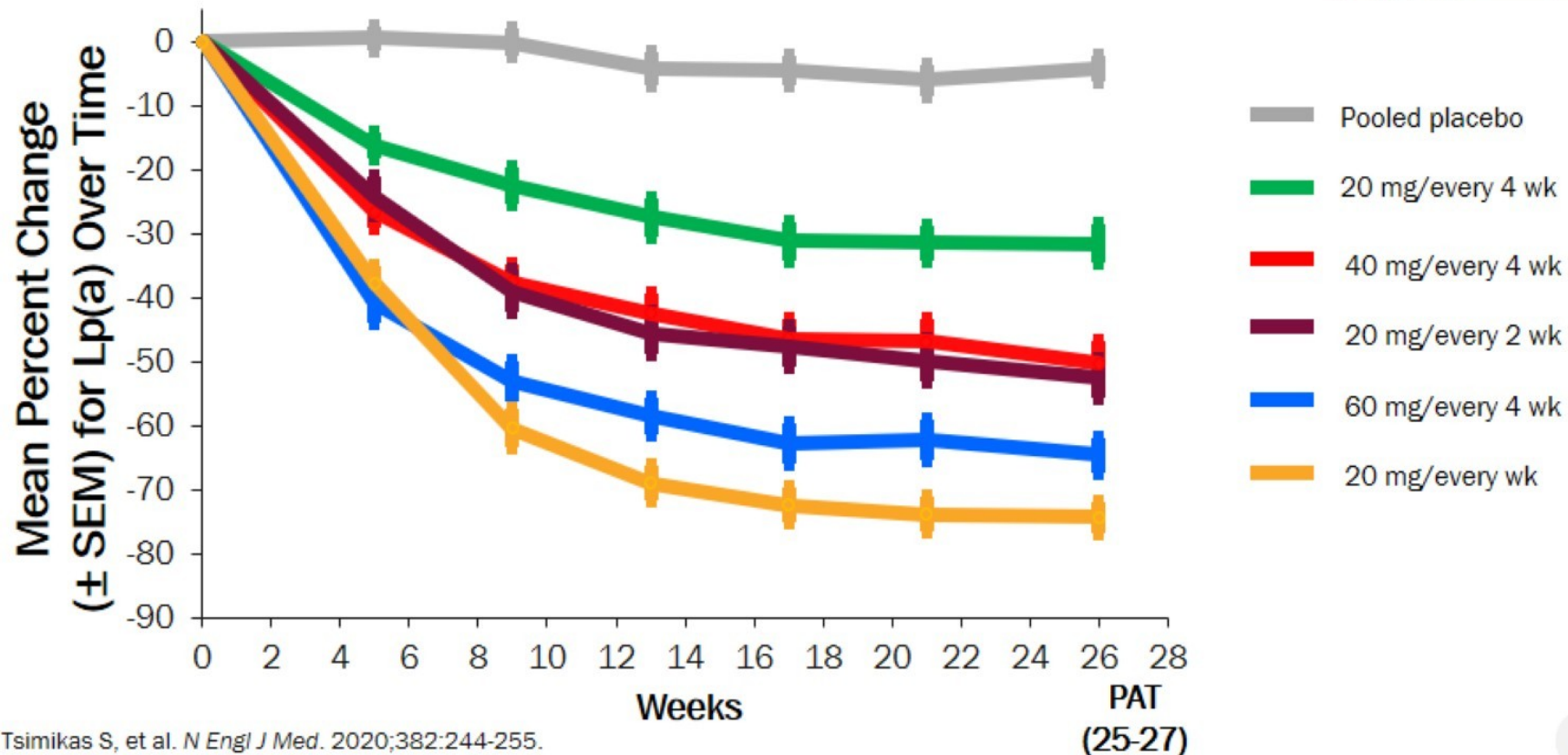


Primary Endpoint Pelacarsen effects on Lp(a) levels

Mean Percent Change (SEM) in Lp(a) From Baseline to Week 25-27

Primary Endpoint

Mean Percent Change (SEM) in Lp(a) From Baseline to Week 25-27



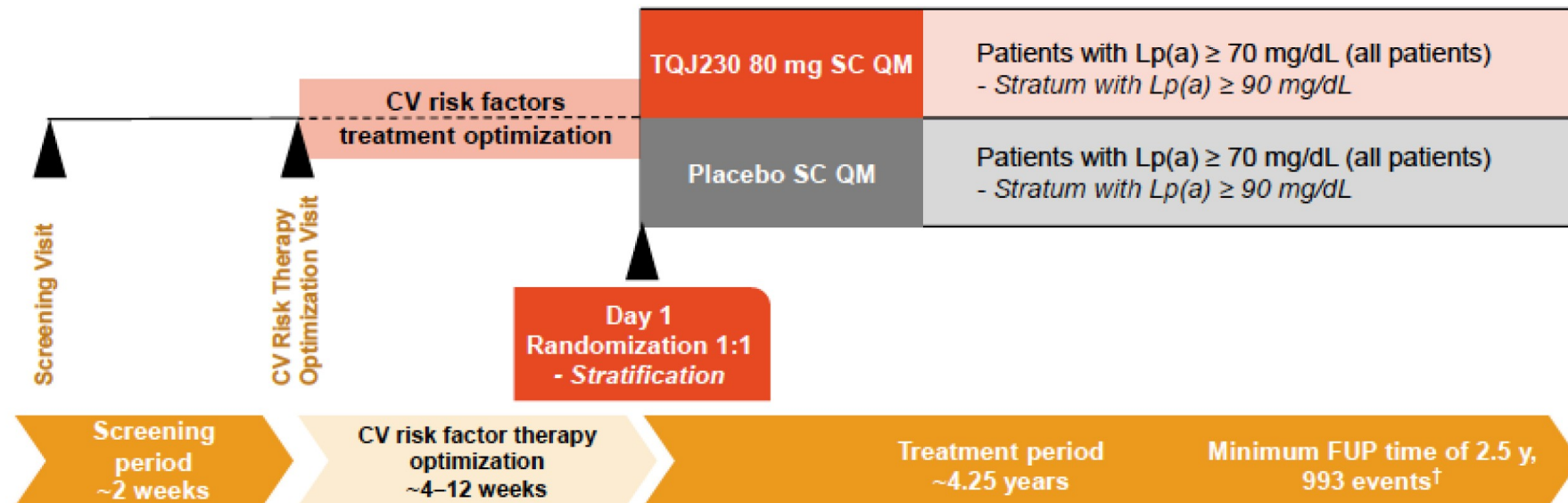
Tsimikas S, et al. *N Engl J Med.* 2020;382:244-255.

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Pelacarsen – CVOT trial

CVOT Targeting Lp(a) – HORIZONS

Study is positive if primary EP is met in either overall or sub-population



- **Objectives:** Demonstrate superiority of TQJ230 vs. placebo in reducing the risk of extended MACE* in the overall study population and in a subpopulation of patients with Lp(a) ≥90 mg/dL
- **Study population:** Patients with established CVD (prior MI, stroke, PAD) and Lp(a) ≥70 mg/dL with optimal therapy for cholesterol lowering and other CV risk factors

*MI, stroke, CV death or urgent coronary revascularization.

[†]A total sample size of 7,680 subjects is required to obtain 993 primary endpoint MACE events.

CV, cardiovascular; MACE, major adverse cardiovascular events; MI, myocardial infarction; PAD, peripheral artery disease; QM, once a month; SC, subcutaneous.

<https://clinicaltrials.gov/ct2/show/NCT04023552> (accessed 06 August 2019)

Business or Operating Unit/Franchise or Department

Restricted

Olpasiran (siRNA)

JAMA

QUESTION Is a single subcutaneous injection of a short interfering RNA (siRNA) targeting hepatic production of apolipoprotein(a) well tolerated and associated with changes in plasma concentrations of lipoprotein(a) (Lp[a]) at different doses?

CONCLUSION In this phase 1 study of individuals with elevated Lp(a) levels and no known clinically overt cardiovascular disease, the siRNA SLN360 was well tolerated and dose-dependent lowering of plasma Lp(a) was observed, supporting further study of the safety and efficacy of SLN360.

POPULATION

17 Women
15 Men



Adults with Lp(a) plasma concentrations ≥ 150 nmol/L and no known clinically overt cardiovascular disease

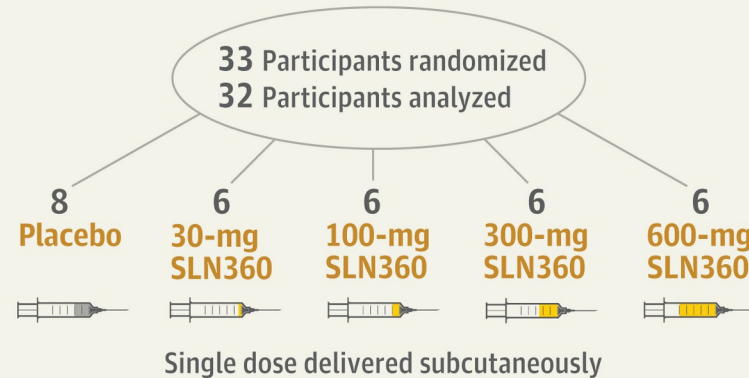
Mean age: 50 years

LOCATIONS

5 Clinical research units in the US, UK, and Australia



INTERVENTION



PRIMARY OUTCOME

Evaluation of safety and tolerability of SLN360

FINDINGS

Safety and tolerability

1 participant in the 30-mg SLN360 group had 2 serious adverse event episodes (admission to hospital for headache and complications of cholecystitis), judged unrelated to study drug.

Range of maximal median percentage changes in Lp(a) from baseline to 150 days:

-10% (placebo)
to
-98% (600-mg SLN360)

© JAMA

Nissen SE, Wolski K, Balog C, et al. Single ascending dose study of a short interfering RNA targeting lipoprotein(a) production in individuals with elevated plasma lipoprotein(a) levels. *JAMA*. Published online April 3, 2022. doi:10.1001/jama.2022.5050

Olpasiran – CVOT trial

Olpasiran

OCEAN(a)-Outcomes Trial

Olpasiran Trials of Cardiovascular Events And LipoproteinN(a) Reduction – Outcomes Trial

Amgen Clinical Study: 20180244

NCT Clinical Study: NCT05581303

A Double-Blind, Randomized, Placebo-Controlled, Multicenter Study Assessing the Impact of Olpasiran on Major CV Events in Participants With ASCVD and Elevated Lp(a)

PHASE 3 STUDY DESIGN:

**Patients with a history of ASCVD
(N = 6,000)***

- Adults aged ≥ 18 to ≤ 85 years
- Lp(a) ≥ 200 nmol/L during screening

Lp(a) > 80 mg/dl


Randomization
1:1

**Olpasiran Dose SC Q12W
+
SoC**

**Placebo SC Q12W
+
SoC**

4 years

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➤ Η ΑΣΘΕΝΗΣ ΔΕΝ ΜΠΟΡΕΙ ΝΑ ΠΕΡΙΜΕΝΕΙ ΜΕΧΡΙ ΤΟ 2025....

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**Lp(a) determination
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Περιστατικό

ΕΠΟΜΕΝΩΣ....

ΜΕ ΒΑΣΗ ΤΗΝ ΥΨΗΛΗ Lp(a)

Η ΑΣΘΕΝΗΣ «ΑΝΕΒΑΙΝΕΙ» ΚΑΤΗΓΟΡΙΑ ΚΙΝΔΥΝΟΥ ΚΑΝ ΣΕ «ΥΨΗΛΟ ΚΙΝΔΥΝΟ»

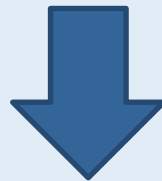


ΣΤΟΧΟΣ LDL-C <70 mg/dl

Περιστατικό

ΣΤΟΧΟΣ LDL-C <70 mg/dl

**Με συνδυασμό ροσουβαστατίνης ή ατορβαστατίνης
+ εζετιμίμη**



➤ LDL CHOL 65 mg/dL

10^ο Πανελλήνιο Συνέδριο των Ομάδων Εργασίας

1-2
Δεκεμβρίου 2023

Ξενοδοχείο Divani Caravel
ΑΘΗΝΑ



Ελληνική Εταιρεία
Αθηροσκλήρωσης

Υπό την Αιγίδα των:



Ευρωπαϊκής Εταιρείας
Αθηροσκλήρωσης



Διεθνούς Εταιρείας
Αθηροσκλήρωσης

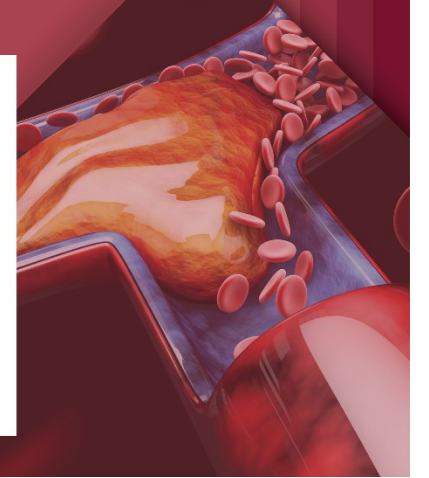
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^{*}Equal contribution



Ευχαριστώ πολύ!

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