Nous fàrmacs en el tractament de les dislipèmies.

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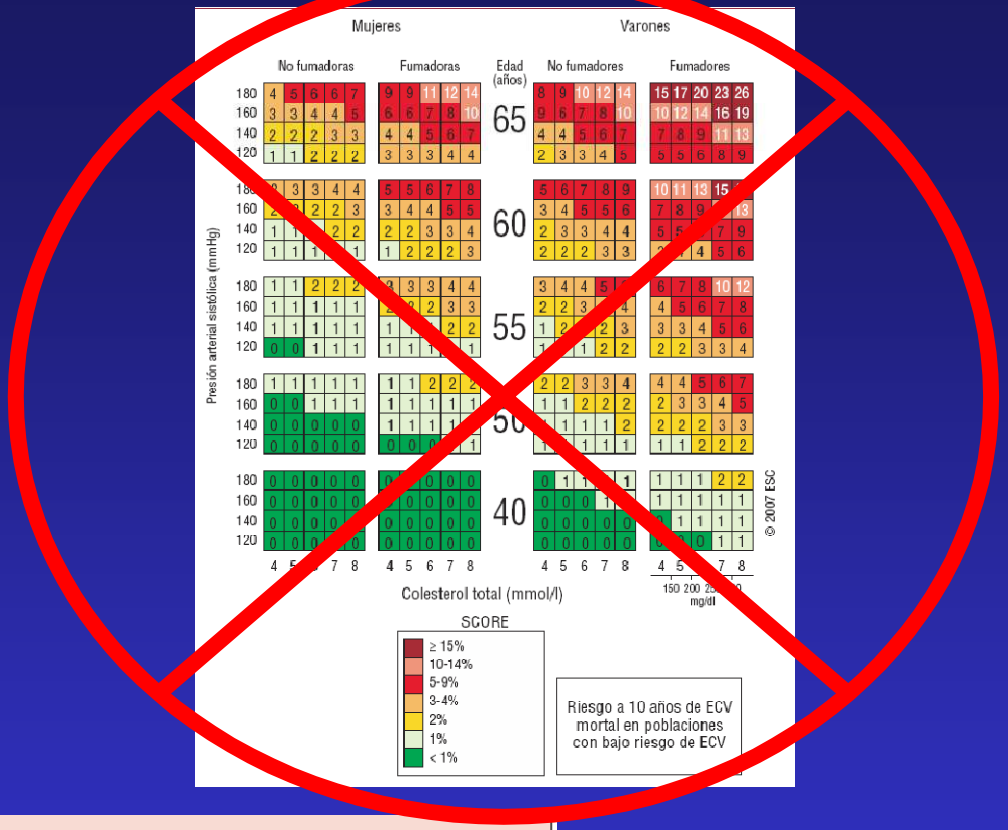
TABLAS DE RIESGO CARDIOVASCULAR



High-risk

OBJ
LDL <100

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.

GUÍA EUROPEA DE RCV

European Heart Journal 2016

HIPERCOLESTEROLEMIA FAMILIAR (HFH)

Herencia

Autosómico dominante (AD)

Heterozigota 1/500
Homozigota 1/1.000.000

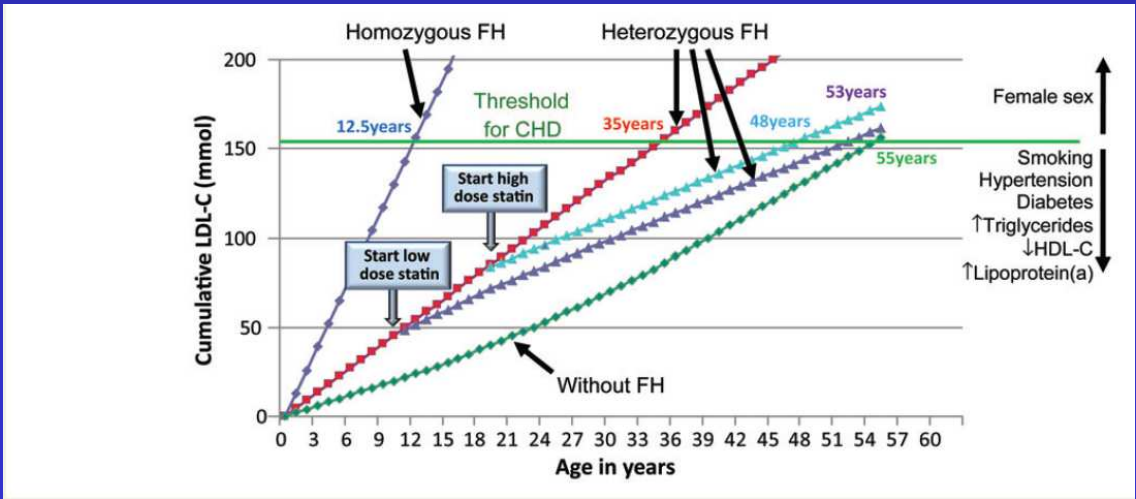
Etiología

- Mutación en gen receptor LDL
- Mutación gen ApoB
- Mutación gen PCSK 9

Colesterol

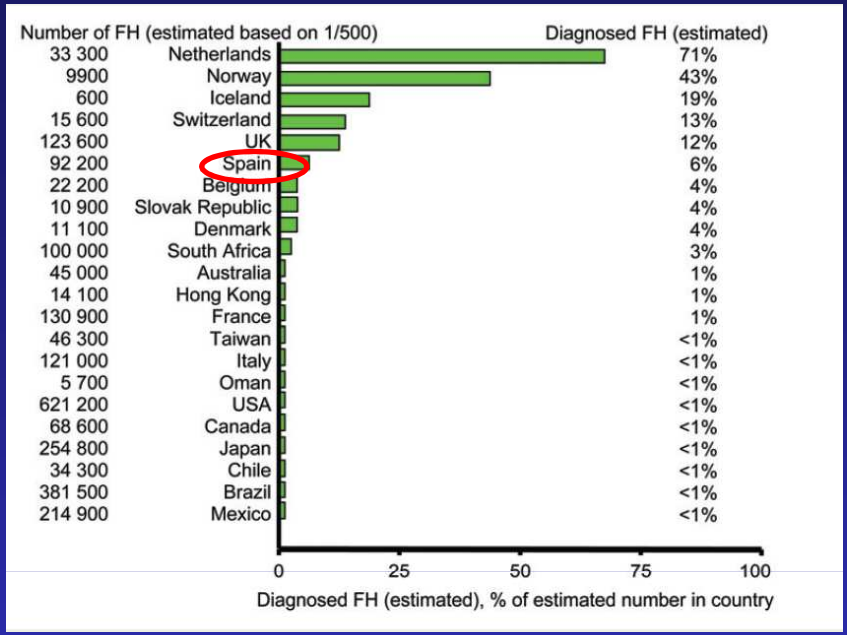
Desde niñez/pubertad
CT 250-450 mg/dl
LDL-C 190-300mg/dl

Aterogenicidad



Nordestgaard B. Eur Heart J 2013

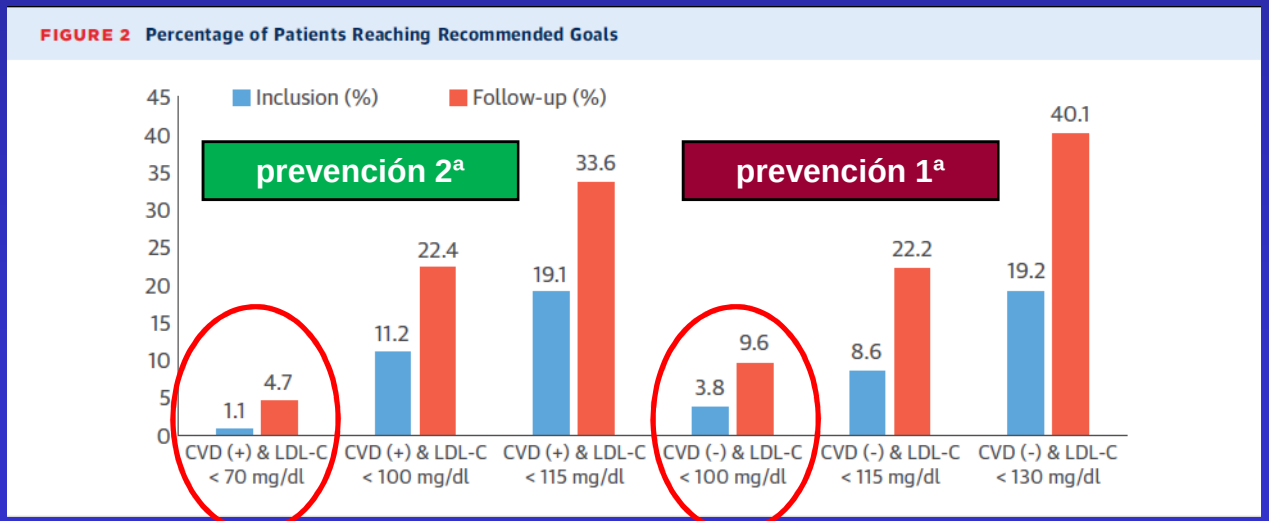
CARATERÍSTICAS CLÍNICAS DE HFH



CRITERIOS DE SOSPECHA

- LDL-C >190 adultos >160 en niños
- A Familiares o personales de CI precoz
- Presencia de xantomas o arco corneal

A pesar de que el 78% estaban a dosis máxima de tto



Huijgen R, Circ Cardiovasc Genet 2012; Starr B, Clin Chem Lab Med 2008 Perez de Isla L. J Am Coll Cardiol 2016

TRATAMIENTO DISLIPEMIAS

- ESTATINAS

- EZETIMIBE

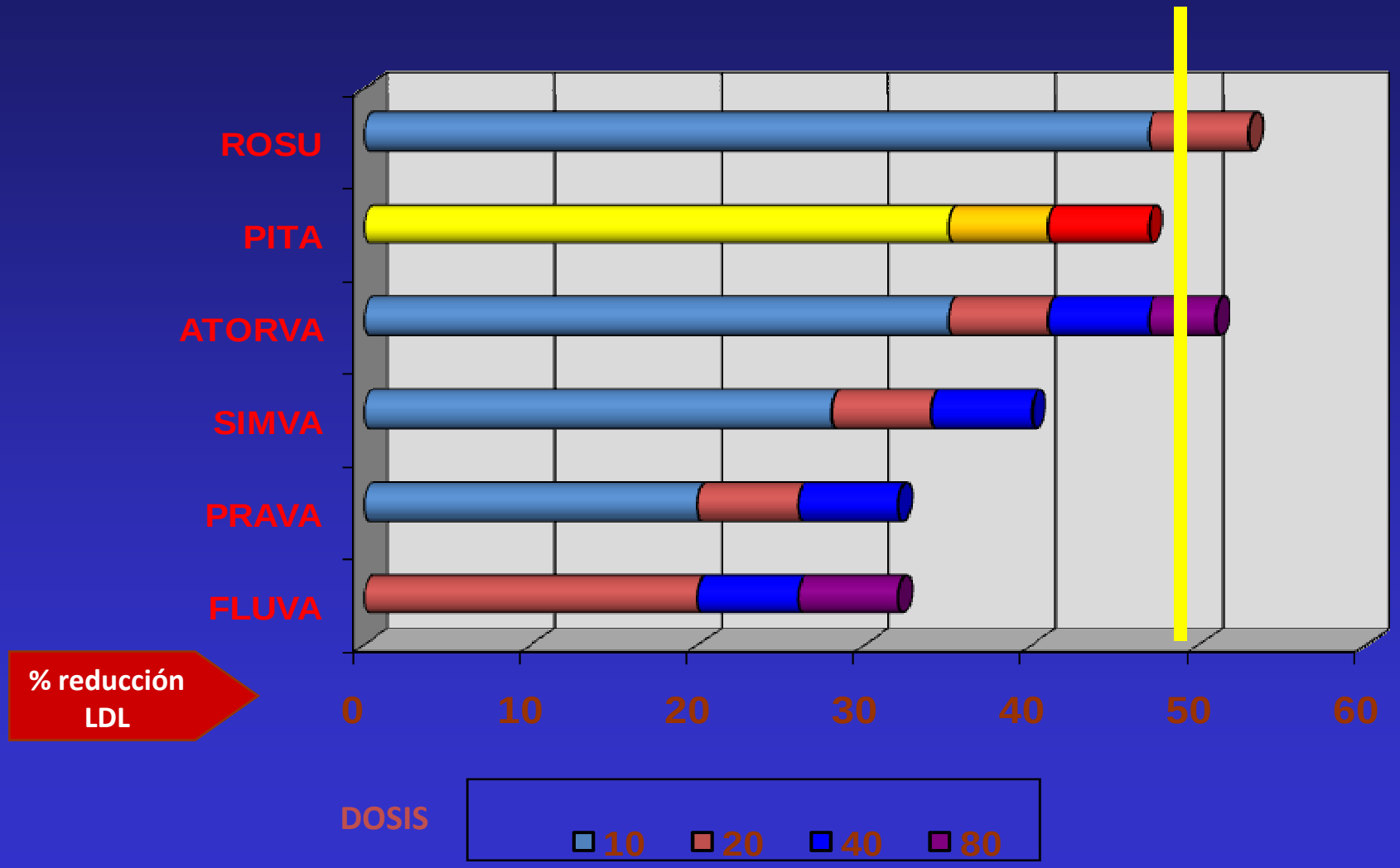
- RESINAS DE INTERCAMBIO IÓNICO/ COLESEVELAM

- LDL AFÉRESIS (HF homocigota)

- NUEVOS TRATAMIENTOS
  - Lomitapide
  - Mimopersen
  - Inhibidores PCSK 9

ESTATINAS

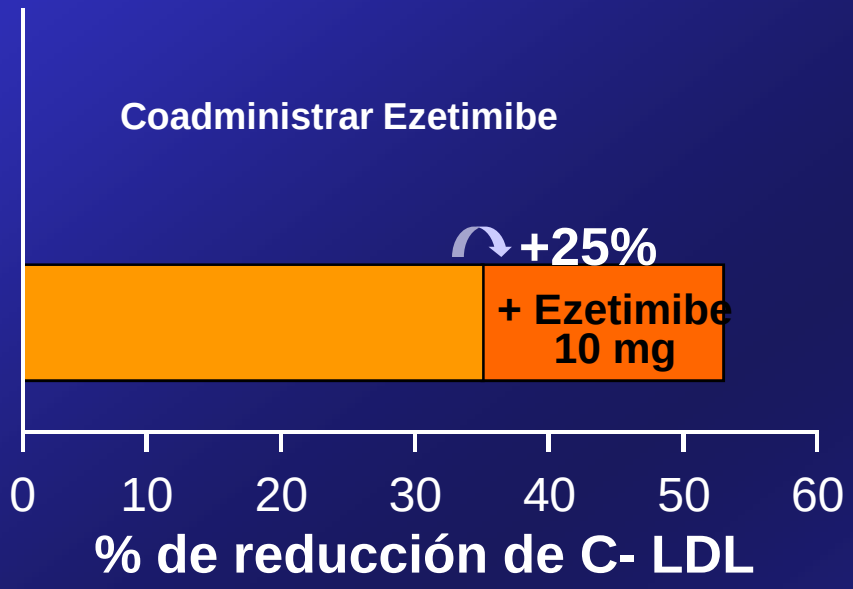
Potencia reductora en cLDL

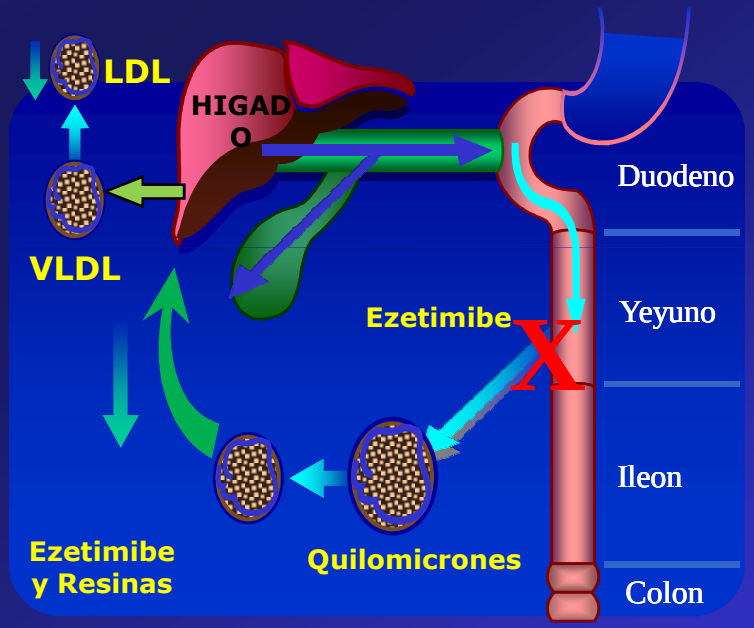


Reckless JPD, et al. Int J Clin Pract 2005;59:239-52. McKenney JM, et al. Curr Med Opin 2003;19:689-98.Schaefer EJ, et al. Am J Cardiol 2004;93:31-9.

EZETIMIBE

- **El efecto de la coadministración de ezetimibe y estatina equivale a duplicar tres veces la dosis de estatina**



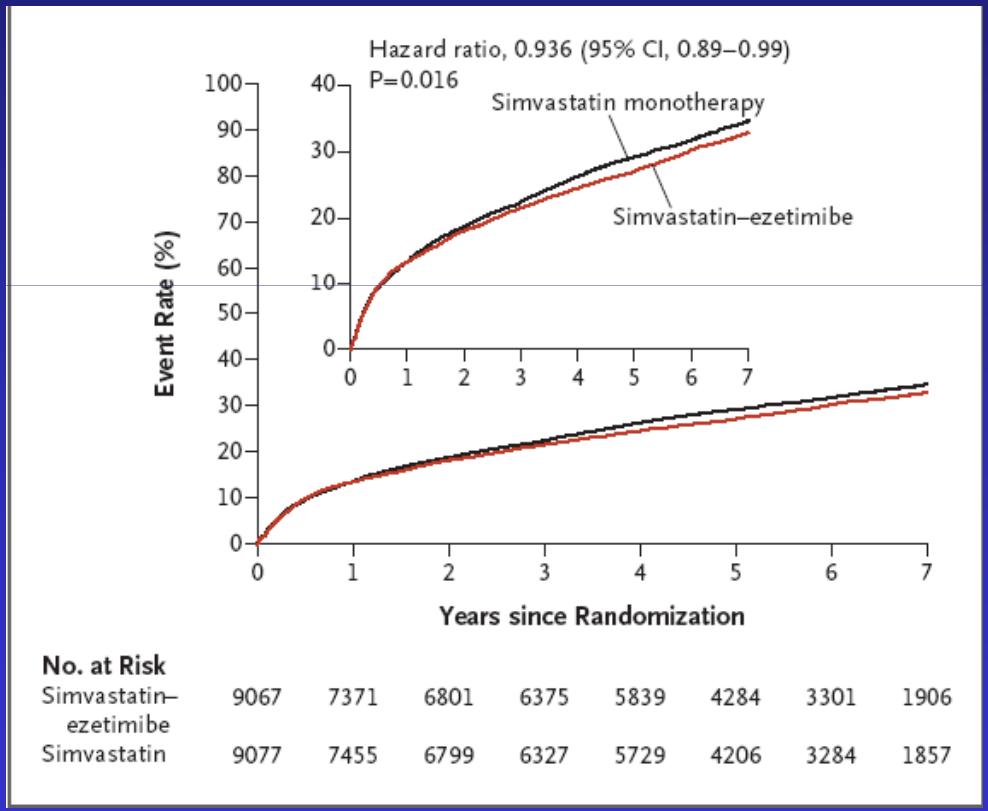


Stein E *Eur Heart J Suppl* 2001

EZETIMIBE

Ezetimibe Added to Statin Therapy after Acute Coronary Syndromes

IMPROVE-IT trial



Prevención 2ª

Ezetimibe o placebo + simvastatina

LDL-C

Ezetimibe 53 mg/dl
Placebo 70 mg/dl

↓ 13% IAM ↓ 14% Ictus

Cannon C. N Engl J Med 2015

NUEVOS TRATAMIENTOS

LIPID-LOWERING AGENT	CHARACTERISTICS						
	MECHANISM	DOSING REGIMEN	MEAN LDL REDUCTION FROM BASELINE	CLINICAL OUTCOME EVIDENCE	CONTRAINDICATIONS	ADVERSE EFFECTS	POTENTIAL DRUG INTERACTIONS
Lomitapide* **LOMITAPIDE**	An MTP inhibitor that prevents assembly of VLDL thereby reducing LDL levels	5-60 mg orally once daily	38%-50%	None	Pregnancy; chronic bowel disease (eg, IBD, malabsorption); moderate or severe hepatic impairment; use of a moderate or strong CYP 3A4 inhibitor; coadministration with simvastatin ≥40 mg/d	Gastrointestinal intolerance, liver enzyme elevations, hepatic steatosis	• Inhibits CYP 3A4 (eg, interacts with atorvastatin, lovastatin, simvastatin, warfarin) • Inhibits P-glycoprotein (eg, interacts with colchicine, dabigatran, digoxin) • CYP 3A4 substrate
Mipomersen† **MIMOPERSEN**	An antisense oligonucleotide targeted against Apo B mRNA, which prevents synthesis of Apo B thereby decreasing LDL levels	200 mg SC once weekly	25%	None	Moderate or severe hepatic impairment	Injection-site reaction, flulike symptoms, liver enzyme elevations, hepatic steatosis	None known

Turgeon R. *Can Fam Physician 2016 ;* Bouhairie V. Endocrinol Metab Clin N Am 2016

Inhibidores PCSK-9

Ac. Monoclonales frente a la proteina convertasa subtilisin/kexin type 9

EVOLOCUMAB **ALIROCUMAB**

Inhibidores PCSK-9

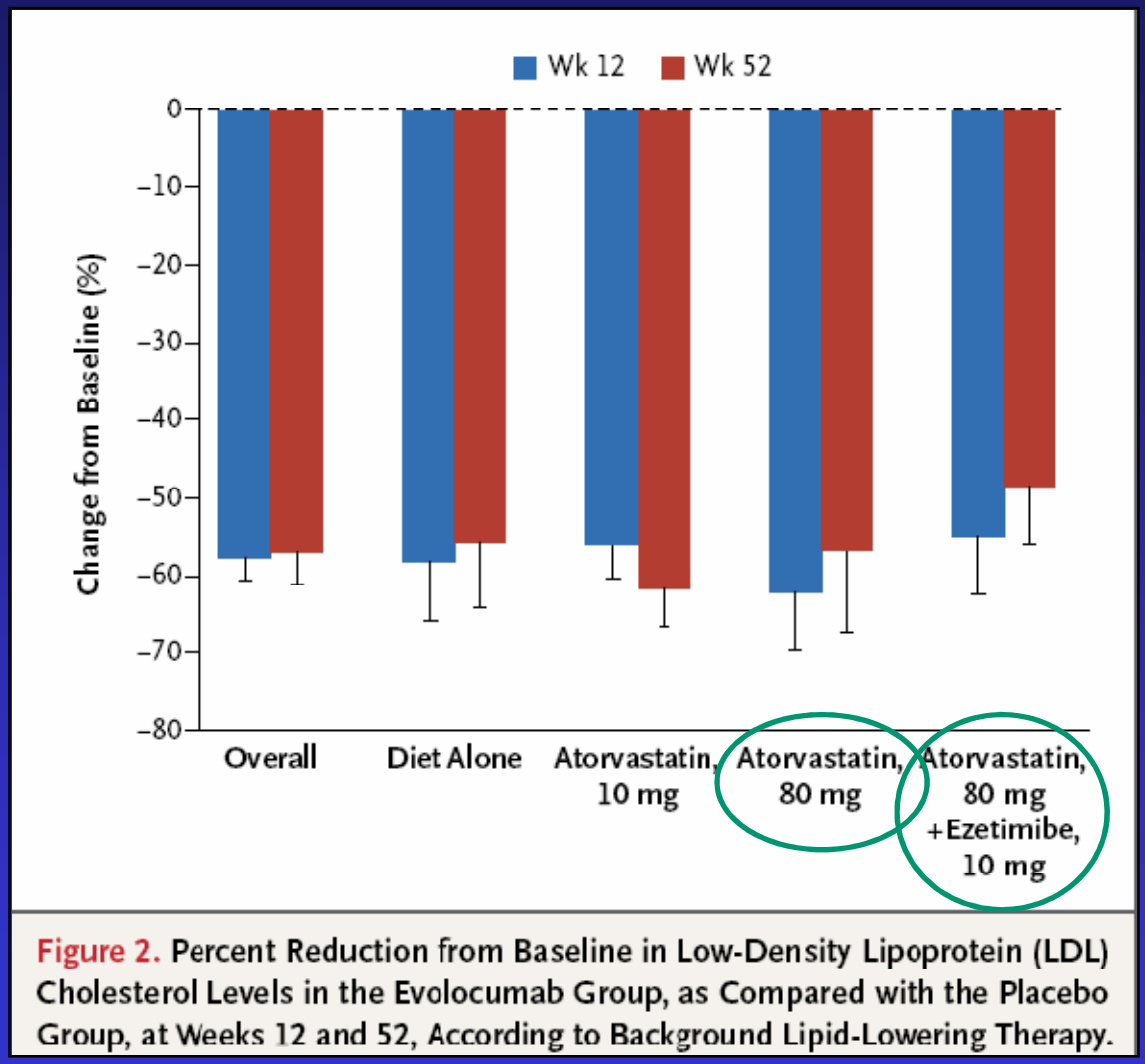
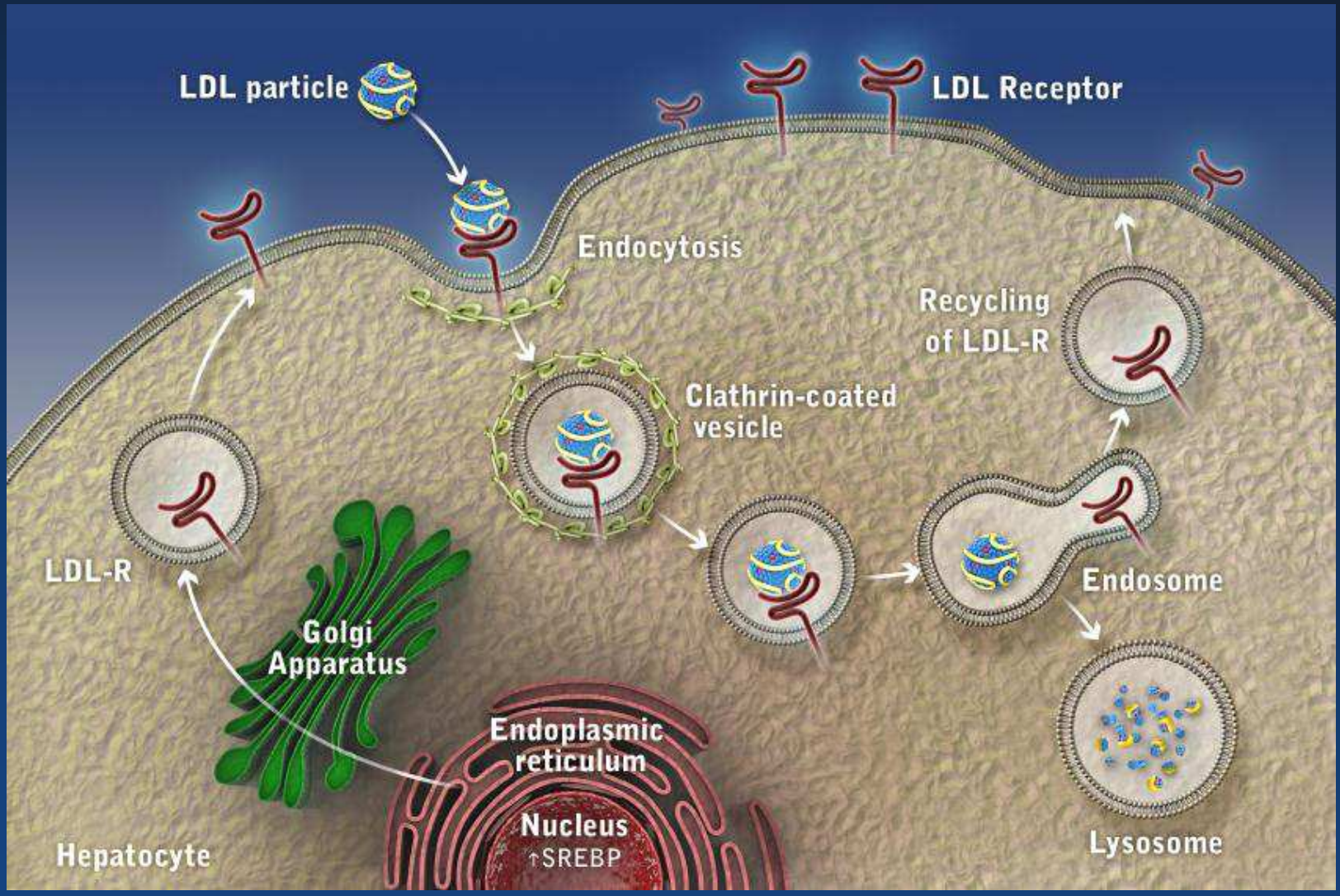


Figure 2. Percent Reduction from Baseline in Low-Density Lipoprotein (LDL) Cholesterol Levels in the Evolocumab Group, as Compared with the Placebo Group, at Weeks 12 and 52, According to Background Lipid-Lowering Therapy.

55-65%

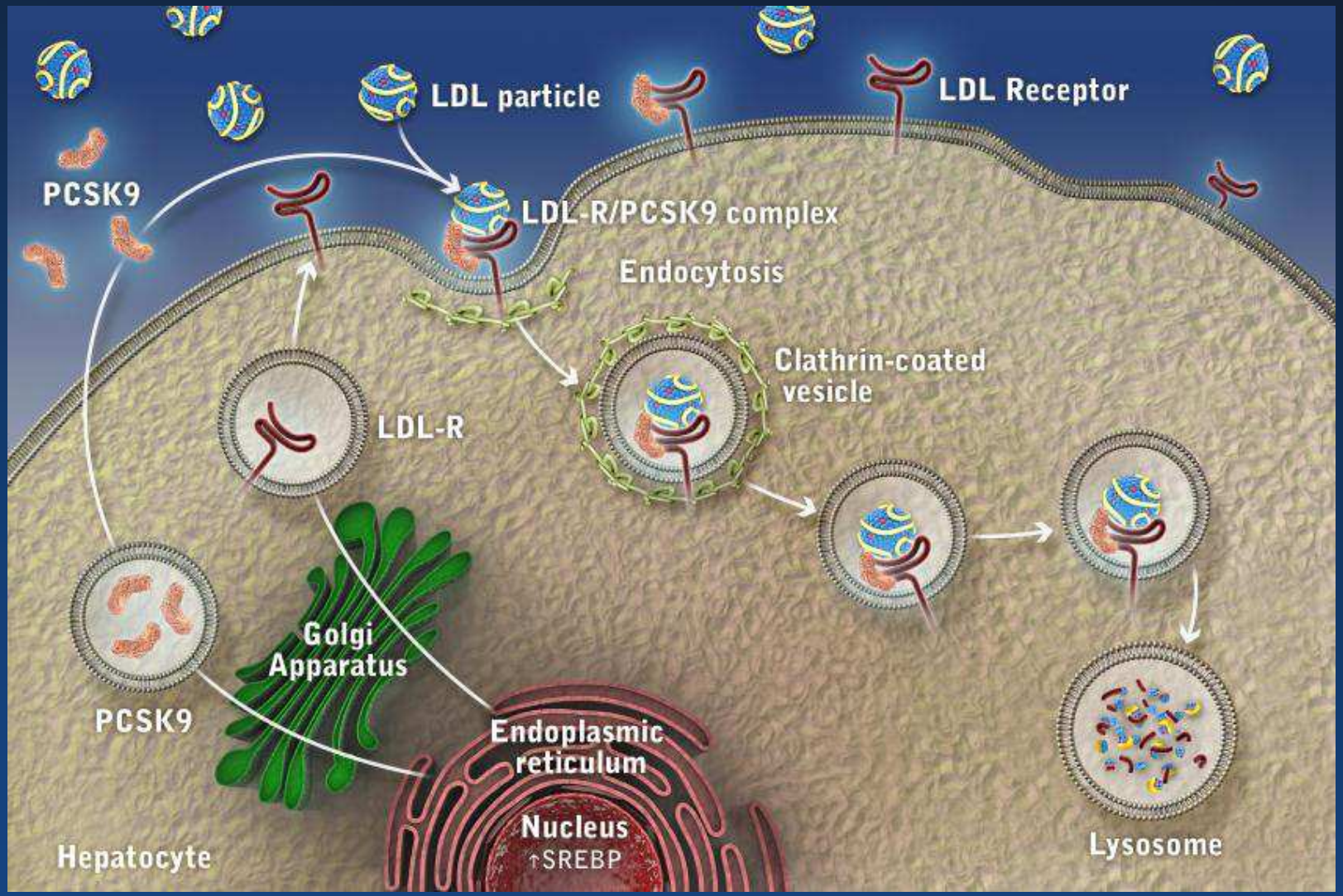
Blom D. N Engl J Med 2014

Función del Receptor LDL y su ciclo de vida



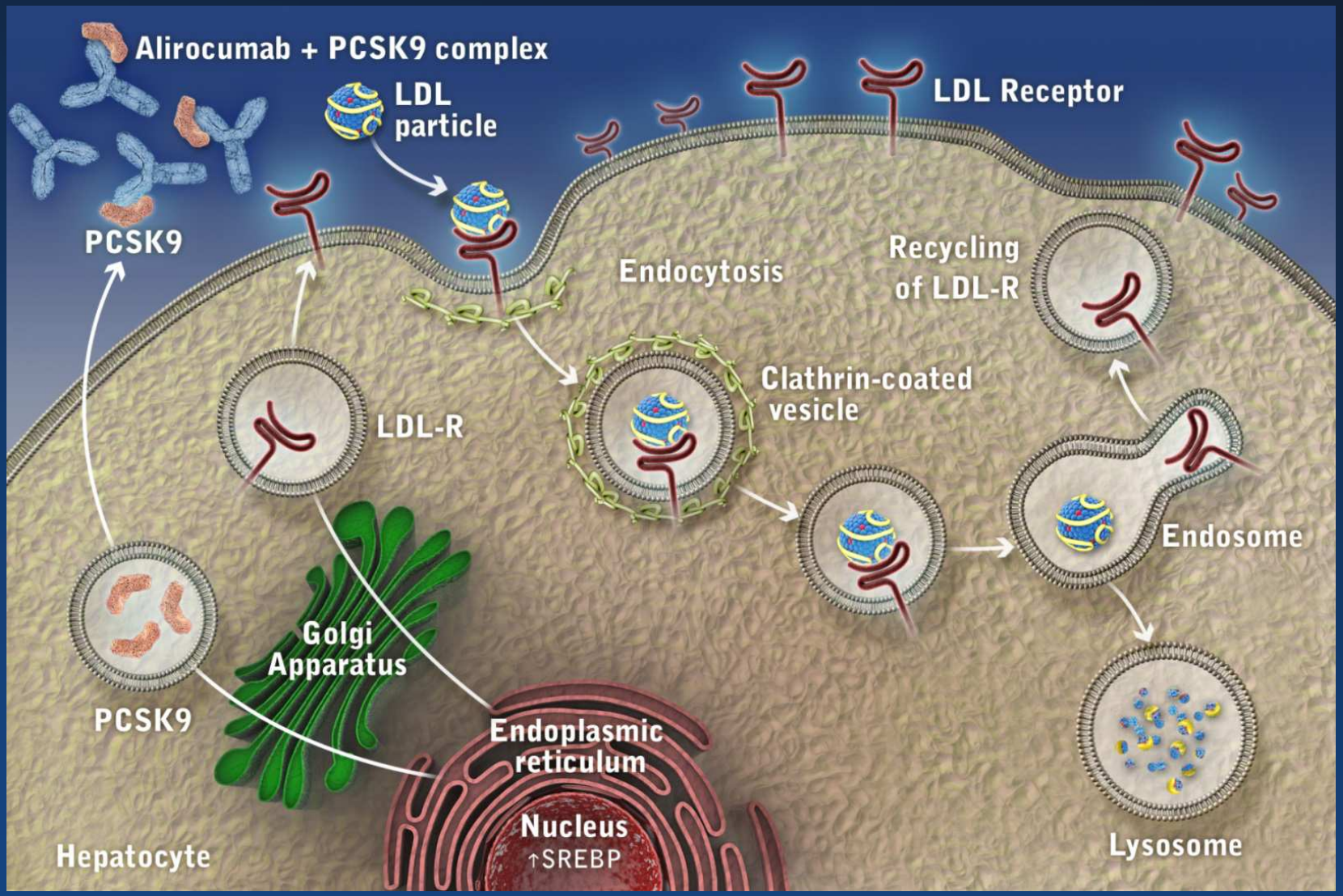
LDL=low-density lipoprotein; LDLR=LDL receptor; SREBP2=sterol regulatory element-binding protein-2.
Source: Semenkovich CF et al. In: *Williams Textbook of Endocrinology*. 12th ed. Philadelphia, PA: Elsevier Saunders; 2011:1633-1674.

El rol del PCSK9 en la regulación de la expresión del Receptor LDL



LDL=low-density lipoprotein; LDLR=LDL receptor; PCSK9=proprotein convertase subtilisin/kexin type 9; SREBP2=sterol regulatory element-binding protein-2.
Source: Lambert G et al. *J Lipid Res.* 2012;53:2515–2524.

Impacto de Alirocumab en la expresión del Receptor LDL

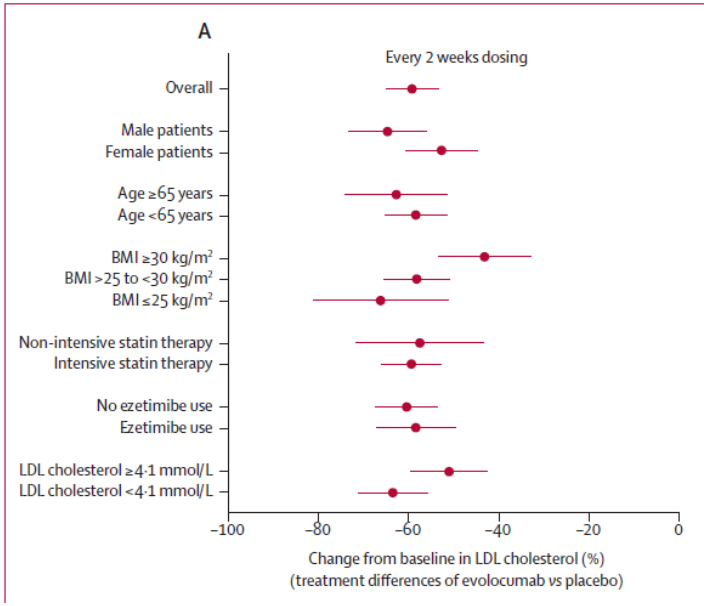


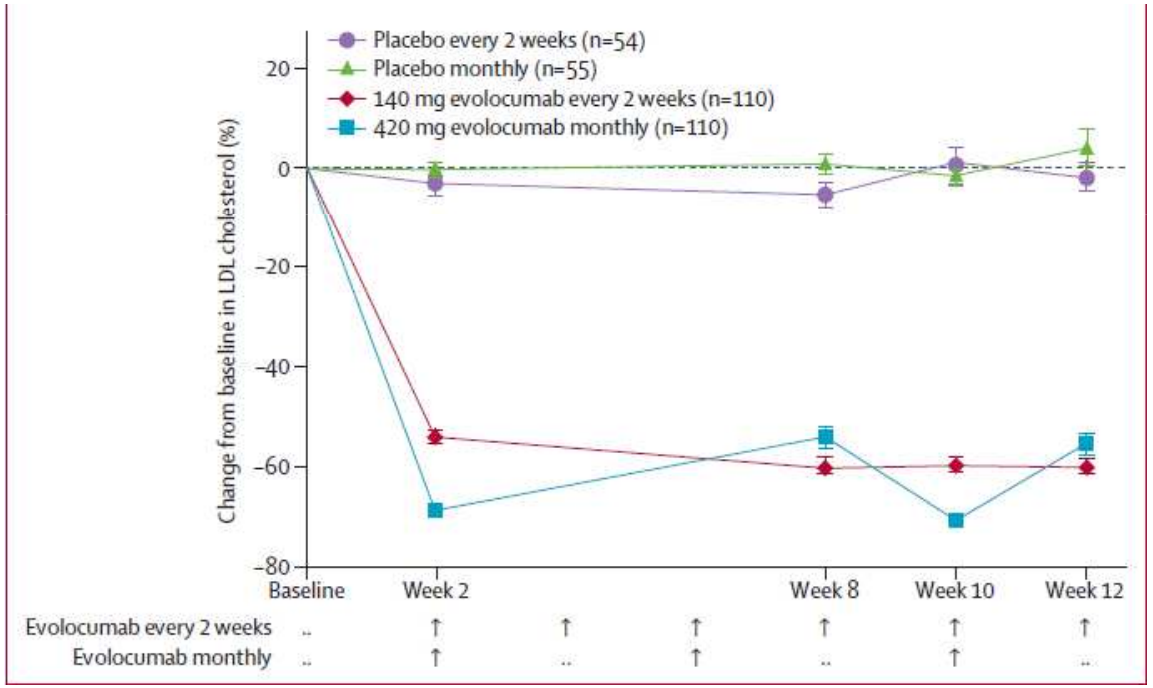
LDL=low-density lipoprotein; LDLR=LDL receptor; PCSK9=proprotein convertase subtilisin/kexin type 9; SREBP2=sterol regulatory element-binding protein-2.
Source: Catapano AL and Papadopoulos N. *Atherosclerosis*. 2013;228(1):18-28.

PCSK9 inhibition with evolocumab (AMG 145) in heterozygous familial hypercholesterolaemia (RUTHERFORD-2): a randomised, double-blind, placebo-controlled trial

	Placebo every 2 weeks (n=54)	Evolocumab 140 mg every 2 weeks (n=110)
Age (years)	51·1 (14·2)	52·6 (12·3)
Female sex	25 (46%)	44 (40%)
Coronary artery disease	16 (30%)	38 (35%)
LDL cholesterol at baseline (mmol/L)*	3·9 (0·9) 154	4·2 (1·3) 162

LDL-C final **68**





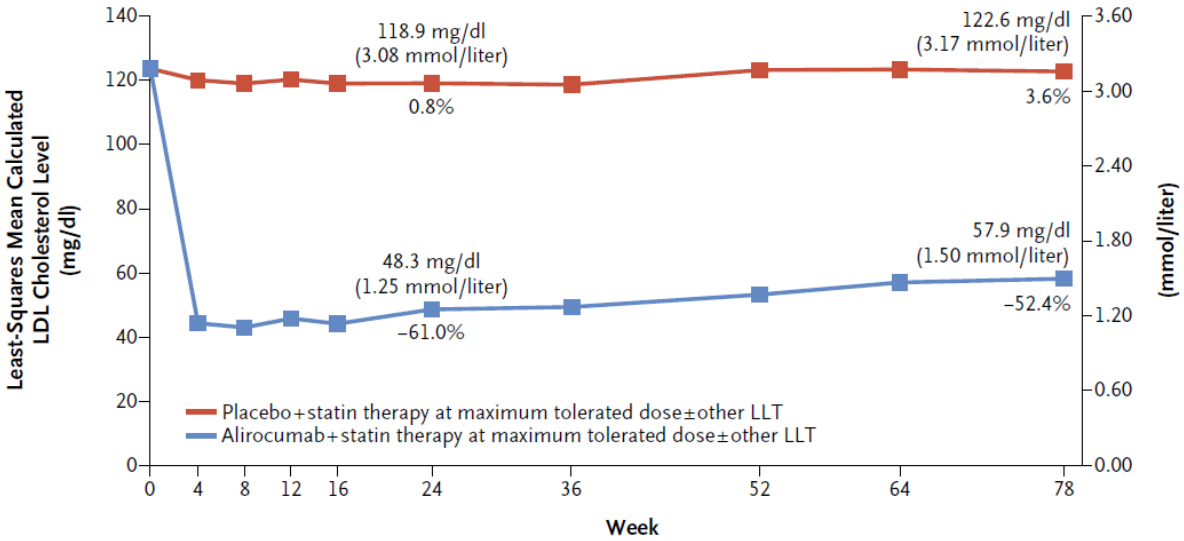
No diferencias según tipo de mutación, o si existe mutación conocida o no

Raal F. Lancet 2015

Efficacy and Safety of Alirocumab in Reducing Lipids and Cardiovascular Events

ODYSSEY LONG TERM

Heterozygous familial hypercholesterolemia — no. (%)§	276 (17.8)	139 (17.6)
Coronary heart disease — no. (%)	1055 (67.9)	552 (70.1)
Coronary heart disease risk equivalent — no. (%)¶	639 (41.1)	323 (41.0)
Type 2 diabetes — no. (%)	542 (34.9)	267 (33.9)
Current smoker — no. (%)	325 (20.9)	159 (20.2)
Lipid-modifying medications — no. (%)		
Any statin	1552 (>99.9)	787 (99.9)
High-dose statin‖	727 (46.8)	368 (46.7)
Other lipid-lowering therapy	437 (28.1)	220 (27.9)
Ezetimibe	216 (13.9)	118 (15.0)
Lipid and lipoprotein levels — mg/dl		
Calculated LDL cholesterol**		
Mean	122.7±42.6	121.9±41.4



Robinson J. N Engl J Med 2015

Efficacy and Safety of Evolocumab in Reducing Lipids and Cardiovascular Events

OSLER 1 Y OSLER 2

Efficacy and Safety of Alirocumab in Reducing Lipids and Cardiovascular Events

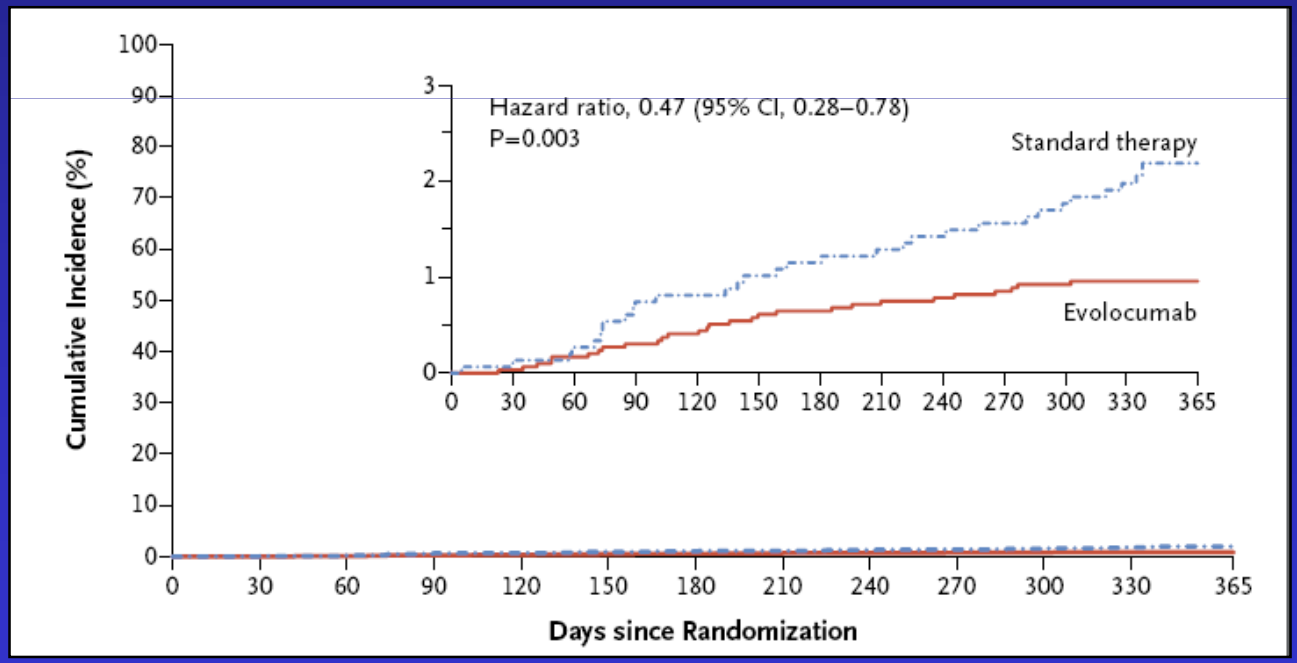
ODYSSEY LONG TERM

Eventos cardiovasculares

Prevención 2ª + HFH + alto RCV

LDL-C basal 120 mg/dl

LDL-C final 48 mg/dl



Robinson J. N Engl J Med 2015

Sabatine MS. N Engl J Med 2015

PCSK9 inhibidores

Evolocumab (Repatha)

140 mg sc cada 15 días

4944 eu/año

Arilocumab (Praluent)

75-150 mg sc cada 15 días

Uso compasivo

-**Prevención secundaria (CI, ACV, Emf. arterial periférica) con LDL >100 con dosis máxima tolerada de estatinas**

-**Pacientes con HF homocigota con LDL >100 con dosis máxima tolerada de estatinas**

- **Pacientes con HF heterocigotacon LDL >100 con dosis máxima tolerada de estatinas**

- **Preveción 2ª o HFH con LDL >100 mg/dl e intolerancia o contraindicación a estatinas**

SEGURIDAD

% (n) **of patients** All patients on background of max tolerated statin ± other lipid-lowering therapy	**Alirocumab (n=1550)**	**Placebo (n=788)**
Treatment-emergent local injection site reactions	**5.8%** (90)	**4.3%** (34)
General allergic reaction events	**9.0%** (140)	**9.0%** (71)
Neurological events‡	**4.2%** (65)	**3.9%** (31)
Neurocognitive disorders‡	**1.2%** (18)	**0.5%** (4)
Ophthalmological events‡	**2.5%** (38)	**1.9%** (15)
Haemolytic anaemia	**0**	**0**

OTROS EFECTOS SECUNDARIOS FRECUENTES

Nasopharyngitis (10.5%), upper respiratory tract infection (9.3%), influenza (7.5%)

Neurocognitive Adverse Events

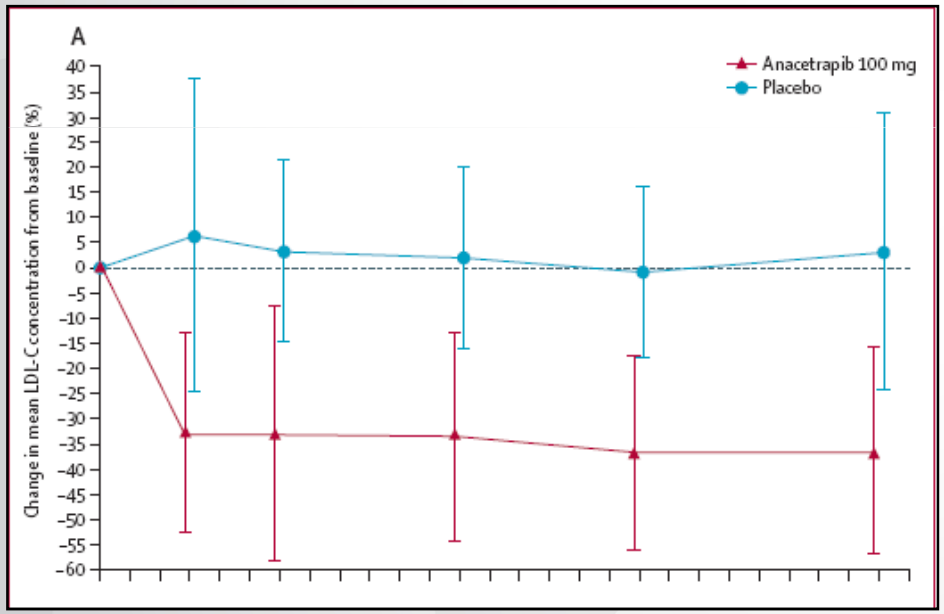
% (n) of patients All patients on background of max tolerated statin ± other lipid-lowering therapy	**Alirocumab (n=1550)**	**Placebo (n=788)**
Any neurocognitive disorder†	**1.2%** (18)	**0.5%** (4)
Amnesia	**0.3%** (5)	**0%** (0)
Memory impairment	**0.3%** (5)	**0.1%** (1)
Confusional state	**0.3%** (4)	**0.1%** (1)
Confusion postoperative	**<0.1%** (1)	**0%** (0)
Dementia	**<0.1%** (1)	**0.1%** (1)
Disorientation	**<0.1%** (1)	**0%** (0)
Disturbance in attention	**<0.1%** (1)	**0.1%** (1)
Frontotemporal dementia	**<0.1%** (1)	**0%** (0)
Transient global amnesia	**<0.1%** (1)	**0%** (0)

No en relación a niveles finales de LDL-C

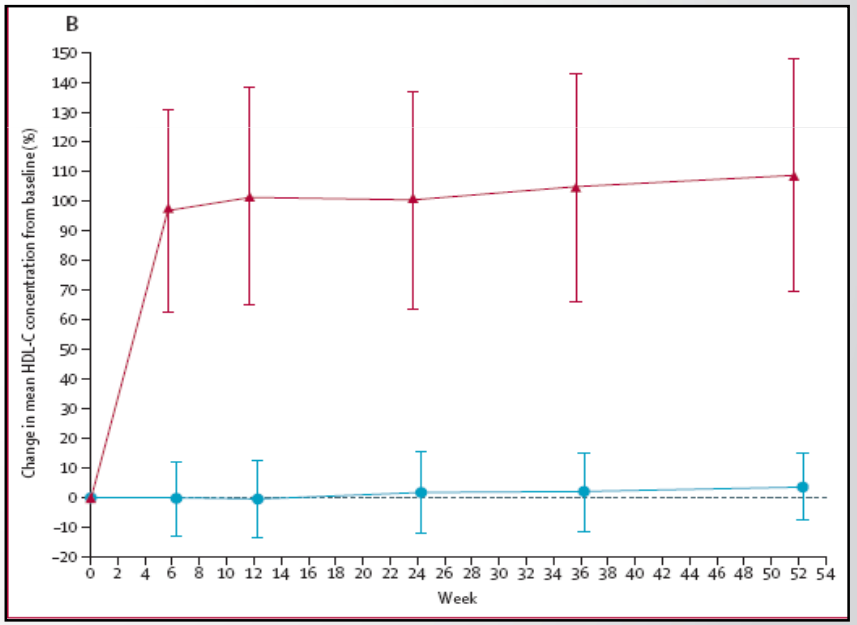
Anacetrapib as lipid-modifying therapy in patients with heterozygous familial hypercholesterolaemia (REALIZE): a randomised, double-blind, placebo-controlled, phase 3 study

Inhibidor de la proteina transportadora esteres de coleterol (CETP)

LDL-C



HDL-C



Use of concomitant lipid-lowering treatment		
Statin only	46 (23%)	25 (25%)
Statin with ezetimibe	145 (71%)	73 (72%)
Other	13 (6%)	4 (4%)

Torcetrapib

Kastelein JP. Lancet 2015

Nous fàrmacs en el tractament de les dislipèmies.

CAT SALUT

GRACIAS ¡¡¡

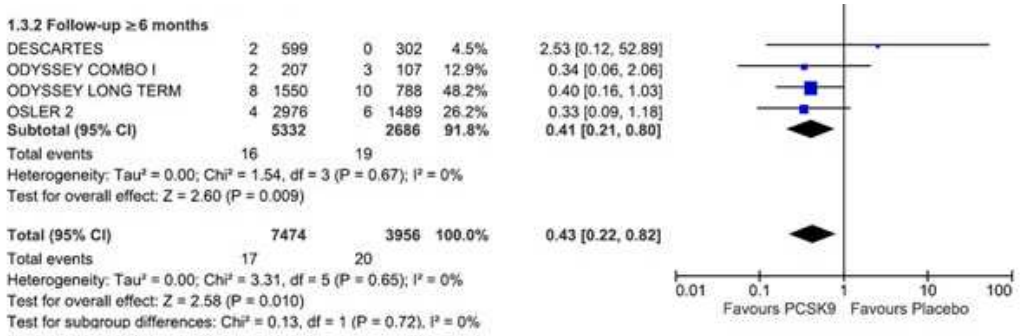
SEGURIDAD

Event	Alirocumab (N=1550)	Placebo (N=788)	P Value¨
Summary of adverse events — no. of patients (%)			
Any adverse event	1255 (81.0)	650 (82.5)	0.40
Serious adverse event	290 (18.7)	154 (19.5)	0.66
Adverse event leading to study-drug discontinuation	111 (7.2)	46 (5.8)	0.26
Adverse event leading to death	8 (0.5)	10 (1.3)	0.08
Other adverse events of interest			
General allergic reaction — no. of patients (%)	156 (10.1)	75 (9.5)	0.71
Local injection-site reaction — no. of patients (%)	91 (5.9)	33 (4.2)	0.10
Myalgia — no. of patients (%)	84 (5.4)	23 (2.9)	0.006
Neurologic event — no. of patients (%)§	65 (4.2)	35 (4.4)	0.83
Neurocognitive disorder — no. of patients (%)¶	18 (1.2)	4 (0.5)	0.17
Amnesia	5 (0.3)	0	0.17
Memory impairment	4 (0.3)	1 (0.1)	0.67
Confusional state	4 (0.3)	1 (0.1)	0.67

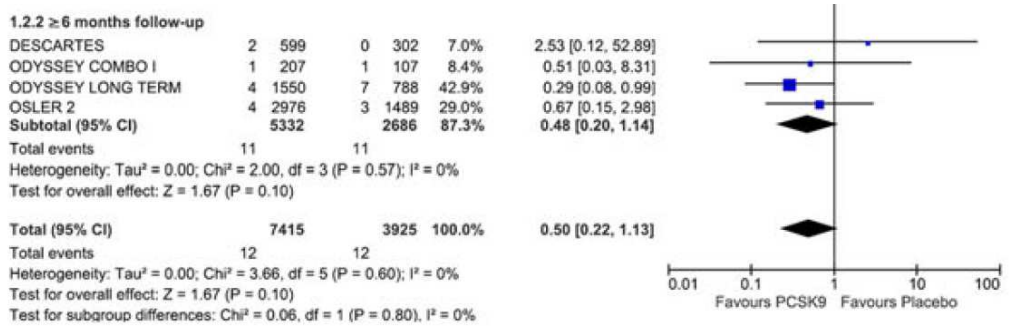
Robinson J. N Engl J Med 2015

Metanálisis eventos CV de PCSK9 en dislipemia familiar

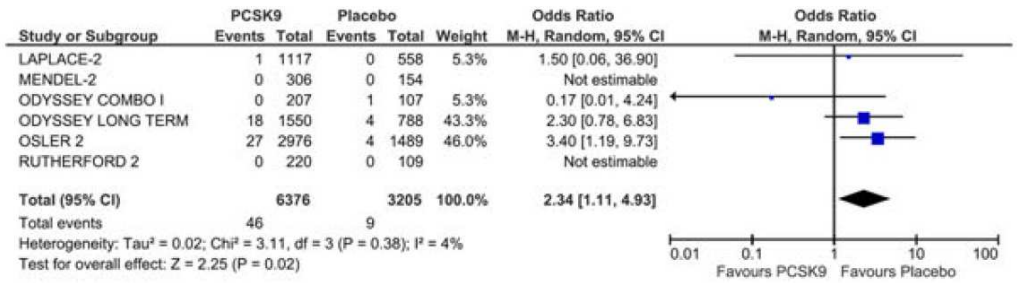
Mortalidad Total



Mortalidad cardiovascular

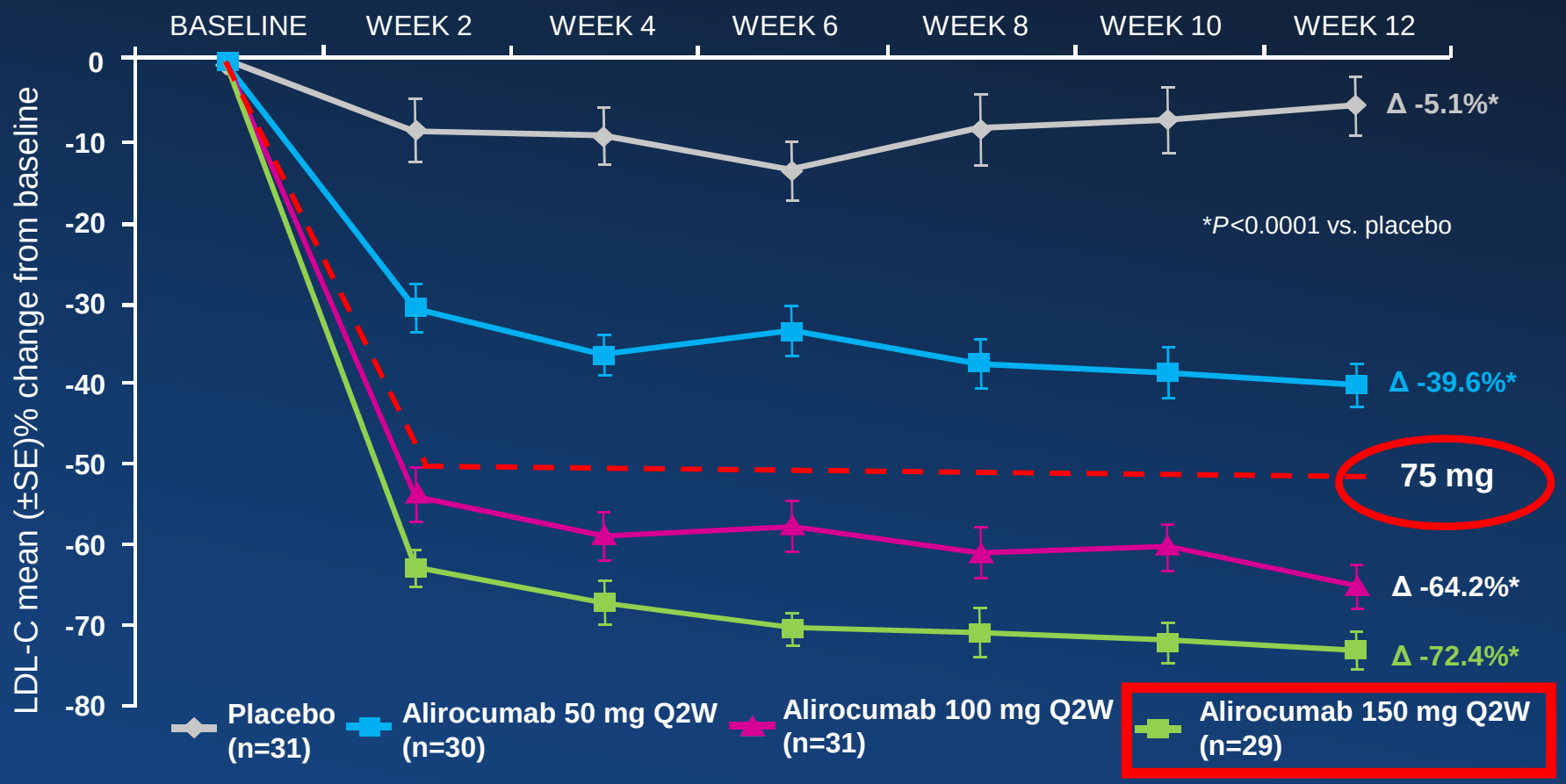


Efectos adversos neurocognitivos



Lipinski MJ. Eur Heart J 2016

Efectos en el cLDL al añadir ALIROCUMAB cada 2 semanas a Atorvastatina



Patients with LDL-C ≥100 mg/dL on stable atorvastatin dose (10 mg, 20 mg, or 40 mg) for at least 6 weeks.
Primary efficacy endpoint: % change in LDL-C from baseline to week 12; *P<0.0001 vs. placebo.

McKenney JM et al. *J Am Coll Cardiol.* 2012;59:2344-2353.

Estudios en pacientes con Hipercolesterolemia Familiar

ODYSSEY FH I
ODYSSEY FH II
ODYSSEY HIGH FH

Características basales

All patients on background of max-tolerated statin ± other lipid-lowering therapy	FH I		FH II		HIGH FH	
	Alirocumab (N=323)	**Placebo** (N=163)	**Alirocumab** (N=167)	**Placebo** (N=82)	**Alirocumab** (N=72)	**Placebo** (N=35)
Diagnosis of HeFH*, % (n) Genotyping Clinical criteria	 **39.9%** (129) **59.8%** (193)†	 **38.0%** (62) **62.0%** (101)	 **70.1%** (117) **29.9%** (50)	 **81.7%** (67) **18.3%** (15)	 **19.4%** (14) **80.6%** (58)	 **14.3%** (5) **85.7%** (30)
Age, years, mean (*SD*)	**52.1** (*12.9*)	**51.7** (*12.3*)	**53.2** (*12.9*)	**53.2** (*12.5*)	**49.8** (14.2)	**52.1** (11.2)
Male, % (n)	**55.7%** (180)	**57.7%** (94)	**51.5%** (86)	**54.9%** (45)	**48.6%** (35)	**62.9%** (22)
Race, white, % (n)	**92.9%** (300)	**88.3%** (144)	**98.2%** (164)	**97.6%** (80)	**88.9%** (64)	**85.7%** (30)
BMI, kg/m^2, mean (*SD*)	**29.0** (*4.6*)	**30.0** (*5.4*)	**28.6** (*4.6*)	**27.7** (*4.7*)	**28.8** (5.2)	**28.9** (4.2)
CHD history, % (n)	**45.5%** (147)	**47.9%** (78)	**34.1%** (57)	**37.8%** (31)	**43.1%** (31)	**62.9%** (22)
Current smoker, % (n)	**12.1%** (39)	**18.4%** (30)	**21.6%** (36)	**15.9%** (13)	**16.7%** (12)	**25.7%** (9)
Hypertension, % (n)	**43.0%** (139)	**43.6%** (71)	**34.1%** (57)	**29.3%** (24)	**55.6%** (40)	**60.0%** (21)
Type 2 diabetes, % (n)	**9.6%** (31)	**15.3%** (25)	**4.2%** (7)	**3.7%** (3)	**12.5%** (9)	**17.1%** (6)

*Diagnosis of HeFH must be made either by genotyping or by clinical criteria. For those patients not genotyped, the clinical diagnosis may be based on either the Simon Broome criteria for definite FH or the WHO/Dutch Lipid Network criteria with a score of >8 points.
† In FH I, one patient was categorized as “probable” FH by clinical criteria – genotyping results for this patient are pending.

A 52-Week Placebo-Controlled Trial of Evolocumab in Hyperlipidemia

PROPROTEIN CONVERTASE SUBTILISIN/KEXIN type 9 (PCSK9), a serine protease that is produced predominantly in the liver, is secreted into the plasma and plays a major role in regulating levels of low-density lipoprotein (LDL) cholesterol by binding to hepatic LDL receptors and promoting their degradation.[1,2] In short-term (8-to-12-week),

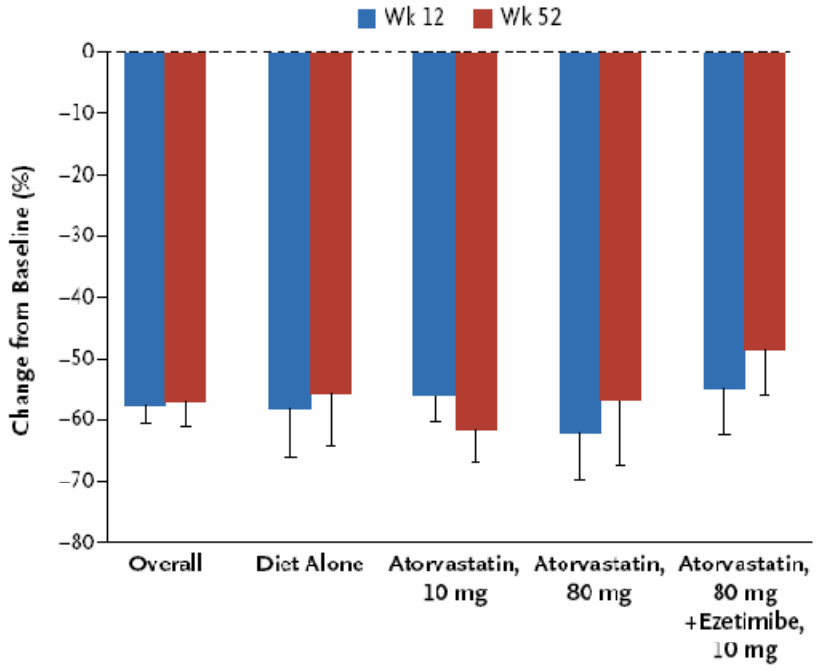


Figure 2. Percent Reduction from Baseline in Low-Density Lipoprotein (LDL) Cholesterol Levels in the Evolocumab Group, as Compared with the Placebo Group, at Weeks 12 and 52, According to Background Lipid-Lowering Therapy.

Blom D. N Engl J Med 2014

Lipid Medication and LDL-C at Baseline

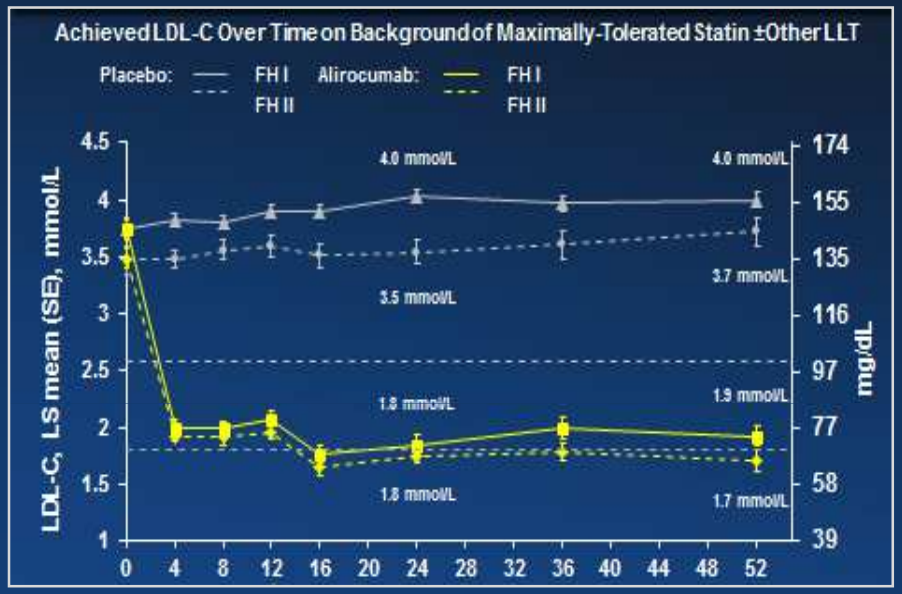
All patients on background of max-tolerated statin ± other lipid-lowering therapy	FH I		FH II		HIGH FH	
	Alirocumab (N=323)	**Placebo** (N=163)	**Alirocumab** (N=167)	**Placebo** (N=82)	**Alirocumab** (N=72)	**Placebo** (N=35)
Any statin*, % (n)	**100%**	**100%**	**100%**	**100%**	**100%**	**100%**
High-intensity statin†, % (n)	**80.8%** (261)	**82.8%** (135)	**86.2%** (144)	**87.8%** (72)	**79.2%** (57)	**80.0%** (28)
Ezetimibe, % (n)	**55.7%** (180)	**59.5%** (97)	**67.1%** (112)	**64.6%** (53)	**19.4%** (14)	**34.3%** (12)
LDL-C, mean (SD)**, mg/dL**	**144.7** (51.2)	**144.4** (46.8)	**134.6** (41.3)	**134.0** (41.6)	**196.3** (57.9)	**201.0** (43.4)

*Patients should receive either rosuvastatin 20-40 mg, atorvastatin 40-80 mg daily, or simvastatin 80 mg daily unless not tolerated and/or appropriate other dose given according to the judgement of the investigator.

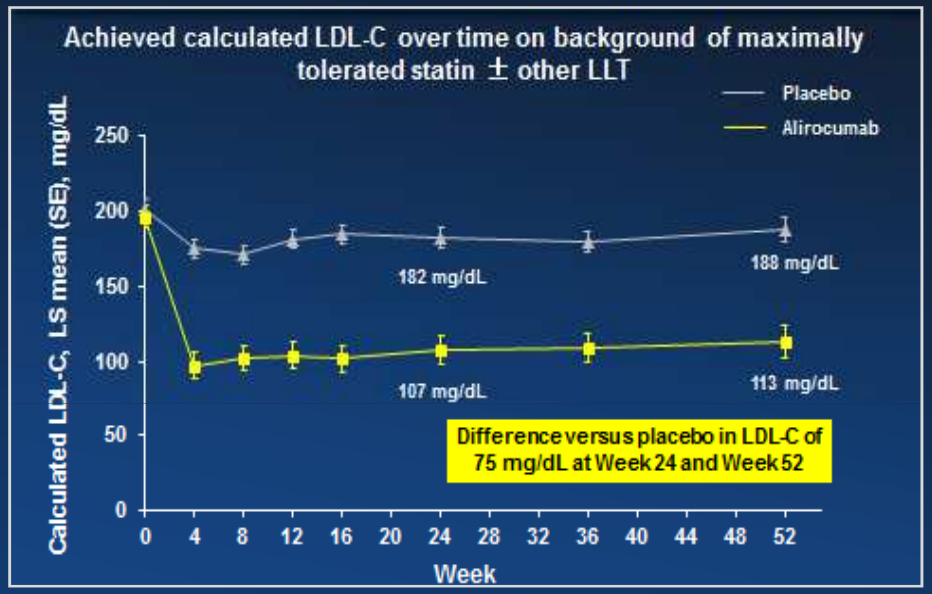
† High-intensity statin: atorvastatin 40-80 mg or rosuvastatin 20-40 mg daily.

Consistent LDL-C Reductions Over 52 Weeks

FH I and FH II



HIGH FH



- Significantly greater LDL-C ↓ vs placebo at week 24 in FH I, FH II, and HIGH FH (*P*<0.001 for all studies)
- Mean achieved LDL-C levels with alirocumab of 65.9-74.3 mg/dL at week 52 in FH I and II and 107 mg/dL at week 24 in HIGH FH
- In HIGH FH, percentage decrease from baseline informed by high baseline LDL-C (196.3 mg/dL):
  - The absolute mean decrease from baseline in LDL-C was –90.8 mg/dL at Week 24 with alirocumab versus 182 mg/dL with placebo

Safety Analysis (Pooled FH I/FH II and HIGH FH)

All Data Collected Until Last Patient Visit at Week 52

% (n) of patients All patients on background of max tolerated statin ± other lipid-lowering therapy	**Pooled FH I and FH II**		**HIGH FH**	
	Alirocumab (N=489)	**Placebo** (N=244)	**Alirocumab** (N=72)	**Placebo** (N=35)
TEAEs	**74.8%** (366)	**75.4%** (184)	**61.1%** (44)	**71.4%** (25)
Treatment-emergent SAEs	**10.0%** (49)	**9.0%** (22)	**11.1%** (8)	**11.4%** (4)
TEAEs leading to death	**0.8%** (4)	**0**	**0**	**0**
TEAEs leading to discontinuation	**3.1%** (15)	**3.7%** (9)	**4.2%** (3)	**2.9%** (1)
Adverse Events of Interest				
Adjudicated CV events*	**1.6%** (8)	**1.2%** (3)	**8.3%** (6)	**0**
Injection-site reactions	**11.5%** (56)	**9.0%** (22)	**8.3%** (6)	**2.9%** (1)
Neurocognitive disorders	**0.2%** (1)	**1.2%** (3)	**1.4%** (1)	**2.9%** (1)
ALT >3 x ULN	**2.1%** (10/488)	**1.2%** (3/244)	**4.2%** (3)	**2.9%** (1)
Creatine kinase >3 x ULN	**3.5%** (17/483)	**6.2%** (15/243)	**2.8%** (2/71)	**0**

- **4 TEAE-related deaths were all in alirocumab arm, 2 due to metastatic cancer (non-small cell lung and pancreatic), 2 due to MI (1 acute, 1 sudden cardiac death)**

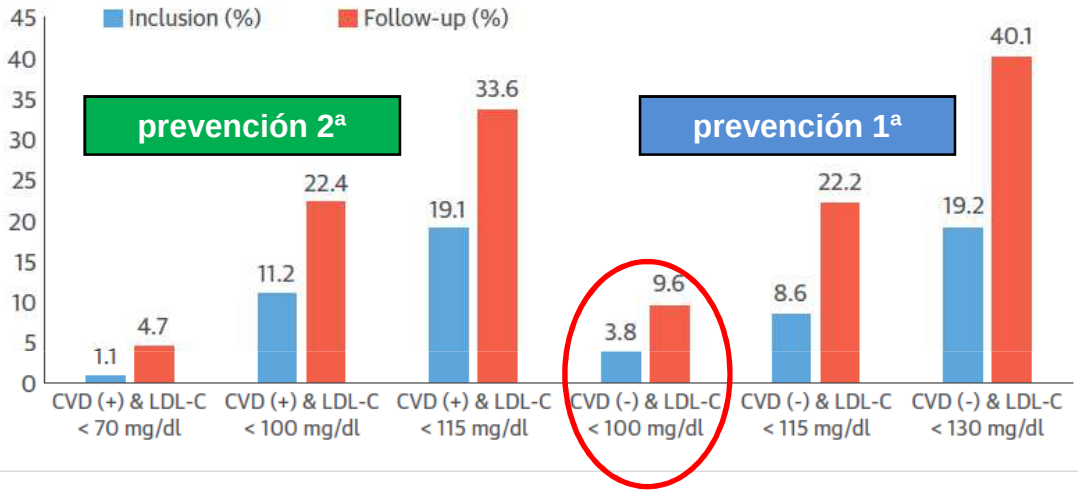
*Adjudicated CV events include all CV AEs positively adjudicated. The adjudication categories are the following: CHD death, non-fatal MI, fatal and non-fatal ischemic stroke, unstable angina requiring hospitalization, congestive heart failure requiring hospitalization, ischemia-driven revascularization procedure (PCI, CABG).
Statistical analyses have not been performed.

Estudio en pacientes intolerantes a estatinas

ODYSSEY ALTERNATIVE

Attainment of LDL-Cholesterol Treatment Goals in Patients With Familial Hypercholesterolemia

FIGURE 2 Percentage of Patients Reaching Recommended Goals

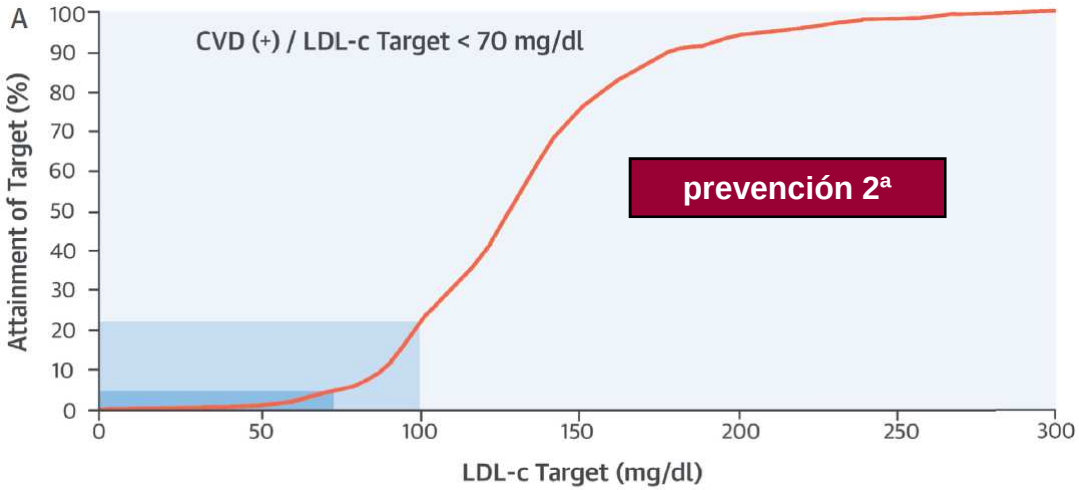


Objetivos tto

LDL-C <100 mg/dl

LDL-C < 70 prevención 2ª

A pesar de que el 78% estaban a dosis máxima de tto



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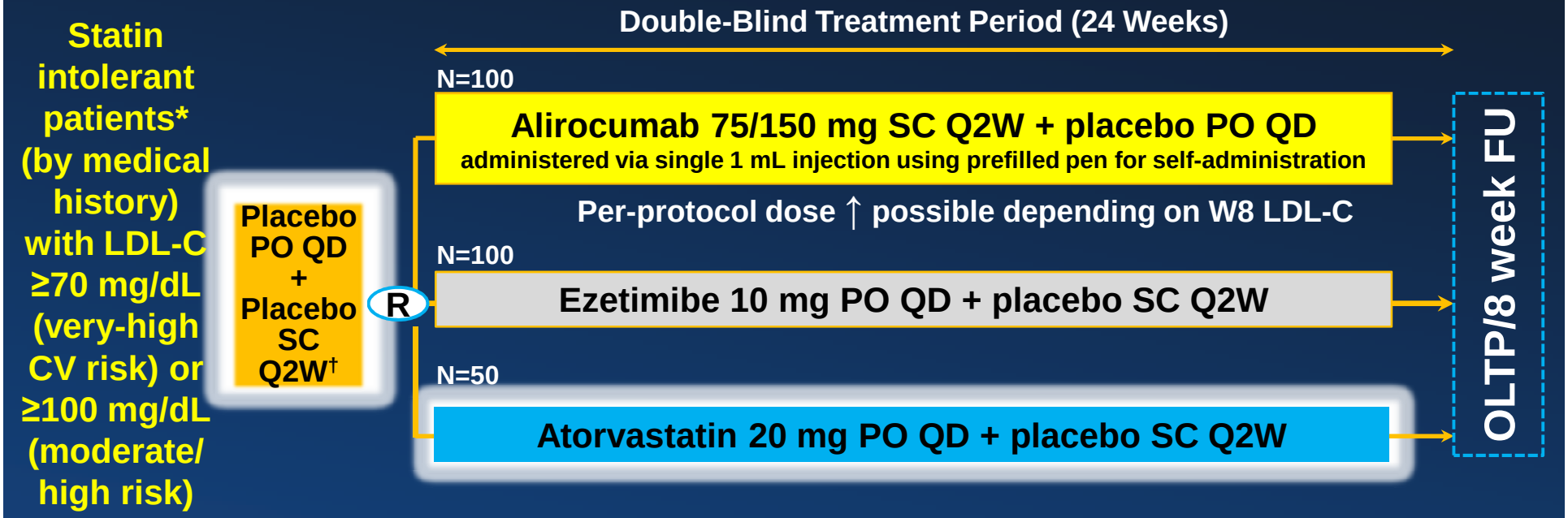
ODYSSEY ALTERNATIVE Study Design



*Unable to tolerate at least two different statins, including one at the lowest dose, due to muscle-related symptoms

†4-week single-blind placebo run-in follows 2-week washout of statins, ezetimibe and red yeast rice.
OLTP: Alirocumab open-label treatment period; W, Week.

Análisis de seguridad - ALTERNATIVE

Safety analysis from double-blind treatment period

% of patients	Alirocumab (N=126)	Ezetimibe (N=124)	Atorvastatin (N=63)
TEAEs*	82.5%	80.6%	85.7%
Treatment-emergent SAEs	9.5%	8.1%	11.1%
TEAEs leading to death	0	0	0
TEAEs leading to discontinuation	18.3%	25.0%	25.4%
Any skeletal-muscle related TEAE†	32.5%	41.1%	46.0%
HR (95% CI) alirocumab vs comparator	-	0.71 (95% CI: 0.47 to 1.06)	0.61 (95% CI: 0.38 to 0.99)
P-value vs alirocumab‡	-	0.096	0.042
Skeletal-muscle related TEAE leading to discontinuation	15.9%	20.2%	22.2%
HR (95% CI) alirocumab vs comparator	-	0.78 (95% CI: 0.43 to 1.41)	0.67 (95% CI: 0.34 to 1.32)
P-value vs alirocumab‡	-	0.409	0.240

*TEAE (treatment emergent adverse event) period = time from first to last injection of study treatment + 70 days.
SAE=serious adverse event.
† Pre-defined category including myalgia, muscle spasms, muscular weakness, musculoskeletal stiffness, muscle fatigue.
‡ Although not pre-planned analysis, the *P*-value is shown for descriptive purposes.

Estudio de eficacia y seguridad en pacientes de alto RCV e HFHe

ODYSSEY LONG-TERM

Características basales

All patients on background of max-tolerated statin ± other lipid-lowering therapy	Alirocumab (n=1553)	Placebo (n=788)
Age, years, mean (*SD*)	**60.4** (*10.4*)	**60.6** (*10.4*)
Male, % (n)	**63.3%** (983)	**60.2%** (474)
Race, White	**92.8%** (1441)	**92.6%** (730)
BMI, kg/m^2, mean (*SD*)	**30.2** (*5.7*)	**30.5** (*5.5*)
HeFH, % (n)	**17.8%** (276)	**17.6%** (139)
CHD history, % (n)	**67.9%** (1055)	**70.1%** (552)
Type 2 diabetes, % (n)	**34.9%** (542)	**33.9%** (267)
Any statin*, % (n)	**99.9%** (1552)	**99.9%** (787)
High-intensity statin†, % (n)	**44.4%** (690)	**43.4%** (342)
Any LLT other than statins, % (n)	**28.1%** (437)	**27.9%** (220)
Ezetimibe, % (n)	**13.9%** (216)	**15.0%** (118)
LDL-C, calculated mean (*SD*)**, mg/dL**	**122.7** (*42.6*)	**121.9** (*41.4*)

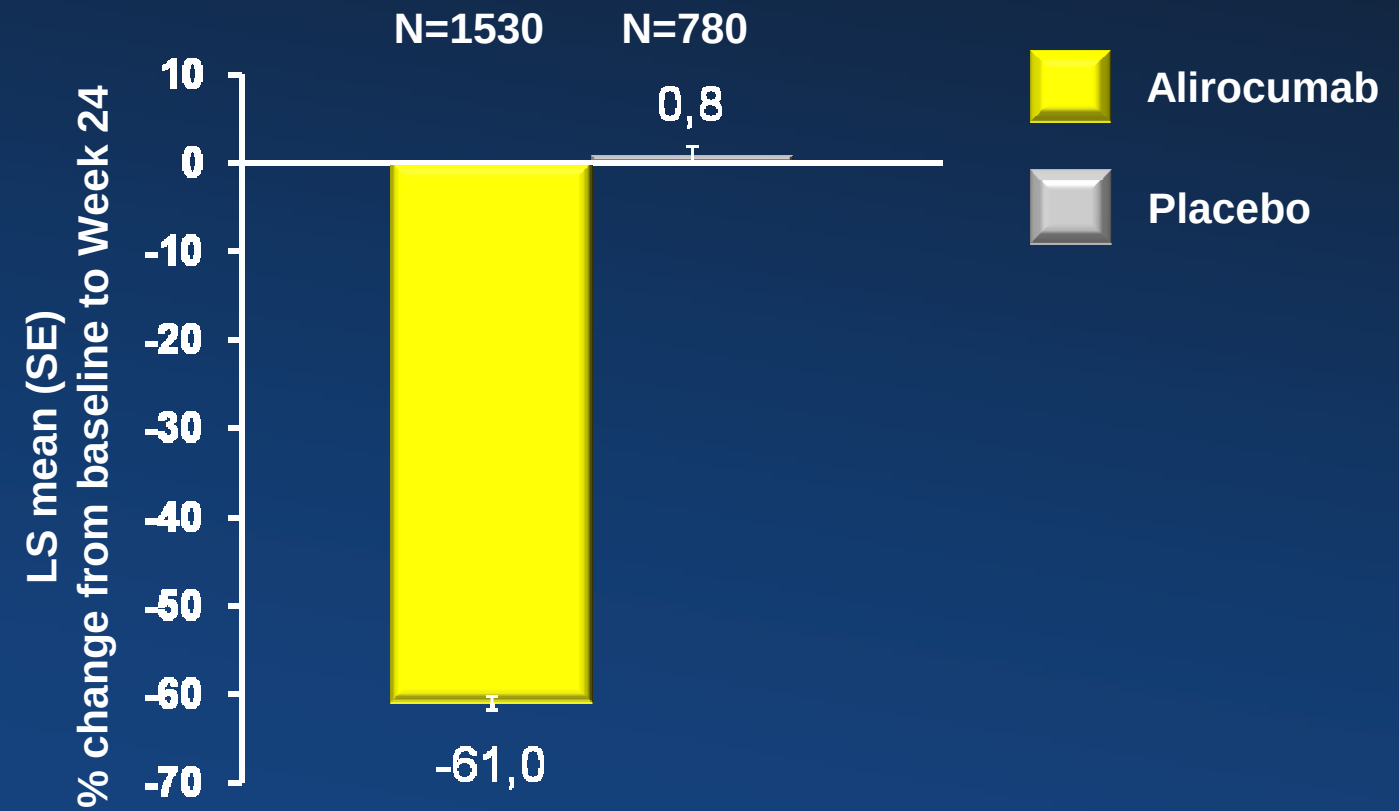
*Patients should receive either rosuvastatin 20-40 mg, atorvastatin 40-80 mg daily, or simvastatin 80 mg daily unless not tolerated and/or appropriate other dose given according to the judgement of the investigator.

† High-intensity statin: atorvastatin 40-80 mg or rosuvastatin 20-40 mg daily.

Alirocumab Significantly Reduced LDL-C from Baseline to Week 24 versus Placebo

Primary Endpoint: Percent Change from Baseline to Week 24 in LDL-C

All patients on background of maximally-tolerated statin ± other lipid-lowering therapy



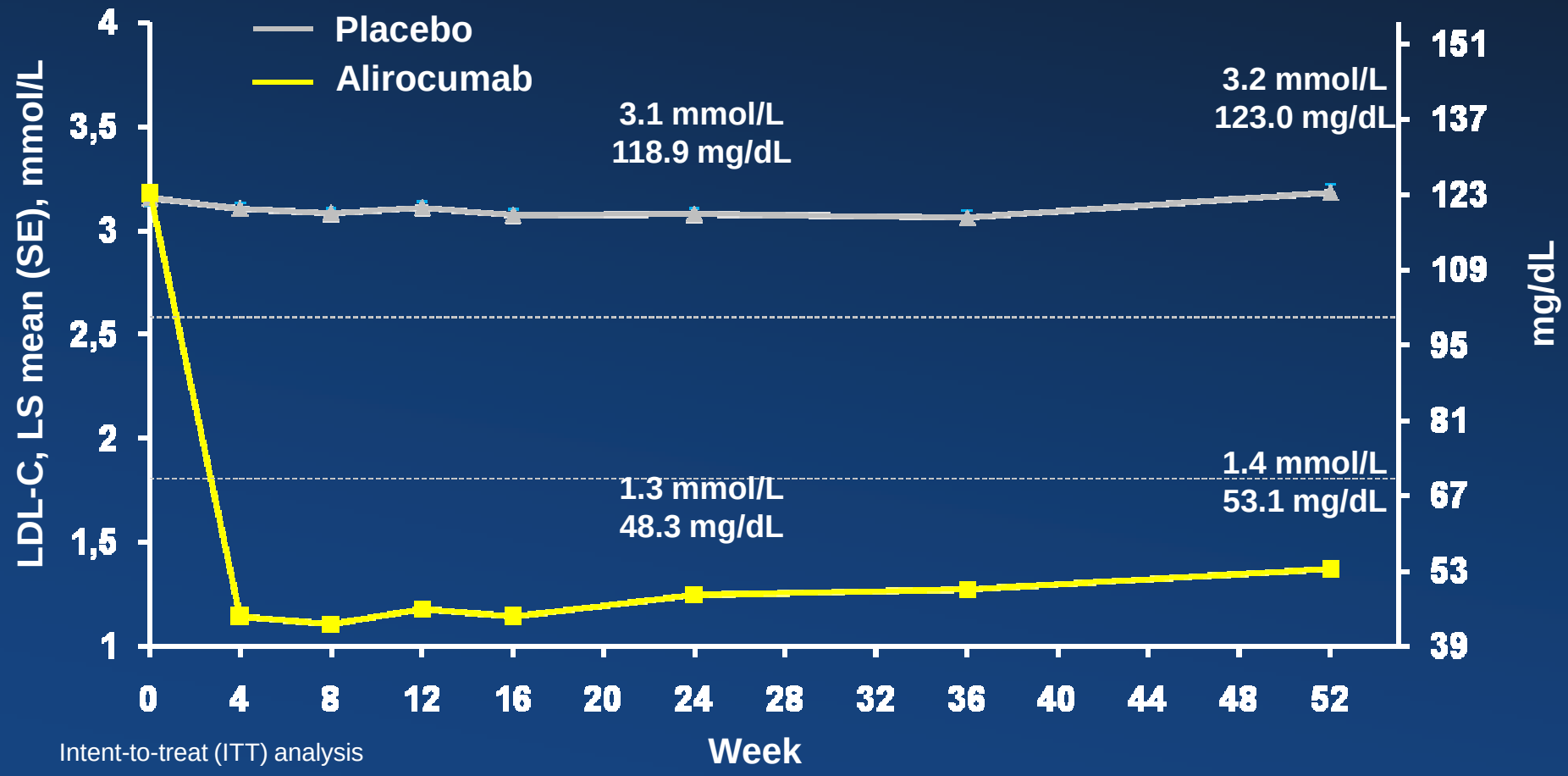
LS mean difference (SE) versus placebo:
−61.9% (1.3); *P*<0.0001

Intent-to-treat (ITT) analysis

Alirocumab Maintained Consistent LDL-C Reductions Over 52 Weeks

Achieved LDL-C Over Time

All patients on background of maximally tolerated statin ±other lipid-lowering therapy



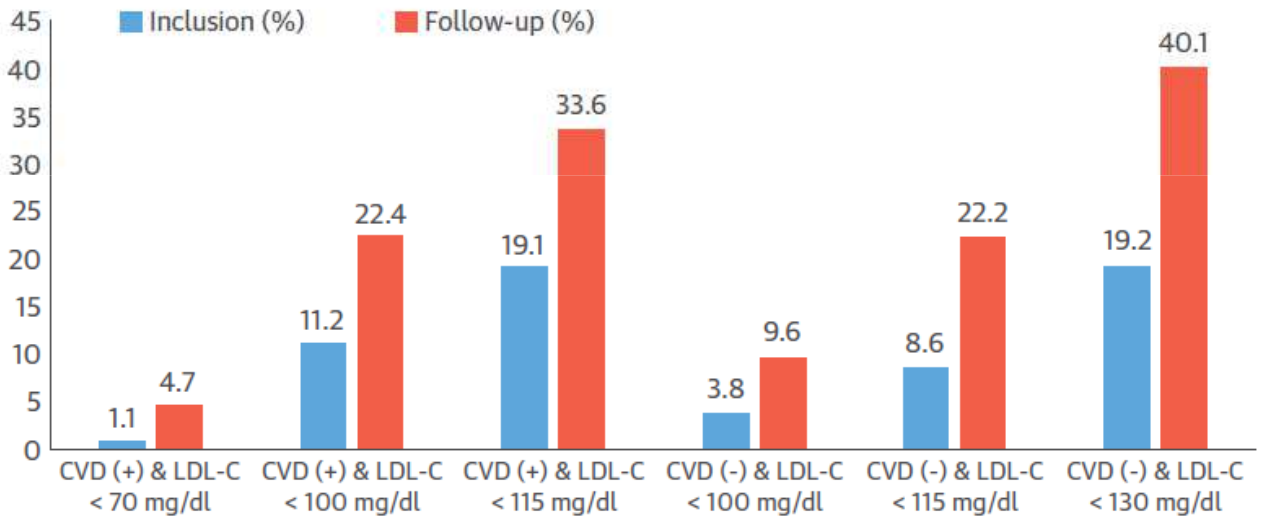
Intent-to-treat (ITT) analysis

Despite the clinical improvement, the proportion of subjects achieving an LDL cholesterol level <100 mg/dl (<2.6 mmol/l) was low throughout the study, increasing from 4.7% at baseline to only 11.2% at

The SAFEHEART investigators followed 2,170 genotyped HeFH patients (mean age, 45 years and ~45% male) for a mean of 5.1 years. Approximately

ictors of goal attainment included the betes, the absence of previous athero- he use of ezetimibe, and the presence defective mutation (9). Better goal

FIGURE 2 Percentage of Patients Reaching Recommended Goals



Although plasma low-density lipoprotein cholesterol (LDL-C) concentration decreased at follow-up, LDL-C goals, as defined by recent international recommendations on familial hypercholesterolemia (FH), were reached in <10% of cases. Nevertheless, there was an increase in the percentage of subjects who reached recommended goals at follow-up compared with at study entry, whether the patient had a history of atherosclerotic cardiovascular disease (CVD [+]) or had no such history (CVD [−]).

Perez de Isla L. J Am Coll Cardiol 2016

TEAEs of Interest Comparable in Patients With 2 Consecutive LDL-C < 0.65 mmol/L (25 mg/dL)

% (n) of patients All pts on background of maximally tolerated statin ± other lipid-lowering therapy	**Alirocumab (n=1550)**	**Alirocumab with 2 consecutive LDL-C <25 mg/dL (n=562)**	**Placebo (n=788)**
General allergic reaction events	**9.0%** (140)	**6.0%** (34)	**9.0%** (71)
Treatment-emergent local injection site reactions	**5.8%** (90)	**3.7%** (21)	**4.3%** (34)
Neurological events‡	**4.2%** (65)	**1.8%** (10)	**3.9%** (31)
All cardiovascular events†	**4.0%** (62)	**3.2%** (18)	**4.4%** (35)
Ophthalmological events‡	**2.5%** (38)	**1.8%** (10)	**1.9%** (15)
Neurocognitive disorders‡	**1.2%** (18)	**0.5%** (3)	**0.5%** (4)
Haemolytic anaemia	0	0	0

Safety Analysis (at least 52 weeks for all patients continuing treatment, including 607 patients overall who completed W78 visit)

† Confirmed by adjudication. Adjudicated CV events include all CV AEs positively adjudicated. The adjudication categories are the following: CHD death, non-fatal MI, fatal and non-fatal ischemic stroke, unstable angina requiring hospitalization, congestive heart failure requiring hospitalization, ischemia driven coronary revascularization procedure [PCI, CABG].

‡Company MedDRA Queries (CMQ).

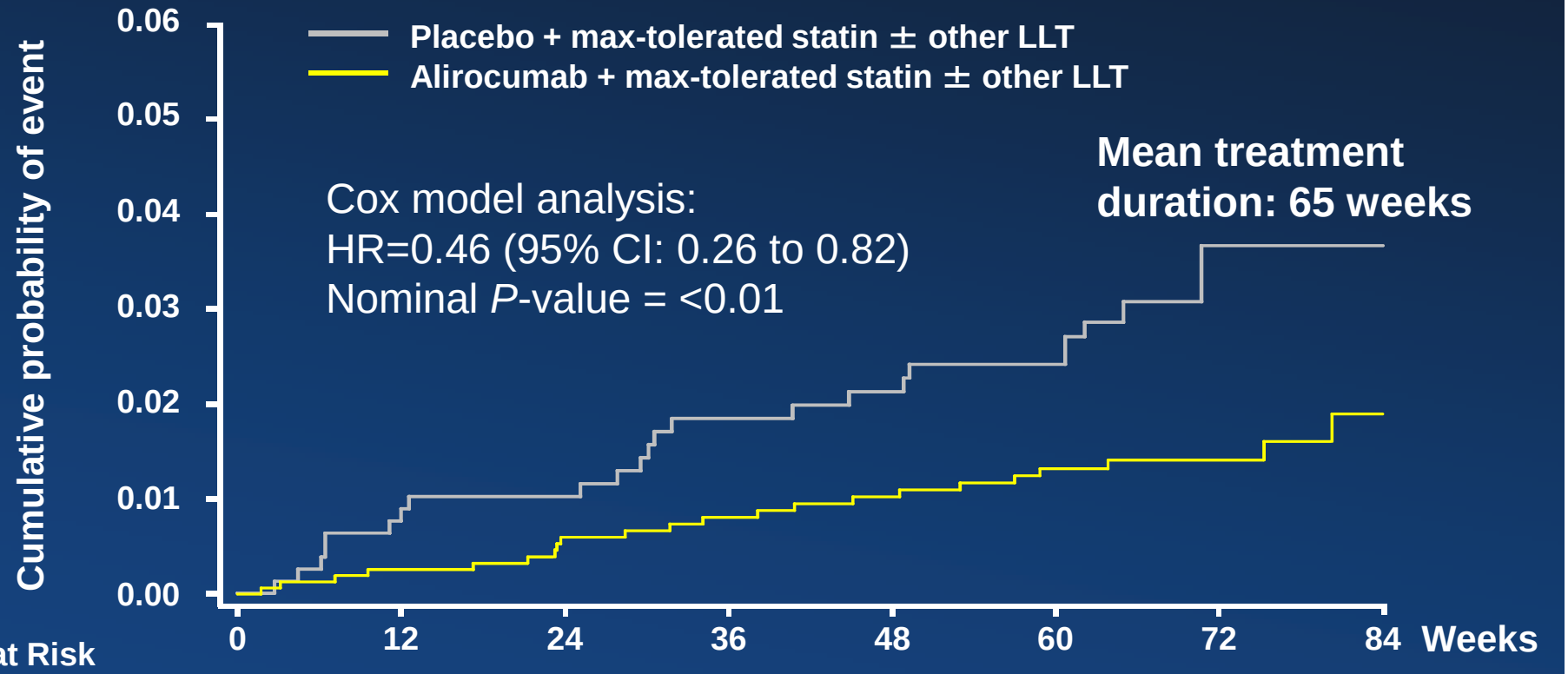
J. Robinson et al., *N Engl J Med* 2015;372(16):1489-1499

Post-hoc Adjudicated Cardiovascular TEAEs*

Safety Analysis (at least 52 weeks for all patients in ongoing study)

Kaplan-Meier Estimates for Time to First Adjudicated Major CV Event

Safety Analysis (at least 52 weeks for all patients continuing treatment, including 607 patients who completed W78 visit)



No. at Risk								
Placebo	788	776	731	703	682	667	321	127
Alirocumab	1550	1534	1446	1393	1352	1335	642	252

*Primary endpoint for the ODYSSEY OUTCOMES trial: CHD death, Non-fatal MI, Fatal and non-fatal ischemic stroke, Unstable angina requiring hospitalization. LLT=lipid-lowering therapy.

Safety Analysis
(Pool of 4x Phase 2 + 10x Phase 3 trials*)

% (n) of patients All pts on background statin	Ezetimibe-controlled pool (N=1482)		Placebo-controlled pool (N=3752)	
	Alirocumab n=864	Ezetimibe n=618	Alirocumab n=2476	Placebo n=1276
TEAEs	70.3% (607)	68.1% (421)	75.8% (1876)	76.4% (975)
Treatment-emergent SAEs	13.1% (113)	11.2% (69)	13.7% (340)	14.3% (182)
TEAEs leading to death	0.2% (2)	1.1% (7)	0.5% (13)	0.9% (11)
TEAEs leading to discontinuation	8.8% (76)	9.7% (60)	5.3% (131)	5.1% (65)
Safety terms of interest				
Adjudicated CV events†	3.1% (27)	1.9% (12)	3.6% (83)	3.5% (41)
HLT: Injection site reactions	3.0% (26)	2.1% (13)	7.3% (180)	5.2% (66)
CMQ: Neurocognitive disorders	0.9% (8)	1.0% (6)	0.8% (21)	0.7% (9)
PCSA: ALT >3 x ULN	1.1% (9/850)	0.2% (1/612)	1.7% (41/2455)	1.4% (18/1266)

*Placebo-controlled studies: phase 3 (LTS11717, FH I, FH II, HIGH FH, COMBO I), phase 2 (DFI11565, DFI11566, CL-1003, DFI12361)
Ezetimibe-controlled studies: phase 3 (COMBO II, MONO, OPTIONS I, OPTIONS II, ALTERNATIVE).
Includes all data collected to last patient visit at 52 wks for COMBO, FH, HIGH FH and LONG TERM studies.
†Includes CHD death, Non-fatal MI, Fatal and non-fatal ischemic stroke, Unstable angina requiring hospitalization, Congestive heart failure requiring hospitalization, Ischemia driven coronary revascularization procedure.
CMQ, Custom MedDRA Query; HLT, High-Level Term, PCSA, Potentially Clinically Significant Abnormalities.

ODYSSEY

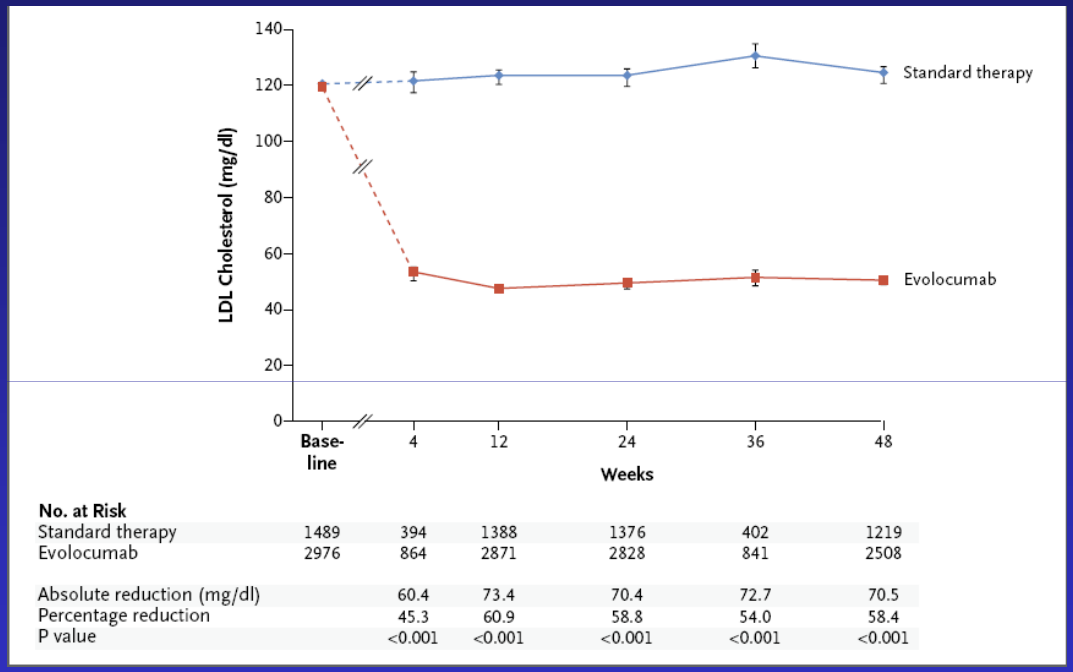
TEAEs Occurring in ≥5% Patients in Any Group (Pool of 4x Phase 2 + 10x Phase 3 trials*)

% (n) of patients All pts on background statin	Ezetimibe-controlled pool (N=1482)		Placebo-controlled pool (N=3752)	
TEAEs by preferred term in ≥5% patients	**Alirocumab n=864**	**Ezetimibe n=618**	**Alirocumab n=2476**	**Placebo n=1276**
Nasopharyngitis	5.4% (37)	5.7% (35)	11.3% (279)	11.1% (141)
Myalgia	6.7% (58)	7.6% (47)	4.2% (104)	3.4% (44)
Upper respiratory tract infection	5.9% (51)	6.0% (37)	6.1% (152)	7.0% (89)
Injection site reaction	2.9% (25)	1.9% (12)	6.7% (166)	4.8% (61)
Influenza	3.7% (32)	2.3% (14)	5.7% (141)	4.6% (59)
Headache	3.9% (34)	3.4% (21)	4.8% (119)	5.2% (66)

*Placebo-controlled studies: phase 3 (LTS11717, FH I, FH II, HIGH FH, COMBO I), phase 2 (DFI11565, DFI11566, CL-1003, DFI12361)
Ezetimibe-controlled studies: phase 3 (COMBO II, MONO, OPTIONS I, OPTIONS II, ALTERNATIVE).
Includes all data collected to last patient visit at 52 wks for COMBO, FH, HIGH FH and LONG TERM studies.

ODYSSEY

Efficacy and Safety of Evolocumab in Reducing Lipids and Cardiovascular Events



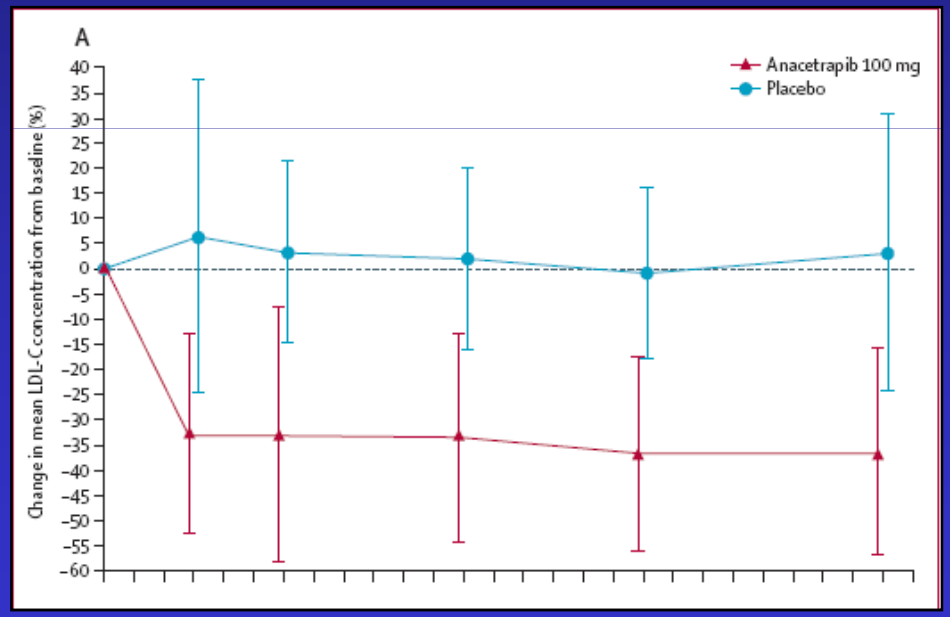
No. at Risk						
Standard therapy	1489	394	1388	1376	402	1219
Evolocumab	2976	864	2871	2828	841	2508
Absolute reduction (mg/dl)		60.4	73.4	70.4	72.7	70.5
Percentage reduction		45.3	60.9	58.8	54.0	58.4
P value		<0.001	<0.001	<0.001	<0.001	<0.001

Sabatine MS: N Engl J Med 2015

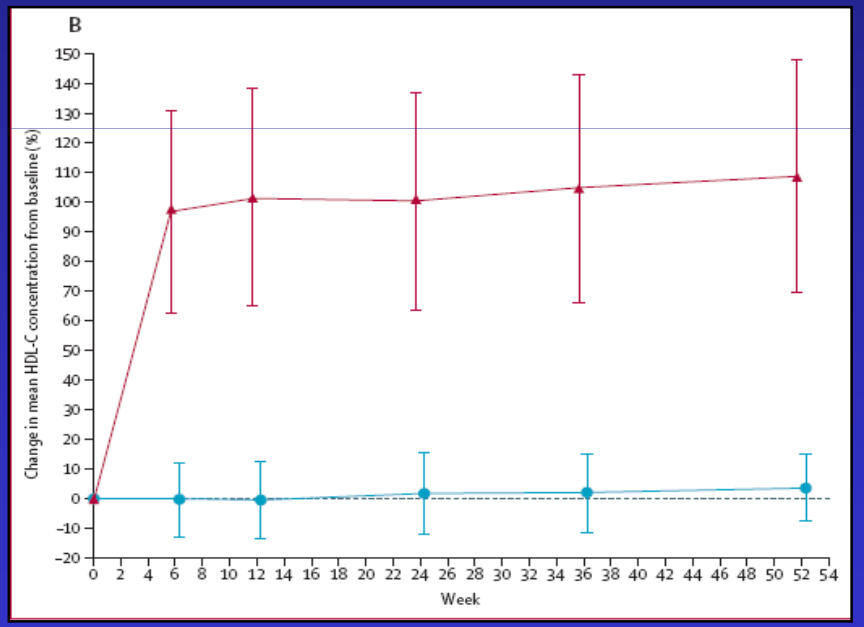
Anacetrapib as lipid-modifying therapy in patients with heterozygous familial hypercholesterolaemia (REALIZE): a randomised, double-blind, placebo-controlled, phase 3 study

Inhibidor de la proteina transportadora esteres de coleterol (CETP)

LDL-C



HDL-C



Use of concomitant lipid-lowering treatment		
Statin only	46 (23%)	25 (25%)
Statin with ezetimibe	145 (71%)	73 (72%)
Other	13 (6%)	4 (4%)

Torcetrapib

Kastelein JP. Lancet 2015

Pregunta 13 (Monitorizar CK y transa)

2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults

2a.CK should not be routinely measured in individuals receiving statin therapy.	A (Strong)	45, 49-51, 54, 55	III: No Benefit	A
2b.Baseline measurement of CK is reasonable for individuals believed to be at increased risk for adverse muscle events based on a personal or family history of statin intolerance or muscle disease, clinical presentation, or concomitant drug therapy that might increase the risk for myopathy.	E (Expert Opinion)	---	IIa	C (90)
2c.During statin therapy, it is reasonable to measure CK in individuals with muscle symptoms, including pain, tenderness, stiffness, cramping, weakness, or generalized fatigue.	E (Expert Opinion)	---	IIa	C (90)

J Am Coll Cardiol. 2014 Jul 1;63(25 Pt B):2889-934.

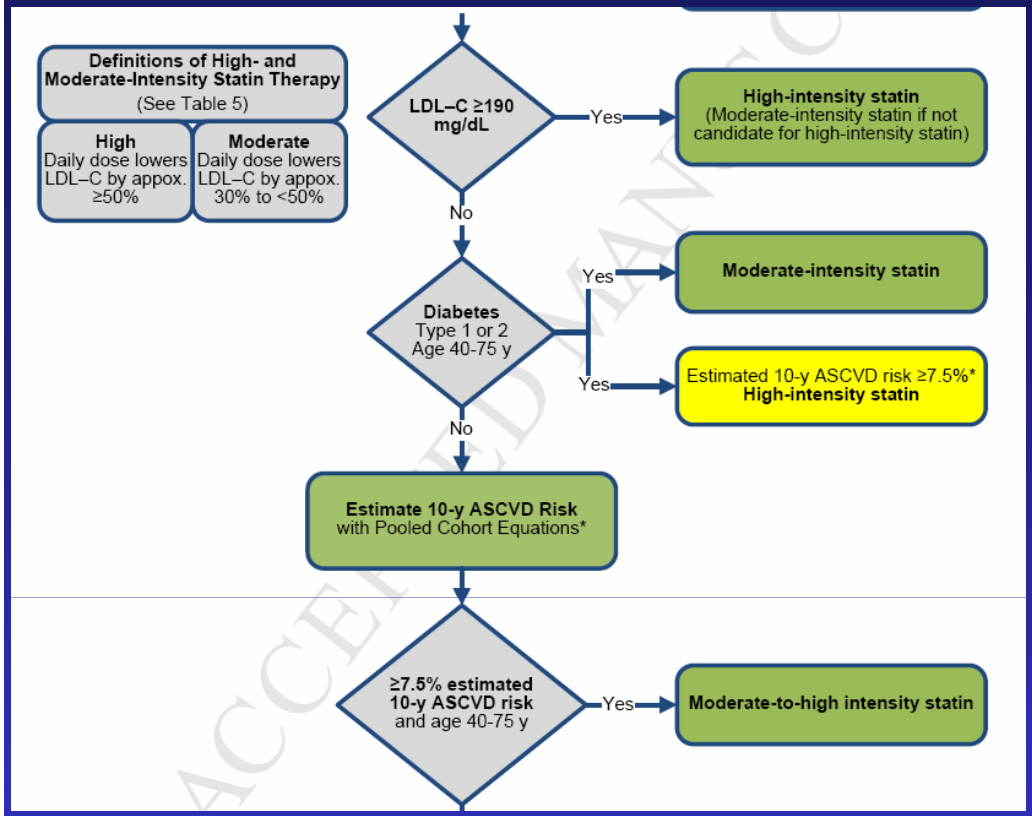
8. It is reasonable to evaluate and treat muscle symptoms, including pain, tenderness, stiffness, cramping, weakness, or fatigue, in statin-treated patients according to the following management algorithm: • To avoid unnecessary discontinuation of statins, obtain a history of prior or current muscle symptoms to establish a baseline before initiating statin therapy. • If unexplained severe muscle symptoms or fatigue develop during statin therapy, promptly discontinue the statin and address the possibility of rhabdomyolysis by evaluating CK, creatinine, and a urinalysis for myoglobinuria. • If mild to moderate muscle symptoms develop during statin therapy: – Discontinue the statin until the symptoms can be evaluated. – Evaluate the patient for other conditions that might increase the risk for muscle symptoms (e.g., hypothyroidism, reduced renal or hepatic function, rheumatologic disorders such as polymyalgia rheumatica, steroid myopathy, vitamin D deficiency, or primary muscle diseases.) – If muscle symptoms resolve, and if no contraindication exists, give the patient the original or a lower dose of the same statin to establish a causal relationship between the muscle symptoms and statin therapy. – If a causal relationship exists, discontinue the original statin. Once muscle symptoms resolve, use a low dose of a different statin. – Once a low dose of a statin is tolerated, gradually increase the dose as tolerated.	E (Expert Opinion)	---	IIa	B (15,90,98-100)

Pregunta 13 (Monitorizar CK y transa)

3a. Baseline measurement of hepatic transaminase levels (ALT) should be performed before initiating statin therapy.	B (Moderate)	46, 52, 53	I†	B
3b. During statin therapy, it is reasonable to measure hepatic function if symptoms suggesting hepatotoxicity arise (e.g., unusual fatigue or weakness, loss of appetite, abdominal pain, dark-colored urine or yellowing of the skin or sclera).	E (Expert Opinion)	---	IIa	C (91)

This guideline recommends that baseline measurement of transaminase (ALT) levels should be performed before initiating statin therapy. This approach was taken in the RCTs reviewed for this report. There is no recommendation to monitor transaminase (ALT) levels because ALT monitoring was performed in the RCTs and there was no significant difference between placebo groups and statin treatment groups in the rates of ALT elevations. In addition, the FDA has indicated that if the baseline hepatic transaminases are normal, further hepatic monitoring is not needed. During statin therapy, it is reasonable to measure hepatic function if symptoms suggesting hepatotoxicity arise (e.g., unusual fatigue or weakness, loss of appetite, abdominal pain, dark-colored urine or yellowing of the skin or sclera).

Pregunta 17 prevención 1



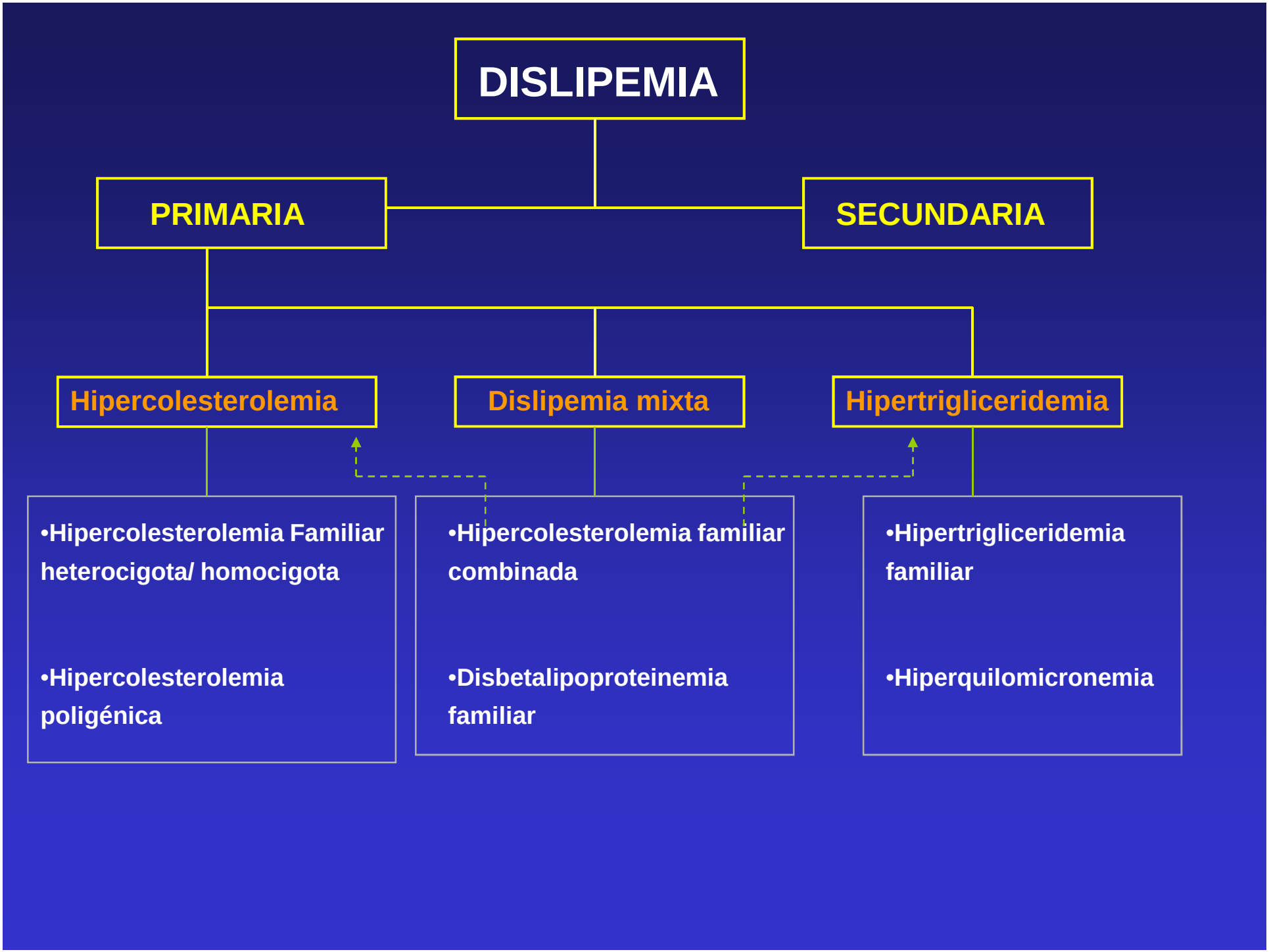
1. Riesgo muy alto

Sujetos con cualquiera de los siguientes factores:

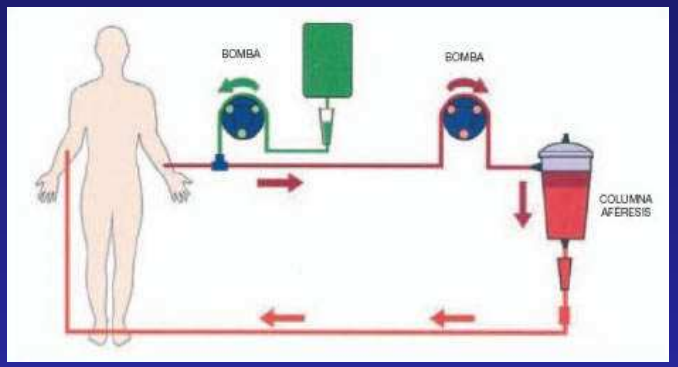
- ECV documentada en pruebas invasivas o no invasivas (como angiografía coronaria, imagen nuclear, ecocardiografía de estrés, placa carotídea por ultrasonidos), infarto de miocardio, SCA, revascularización coronaria (ICP, CABG) y otros procedimientos de revascularización arterial, ictus isquémico, enfermedad arterial periférica (EAP).
- DM1 o DM2 con uno o más factores de riesgo CV o lesión de órgano diana (como microalbuminuria 30-300 mg/24 h).
- ERC grave (TFG < 30 ml/min/1,73 m²).
- Una estimación SCORE ≥ 10%.

Riesgo CV total (SCORE) %	Concentración de cLDL				
	< 70 mg/dl < 1,8 mmol/l	70 a < 100 mg/dl 1,8 a < 2,5 mmol/l	100 a < 155 mg/dl 2,5 a < 4,0 mmol/l	155 a < 190 mg/dl 4,0 a < 4,9 mmol/l	> 190 mg/dl > 4,9 mmol/l
> 5 a < 10, o alto riesgo	Intervención en estilo de vida, considerar tratamiento farmacológico	Intervención en estilo de vida, considerar tratamiento farmacológico	Intervención en estilo de vida y tratamiento farmacológico inmediato	Intervención en estilo de vida y tratamiento farmacológico inmediato	Intervención en estilo de vida y tratamiento farmacológico inmediato
Clase[a]/Nivel[b]	IIa/A	IIa/A	IIa/A	I/A	I/A
≥10 o riesgo muy alto	Intervención en estilo de vida, considerar tratamiento farmacológico[c]	Intervención en estilo de vida y tratamiento farmacológico inmediato	Intervención en estilo de vida y tratamiento farmacológico inmediato	Intervención en estilo de vida y tratamiento farmacológico inmediato	Intervención en estilo de vida y tratamiento farmacológico inmediato

ECV mortal.


DISLIPEMIA
PRIMARIA
SECUNDARIA
Hipercolesterolemia
Dislipemia mixta
Hipertrigliceridemia
•Hipercolesterolemia Familiar heterocigota/ homocigota
•Hipercolesterolemia poligénica
•Hipercolesterolemia familiar combinada
•Disbetalipoproteinemia familiar
•Hipertrigliceridemia familiar
•Hiperquilomicronemia

LDL-aféresis



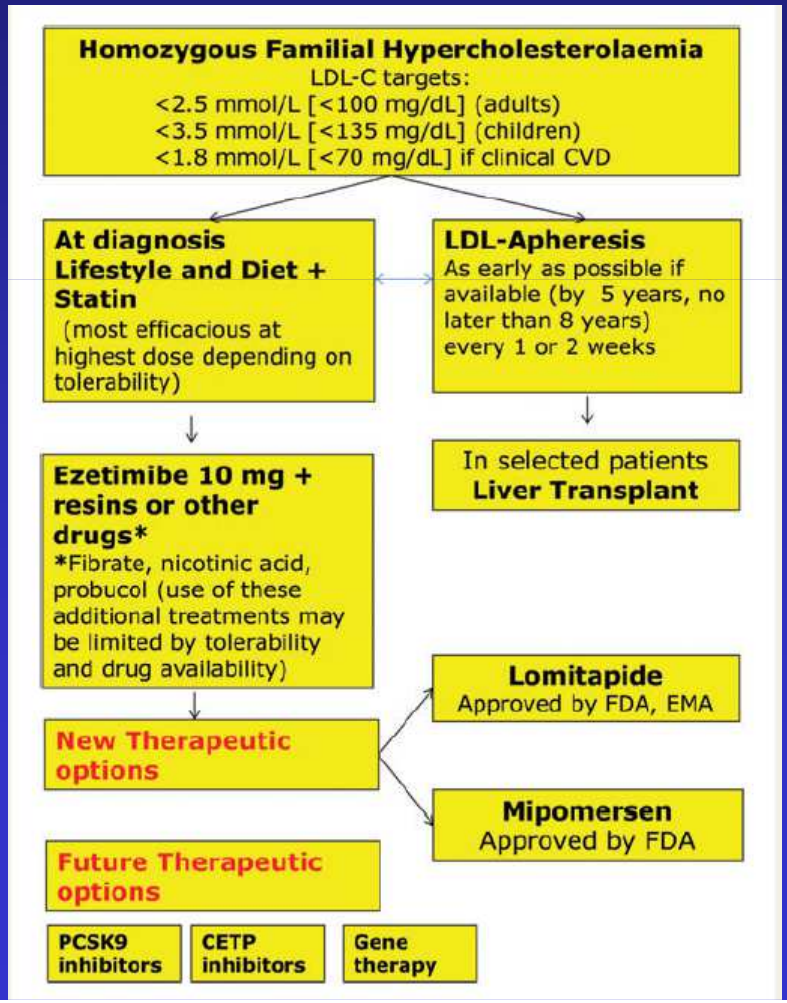
Homocigotos HFH
Heterocigotos prevención 2ª y LDL-C >200

Reducción LDL-C 55–70%

Senmanal/bisemanal

Reduce Lipoproteína (a)

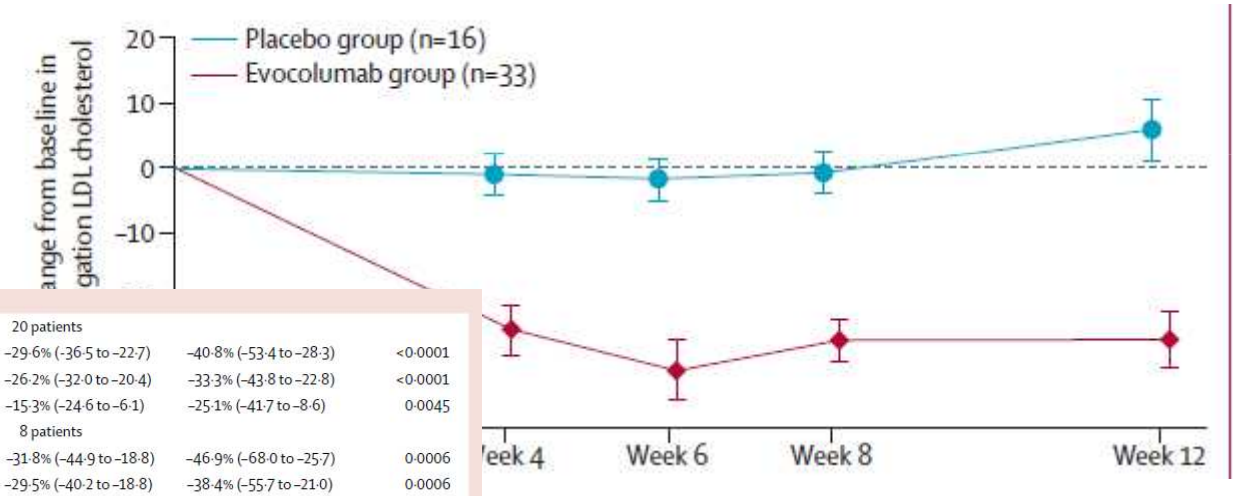
Inicio entre 5-8 años



Cuchel M. Eur Heart J 2014

Inhibition of PCSK9 with evolocumab in homozygous familial hypercholesterolaemia (TESLA Part B): a randomised, double-blind, placebo-controlled trial

	Placebo group (n=16)	Evolocumab group (n=33)
Lipid parameters	336	355
LDL cholesterol, ultracentrifugation (mmol/L)	8·7 (3·8)	9·2 (3·5)

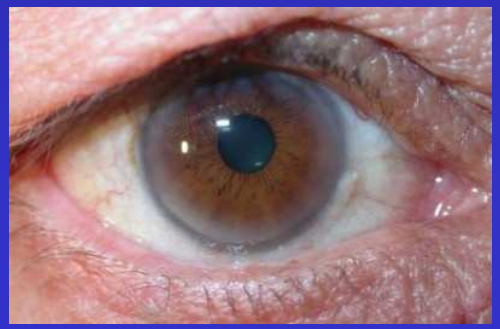


LDL receptor mutations status				
Patients defective in one or both alleles	8 patients	20 patients		
Ultracentrifugation LDL cholesterol	11·2% (0·8 to 21·7)	−29·6% (−36·5 to −22·7)	−40·8% (−53·4 to −28·3)	<0·0001
Apolipoprotein B	7·1% (−1·7 to 15·9)	−26·2% (−32·0 to −20·4)	−33·3% (−43·8 to −22·8)	<0·0001
Lipoprotein(a)	9·8% (−4·0 to 23·6)	−15·3% (−24·6 to −6·1)	−25·1% (−41·7 to −8·6)	0·0045
Patients with defective/defective status	5 patients	8 patients		
Ultracentrifugation LDL cholesterol	15·1% (−1·2 to 31·3)	−31·8% (−44·9 to −18·8)	−46·9% (−68·0 to −25·7)	0·0006
Apolipoprotein B	8·9% (−4·4 to 22·2)	−29·5% (−40·2 to −18·8)	−38·4% (−55·7 to −21·0)	0·0006
Lipoprotein(a)	9·8% (−9·3 to 28·9)	−10·0% (−25·4 to 5·3)	−19·8% (−44·8 to 5·1)	0·11
Patients with defective/negative status	3 patients	6 patients		
Ultracentrifugation LDL cholesterol	3·5% (−10·6 to 17·5)	−21·0% (−30·7 to −11·2)	−24·5% (−41·6 to −7·3)	0·0128
Apolipoprotein B	4·8% (−3·2 to 12·9)	−17·6% (−23·1 to −12·1)	−22·4% (−32·1 to −12·6)	0·0013
Lipoprotein(a)	9·1% (7·1)†	−14·7% (7·7)†	−23·8%†	NC†
Patients with unclassified mutation status‡	6 patients	16 patients		
Ultracentrifugation LDL cholesterol	3·8% (−20·7 to 28·3)	−17·9% (−36·0 to 0·3)	−21·7% (−50·6 to 7·3)	0·13
Apolipoprotein B	−0·2% (−21·3 to 20·9)	−16·4% (−32·3 to −0·6)	−16·2% (−41·5 to 9·0)	0·19
Lipoprotein(a)	−2·0% (−21·7 to 17·8)	−5·4% (−21·7 to 10·8)	−3·5% (−27·7 to 20·8)	0·77
Patients with negative/negative mutation status	0 patients	1 patient		
Ultracentrifugation LDL cholesterol	..	10·3%	..	..
Apolipoprotein B	..	9·3%	..	..
Lipoprotein(a)	..	38·0%	..	..

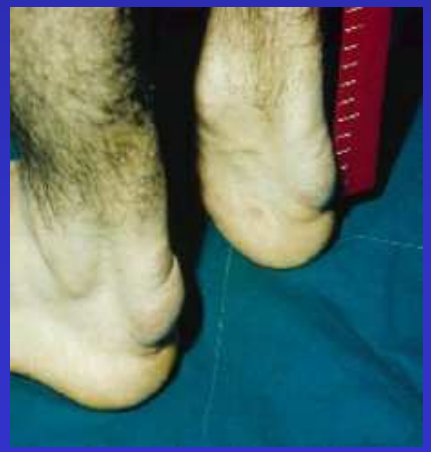
Raal F. Lancet 2015

CARATERÍSTICAS CLÍNICAS DE HFH

	Heterocigotos	Homocigotos
Colesterol	Desde niñez/pubertad CT 250-450 mg/dl LDL-C 190-300mg/dl	Desde nacimiento CT 600-1200 mg/dl LDL-C >500 mg/dl
Aterogenicidad	4ª década	Adolescencia



Arco corneal



Xantomas tendinosos

xantelasmas

Cual es el objetivo LDL-C de tratamiento en la HFH ?

National Lipis Association 2011

Reducción 50% LDL-C

<100 mg/dl si alto riesgo

GUÍA EUROPEA 2013

Niños LDL-C <135 mg/dl

Adultos LDL-C <100 mg/dl

GUÍA ACC/AHA 2013

Reducción 50% LDL-C

GUÍA INTERNACIONAL 2014

LDL-C <100 mg/dl

LDL-C < 70 mg/dl si F de R

LDL-C 135 niños >8-10a

GUÍA NICE 2013

Reducción 50% LDL-C

Robinson J. J Clin Lipidol 2011. Stone JACC 2013 . Nordestgaard B. Eur Heart J 2013. Watts G. J Clin Lipidol 2014

Cuando comenzar a tratar la HF ?

GUÍA AMERICANA 2011

GUÍA EUROPEA 2013

Adultos

Considerar entre 8-10 años

- AF de ECV
- Lipoproteina (a) elevada
- Obesidad, tabaquismo

GUÍA INTERNACIONAL 2014

Antes de los 18a
Considerar 8-10 años si LDL>135 mg/dl

GUÍA NICE 2013

10 años

GUÍA ACC/AHA 2013

Lovastatina, atorvastatina, simvastatina, and rosuvastatina en niños >10a
Pravastatina o rosuvastatina a partir de 8a

Robinson J. J Clin Lipidol 2011. Stone. JACC 2013 ; Nordestgaard B. Eur Heart J 2013. Watts G. J Clin Lipidol 2014; Deschamps OS. Atherosclerosis 2011

Interacciones con estatinas

Metabolismo de las estatinas

The Statin Armamentarium: Individual Metabolism Characteristics

Factor	Pitava	Rosuva	Fluva	Atorva	Simva	Lova	Prava
Absorption (%)	80	50	98	30	60-85	30	35
Bioavail (%)	60	20	30	12	< 5	5	18
T ½ (h)	10-13	20	1-3	7-20	2-5	2-5	1-3
CYP metabolism	2C9/2C8 +/-	2C9/2C19 +/-	2C9	3A4	3A4	3A4	None
OATP1B1	+	+	+	+	+	+	+
MDR1	+		?	+	+	+	+

+/- = minimal metabolism by pathway

MDR1 = multidrug resistance protein 1; OATP1B1 = organic anion transporter polypeptide 1B1

LIPID & METABOLIC Corsini A, et al. *Curr Med Res Opin*. 2011;27:1551-1562. theheart.org Medscape EDUCATION

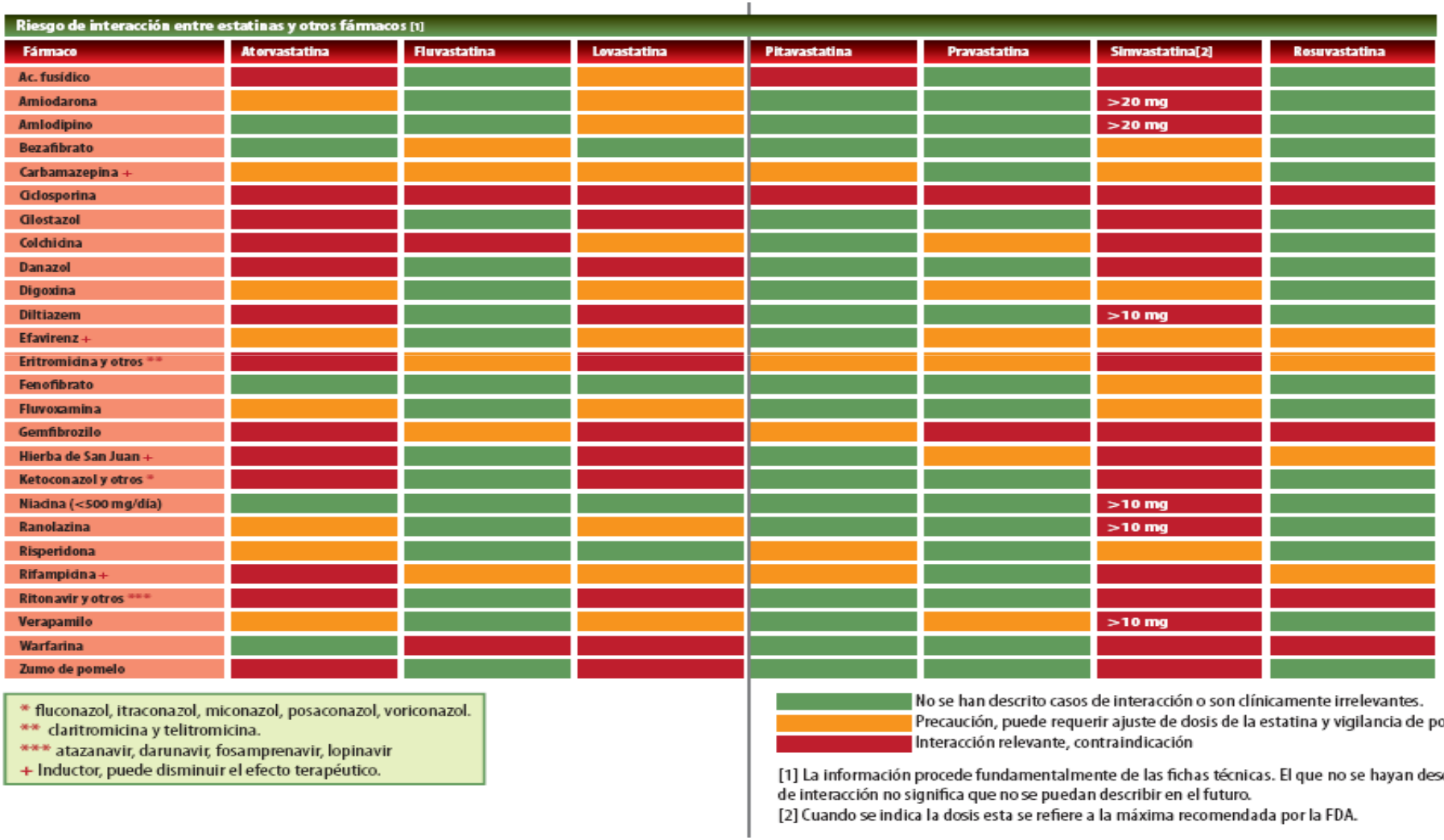
la pitavastatina se elimina por la bilis sin cambios hepáticos, y menos del 5% se excreta en la orina

METABOLIZACIÓN HEPÁTICA ESTATINAS

CYP3A4	**Atorvastatina** **Sinvastatina** **Lovastatina**
CYP 2C9	**Rosuvastatina** **Fluvastatina**
Sulfatación	**Pravastatina**
Glucoronización/Lactonización Escaso por CYP 2C9y CYP2C8	**PITAVASTATINA**

Interacciones con estatinas

Perfil de interacciones farmacológica entre estatinas



Riesgo de interacción entre estatinas y otros fármacos [1]

Fármaco	Atorvastatina	Fluvastatina	Lovastatina	Pitavastatina	Pravastatina	Simvastatina[2]	Rosuvastatina
Ac. fusídico							
Amiodarona						>20 mg	
Amlodipino						>20 mg	
Bezafibrato							
Carbamazepina +							
Ciclosporina							
Cilostazol							
Colchicina							
Danazol							
Digoxina							
Diltiazem						>10 mg	
Efavirenz +							
Eritromicina y otros **							
Fenofibrato							
Fluvoxamina							
Gemfibrozilo							
Hierba de San Juan +							
Ketoconazol y otros *							
Niacina (<500 mg/día)						>10 mg	
Ranolazina						>10 mg	
Risperidona							
Rifampicina +							
Ritonavir y otros ***							
Verapamilo						>10 mg	
Warfarina							
Zumo de pomelo							

* fluconazol, itraconazol, miconazol, posaconazol, voriconazol.
** claritromicina y telitromicina.
*** atazanavir, darunavir, fosamprenavir, lopinavir
\+ Inductor, puede disminuir el efecto terapéutico.

No se han descrito casos de interacción o son clínicamente irrelevantes.
Precaución, puede requerir ajuste de dosis de la estatina y vigilancia de posibles RAM
Interacción relevante, contraindicación

[1] La información procede fundamentalmente de las fichas técnicas. El que no se hayan descrito casos de interacción no significa que no se puedan describir en el futuro.
[2] Cuando se indica la dosis esta se refiere a la máxima recomendada por la FDA.

Morales FJ, Pascual V. Relevancia clínica de las interacciones farmacológicas 2012.

Table 1
Diagnosis of FH in children.

High probability of FH if LDL cholesterol is: • ≥5 mmol/L (190 mg/dL) after 3 months dietary intervention • ≥4 mmol/L (160 mg/dL) plus family history of premature CHD and/or high cholesterol in one parent (untreated) • ≥3.5 mmol/L (130 mg/dL) and parent has a genetic diagnosis of FH Detection of an FH-causing mutation (usually in the *LDLR* gene), is the gold standard for diagnosis

Table 2
Key points about screening for FH in children.

• The EAS Consensus Panel recommend phenotypic screening based on count • Children (both boys and girls) with su • If homozygous FH is suspected (both • Universal screening of children may b

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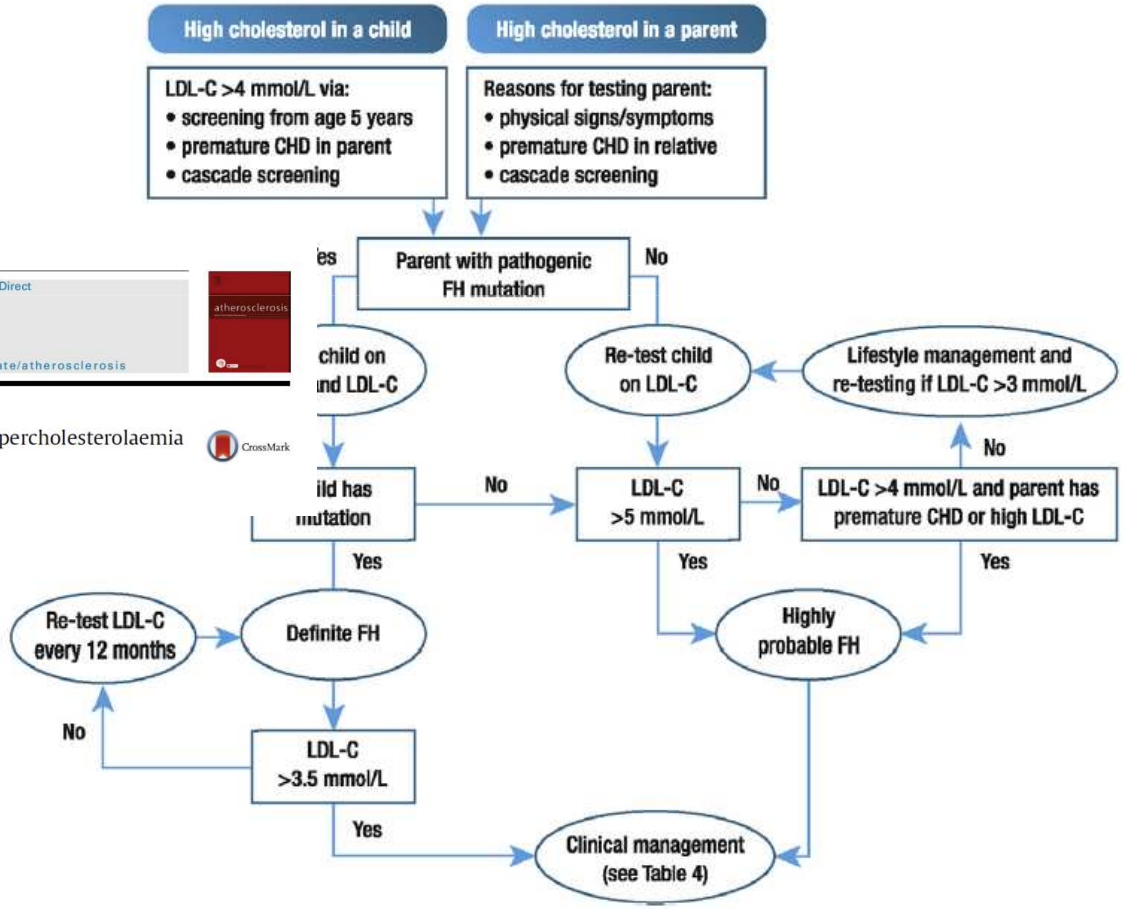
Discussion

Landmark position paper on paediatric familial hypercholesterolaemia from the EAS Consensus Panel

Jane Stock*



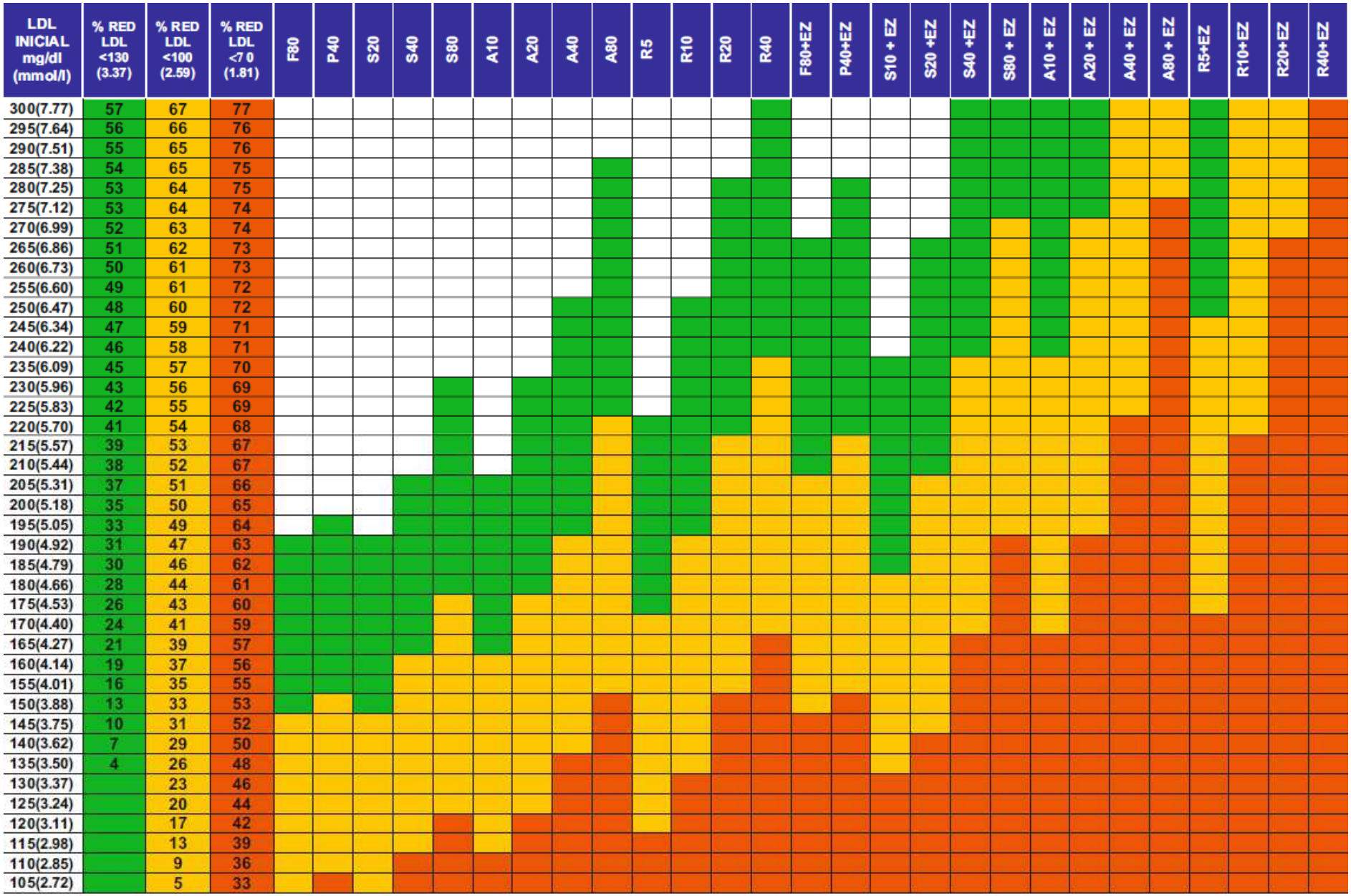
The NLA has proposed a pragmatic working definition of statin intolerance that may be useful in assisting clinicians, researchers, insurers, and regulatory authorities.

Statin intolerance is a clinical syndrome that may be characterized by:

B The inability to tolerate at least 2 statins: one statin at a low or lowest starting daily dose AND another statin at any daily dose.

B Either objectionable symptoms (real or perceived) or abnormal laboratory determinations, which are temporally related to statin treatment.

B Reversible upon statin discontinuation, but reproducible by rechallenge with other known determinants being excluded (such as hypothyroidism, interacting drugs, concurrent illnesses, significant changes in physical activity or exercise, and underlying muscle disease).



Masana . Med Clin (Barc) 2010

Ldl aféresis

Familial Hypercholesterolemia
Victoria Enchia Bouhairie, MD, Anne Carol Goldberg, MD*

Low-Density Lipoprotein Apheresis
LDL apheresis is an important treatment modality for homozygous FH patients and for heterozygous patients who have not met treatment goals despite optimal tolerated medical therapy (Box 5).24,36 It is an extracorporeal treatment that uses various methods to remove LDL from the circulation. LDL apheresis is currently FDA approved and has been shown in clinical trials to prevent and slow the progression of CHD.13,37,38 Apheresis is generally done every 1 to 2 weeks, with each session taking about 3 hours and removing greater than 60% of Apo-B-containing lipoproteins.38 The LDL reduction with LDL apheresis is temporary and associated with a rebound elevation in lipid levels after the procedure. The efficacy of LDL apheresis can be enhanced by the addition of statin therapy. LDL apheresis treatment in homozygous FH patients has improved their life expectancy to more than 50 years.38 Cost and limited availability decrease widespread use of LDL apheresis.
Homozygous Familial Hypercholesterolemia: Treatment Considerations
Treatment starts at the time of diagnosis and involves age-appropriate diet, statin, ezetimibe, and often apheresis.3,13 The FDA has approved 2 novel treatments for homozygous FH individuals older than 18 years of age: lomitapide and mipomersen (Table 4).39 Lomitapide also has European approval. Lomitapide is a microsomal triglyceride transfer (MTP) protein inhibitor available as a capsule and used as an adjunct to other cholesterol-lowering medications, lifestyle changes, and LDL apheresis if needed. The function of MTP, which resides in the lumen of endoplasmic ret

Anti-PCSK9 Antibody Effectively Lowers Cholesterol in Patients With Statin Intolerance

The GAUSS-2 Randomized, Placebo-Controlled Phase 3 Clinical Trial of Evolocumab

Erik Stroes, MD, PHD,* David Colquhoun, MD,† David Sullivan, MD,‡ Fernando Civeira, MD,§