DAL DIABETOLOGO AL CARDIOLOGO: L'ORIZZONTE È PIÙ LONTANO

MODERATORI:
Alessandra Clerico,
Maria Chantal Ponziani

Gestione clinica dell'ipercolesterolemia nel diabetico: focus sulle terapie che agiscono su PCSK9

Maria Chantal Ponziani

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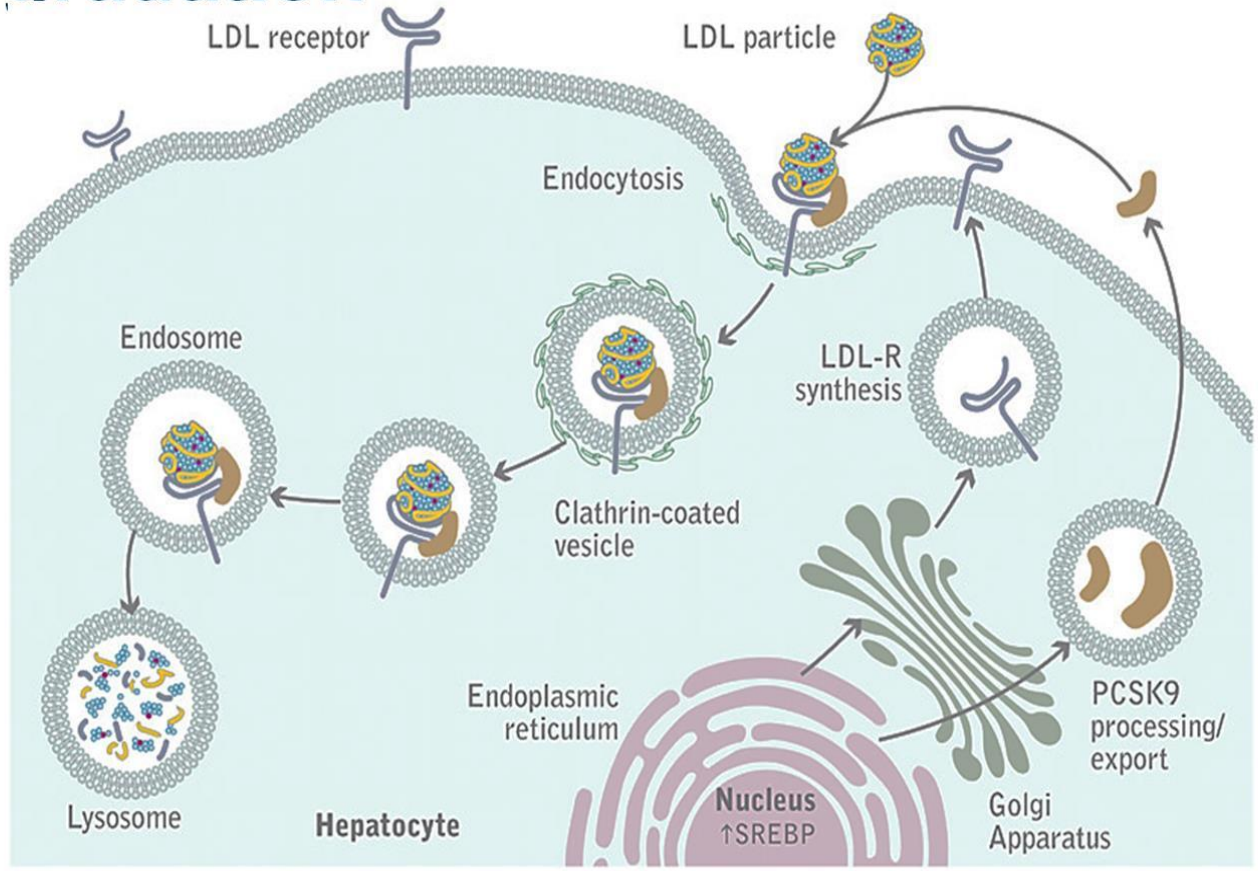
PCSK9 Regulates LDLR Turnover Through Increased Intracellular Degradation



Loss-of-Function Mutations in PCSK9 Are Associated With Decreased LDL-C and CHD Risk

PCSK9 Variant	Population	LDL-C	CHD Risk
R46L	ARIC, DHS	↓ 15%[1]	↓ 47%[1]
Y142X or C679X	ARIC, DHS	↓ 28%-40%[1,2]	↓ 88%[1]
R46L	CGPS	↓ 11%[3]	↓ 46%[3]

- Heterozygous LOF mutations found in 1% to 3% of population[1]
- Associated with
  - Lower serum LDL-C[1]
  - Lower incidence of coronary heart disease[1]
- PCSK9 null individual identified (compound heterozygote for two inactivating mutations)
  - No detectable circulating PCSK9 with strikingly low LDL-C (14 mg/dL)[4]
  - Healthy and fertile college graduate in apparent good health[4]
- Inhibiting LDLR/PCSK9 interaction may lower plasma LDL-C levels[5]

LOF = loss of function.

Adapted from 1. Cohen JC, et al. *N Engl J Med.* 2006;354:1264-1272.
Adapted from 2. Cohen J, et al. *Nat Genet.* 2005;37:161-165.
Adapted from 3. Benn M, et al. *J Am Coll Cardiol.* 2010;55:2833-2842.
Adapted from 4. Zhao et al. *Am Journal of Hum Gen.* 2006;79:514-534.
Adapted from 5. Steinberg D, et al. *Proc Natl Acad Sci U S A.* 2009;106:9546-9547.

Table 1. Plasma Lipid and Lipoprotein Levels in Family Members of an Individual Who Is a Compound Heterozygote for Loss-of-Function Mutations in *PCSK9*

Individual	Age (years)	Sex	Fasting Plasma Levels, in mg/dL (Percentile)				*PCSK9* Allele[a]	
			Cholesterol	LDL-C	HDL-C[b]	TG[c]	1	2
I.1	51	M	96 (<1st)	39 (<1st)	44 (55th)	88 (25th)	ΔR97	WT
I.2	53	F	144 (<1st)	49 (<1st)	88 (90th)	51 (<1st)	Y142X	WT
II.1	10	F	137 (15th)	77 (20th)	49 (45th)	78 (50th)	ΔR97	WT
II.2	32	F	96 (<1st)	14 (<1st)	65 (80th)	119 (70th)	ΔR97	Y142X
II.3	28	F	152 (20th)	80 (15th)	59 (65th)	92 (55th)	WT	WT
III.1	6	M	106 (<1st)	30 (<1st)	65 (75th)	77 (75th)	Y142X	WT
III.2	3	F	106 (<1st)	37 (<1st)	59 (70th)	71 (55th)	Y142X	WT
III.3	13	F	174 (60th)	104 (60th)	55 (65th)	110 (75th)	WT	WT

NOTE.—Plasma lipid and lipoprotein levels were measured after a 12-h fast. The percentile of the lipid and lipoprotein levels are compared with age- and sex-matched African American control individuals.

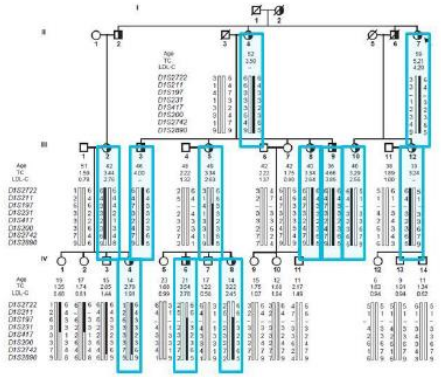
[a] WT = wild type.
[b] HDL-C = high-density lipoprotein cholesterol.
[c] TG = triglycerides.

PCSK9 GAIN-of-Function Mutation: Identifying the Cause and a Potential Treatment Target

Mutations in *PCSK9* cause autosomal dominant hypercholesterolemia

Marianne Abifadel[1,2], Mathilde Varret[1], Jean-Pierre Rabès[1,3], Delphine Allard[1], Khadija Ouguerram[4], Martine Devillers[1], Corinne Cruaud[5], Suzanne Benjannet[6], Louise Wickham[6], Danièle Erlich[1], Aurélie Derré[1], Ludovic Villéger[1], Michel Farnier[7], Isabel Beucler[8], Eric Bruckert[9], Jean Chambaz[10], Bernard Chanu[11], Jean-Michel Lecerf[12], Gerald Luc[12], Philippe Moulin[13], Jean Weissenbach[5], Annick Prat[6], Michel Krempf[4], Claudine Junien[1,3], Nabil G Seidah[6] & Catherine Boileau[1,3]

Autosomal dominant hypercholesterolemia (ADH; OMIM144400), a risk factor for coronary heart disease, is characterized by an increase in low-density lipoprotein cholesterol levels that is associated with mutations in the genes *LDLR* (encoding low-density lipoprotein receptor) or *APOB* (encoding apolipoprotein B). We mapped a third locus associated with ADH, *HCHOLA3* at 1p32, and now report two mutations in the gene *PCSK9* (encoding proprotein convertase subtilisin/kexin type 9) that cause ADH. *PCSK9* encodes NARC-1 (neural apoptosis regulated convertase), a newly identified human subtilase that is highly expressed in the liver and contributes to cholesterol homeostasis.



Affected family members with:

- Total cholesterol in 90th percentile
- Tendon xanthomas
- CHD
- Early MI
- Stroke

CHD, coronary heart disease.

Vascular Pharmacology xxx (2014) xxx–xxx

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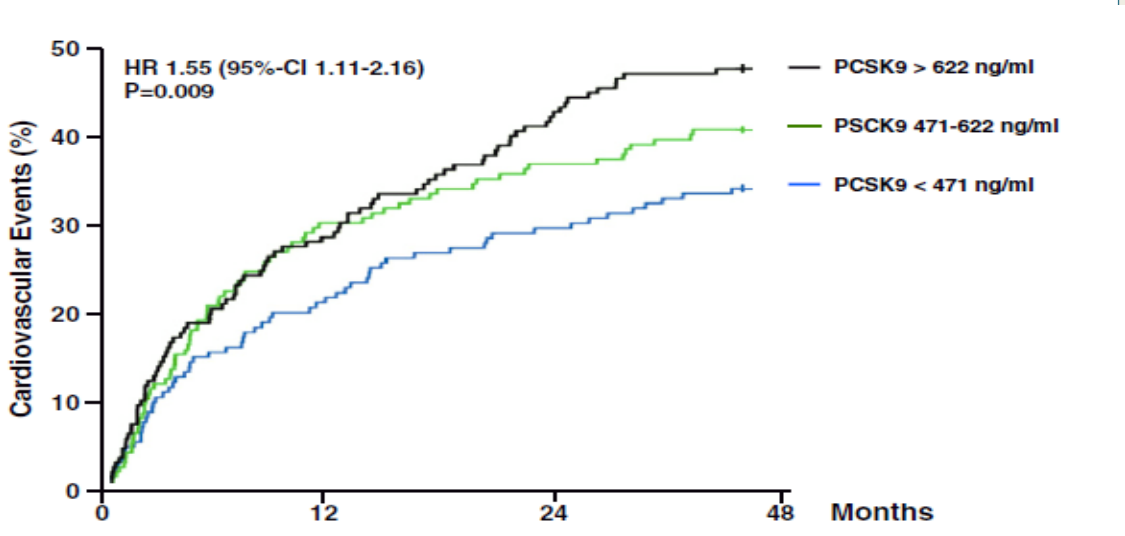
Vascular Pharmacology

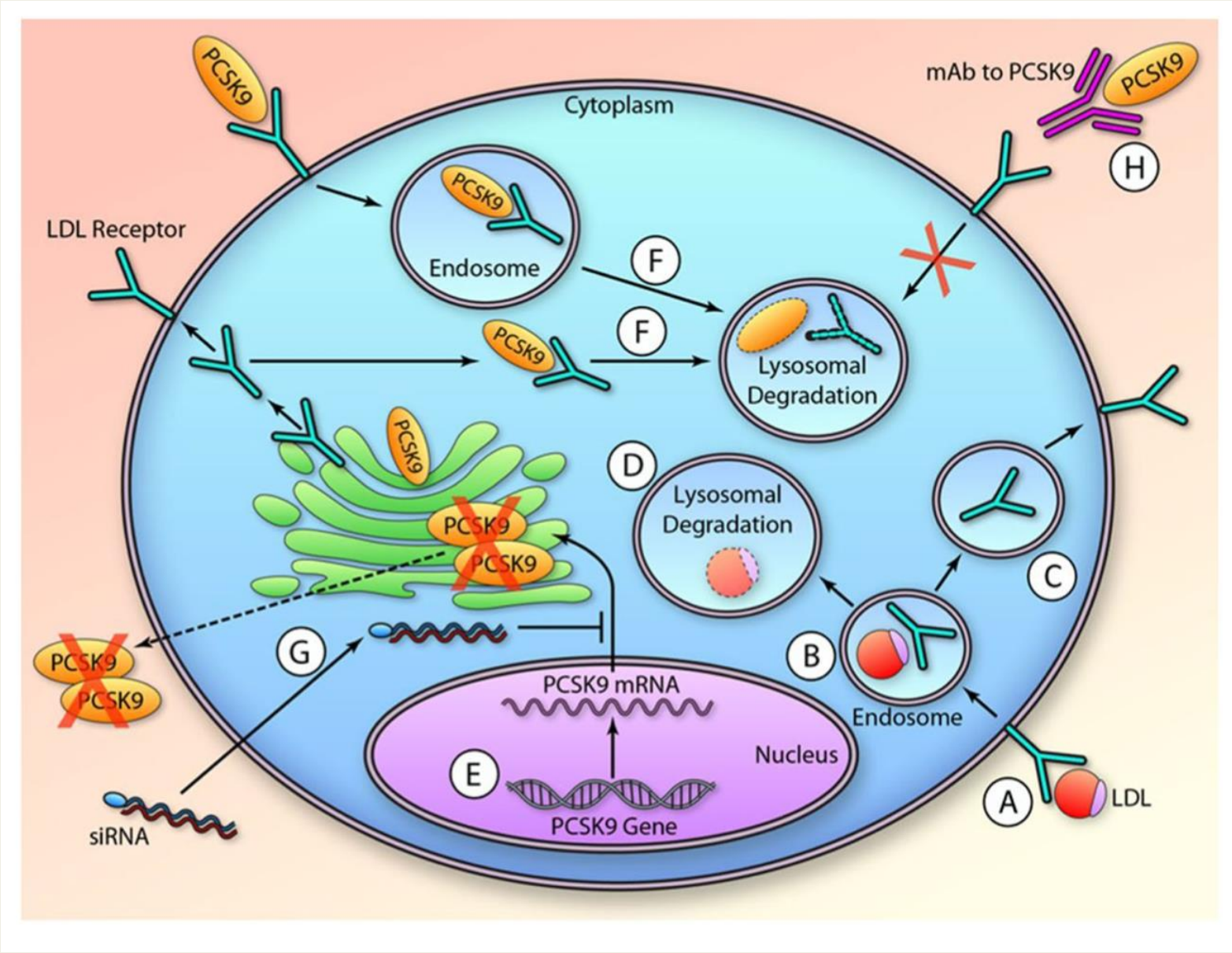
journal homepage: www.elsevier.com/locate/vph

Risk prediction with proprotein convertase subtilisin/kexin type 9 (PCSK9) in patients with stable coronary disease on statin treatment

Christian Werner [a], Michael M. Hoffmann [b], Karl Winkler [b], Michael Böhm [a], Ulrich Laufs [a,*]



Alirocumab
Evolocumab



Inclisiran

I livelli di PCSK9 sono aumentati nel diabete mellito di tipo 2

Circulating PCSK9 levels and 2-hPG are positively correlated in metabolic diseases in a Chinese Han population

Wen Guo[1,2†], Yingyun Gong[1†], Yong Gu[1†], Zhenzhen Fu[1], Hongqi Fan[1], Beibei Gao[1], Xiaohui Zhu[1], Jinxiang Fu[1], Yang Zhao[3], Min Sun[1], Xing Liu[4], Xian-Cheng Jiang[5], Tao Yang[1] and Hongwen Zhou[1*]

Guo *et al. Lipids in Health and Disease* (2018) 17:15
DOI 10.1186/s12944-018-0658-z

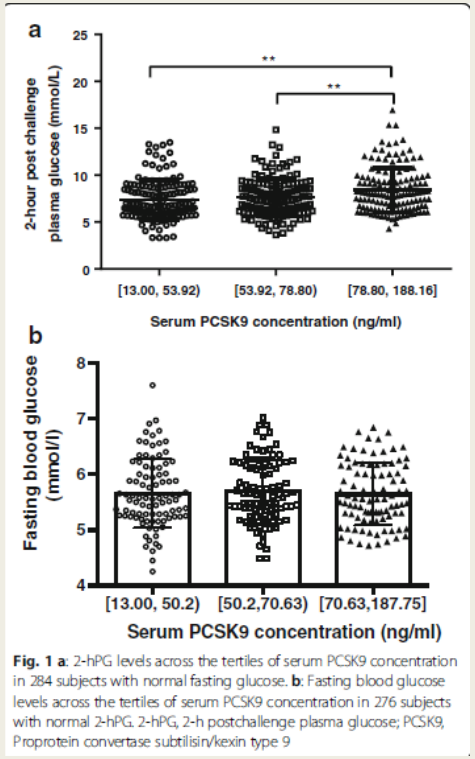


Fig. 1 a: 2-hPG levels across the tertiles of serum PCSK9 concentration in 284 subjects with normal fasting glucose. **b**: Fasting blood glucose levels across the tertiles of serum PCSK9 concentration in 276 subjects with normal 2-hPG. 2-hPG, 2-h postchallenge plasma glucose; PCSK9, Proprotein convertase subtilisin/kexin type 9

I livelli di PCSK9 sono aumentati nel diabete mellito di tipo 2

Obesity and type 2 diabetes are associated with elevated PCSK9 levels in young women

Amy E. Levenson[1] | Amy S. Shah[2] | Philip R. Khoury[3] | Thomas R. Kimball[3] | Elaine M. Urbina[3] | Sarah D. de Ferranti[4] | David M. Maahs[5] | Lawrence M. Dolan[2] | R. Paul Wadwa[5] | Sudha B. Biddinger[1]

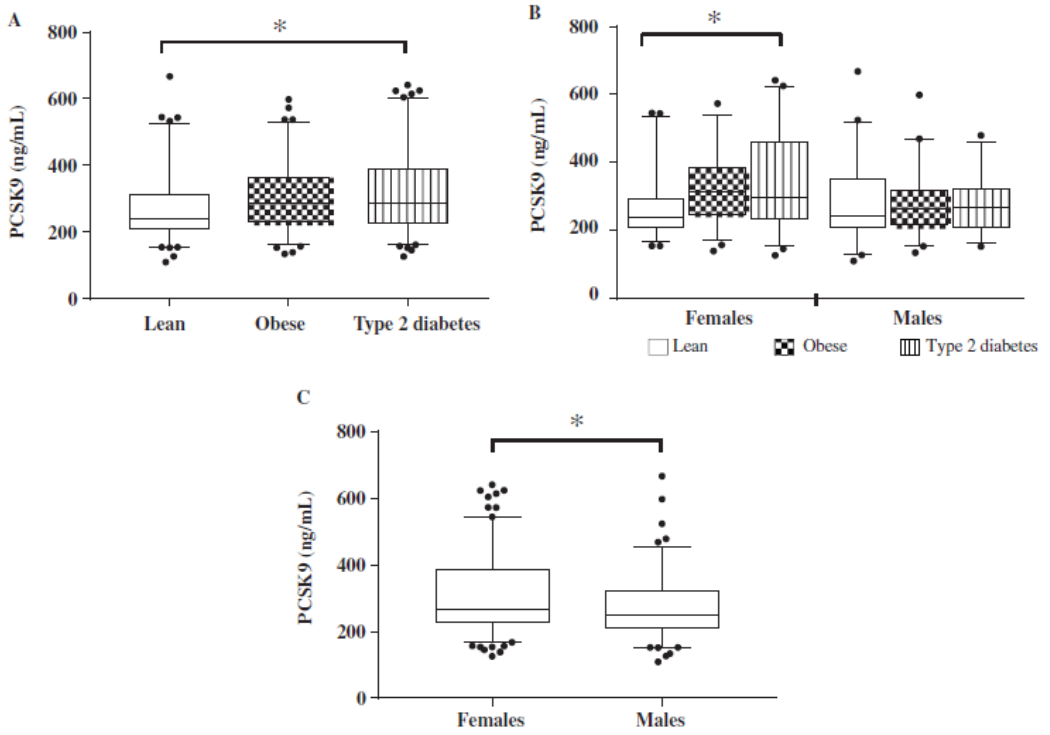


FIGURE 1 A, Comparison of proprotein convertase subtilisin/kexin type 9 (PCSK9) levels by group. B, Comparison of PCSK9 levels by group within each sex. C, Comparison of PCSK9 levels by sex. The boxes denote the distribution between the 75th and 25th percentiles; the horizontal lines within the boxes denote the median values; the whiskers represent the 5th and 95th percentiles. Closed circles represent individuals below the 5th or above the 95th percentiles. The asterisk indicates a *P*-value of <.01 between the groups by ANOVA (A, B) or independent *t* test (C).

L'INSULINA AUMENTA L'ESPRESSIONE DI PCSK9 A LIVELLO EPATICO

Published in final edited form as:
Arterioscler Thromb Vasc Biol. 2015 July ; 35(7): 1589–1596

The Role of Insulin in the Regulation of PCSK9

Ji Miao[1], **Praveen V. Manthena**[1], **Mary E. Haas**[1], **Alisha V. Ling**[1], **Dong-Ju Shin**[1], **Mark J. Graham**[2], **Rosanne M. Crooke**[2], **Jingwen Liu**[3], and **Sudha B. Biddinger**[1]

Approach and Results—*Using* rat hepatoma cells and primary rat hepatocytes, we found that insulin increased PCSK9 expression and increased LDL receptor degradation in a PCSK9-dependent manner. In parallel, hepatic *Pcsk9* mRNA and plasma PCSK9 protein levels were reduced by 55-75% in mice with liver-specific knockout of the insulin receptor; 75-88% in mice made insulin deficient with streptozotocin; and 65% in *ob/ob* mice treated with antisense oligonucleotides against the insulin receptor. However, antisense oligonucleotide mediated knockdown of insulin receptor in lean, wildtype mice had little effect. In addition, we found that fasting was able to reduce PCSK9 expression by 80% even in mice that lack hepatic insulin signaling.

SYSTEMATIC REVIEWS AND META-ANALYSES

Efficacy and safety of PCSK9 inhibitors in patients with diabetes: A systematic review and meta-analysis

Tian Chen [a], Zhenwei Wang [a], Jing Xie [b], Shengjue Xiao [a], Wei Li [a,c], Naifeng Liu [a,*]

[a] Department of Cardiology, Zhongda Hospital, School of Medicine, Southeast University, Nanjing, Jiangsu, China
[b] College of Basic Medicine and Clinical Pharmacy, China Pharmaceutical University, Nanjing, Jiangsu, China
[c] Department of Cardiology, Affiliated Hospital of Yangzhou University, Yangzhou, Jiangsu, China

Nutrition, Metabolism & Cardiovascular Diseases (2023) **33**, 1647–1661

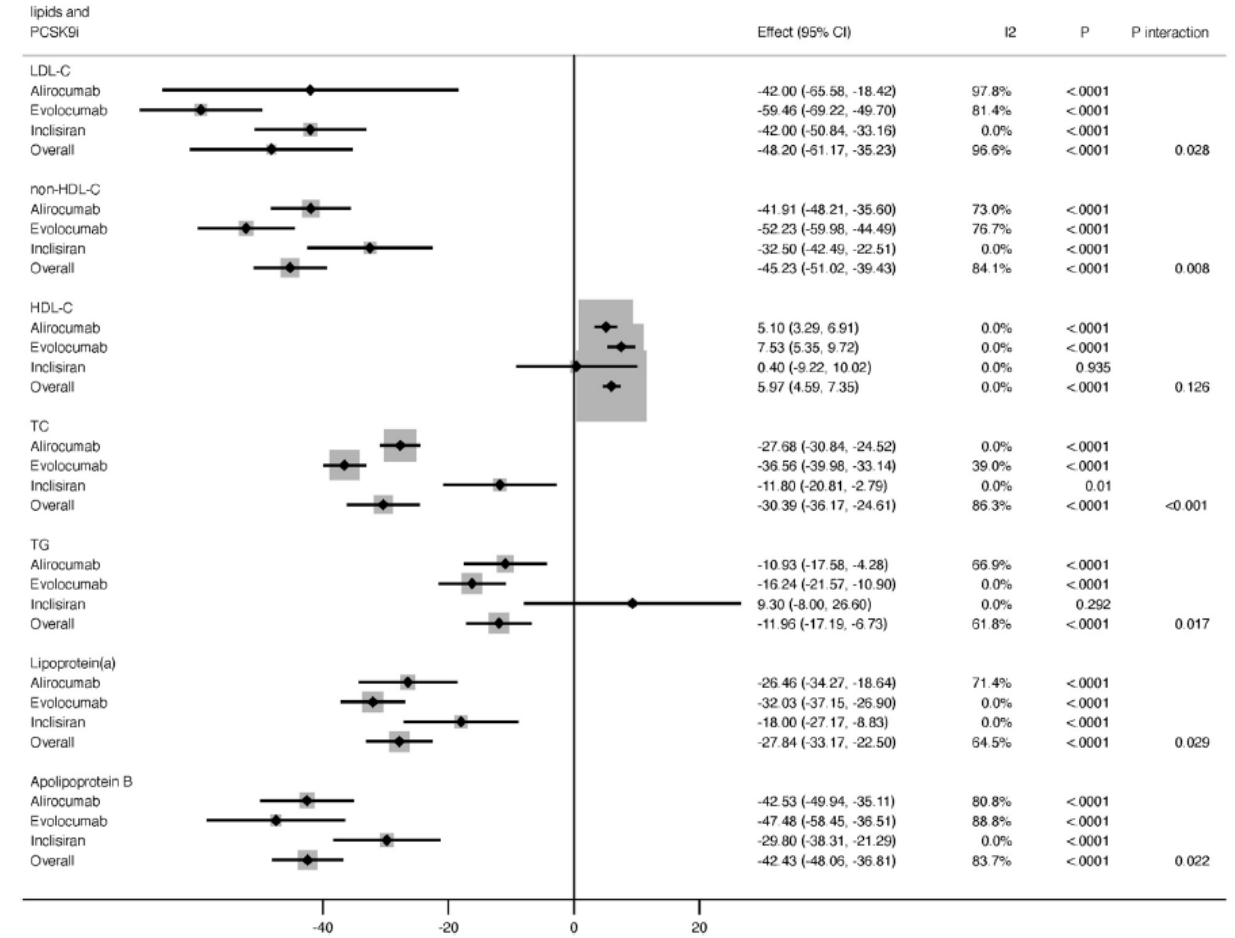


Figure 2 Primary Efficacy Endpoints for PCSK9 Inhibitors versus Control. Results are reported as weighted mean differences and 95% confidence intervals estimated using DerSimmonian-Laird random effect model.

PCSK9 inhibitor therapy: A systematic review and meta-analysis of metabolic and cardiovascular outcomes in patients with diabetes

Matteo Monami MD[1] | Giorgio Sesti MD[2] | Edoardo Mannucci MD[1]

Diabetes Obes Metab. 2019;21:903–908.

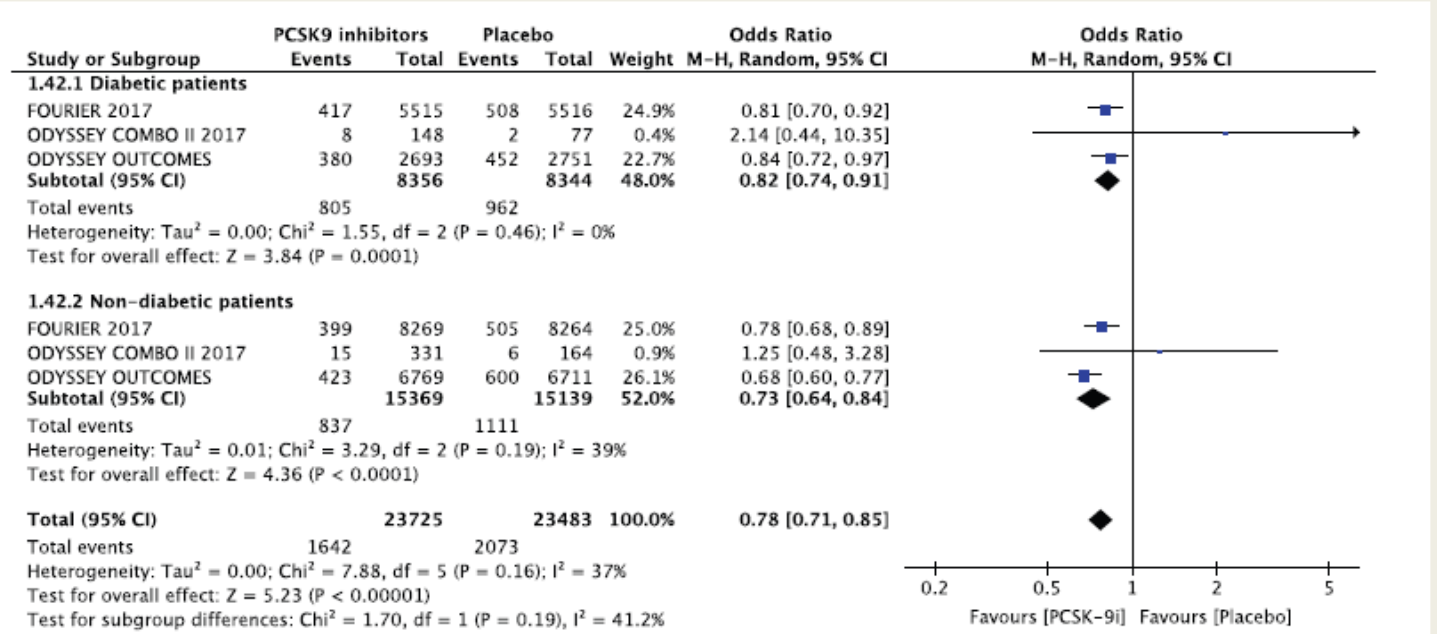


FIGURE 2 Effect of PCSK9 inhibitors on the incidence of major cardiovascular events in individuals with and without diabetes in placebo-controlled trials

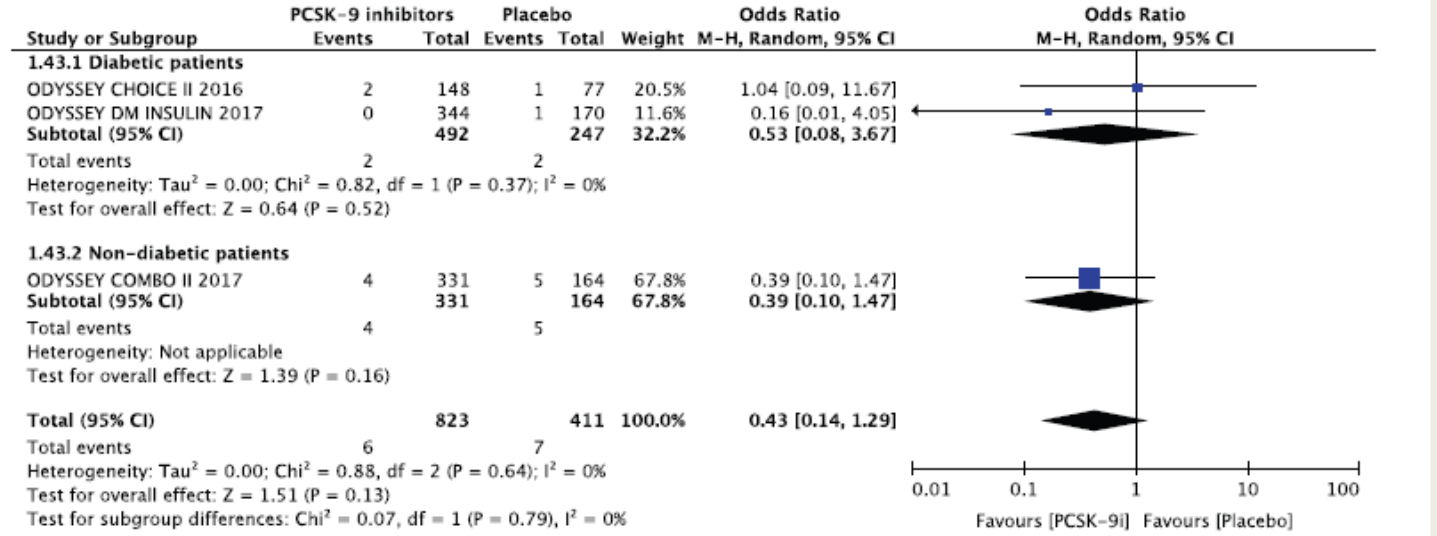


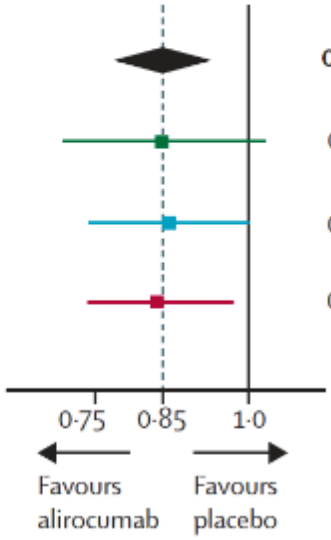
FIGURE 3 Effect of PCSK9 inhibitors on all-cause mortality in individuals with and without diabetes in placebo-controlled trials

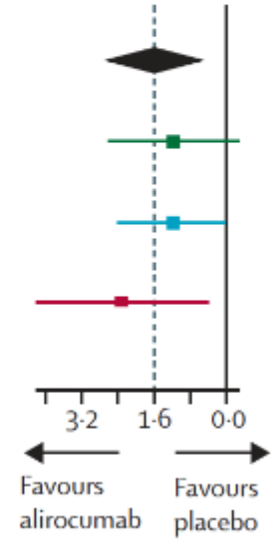
ODYSSEY OUTCOMES
diabete

Effects of alirocumab on cardiovascular and metabolic outcomes after acute coronary syndrome in patients with or without diabetes: a prespecified analysis of the ODYSSEY OUTCOMES randomised controlled trial

Kausik K Ray*, Helen M Colhoun*, Michael Szarek*, Marie Baccara-Dinet, Deepak L Bhatt, Vera A Bittner, Andrzej J Budaj, Rafael Diaz, Shaun G Goodman, Corinne Hanotin, Robert A Harrington, J Wouter Jukema, Virginie Lecorps, Renato D Lopes, Anjèle Moryusef, Jan Murin, Robert Pordy, Arsen D Ristic, Matthew T Roe, José Tuñón, Harvey D White, Andreas M Zeiher, Gregory G Schwartz*, Philippe Gabriel Steg*, for the ODYSSEY OUTCOMES Committees and Investigators†

	MACE incidence		Relative risk reduction $p_{interaction}$=0·98	Hazard ratio (95% CI)	Absolute risk reduction $p_{interaction}$=0·0019	Absolute risk reduction (95% CI)
	Alirocumab n/N (%)	Placebo n/N (%)				
Overall	**903/9462 (9·5%)**	**1052/9462 (11·1%)**		**0·85 (0·78–0·93)**		**1·6% (0·7 to 2·4)**
Normoglycaemia	192/2639 (7·3%)	220/2595 (8·5%)		0·85 (0·70–1·03)		1·2% (–0·3 to 2·7)
Prediabetes	331/4130 (8·0%)	380/4116 (9·2%)		0·86 (0·74–1·00)		1·2% (0·0 to 2·4)
Diabetes	380/2693 (14·1%)	452/2751 (16·4%)		0·84 (0·74–0·97)		2·3% (0·4 to 4·2)





riduzione relativa (RRR) e assoluta (ARR) della incidenza di eventi cardiovascolari nel gruppo placebo in base allo stato glicemico di base :
dal momento che il rischio assoluto è maggiore la sua riduzione più evidente

Ray KK, Colhoun HM, Szarek M et al. Lancet Diabetes Endocrinol 2019

PCSK9 genetic variants and risk of type 2 diabetes: a mendelian randomisation study

www.thelancet.com/diabetes-endocrinology **Vol 5 February 2017**

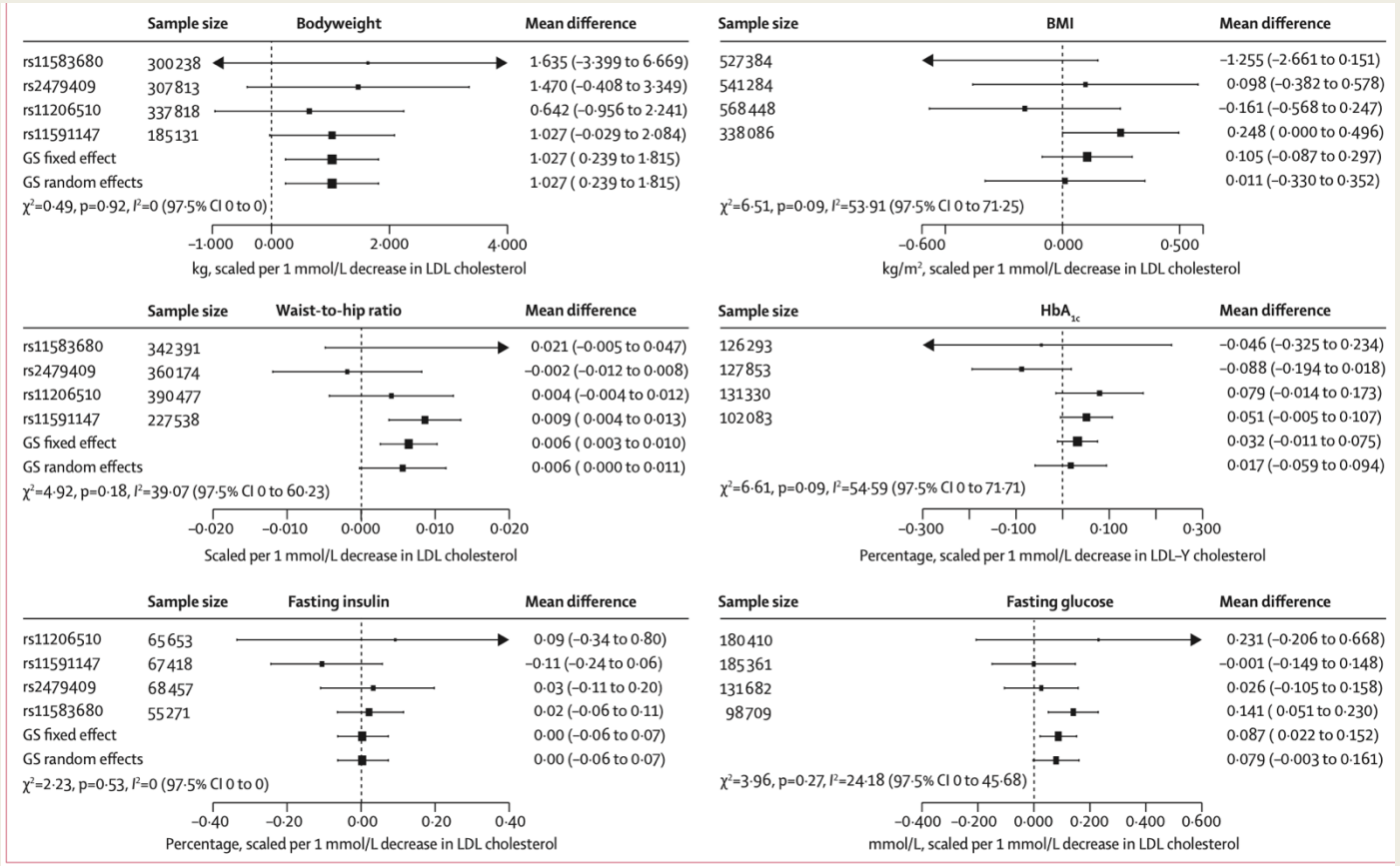


Figure 2: **Association of genetic variants in *PCSK9* with glycaemic and anthropometric biomarkers**
Effect estimates are presented as mean difference with 95% CIs. Associations were scaled to a 1 mmol/L reduction in LDL cholesterol. SNP-specific results are pooled by use of a fixed-effect model; weighted gene-centric score (GS) models combining all four SNP-specific estimates are presented as fixed-effect and random-effects estimates. The size of the black dots representing the point estimates is proportional to the inverse of the variance. Between-SNP heterogeneity was measured as a two-sided Q-test (χ^2) and an I^2 with one-sided 97·5% CI. Note that results from individual participant data are supplemented by repository data from the Global Lipids Genetics Consortium, the Meta-Analyses of Glucose and Insulin-related traits Consortium, and the Genetic Investigation of Anthropometric Traits consortium.

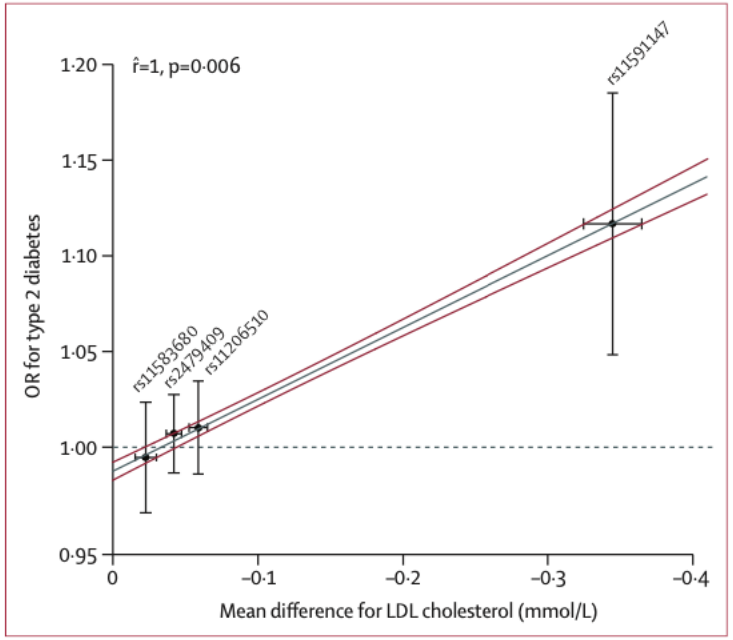


Figure 4: **Correlation between *PCSK9* associations with LDL cholesterol concentration and type 2 diabetes**
Effect estimates are presented as mean difference in LDL cholesterol concentration (mmol/L) and odds ratios (ORs) for the incidence or prevalence of type 2 diabetes, with 95% CIs. Associations are presented per LDL cholesterol-decreasing allele. The Pearson correlation coefficient, regression line (grey), and its 95% CI (red) were calculated by weighting the SNPs for the inverse of the variance in the type 2 diabetes association. Excluding the SNP with the largest effect on LDL cholesterol (rs11591147) resulted in a correlation coefficient of 0·993 and a p value of 0·437.

PCSK9-deficient mice exhibit impaired glucose tolerance and pancreatic islet abnormalities

Majambu Mbikay [a,b,c,*], Francine Sirois [a], Janice Mayne [a], Gen-Sheng Wang [a], Andrew Chen [a], Thilina Dewpura [a], Annik Prat [d], Nabil G. Seidah [d], Michel Chretien [a,b,c], Fraser W. Scott [a,b,c]

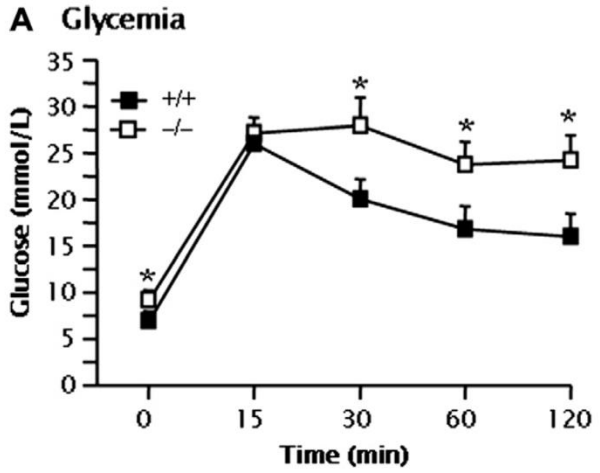


Fig. 3. OGTT. *Pcsk9*$^{+/+}$ and *Pcsk9*$^{-/-}$ male mice (n = 9/genotype) were subjected to an OGTT. (A) Plasma glucose was not different between the two genotypes at 15 min, but was significantly higher in mutant mice at later time points. (B) Plasma insulin was significantly lower in mutant mice at all time points, most noticeably at 15 min. *P < 0.05; ***P < 0.001.

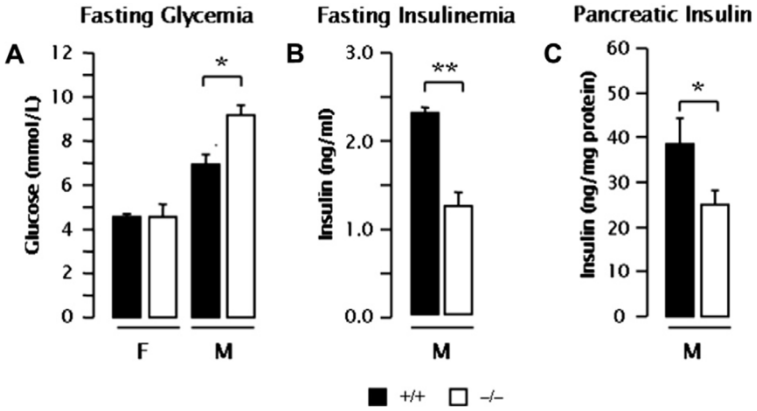


Fig. 2. Glucose homeostasis is altered in PCSK9-deficient mice. Female (F) and male (M), *Pcsk9*$^{+/+}$ and *Pcsk9*$^{-/-}$ 4-month-old mice (n = 8/gender/genotype) were phenotyped for glucose homeostasis parameters. (A) Fasting glycemia was similar in females; but was increased (P < 0.05) in male *Pcsk9*$^{-/-}$ mice. (B) Insulinemia was reduced (P < 0.01) in male *Pcsk9*$^{-/-}$ mice. (C) Pancreatic insulin content was reduced (P < 0.05) in *Pcsk9*$^{-/-}$ mice.

PCSK9 deficiency reduces insulin secretion and promotes glucose intolerance: the role of the low-density lipoprotein receptor

European Heart Journal (2018) **00**, 1–13
doi:10.1093/eurheartj/ehy357

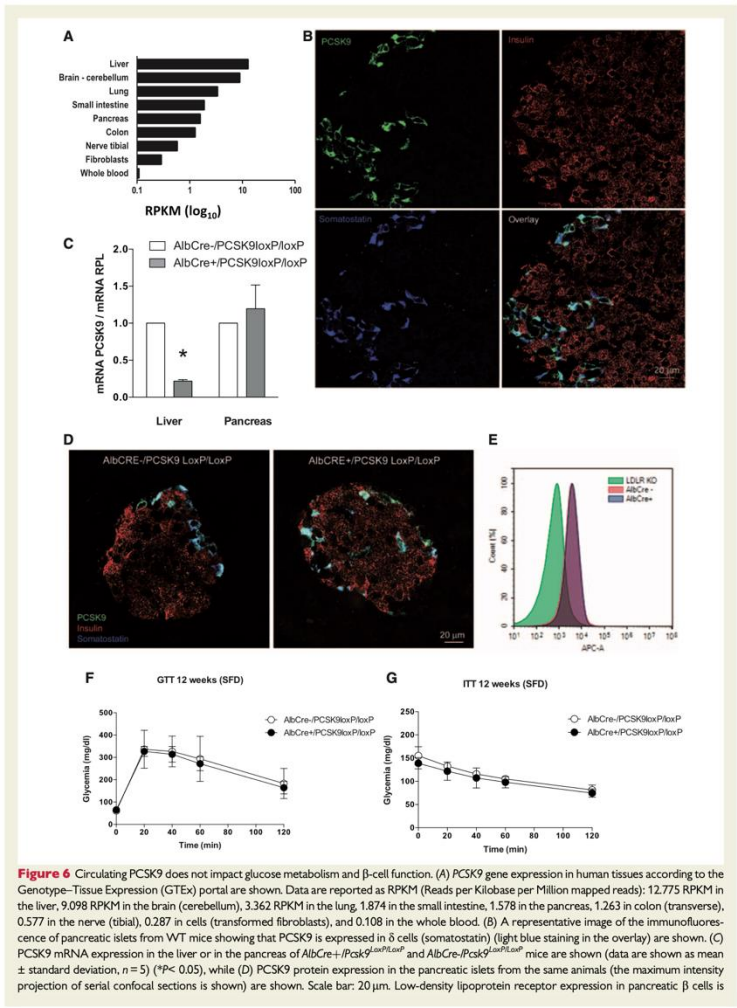


Figure 6 Circulating PCSK9 does not impact glucose metabolism and β-cell function. (*A*) *PCSK9* gene expression in human tissues according to the Genotype–Tissue Expression (GTEx) portal are shown. Data are reported as RPKM (Reads per Kilobase per Million mapped reads): 12.775 RPKM in the liver, 9.098 RPKM in the brain (cerebellum), 3.362 RPKM in the lung, 1.874 in the small intestine, 1.578 in the pancreas, 1.263 in colon (transverse), 0.577 in the nerve (tibial), 0.287 in cells (transformed fibroblasts), and 0.108 in the whole blood. (*B*) A representative image of the immunofluorescence of pancreatic islets from WT mice showing that PCSK9 is expressed in δ cells (somatostatin) (light blue staining in the overlay) are shown. (*C*) PCSK9 mRNA expression in the liver or in the pancreas of *AlbCre+/Pcsk9*$^{LoxP/LoxP}$ and *AlbCre-/Pcsk9*$^{LoxP/LoxP}$ mice are shown (data are shown as mean ± standard deviation, $n = 5$) (*$P < 0.05$), while (*D*) PCSK9 protein expression in the pancreatic islets from the same animals (the maximum intensity projection of serial confocal sections is shown) are shown. Scale bar: 20 μm. Low-density lipoprotein receptor expression in pancreatic β cells is

PCSK9 in diabetes: sweet, bitter or sour?

Francesco Paneni[1,2]* and Sarah Costantino[2]

[1]University Heart Center, Clinic for Cardiology, University Hospital Zürich, Switzerland; and [2]Center for Molecular Cardiology, University of Zürich, Wagistrasse 12, Schlieren CH-8952, Zürich, Switzerland

Online publish-ahead-of-print 31 July 2018

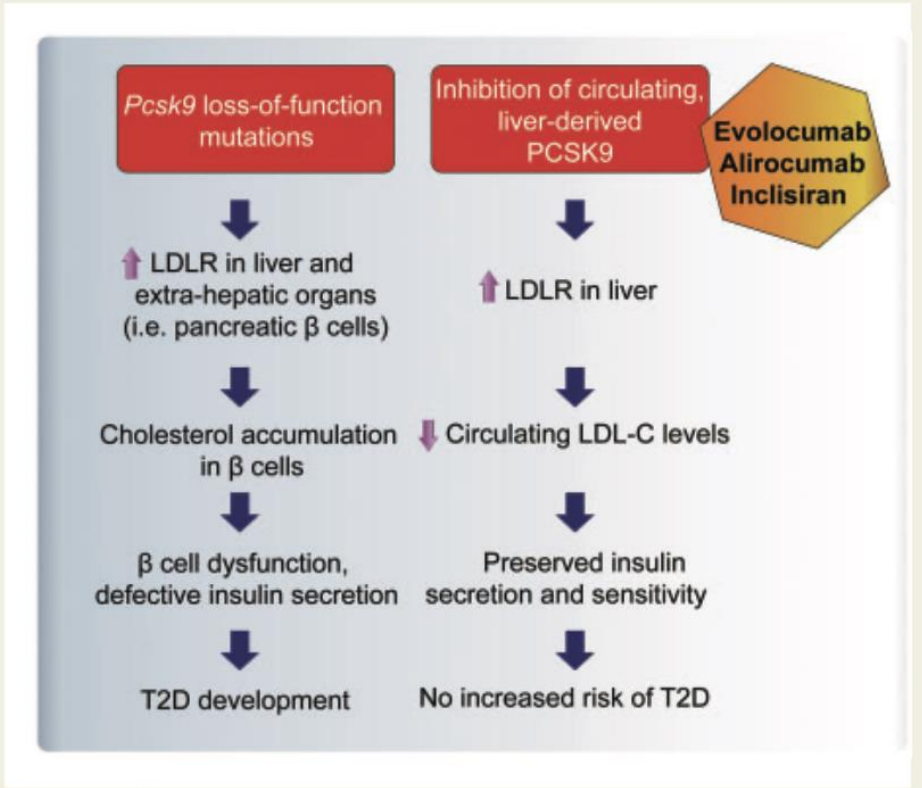


Figure 1 Effects of proprotein convertase subtilisin/kexin type 9 loss-of function vs. blockade of circulating, liver-derived proprotein convertase subtilisin/kexin type 9. LDL-C, low density lipoprotein-cholesterol; LDLR, low density lipoprotein receptor; PCSK9, proprotein convertase subtilisin/kexin type 9; T2D, type 2 diabetes.

PCSK9 Inhibitor Safety Data

FOURIER[a]

Outcome	Evolocumab (n = 13,769)	Placebo (n = 13,756)
Injection-site reaction, %*	2.1	1.6
Allergic reaction, %	3.1	2.9
Muscle-related event, %	5.0	4.8
Rhabdomyolysis, %	0.1	0.1
Cataract, %	1.7	1.8
Adjudicated case of new-onset diabetes, %	8.1	7.7
Neurocognitive event, %	1.6	1.5

ODYSSEY [b]

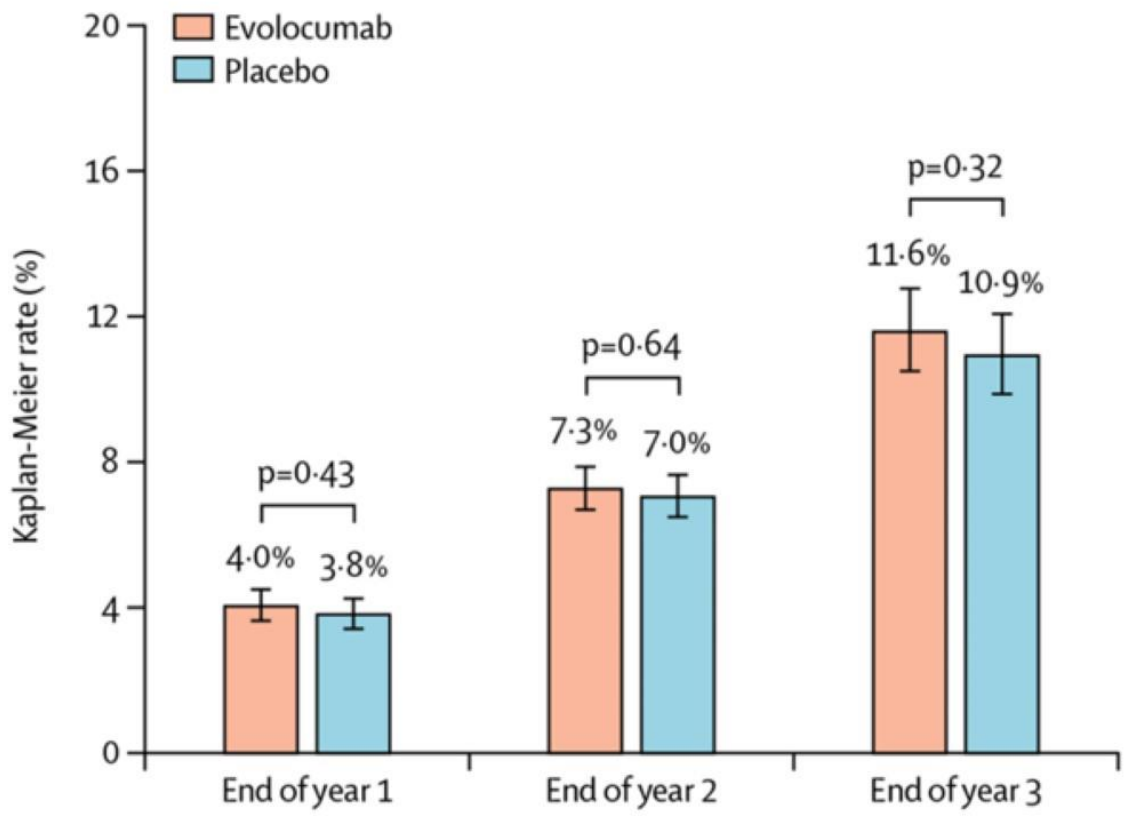
Event	Alirocumab (n = 9451)	Placebo (n = 9443)
Diabetes worsening or diabetic complications: patients w/ DM at baseline, %	18.8	21.2
New-onset diabetes: patients w/o DM at baseline, %	9.6	10.1
General allergic reaction, %	7.9	7.8
Hepatic disorder, %	5.3	5.7
Local injection-site reaction, %†	3.8	2.1
Neurocognitive disorder, %	1.5	1.8
Cataracts, %	1.3	1.4
Hemorrhagic stroke, %	<0.1	0.2

*The between-group difference was nominally significant (P <.001).
†HR vs placebo = 1.82 (95% CI 1.54, 2.17).

a. Sabatine MS, et al. *N Engl J Med*. 2017;376:1713-1722.
b. Schwartz GG, et al. ACC 2018.

FOURIER

New-Onset Diabetes in FOURIER



In all patients without diabetes at baseline (1294 incident cases in 16,510 patients):

HR 1.05
(95% CI: 0.94, 1.17)

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

HR 1.00
(95% CI: 0.89, 1.13)

Reprinted from *Lancet Diabetes Endocrinol*, 5, Sabatine MS, et al., Cardiovascular safety and efficacy of the PCSK9 inhibitor evolocumab in patients with and without diabetes and the effect of evolocumab on glycaemia and risk of new-onset diabetes: a prespecified analysis of the FOURIER randomised controlled trial, 941–950., Copyright 2017, with permission from Elsevier.

Studi ORION 9-10-11: le sole reazioni avverse associate a inclisiran sono state le reazioni in sede di iniezione (8.2%)

ORION 9 n° pazienti 240/241 Inclisiran/Pbo
ORION 10 781/778 Inclisiran/Pbo
ORION 11 811/804 Inclisiran/Pbo
Adverse events recorded over trial period of 540 days

AEs	Rachialgia
SAEs	Gastroenterite
AEs interruzione T	Diabete mellito
Nasofaringite	Ipertensione
URTI	Artralgia
Dispnea	Osteoartrite

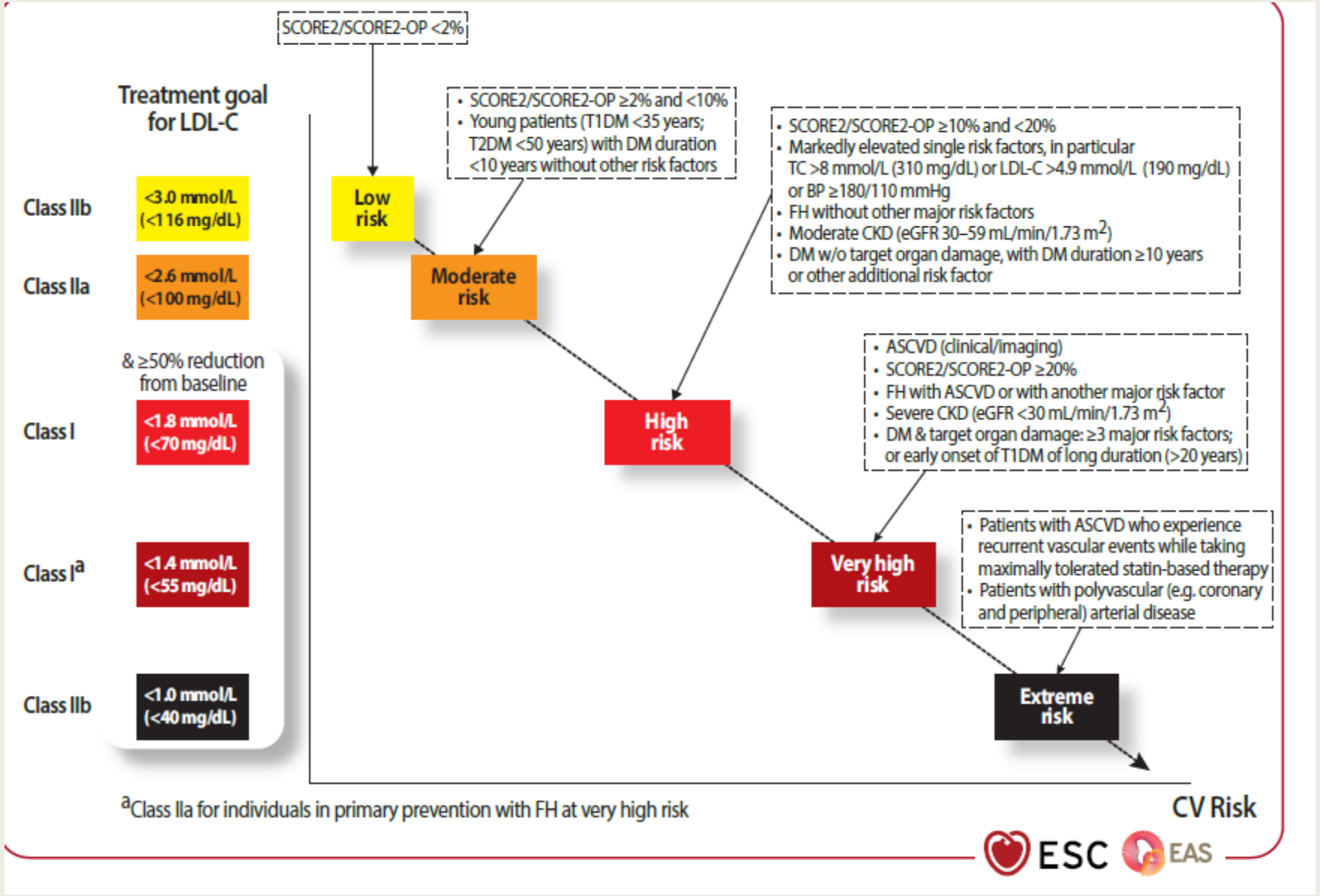
Differenze
tutte non significative

Le reazioni al sito di iniezione sono state prevalentemente lievi, nessuna severa o persistente

Raal FJ, et al. N Engl J Med. 2020;382(16):1520-1530.

Ray KK, et al. N Engl J Med. 2020;382(16):1507-1519.
Leqvio, SmPC

2025 Focused Update of the 2019 ESC/EAS Guidelines for the management of dyslipidaemias



CONSENSUS

DOCUMENTO DI CONSENSO SULLA DIAGNOSI E GESTIONE DELLA IPERCOLESTEROLEMIA FAMILIARE DELLA SOCIETÀ ITALIANA PER LO STUDIO DELL'ATEROSCLEROSI

Consensus document on diagnosis and management of familial hypercholesterolemia from the Italian Society for the Study of Atherosclerosis (SISA)

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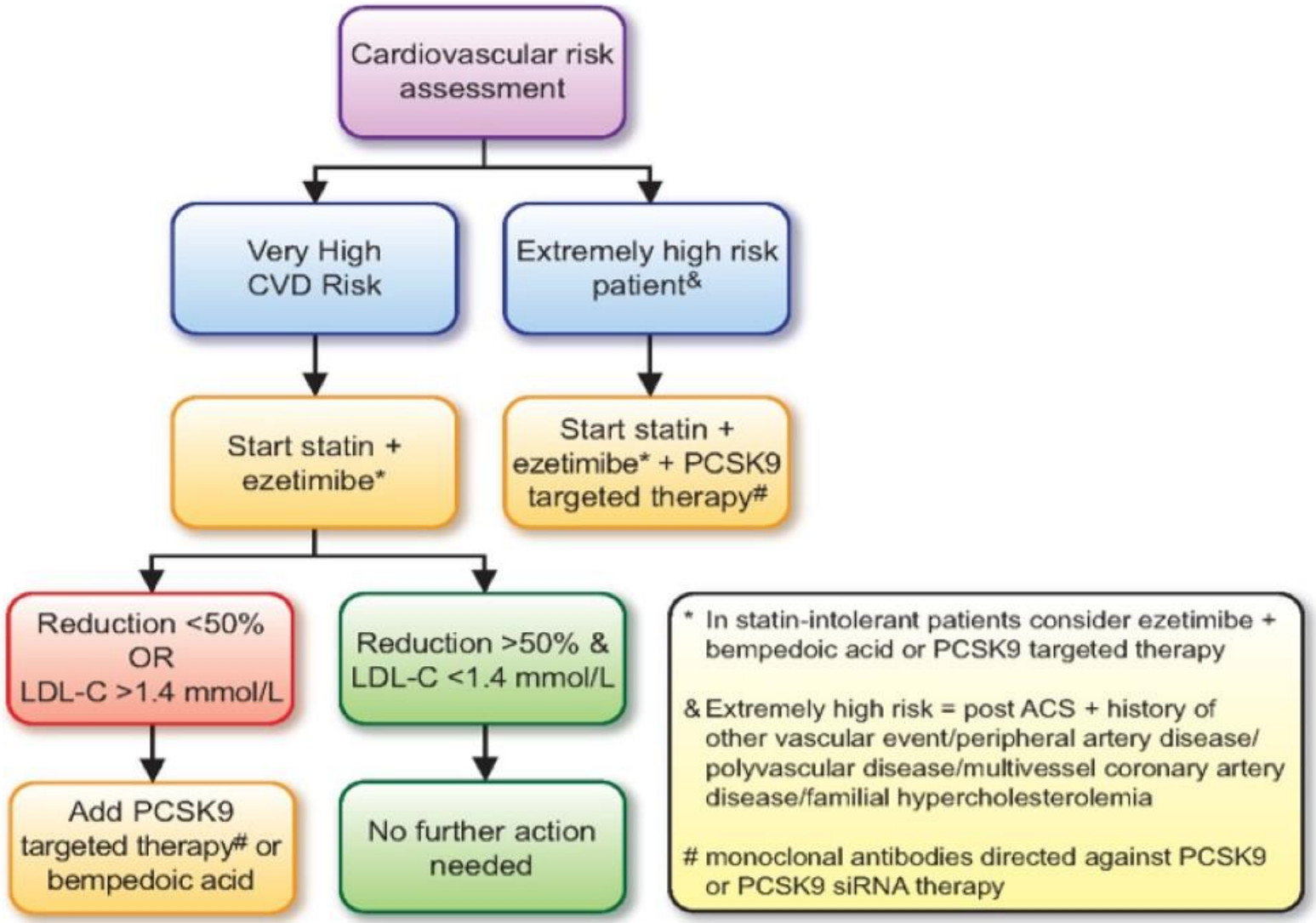
Tabella 4 - Percentuale di riduzione dei livelli plasmatici di colesterolo LDL indotta da diversi trattamenti ipocolesterolemizzanti.

Trattamento farmacologico	% di riduzione di LDL-C
Statine di moderata intensità (*atorvastatina* 10-20 mg; *rosuvastatina* 5-10 mg; *simvastatina* 20-40 mg; *pravastatina* 40-80 mg)	30%
Statine ad alta intensità (*atorvastatina* 40-80 mg; *rosuvastatina* 20-40 mg)	50%
Statine ad alta intensità + ezetimibe 10 mg	65%
Inibitori di PCSK9 (*alirocumab*, *evolocumab*, sottocute ogni due settimane)	60%
Statine ad alta intensità + Inibitori di PCSK9	75%
Statine ad alta intensità + Inibitori di PCSK9 + ezetimibe 10 mg	80%
Acido bempedoico 180 mg	20%
Acido bempedoico 180 mg + ezetimibe 10 mg	40%

Combination Therapy as First-Line Strategy in Very High-Risk Patients



siRNA, small interfering RNA.

Ray KK, et al. Eur Heart J. 2022;43:830-833.

Evolocumab

- *pazienti di età ≤80 aa con ipercolesterolemia familiare omozigote - in prevenzione primaria in pazienti di età ≤80 aa con ipercolesterolemia familiare eterozigote e livelli di LDL-C ≥130 mg/dL nonostante terapia da almeno 6 mesi con statina ad alta potenza alla massima dose tollerata + ezetimibe oppure con dimostrata intolleranza alle statine (vedere successivamente la definizione di intolleranza) e/o all'ezetimibe;*
- ***in prevenzione secondaria** in pazienti di età ≤80 aa con ipercolesterolemia familiare eterozigote o ipercolesterolemia non familiare o dislipidemia mista con livelli di LDL-C ≥ 70 mg/dL nonostante terapia da almeno 6 mesi con statina ad alta potenza alla massima dose tollerata + ezetimibe oppure dopo una sola rilevazione di C-LDL in caso di IMA recente (ultimi 12 mesi) o eventi CV mulitpli oppure con dimostrata intolleranza alle statine (vedere successivamente la definizione di intolleranza) e/o all'ezetimibe.*

Alirocumab
Inclisiran

- *in prevenzione primaria in pazienti di età ≤80 aa con ipercolesterolemia familiare eterozigote e livelli di LDL-C ≥130 mg/dL nonostante terapia da almeno 6 mesi con statina ad alta potenza alla massima dose tollerata + ezetimibe oppure con dimostrata intolleranza alle statine (vedere successivamente la definizione di intolleranza) e/o all'ezetimibe;*
- ***in prevenzione secondaria** in pazienti di età ≤80 aa con ipercolesterolemia familiare eterozigote o ipercolesterolemia non familiare o dislipidemia mista e livelli di LDL-C ≥ 70 mg/dL nonostante terapia da almeno 6 mesi con statina ad alta potenza alla massima dose tollerata + ezetimibe oppure dopo una sola rilevazione di C-LDL in caso di IMA recente (ultimi 12 mesi) o eventi CV multipli oppure con dimostrata intolleranza alle statine (vedere successivamente la definizione di intolleranza) e/o all'ezetimibe.*

Le dosi raccomandate di alirocumab sono 75 mg una volta ogni 2 settimane, 150 mg una volta ogni 2 settimane, 300 mg una volta ogni 4 settimane (mensilmente), somministrate per via sottocutanea. Tutte le dosi possono essere utilizzate per l'inizio del trattamento.

La dose raccomandata di evolocumab è 140 mg ogni due settimane o 420 mg una volta al mese; le due dosi sono clinicamente equivalenti.

Somministrazione[1,2]

Uso sottocutaneo.

Inclisiran è somministrato tramite iniezione sottocutanea nell'addome; siti di iniezione alternativi comprendono il braccio o la coscia.

Ogni dose da 284 mg viene somministrata utilizzando una singola siringa preriempita.

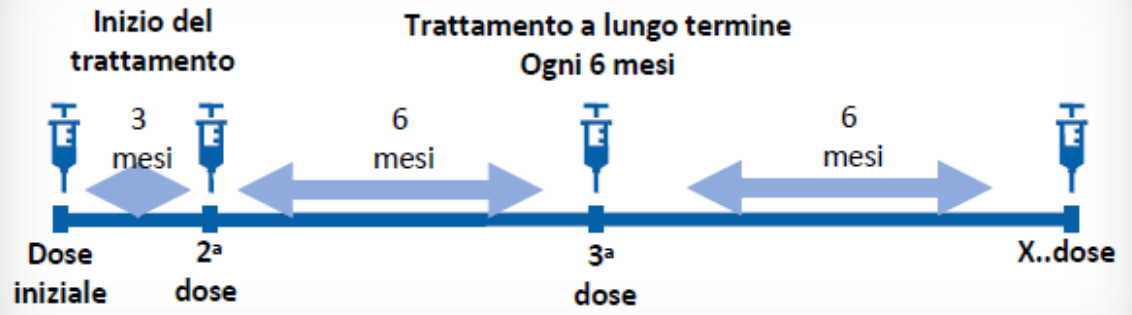
Ogni siringa preriempita è solo monouso.

Inclisiran è destinato alla somministrazione da parte di un operatore sanitario.

Formulazione[1,2]

- Siringa preriempita
- Ogni siringa preriempita contiene inclisiran sodico equivalente a 284 mg di inclisiran in 1,5 mL di soluzione
- Conservazione a temperatura ambiente

Regime posologico[1,2]



Semplicemente

- I diabetici hanno nella maggior parte dei casi un rischio cardiovascolare alto o molto alto
- L'obiettivo di c LDL per tale rischio non sempre viene raggiunto con la dose massima tollerata di statina + ezetimibe
- I farmaci che agiscono su PCSK9 rappresentano una opzione terapeutica efficace e sicura
- Dai trial clinici non risulta un aumento del rischio di diabete

Grazie per l’ascolto