EVALUATION DU RISQUE LIPIDIQUE APRÈS UN AVC : REGARDS CROISÉS NEUROLOGUE & CARDIOLOGUE

Session avec le soutien de Novartis

27ème journées SNFV

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Liens d’intérêts

Consultant: Amgen, Sanofi, Novartis

Conférences: AstraZeneca, MSD France, NovoNordisk, ViiV Healthcare, Aegerion, Gilead, Servier

Subvention de recherche: Amgen

Sommaire

- **Quelle cible de LDL-cholestérol visée ?**
- - **Point de vue du cardiologue / Franck Boccara (Paris)**
- - Point de vue du neurologue / David Calvet (Paris)

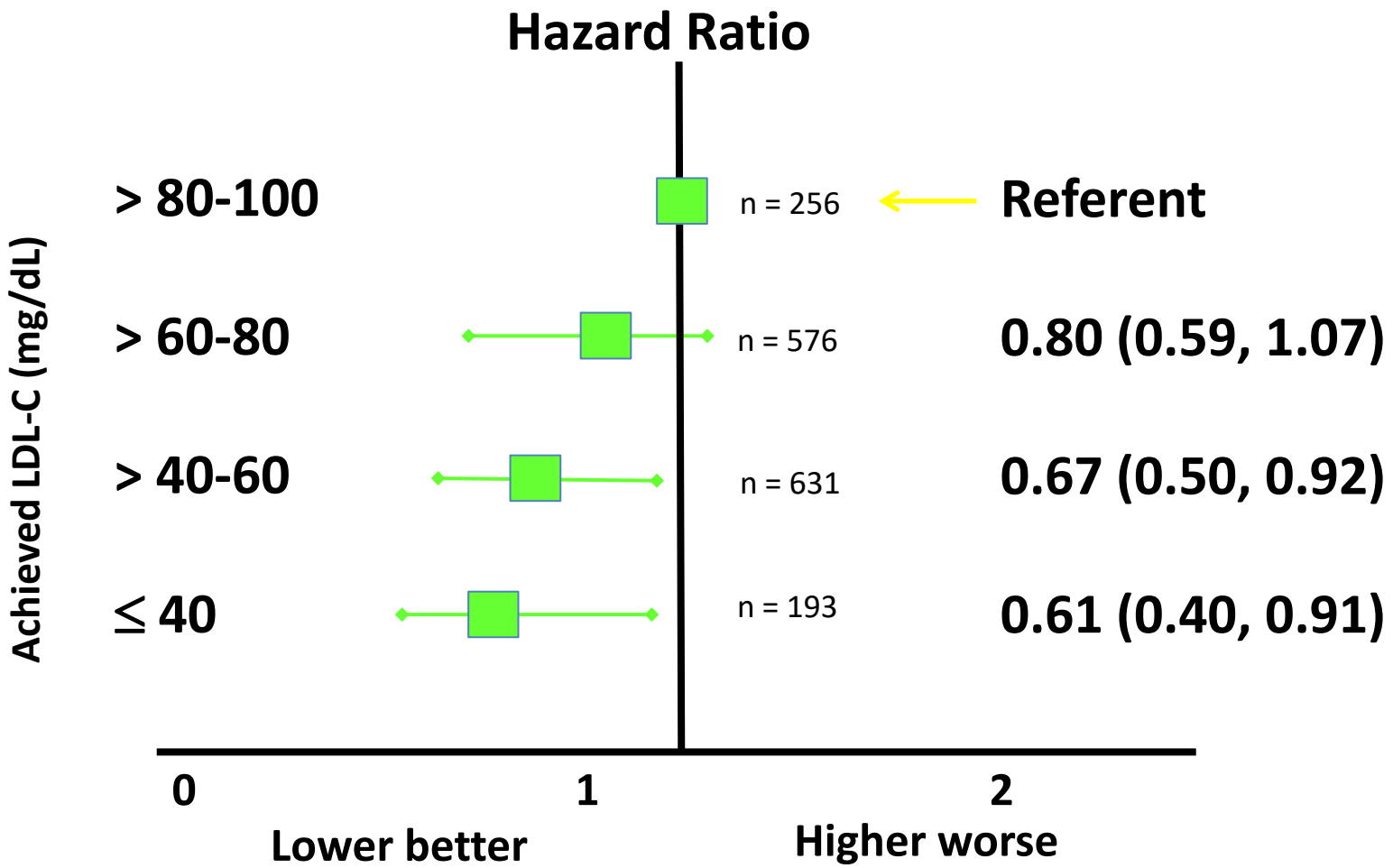
- **Lp(a) et AVC : où en est-on ?**
- - Lien Lp(a) et risque d'AVC / David Calvet (Paris)
- - **Recommandations et usage en pratique / Franck Boccara (Paris)**

Sommaire

- **Lower is better**
- **Recommandations ESC**
- **Real life**
- **Optimiser le traitement de sortie**

Hazard Ratio of the Primary Endpoint Compared with Achieved LDL-C < 100 PROVE-IT (TIMI 22) Substudy*

Atorvastatin 80 mg vs pravastatin 40 mg in 2099 ACS patients for 24 months



Endpoint: CHD death, nonfatal MI, CVA, recurrent ischemia, revascularization

*Adjusted for age, gender, baseline LDL-C, diabetes mellitus, and prior MI.

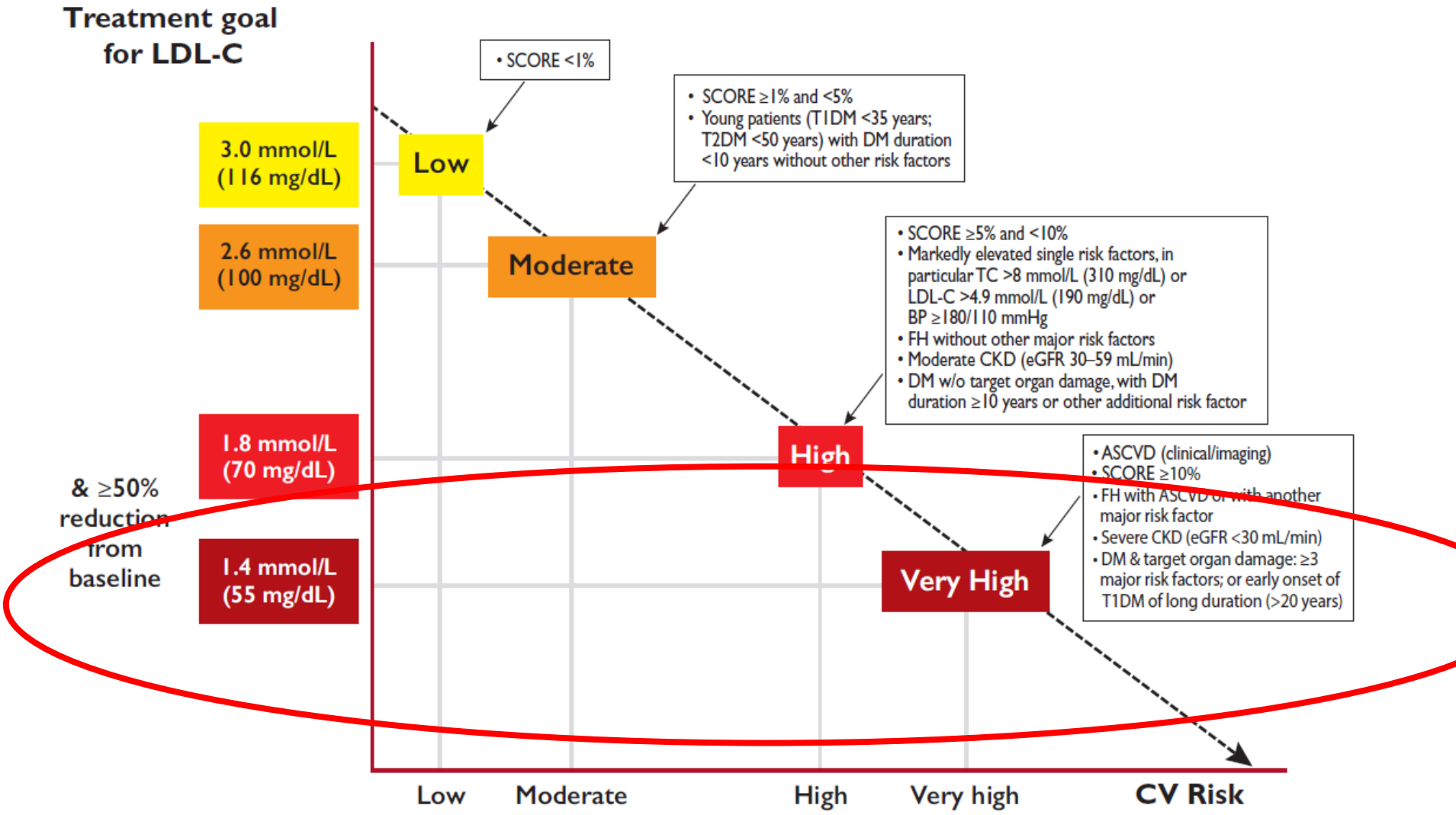
Wiviott SD et al. *JACC.* 2005;46:1411-1416.

Risque résiduel post SCA diminué grâce au traitement hypolipémiant

- **Statine forte intensité *PROVE-IT (TIMI 22) Substudy***
- **Combinaison statine + ezetimibe *IMPROVE IT***
- **iPCSK9 ; Alirocumab et Evolocumab, *ODISSEY, FOURIER***
- **Omega-3 oil (eicosapentaenoic acid : EPA) (*REDUCE-IT*)**

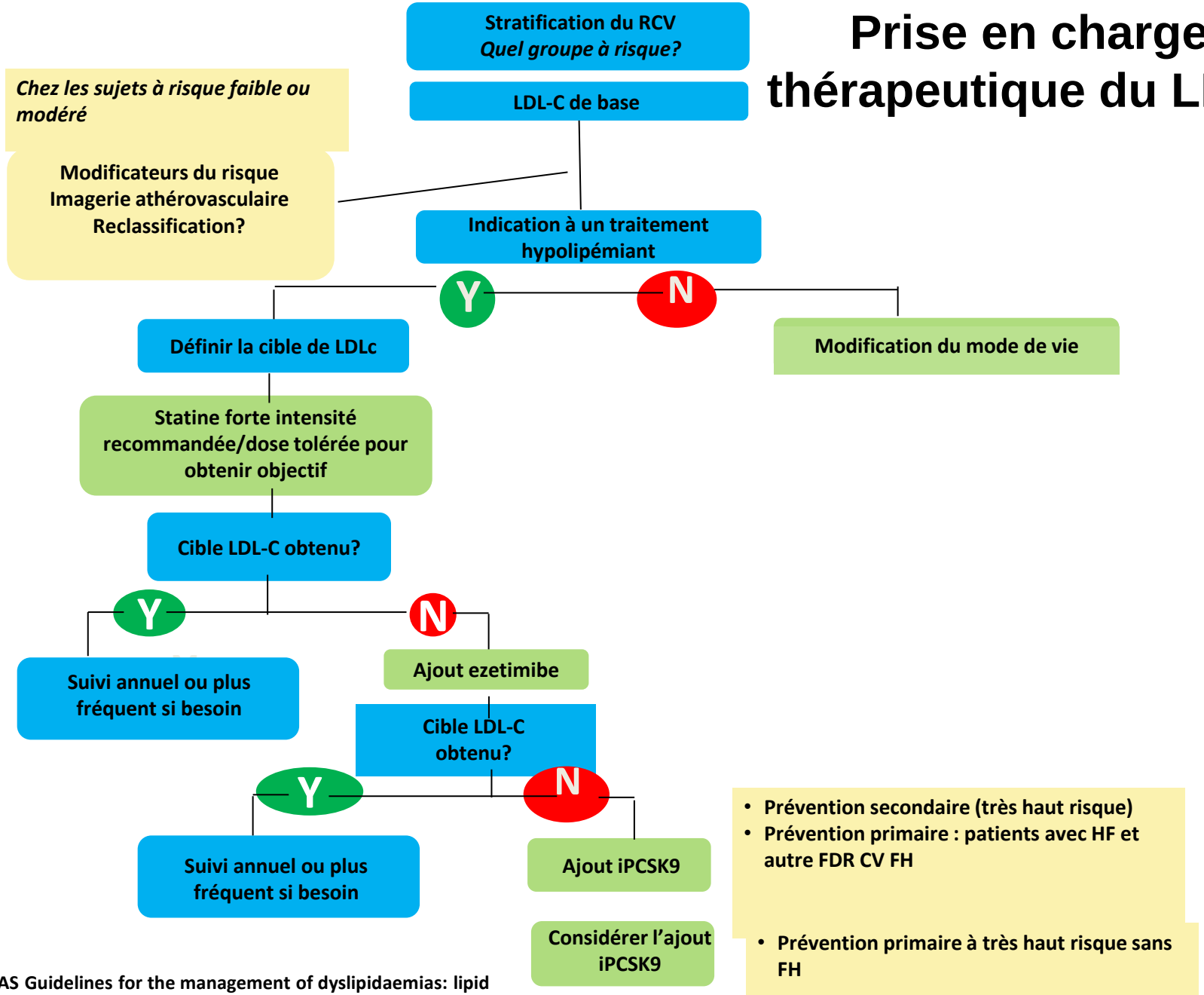
Wiviott SD et al. JACC. 2005;46:1411-1416.
Cannon C et al. NEJM 2015
Sabatine MS et al. NEJM 2017;376:1713-22
Schwartz GG et al. N Engl J Med 2018

Objectifs de LDLc en fonction du niveau de risque



ESC/EAS 2019 Guidelines
EHJ 2019

Arbre décisionnel Prise en charge thérapeutique du LDLc

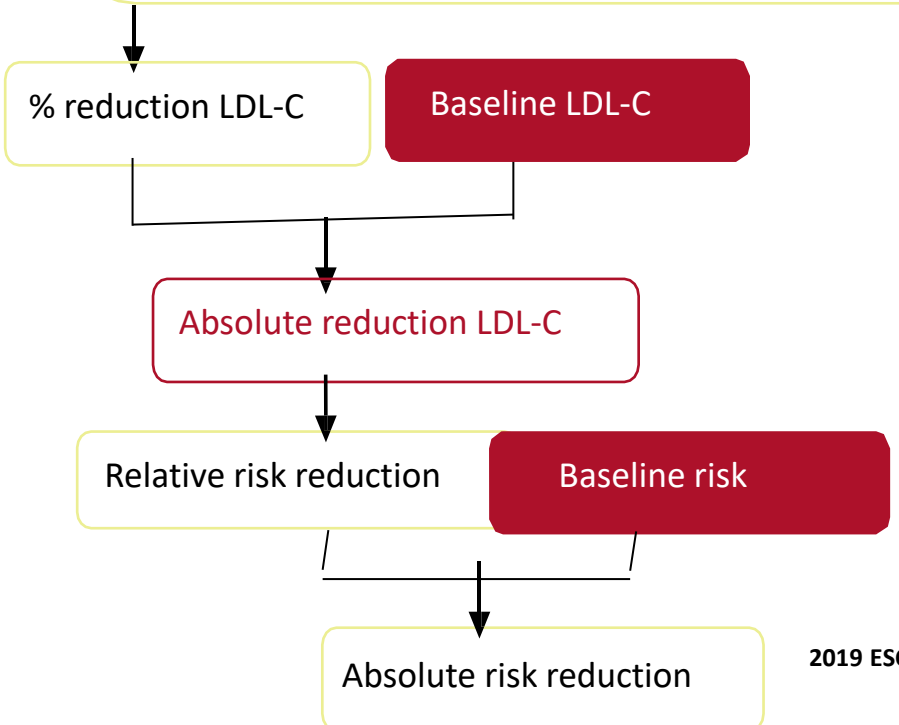


2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019

Bénéfice biologique attendu de la réduction du LDLc

Intensity of lipid lowering treatment

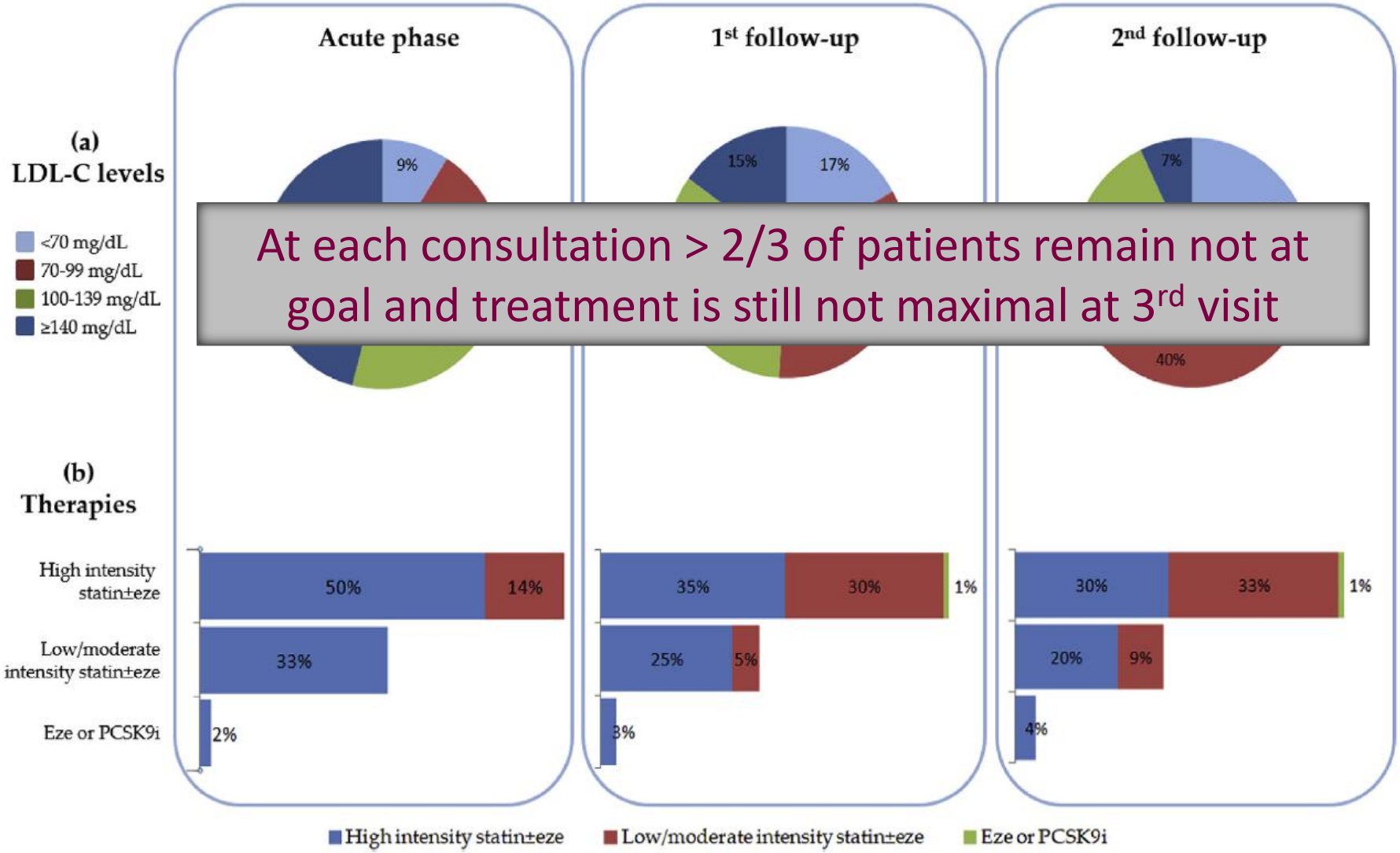
Treatment	Average LDL-C reduction
Moderate intensity statin	≈ 30%
High intensity statin	≈ 50%
High intensity statin plus ezetimibe	≈ 65%
PCSK9 inhibitor	≈ 60%
PCSK9 inhibitor plus high intensity statin	≈ 75%
PCSK9 inhibitor plus high intensity statin plus ezetimibe	≈ 85%



LDL-C = low-density lipoprotein cholesterol;
PCSK9 = proprotein convertase subtilisin/kexin type 9.

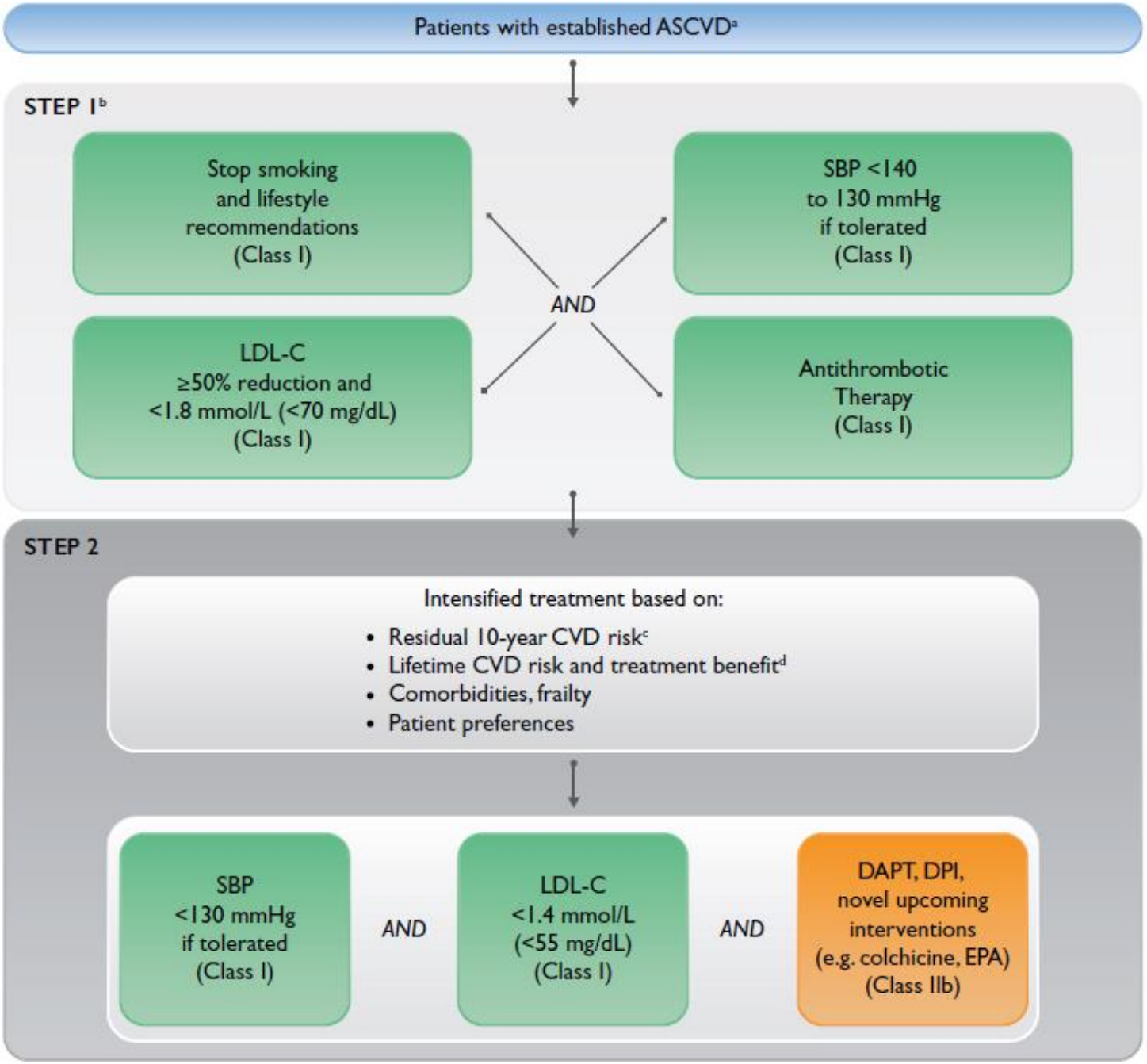
2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019

Atteintes des objectifs postSCA
Cardiologists survey



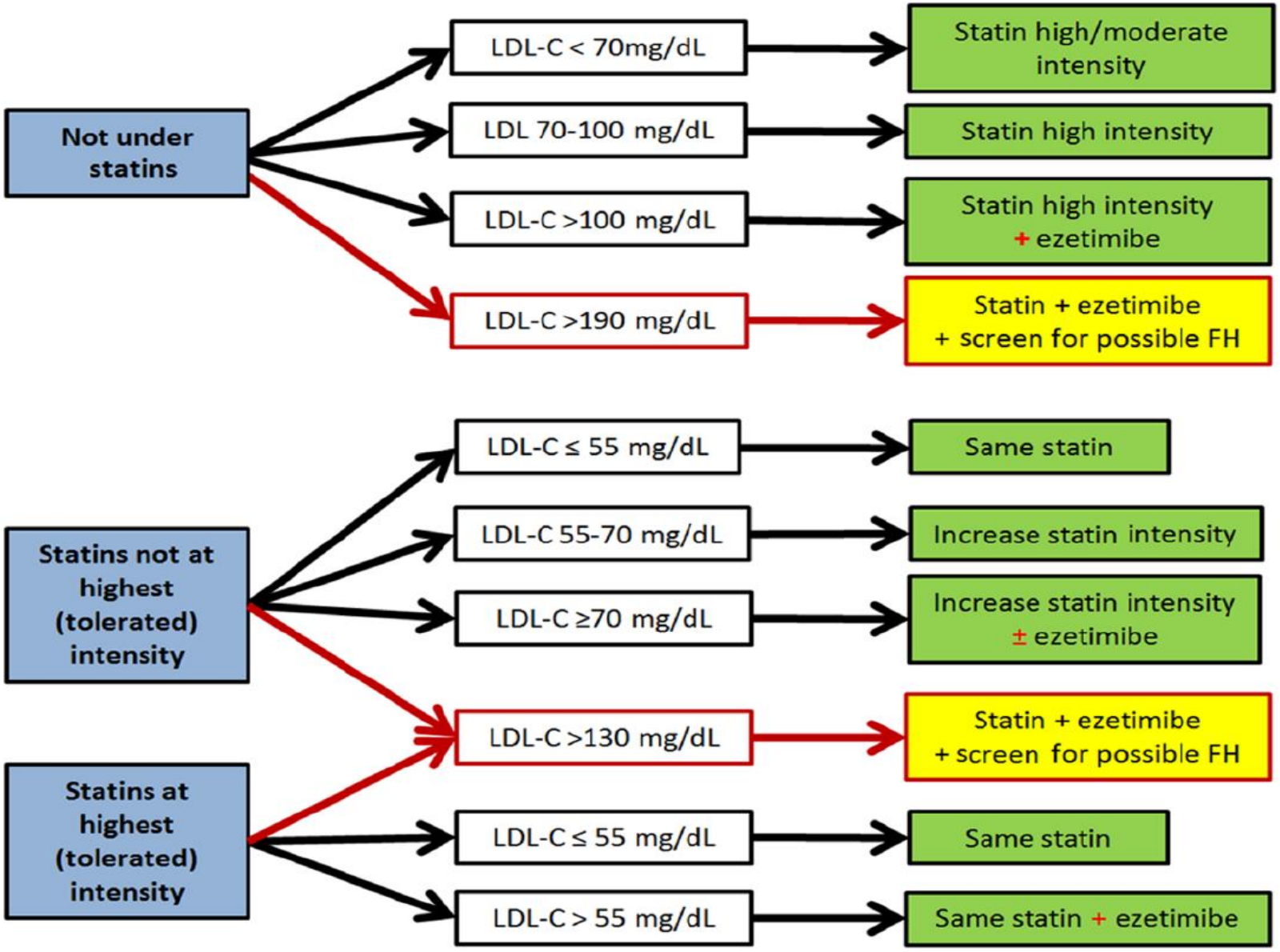
At each consultation > 2/3 of patients remain not at goal and treatment is still not maximal at 3rd visit

Landmesser U. et al. Atherosclerosis Supplements 42 (2020) e49ee58



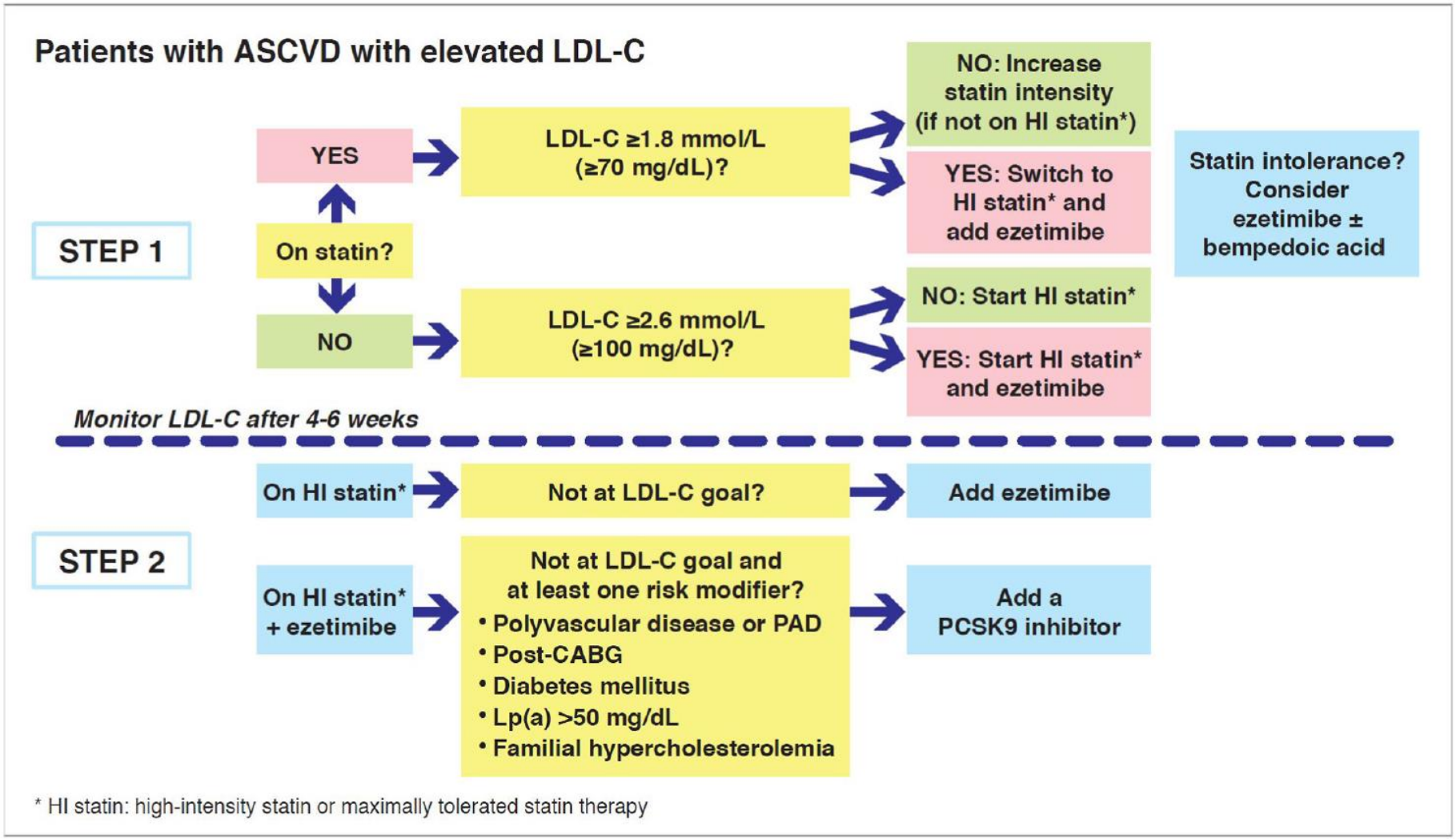
ESC 2021 CVD prevention guidelines
European Heart Journal 2021:42,227-3337

Algorithme à l'admission pour SCA



Schiele F. et al. European Heart Journal: Acute Cardiovascular Care 2016; 1-12.

EAS TASK FORCE 2021



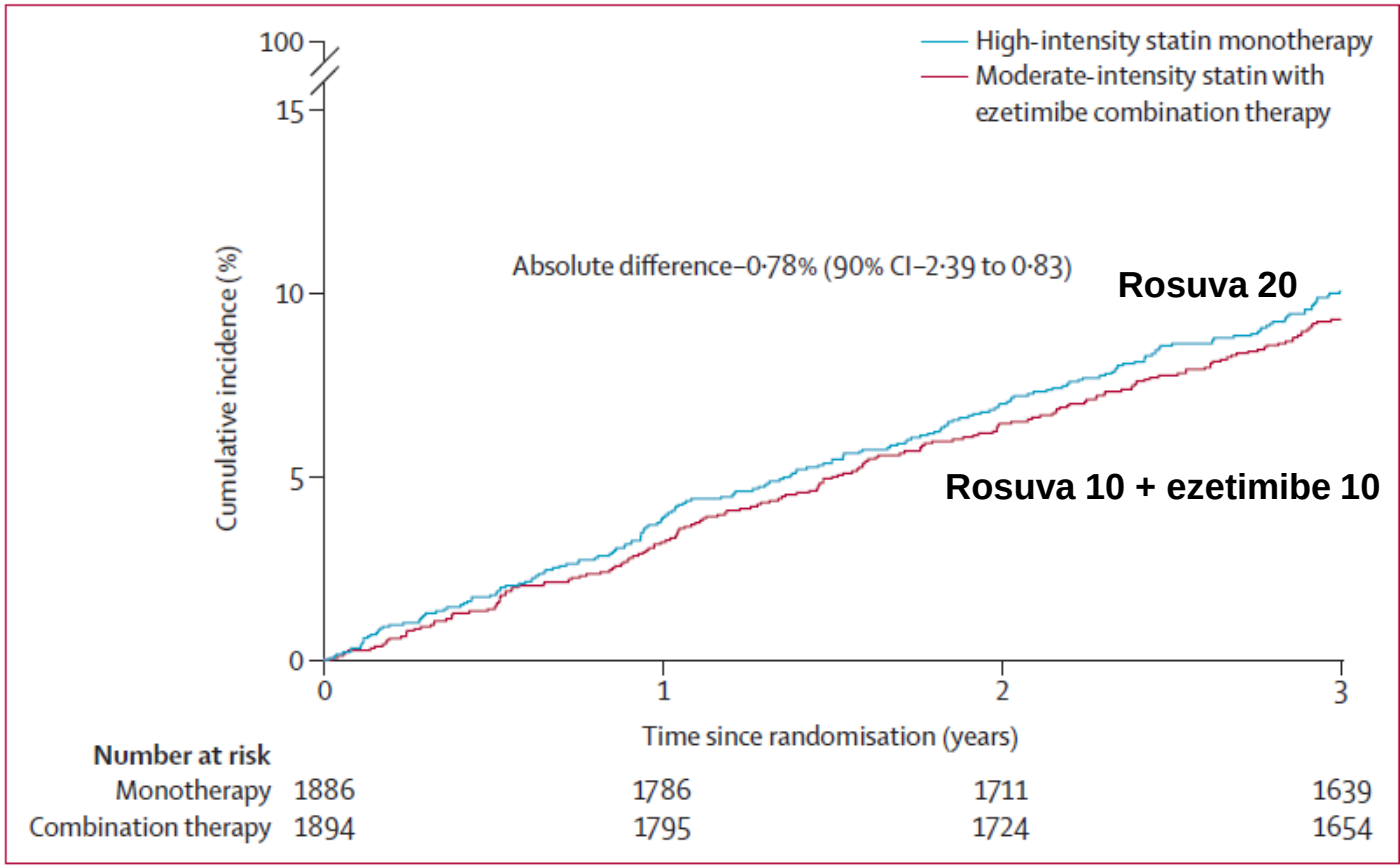
EAS TASK FORCE 2021. Atherosclerosis 329 (2021) 32–35

RACING study. Statin and ezetimibe combination

Corée du Sud. Prévention secondaire

LDL < 70 mg/dL at 1, 2, and 3 years
73%, 75%, and 72% **(rosuva 10 + eze 10)**
Vs 55%, 60%, and 58% **(rosuva 20)**

Discontinuation
4·8% (rosuva 10 + eze 10)
8·2% (rosuva 20)



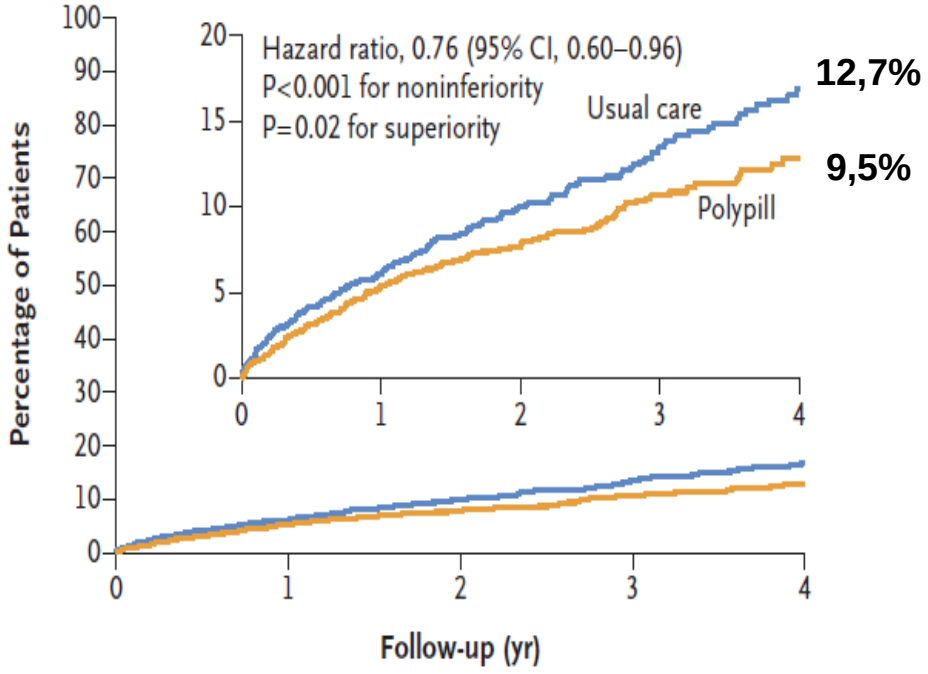
The primary endpoint was the 3-year composite of cardiovascular death, major cardiovascular events, or non-fatal stroke, in the intention-to-treat population with a non-inferiority margin of 2·0%.

Kim BK et al. Lancet 2022; 400: 380–90

SECURE TRIAL

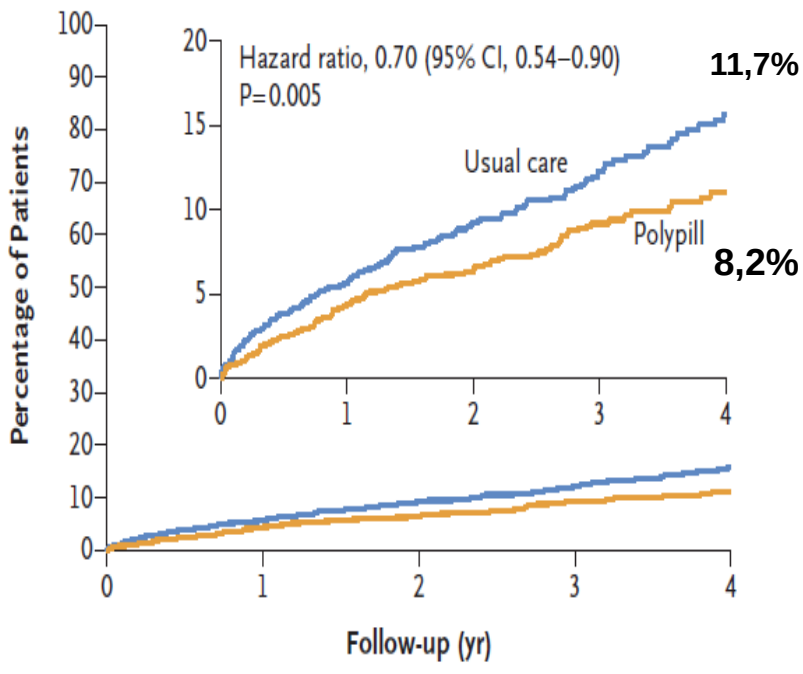
2500 sujets en prévention secondaire. Europe dont France. IDM type 1 < 6m
Et ≥ 75a ou ≥ 65a avec un critère enrichissement (diabète, IRC (DFG 30-60), ACTD CABG, CPI, AVC
ASA 100mg + Ramipril 2,5; 5, 10mg + Atorva 20 ou 40mg

A Primary Outcome **Décès CV +IDM , AVC non fatal, ou Revx urg**



No. at Risk					
Usual care	1229	1075	852	518	196
Polypill	1237	1064	848	511	192

B Key Secondary Outcome **Décès CV + IDM , AVC non fatal**



No. at Risk					
Usual care	1229	1079	857	522	196
Polypill	1237	1074	859	521	201

Castellano JM et al. NEJM 2022;Sept15

Conclusions

- Risque résiduel important postSCA et peut diminuer avec obtention objectifs LDLc

- Lutter contre l'inertie médicale : meilleur connaissance des objectifs, algorithmes décisionnels dès la sortie USIC, CRH, ordonnances, association statine + ezetimibe d'emblée **(Fire and Forget)** puis iPCSK9 si non atteinte objectif après 4 à 8 semaines.

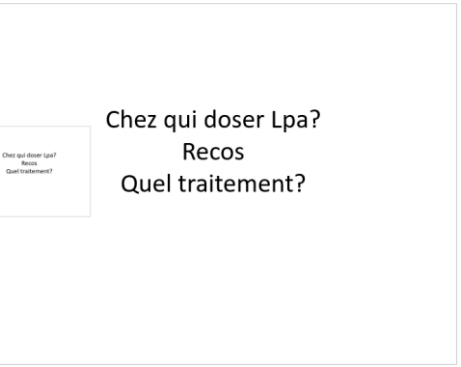
- Rôle du centre de rééducation CV, MG, Cardiologues libéraux

- Améliorer adhérence du patient (acteur informé)

Lp(a) et AVC : où en est-on ?

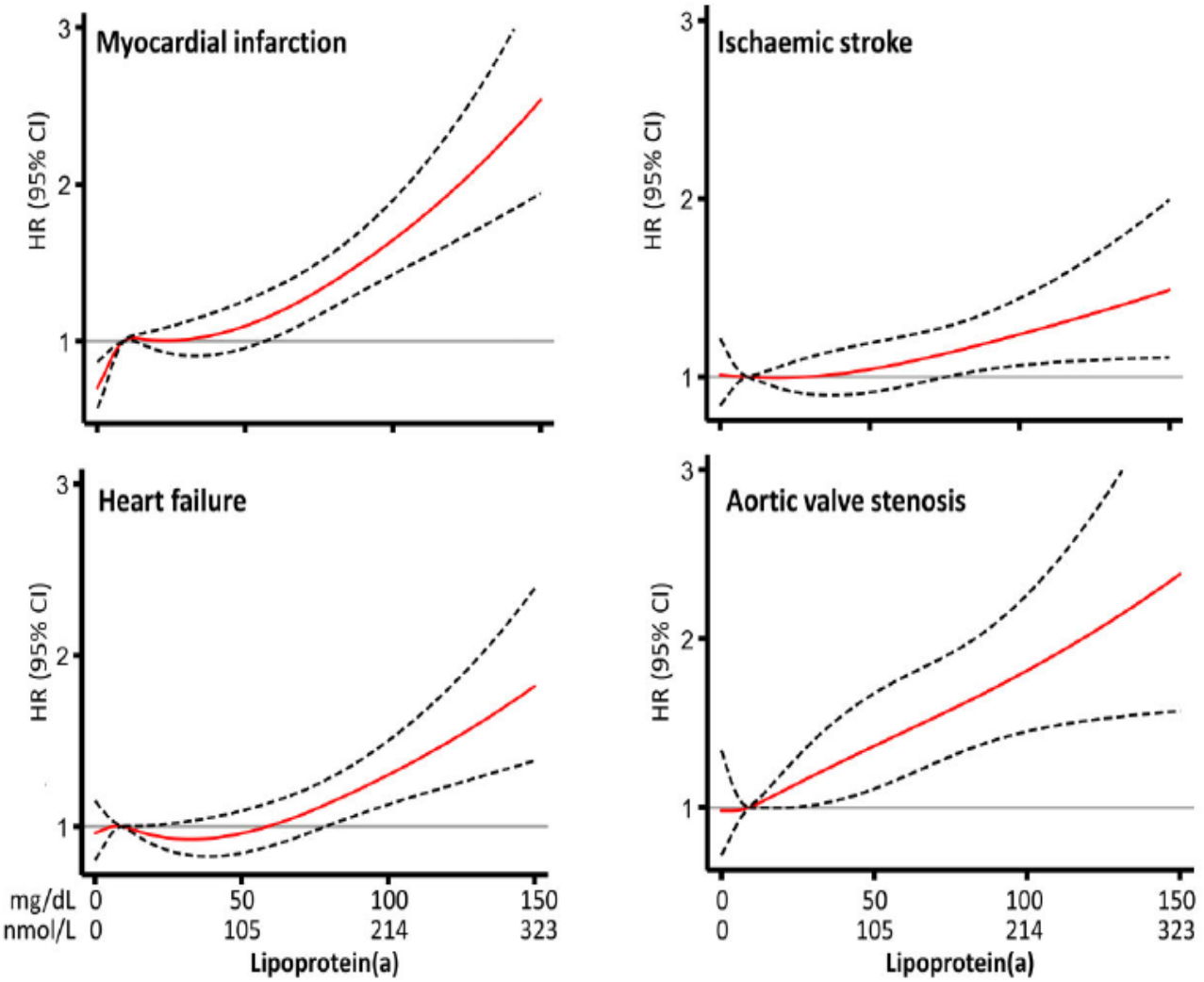
- Lien Lp(a) et risque d'AVC / David Calvet (Paris)

- **Recommandations et usage en pratique / Franck Boccara (Paris)**



Chez qui doser Lpa?
Recos
Quel traitement?

Risque d'événement CV en fonction de la concentration de Lpa

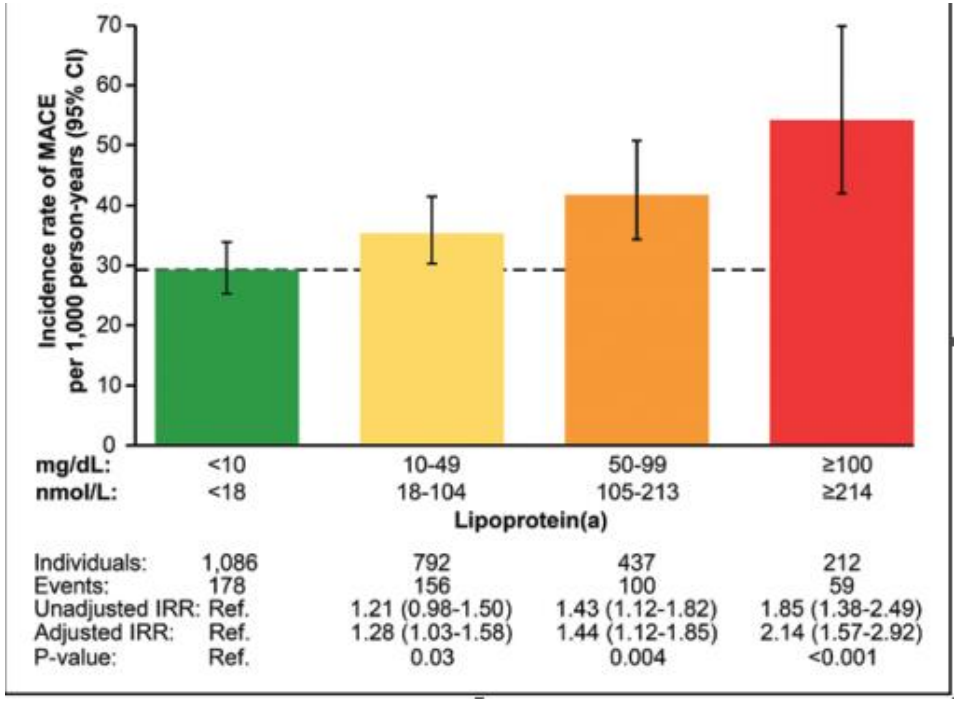


Based on data from 70 286 White individuals in the Copenhagen General Population Study with a median 7.4 years of follow-up.

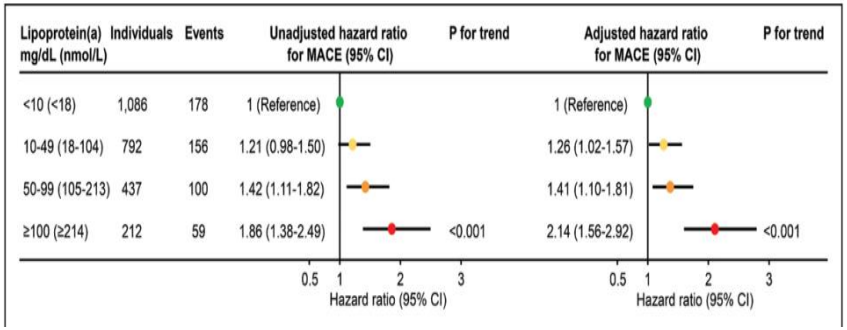
Kronenberg et al., European Heart Journal (2022) 0, 1–2

RCV et Lpa en prevention secondaire

Absolute risk of major adverse cardiovascular event (MACE) according to concentrations of Lp(a) (lipoprotein[a]).



Hazard ratios for major adverse cardiovascular event (MACE) according to concentrations of Lp(a) (lipoprotein[a])



***This prospective study included 2527 individuals aged 20 to 79 with a history of CV disease.**
Error bars indicate 95% confidence intervals. ASCVD, atherosclerotic cardiovascular disease; CV, cardiovascular; IRR, incidence rate ratio; LDL-C_{corr}, low-density lipoprotein cholesterol corrected for Lp(a); **MACE, major adverse cardiovascular event: CV death, non fatal MI, PCI/CABG, stroke**

Madsen CM et al. Arterioscler Thromb Vasc Biol. 2020;40(1):255–266.

Chez qui doser la Lp(a)?

2019 Recommendations for lipid analyses for cardiovascular disease risk estimation (3)

EAS ESC European Society of Cardiology

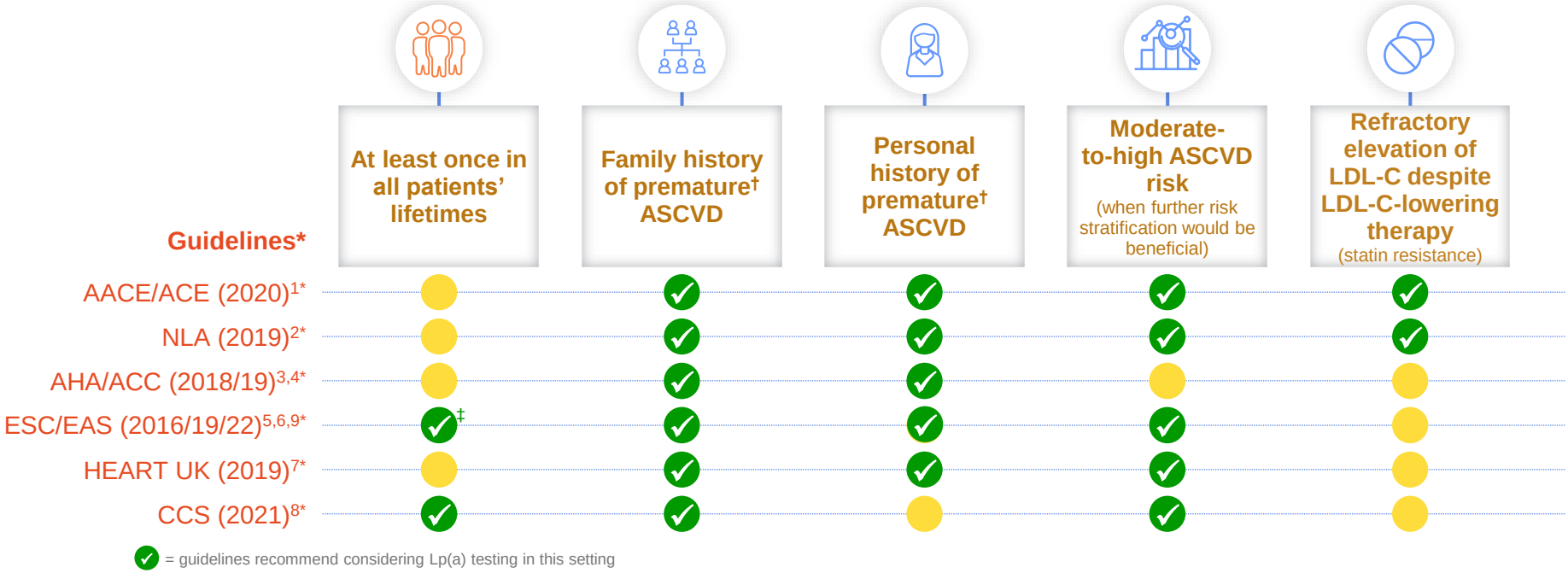
Recommendations	Class	Level
Lp(a) measurement should be considered at least once in each adult person's lifetime to identify those with very high inherited Lp(a) levels >180 mg/dL (>430 nmol/L) who may have a lifetime risk of ASCVD equivalent to the risk associated with heterozygous familial hypercholesterolaemia.	IIa	C
Lp(a) should be considered in selected patients with a family history of premature CVD, and for reclassification in people who are borderline between moderate and high-risk.	IIa	C

www.escardio.org/guidelines

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Guidelines recommend considering Lp(a) testing for a variety of patients

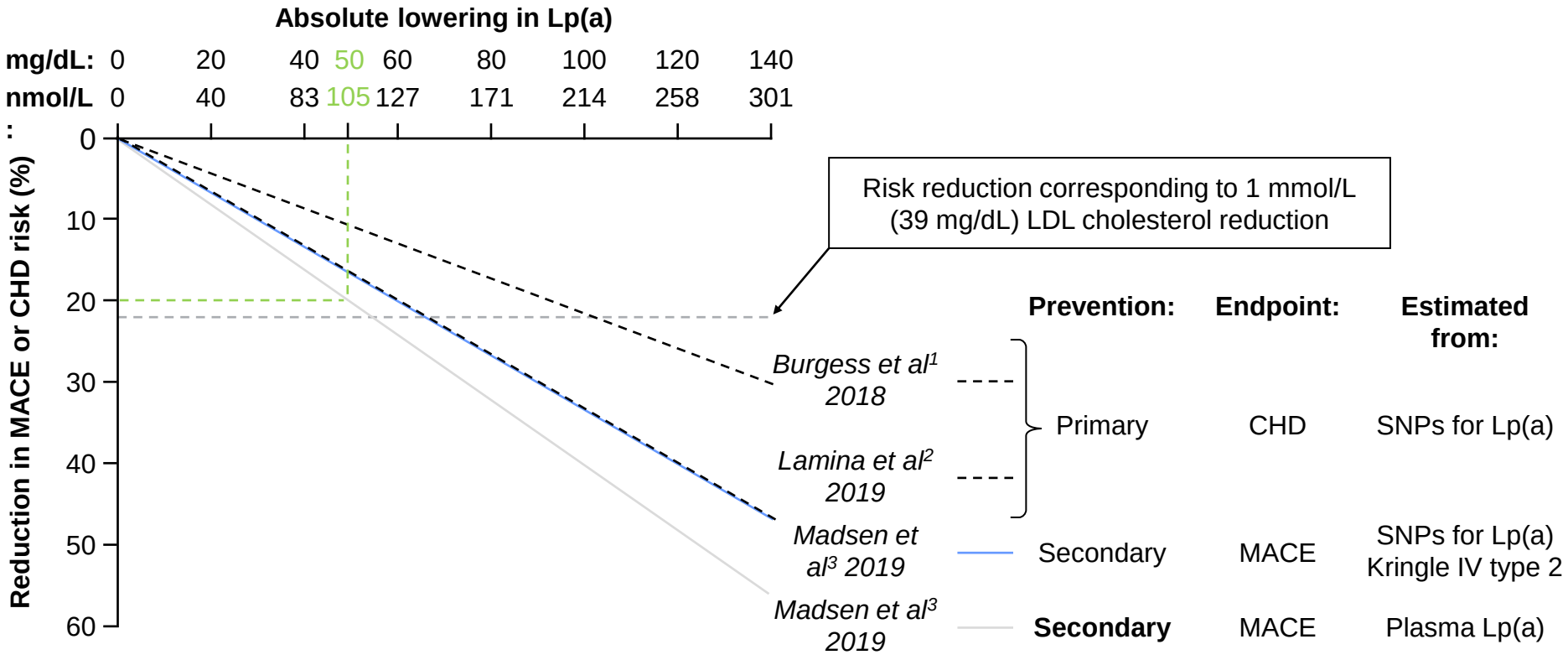
Dyslipidemia management and CVD prevention guidelines **recommend considering Lp(a) testing for a variety of patients for ASCVD risk assessment:**



***Synopsis of guideline recommendations – please refer to the notes for full details. †'Premature' defined as ASCVD occurring in males aged <55 years or females aged <65 years.[1–6] ‡Recommended once in each person's lifetime in 2019 dyslipidemias guidelines,[5] but not in 2016 CVD prevention guidelines.[6] See notes for abbreviations and references.**

Quel traitement en cas d’élévation ?

In a secondary prevention setting, lowering Lp(a) by 50 mg/dL over a short-term period may reduce MACE risk by 20%



MACE risk reduction in secondary prevention[3]		10 %	20 %	30 %	40 %	50 %
Estimated Lp(a)-lowering required (95% CI)[3]						
	Plasma Lp(a) mg/dL	25 (13–66)	50 (27–138)	74 (41–206)	99 (54–273)	124 (69–344)
	Plasma Lp(a) nmol/L	51 (25–140)	105 (55–297)	157 (86–445)	212 (114–592)	266 (147–681)

ASCVD, atherosclerotic cardiovascular disease; CHD, coronary heart disease; CI, confidence interval; LDL, low-density lipoprotein; MACE, major adverse cardiovascular event; SNP, single nucleotide polymorphism.

1. Burgess S et al. JAMA Cardiol. 2018;3(7):619–627; 2. Lamina C et al. JAMA Cardiol. 2019;4(6):575–577;
3. Madsen CM et al. Arterioscler Thromb Vasc Biol. 2020;40(1):255–266.

Managing high Lp(a) concentration

No treatment is approved specifically for cardiovascular reduction risk in patients with high Lp(a), except apheresis in some countries with additional restrictions & various indications (GER, UK, US).

Box 3 : Recommendations for the treatment of patients with a high lipoprotein(a) concentration.

In patients with Lp(a) > 250 nmol/L (≈ 1 g/L), cardiovascular risk is elevated, and therefore lipid-lowering treatment should be intensified (LOE B/Class IIb)

A discrete rise in Lp(a) under statin treatment does not limit the use of statins, given the net overall cardiovascular benefit of the treatment, even in patients with high Lp(a) (LOE A/Class I)

In primary prevention, aspirin treatment should be considered in patients with Lp(a) > 250 nmol/L (≈ 1 g/L) and subclinical atherosclerosis (i.e. coronary artery calcium score > 400 Agatston units) or significant carotid stenosis > 50% (LOE B/Class IIa)

Class: class of recommendation; LOE: level of evidence; Lp(a): lipoprotein(a).

Consensus panel recommendations for managing high Lp(a) concentration

- In the absence of specific Lp(a)-lowering therapies, early risk factor management is recommended for individuals with elevated Lp(a), taking into account their absolute global cardiovascular risk and Lp(a) level.
- Among patients with high Lp(a), all cardiovascular risk factors should be comprehensively addressed as per guideline recommendations.
- Lipoprotein apheresis can be considered in patients with very high Lp(a) and progressive cardiovascular disease despite optimal management of risk factors.
- Niacin is not recommended for Lp(a) lowering.

Durlach et al., 2021, ACVD

Kronenberg et al., European Heart Journal (2022) 0, 1–22 https://doi.org/10.1093/eurheartj/ehac361

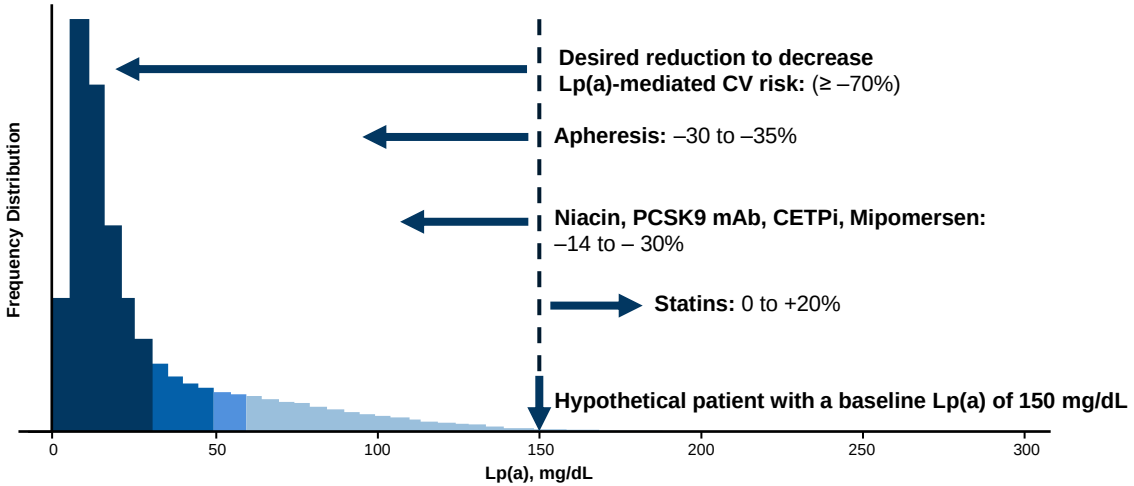
The most effective current lipid-lowering therapies only modestly reduce Lp(a) levels and the burden of residual CV risk remains

Thresholds that are considered important for reducing Lp(a)-associated CV risk[1–3]

- (<30 mg/dL) U.S. & CN normal levels, represents negligible risk for CVD and CAVS
- (<50 mg/dL) Mentioned in several guidelines (not present in the 2019 ESC/EAS Guidelines)
- (<60 mg/dL) Cutoff for apheresis eligibility in Germany and U.K.

% increase/decrease in Lp(a) levels from hypothetical baseline

Effects of several drugs/procedure on Lp(a) levels[1]

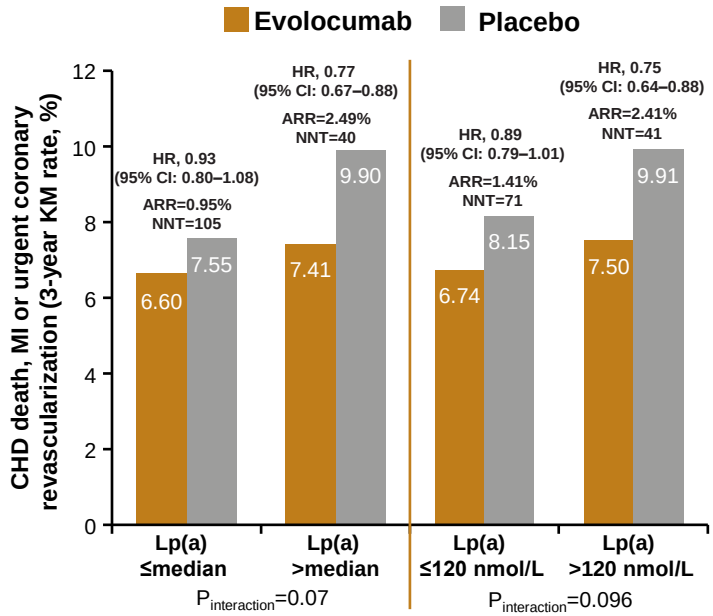


Novel RNA-targeted therapies, such as antisense oligonucleotides, have the potential to reduce Lp(a) to levels whereby the risk of Lp(a)-mediated CVD is relatively low in most patients[1]

CAVS, calcific aortic valve stenosis; CETPi, cholesterol ester transfer protein inhibitors; CV, cardiovascular; CVD, cardiovascular disease; EAS, European Atherosclerosis Society; ESC, European Society of Cardiology; Lp(a), lipoprotein(a); mAb, monoclonal antibodies; PCSK9, proprotein convertase subtilisin/kexin-type 9; RNA, ribonucleic acid.

1. Tsimikas S. *J Am Coll Cardiol.* 2017;69:692–711. 2. Grundy SM, et al. *Circulation.* 2019;139:e1082–e1143. 3. Wilson DP, et al. *J Clin Lipidol.* 2019;13:374–392.

Patients with higher baseline Lp(a) levels experienced greater CV risk reduction with evolocumab



Overall, evolocumab reduced the risk of CHD death, MI, or urgent coronary revascularization by **16%**; however, this **response varied by baseline Lp(a)**:

- **23%** vs **7%** reduction in patients above or below **median** baseline value: **37 nmol/L** (~15 mg/dL)
- **25%** vs **11%** reduction in patients above or below **120 nmol/L** (~50 mg/dL)

Higher levels of Lp(a) are independently associated with an increased risk of CV events in patients with established CV disease, irrespective of their LDL-C levels

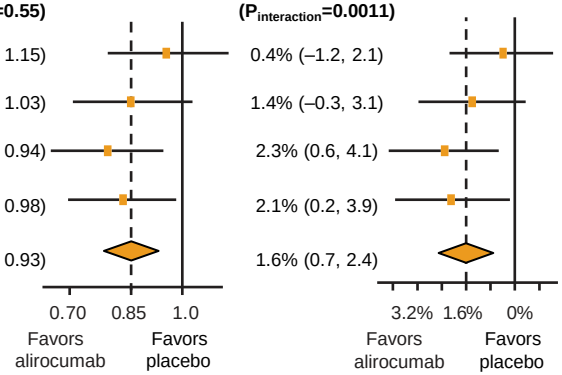
O'Donoghue ML, et al. Circulation. 2019;139(12):1483–1492.

Lp(a) reduction with alirocumab appears to contribute independently to CV risk reduction

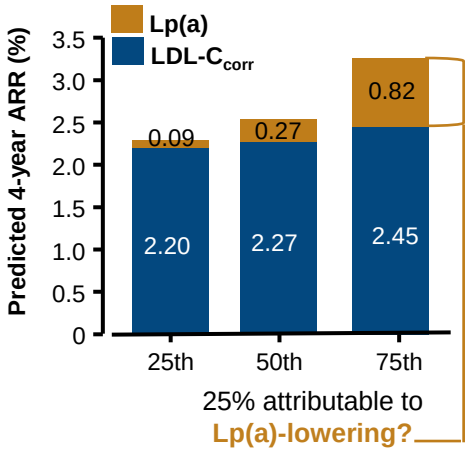
ODYSSEY OUTCOMES

Relative and absolute treatment effects on MACE stratified by baseline Lp(a) quartile

Sub-group	Alirocumab n/N (%)	Placebo n/N (%)	HR (95% CI) ($P_{interaction}$=0.55)	ARR (95% CI) ($P_{interaction}$=0.0011)
Q1	211/2,327 (9.1)	228/2,403 (9.5)	0.95 (0.79, 1.15)	0.4% (–1.2, 2.1)
Q2	219/2,438 (9.0)	239/2,293 (10.4)	0.85 (0.71, 1.03)	1.4% (–0.3, 3.1)
Q3	212/2,356 (9.0)	269/2,373 (11.3)	0.79 (0.66, 0.94)	2.3% (0.6, 4.1)
Q4	261/2,341 (11.2)	316/2,393 (13.2)	0.83 (0.70, 0.98)	2.1% (0.2, 3.9)
Overall	903/9,462 (9.5)	1052/9,462 (11.1)	0.85 (0.78, 0.93)	1.6% (0.7, 2.4)



Relative contributions of changes in lipids and lipoproteins to CV risk reduction



The **relative contribution of Lp(a) reduction to reduced risk of MACE** was negligible when baseline Lp(a) concentration was low but **became substantial** when baseline **Lp(a) concentration was high** (≥59.6 mg/dL)

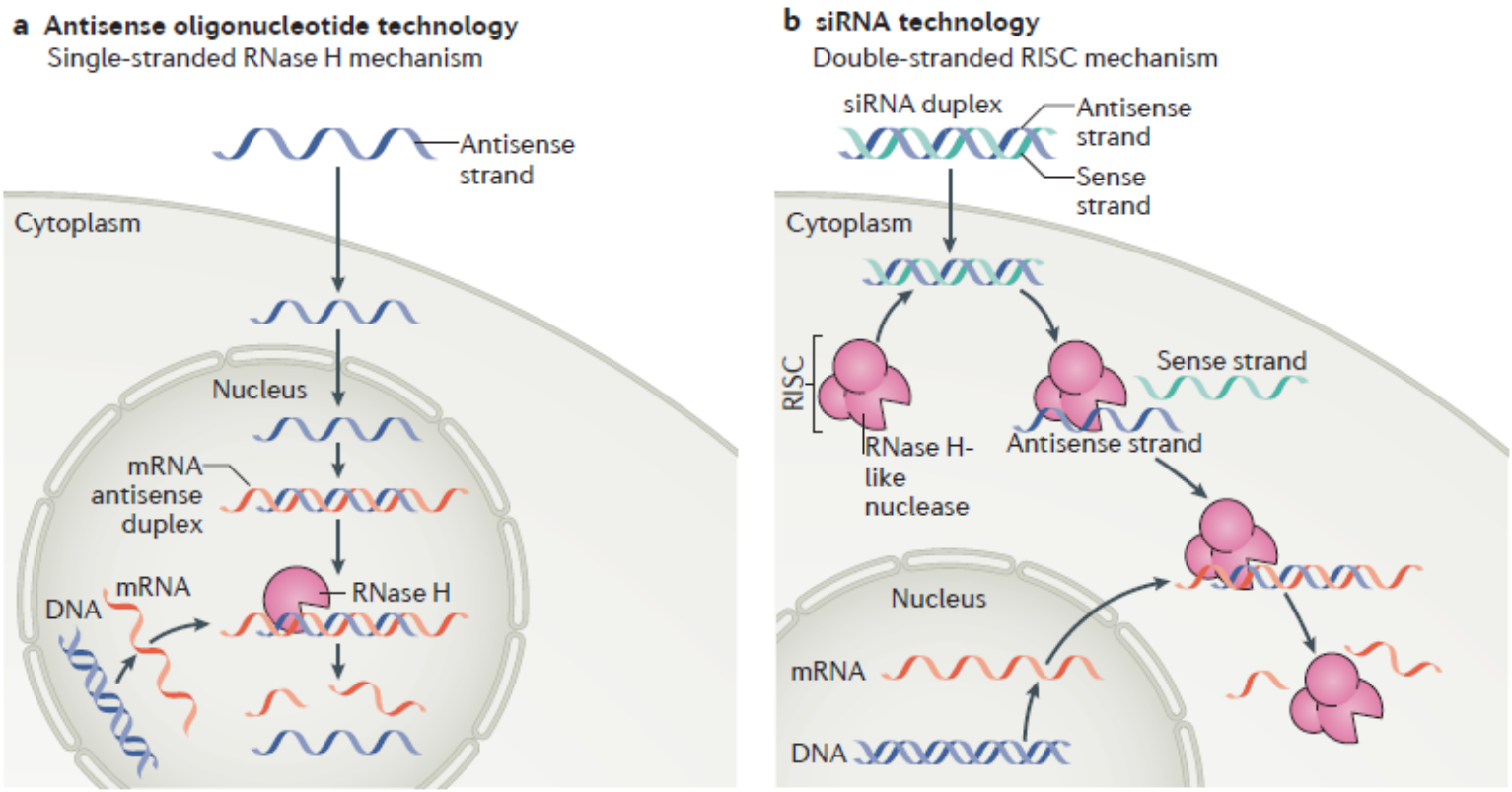
Reductions in Lp(a) and LDL-C_{corr} were **independently associated** with the absolute reduction in MACE

LDL-C_{corr} levels calculated using the formula LDL-C_{corr} = LDL-C – 0.3 × Lp(a) mass.
Bittner VA, et al. J Am Coll Cardiol. 2020;75(2):133–144.

Lp(a) inhibitors

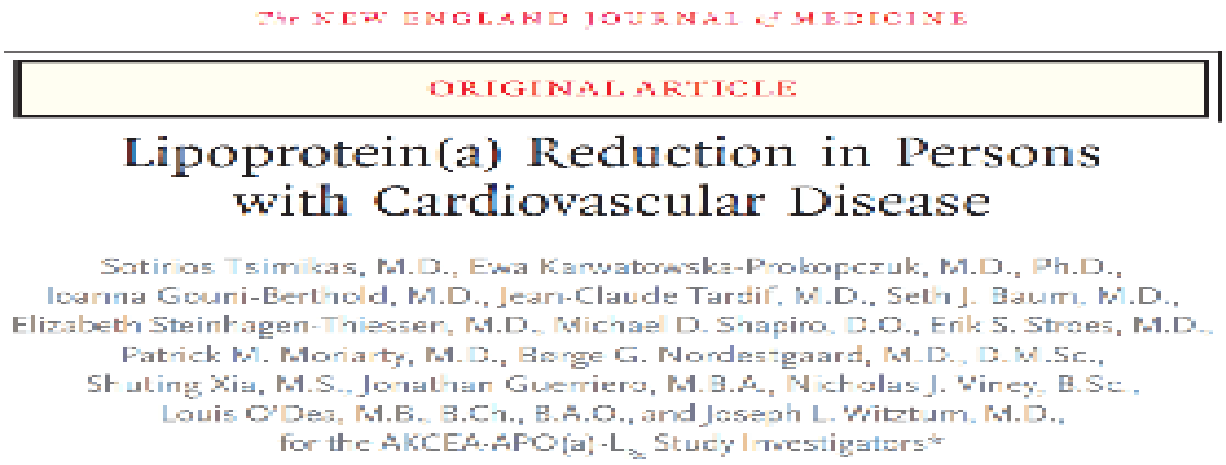
- ***Pelacarsen (ASO)***
- ***Olpasiran (siRNA)***

siRNA-based versus antisense oligonucleotide-based approaches



Nordestgaard et al. Nat Rev Cardiol 2018; 15: 261-272

PELACARSEN



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Lipoprotein(a) Reduction in Persons with Cardiovascular Disease

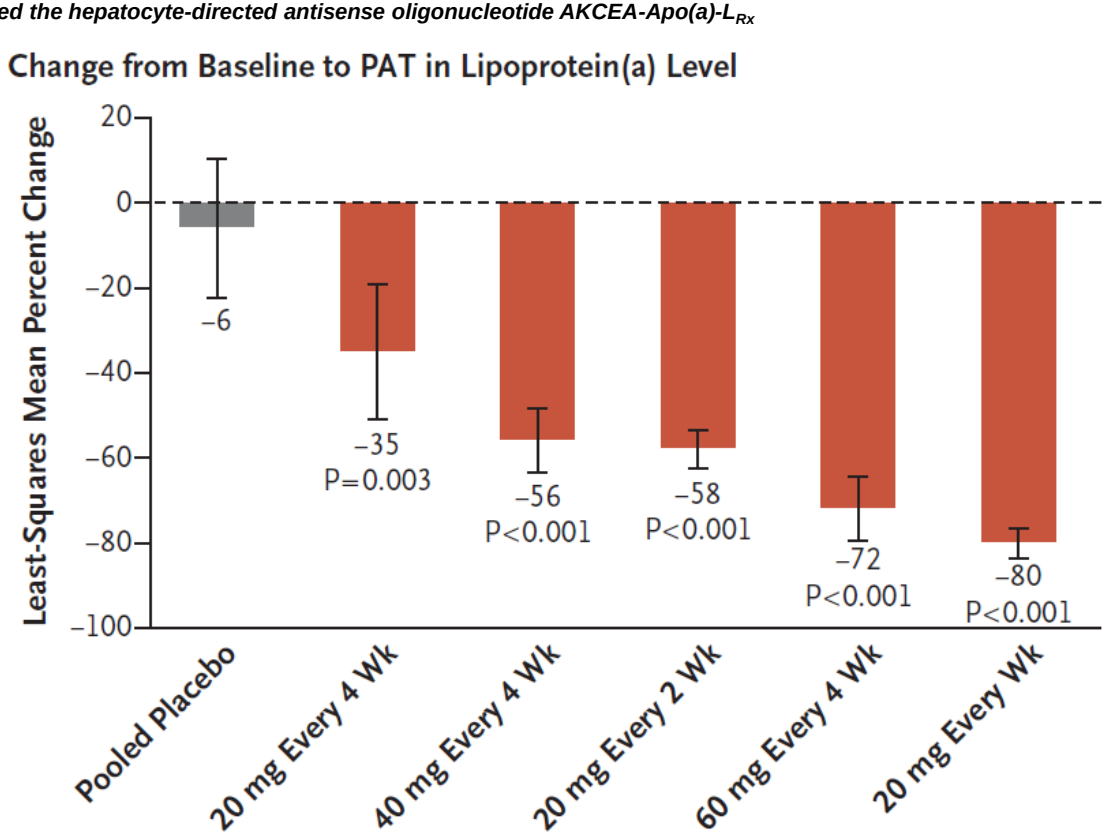
Sotirios Tsimikas, M.D., Ewa Karwatowska-Prokopczuk, M.D., Ph.D., Ioanna Gouni-Berthold, M.D., Jean-Claude Tardif, M.D., Seth J. Baum, M.D., Elizabeth Steinhagen-Thiessen, M.D., Michael D. Shapiro, D.O., Erik S. Stroes, M.D., Patrick M. Moriarty, M.D., Børge G. Nordestgaard, M.D., D.M.Sc., Shuting Xia, M.S., Jonathan Guerriero, M.B.A., Nicholas J. Viney, B.Sc., Louis C'Dea, M.B., B.Ch., B.A.O., and Joseph L. Witztum, M.D., for the AKCEA-APO(a)-L_{Rx} Study Investigators*

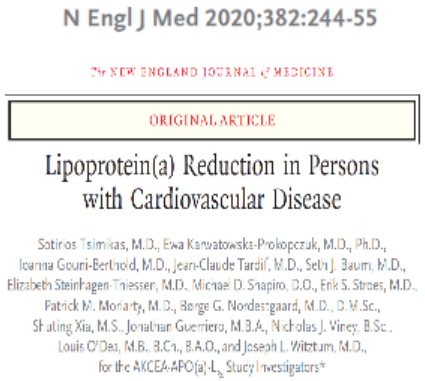
- ***286 patients with established CV disease and Lp(a) ≥ 60 mg/dL (150 nmol/L)***
- ***Patients received the hepatocyte-directed antisense oligonucleotide AKCEA-Apo(a)-L_{Rx}***

Tsimikas et al. N Engl J Med 2020; 382: 244-55

Effect of APO(a)-L_{Rx} on lipoprotein(a) level

- *286 patients with established CV disease and Lp(a) ≥ 60 mg/dL (150 nmol/L)*
- *Patients received the hepatocyte-directed antisense oligonucleotide AKCEA-Apo(a)-L_{Rx}*




N Engl J Med 2020;382:244-55

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ORIGINAL ARTICLE

Lipoprotein(a) Reduction in Persons with Cardiovascular Disease

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PAT: primary analysis time point

Tsimikas et al. N Engl J Med 2020; 382: 244-55

ORIGINAL ARTICLE

Olpasiran. Etude de phase II

Small Interfering RNA to Reduce Lipoprotein(a) in Cardiovascular Disease

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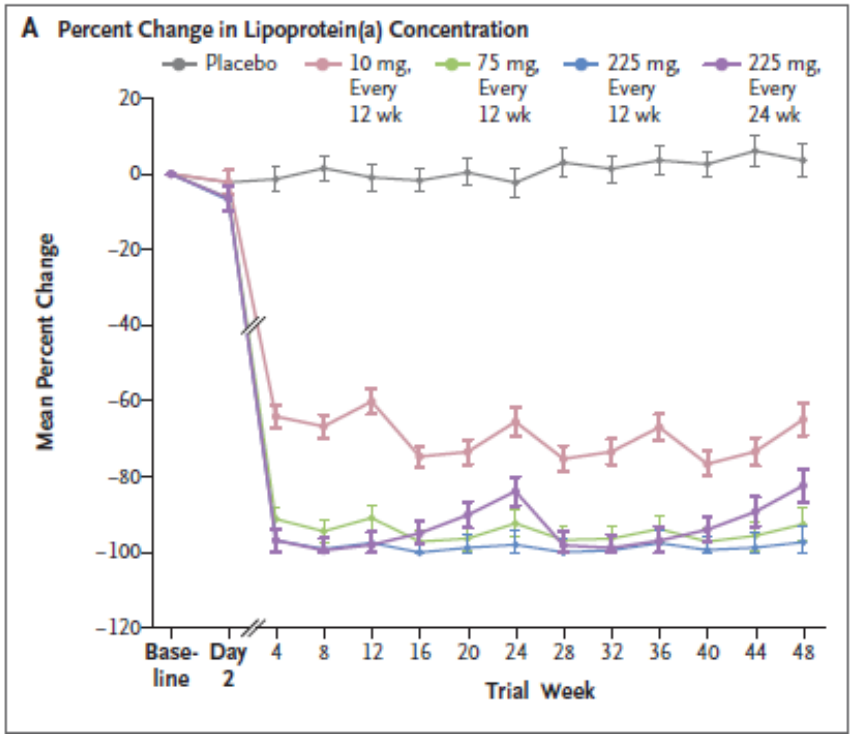
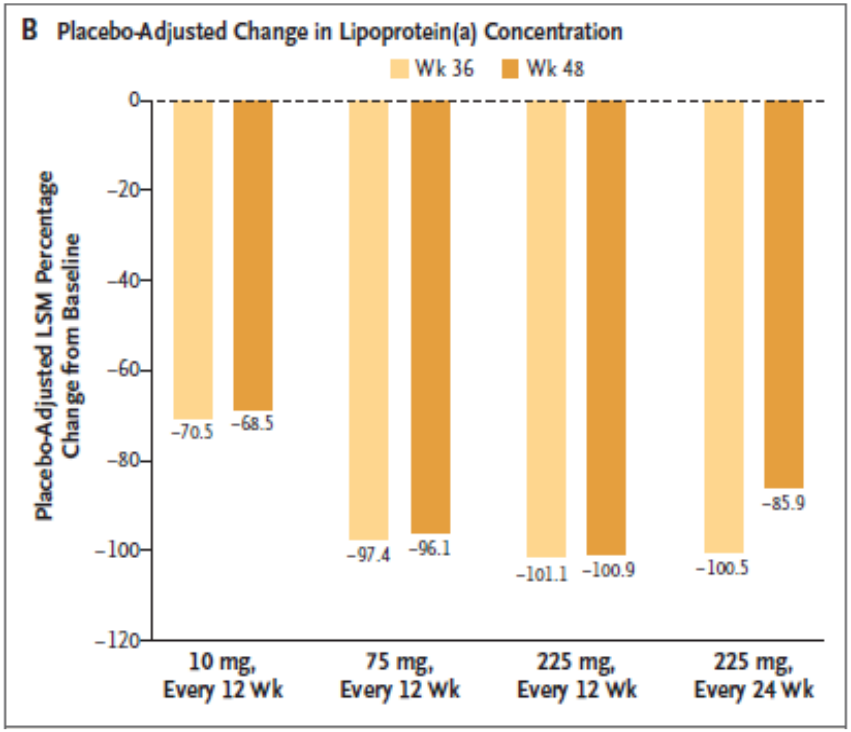
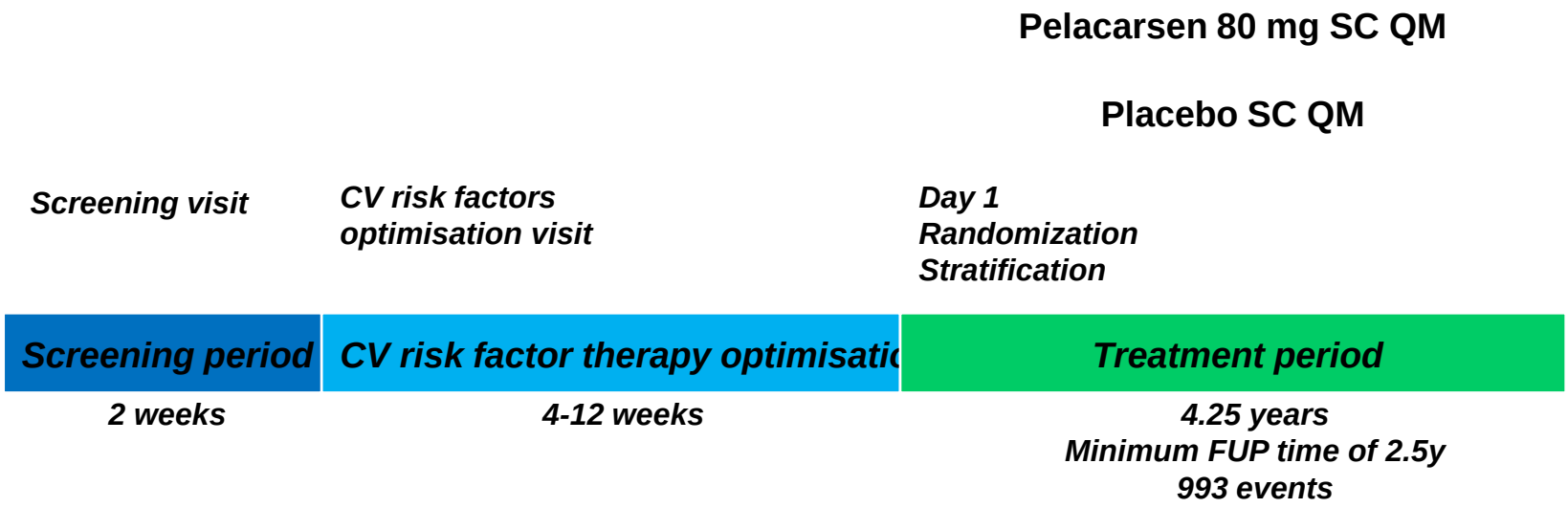




NEJM 2022; Nov 6

CVOT Targeting Lp(a) - HORIZONS

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



Study is positive if primary EP is met in either overall (patients with Lp(a) ≥ 70 mg/dL) or sub-population (stratum with Lp(a) ≥ 90 mg/dL)

Primary Endpoint: MI, stroke, CV death or urgent coronary revascularization

Conclusions

- **Why?** Lp(a) is a strong and causal risk factor for CVD. However, the lack of clinical trial data has resulted in Lp(a) being largely ignored by clinical guidelines assessing the prevention of CVD.

- No clinical trials have adequately tested the hypothesis that Lp(a) reduction reduces the incidence of first or recurrent CVD events
- Screening for Lp(a) excess is indicated in selected individuals

- **When? Who?**

  Primary prevention: FH, Score > 5%, Familial Hx of premature CVD or Lp(a)
  Secondary prevention: premature CVD, recurrent CVD with max statin

- New therapeutics decrease Lp(a) levels may have important clinical benefit

Back up

CRH de sortie postSCA

Lipides

- Indiquer objectif LDLc < 0.55 g/L
- Date nouveau BL et ordonnance
- Indiquer escalade thérapeutique si non atteinte objectif
- Identifier les visites de suivi (1ère visite avec BL)

Conclusions

SCA STEMI inaugural chez une femme de 65 ans hypertendue, diabétique pris en charge à H5 avec atteinte bitronculaire (occlusion CD2 responsable STEMI et sténose serrée IVA2). Angioplasties + stents actifs CD2 et IVA2. FEVG 52%. Biantiaggrégation plaquetaire pendant 12 mois

Objectif LDLc < 0.55 g/L mise sous statine forte intensité + IAC

Nouveau bilan lipidique entre 4 et 8 semaines avec consultation cardiologique en ville entre un et 3 mois.

Si LDLc > 0.7 g/L indication à la prescription d'un iPCSK9

Schiele F. et al. European Heart Journal: Acute Cardiovascular Care 2019

Gestion objectifs et tolérance après la sortie USIC

Sortie avec CRH indiquant

Objectif LDLc

ASAT/ ALAT +/- CPK

+ Ordonnance bilan lipidique et

ASAT/ALAT +/- CPK

Préciser escalade thérapeutique

6-8 semaines

Centre réadaptation CV

Objectif, Tolérance

Dépistage FH

Cardiologue libéral

Médecin traitant

Objectif, Tolérance

Dépistage FH

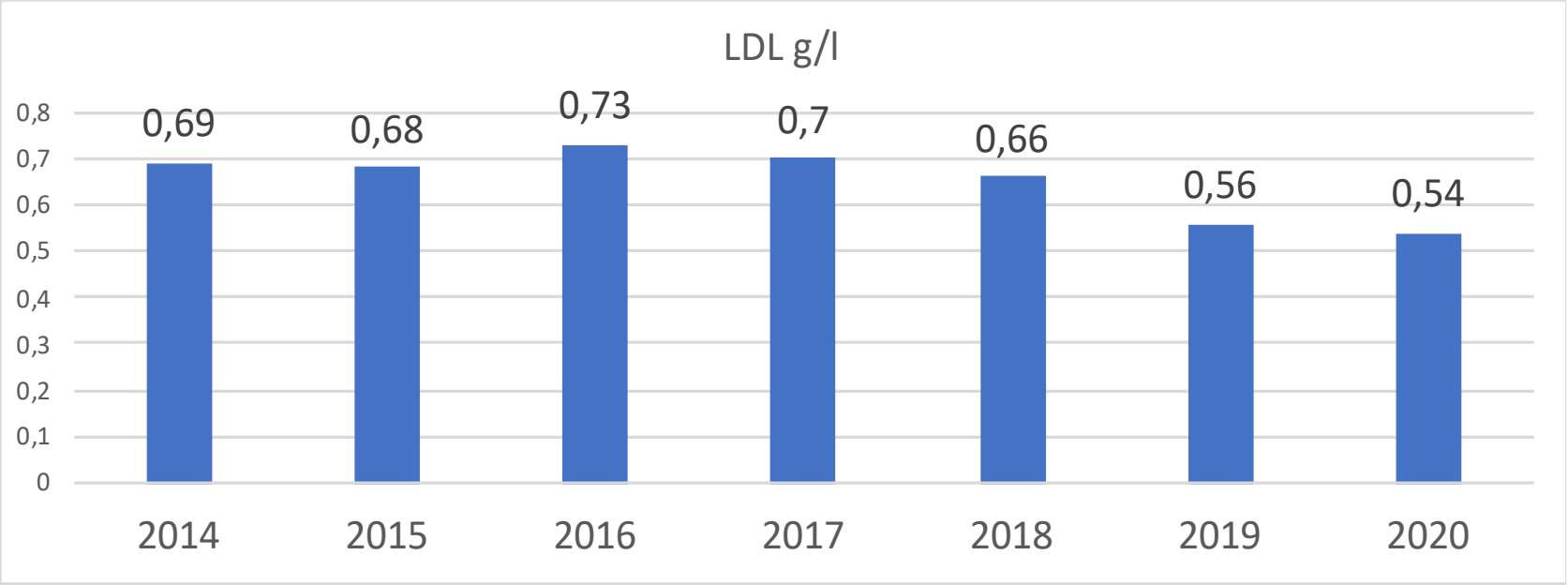
Rôle du centre de réadaptation cardiovasculaire

- Surveillance efficacité et tolérance du traitement par statine
- Intensification du traitement hypolipémiant ajout ézétimibe
- Education et information du patient sur les bénéfices des statines et leurs effets indésirables potentiels
- Identification des sujets avec hypercholestérolémie familiale.

Dépistage et collaboration avec centre de référence/Avis spécialisé

Le diagnostic doit être suspecté lorsque le LDL-C est = 1,9 g/L (4,9 mmol/L) chez l'adulte et 1,6 g/L (4,1 mmol/L) chez l'enfant.
Il est recommandé de confirmer le diagnostic par un score établi sur les critères clinico-biologiques du Dutch Lipid Clinic Network ou si possible par une analyse génétique.

Evolution du LDLc à la sortie du service de réadaptation cardiaque de Machecoul



Nb patients	143	161	176	172	171	210	129
% LDL<0,55	36%	33%	26%	37%	43%	56%	63%

Avec l'autorisation de Bruno PAVY, LDL après SCA. Cardio Online, 2020

Payer's guidelines

MINISTÈRE DES SOLIDARITÉS ET DE LA SANTÉ

Arrêté du 8 décembre 2020 relatif à la procédure d'accord préalable pour bénéficier de la prise en charge de la spécialité PRALUENT® (alirocumab)

remboursables aux assurés sociaux, était limitée aux seules indications thérapeutiques suivantes, plus restreintes que celles issues de son autorisation de mise sur le marché:

– en association à un traitement hypolipémiant optimisé, des patients adultes ayant une **hypercholestérolémie familiale hétérozygote**, insuffisamment contrôlée et nécessitant un traitement par LDL-aphérèse (3 g/L en prévention primaire et 2 g/L en prévention secondaire)

– en association à un traitement hypolipémiant optimisé chez les patients adultes ayant une maladie cardiovasculaire athéroscléreuse établie par un **antécédent de SCA récent** (prévention secondaire) et qui ne sont pas contrôlés **(LDL-c ≥ 0,7 g/L**) malgré un traitement hypolipémiant optimisé comprenant au moins une statine à la dose maximale tolérée;

Payer's guidelines

MINISTÈRE DES SOLIDARITÉS ET DE LA SANTÉ

Arrêté du 8 décembre 2020 relatif à la procédure d'accord préalable pour bénéficier de la prise en charge de la spécialité REPATHA® (evolocumab)

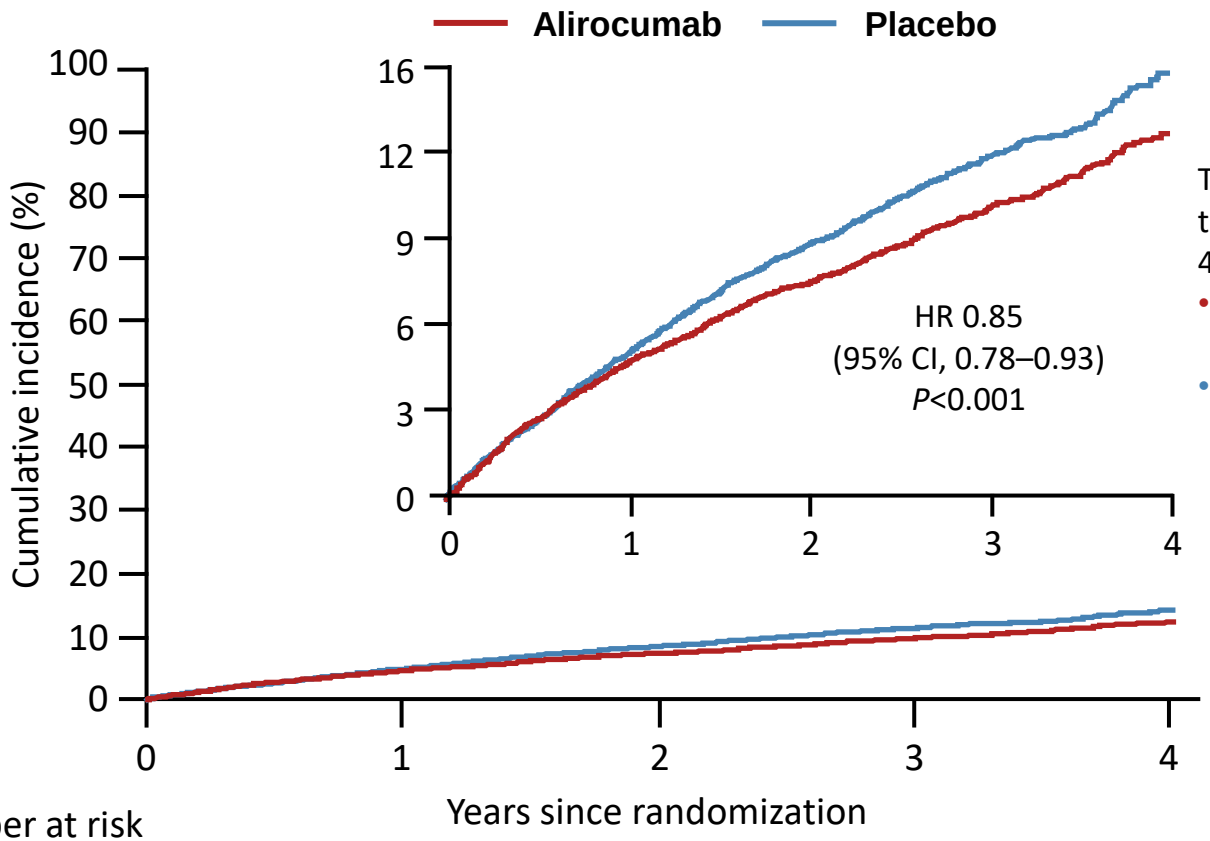
remboursables aux assurés sociaux, était limitée aux seules indications thérapeutiques suivantes, plus restreintes que celles issues de son autorisation de mise sur le marché:

– en association avec d'autres thérapies hypolipidémiantes, chez l'adulte et l'adolescent à partir de 12 ans présentant une **hypercholestérolémie familiale homozygote**;
– en association à un traitement hypolipémiant optimisé chez les patients adultes présentant une **hypercholestérolémie familiale hétérozygote (HFHe), insuffisamment** contrôlée par un traitement optimisé et nécessitant une prise en charge par LDL-aphérèse (3 g/L en prévention primaire et 2 g/L en prévention secondaire)

– en association à un traitement hypolipémiant optimisé chez les patients adultes à très haut risque cardiovasculaire, avec hypercholestérolémie primaire ou dyslipidémie mixte, présentant une **maladie cardiovasculaire athéroscléreuse établie par un antécédent d'infarctus du myocarde (IDM), d'accident vasculaire cérébral (AVC) non hémorragique et/ou d'artériopathie oblitérante des membres inférieurs (AOMI) symptomatique (prévention secondaire),** et non contrôlés (LDL-c ≥ 0,7 g/L) malgré un traitement optimisé comprenant au moins une statine à dose maximale tolérée.

ALIROCUMAB (iPCSK9)

Cumulative Incidence of the Composite Primary Endpoint



Number at risk

Placebo	9462	8805	8201	3471	629
Alirocumab	9462	8846	8345	3574	653

The Kaplan–Meier rates for the primary endpoint at 4 years were:

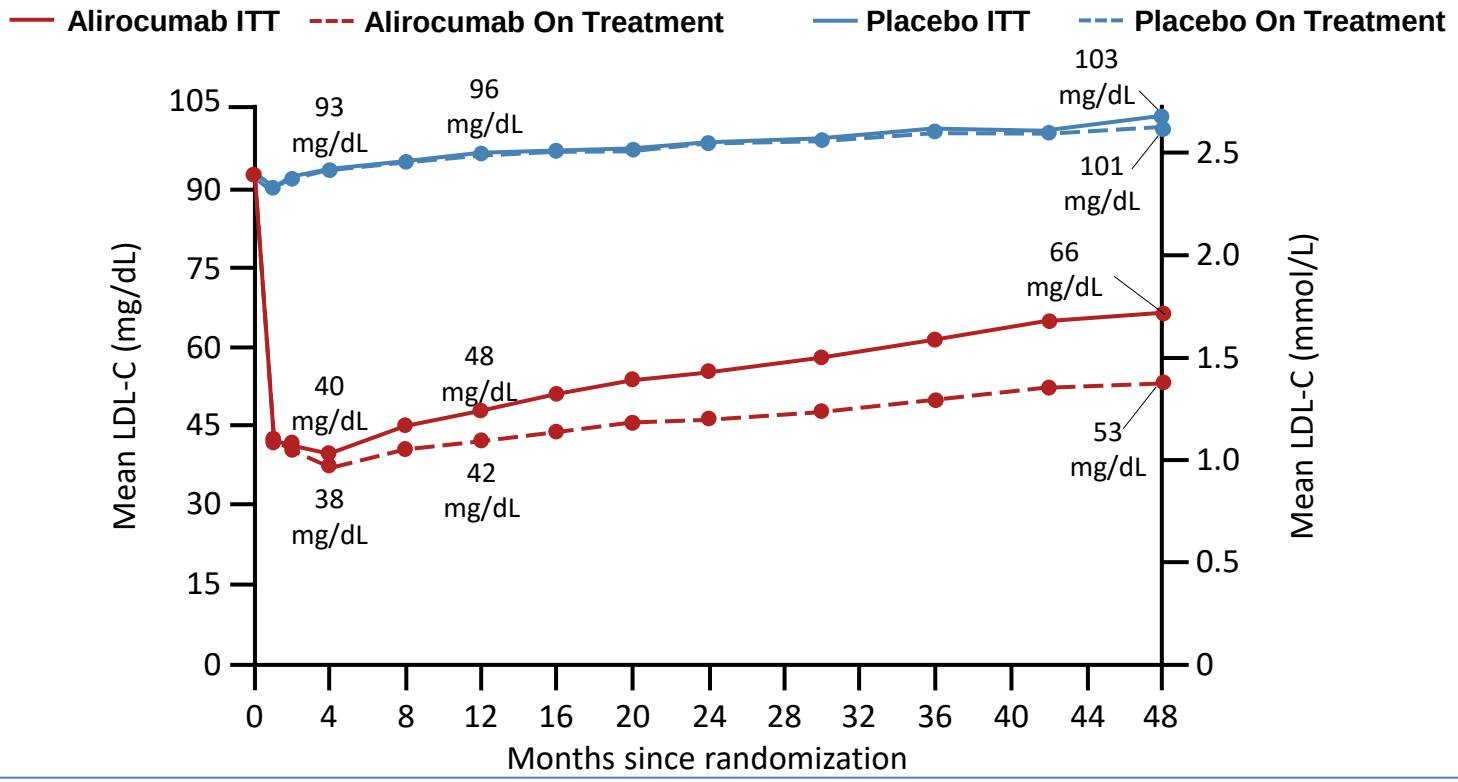
- 12.5% (95% CI: 11.5–13.5) for alirocumab
- 14.5% (95% CI: 13.5–15.6) for placebo

To prevent one primary end point event, 49 patients (95% CI: 28–164) would need to be treated for 4 years

The inset shows the same data on an enlarged y-axis.
CI, confidence interval; HR, hazard ratio.

Schwartz GG et al. *N Engl J Med* 2018 .

LDL-C Levels Over Time (ITT† and On-Treatment‡ Analyses)



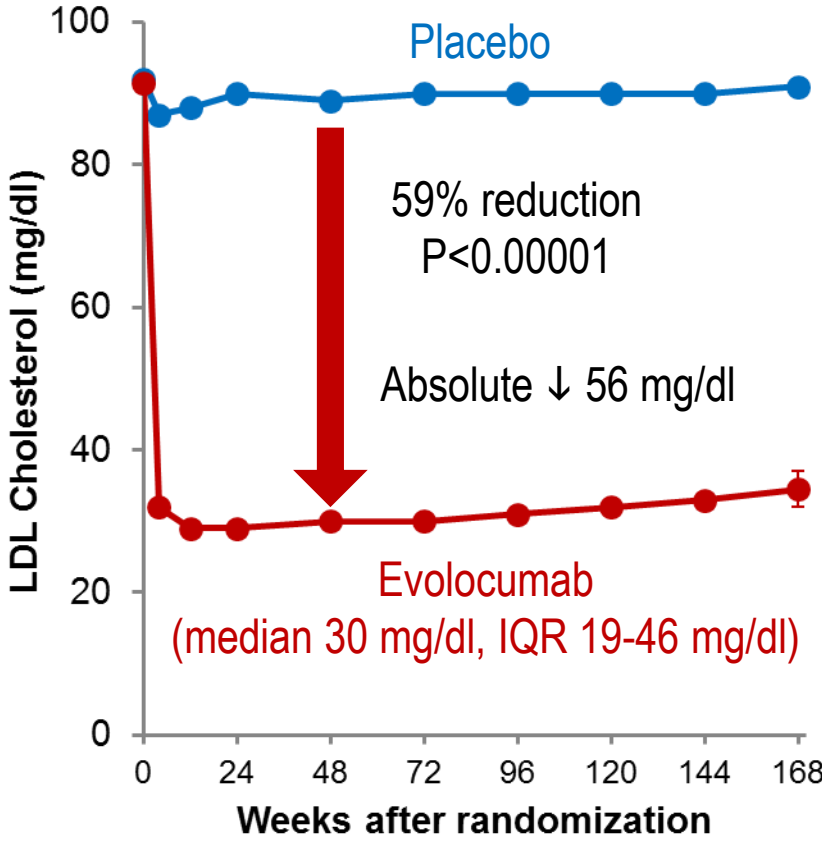
In the on-treatment analyses, at 4, 12, and 48 months, average LDL-C levels in patients treated with alirocumab were 62.7%, 61.1%, and 54.7% lower than the respective levels in the placebo group.
Earliest down-titration of alirocumab (including placebo substitution) could not occur before the Month 4 visit

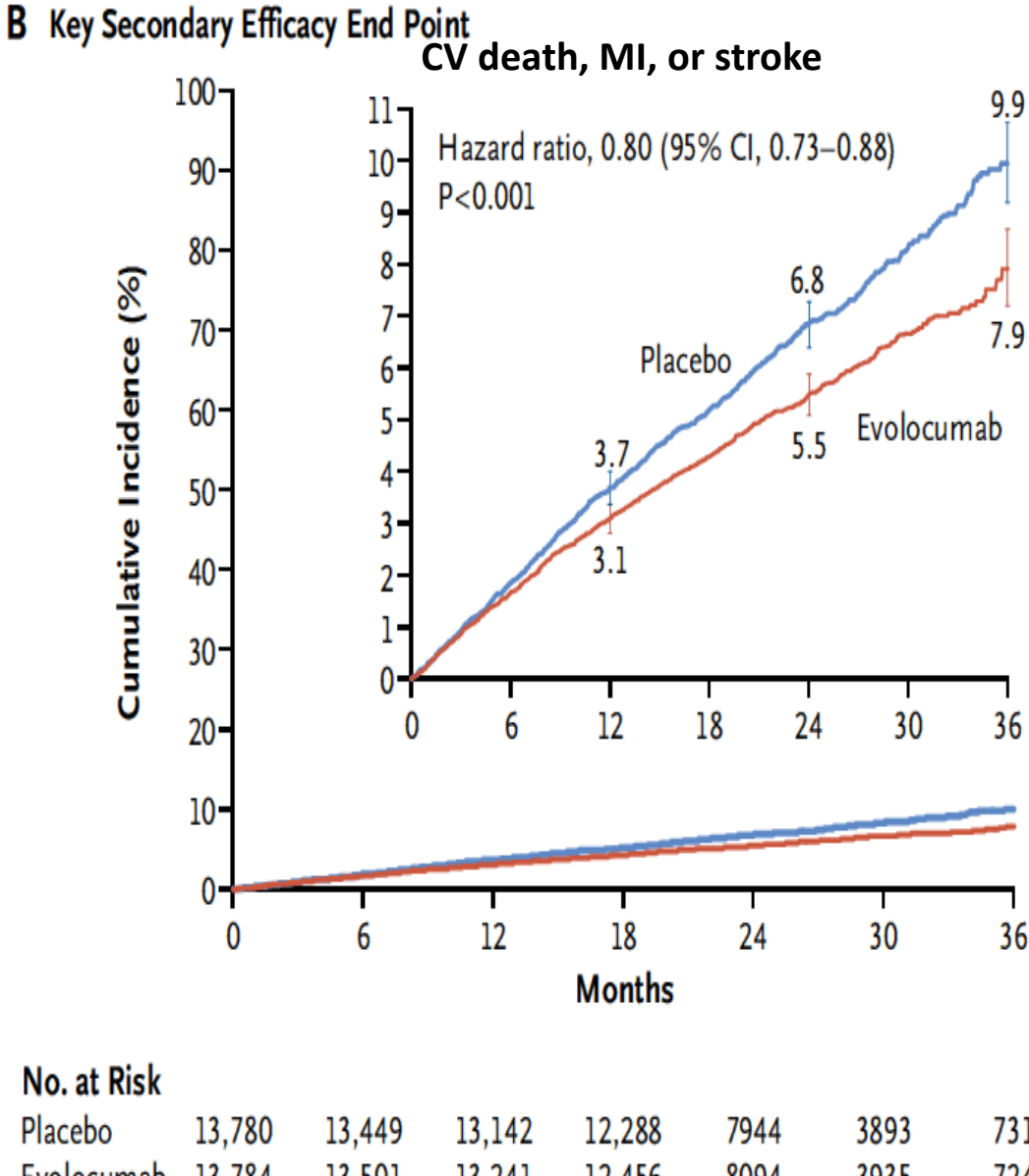
†All LDL-C values, including those after premature treatment discontinuation, blinded dose decrease, and blinded switch to placebo.
‡Excludes LDL-C values obtained after premature treatment discontinuation or blinded switch from alirocumab to placebo (but includes LDL-C values obtained after blinded titration of alirocumab between the 75 and 150 mg doses). ITT, intention-to-treat; LDL-C, low-density lipoprotein cholesterol.

Schwartz GG et al. *N Engl J Med* 2018 .

Evolocumab. iPCSK9
Primary efficacy endpoint

- ↓ LDL-C by 59% to a median of 30 m
- ↓ CV outcomes in patients on statin
- Safe and well-tolerated





Parcours patient structuré

Optimisation de la coordination ville-hôpital :

→ CRH clair avec **objectif lipidique** inscrit en fin de CRH dans la conclusion par ex pour le cardiologue de ville et médecin traitant. Interactions médicamenteuses potentielles.

→ **Ordonnance bilan lipidique et surveillance hépatique et musculaire** à donner au patient pour sa prochaine visite avec le cardio ou MT **(indiquer dans CRH niveau ASAT/ALAT avant statine)**

Quel objectif de LDLc? Quelle surveillance?

Double rôle :

1/ Atteinte des objectifs lipidiques **entre 4 et 8 semaines**

2/ Surveillance des effets indésirables potentiels : **hépatique, musculaire à 8 semaines et apparition diabète**

LETTRE DE SORTIE POST-SCA

Table 1. The eight headings of the structured discharge letter after acute myocardial infarction.

Syndrome
1. Patient identification: name, date of birth. Risk factors and history: cardiovascular risk factors, cardiovascular history, important non-cardiovascular history.
2. Reason for admission (symptoms, ECG changes, troponin) and diagnosis: • Main diagnosis: STEMI, NSTEMI, UA • Additional diagnosis (heart failure, arrhythmia, diabetes, renal dysfunction…).
3. Invasive strategy: coronary angiography, extent of coronary disease, culprit lesion, angioplasty, complete revascularization. Onset of symptoms to balloon time.
4. Left ventricular ejection fraction at discharge (%).
5. Main biological results: peak troponin, eGFR, HbA1c, LDL-C admission.
6. Discharge treatment: • Standard: aspirin (dose), type of P2Y12 inhibitor (reason for choice), beta-blocker, ACE inhibitor, lipid-lowering, proton-pump inhibitor • Specific: diabetes, hypertension, additional lipid-lowering, heart failure, anticoagulant, anti-arrhythmic treatment, implanted cardioverter defibrillator
7. Therapeutic targets (tailored to the patient's profile): • LDL-C: reasons for addition of ezetimibe • HbA1c: reason for increase/change in treatment • Duration of DAPT: type and duration; mention of high bleeding or high ischaemic risk, strategy if use of chronic anticoagulation • Other risk factors of lifestyle, tailored to patient's profile (diet, smoking cessation, body weight, exercise)
8. Structured follow-up: • Time of first cardiology visit, rehabilitation • Time of complementary tests: ischaemic test, extension of the arterial disease

Schiele F. et al. European Heart Journal: Acute Cardiovascular Care 2019

HAS IPAQSS 2017 - IDM : Indicateurs de qualité et de sécurité des soins (IQSS) du thème « Prise en charge hospitalière de l'infarctus du myocarde »

Indicateurs du thème IDM
Dix indicateurs évaluant la prise en charge des patients hospitalisés pour un infarctus du myocarde (IDM) peuvent être recueillis en hors-protocole :

1.Taux de patients SCA ST+ avec délai arrivée en établissement de santé – ponction ≤ 60 minutes (PON).
2.Administration d'aspirine et autre antiagrégant plaquettaire et d'anticoagulant à la phase aiguë (AAP).
3.Tenue du dossier patient pris en charge pour un SCA ST+ (TDP-SCA).

4. **Score agrégé des indicateurs évaluant les prescriptions médicamenteuses** appropriées à la sortie (BASI : composé des 5 indicateurs ci-dessous)
1. Prescription appropriée d'aspirine et de clopidogrel ou de prasugrel ou ticagrelor à la sortie (ASP).
2. Mesure de la fraction d'éjection systolique du ventricule gauche (FEVG).
3. Prescription appropriée de bêtabloquant à la sortie (BBL)*.
4. Prescription appropriée d'inhibiteur de l'enzyme de conversion à la sortie (IEC)*.
5. Prescription appropriée de statine à la sortie (STA).

10. Sensibilisation aux règles hygiéno-diététiques (HYG).

*conformité recherchée dans la population IDM avec ICS (FEVG ≤ 40%)

https://www.has-sante.fr/jcms/c_1242619/fr/ipaqss-2017-idm-indicateurs-de-qualite-et-de-securite-des-soins-iqss-du-theme-prise-