

Papel de los iPCSK9

Datos en vida real

Dr. Juan Rondán | *Hospital Universitario de Cabueñes*

¡PCSK9: 7 años después...

Long-Term Evolocumab in Patients With Established Atherosclerotic Cardiovascular Disease.
O'Donoghue ML, Giugliano RP, Wiviott SD, Atar D, Keech A, Kuder JF, Im K, Murphy SA, Flores-Arredondo JH, López JAG, Elliott-Davey M, Wang B, Monsalvo ML, Abbasi S, Sabatine MS.
Circulation. 2022 Oct 11;146(15):1109-1119. doi: 10.1161/CIRCULATIONAHA.122.061620. Epub 2022 Aug 29.
PMID: 36031810 Clinical Trial

Efficacy and Safety of PCSK9 Monoclonal Antibodies in Patients at High Cardiovascular Risk: An Updated Systematic Review and Meta-Analysis of 32 Randomized Controlled Trials.
Mu G, Xiang Q, Zhou S, Liu Z, Qi L, Jiang J, Gong Y, Xie Q, Wang Z, Zhang H, Huo Y, Cui Y.
Adv Ther. 2020 Apr;37(4):1496-1521. doi: 10.1007/s12325-020-01259-4. Epub 2020 Feb 27.
PMID: 32108309

[Real-life efficacy and safety of PCSK9 inhibitors treatment: Experience in three hospitals in Asturias].
Rodríguez Escobedo R, González Martínez S, Díaz Naya L, Suárez Gutiérrez L, Fernández Morera JL, Riestra Fernández M, Martínez Faedo C, Villazón González F, Menéndez Torre EL.
Semergen. 2021 Sep;47(6):369-375. doi: 10.1016/j.semerg.2021.03.008. Epub 2021 Jun 8.
PMID: 34112592 Spanish.

Remnant cholesterol and lipid residual risk: The
... descriptive study. We collected data from all patients that... in three hospitals in Asturias... its use
... of PCSK9...
...ez Quiroga GA, Romero-Menor C, Fácila L, Seijas-Amigo J, ...z-Mañero M, Bello Mora MC, Valle A, Fornovi A, Freixa Pamias ...nte Lorenzo MM, Sánchez-Álvarez S, López-Rodríguez L,
...e13863. doi: 10.1111/eci.13863. Epub 2022 Sep 5.
...rospective registry of patients treated with PCSK9 inhibitors from 14 ...ore and on-treatment lipid parameters were recorded. ...By contrast, ...observed according to baseline LDLc ...



**DICTAMEN DE LA COMISIÓN DE USO RACIONAL DE LOS MEDICAMENTOS Y PRODUCTOS SANITARIOS
(CURMP) SOBRE LA INCLUSIÓN EN LA GUÍA FARMACOTERAPÉUTICA DEL SESPA DE
ALIROCUMAB Y EVOLOCUMAB PARA EL TRATAMIENTO DE LA HIPERCOLESTEROLEMIA**

En Prevención Secundaria:

Para los pacientes mayores de 18 años de edad que han sufrido un evento aterotrombótico (ictus aterotrombóticos, infarto agudo de miocardio y arteriopatía periférica) previo y en tratamiento con dosis

➤ **Identificar al paciente de **muy muy** alto riesgo fuera de visado:
Que no fuera necesario tratamiento con Ezetimibe.**

Para los pacientes de cualquiera de los grupos anteriores con intolerancia demostrada a las estatinas o contraindicación y que presentan cLDL por encima de los límites fijados.

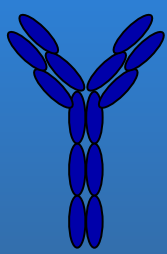
ROSUVASTATINA 40 ó ATORVASTATINA 80

+ EZETIMIBA

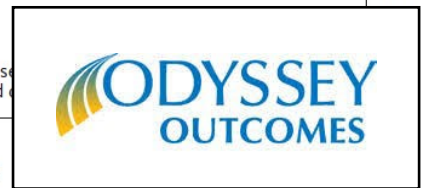
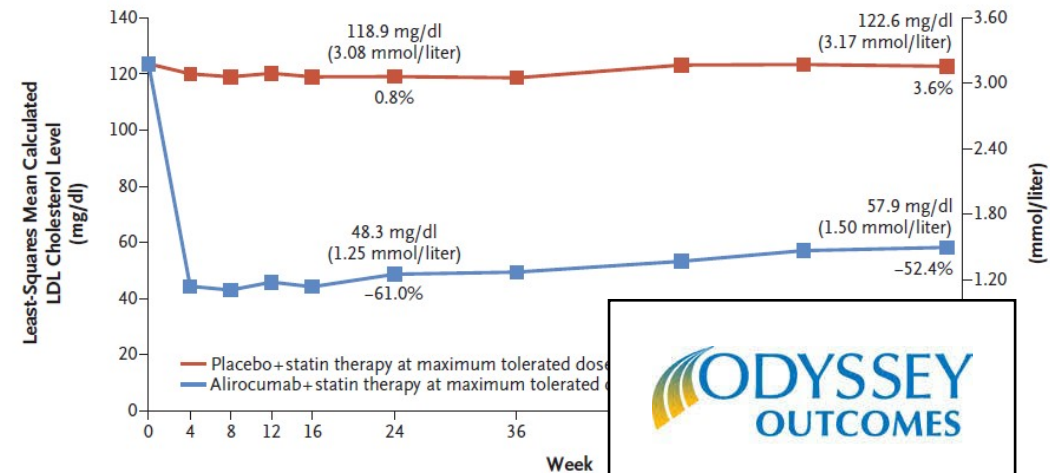
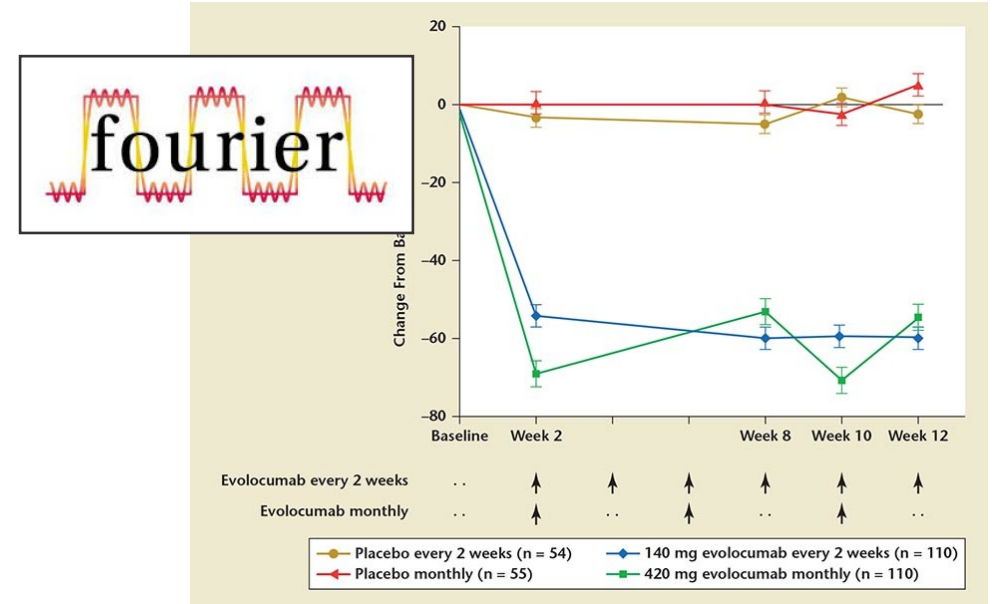
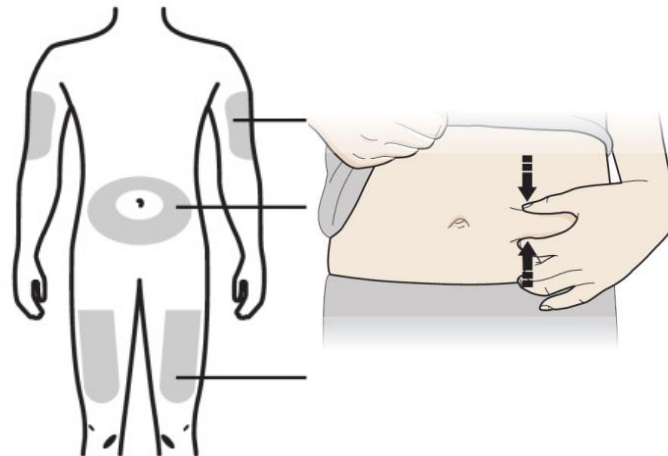
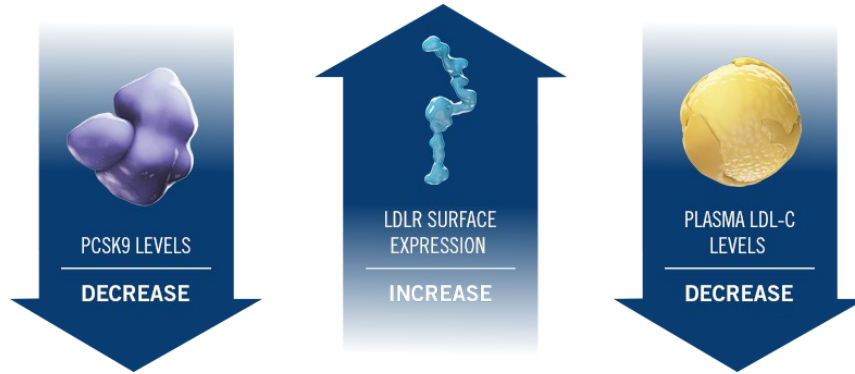
LDL > 100 mgdL

iPCSK9: Evolocumab y Alirocumab

human mAb



- human variable
- human constant
- repeated dosing possible

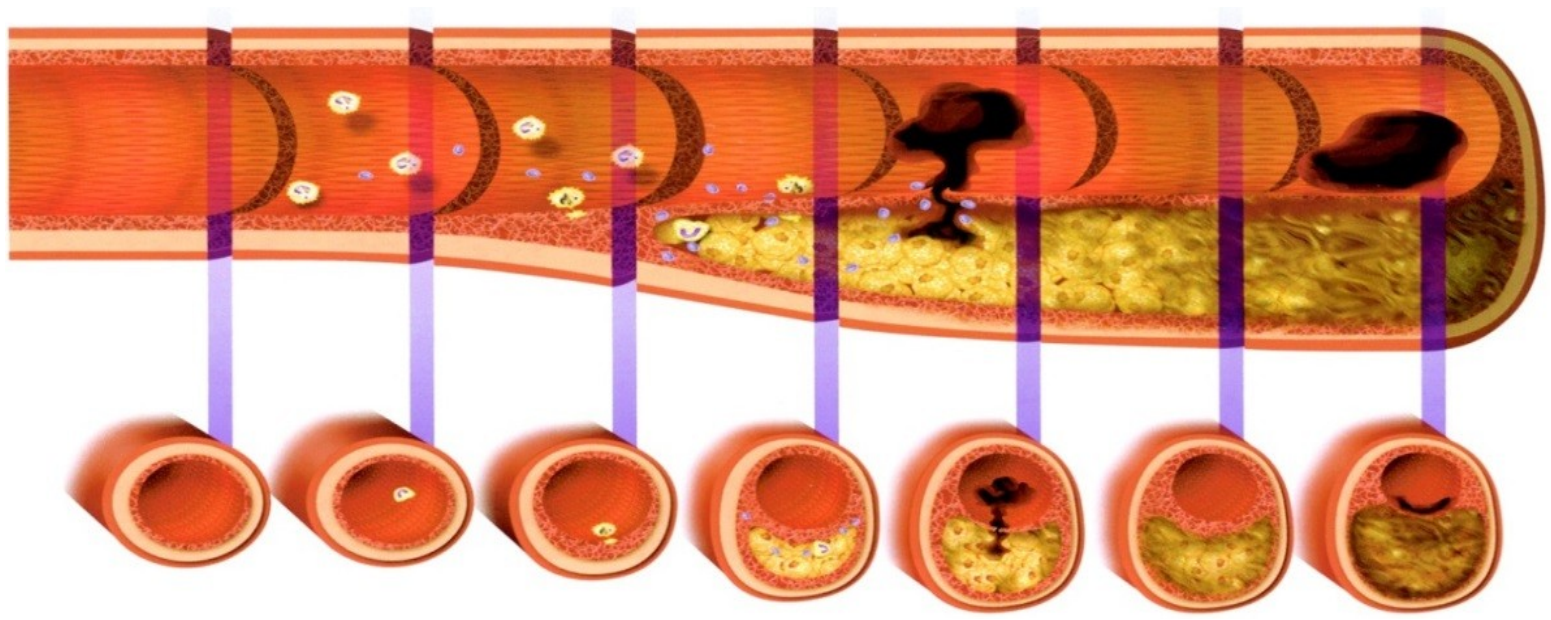


¿Por qué reducen MACE?
Eficacia y Seguridad a largo plazo
Vida real

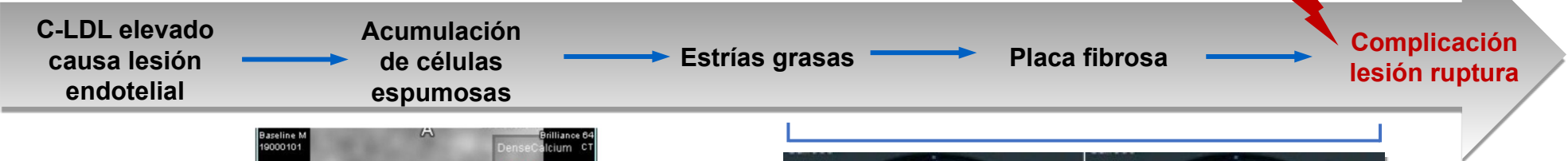
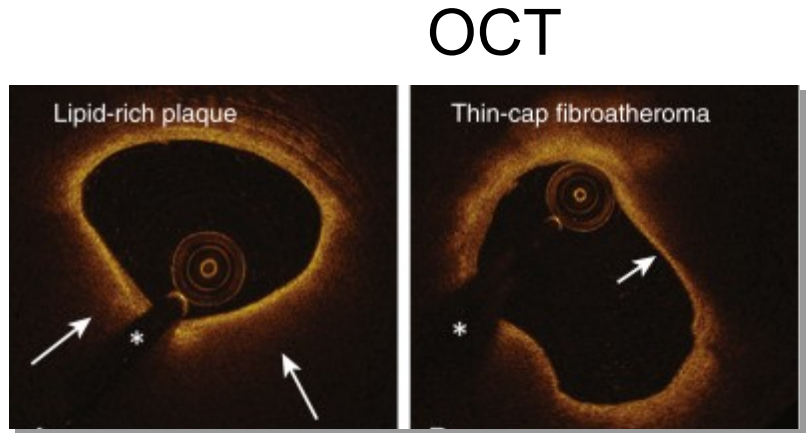
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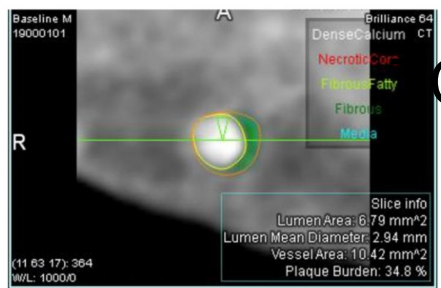
Vida real



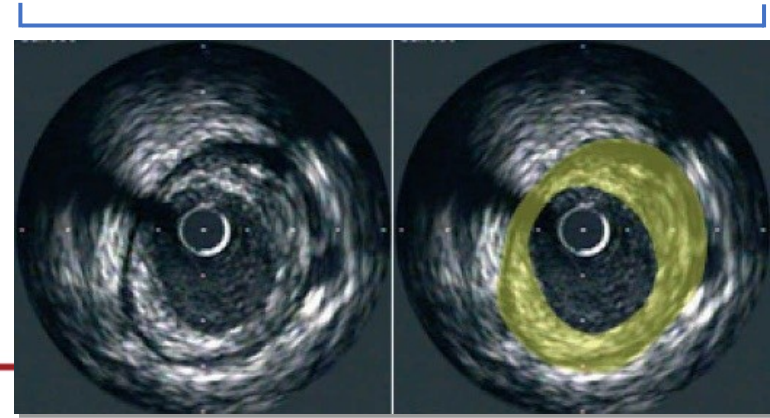
Biomarcador y FRCV



Eventos clínicos



IVUS



Congreso **SAC24**



IVUS: Reducción de placa

Randomized Controlled Trial > [JAMA](#). 2016 Dec 13;316(22):2373-2384.

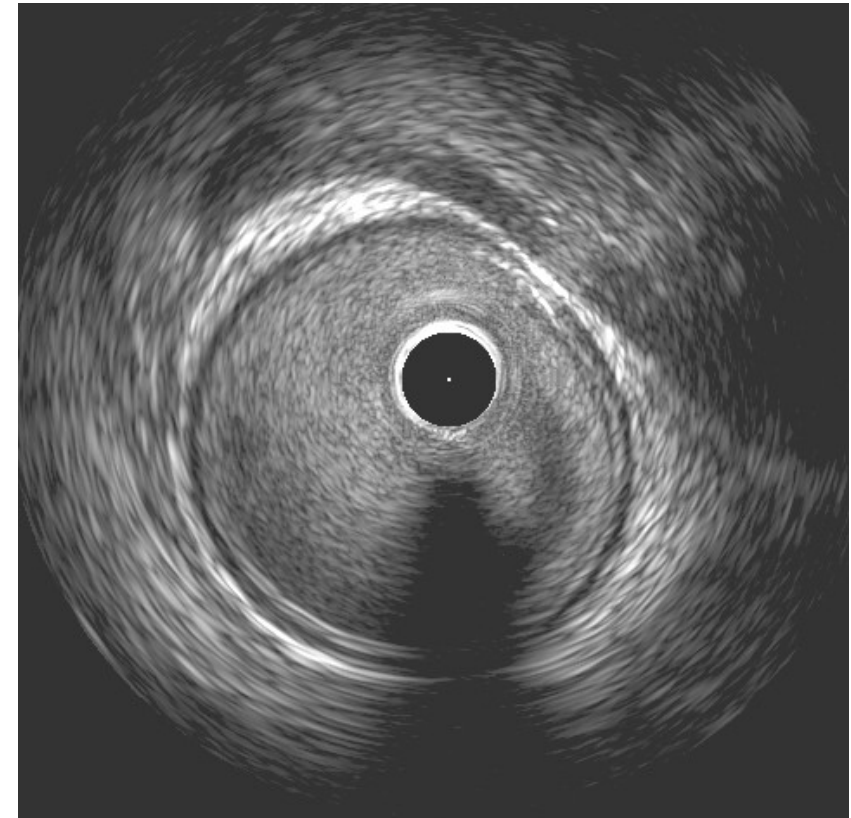
doi: 10.1001/jama.2016.16951.

Effect of Evolocumab on Progression of Coronary Disease in Statin-Treated Patients: The GLAGOV Randomized Clinical Trial

Randomized Controlled Trial > [JAMA](#). 2022 May 10;327(18):1771-1781.

doi: 10.1001/jama.2022.5218.

Effect of Alirocumab Added to High-Intensity Statin Therapy on Coronary Atherosclerosis in Patients With Acute Myocardial Infarction: The PACMAN-AMI Randomized Clinical Trial



IVUS: Reducción de placa

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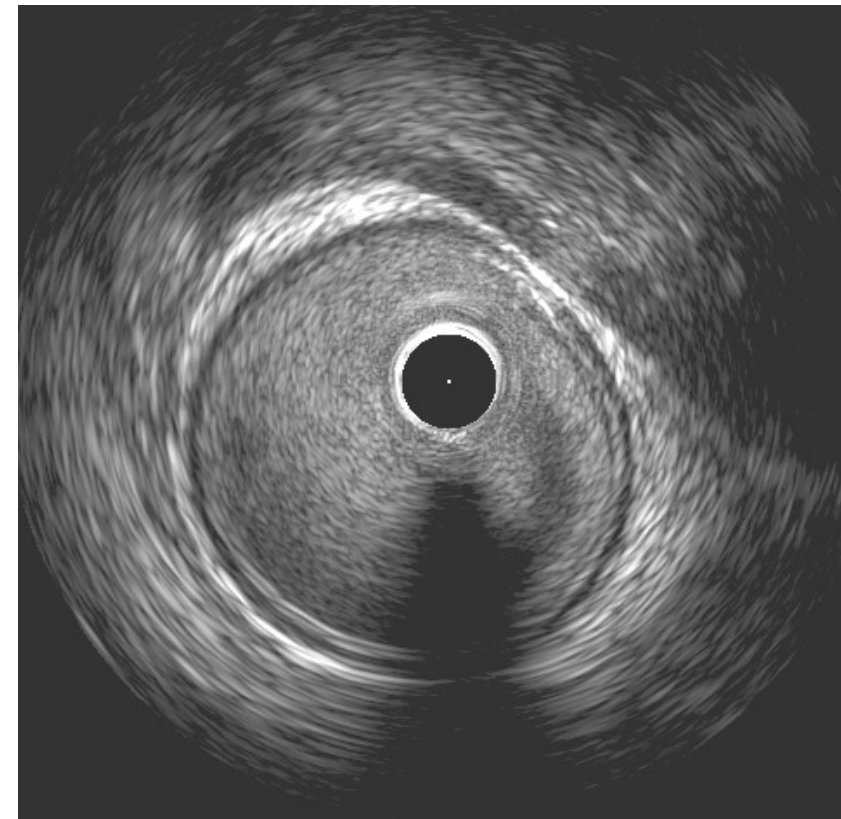
GLAGOV
↓ 1% PAV

Randomized Controlled Trial > JAMA. 2022 May 10;327(18):1771-1781.

doi: 10.1001/jama.2022.5218.

Effect of Alirocumab Added to High-Intensity Statin Therapy on Coronary Atherosclerosis in Patients With Acute Myocardial Infarction: The PACMAN-AMI Randomized Clinical Trial

PACMAN-AMI
↓ 1.2% PAV



IVUS

JAMA Cardiology | Original Investigation

Atherosclerotic Coronary Plaque Regression and Risk of Adverse Cardiovascular Events A Systematic Review and Updated Meta-Regression Analysis

Iulia Iatan, MD, PhD; Meijiao Guan, PhD; Karin H. Humphries, DSc; Eunice Yeoh, BSc; G. B. John Mancini, MD

La reducción en el porcentaje de placa arterioesclerótica en un 1% se asociaba a una reducción del 25% en la probabilidad de MACE

Randomized Controlled Trial

doi: 10.1001/jama.2016.16951.

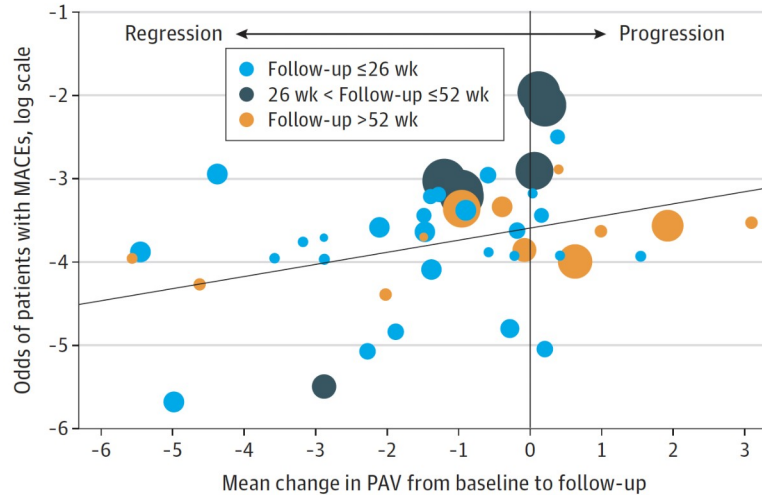
Effect of Evolocumab on Atherosclerosis in Statin-Treated Patients: A Randomized Clinical Trial

Randomized Controlled Trial > J

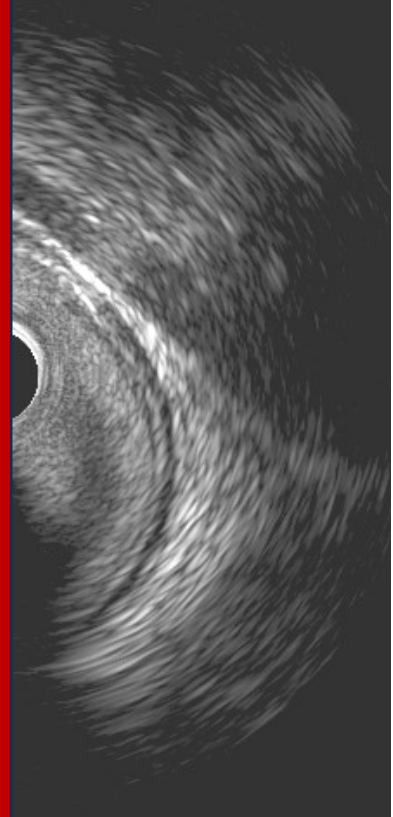
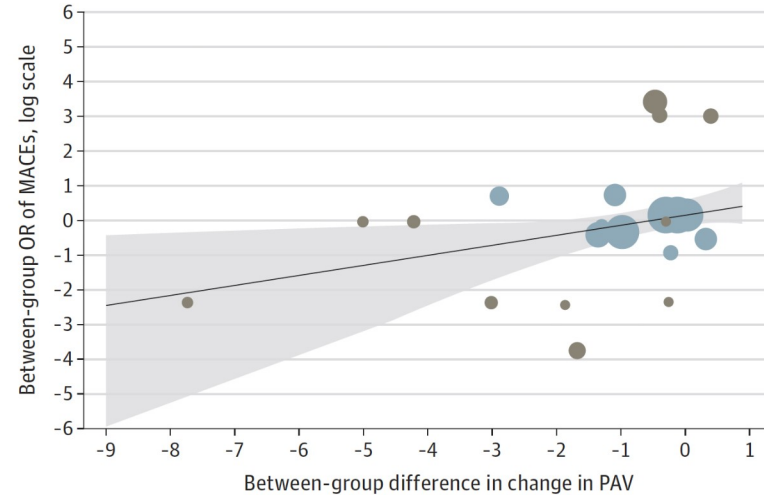
doi: 10.1001/jama.2022.5218.

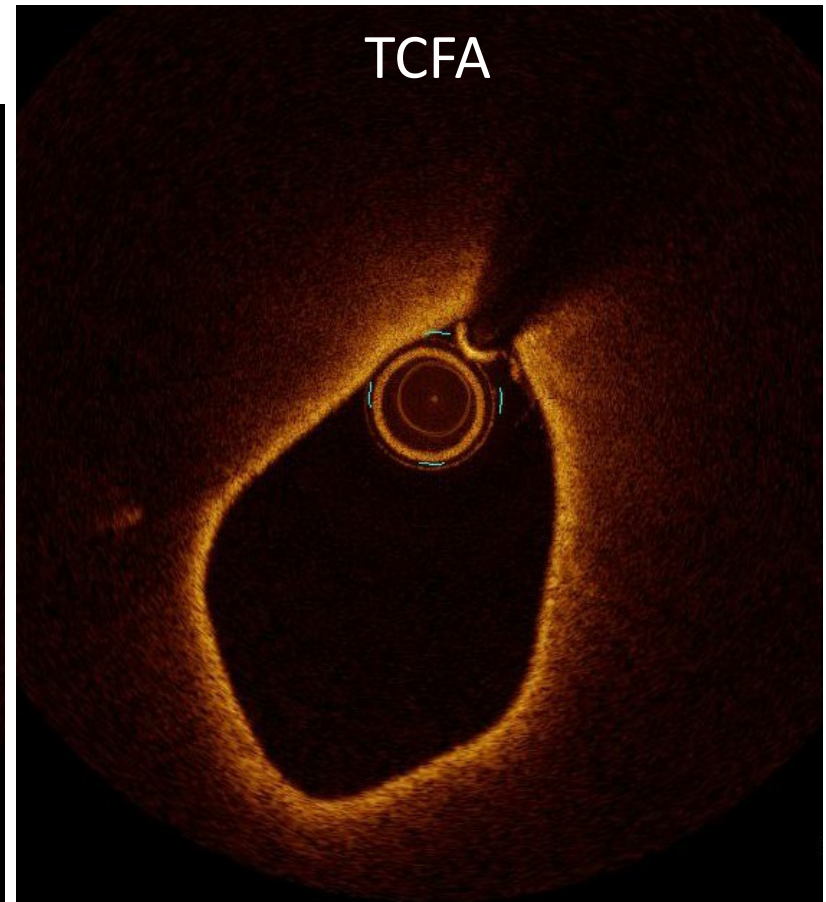
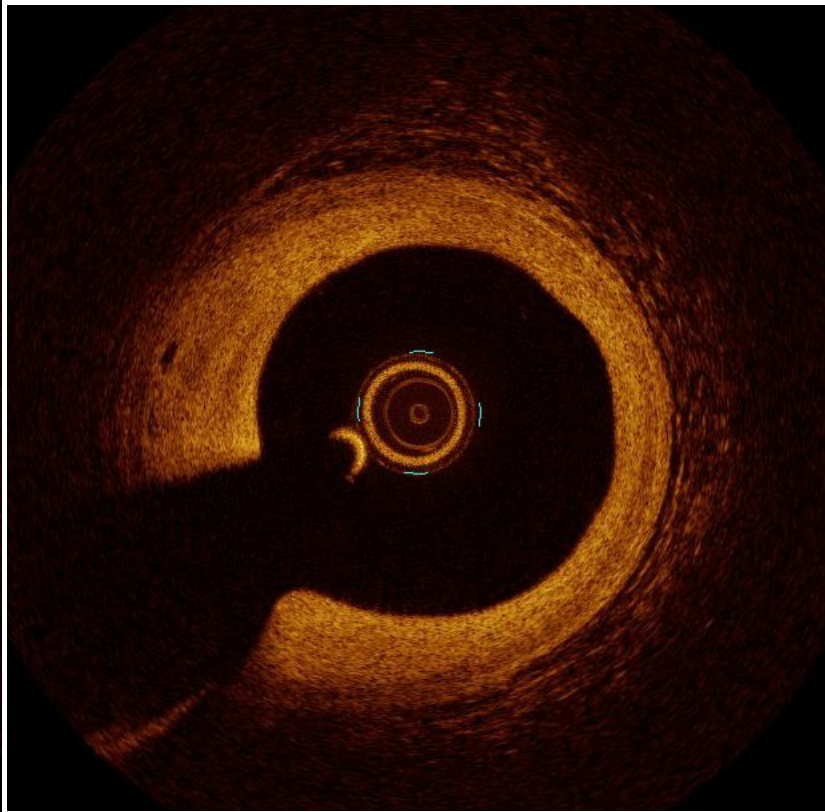
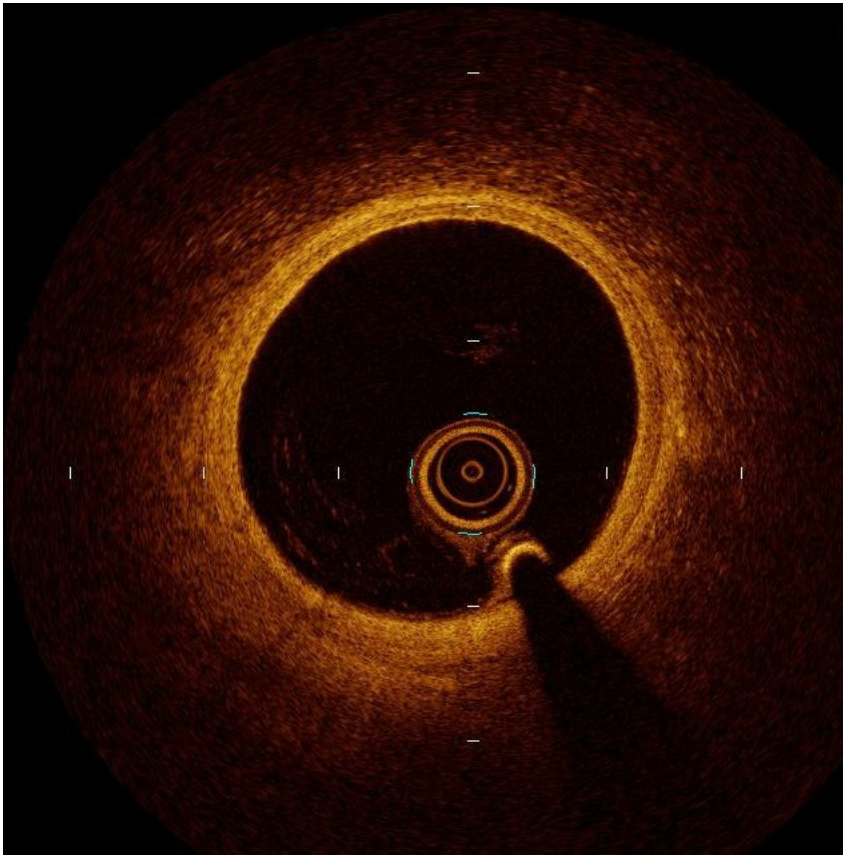
Effect of Alirocumab Therapy on Coronary Atherosclerosis in Patients With Acute Myocardial Infarction: A Randomized Clinical Trial

A Association between mean change in PAV and odds of patients with MACEs (log scale)



B Association of between-group differences in PAV and OR of MACEs





OCT: Estabilización de placa

Randomized Controlled Trial > [JACC Cardiovasc Imaging](#). 2022 Jul;15(7):1308-1321.

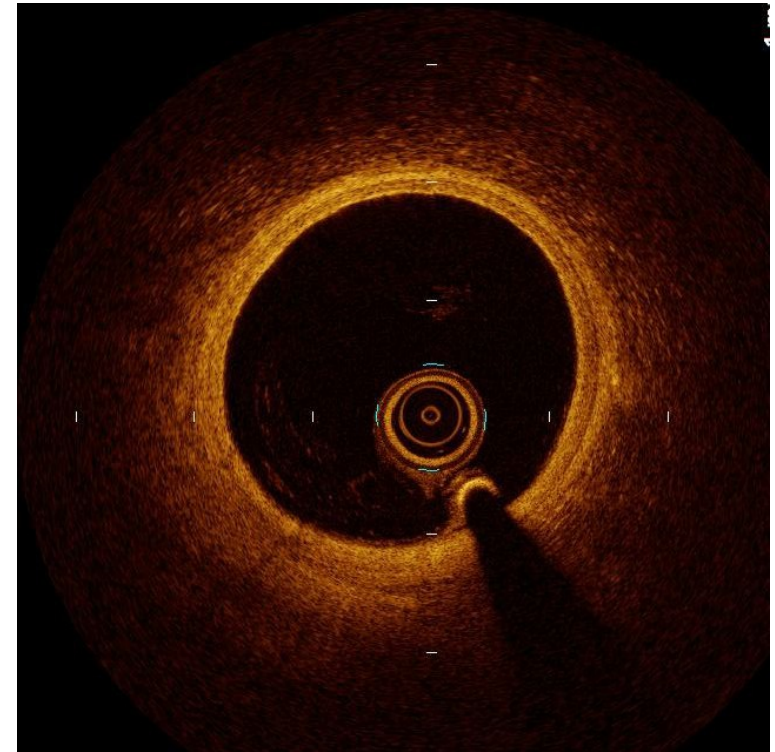
doi: 10.1016/j.jcmg.2022.03.002. Epub 2022 Mar 16.

Effect of Evolocumab on Coronary Plaque Phenotype and Burden in Statin-Treated Patients Following Myocardial Infarction

Randomized Controlled Trial > [JAMA](#). 2022 May 10;327(18):1771-1781.

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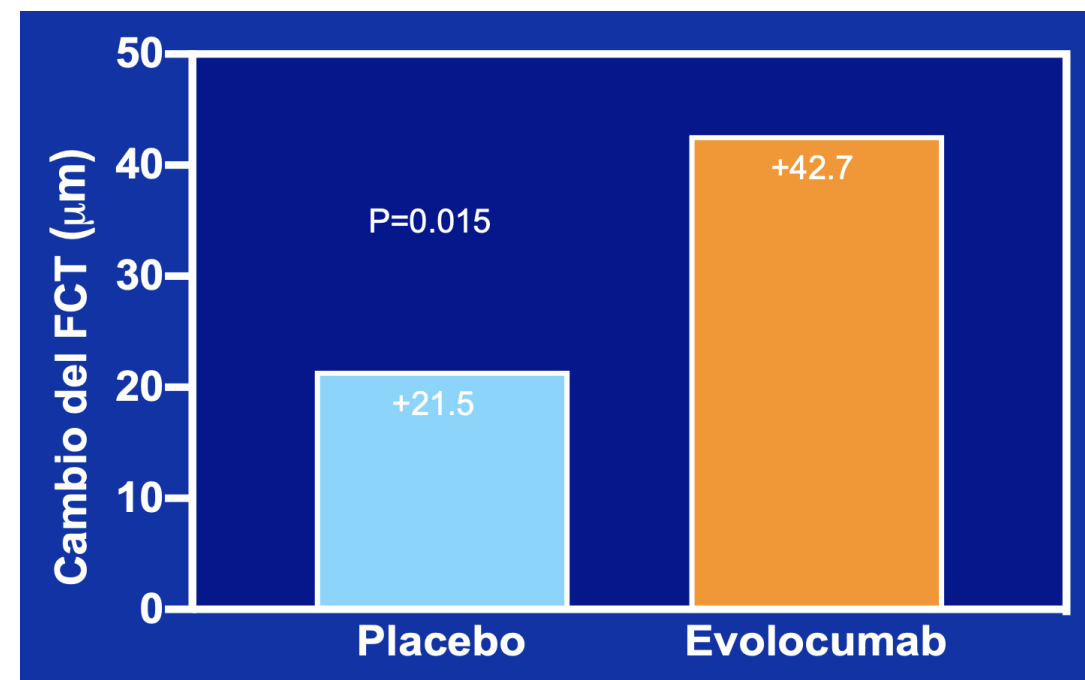
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Effect of Alirocumab Added to High-Intensity Statin Therapy on Coronary Atherosclerosis in Patients With Acute Myocardial Infarction: The PACMAN-AMI Randomized Clinical Trial

HUYGENS

Cambio en el espesor mínimo del FCT



OCT: Estabilización de placa

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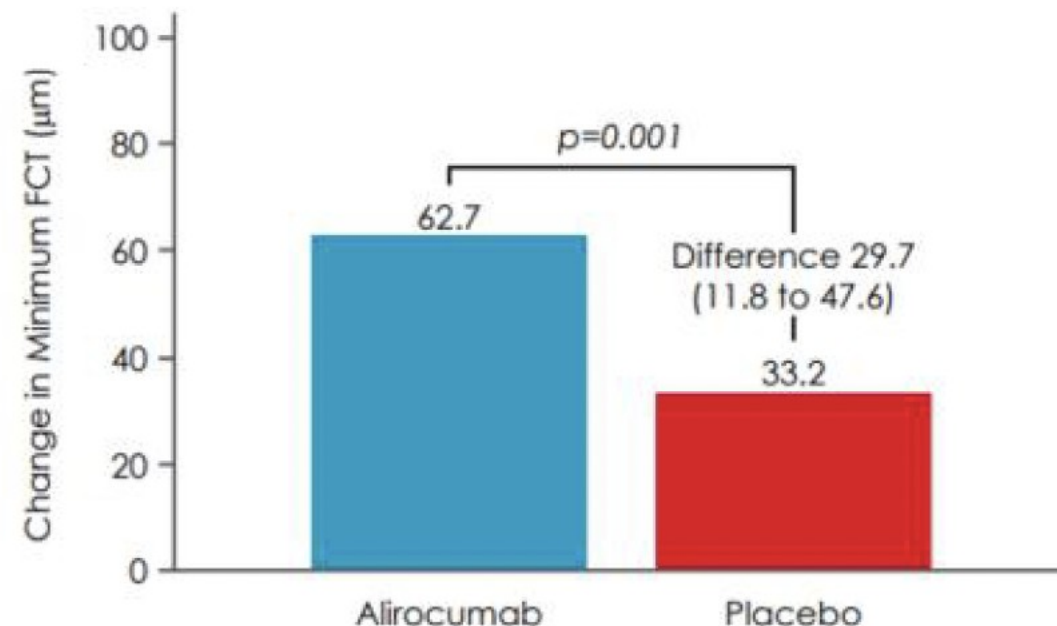
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PACMAN-AMI



TC coronario

Multicenter Study > [Circulation](#). 2023 May 9;147(19):1436-1443.

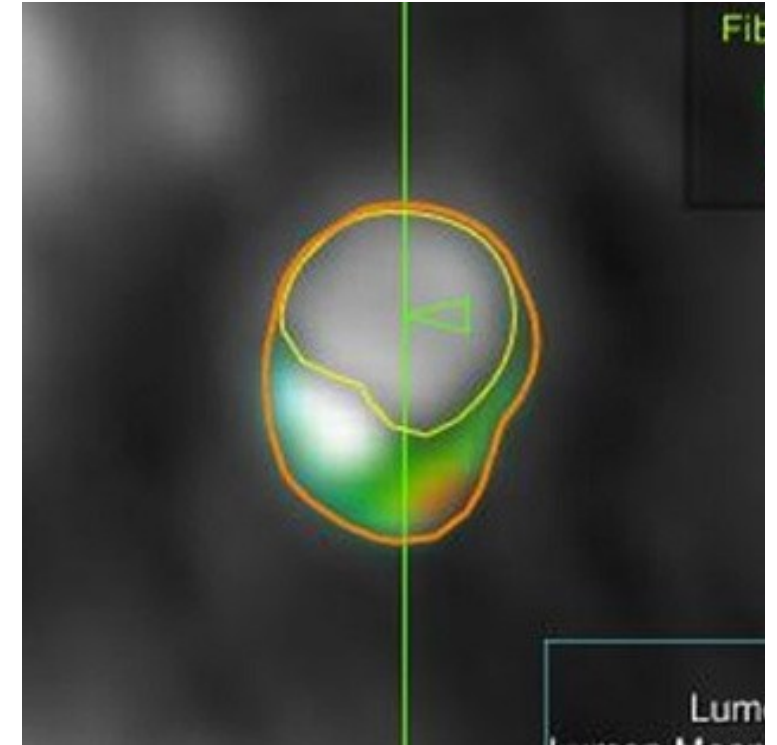
doi: 10.1161/CIRCULATIONAHA.122.062557. Epub 2023 Apr 3.

Alirocumab and Coronary Atherosclerosis in Asymptomatic Patients with Familial Hypercholesterolemia: The ARCHITECT Study

Multicenter Study > [Circ Cardiovasc Imaging](#). 2024 Jan;17(1):e016206.

doi: 10.1161/CIRCIMAGING.123.016206. Epub 2024 Jan 11.

Characteristics of Coronary Atherosclerosis Related to Plaque Burden Regression During Treatment With Alirocumab: The ARCHITECT Study



TC coronario

Multicenter Study > [Circulation](#). 2023 May 9;147(19):1436-1443.

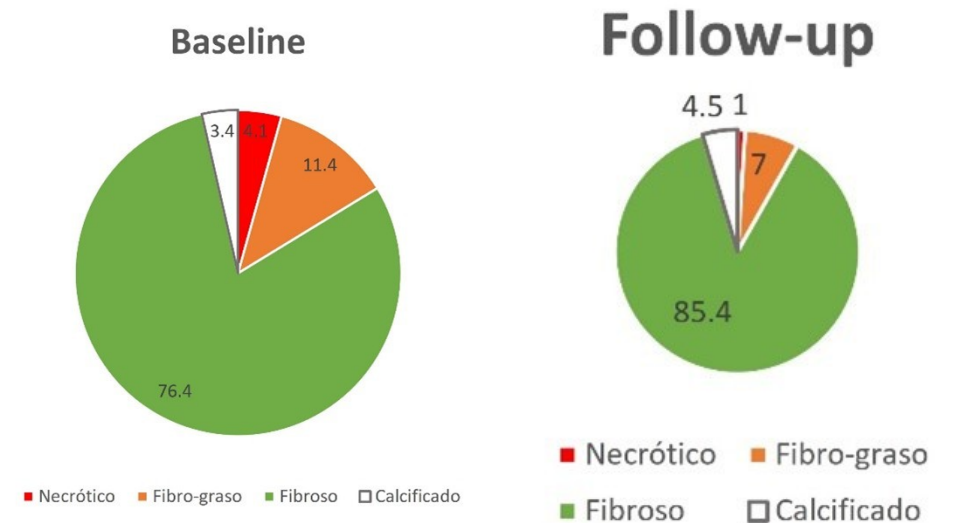
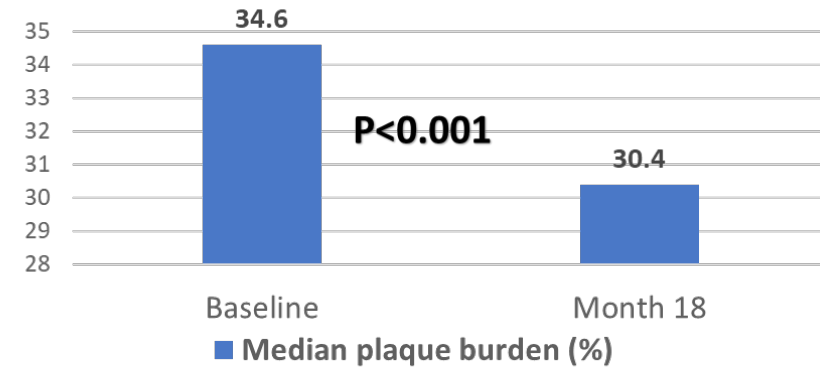
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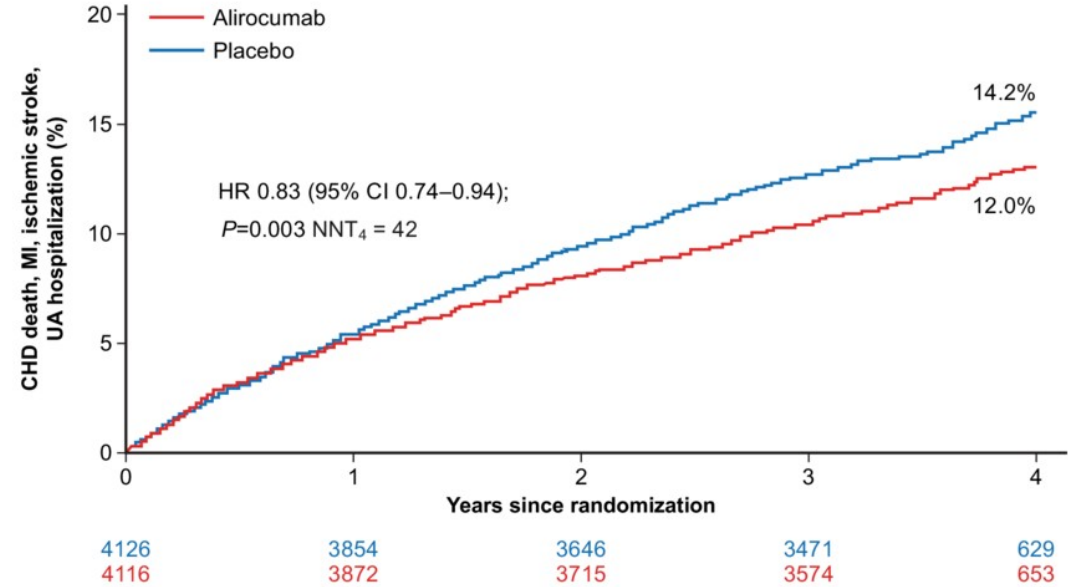
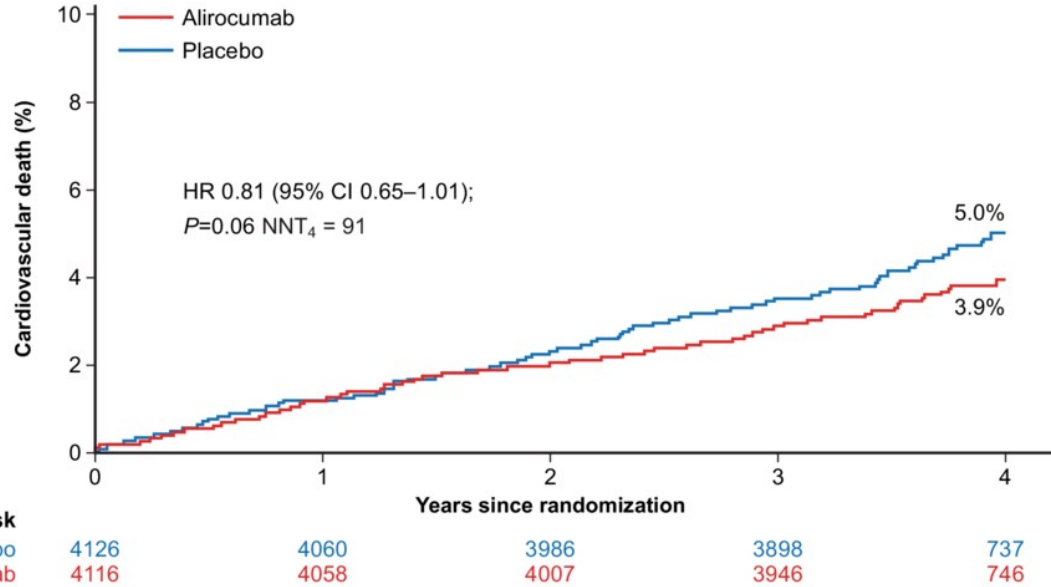
Characteristics of Coronary Atherosclerosis Related to Plaque Burden Regression During Treatment With Alirocumab: The ARCHITECT Study



¿Por qué reducen MACE?
Eficacia y Seguridad a largo plazo
Vida real

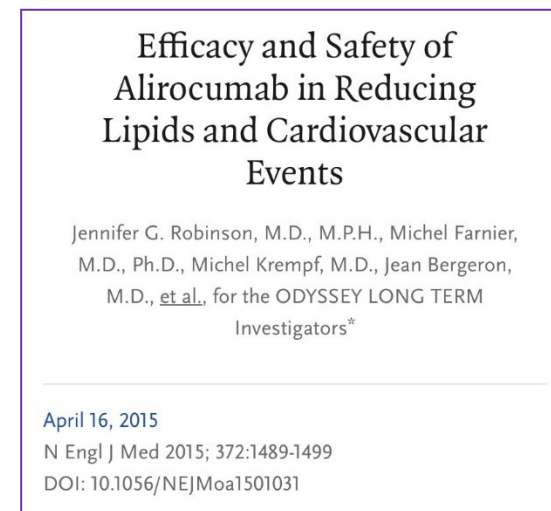
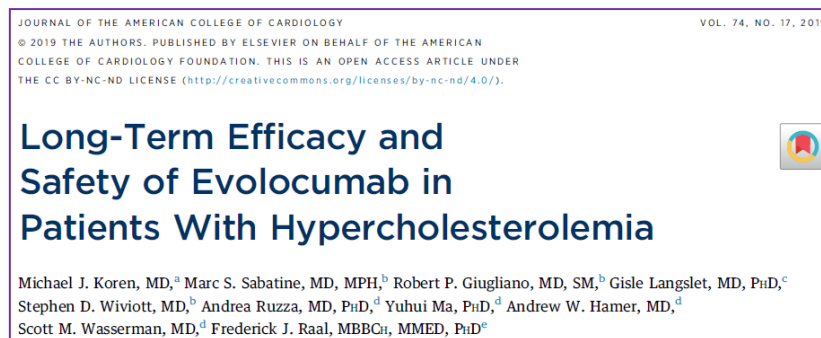
RESEARCH LETTERS

Long-Term Efficacy, Safety, and Tolerability of Alirocumab in 8242 Patients Eligible for 3 to 5 Years of Placebo-Controlled Observation in the ODYSSEY OUTCOMES Trial



Seguridad

- Han demostrado un buen perfil de seguridad, comparable a placebo



Safety of proprotein convertase subtilisin/kexin 9 inhibitors: a systematic review and meta-analysis.

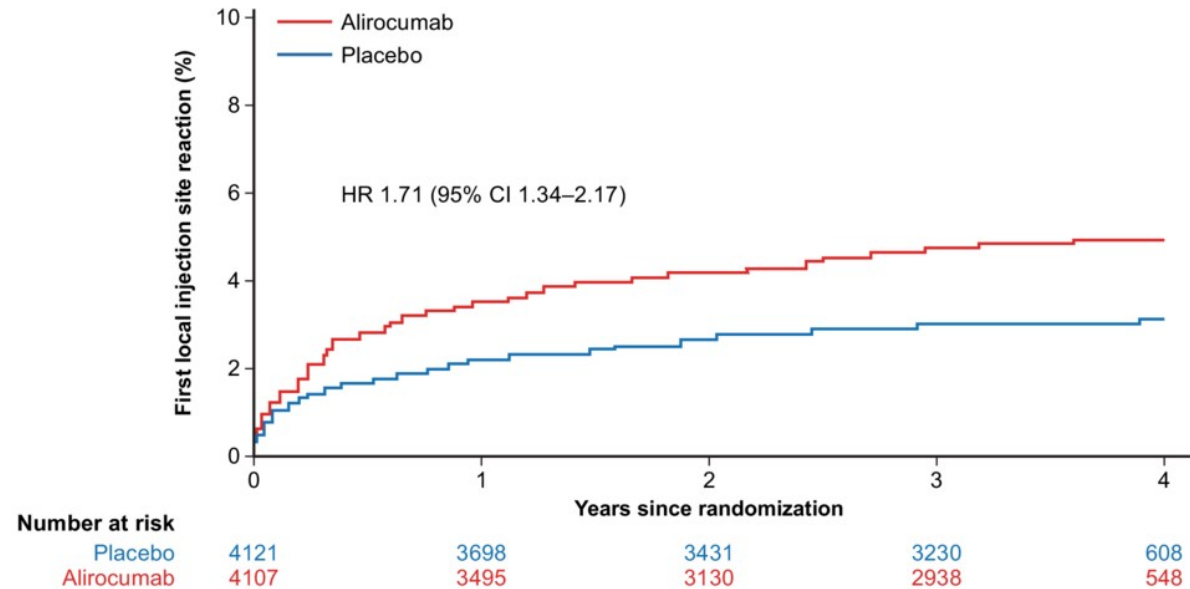
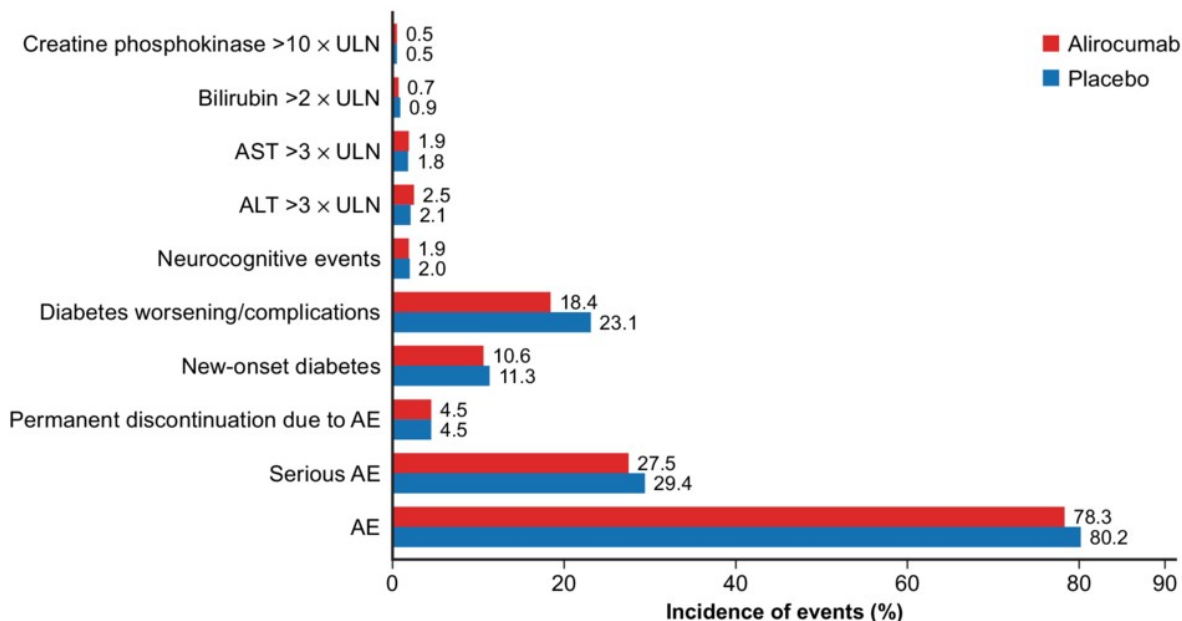
Li J, Du H, Wang Y, Aertgeerts B, Guyatt G, Hao Q, Shen Y, Li L, Su N, Delvaux N, Bekkering G, Khan SU, Riaz IB, Vandvik PO, Su B, Tian H, Li S.

Heart. 2022 Jul 27;108(16):1296-1302. doi: 10.1136/heartjnl-2021-320556.

Conclusions: PCSK9 inhibitors slightly increase the risk of severe **injection-site reaction** but not cataracts, gastrointestinal haemorrhage, neurocognitive events, new-onset diabetes or severe myalgia or muscular pain.

RESEARCH LETTERS

Long-Term Efficacy, Safety, and Tolerability of Alirocumab in 8242 Patients Eligible for 3 to 5 Years of Placebo-Controlled Observation in the ODYSSEY OUTCOMES Trial

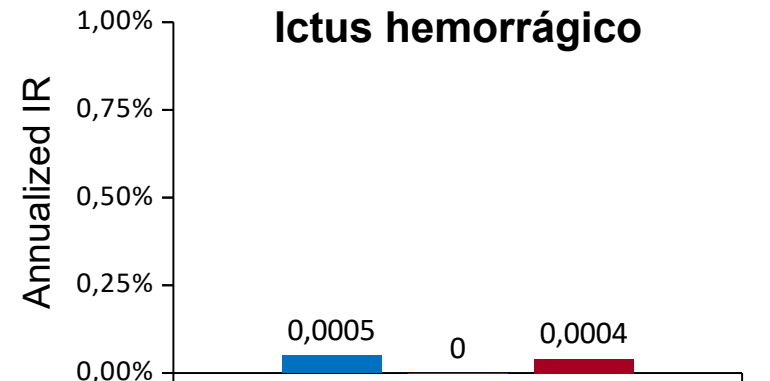
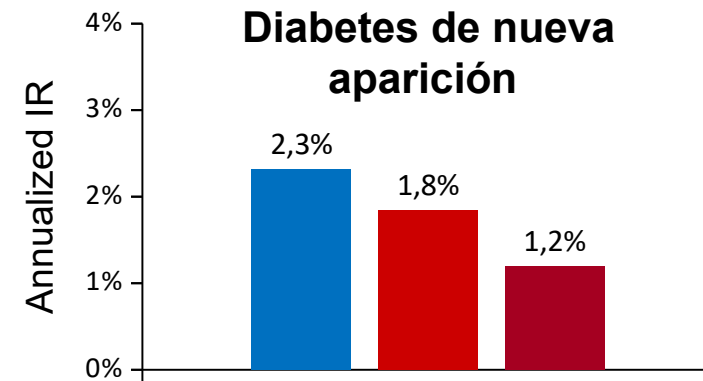
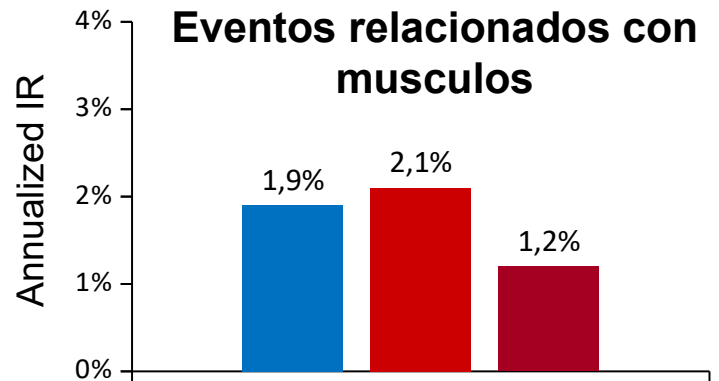
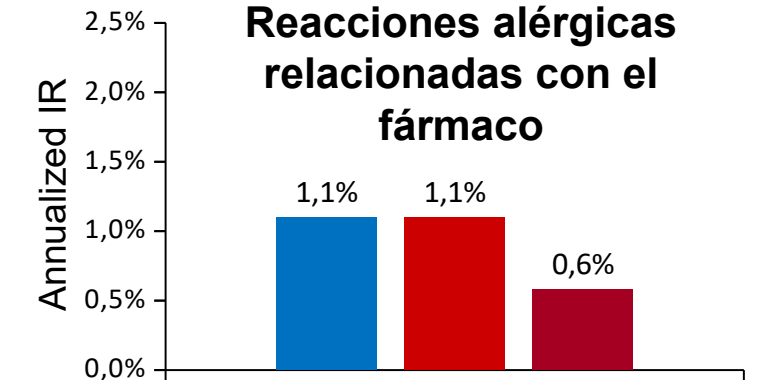
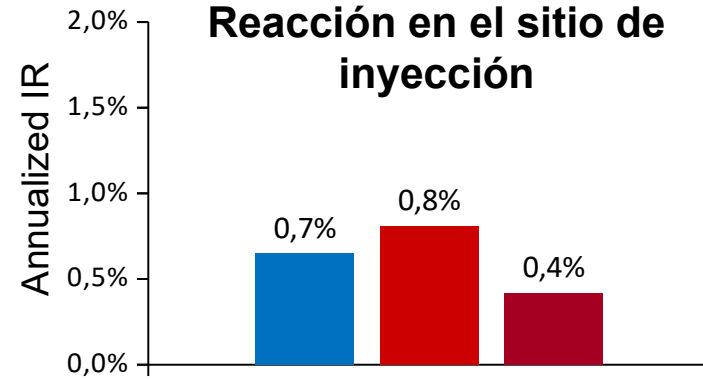
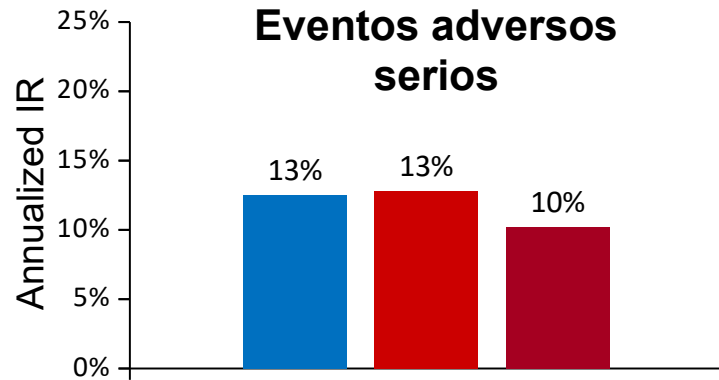
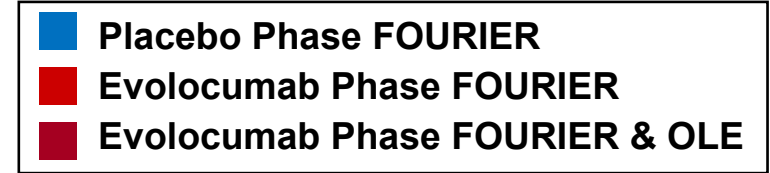




ORIGINAL RESEARCH ARTICLE

Long-Term Evolocumab in Patients With Established Atherosclerotic Cardiovascular Disease

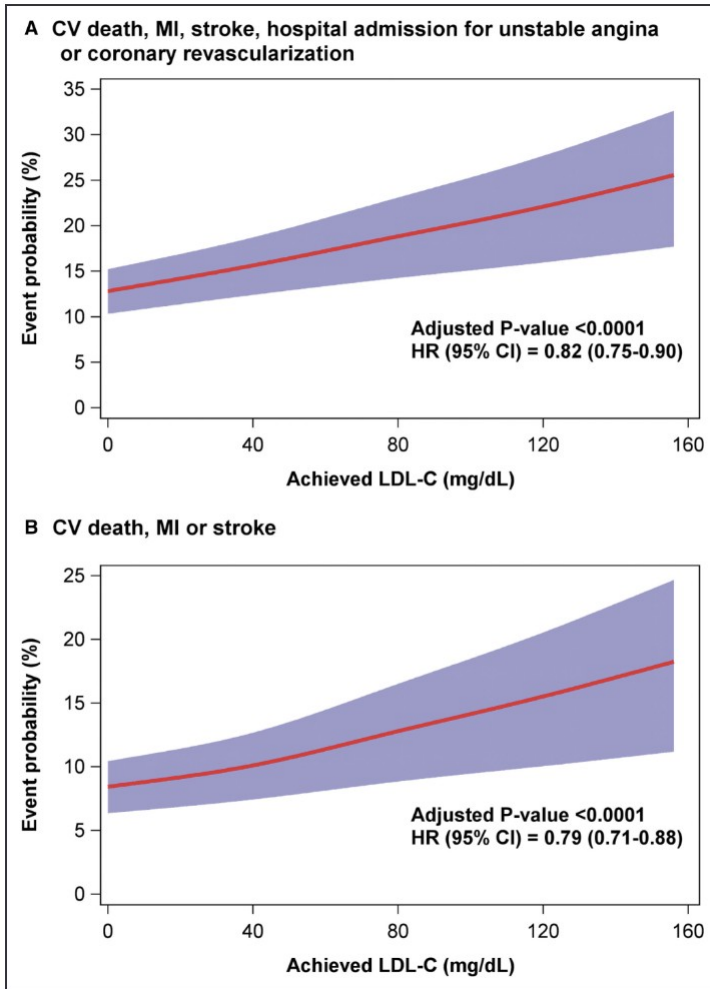
> 8 años



Association Between Achieved Low-Density Lipoprotein Cholesterol Levels and Long-Term Cardiovascular and Safety Outcomes: An Analysis of FOURIER-OLE

Circulation

Volume 147, Issue 16, 18 April 2023; Pages 1192-1203
<https://doi.org/10.1161/CIRCULATIONAHA.122.063399>



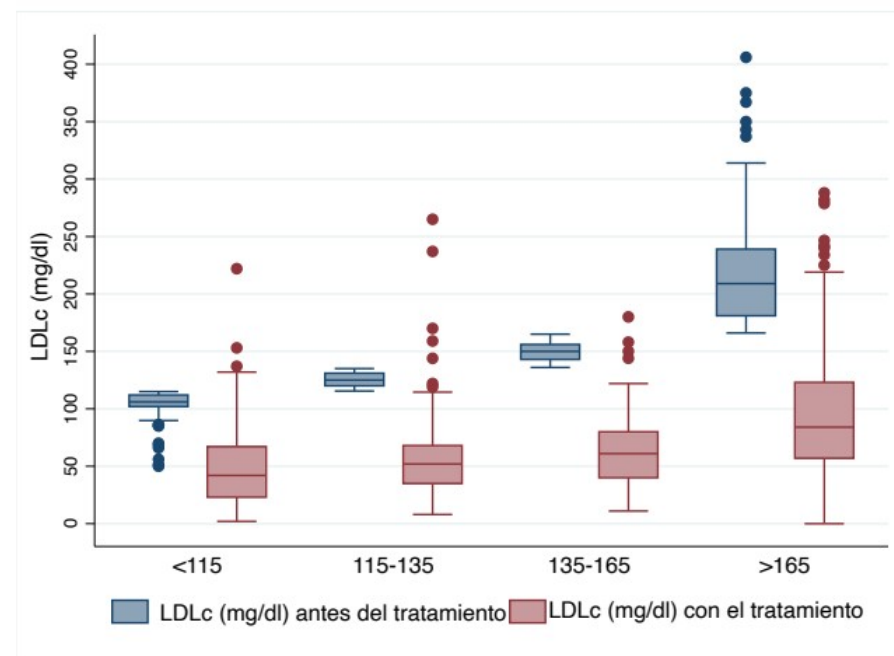
	Achieved LDL-C level, mg/dL					Adjusted <i>P</i> trend
	<20 (n=1604)	20–<40 (n=2627)	40–<55 (n=1031)	55–<70 (n=486)	≥70 (n=811)	
Safety outcomes						
Serious adverse events	12.15 (10.34, 14.27)	12.64 (10.89, 14.67)	12.65 (10.70, 14.97)	12.90 (10.63, 15.65)	12.18 (10.27, 14.43)	0.88
Neurocognitive events	0.50 (0.25, 0.98)	0.53 (0.28, 1.00)	0.53 (0.27, 1.07)	0.30 (0.12, 0.73)	0.43 (0.21, 0.89)	0.35
Cataract-related adverse events	0.82 (0.47, 1.44)	0.87 (0.51, 1.49)	0.91 (0.51, 1.62)	0.33 (0.14, 0.79)	0.64 (0.35, 1.20)	0.11
New or progressive malignancy	1.83 (1.26–2.66)	1.76 (1.23–2.50)	1.73 (1.17–2.57)	1.89 (1.21–2.96)	1.36 (0.89–2.10)	0.23
New-onset diabetes*	0.66 (0.32, 1.39)	0.52 (0.25, 1.05)	0.46 (0.20, 1.02)	0.45 (0.18, 1.12)	0.43 (0.20, 0.95)	0.13
Hemorrhagic stroke†	0.06 (0.02, 0.15)	0.09 (0.05, 0.17)	0.07 (0.02, 0.20)	—	0.06 (0.01, 0.23)	0.55
Muscle-related events	0.67 (0.38, 1.18)	0.62 (0.36, 1.07)	0.69 (0.38, 1.24)	0.76 (0.39, 1.46)	0.56 (0.30, 1.05)	0.84
Noncardiovascular death	1.33 (0.87, 2.04)	1.14 (0.76, 1.71)	1.65 (1.07, 2.56)	2.32 (1.46, 3.67)	1.49 (0.94, 2.36)	0.04
All-cause mortality	2.65 (1.98, 3.56)	2.87 (2.20, 3.76)	3.72 (2.77, 5.00)	4.30 (3.10, 5.98)	3.93 (2.92, 5.29)	0.0001

¿Por qué reducen MACE?
Eficacia y Seguridad a largo plazo
Vida real

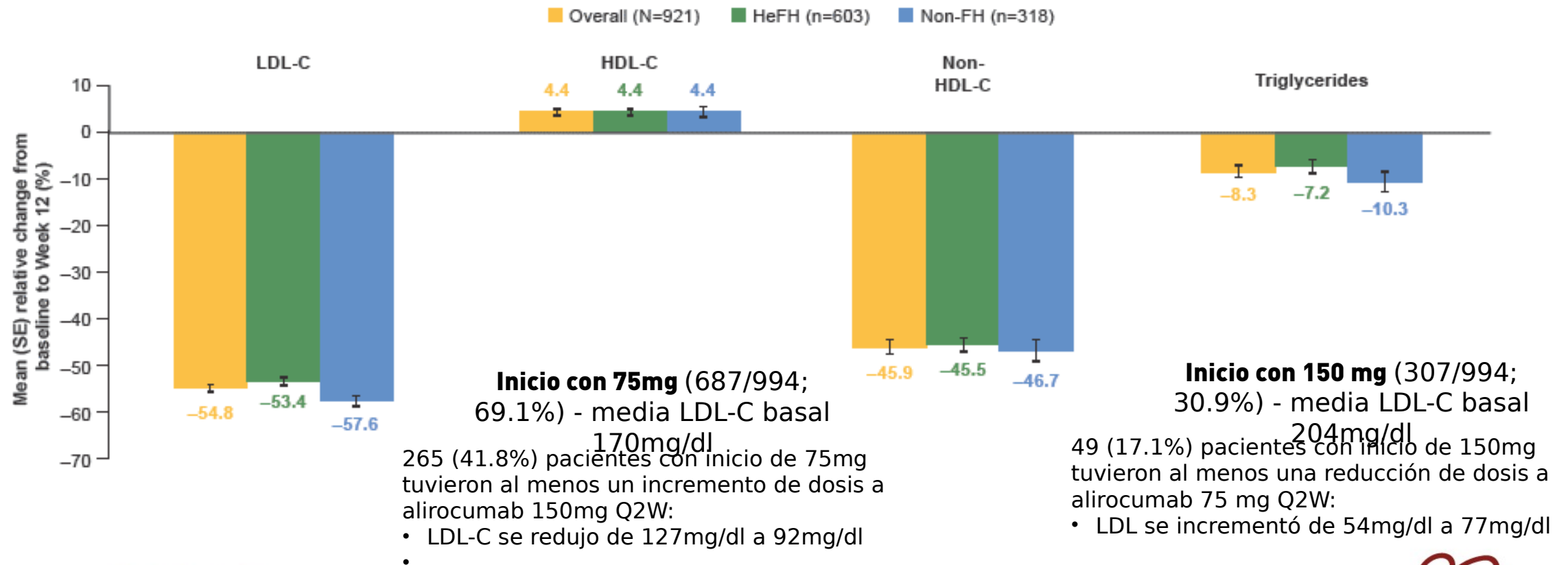
Registro LIPID-REAL

- 14 hospitales, 552 pacientes
- Edad media 60.2, 79,2% varones y 73,3% enfermedad cardiovascular
- 92,3% recibían tratamiento con estatinas y 54,1% con ezetimibe
- Evolocumab 140 en 318 (56,6%); alirocumab 75 en 229 (40,7%) y alirocumab 150 en 15 (2,7%)
-

La mediana de LDLc fue 135 (RIQ 115,0-165,0) mg/dl y con el tratamiento 57 (RIQ 36,4-83,0). La reducción media de LDLc fue del 54,7%

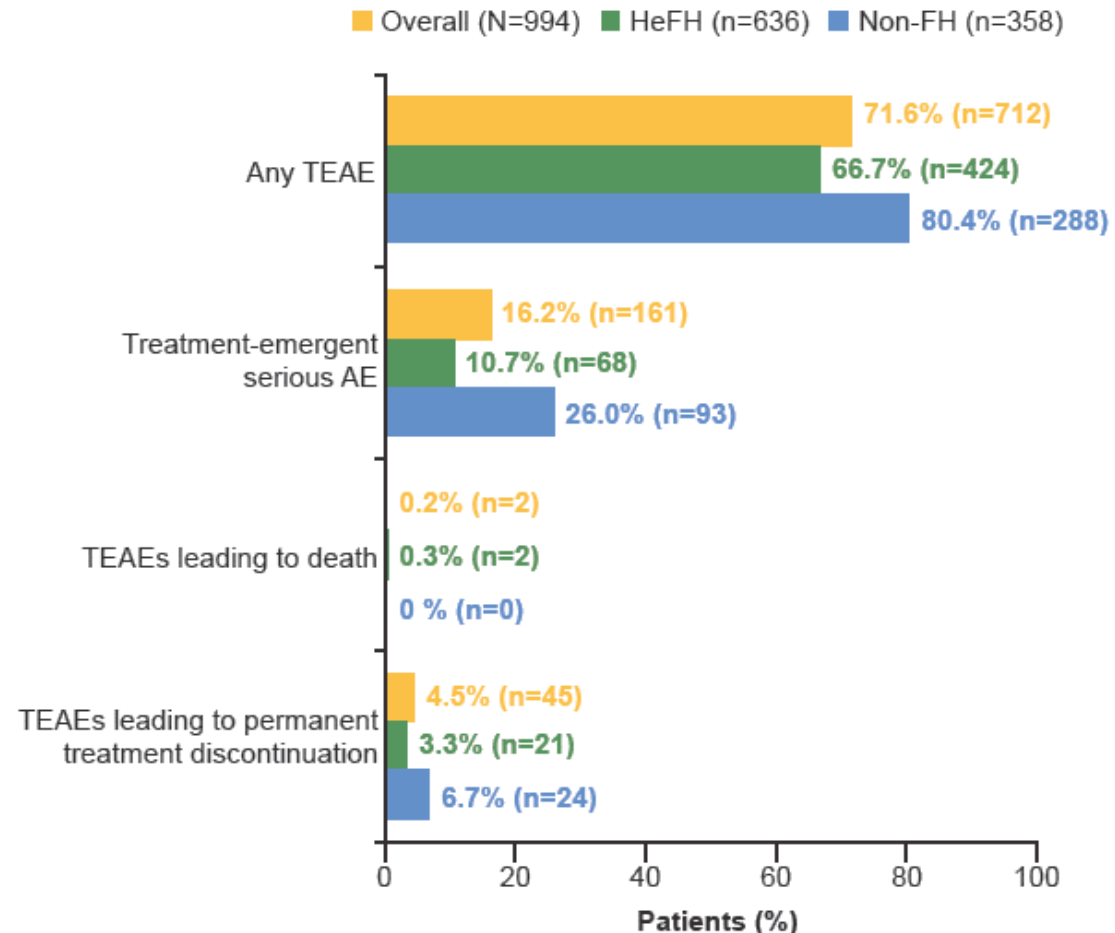


Efficacy and safety of alirocumab in a real-life setting in patients with or without familial hypercholesterolemia: The ODYSSEY APPRISE study



Efficacy and safety of alirocumab in a real-life setting in patients with or without familial hypercholesterolemia: The ODYSSEY APPRISE study

En general, los TEAE comunes incluyeron nasofaringitis (7,8 %), mialgia (7,1 %), dolor de cabeza (6,2 %) e influenza (5,3 %).



HEYMANS registry

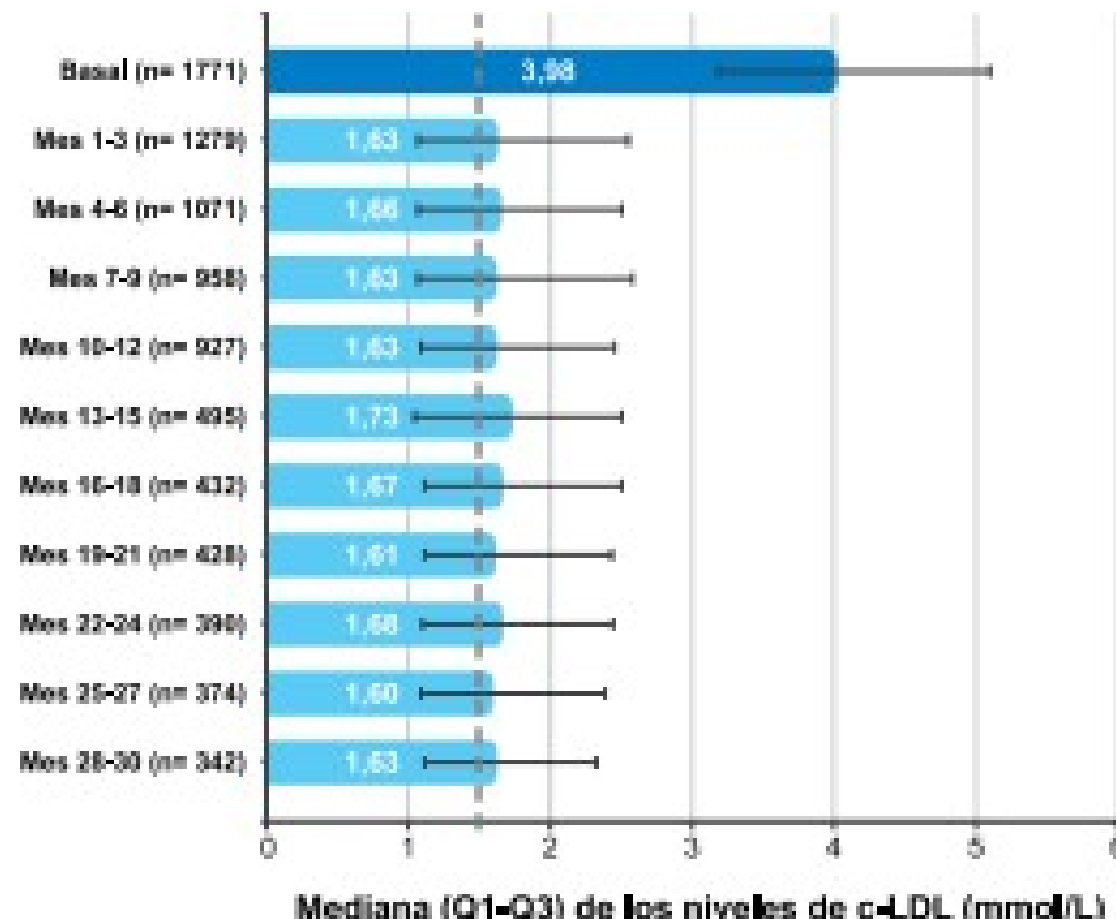
La mediana de los niveles de c-LDL disminuyó en un **58%** en los 3 meses siguientes al inicio del tratamiento **evolocumab**



Estas reducciones **se mantuvieron a lo largo de todo el estudio** (-58% desde el valor basal a los 30 meses de seguimiento)

A los 30 meses de seguimiento, el **92,2%** (921/999) de los pacientes **permanecían en tratamiento con evolocumab**

Evolución de los niveles totales de c-LDL



“Mini-Conclusiones” iPCSK9

- Reducen un 55-60% el LDLc mantenido en el tiempo
- Reducen un 15-20% MACE
- Reducen volumen placa y la estabilizan
- Son seguros a largo plazo, también LDL-c muy bajo
- LDL>100 con estatina dosis máxima tolerada + ezetimibe

Gracias

Dr. Juan Rondán | *Hospital Universitario de Cabueñes*