UPDATE CARDIOLOGIA

GIUBIASCO 26.09.2018

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…nell’invito stava scritto…

- …parlare di tematiche recenti (pubblicazioni degli ultimi 3-4 anni) apparse nella propria specialità…

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…nell’invito stava scritto…

- …parlare di tematiche recenti (ultimi 3-4 anni) apparse nella propria specialità…
- …CHE HANNO o AVREBBERO DOVUTO MODIFICARE IL MODO DI AGIRE…

3 Argomenti

- 1. Dislipidemia
- 2. NOAC
- 3. Insufficienza cardiaca

3 Argomenti

- 1. Dislipidemia
  - Inibitori PCSK 9 -> se e quando

3 Argomenti

- 1. Dislipidemia
  - Inibitori PCSK 9 -> se e quando

Repatha (evolocumab) injection 140 mg/mL

Praluent (alirocumab) Injection 75mg/mL 150mg/mL

- 2. NOAC
  - → quale e quanto

Xarelto® rivaroxaban

Eliquis® apixaban

Pradaxa® dabigatran etexilate

Lixiana® edoxaban

3 Argomenti

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Lixiana® edoxaban

- 3. Insufficienza cardiaca
  - → Sacubitril/Valsartan: quando e perché

Entresto™ (sacubitril/valsartan) table

24/26mg · 49/51mg · 97/103mg

3. Argomenti

- 1. Dislipidemia
  - Inibitori PCSK 9 -> se e quando
- 2. NOAC
  - → quale e quanto
- 3 Insufficienza cardiaca
  - Valsartan/Sacubitril → come e a chi

Table 4 Risk categories

Very high-risk	Subjects with any of the following: • Documented cardiovascular disease (CVD), clinical or unequivocal on imaging. Documented CVD includes previous myocardial infarction (MI), acute coronary syndrome (ACS), coronary revascularisation (percutaneous coronary intervention (PCI), coronary artery bypass graft surgery (CABG)) and other arterial revascularization procedures, stroke and transient ischaemic attack (TIA), and peripheral arterial disease (PAD). Unequivocally documented CVD on imaging is what has been shown to be strongly predisposed to clinical events, such as significant plaque on coronary angiography or carotid ultrasound. • DM with target organ damage such as proteinuria or with a major risk factor such as smoking, hypertension or dyslipidaemia. • Severe CKD (GFR <30 mL/min/1.73 m^2). • A calculated SCORE ≥10% for 10-year risk of fatal CVD.
High-risk	Subjects with: • Markedly elevated single risk factors, in particular cholesterol >8 mmol/L (>310 mg/dL) (e.g. in familial hypercholesterolaemia) or BP ≥180/110 mmHg. • Most other people with DM (some young people with type 1 diabetes may be at low or moderate risk). • Moderate CKD (GFR 30–59 mL/min/1.73 m^2). • A calculated SCORE ≥5% and <10% for 10-year risk of fatal CVD.
Moderate-risk	SCORE is ≥1% and <5% for 10-year risk of fatal CVD.
Low-risk	SCORE <1% for 10-year risk of fatal CVD.

ACS = acute coronary syndrome; AMI = acute myocardial infarction; BP = blood

Arteriosclerosi documentata , significativa e/o già manifestatasi clinicamente

Diabete mellito con danno d'organo

GFR <30 ml/min/1.73 m2

Score > 10%

Singoli FRCV molto elevati

Diabete mellito

GFR tra 30 e 59 ,l/min/1.73 m2

SCORE tra 5 e 10 %

Dislipidemia: target terapeutici

Table 11 Recommendations for treatment goals for low-density lipoprotein-cholesterol

Recommendations	Class [a]	Level [b]	Ref [c]
In patients at VERY HIGH CV risk[d], an LDL-C goal of <1.8 mmol/L (70 mg/dL) or a reduction of at least 50% if the baseline LDL-C[e] is between 1.8 and 3.5 mmol/L (70 and 135 mg/dL) is recommended.	I	B	61, 62, 65, 68, 69, 128
In patients at HIGH CV risk[d], an LDL-C goal of <2.6 mmol/L (100 mg/dL), or a reduction of at least 50% if the baseline LDL-C[e] is between 2.6 and 5.2 mmol/L (100 and 200 mg/dL) is recommended.	I	B	65, 129
In subjects at LOW or MODERATE risk[d] an LDL-C goal of <3.0 mmol/L (<115 mg/dL) should be considered.	IIa	C	-

CV = cardiovascular; LDL-C = low-density lipoprotein-cholesterol.

Numeri da memorizzare

- **1.8**
  - **50%**
- **2.6**
- **3**

Linee guida: dove stanno gli iPCSK9

Table 16 Recommendations for the pharmacological treatment of hypercholesterolaemia

Recommendations	Class [a]	Level [b]	Ref [c]
Prescribe statin up to the highest recommended dose or highest tolerable dose to reach the goal.	I	A	62, 64, 68
In the case of statin intolerance, ezetimibe or bile acid sequestrants, or these combined, should be considered.	IIa	C	239, 256, 257
If the goal is not reached, statin combination with a cholesterol absorption inhibitor should be considered.	IIa	B	63
If the goal is not reached, statin combination with a bile acid sequestrant may be considered.	IIb	C	
In patients at very high-risk, with persistent high LDL-C despite treatment with maximal tolerated statin dose, in combination with ezetimibe or in patients with statin intolerance, a PCSK9 inhibitor may be considered.	IIb	C	115, 116

Linee guida: dove stanno gli iPCSK9 (nella sindrome coronarica acuta)

Recommendations	Class [a]	Level [b]	Ref [c]
It is recommended to initiate or continue high dose statins early after admission in all ACS patients without contra-indication or history of intolerance, regardless of initial LDL-C values.	I	A	64, 358–360
If the LDL-C target is not reached with the highest tolerable statin dose, ezetimibe should be considered in combination with statins in post-ACS patients.	IIa	B	63
If the LDL-C target is not reached with the highest tolerable statin dose and/or ezetimibe, PCSK9 inhibitors may be considered on top of lipid-lowering therapy; or alone or in combination with ezetimibe in statin intolerant patients or in whom a statin is contra-indicated.	IIb	C	115, 116
Lipids should be re-evaluated 4–6 weeks after ACS to determine whether target levels of LDL-C <1.8 mmol/L (<70 mg/dL) or a reduction of at least 50% if the baseline is between 1.8 and 3.5 mmol/L (70 and 135 mg/dL) have been reached and whether there are any safety issues. The therapy dose should then be adapted accordingly.	IIa	C	
Routine short pretreatment or loading (on the background of chronic therapy) with high-dose statins before PCI should be considered in elective PCI or in NSTE-ACS.	IIa	A	363–365

Linee guida ESC 2016

3 Argomenti

- 1. Dislipidemia
  - Inibitori PCSK 9 -> se e quando

Repatha (evolocumab) injection 140 mg/mL

Praluent (alirocumab) Injection 75mg/mL 150mg/mL

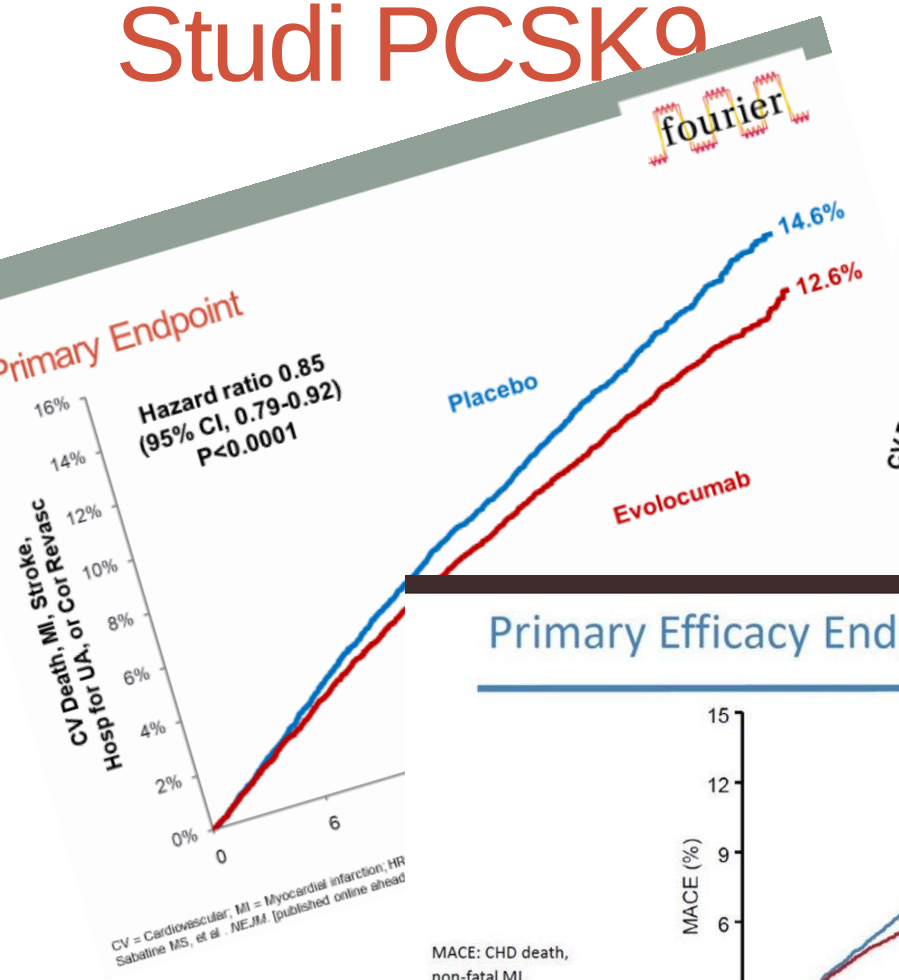
Fourier

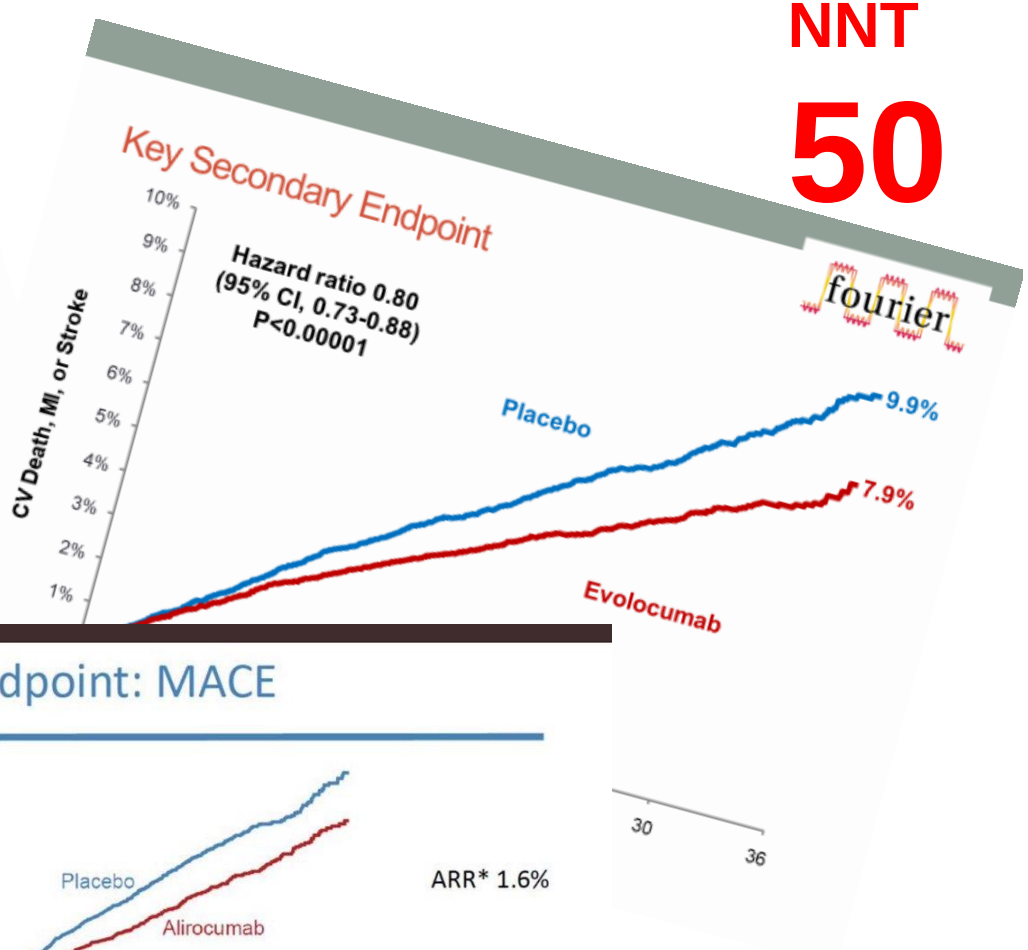
Odissey

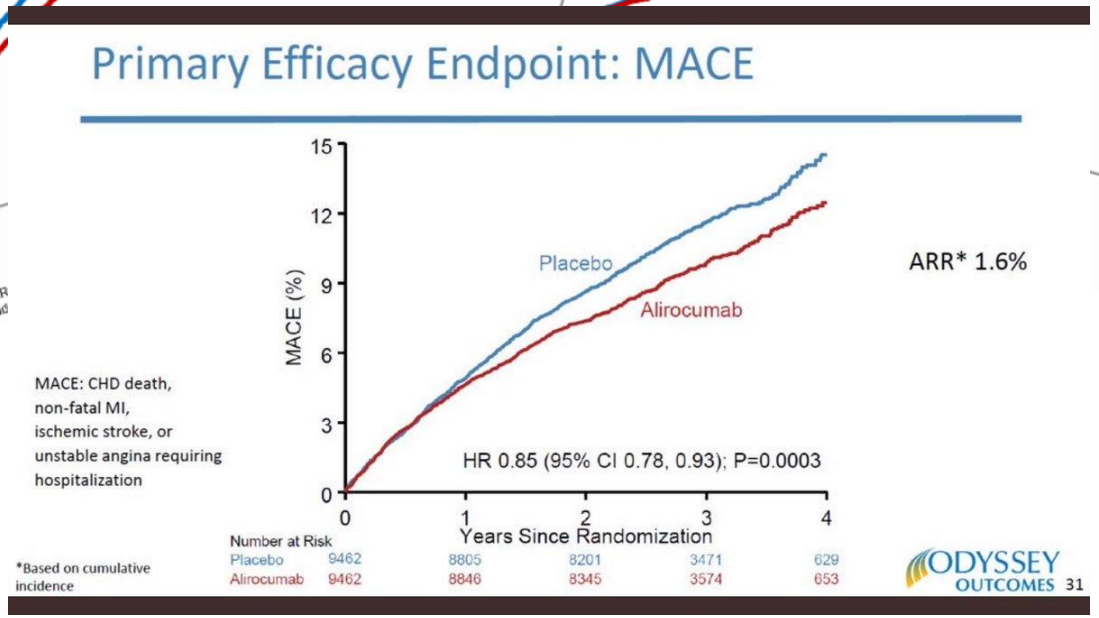
Studi PCSK9

NNT

50







62

* Alirocumab ist ein vollständig humaner monoklonaler Antikörper (Isotyp IgG1), der an Proproteinkonvertase Subtilisin Kexin Typ 9 (PCSK9) bindet. Alirocumab wird mittels rekombinanter DNA-Technologie aus einer Suspensionskultur von Ovarialzellen des chinesischen Hamsters gewonnen.

Galenische Form und Wirkstoffmenge pro Einheit

Praluent 75 mg, Injektionslösung in einer Fertigspritze: Jede 1-ml-Fertigspritze zur einmaligen Anwendung enthält 75 mg Alirocumab zur subkutanen Verabreichung.

Praluent 150 mg, Injektionslösung in einer Fertigspritze: Jede 1-ml-Fertigspritze zur einmaligen Anwendung enthält 150 mg Alirocumab zur subkutanen Verabreichung.

Praluent 75 mg, Injektionslösung in einem Fertigpen: Jeder 1-ml-Fertigpen zur einmaligen Anwendung enthält 75 mg Alirocumab zur subkutanen Verabreichung.

Praluent 150 mg, Injektionslösung in einem Fertigpen: Jeder 1-ml-Fertigpen zur einmaligen Anwendung enthält 150 mg Alirocumab zur subkutanen Verabreichung.

Indikationen/Anwendungsmöglichkeiten

Praluent ist indiziert begleitend zu einer Diät und zusätzlich zu einer maximal tolerierten Statin-Dosis, mit oder ohne weitere lipidmodifizierende Therapien zur Behandlung von Erwachsenen mit schwerer heterozygoter familiärer Hypercholesterinämie, oder mit klinisch manifester atherosklerotischer kardiovaskulärer Erkrankung, welche eine zusätzliche Low-Density-Lipoprotein-Cholesterin (LDL-C) Senkung benötigen.

Die Wirkung von Praluent auf die kardiovaskuläre Morbidität und Mortalität wurde bislang noch nicht nachgewiesen.

Con o senza antiipolimidizzante suppelementare

Nessuna indicazione sul target...

Dosierung/Anwendung

Um die Rückverfolgbarkeit von biotechnologisch hergestellten Arzneimitteln sicherzustellen, wird empfohlen, Handelsname und Chargennummer bei jeder Behandlung zu dokumentieren.

Dosierung

Die empfohlene Anfangsdosis für Praluent beträgt 75 mg. Diese Dosis kann bis auf die Maximaldosis von 150 mg erhöht werden, wenn die LDL-C-Senkung nicht ausreichend ist. Der LDL-C-Spiegel kann 4 bis 8 Wochen nach Beginn der Behandlung untersucht und die Dosis von Praluent entsprechend angepasst werden. Praluent wird einmal alle zwei Wochen subkutan injiziert.

Wenn eine Dosis vergessen wurde, sollte die vergessene Injektion so bald wie möglich verabreicht werden und danach die Behandlung zwei Wochen nach dem Tag, an dem die Dosis vergessen wurde, fortsetzt werden.

Besondere Patientengruppen

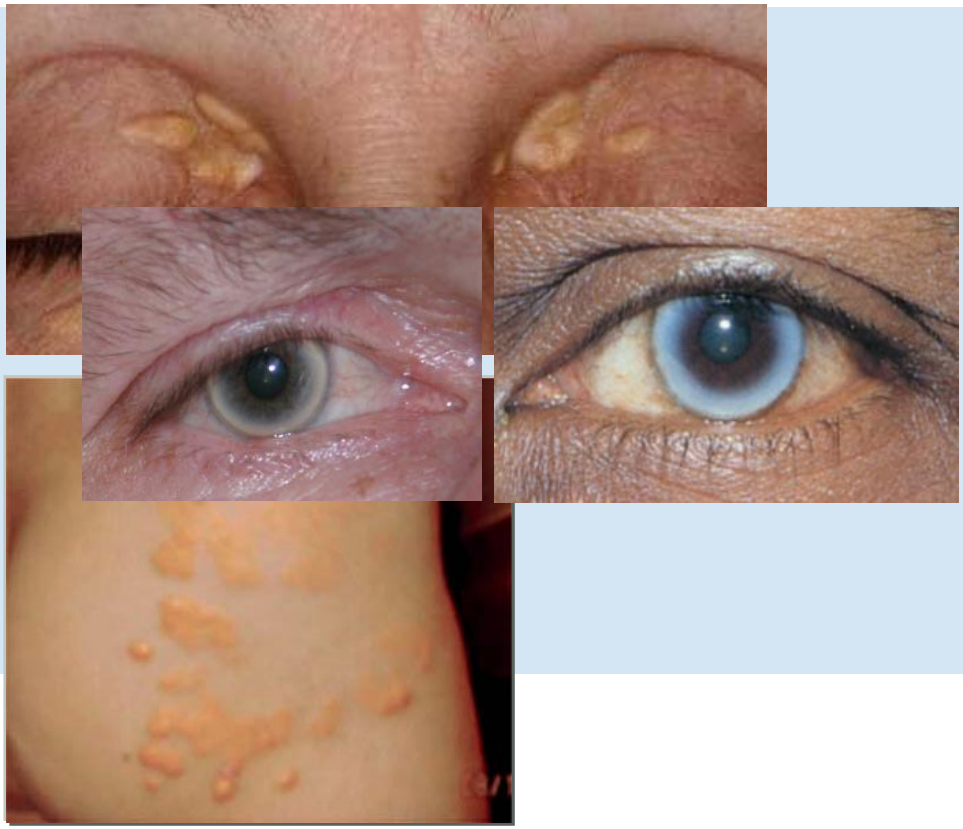
Kinder und Jugendliche

Die Sicherheit und Wirksamkeit von Praluent bei Kindern und Jugendlichen unter 18 Jahren wurde bisher noch nicht erwiesen. Es liegen keine Daten vor.

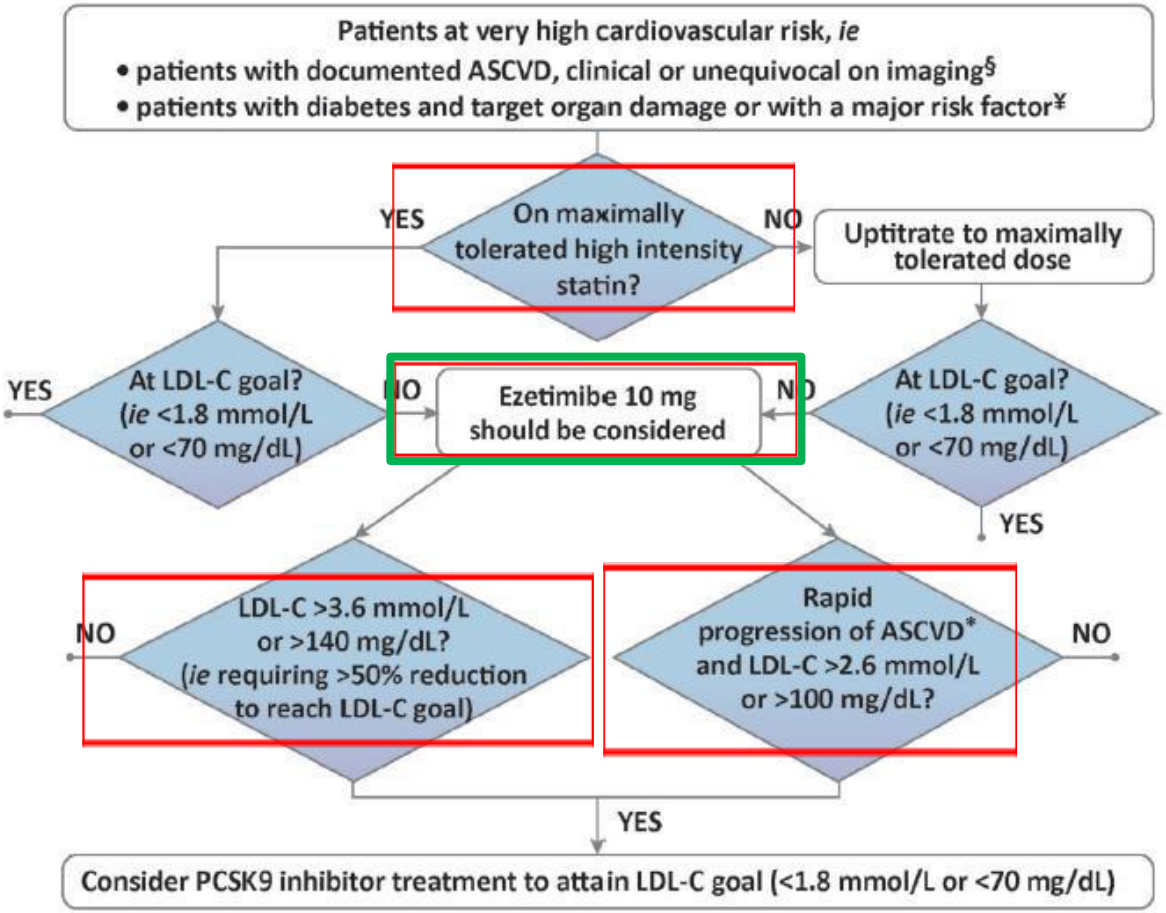
Ältere Patienten

Criteri diagnostici della ipercolesterolemia famigliare

Criteria	Points
1) Family history	
First-degree relative with known premature (men: <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 <18 years of age with LDL-C above the 95th percentile (see 9.1.2.3)	2
2) Clinical history	
Patient with premature (men: <55 years; women: <60 years) coronary artery disease	2
Patient with premature (men: <55 years; women: <60 years) cerebral or peripheral vascular disease	1
3) Physical examination	
Tendinous xanthomata	6
Arcus cornealis before age 45 years	4
4) LDL-C levels	
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 gene	8
Choose only one score per group, the highest applicable Diagnosis (diagnosis is based on the total number of points obtained)	
A 'definite' FH diagnosis requires >8 points	
A 'probable' FH diagnosis requires 6–8 points	
A 'possible' FH diagnosis requires 3–5 points	



PCSK9 Indicazioni e limiti

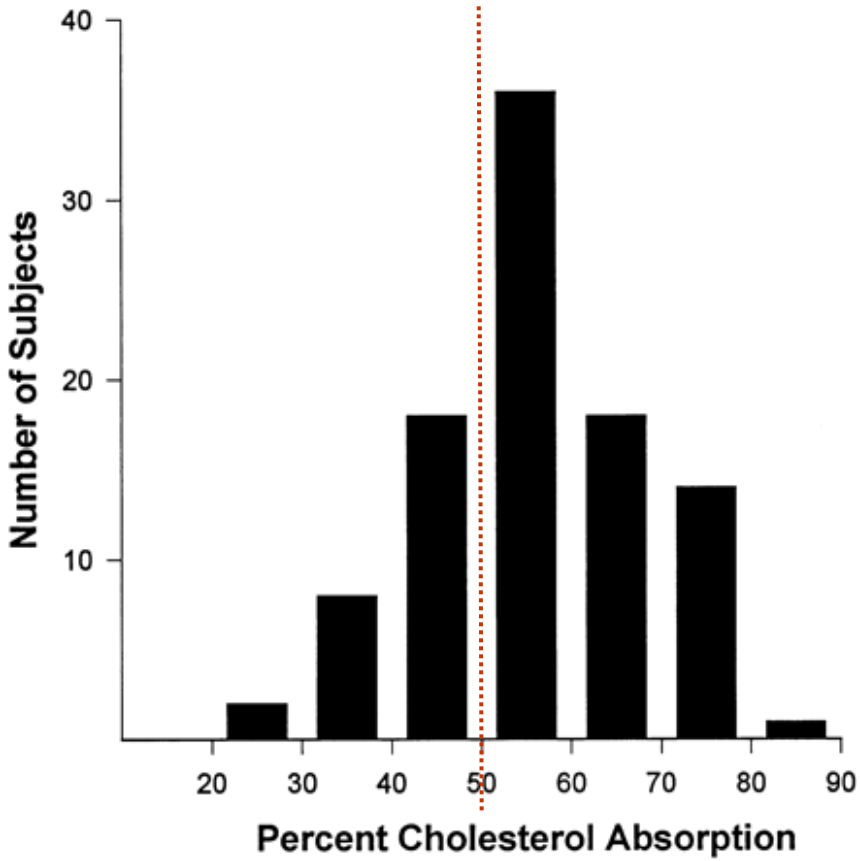


3.6 **2.6**

	Con ASCVD* a progressione rapida	Intolleranza alle statine e ASCVD*	Evento CV < 1 anno fa
	Primo (64 anni) • Stile di vita sano • Sposato • Padre di due adolescenti • Capo del dipartimento di un assicuratore	**Priscilla** (58 anni) • Organizzatrice di eventi • Attiva nella comunità locale • Tre figli adulti	**Prosper** (63 anni) • Direttore finanziario in una PMI • Celibe • Quattro figliocci
I	Diagnostica d'AOP a 60 anni, infarto miocardico 1.5 anni fa	Infarto miocardico 14 mesi fa	Infarto del miocardio 6 mesi fa
NTE	Effetti collaterali con simvastatina 40 mg, attualmente rosuvastatina 20 mg	Mialgia con simvastatina 40 mg e atorvastatina 10 mg, attualmente solo ezetimibe 10 mg	Effetti collaterali con simvastatina 40 mg, attualmente atorvastatina 40 mg
	2.8 mmol/L	**3.9 mmol/L**	**3.6 mmol/L**

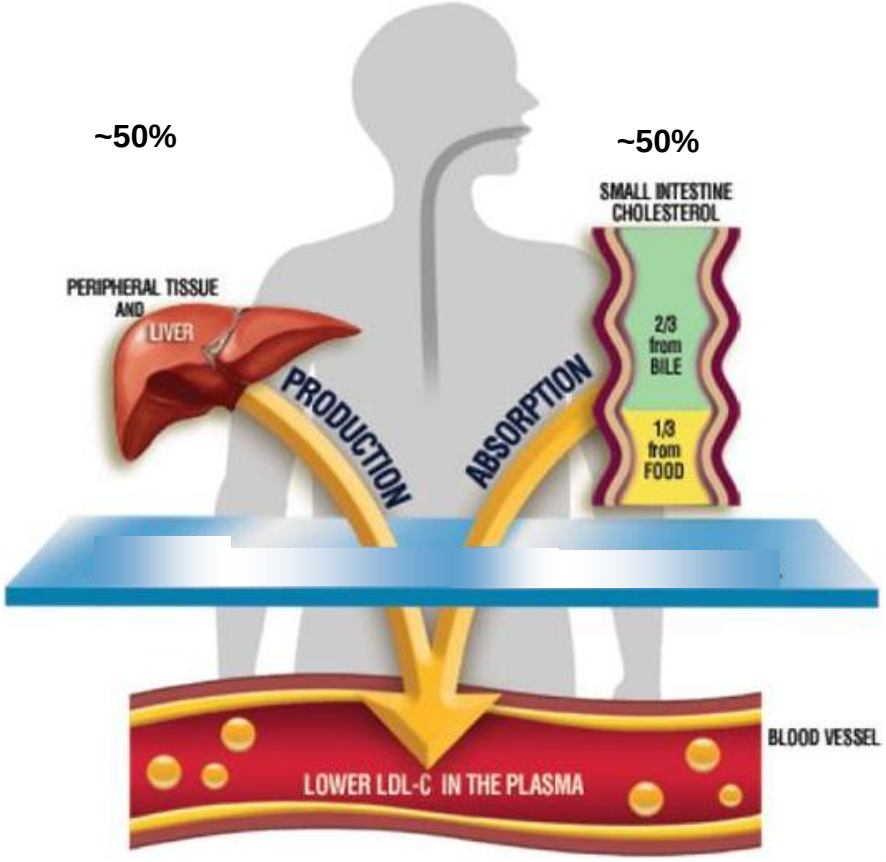
Variabilità genetica fra assorbimento e sintesi colesterolo

Persone con50% Sintesi e 50% Riassorbimento



n = 94
Range: 29-80%
Valore mediot: 56.2±12.1%

Regolazione inversa fra assorbimento e sintesi del colesterolo



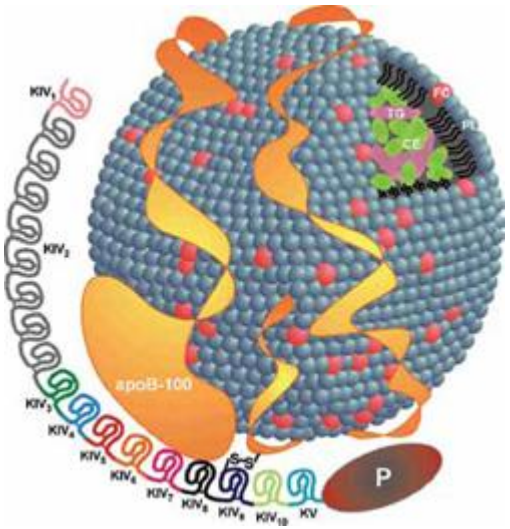
Nach Sheperd J et al.

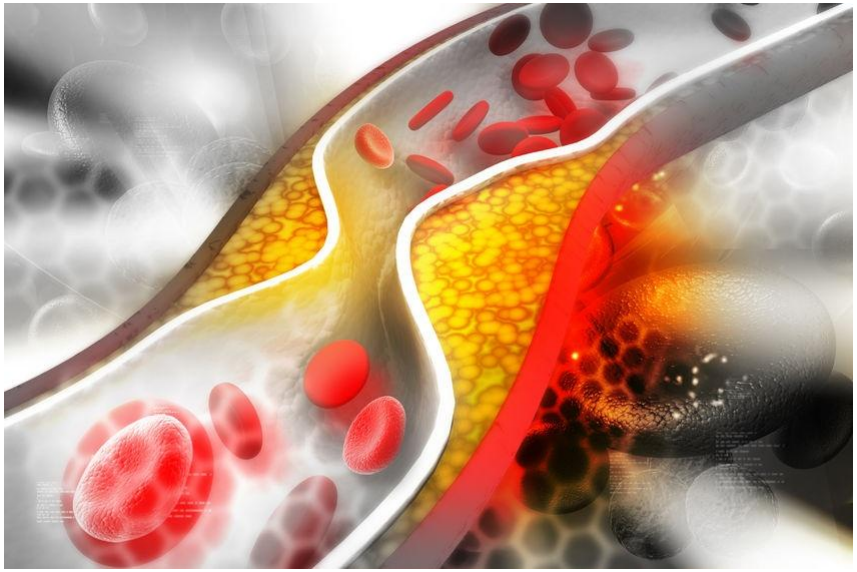
	Statin	Ezetimibe	Statin + Ezetimibe
Cholesterol synthesis in liver	↓	↑	↓
Cholesterol absorption in intestine	↑	↓	↓

SheperdJ. *EurHeart J* 2001; 3(suppl E):E2-E5 Assmann G, et al. Curr Med Res Opin. 2008;24(1):249–259.
Bays H et al. *ClinTher*2004; 26(11):1758-1773

SantosaS et al. *Life Sci*2007; 80:505-51414
Bays H. *Expert Opin Investig Drugs* 2002; 11:1587-1604

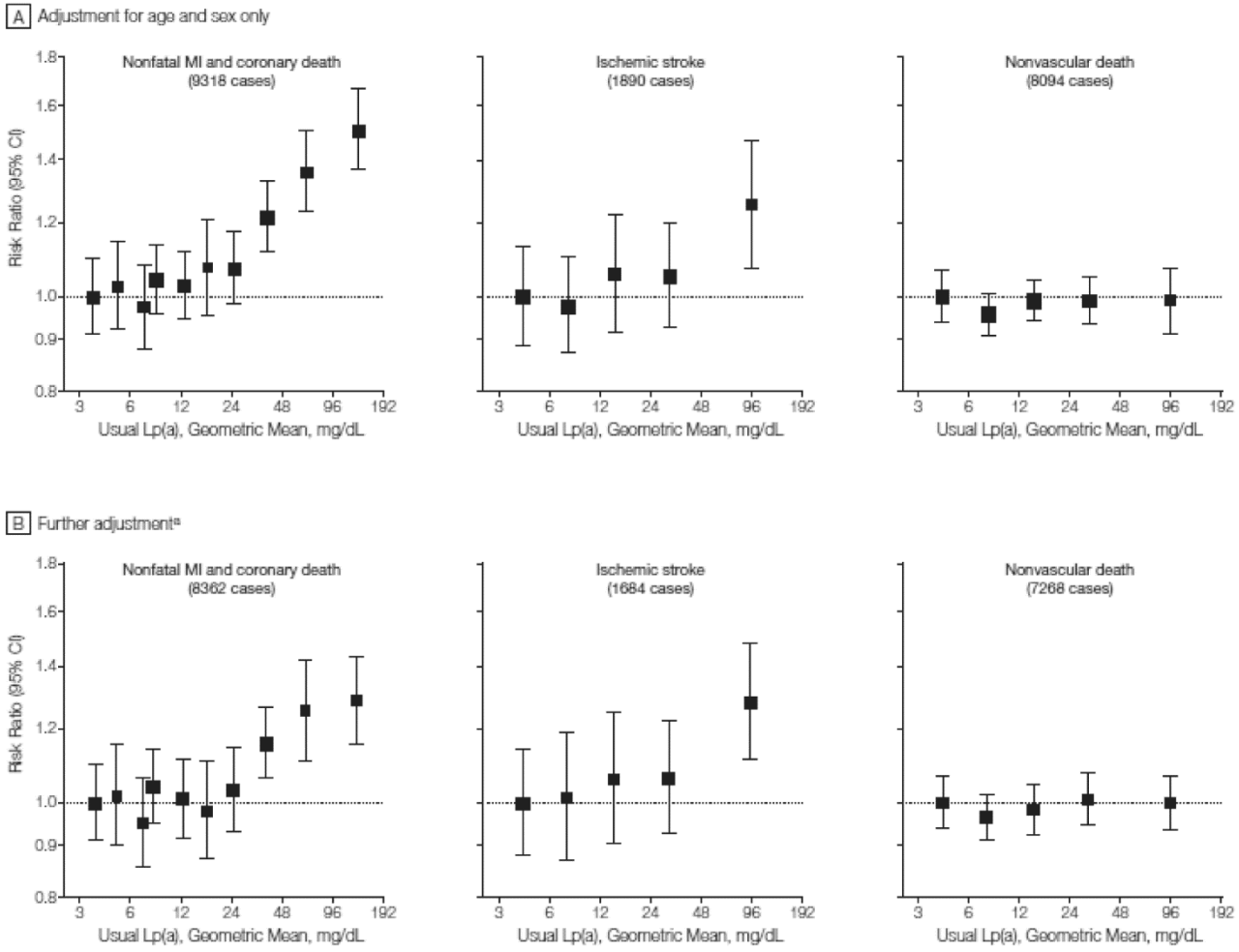
Ruolo Lp(a)





- PCSK9 i →Riduzione 25-30 %

Rischio di malattia coronarica e Lp(a)



- The Emerging Risk Factors Collaboration: Lipoprotein(a) concentration and the risk of coronary heart disease, stroke, and nonvascular mortality. JAMA 2009; 302:412-23

Dislipidemia: statement importante

Table 3 Suggestions for implementing healthy lifestyles

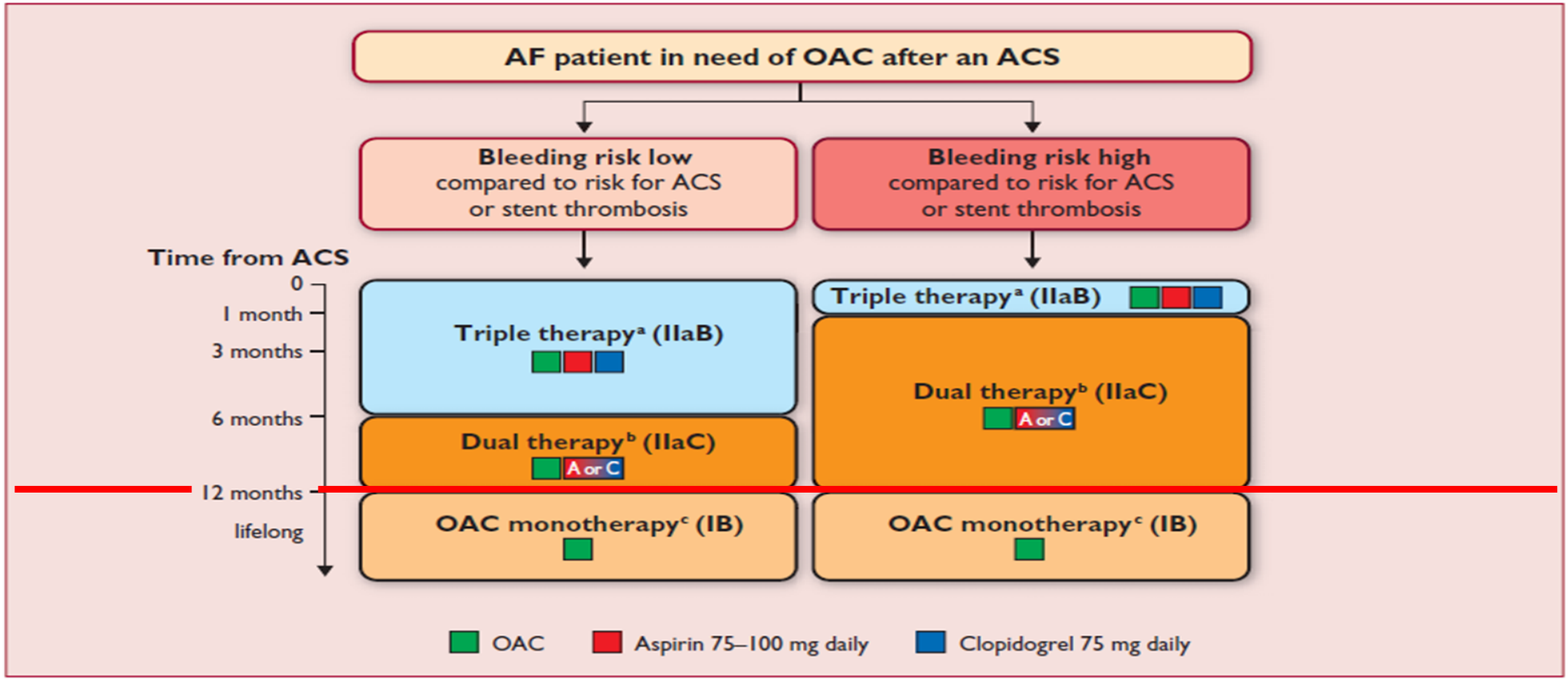
Recommendation	Class [a]	Level [b]	Ref [c]
Measures aimed at implementing healthy lifestyles are more cost-effective than drug interventions at the population level.	IIa	B	7

[a]Class of recommendation.
[b]Level of evidence.
[c]Reference(s) supporting recommendations.

3. Argomenti

- NOAC
  → quale e quanto

Durata dell'anticoagulazione



ACS = acute coronary syndrome; AF = atrial fibrillation; OAC = oral anticoagulation (using vitamin K antagonists or non-vitamin K antagonist oral anticoagulants); PCI = percutaneous coronary intervention.

[a]Dual therapy with OAC and aspirin or clopidogrel may be considered in selected patients, especially those not receiving a stent or patients at a longer time from the index event.

[b]OAC plus single antiplatelet.

[c]Dual therapy with OAC and an antiplatelet agent (aspirin or clopidogrel) may be considered in patients at high risk of coronary events.

Studio Compass

- NOAC basso dosato (2.5 mg 2 x di) + Aspirina sul lungo termine in pazienti con ateromatosi coronarica o periferica cronica

Outcome	Rivaroxaban 2.5 mg bid + aspirin 100 mg N=9152	Aspirin 100 mg N=9126	Rivaroxaban 2.5 mg bid + aspirin 100 mg vs aspirin 100 mg	
			HR (95% CI)	*p*-value*
CHD death, ischaemic stroke, MI, ALI	329 (3.6%)	450 (4.9%)	0.72 (0.63–0.83)	<0.001
CV death, ischaemic stroke, MI, ALI	389 (4.3%)	516 (5.7%)	0.74 (0.65–0.85)	<0.001
Mortality (all-cause)	313 (3.4%)	378 (4.1%)	0.82 (0.71–0.96)	0.01

Studio Compass

- NOAC basso dosato (2.5 mg 2 x di) + Aspirina sul lungo termine in pazienti con ateromatosi coronarica o periferica cronica

Outcome	Rivaroxaban 2.5 mg bid + aspirin 100 mg N=9152	Aspirin 100 mg N=9126	Rivaroxaban 2.5 mg bid + aspirin 100 mg vs aspirin 100 mg		NNT
			HR (95% CI)	*p*-value*	
CHD death, ischaemic stroke, MI, ALI	329 (3.6%)	450 (4.9%)	0.72 (0.63–0.83)	<0.001	76
CV death, ischaemic stroke, MI, ALI	389 (4.3%)	516 (5.7%)	0.74 (0.65–0.85)	<0.001	71
Mortality (all-cause)	313 (3.4%)	378 (4.1%)	0.82 (0.71–0.96)	0.01	142

Brilique o Xarelto sul lungo termine ?

NNT

84

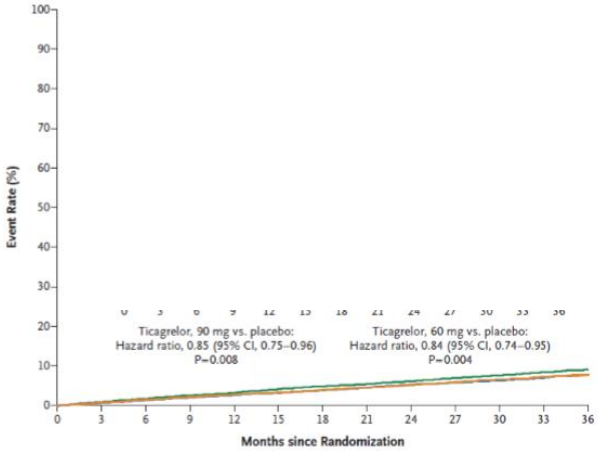
Rivaroxaban with or without Aspirin in Stable Cardiovascular Disease

www.phri.ca

Population Health Research Institute
HEALTH THROUGH KNOWLEDGE

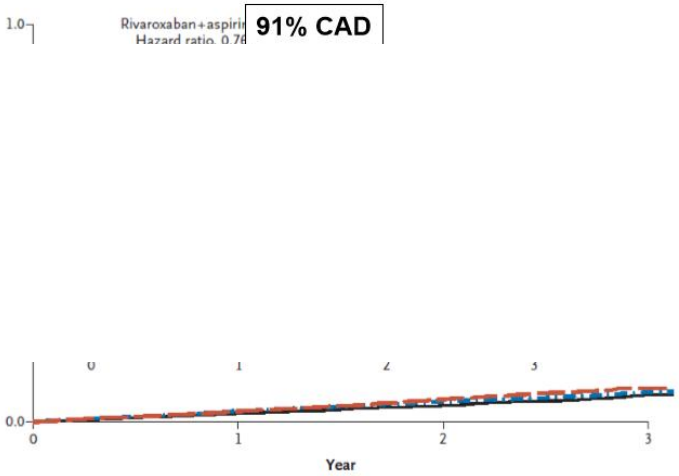
PEGASUS TIMI 54

100% CAD



COMPASS

91% CAD



Bonaca M, et al. N Engl J Med 2015; 372: 1791-800. Eikelboom JW, et al. N Engl J Med 2017; 377: 1319-30.

www.phri.ca

Nuovi Anticoagulanti Orali
Adattamento della dose

Nuovi Anticoagulanti Orali
Adattamento della dose

- **Apixaban**
  - Se 2 criteri su 3
    - Peso < 60 Kg
    - CreaCl 133 mcmol/L
    - Età > 80 anni

- **Dabigatran**
  - Età > 80 anni
  - CreaCl 30-50 ml/min

Nuovi Anticoagulanti Orali
Adattamento della dose

- **Rivaroxaban**
  - CrCl < 50 ml/min

- **Edoxaban**
  - Peso < 60 kg
  - CrCl < 50 ml/min
  - Terapia con forti P-Gp-Inibitori

CAVE Adattamento vs. Riduzione della dose

- Ridurre solo in caso di chiara indicazione
- Negli anziani NNT minore che nei giovani
- Almeno 300 cadute necessarie per un ematoma subdurale che annulli il rischio di un Ictus
- Considerare le interazioni !

Nuovi Anticoagulanti Orali: Interazioni

Komedikation	Dabigatran	Apixaban	Rivaroxaban	Edoxaban
Amiodaron	mit Vorsicht[bj,bk]	keine Daten	keine Anpassung[bl]	keine Anpassung
Chinidin	kontraindiziert	keine Daten	keine Daten	1 x 30 mg
Ciclosporin	kontraindiziert	keine Daten	keine Daten	1 × 30 mg
Diltiazem	keine Daten	keine Anpassung	keine Anpassung[bl]	keine Daten
Dronedaron	kontraindiziert	keine Daten	keine Daten	1 × 30 mg
Erythromycin	keine Daten	keine Daten	keine Anpassung[bl]	1 × 30 mg
Fluconazol	keine Daten	keine Daten	keine Anpassung	keine Daten
HIV-Protease Inhibitoren (z.B. Ritonavir)	kontraindiziert	nicht empfohlen	nicht empfohlen	keine Daten
Itraconazol	kontraindiziert	nicht empfohlen	nicht empfohlen	keine Daten
Ketoconazol (systemisch)	kontraindiziert	nicht empfohlen	nicht empfohlen	1 × 30 mg
Naproxen	keine Daten	keine Anpassung	mit Vorsicht	nicht längerfristig kombinieren
Posaconazol	mit Vorsicht	nicht empfohlen	nicht empfohlen	keine Daten
Ticagrelor	mit Vorsicht	keine Daten	keine Daten	keine Daten
Verapamil	mit Vorsicht[bj, bk]	keine Daten	keine Anpassung[bl]	1 x 30 mg
Voriconazol	keine Daten	nicht empfohlen	nicht empfohlen	keine Daten
Induktoren (Rifampicin, Carbamazepin, Johanniskraut, Phenobarbital, Phenytoin)	mit Vorsicht	nvVHF, Sekundärprophylaxe TVT / LE: mit Vorsicht Behandlung TVT / LE: nicht empfohlen	mit Vorsicht	mit Vorsicht

3 Argomenti

- 1. Dislipidemia
  - Inibitori PCSK 9 -> se e quando
- 2. NOAC
  - → quale e quanto
- 3. Insufficienza cardiaca
  - → Sacubitril/Valsartan: quando e perché?

Insufficienza cardiaca

Table 3.1 Definition of heart failure with preserved (HFpEF), mid-range (HFmrEF) and reduced ejection fraction (HFrEF)

Type of HF		HFrEF	HFmrEF	HFpEF
CRITERIA	1	Symptoms ± Signs[a]	Symptoms ± Signs[a]	Symptoms ± Signs[a]
	2	LVEF <40%	LVEF 40–49%	LVEF ≥50%
	3	–	1. Elevated levels of natriuretic peptides[b]; 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2).	1. Elevated levels of natriuretic peptides[b]; 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2).

BNP = B-type natriuretic peptide; HF = heart failure; HFmrEF = heart failure with mid-range ejection fraction; HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction; LAE = left atrial enlargement; LVEF = left ventricular ejection fraction; LVH = left ventricular hypertrophy; NT-proBNP = N-terminal pro-B type natriuretic peptide.

[a]Signs may not be present in the early stages of HF (especially in HFpEF) and in patients treated with diuretics.

[b]BNP>35 pg/ml and/or NT-proBNP>125 pg/mL.

Insufficienza cardiaca con normale FE

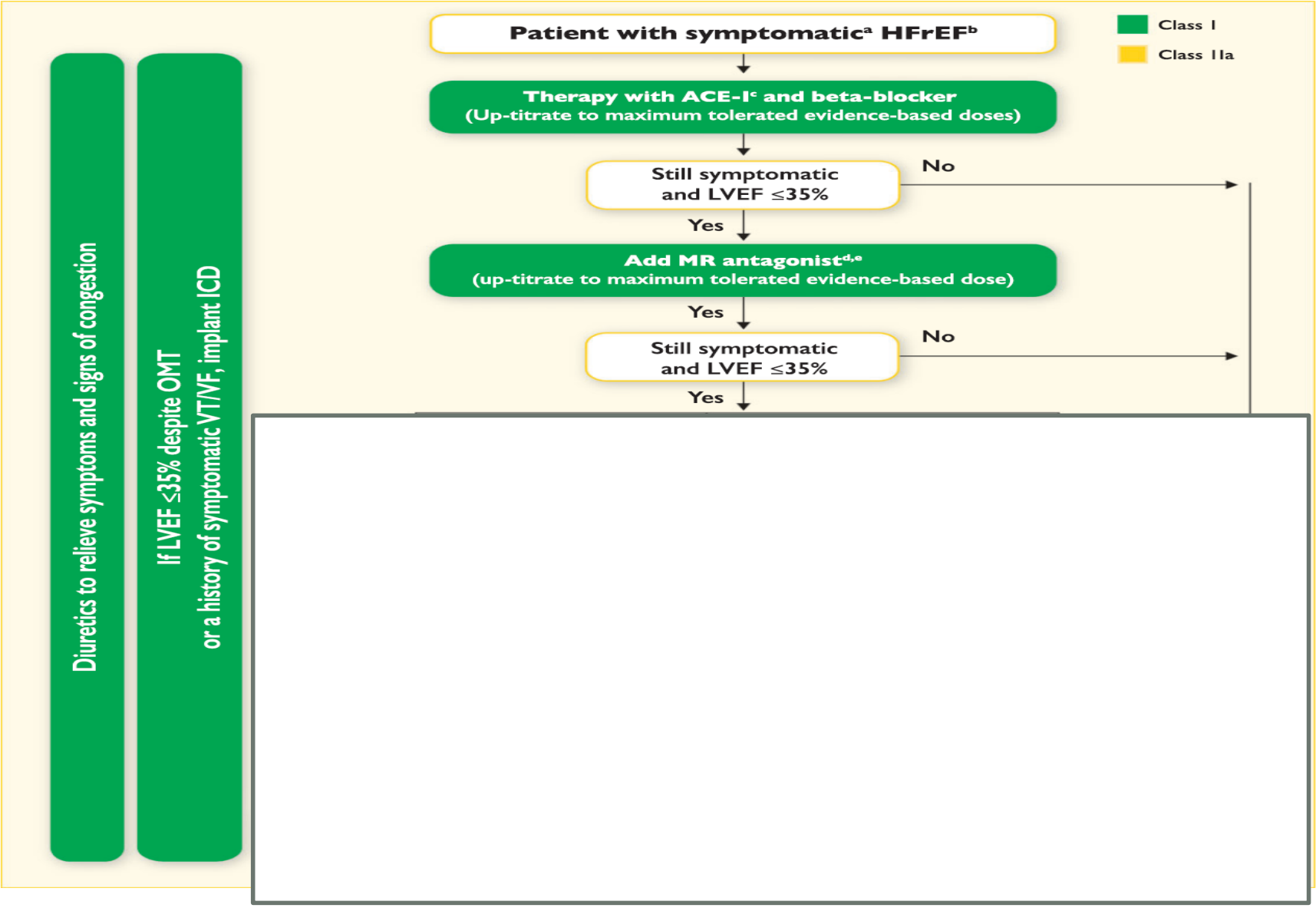
Recommendations for treatment of patients with heart failure with preserved ejection fraction and heart failure with mid-range ejection fraction

Recommendations	Class[a]	Level[b]	Ref[c]
it is recommended to screen patients with HFpEF or HFmrEF for both cardiovascular and non-cardiovascular comorbidities, which, if present, should be treated provided safe and effective interventions exist to improve symptoms, well-being and/or prognosis.	I	C	
Diuretics are recommended in congested patients with HFpEF or HFmrEF in order to alleviate symptoms and signs.	I	B	178, 179

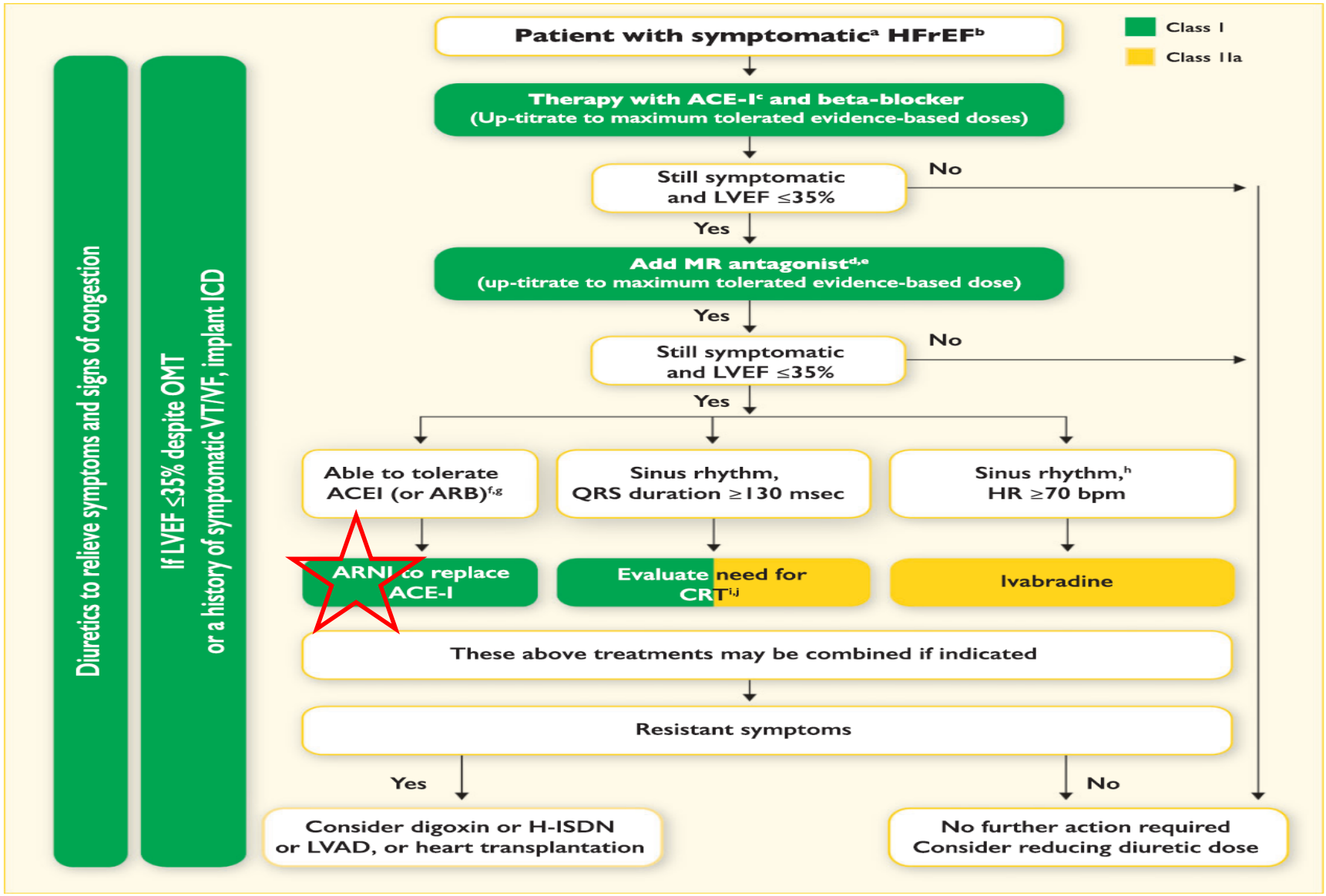
HFmrEF = heart failure with mid-range ejection fraction; HFpEF = heart failure with preserved ejection fraction.

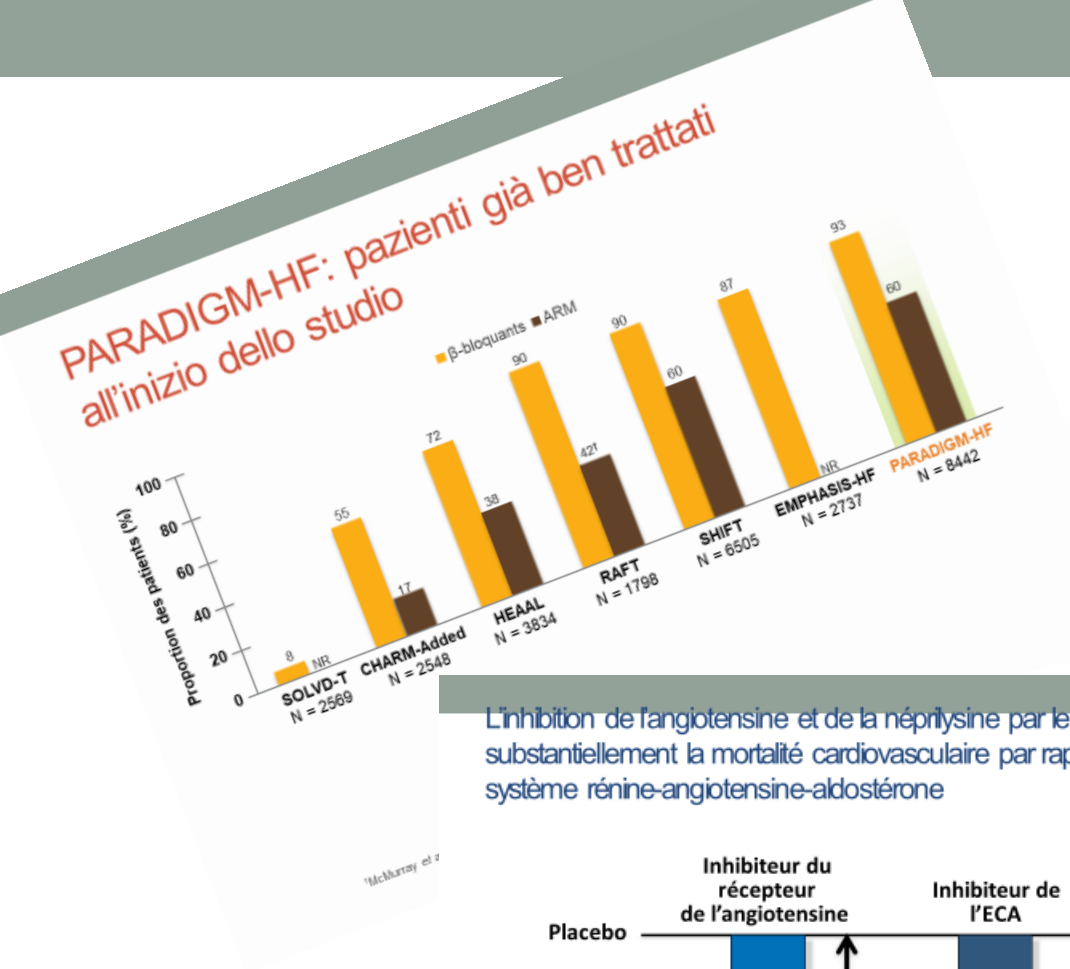
Ma nessuna raccomandazione di terapia migliorativa di mortalità e morbidità !!!

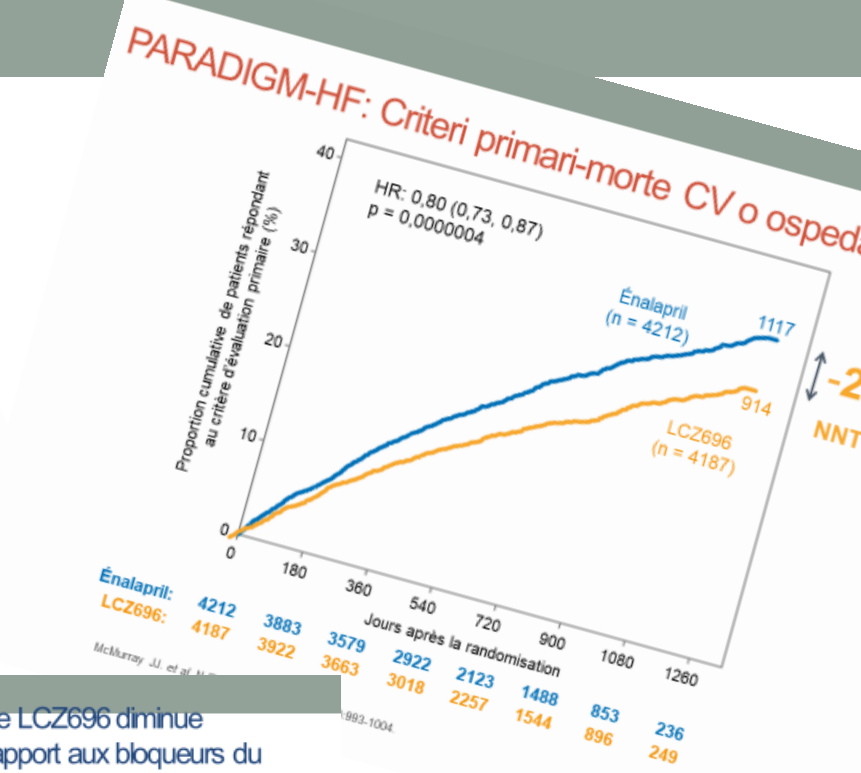
Insufficienza cardiaca: Algoritmo terapeutico



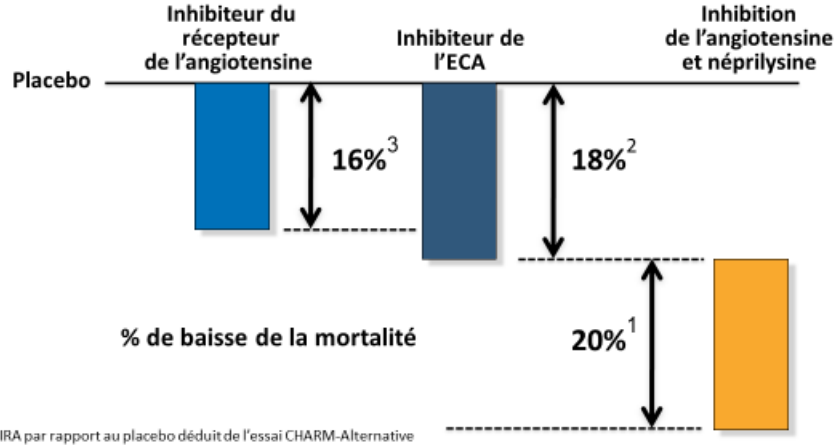
Insufficienza cardiaca: Algoritmo terapeutico







L'inhibition de l'angiotensine et de la néprilysine par le LCZ696 diminue substantiellement la mortalité cardiovasculaire par rapport aux bloqueurs du système rénine-angiotensine-aldostérone



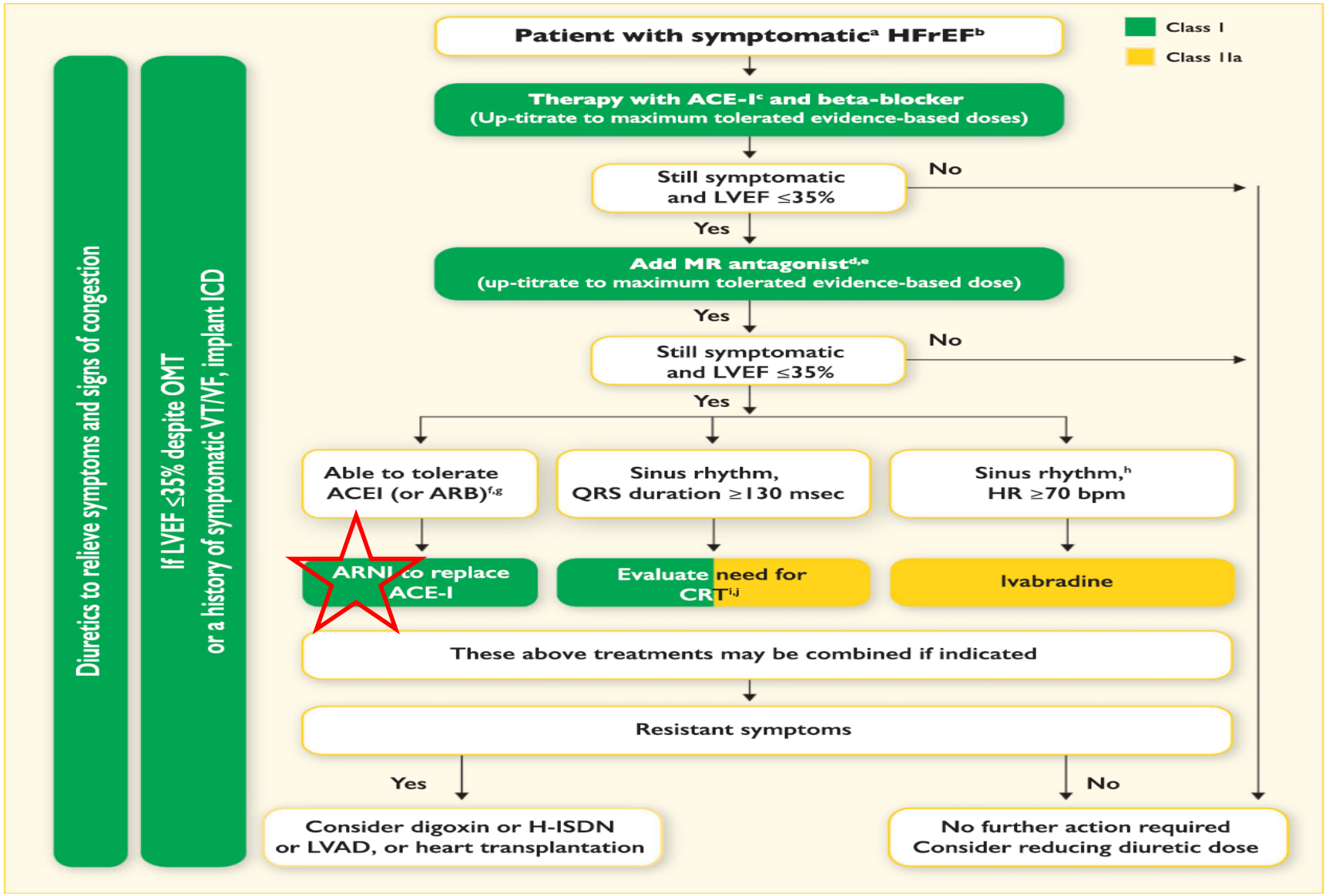
Effet de l'IRA par rapport au placebo déduit de l'essai CHARM-Alternative
Effet de l'inhibiteur de l'ECA par rapport au placebo déduit de l'essai thérapeutique SOLVD-T
Effet du LCZ696 comparé à l'inhibiteur de l'ECA déduit de l'essai PARADIGM-HF

[1]McMurray *et al.* Eur Heart J 2012; 33:1787–847; [2]Investigateurs des SOLVD. N Engl J Med 1991; 325:293–302; [3]Granger *et al.* Lancet 2003; 362:772–66;

NNT

21

Quando iniziare Sacubitril/Valsartan ?



Aspetti pratici dell'uso di Sacubitril/valsartan

- Aspettare almeno 36 ore senza ACE Inibitore

Terapia attuale	Dose iniziale raccomandata di LCZ696
Inibitore ACE Sartano	100 mg 1-0-1 se ACE o Sartano alto dosato 50 mg 1-0-1 se ACE o Sartano basso dosato
Nessuna terapia	50 mg 1-0-1

- **<u>Controindicato se :</u>**

In combinazione con ACE inibitore.
Antecedenti di angioedema con ACE o Sartano
Utilizzazione di Aliskirene
Gravidanza.
PA sist. < 100 mmHg

Aspetti pratici dell’uso di Sacubitril/Valsartan

In caso di insufficienza renale

	Dose iniziale raccomandata di LCZ696
GFR > 30 ml/min1.73 m2	Nessun adattamento della dose
GFR < 30 ml/min/1.73 m2	50 mg 1-0-1
GFR < 10 ml/min/1.73 m2	CONTROINDICATO

Aumento del dosaggio ogni 2-3 settimane

Sacubitril/Valsartan: Chi fa cosa ?

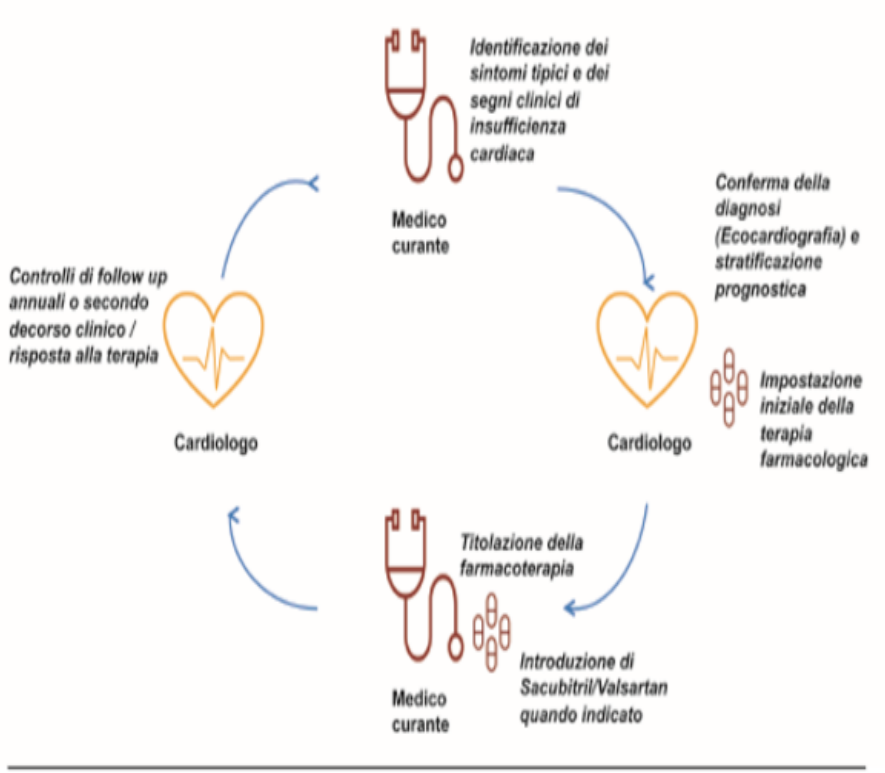


Illustrazione 2: Gestione delle insufficienza cardiaca

Sacubitril/Valsartan

La domanda non è

SE…

ma

QUANDO iniziare.

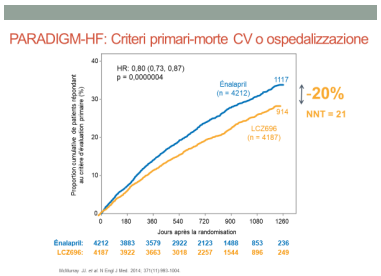
Sacubitril/Valsartan: quando iniziare

Dopo titolazione dei farmaci tradizionali

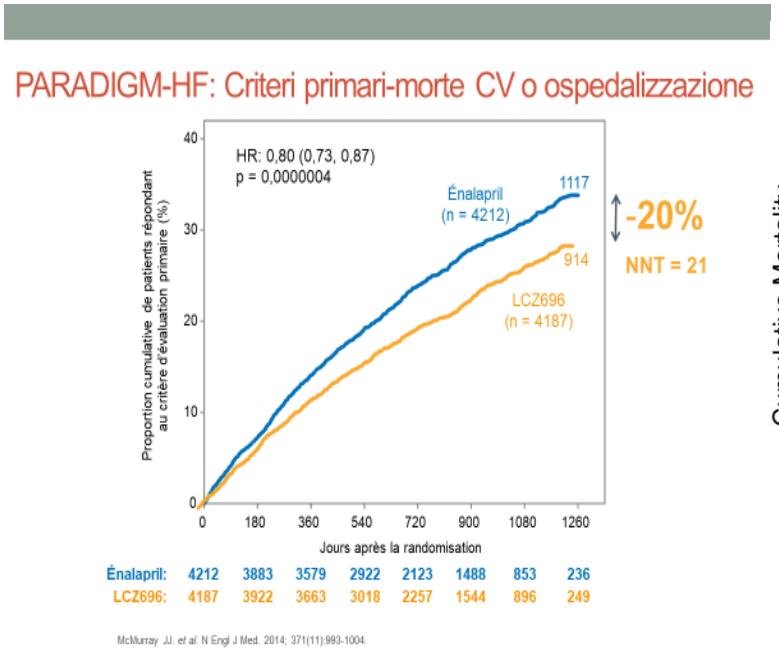
- In accordo ai criteri dello studio
- Rischio di deposito di Amilode nel cervello ?

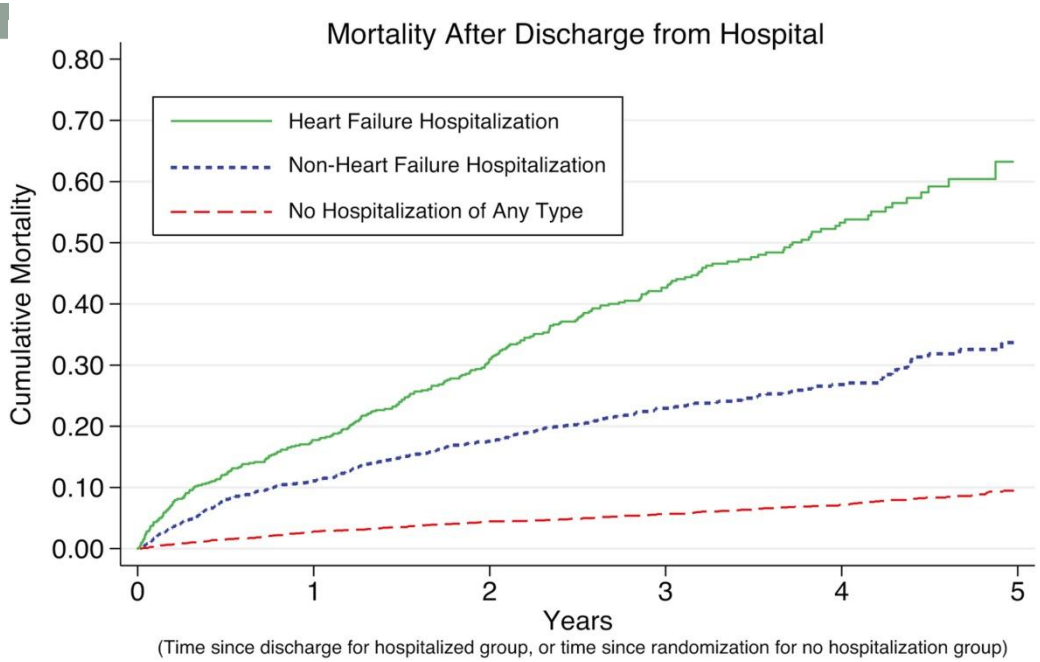
In prima intenzione appena fatta la diagnosi

- Spesso criteri non rispettati anche per ACE i
- Meno iperpotassiemia in caso di Antagonisti Aldosterone
- I pazienti intanto muoiono



Sacubitril/Valsartan: quando iniziare





Sacubitril/Valsartan, perché ?

Solo per la mortalità ?

Sacubitril/Valsartan: perché ?
Effetto sulle attività della vita quotidiana

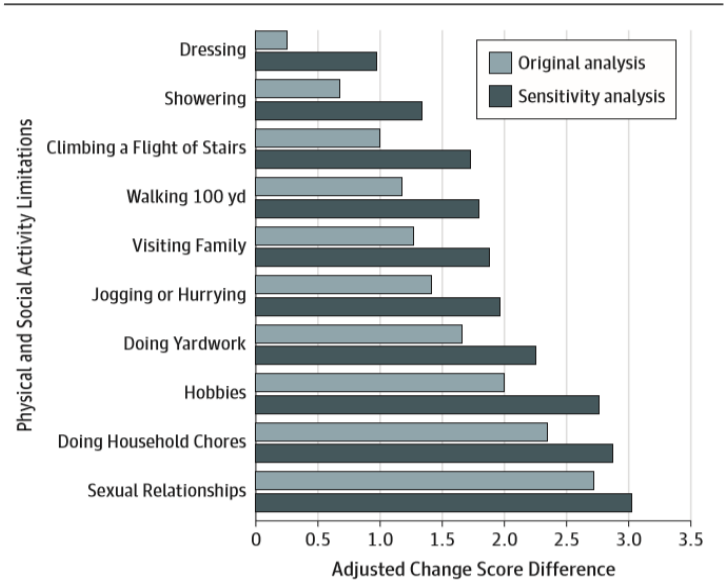
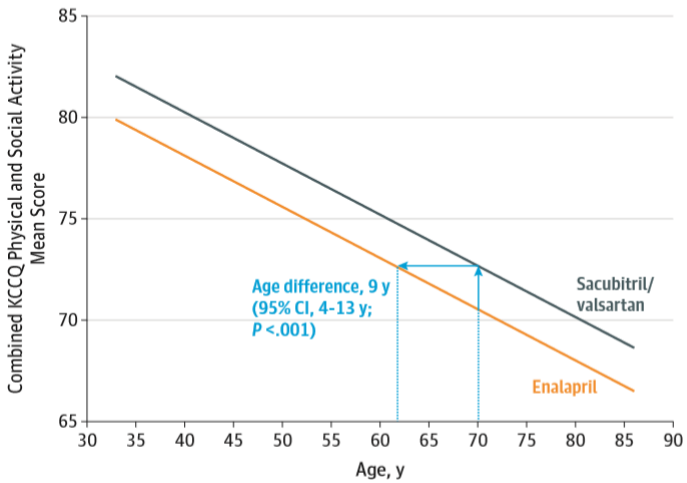


Figure 2. Unadjusted Age Equivalency Analysis of Kansas City Cardiomyopathy Questionnaire (KCCQ) Physical and Social Activity Mean Score at 8-Month Follow-up Comparing Sacubitril/Valsartan and Enalapril



Insufficienza cardiaca: co-morbidità

Recommendations for the treatment of other co-morbidities in patients with heart failure

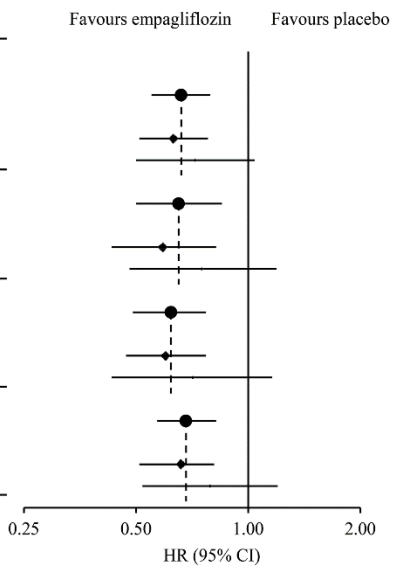
Recommendations	Class [a]	Level [b]	Ref [c]
Iron deficiency			
Intravenous FCM should be considered in symptomatic patients with HFrEF and iron deficiency (serum ferritin <100 μg/L, or ferritin between 100–299 μg/L and transferrin saturation <20%) in order to alleviate HF symptoms, and improve exercise capacity and quality of life.	IIa	A	469, 470
Diabetes			
Metformin should be considered as a first-line treatment of glycaemic control in patients with diabetes and HF, unless contra-indicated.	IIa	C	440 ,441

SGLT2 inibitori

FCM = ferric carboxymaltose; HF = heart failure; HFrEF = heart failure with reduced ejection fraction.

Empagliflozina e insufficienza cardiaca

	Empagliflozin		Placebo		HR (95% CI)
	n with event/*n*	%	*n* with event/*n*	%	
Heart failure hospitalization or cardiovascular death					
All patients	265/4687	5.7	198/2333	8.5	0.66 (0.55–0.79)
Heart failure at baseline					
No	190/4225	4.5	149/2089	7.1	0.63 (0.51–0.78)
Yes	75/462	16.2	49/244	20.1	0.72 (0.50–1.04)
Hospitalization for heart failure					
All patients	126/4687	2.7	95/2333	4.1	0.65 (0.50–0.85)
Heart failure at baseline					
No	78/4225	1.8	65/2089	3.1	0.59 (0.43–0.82)
Yes	48/462	10.4	30/244	12.3	0.75 (0.48–1.19)
Cardiovascular death					
All patients	172/4687	3.7	137/2333	5.9	0.62 (0.49–0.77)
Heart failure at baseline					
No	134/4225	3.2	110/2089	5.3	0.60 (0.47–0.77)
Yes	38/462	8.2	27/244	11.1	0.71 (0.43–1.16)
All-cause mortality					
All patients	269/4687	5.7	194/2333	8.3	0.68 (0.57–0.82)
Heart failure at baseline					
No	213/4225	5.0	159/2089	7.6	0.66 (0.51–0.81)
Yes	56/462	12.1	35/244	14.3	0.79 (0.52–1.20)



Heart failure outcomes with empagliflozin in patients with type 2 diabetes at high cardiovascular risk: results of the EMPA-REG OUTCOME® trial

Eur Heart J. 2016;37(19):1526-1534. doi:10.1093/eurheartj/ehv728

Insufficienza cardiaca: approccio globale

Recommendations for exercise, multidisciplinary management and monitoring of patients with heart failure

Recommendations	Class [a]	Level [b]	Ref [c]
It is recommended that regular aerobic exercise is encouraged in patients with HF to improve functional capacity and symptoms.	I	A	321, 618–621
It is recommended that regular aerobic exercise is encouraged in stable patients with HFrEF to reduce the risk of HF hospitalization.	I	A	618, 619
It is recommended that patients with HF are enrolled in a multidisciplinary care management programme to reduce the risk of HF hospitalization and mortality.	I	A	622–625
Referral to primary care for long-term follow-up may be considered for stable HF patients who are on optimal therapy to monitor for effectiveness of treatment, disease progression and patient adherence.	IIb	B	626, 627

Considerazioni finali
Come é cambiato il modo di agire ?

- **Dislipidemia**
  - → aumentato l'uso di Ezetimibe (CON SUCCESSO !!)
  - → stratificazione rischio con Lp(a)

Considerazioni finali
Come é cambiato il modo di agire ?

- **NOAC**

→Aumentato l’uso di anticoagulanti

→Diminuito l’uso di Cumarinici

→Diminuito il Bridge con Eparina in caso di sospensione pre intrvento chirurgico

→Diminuito uso di ASS dopo un anno in pazienti anticoagulati

Considerazioni finali
Come é cambiato il modo di agire ?

- **Insufficienza cardiaca**

→migliorata la titolazione verso l'alto dei farmaci prognostici (ACE, Betabloccante e Aldactone, Ivabradina, Sacubitril/Valsartan)

→Maggiore sensibilità sullo stato marziale

→Nei diabetici prima scelta SGLT2 inibitori

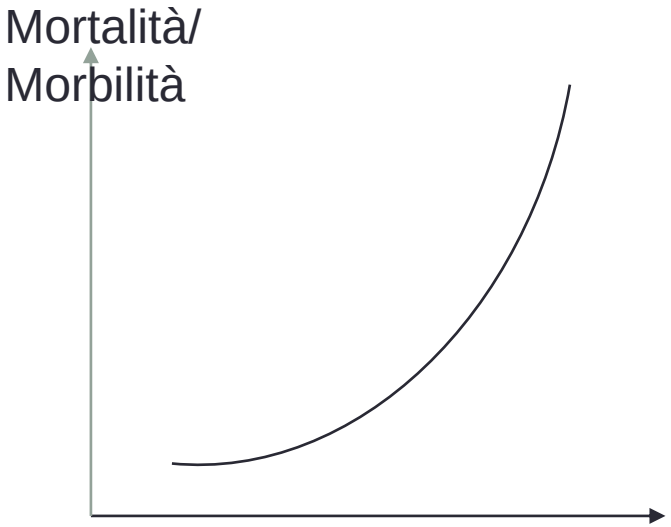

Spauracchio delle Schegge
2
Creatura — Elementale
Travolgere
La forza e la costituzione dello
Spauracchio delle Schegge sono pari al

Tendenza discutibile

Tocca a NOI usare il buonsenso


ACME CO.


HOW ABOUT ENDING THIS CARTOON BEFORE I HIT?


Mortalità/
Morbilità


SUPERB wallpapers
That's all Folks!
Statistics !

Relazione fra comsumo di cioccolata e quantità di premi Nobel per Nazione

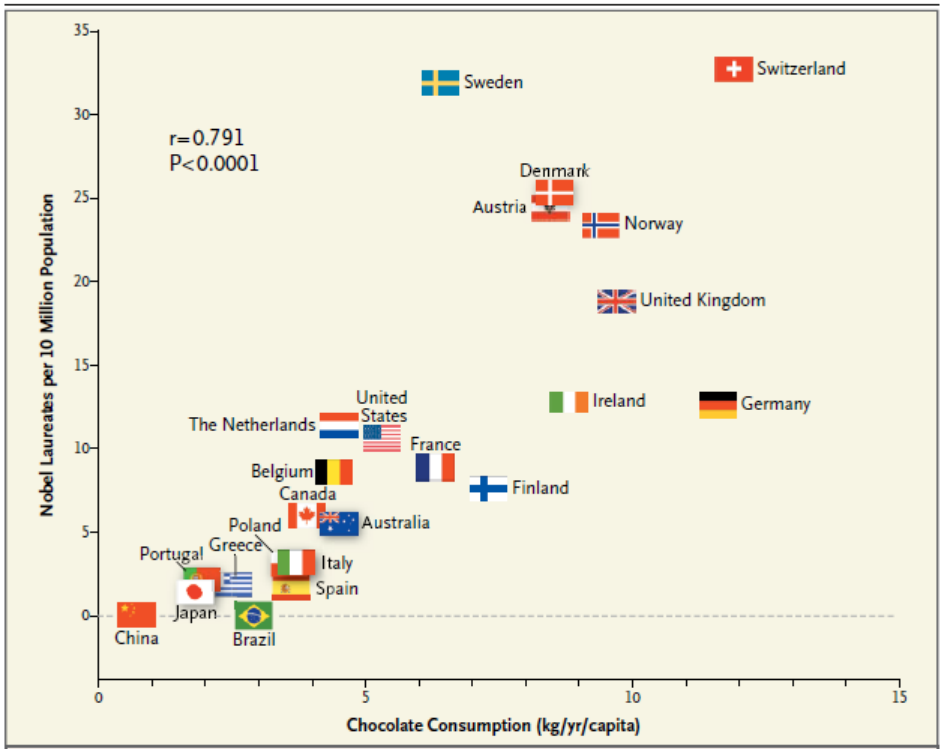


Figure 1. Correlation between Countries' Annual Per Capita Chocolate Consumption and the Number of Nobel Laureates per 10 Million Population.

GRAZIE
per l'attenzione

Dr.med. Mauro Capoferri

maurocapoferri@bluewin.ch

Insufficienza cardiaca: trattamenti dannosi

Treatments (or combinations of treatments) that may cause harm in patients with symptomatic (NYHA Class II–IV) heart failure with reduced ejection fraction

Recommendations	Class [a]	Level [b]	Ref [c]
Thiazolidinediones (glitazones) are not recommended in patients with HF, as they increase the risk of HF worsening and HF hospitalization.	III	A	209, 210
NSAIDs or COX-2 inhibitors are not recommended in patients with HF, as they increase the risk of HF worsening and HF hospitalization.	III	B	211–213
Diltiazem or verapamil are not recommended in patients with HFrEF, as they increase the risk of HF worsening and HF hospitalization.	III	C	214
The addition of an ARB (or renin inhibitor) to the combination of an ACE-I and an MRA is not recommended in patients with HF, because of the increased risk of renal dysfunction and hyperkalaemia.	III	C	

ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; COX-2 inhibitor = cyclooxygenase-2 inhibitor; HF = heart failure; HFrEF = heart failure with reduced ejection fraction; MRA = mineralocorticoid receptor antagonist; NSAIDs = non-steroidal anti-inflammatory drugs.

aflet.pdf

170%

Normaler Blutdruck

• In der Praxis:	< 140/90 mmHg
• Selbstmessung:	< 135/85 mmHg
• Mittelwert der 24h ambulanten BD-Messung:	
– Tag + Nacht:	< 130/80 mmHg
– Tag (Wach):	< 135/85 mmHg
– Nacht (Schlaf)	< 120/70 mmHg
– Dipping profile:	Nachtabfall >10 – 15% Tagesmittelwert

Hypertonie-Beurteilung (Erwachsene >18 Jahre)[1]

Klasse	systolisch (mmHg)		diastolisch (mmHg)
Normaler Blutdruck	<140	und	<90
Hypertonie 1. Grades (leicht)	140 – 159	und/oder	90 – 99
Hypertonie 2. Grades (mässig)	160 – 179	und/oder	100 – 109
Hypertonie 3. Grades (schwer)	≥ 180	und/oder	≥ 110
Isolierte systolische Hypertonie	≥ 140	und	<90

Weisskittelhypertonie: Erhöhter Blutdruck nur in der Praxis
Maskierte Hypertonie: Erhöhte Blutdruckwerte nur ausserhalb der Praxis

[1] Mittelwert von zwei bis drei Messungen an verschiedenen Tagen bzw. Wochen bis Monaten

Hypertonie bei Kindern

Systolische Hypertonie:

1 bis 17 Jahre:	> 100 + (Alter x 2)	mmHg

Diastolische Hypertonie:

1 bis 10 Jahre:	> 60 + (Alter x 2)	mmHg
11 bis 17 Jahre:	> 70 + Alter	mmHg

Isolierte systolische Hypertonie bei jungen Erwachsenen

Ultimissime dal congresso Europeo di Cardiologia 2018

Insufficienza cardiaca

- Nuova definizione
- Nuovo algoritmo diagnostico
- Raccomandazioni sulla prevenzione della insufficienza cardiaca prima del suo sviluppo
- Nuovo algoritmo terapeutico
- Importanza delle comorbidità e della multidisciplinarietà

Table 23 **Genetic disorders of lipoprotein metabolism**

Disorder	Prevalence	Gene(s)	Effect on lipoproteins
HeFH	1 in 200–250	*LDLR* *APO B* *PCSK9*	↑LDL-C
HoFH	1 in 160 000–320 000	*LDLR* *APO B* *PCSK9*	↑↑LDL-C
FCH	1 in 100/200	*USF1 + modifying genes*	↑LDL-C ↑VLDL-C ↑apoB
Familial dysbetalipoproteinaemia	1 in 5000	*APO E*	↑↑ IDL and chylomicron remnants (βVLDL)
Familial lipoprotein lipase deficiency	1 in 10^6	*LPL* *APO C2*	↑↑ chylomicrons and VLDL-C
Tangier disease (analphalipoproteinaemia)	1 in 10^6	*ABCA1*	↓↓HDL-C
Familial LCAT deficiency	1 in 10^6	*LCAT*	↓HDL-C

apo = apolipoprotein; FCH = familial combined hyperlipidaemia; HeFH = heterozygous familial hypercholesterolaemia; HoFH = homozygous familial hypercholesterolaemia; HDL-C = high-density lipoprotein-cholesterol; IDL = intermediate-density lipoprotein; LCAT = lecithin cholesterol acyltransferase; LDL-C = low-density lipoproteincholesterol; VLDL = very low-density lipoprotein-cholesterol.

Table 12 Impact of specific lifestyle changes on lipid levels

	Magnitude of the effect	Level of evidence	References
Lifestyle interventions to reduce TC and LDL-C levels			
Reduce dietary trans fat	+++	A	136, 139
Reduce dietary saturated fat	+++	A	136, 137
Increase dietary fibre	++	A	140, 141
Use functional foods enriched with phytosterols	++	A	142, 143
Use red yeast rice supplements	++	A	144–146
Reduce excessive body weight	++	A	147, 148
Reduce dietary cholesterol	+	B	149
Increase habitual physical activity	+	B	150
Use soy protein products	+/-	B	151
Lifestyle interventions to reduce TG-rich lipoprotein levels			
Reduce excessive body weight	+++	A	147, 148
Reduce alcohol intake	+++	A	152, 153
Increase habitual physical activity	++	A	150, 154
Reduce total amount of dietary carbohydrate	++	A	148, 155
Use supplements of n-3 polyunsaturated fat	++	A	156, 157
Reduce intake of mono- and disaccharides	++	B	158, 159
Replace saturated fat with mono- or polyunsaturated fat	+	B	136, 137
Lifestyle interventions to increase HDL-C levels			
Reduce dietary trans fat	+++	A	136, 160
Increase habitual physical activity	+++	A	150, 161
Reduce excessive body weight	++	A	147, 148
Reduce dietary carbohydrates and replace them with unsaturated fat	++	A	148, 162
Modest consumption in those who take alcohol may be continued	++	B	152
Quit smoking	+	B	163
Among carbohydrate-rich foods prefer those with low glycaemic index and high fibre content	+/-	C	164
Reduce intake of mono- and disaccharides	+/-	C	158, 159

HDL-C = high-density lipoprotein-cholesterol; LDL-C = low-density lipoprotein-cholesterol; TC = total cholesterol; TG = triglycerides.
The magnitude of the effect (+++ = marked effects, ++ = less pronounced effects, + = small effects, − = not effective) and the level of evidence refer to the impact of each dietary modification on plasma levels of a specific lipoprotein class.

Dislipidemia: Ipercolesterolemia famigliare

Table 21 Dutch Lipid Clinic Network diagnostic criteria for familial hypercholesterolaemia[391]

Criteria	Points
1) Family history	
First-degree relative with known premature (men: <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 <18 years of age with LDL-C above the 95th percentile (see 9.1.2.3)	2
2) Clinical history	
Patient with premature (men: <55 years; women: <60 years) coronary artery disease	2
Patient with premature (men: <55 years; women: <60 years) cerebral or peripheral vascular disease	1
3) Physical examination	
Tendinous xanthomata	6
Arcus cornealis before age 45 years	4
4) LDL-C levels	
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 gene	8
Choose only one score per group, the highest applicable Diagnosis (diagnosis is based on the total number of points obtained)	
A 'definite' FH diagnosis requires >8 points	
A 'probable' FH diagnosis requires 6–8 points	
A 'possible' FH diagnosis requires 3–5 points	

Table 12.3 Causes of elevated concentrations of natriuretic peptides[522–524]

Cardiac	Heart failure Acute coronary syndromes Pulmonary embolism Myocarditis Left ventricular hypertrophy Hypertrophic or restrictive cardiomyopathy Valvular heart disease Congenital heart disease Atrial and ventricular tachyarrhythmias Heart contusion Cardioversion, ICD shock Surgical procedures involving the heart Pulmonary hypertension
Non-cardiac	Advanced age Ischaemic stroke Subarachnoid haemorrhage Renal dysfunction Liver dysfunction (mainly liver cirrhosis with ascites) Paraneoplastic syndrome Chronic obstructive pulmonary disease Severe infections (including pneumonia and sepsis) Severe burns Anaemia Severe metabolic and hormone abnormalities (e.g. thyrotoxicosis, diabetic ketosis)

HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction; ICD = implantable cardioverter defibrillator.

PARADIGM-HF: Principaux critères d'exclusion

- Antécédents d'angiœdème
- Taux de filtration glomérulaire < 30 ml/min/1,73 m^2
  ou une baisse > 35% du TFG entre le screening et la fin de la préinclusion sous énalapril ou la randomisation
- Potassium > 5,2 mmol/l au screening ou > 5,4 mmol/l à la fin de la préinclusion sous énalapril ou la fin de la préinclusion sous LCZ696
- Nécessité de traitement avec des IECA et des sartans
- Hypotension symptomatique et/ou TAS < 100 mmHg lors du screening, ou TAS < 95 mmHg à la fin de la préinclusion sous énalapril ou à la randomisation
- IC aiguë décompensée
- Antécédents de maladie pulmonaire sévère
- Syndrome coronarien aigu, AVC, AIT, opération du cœur, de la carotide ou autre opération chirurgicale cardiovasculaire majeure, angioplastie coronarienne ou carotidienne dans les 3 mois précédant la sélection

McMurray *et al*. Eur J Heart Fail. 2013; 15:1062–73;

Safety

	Evolocumab (N=13,769)	Placebo (N=13,756)
Adverse events (%)		
Any	77.4	77.4
Serious	24.8	24.7
Allergic reaction	3.1	2.9
Injection-site reaction	2.1	1.6
Treatment-related and led to d/c of study drug	1.6	1.5
Muscle-related	5.0	4.8
Cataract	1.7	1.8
Diabetes (new-onset)	8.1	7.7
Neurocognitive	1.6	1.5
Laboratory results (%)		
Binding Ab	0.3	n/a
Neutralizing Ab	*none*	n/a

New-onset diabetes assessed in patients without diabetes at baseline; adjudicated by CEC

Sabatine MS, et al . *NEJM*. [published online ahead of print March 17, 2017]. doi: 10.1056/NEJMoa1615664

Trattamento terapeutico

ANAMNESI

Prevenzione primaria
ipercolesterolemia familiare eterozigote

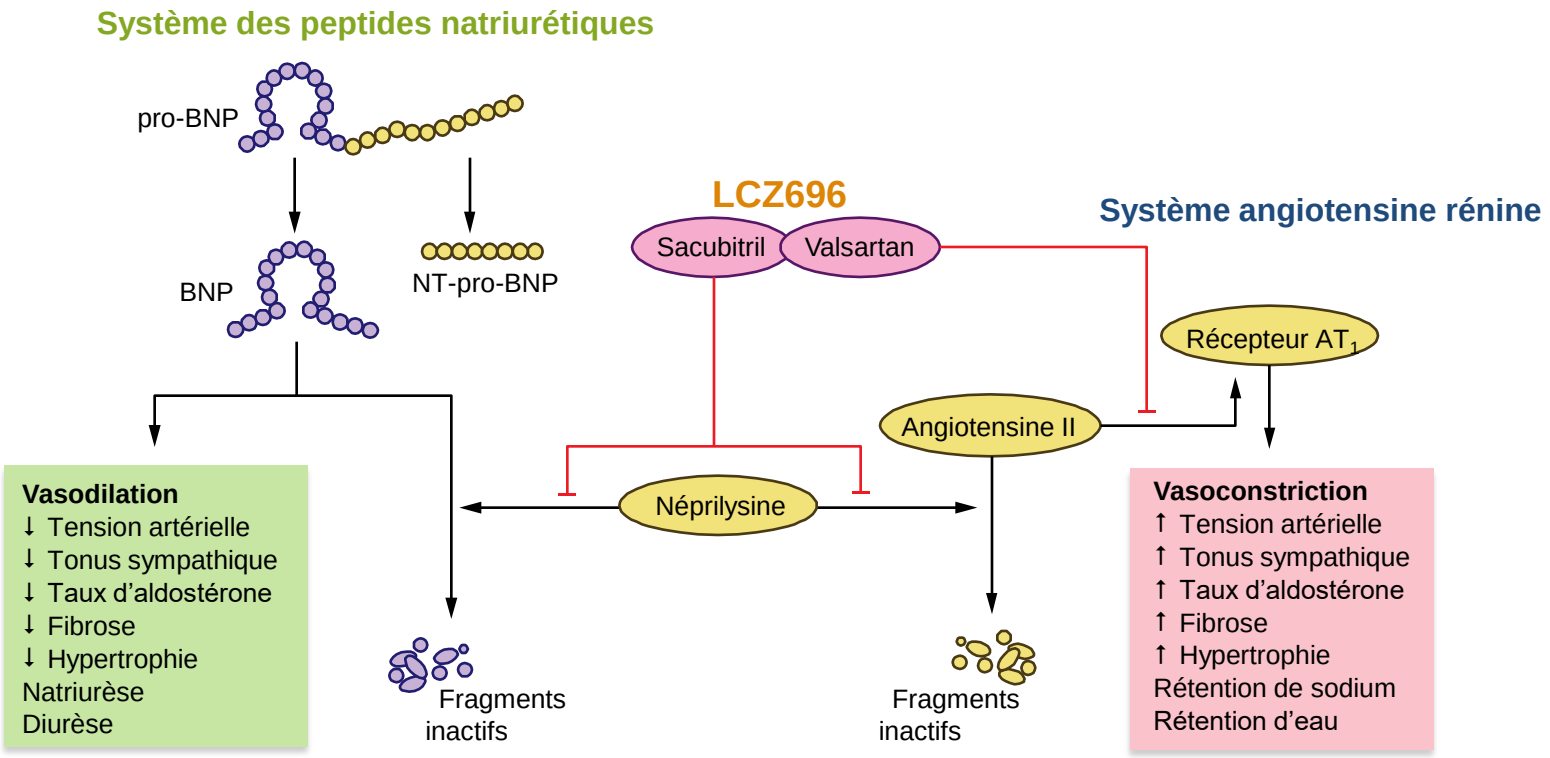
C-LDL con terapia precedente **> 5.0 mmol/L**

C-LDL con terapia precedente **> 4.5 mmol/L**

Con min. 1 ulteriore fattore di rischio tra:

- Diabete mellito,
- Aumento della lipoproteina (a) > 50 mg/dL,
- Ipertensione arteriosa elevata,
- ASCVD° familiare precoce§ clinicamente manifesta.

LCZ696: inibitore a doppia azione



Swedberg K. Nat Rev Cardiol. 2015; 12(2):73-5.

Riduzione significativa anche di altri parametri lipidici alla settimana 24