2019 ESC/EAS Guidelines for the management of dyslipidaemias: *lipid modification to reduce cardiovascular risk*: The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS)

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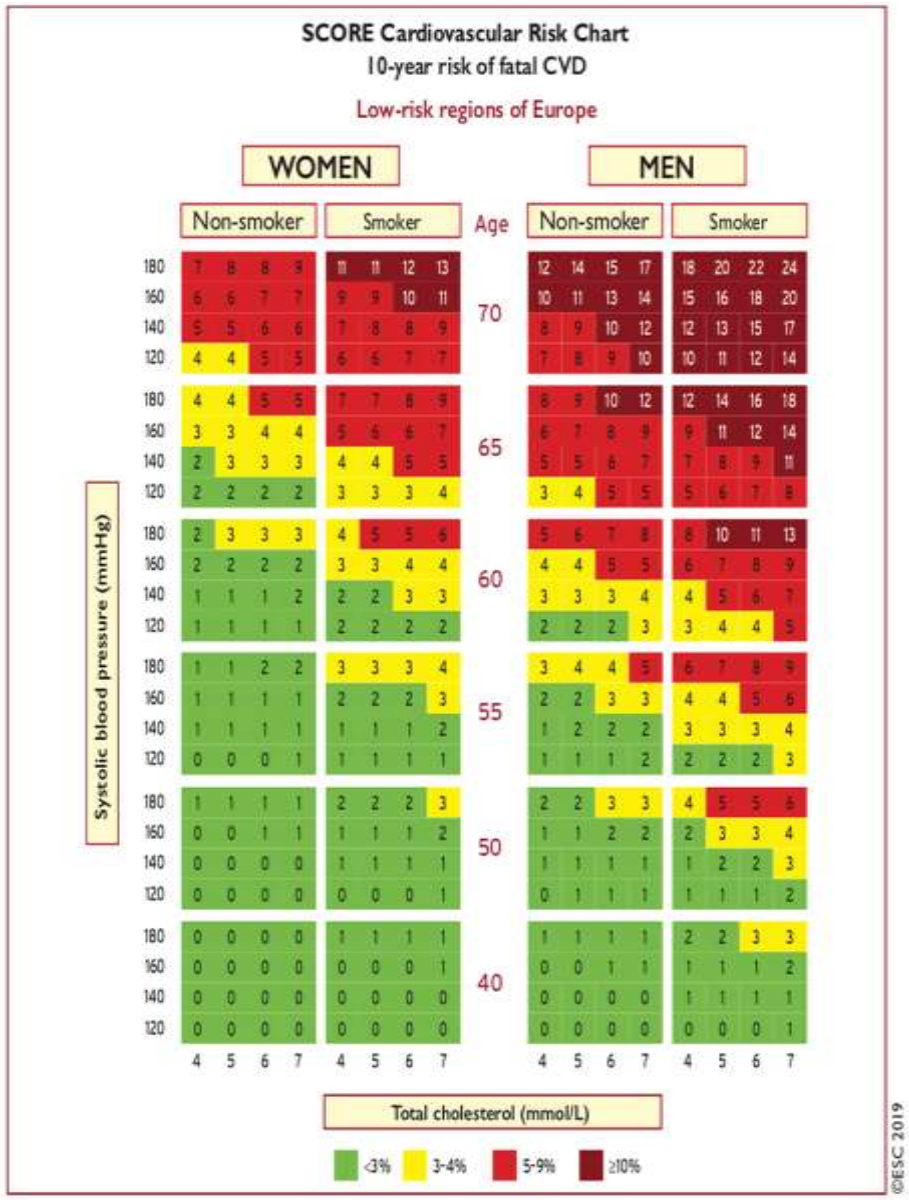
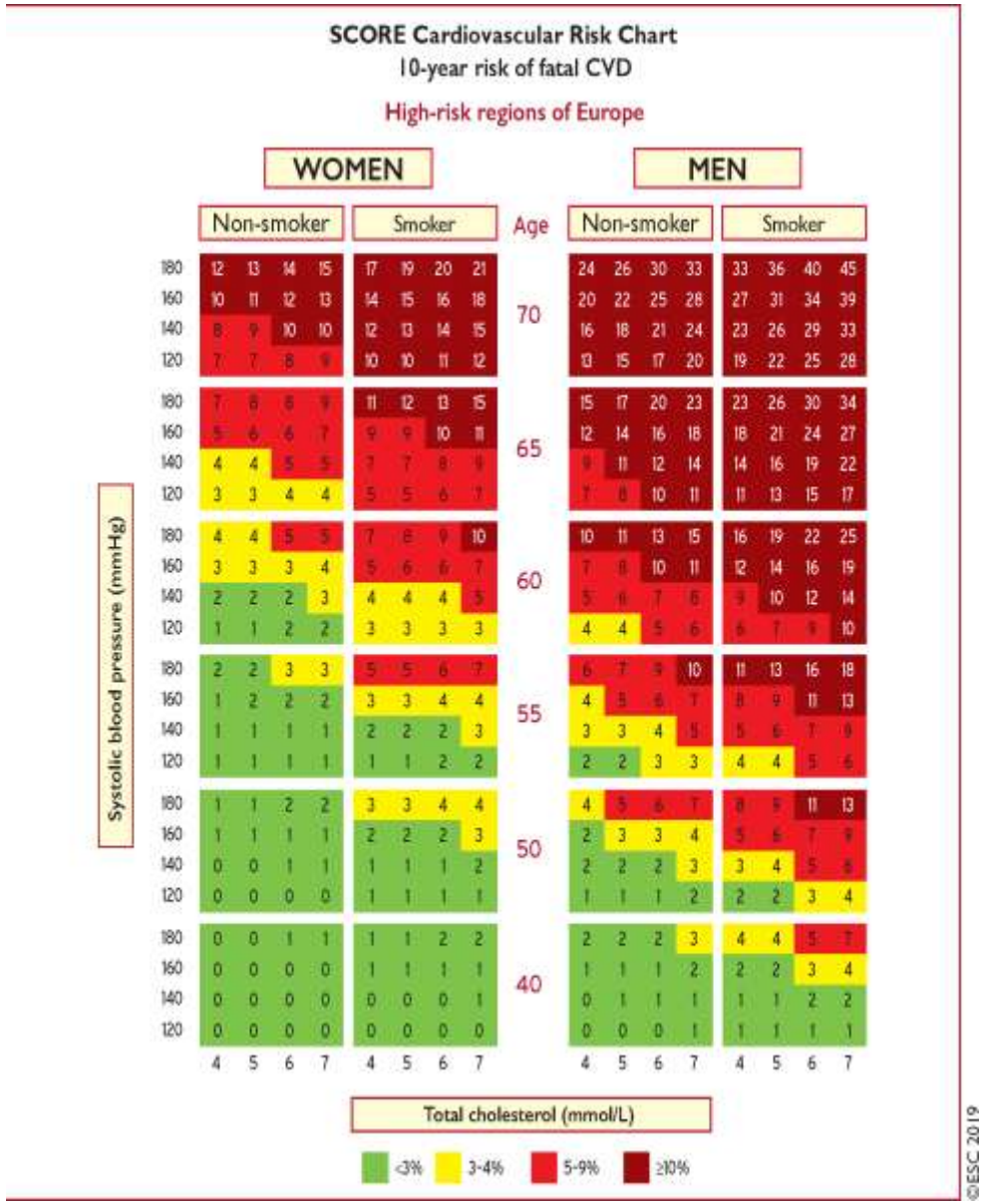
Evaluation du risque cardio vasculaire

SCORE : Risque à 10 ans d évènements CVX fatals





Risk estimation charts for different countries

The low-risk charts should be considered for use in
Austria, Belgium, Cyprus, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Luxembourg, Netherlands, Norway, Malta, Portugal, Slovenia, Spain, Sweden, Switzerland, and the UK.

The high-risk charts should be considered for use in
Albania, Algeria, Armenia, Bosnia and Herzegovina, Croatia, Czech Republic, Estonia, Hungary, Latvia, Lebanon, Libya, Lithuania, Montenegro, **Morocco,** Poland, Romania, Serbia, Slovakia, Tunisia, and Turkey

Some countries have a cardiovascular disease mortality rate >350/100 000, and the **high-risk chart may underestimate risk**. These are Azerbaijan, Belarus, Bulgaria, Egypt, Georgia, Kazakhstan, Kyrgyzstan, North Macedonia, Republic of Moldova, Russian Federation, Syria, Tajikistan, Turkmenistan, Ukraine, and Uzbekistan.

How to use the risk estimation charts

To estimate a person's 10-year risk of CVD death, find the table for his/her gender, smoking status, and age. Within the table, find the cell nearest to the person's BP and TC. Risk estimates will need to be adjusted upwards as the person approaches the next age category

Risk is initially assessed on the level of TC and systolic BP before treatment, if known. The longer the treatment and the more effective it is, the greater the reduction in risk, but in general it will not be more than about one-third of the baseline risk. For example, for a person on antihypertensive drug treatment in whom the pre-treatment BP is not known, if the total CV SCORE risk is 6%, then the pre-treatment total CV risk may have been 9%.

Low-risk persons should be offered advice to maintain their low-risk status. While no threshold is universally applicable, the intensity of advice should increase with increasing risk.

The charts may be used to give some indication of the effects of reducing risk factors, given that there is apparently a time lag before the risk reduces. In general, people who stop smoking halve their cumulative risk over a relatively short period of time.

In apparently healthy persons, CVD risk is most frequently the result of multiple, interacting risk factors. This is the basis for total CV risk estimation and management.
Risk factor screening including the lipid profile should be considered in men >40 years old, and in women >50 years of age or post-menopausal
A risk estimation system such as SCORE can assist in making logical management decisions, and may help to avoid both under- and overtreatmen
Certain individuals declare themselves to be at high or very high CVD risk without needing risk scoring, and all risk factors require immediate attention. This is true for patients with documented CVD, older individuals with long-standing DM, familial hypercholesterolaemia, chronic kidney disease, carotid or femoral plaques, coronary artery calcium score >100, or extreme Lp(a) elevation.
All risk estimation systems are relatively crude and require attention to qualifying statements.
Additional factors affecting risk can be accommodated in electronic risk estimation systems such as HeartScore (www.heartscore.org)
The total risk approach allows flexibility; if optimal control cannot be achieved with one risk factor, trying harder with the other factors can still reduce risk.

Evaluation du risque cardio vasculaire

- SCORE : Personnes apparemment en bonne santé

- Prévention secondaire
- Diabète
- Insuffisance rénale
- Hypercholestérolémie familiale

} Haut ou très haut risque cardio vasculaire

Cardiovascular risk categories

Very-high-risk	People with any of the following:
*	Documented ASCVD, either clinical or unequivocal on imaging. Documented ASCVD includes previous ACS (MI or unstable angina), stable angina, coronary revascularization (PCI, CABG, and other arterial revascularization procedures), stroke and TIA, and peripheral arterial disease. Unequivocally documented ASCVD on imaging includes those findings that are known to be predictive of clinical events, such as significant plaque on coronary angiography or CT scan (multivessel coronary disease with two major epicardial arteries having >50% stenosis), or on carotid ultrasound.
*	DM with target organ damage,[a] or at least three major risk factors, or early onset of T1DM of long duration (>20 years).
*	Severe CKD (eGFR <30 mL/min/1.73 m^2).
*	A calculated SCORE ≥10% for 10-year risk of fatal CVD.
*	FH with ASCVD or with another major risk factor.
High-risk	People with:
*	Markedly elevated single risk factors, in particular TC >8 mmol/L (>310 mg/dL), LDL-C >4.9 mmol/L (>190 mg/dL), or BP ≥180/110 mmHg.
*	Patients with FH without other major risk factors.
*	Patients with DM without target organ damage,[a] with DM duration ≥10 years or another additional risk factor.
*	Moderate CKD (eGFR 30–59 mL/min/1.73 m^2).
*	A calculated SCORE ≥5% and <10% for 10-year risk of fatal CVD.
Moderate-risk	Young patients (T1DM <35 years; T2DM <50 years) with DM duration <10 years, without other risk factors. Calculated SCORE ≥1 % and <5% for 10-year risk of fatal CVD.
Low-risk	Calculated SCORE <1% for 10-year risk of fatal CVD.

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Target organ damage is defined as microalbuminuria, retinopathy, or neuropathy.

Recommendations for cardiovascular imaging for risk assessment of atherosclerotic cardiovascular disease

Recommendations	Class[a]	Level[b]
Arterial (carotid and/or femoral) plaque burden on arterial ultrasonography should be considered as a risk modifier in individuals at low or moderate risk.[29,30]	IIa	B
CAC score assessment with CT should be considered as a risk modifier in the CV risk assessment of asymptomatic individuals at low or moderate risk.[14–16,24,26]	IIa	B

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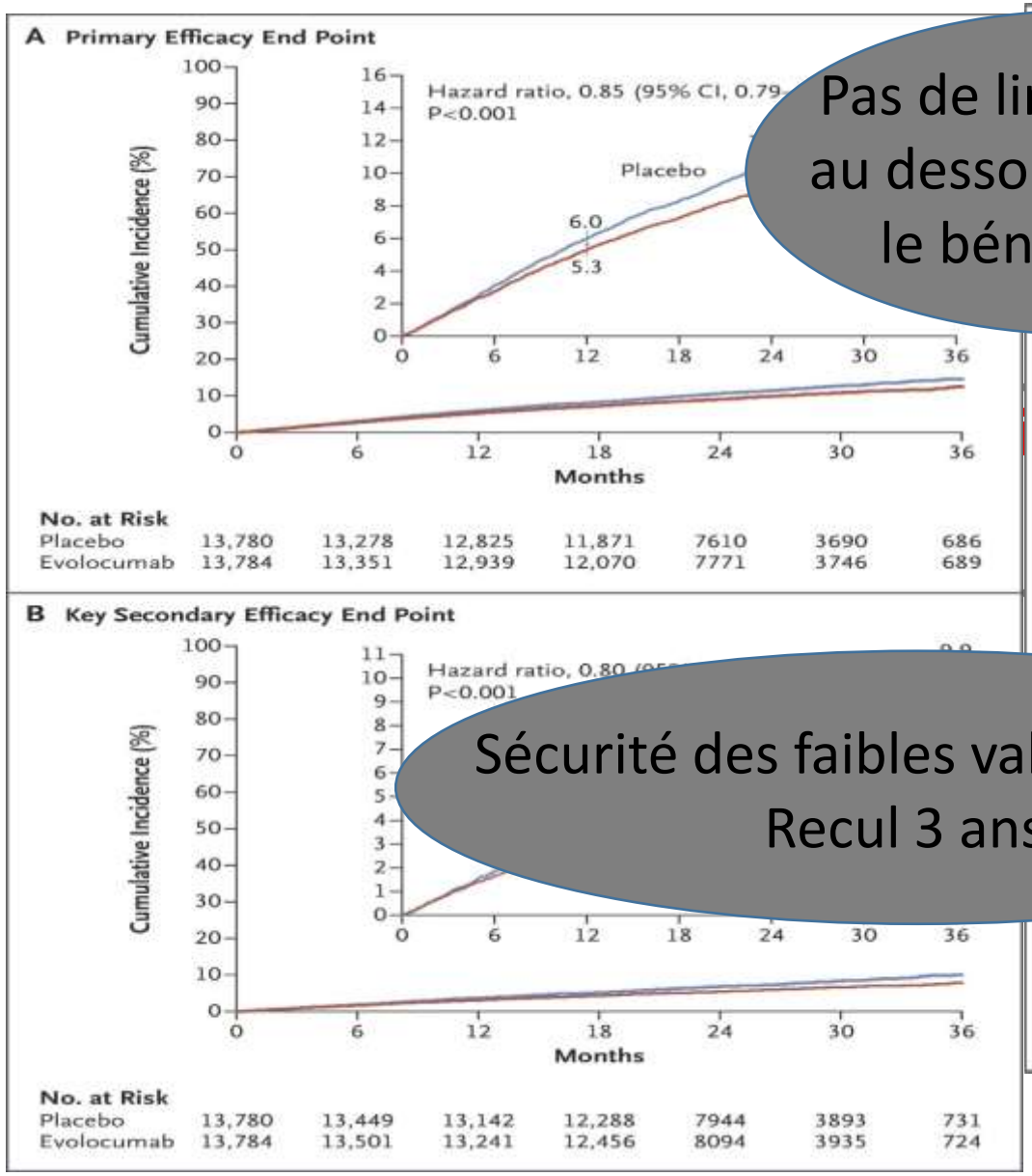
Stratégies d'intervention en fonction du risque cardiovasculaire total et selon le taux de LDLc

	Total CV risk (SCORE) %	Untreated LDL-C levels					
		<1.4 mmol/L (55 mg/dL)	1.4 to <1.8 mmol/L (55 to <70 mg/dL)	1.8 to <2.6 mmol/L (70 to <100 mg/dL)	2.6 to <3.0 mmol/L (100 to <116 mg/dL)	3.0 to <4.9 mmol/L (116 to <190 mg/dL)	≥4.9 mmol/L (≥190 mg/dL)
Primary prevention	<1, low-risk	Lifestyle advice	Lifestyle advice	Lifestyle advice	Lifestyle advice	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention and concomitant drug intervention
	Class[a]/Level[b]	I/C	I/C	I/C	I/C	IIa/A	IIa/A
	≥1 to <5, or moderate risk (see *Table 4*)	Lifestyle advice	Lifestyle advice	Lifestyle advice	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention and concomitant drug intervention
	Class[a]/Level[b]	I/C	I/C	IIa/A	IIa/A	IIa/A	IIa/A
	≥5 to <10, or high-risk (see *Table 4*)	Lifestyle advice	Lifestyle advice	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention
	Class[a]/Level[b]	IIa/A	IIa/A	IIa/A	I/A	I/A	I/A
	≥10, or at very-high risk due to a risk condition (see *Table 4*)	Lifestyle advice	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention
	Class[a]/Level[b]	IIa/B	IIa/A	I/A	I/A	I/A	I/A
Secondary prevention	Very-high-risk	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention
	Class[a]/Level[b]	IIa/A	I/A	I/A	I/A	I/A	I/A

Prise en charge thérapeutique

Objectifs LDLC

Evolocumab Cumulative Incidence of Cardiovascular Events.



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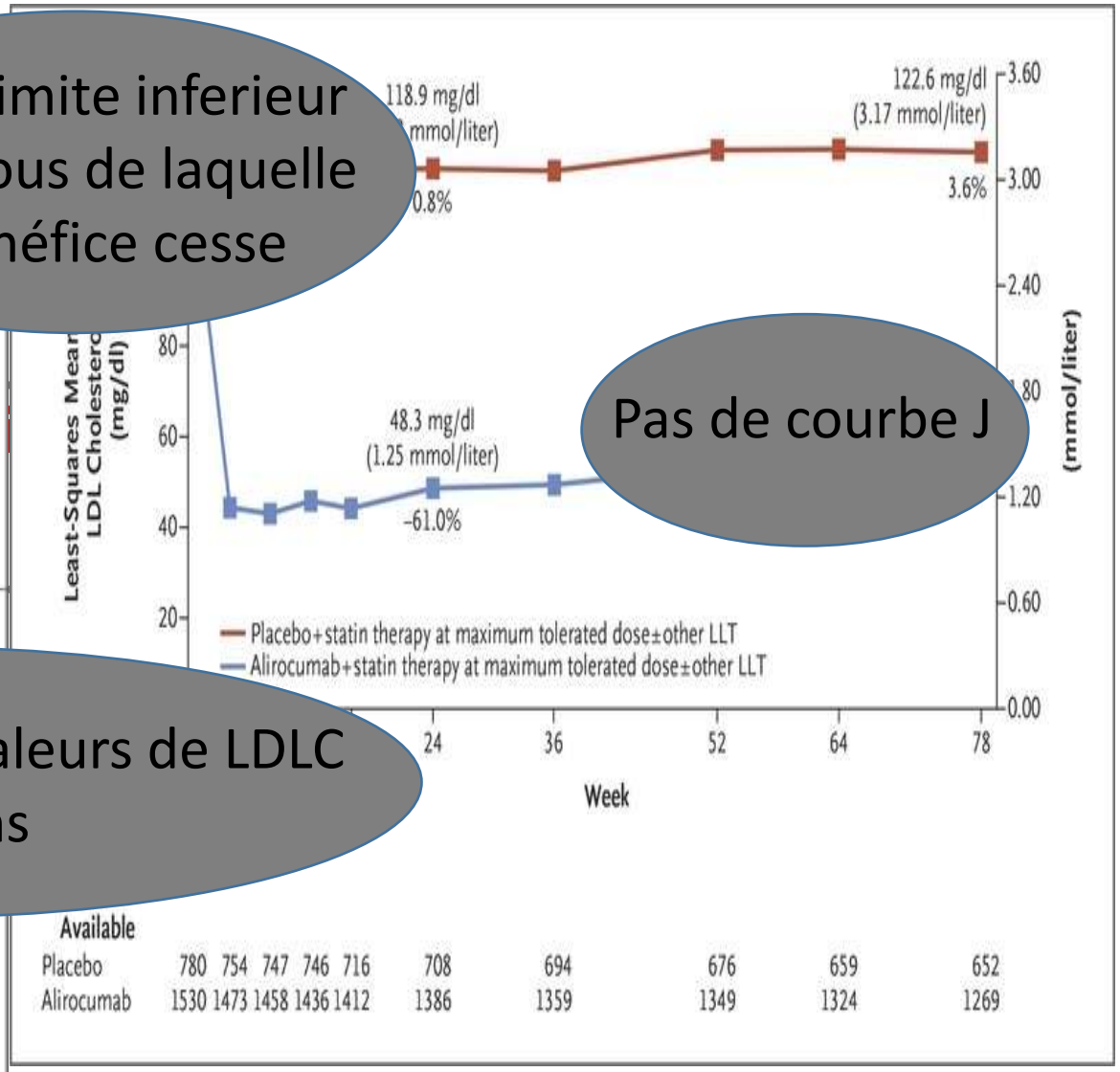
Sécurité des faibles valeurs de LDLC
Recul 3 ans

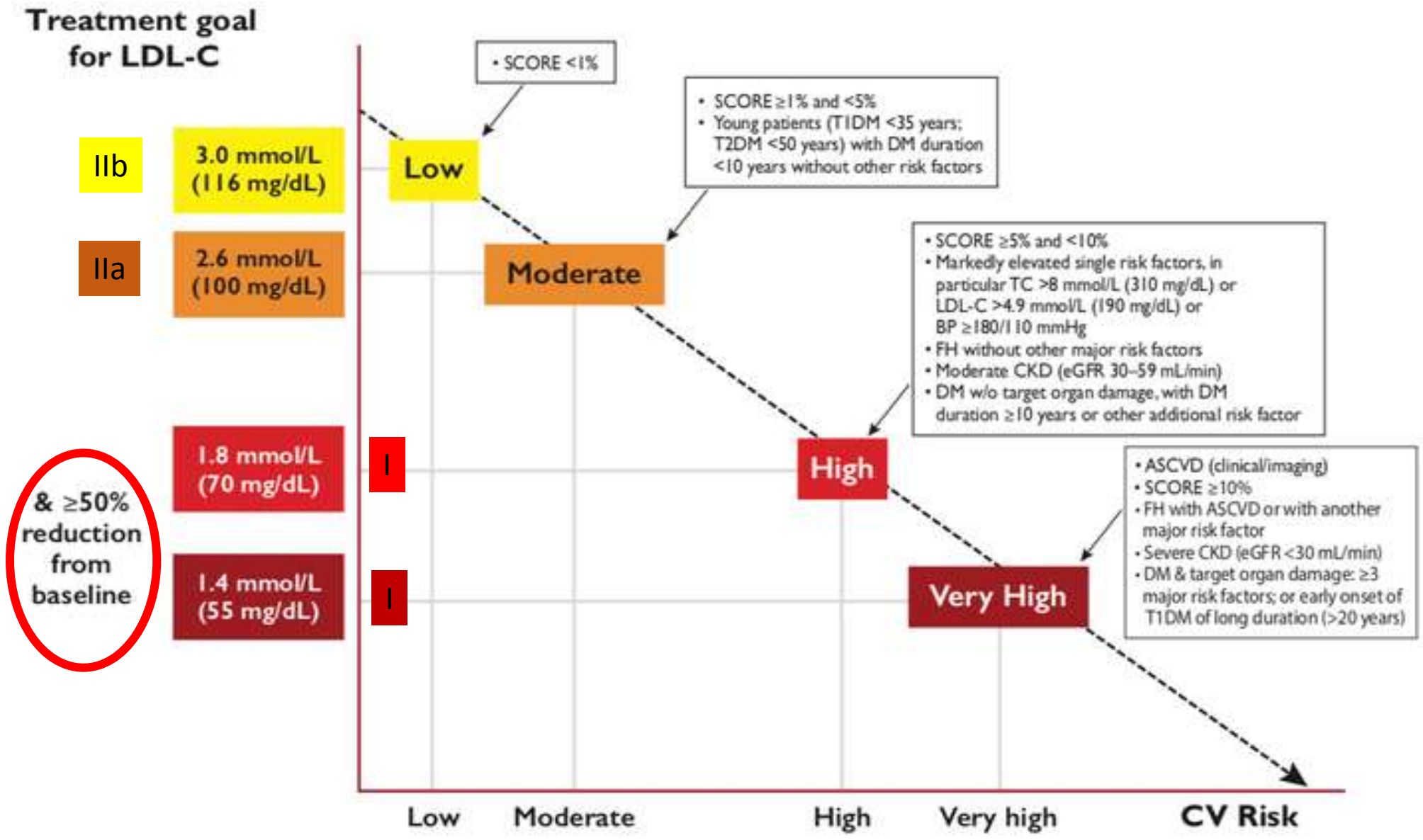
Efficacy and Safety of Alirocumab in Reducing Lipids



Pas de courbe J

for the ODYSSEY LONG TERM Investigators

For the FOURIER Steering Committee and Investigators


Treatment goal for LDL-C
IIb
3.0 mmol/L (116 mg/dL)
IIa
2.6 mmol/L (100 mg/dL)
1.8 mmol/L (70 mg/dL)
I
1.4 mmol/L (55 mg/dL)
I
& ≥50% reduction from baseline
• SCORE <1%
Low
• SCORE ≥1% and <5%
• Young patients (T1DM <35 years; T2DM <50 years) with DM duration <10 years without other risk factors
Moderate
• SCORE ≥5% and <10%
• Markedly elevated single risk factors, in particular TC >8 mmol/L (310 mg/dL) or LDL-C >4.9 mmol/L (190 mg/dL) or BP ≥180/110 mmHg
• FH without other major risk factors
• Moderate CKD (eGFR 30–59 mL/min)
• DM w/o target organ damage, with DM duration ≥10 years or other additional risk factor
High
• ASCVD (clinical/imaging)
• SCORE ≥10%
• FH with ASCVD or with another major risk factor
• Severe CKD (eGFR <30 mL/min)
• DM & target organ damage: ≥3 major risk factors; or early onset of T1DM of long duration (>20 years)
Very High
Low
Moderate
High
Very high
CV Risk

Objectifs thérapeutiques LDLC

Recommendations	Class[a]	Level[b]
In secondary prevention for patients at very-high risk,[c] an LDL-C reduction of ≥50% from baseline[d] and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) are recommended.[33–35,119,120]	I	A
In primary prevention for individuals at very-high risk but without FH,[c] an LDL-C reduction of ≥50% from baseline[d] and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) are recommended.[34–36]	I	C
In primary prevention for individuals with FH at very-high risk, an LDL-C reduction of ≥50% from baseline and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) should be considered.	IIa	C
For patients with ASCVD who experience a second vascular event within 2 years (not necessarily of the same type as the first event) while taking maximally tolerated statin-based therapy, an LDL-C goal of <1.0 mmol/L (<40 mg/dL) may be considered.[119,120]	IIb	B
In patients at high risk,[c] an LDL-C reduction of ≥50% from baseline[d] and an LDL-C goal of <1.8 mmol/L (<70 mg/dL) are recommended.[34,35]	I	A
In individuals at moderate risk,[c] an LDL-C goal of <2.6 mmol/L (<100 mg/dL) should be considered.[34]	IIa	A
In individuals at low risk,[c] an LDL-C goal <3.0 mmol/L (<116 mg/dL) may be considered.[34]	IIb	A

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Prise en charge thérapeutique

Objectifs Secondaires

Objectifs thérapeutiques secondaires : NON HDLC

Profil lipidique disséqué

- Non HDLc : Cholesterol total - HDLC
  - Chylomicrons remnannts
  - VLDL
  - IDL
  - Lpa
  - LDLc

Liporoteines athérogénes contenant l'APOB

- HDLc

Recommendations	Class[a]	Level[b]
TC is to be used for the estimation of total CV risk by means of the SCORE system.	I	C
HDL-C analysis is recommended to further refine risk estimation using the online SCORE system.	I	C
LDL-C analysis is recommended as the primary lipid analysis method for screening, diagnosis, and management.	I	C
TG analysis is recommended as part of the routine lipid analysis process.	I	C
Non-HDL-C evaluation is recommended for risk assessment, particularly in people with high TG levels, DM, obesity, or very low LDL-C levels.	I	C
ApoB analysis is recommended for risk assessment, particularly in people with high TG levels, DM, obesity, metabolic syndrome, or very low LDL-C levels. It can be used as an alternative to LDL-C, if available, as the primary measurement for screening, diagnosis, and management, and may be preferred over non-HDL-C in people with high TG levels, DM, obesity, or very low LDL-C levels.	I	C
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

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Treatment Targets and goals for cardiovascular disease prevention

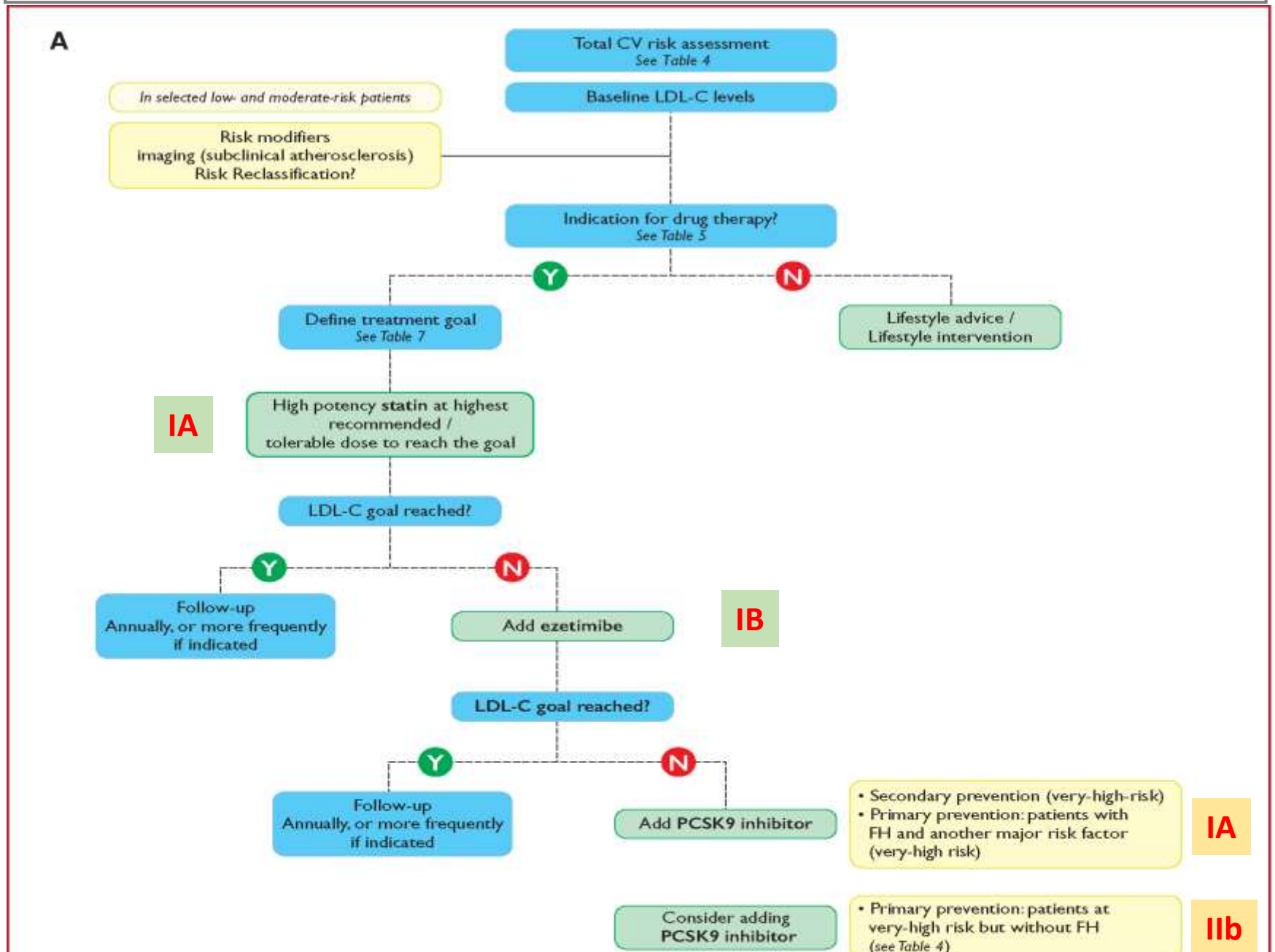
Objectifs secondaires : personnes à très haut risque cardio vasculaire apres atteinte de l objectif LDL

Non-HDL-C	**Non-HDL-C secondary goals < 2.2, 2.6, and 3.4 mmol/L (< 85, 100, and 130 mg/dl) for very high- high, and moderate risk people respectively**
Apo B	Apo B secondary goals are < 65,80, and 100 mg/dl for very high, high and moderate risk people respectively
Triglycerides	No goal but < 1.7 mmol/l (150 mg/dl) indicates lower risk and higher levels indicate a need to look for ather risk factors

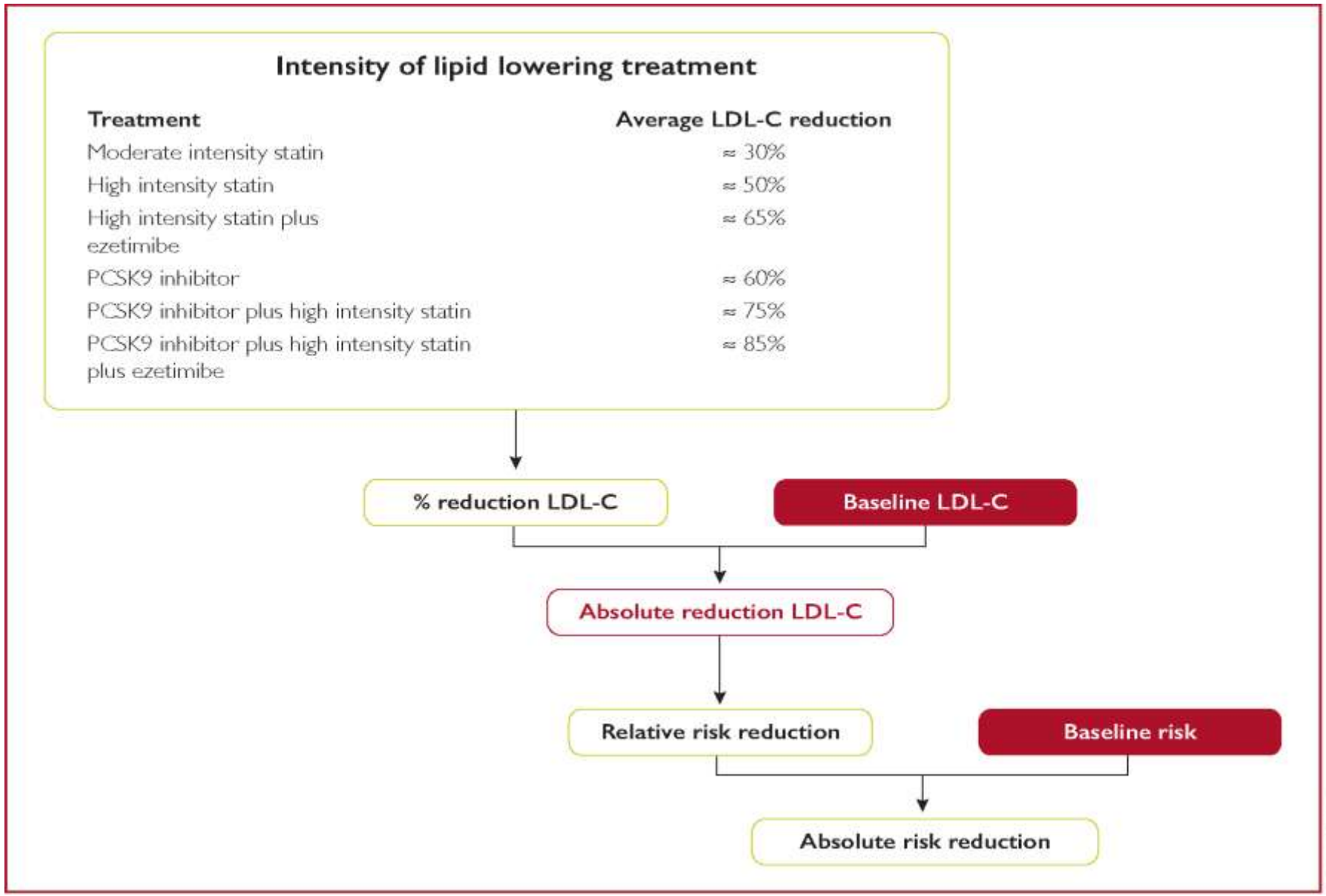
Prise en charge thérapeutique

Stratégie thérapeutique

Treatment algorithm for pharmacological low-density lipoprotein cholesterol lowering.



Expected clinical benefits of low-density lipoprotein cholesterol-lowering therapies. The expected clinical ...



Recommendations for drug treatments of patients with hypertriglyceridemia

Recommendations	Class[a]	Level[b]
Statin treatment is recommended as the first drug of choice to reduce CVD risk in high-risk individuals with hypertriglyceridaemia [TG levels >2.3 mmol/L (>200 mg/dL)].[355]	I	B
In high-risk (or above) patients with TG levels between 1.5–5.6 mmol/L (135–499 mg/dL) despite statin treatment, n-3 PUFAs (icosapent ethyl 2×2 g/day) should be considered in combination with a statin.[194]	IIa	B
In primary prevention patients who are at LDL-C goal with TG levels >2.3 mmol/L (>200 mg/dL), fenofibrate or bezafibrate may be considered in combination with statins.[305–307,356]	IIb	B
In high-risk patients who are at LDL-C goal with TG levels >2.3 mmol/L (>200 mg/dL), fenofibrate or bezafibrate may be considered in combination with statins.[305–307,356]	IIb	C

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Dutch Lipid Clinic Network dignostic criteria for familial hypercholesterolemia

Criteria	Points
1) Family history	
First-degree relative with known premature (men aged <55 years; women <60 years) coronary or vascular disease, or first-degree relative with known LDL-C above the 95th percentile	1
First-degree relative with tendinous xanthomata and/or arcus cornealis, or children aged <18 years with LDL-C above the 95th percentile	2
2) Clinical history	
Patient with premature (men aged <55 years; women <60 years) CAD	2
Patient with premature (men aged <55 years; women <60 years) cerebral or peripheral vascular disease	1
3) Physical examination[a]	
Tendinous xanthomata	6
Arcus cornealis before age 45 years	4

Dutch Lipid Clinic Network dignostic criteria for familial hypercholesterolemia

4) LDL-C levels (without treatment)	
LDL-C ≥8.5 mmol/L (≥325 mg/dL)	8
LDL-C 6.5–8.4 mmol/L (251–325 mg/dL)	5
LDL-C 5.0–6.4 mmol/L (191–250 mg/dL)	3
LDL-C 4.0–4.9 mmol/L (155–190 mg/dL)	1
5) DNA analysis	
Functional mutation in the *LDLR*, *apoB*, or *PCSK9* genes	8

‘definite’ FH diagnosis requires >8 points
A ‘probable’ FH diagnosis requires 6–8 points
A ‘possible’ FH diagnosis requires 3–5 points

Tester les lipides

À quelle fréquence les lipides doivent-ils être testés?

Avant de commencer un traitement hypolipidémiant, au moins deux mesures doivent être effectuées, avec un intervalle de 1 à 12 semaines, à l'exception des conditions dans lesquelles un traitement rapide est suggéré, telles que le SCA et les patients à risque très élevé

À quelle fréquence les lipides d'un patient doivent-ils être testés après le début d'un traitement hypolipidémiant?

Après le début du traitement: 8 (± 4) semaines.
Après ajustement du traitement: 8 (± 4) semaines jusqu'à ce que l'objectif soit atteint.

À quelle fréquence les lipides doivent-ils être testés une fois que le patient a atteint le niveau lipidique cible ou optimal?

Annuellement (à moins qu'il y ait des problèmes d'adhésion ou d'autres raisons spécifiques pour des examens plus fréquents)

Surveillance des enzymes hépatiques et musculaires

À quelle fréquence les enzymes hépatiques (ALT) doivent-elles être systématiquement mesurées chez les patients prenant des médicaments hypolipidémiants?

- Avant traitement
- Une fois, 8 à 12 semaines après le début du traitement médicamenteux ou après l'augmentation de la dose.
- Le contrôle de routine de l'ALAT par la suite n'est pas recommandé pendant le traitement par la statine, sauf en cas de symptômes évocateurs d'une maladie du foie. Pendant le traitement par les fibrates, le contrôle de l'ALT est toujours recommandé

Que faire si les enzymes hépatiques deviennent élevées chez une personne prenant des médicaments hypolipidémiants?

- Si ALT <3 × ULN : Continuer la thérapie. Revérifier les enzymes hépatiques dans 4–6 semaines.
- Si ALT augmente à ≥3 × LSN Arrêtez le traitement hypolipidémiant ou réduisez la dose et revérifiez les enzymes hépatiques dans les 4 à 6 semaines.
  Une réintroduction prudente du traitement peut être envisagée après le retour à la normale des ALAT
- Si ALT reste élevé Cherchez d autres étiologies .

Surveillance des enzymes hépatiques et musculaires

À quelle fréquence faut-il mesurer la CPK chez les patients prenant des médicaments hypolipidémiants?

- *Pré-traitement*

  Avant de commencer le traitement.

  Si la CPK de base est> 4 × LSN, ne commencez pas le traitement médicamenteux; revérifier.

- *Surveillance:*

  La surveillance de routine de la CK n'est pas nécessaire.

  Vérifiez CK si le patient développe une myalgie . Faites preuve de vigilance face à la myopathie et à l'élévation de la CK chez les patients à risque, tels que les patients âgés, ceux qui suivent un traitement interférant concomitant, la prise de multiples médicaments, une maladie hépatique , rénale et chez les athlètes.

Surveillance des enzymes hépatiques et musculaires

Que faire si la CK devient élevée chez une personne prenant des médicaments hypolipidémiants?
Réévaluer l'indication pour le traitement par statine.

- Si ≥4 × ULN:
  - Si CK> 10 × LSN: arrêtez le traitement, vérifiez la fonction rénale et surveillez la CK toutes les 2 semaines.
  - Si CK <10 × LSN: en l'absence de symptômes, poursuivre le traitement hypolipidémiant tout en surveillant la CK entre 2 et 6 semaines.
  - Si CK <10 × LSN: en cas de symptômes, arrêter la statine et surveiller la normalisation de la CK, avant de reprendre le traitement avec une dose de statine plus faible.
  - Envisagez la possibilité d'une élévation transitoire de la CK pour d'autres raisons, telles que l'effort.
  - Evoquer une myopathie si la CK reste élevée.
  - Envisager un traitement d'association ou un médicament alternatif.

- Si <4 × ULN:
  - En l'absence de symptômes musculaires, continuer la statine (le patient doit être averti de signaler les symptômes; vérifier la CK).
  - En cas de symptômes musculaires, surveillez les symptômes et la CK régulièrement.
  - Si les symptômes persistent, arrêtez la statine et réévaluez les symptômes après 6 semaines; réévaluer l'indication de traitement par statines.
  - Envisagez de reprendre le traitement avec la même ou une autre statine.
  - prendre la statine à faible dose, tous les deux jours ou une ou deux fois par semaine, ou un traitement d'association.

Drugs potentially interacting with statins metabolized by cytochrome P450 3A4 leading to increased risk of myopathy and rhabdomyolysis

Anti-infective agents	Calcium antagonists	Other
Itraconazole	Verapamil	Ciclosporin
etoconazole	Diltiazem	Danazol
Posaconazole	Amlodipine	Amiodarone
Erythromycin		Ranolazine
Clarithromycin		Grapefruit juice
Telithromycin		Nefazodone
HIV protease inhibitors		Gemfibrozil

Chez quels patients l'HbA1c ou la glycémie devraient-ils être contrôlés?

- Un contrôle régulier de l'HbA1c ou de la glycémie doit être envisagé chez les patients présentant un risque élevé de développer un diabète et sous traitement à haute dose de statines.
- Les groupes à prendre en compte pour le contrôle du glucose sont les personnes âgées et les patients atteints de syndrome métabolique, d'obésité ou d'autres signes de résistance à l'insuline.

Recommendations for lipid management with moderate – to severe chronic kidney disease

Recommendations	Class[a]	Level[b]
It is recommended that patients with Kidney Disease Outcomes Quality Initiative stage 3–5[c] CKD are considered to be at high or very-high risk of ASCVD.[489–493]	I	A
The use of statins or statin/ezetimibe combination is recommended in patients with non-dialysis-dependent stage 3–5 CKD.[214,222,495,496]	I	A
In patients already on statins, ezetimibe, or a statin/ezetimibe combination at the time of dialysis initiation, continuation of these drugs should be considered, particularly in patients with ASCVD.	IIa	C
In patients with dialysis-dependent CKD who are free of ASCVD, commencement of statin therapy is not recommended.[220,221]	III	A

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Association statines ézétimibe ou anti PCSK9

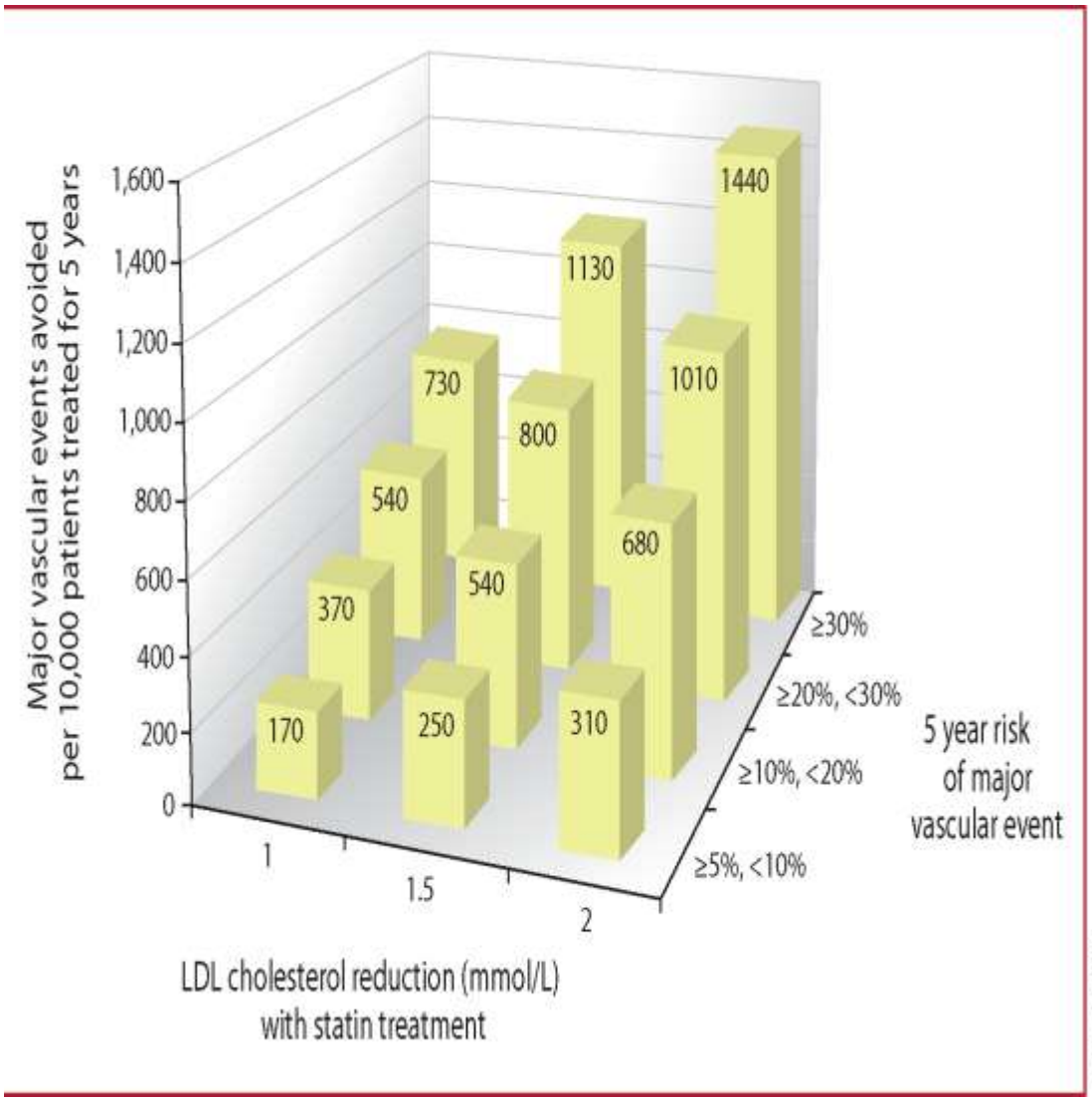
plus le LDL obtenu est bas plus le risque évenement CVX futurs est faible

Pas de limite inferieure pour le LDL ni d effet de courbe J

Sécurité des très faibles valeurs du LDLc ; terme Long ?

Nouveaux objectifs

Nouvelles stratification du risque cardio VX



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Pas de courbe J

Baisse drastique des Objectifs LDLC

Sécurité des faibles valeurs de LDLC
Recul 3 ans

Collins et al . The Lancet 2016 ; 388/10059, 2532-2561