Alirocumab and Reduction of Cardiovascular Event

Current Evidence and Future Perspectives

Hyuck-Jun Yoon

Division of Cardiology, Department of Internal Medicine, Keimyung University Dongsan Hospital

계명대학교 동산병원
KEIMYUNG UNIVERSITY DONGSAN HOSPITAL

1

Lipid lowering strategies for Post-ACS

Patients of CV high-risk[1]

Praluent® alirocumab

2019 ESC/EAS Guidelines[1]

ACS
(MI or unstable angina)

Stable angina

Coronary revascularization
(PCI, CABG, and other arterial revascularization procedures)

stroke and TIA

Peripheral arterial disease*

CV very-high risk: ASCVD[1]

*Unequivocally documented ASCVD on imaging includes those findings that are known to be predictive of clinical events, such as significant plaque on coronary angiography or CT scan (multivessel coronary disease with two major epicardial arteries having >50% stenosis), or on carotid ultrasound.

ACS, acute coronary syndrome; ASCVD, atherosclerotic cardiovascular disease; CABG, coronary artery bypass graft; CT, computed tomography CV, cardiovascular; EAS, European Atherosclerosis Society; ESC, European Society of Cardiology; MI, myocardial infarction; PCI, percutaneous coronary intervention; TIA, transient ischemic attacks.

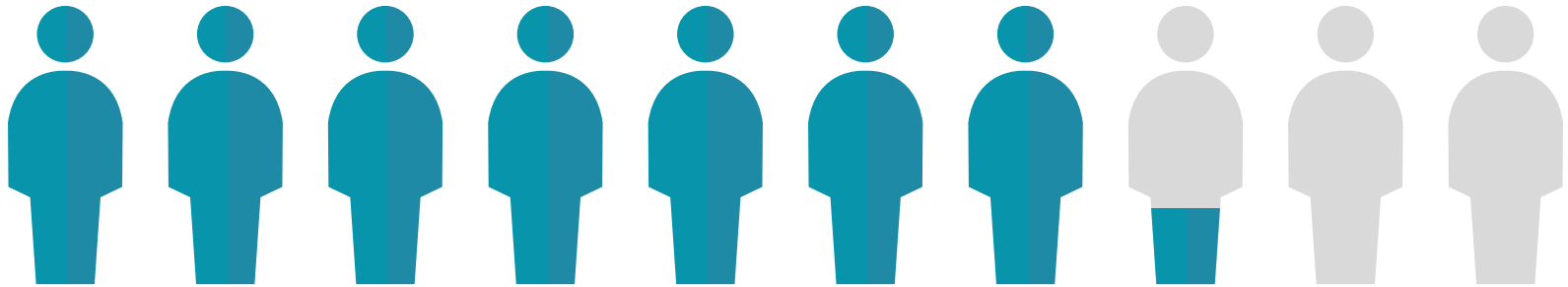
Reference. 1. Mach F, et al. Eur Heart J. 2020;41:111-188.

After the first ACS event, the risk of a recurrent CV event increases if LDL-C is not rapidly recontrolled[1]

Praluent® alirocumab

RECURRENCE OF CV EVENTS[1]

73% *IN THE FIRST 6 MONTHS COMPARED TO THE FIRST 12 MONTHS*



ACS, acute coronary syndrome; CV, cardiovascular; LDL, low-density lipoprotein.
[Study design[1]] This was a retrospective, cohort study linking morbidity, mortality, and medication data from Swedish national registries. Of 108 315 patients admitted to hospital with a primary MI between 1 July 2006 and 30 June 2011 (index MI), 97 254 (89.8%) were alive 1 week after discharge and included in this study. Analysed data from mandatory Swedish national registries: the National Inpatient Register (IPR) [inpatient admission and discharge dates. The primary endpoint was a composite of risk for non-fatal MI, non-fatal stroke, or cardiovascular death was estimated for the first 365 days post-index MI and Day 366 to study completion.

Reference. 1. Jernberg T, et al.Eur Heart J. 2015;36(19):1163–1170.

1 in 4 patients with ACS experienced a recurrence after their first stenting procedure[1]

Praluent® alirocumab

Recurrence within 6-8 month in first ACS **25%**

Patients at high risk of CV events, such as ACS, need a robust LDL-C management strategy to reduce the risk of recurrence and death.[1]

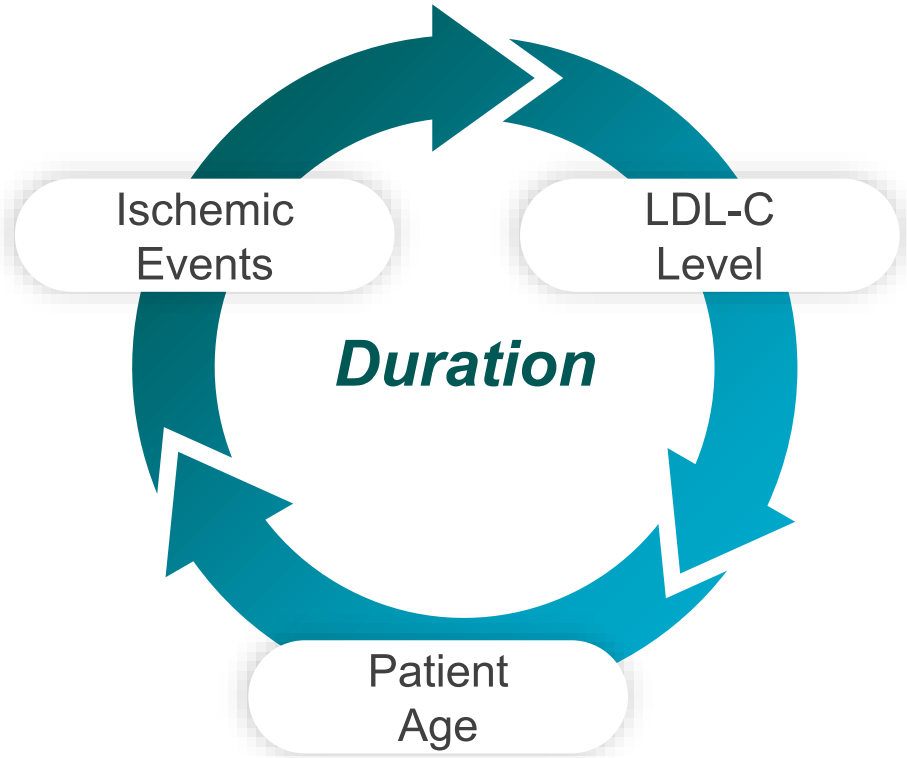
ACS, acute coronary syndrome; CV, cardiovascular; LDL, low-density lipoprotein.

Reference. 1. 급성관상동맥증후군 백서. 심혈관연구원. 2012.02.

What to consider Treatment *Strategies*

Praluent® alirocumab

- Establish patient risk level
- Patients post-ACS need lipid levels reevaluated at 4 to 6 weeks to assess safety issues and adjust treatment, if necessary
  - Restrafity patients by risk
  - Assess statins and ezetimibe
  - Consider PCSK9 inhibitors

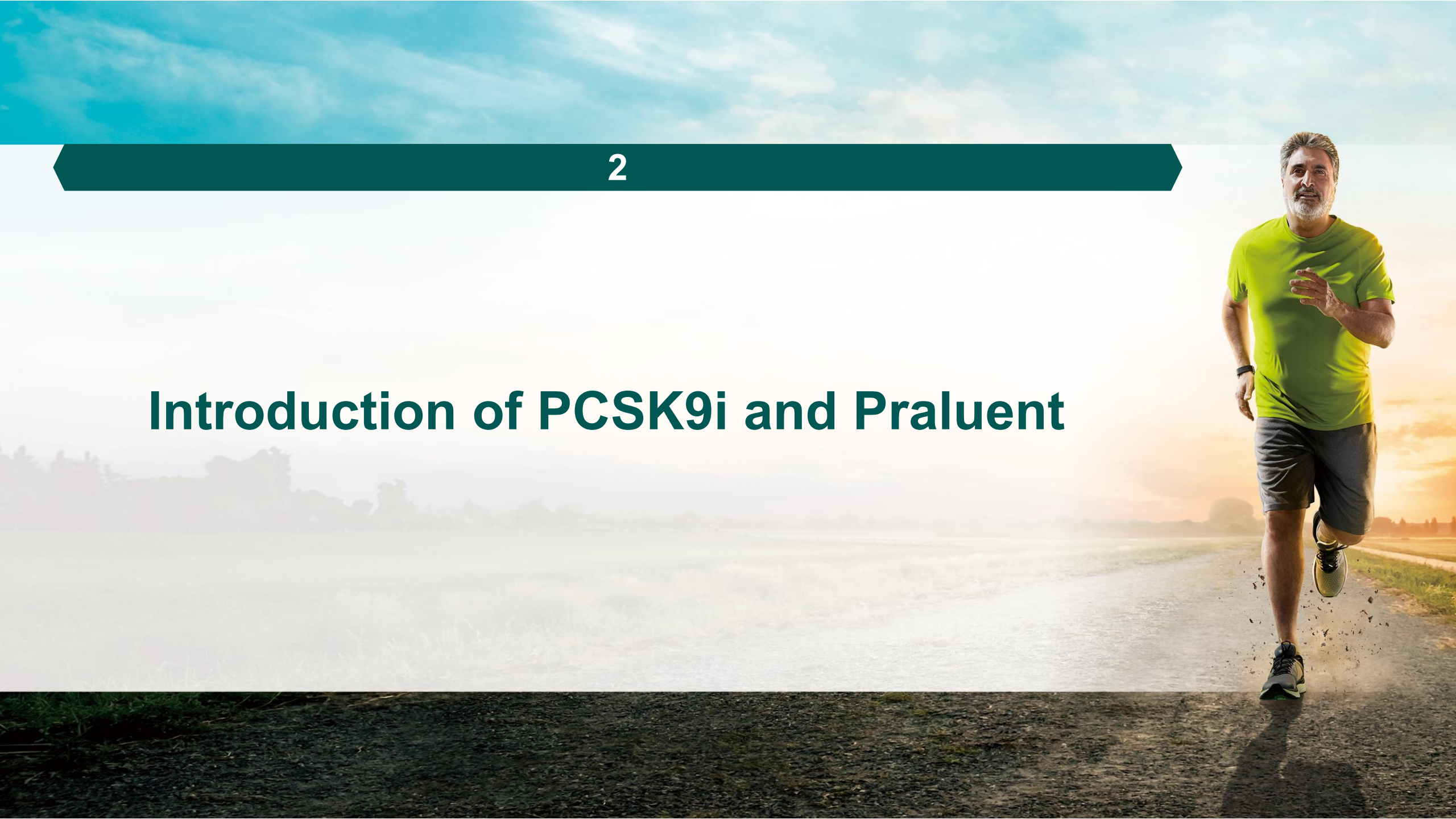


ACS, acute coronary syndrome; LDL-C, low-density lipoprotein cholesterol; PCSK9, proprotein convertase subtilisin/kexin type 9.

Reference. 1. Mach F, et al. Eur Heart J. 2020 Jan 1;41(1):111-188.

2

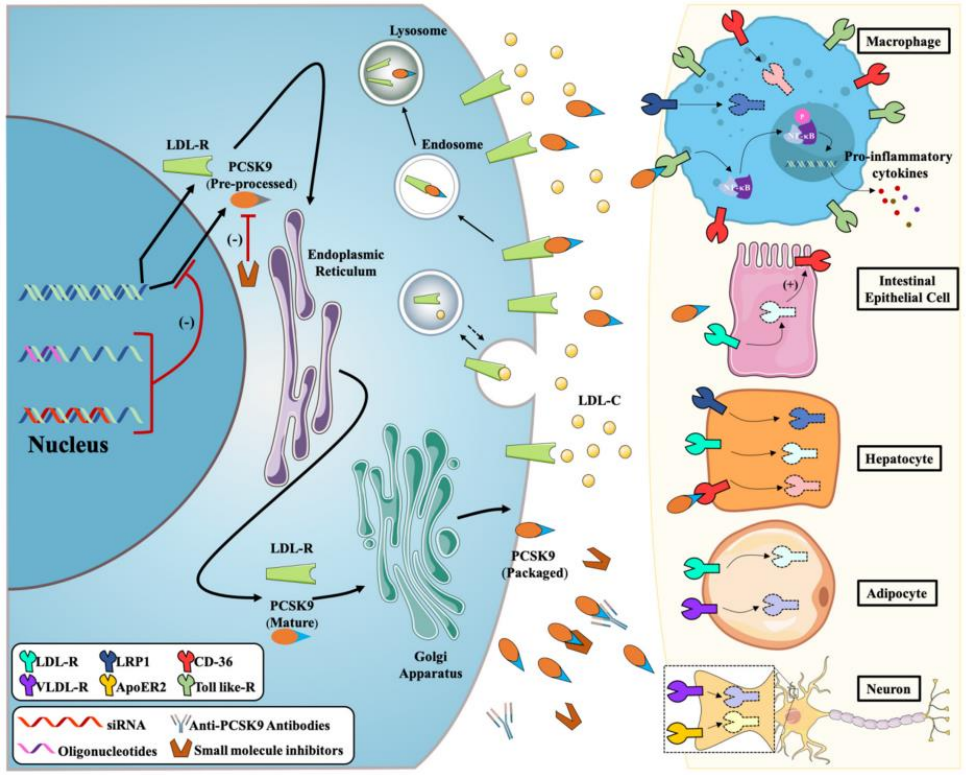
Introduction of PCSK9i and Praluent



Molecular mechanisms of PCSK9 inhibitors with different strategies[1]

Praluent® alirocumab

Molecular Mechanism of PCSK9[1]



adapted from Liu C, et al. 2022.

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

Reference. 1. Liu C, et al. Cells. 2022 Sep 23;11(19):2972.

PCSK 9 inhibitor

PRALUENT® has an established mechanism of action

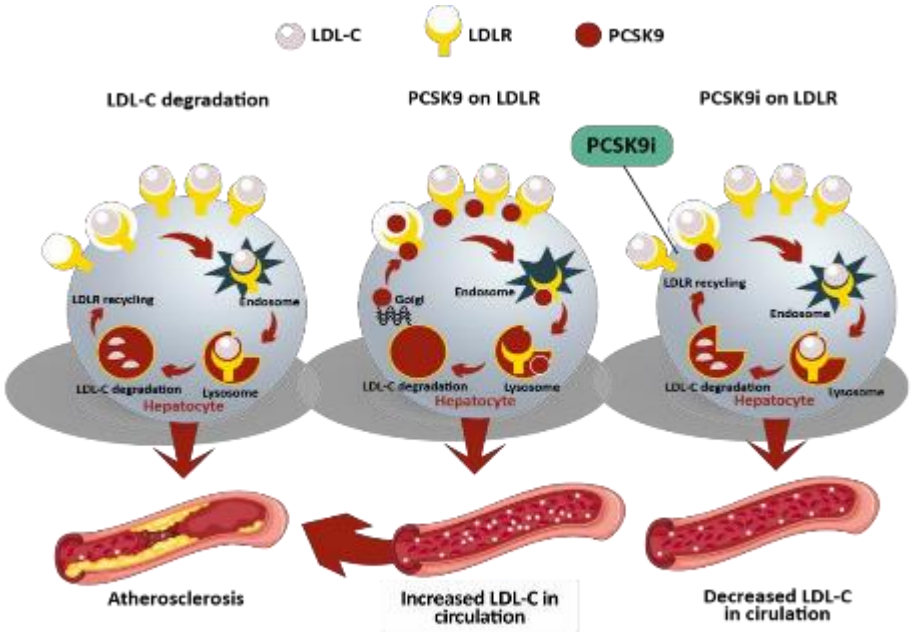
Praluent® alirocumab

Alirocumab makes LDL-R recycle to the surface of hepatocyte, which means lowering LDL-C consistently

- PCSK9 inhibition is an effective way of reducing LDL-C
- PSCK9 inhibitors decrease LDL-R degradation, resulting in improved lipid metabolism, reducing plasma LDL-C, leading to reduced risk of atherosclerosis[1]

Specific characteristics of PRALUENT®

- **Time to steady state:** Reached after 2 or 3 doses[2]
- **High bioavailability:** Absolute bioavailability of ~85%[2]
- **High binding affinity[2]:** Dissociation constant of 0.58 nM[3]



PCSK9, proprotein convertase subtilisin/kexin type 9; LDL-R, low-density lipoprotein receptor; LDL-C, low-density lipoprotein cholesterol

Reference. 1. Amput P, et al. Biomed Pharmacother. 2019 Jan;109:1171-1180; 2. Alirocumab SmPC; 3. Djebli N, et al. Clin Pharmacokinet. 2017 Oct;56(10):1155-1171.

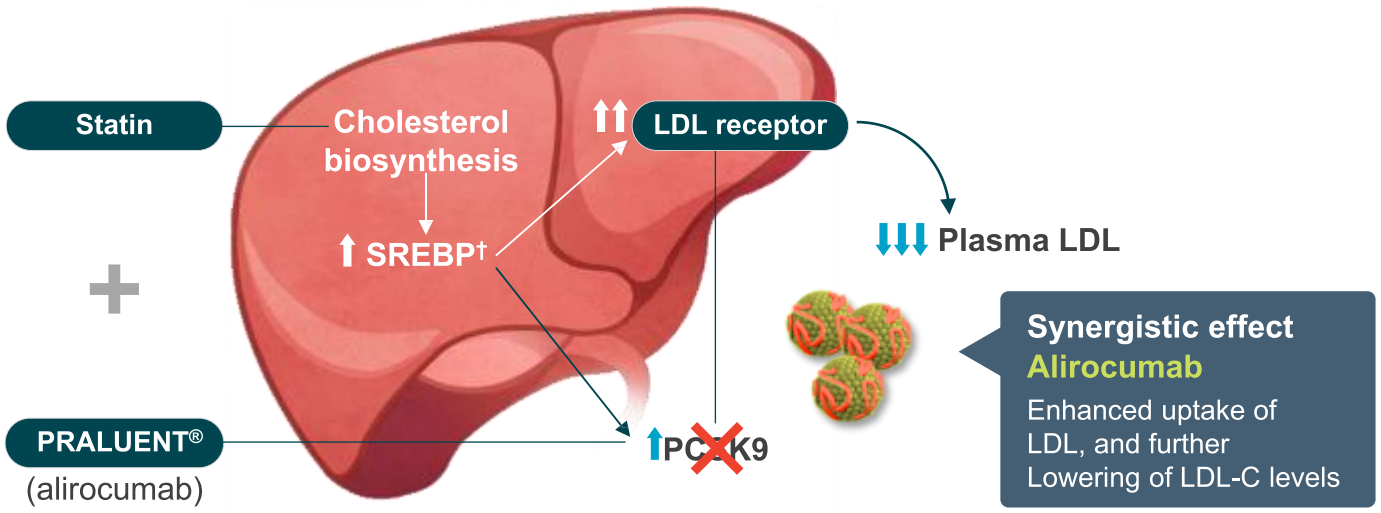
PCSK 9 inhibitor

Synergistic effect of PCSK9 inhibitor and Statin

Praluent® alirocumab

- Alirocumab would be predicted to lower LDL-C levels alone and in combination with statins by increasing cell-surface expression of LDLR

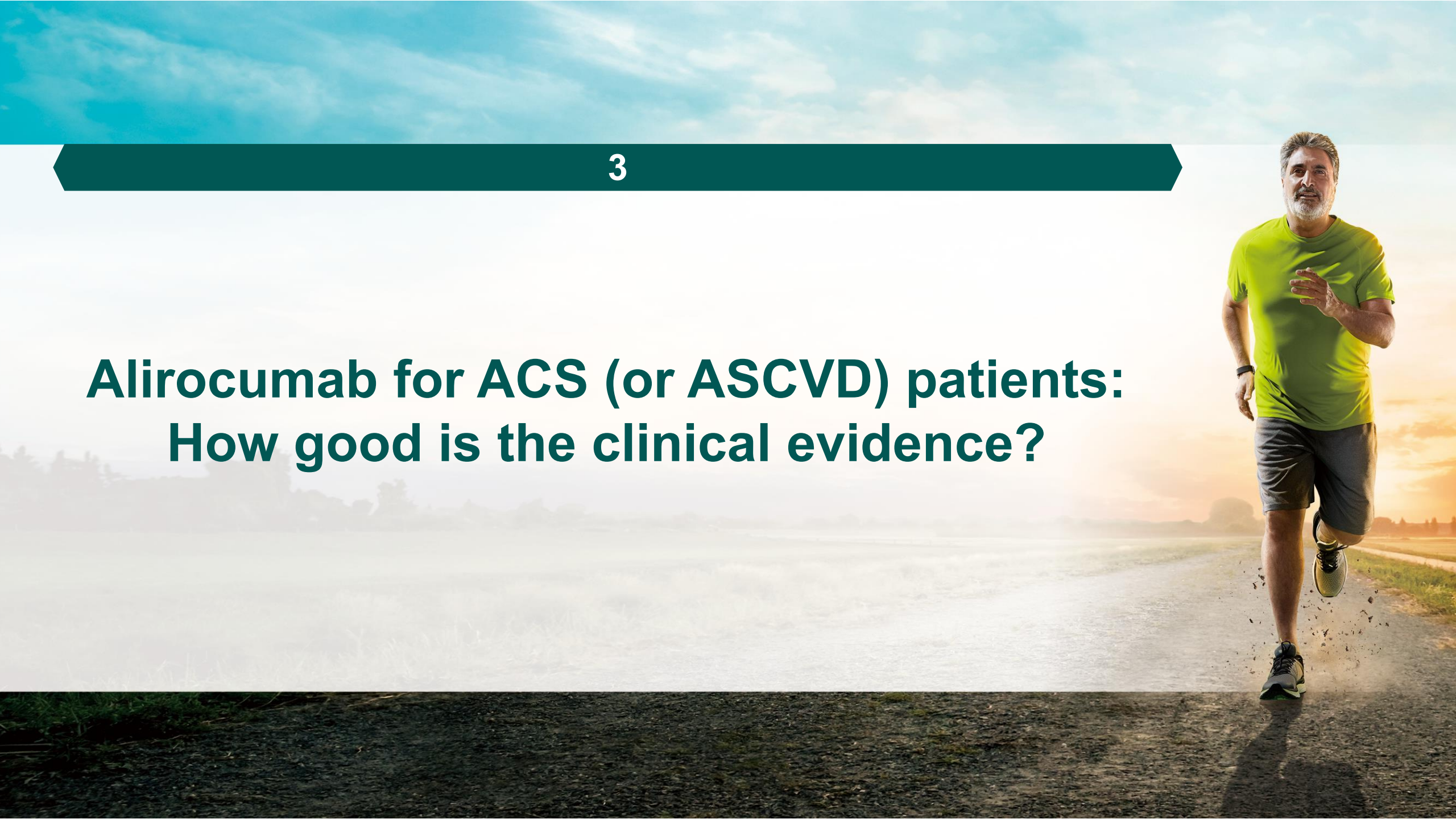
Lowering plasma LDL-C levels by increasing cellular LDL-Rs



*SREBP transcription factor : upregulates transcription of the LDL-R → LDL-C ↓
LDL-C, low-density lipoprotein cholesterol; LDL-R, low-density lipoprotein receptor.

Reference. 1. Maxwell KN, *et al*. Circ Res. 2012;111(3):274-277.

Alirocumab for ACS (or ASCVD) patients: How good is the clinical evidence?



Case 1. Acute Coronary Syndrome

Case

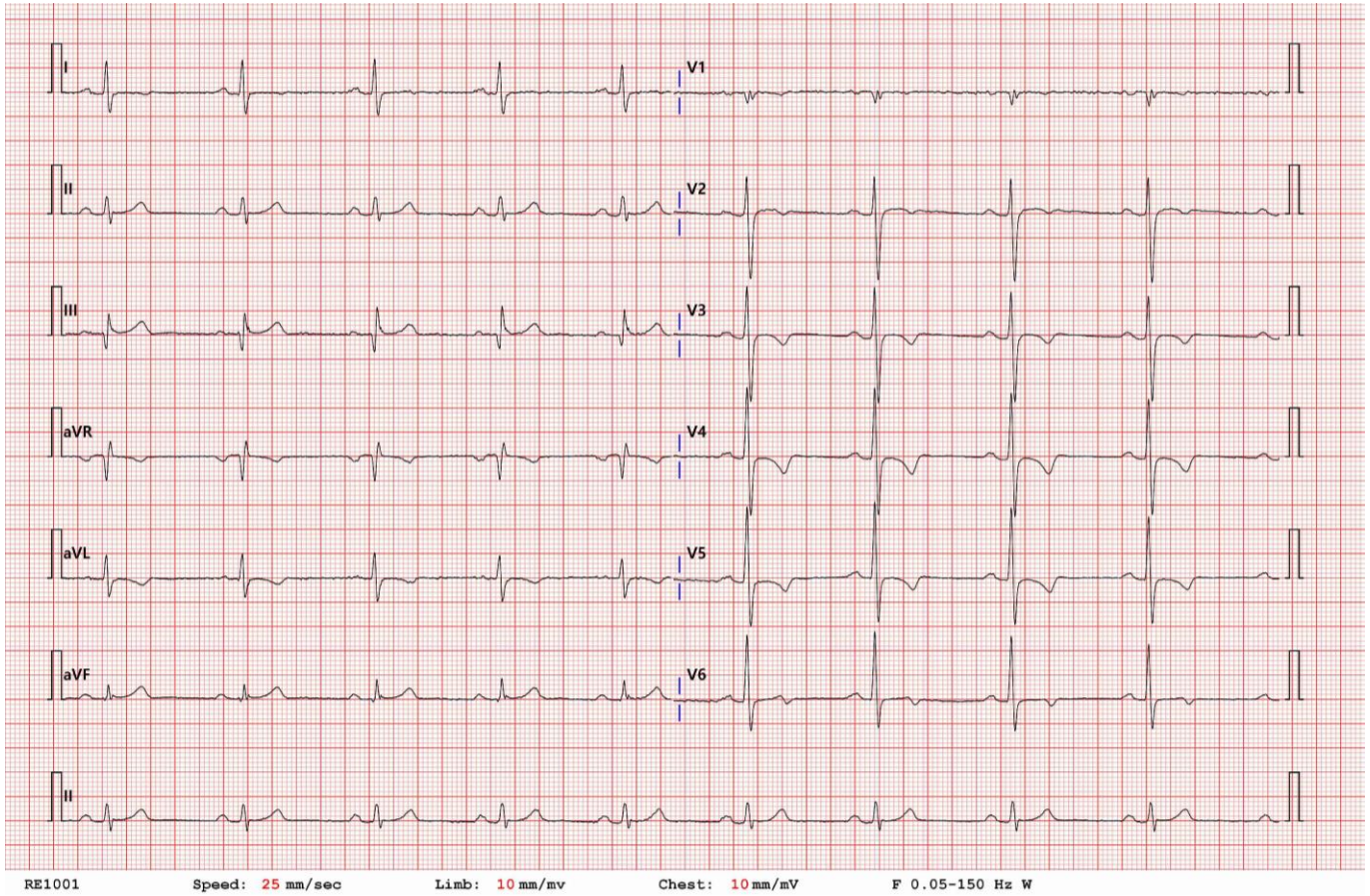
- 46YR , Male, 184cm/95kg, BMI 28.0

Coronary Risk Factors

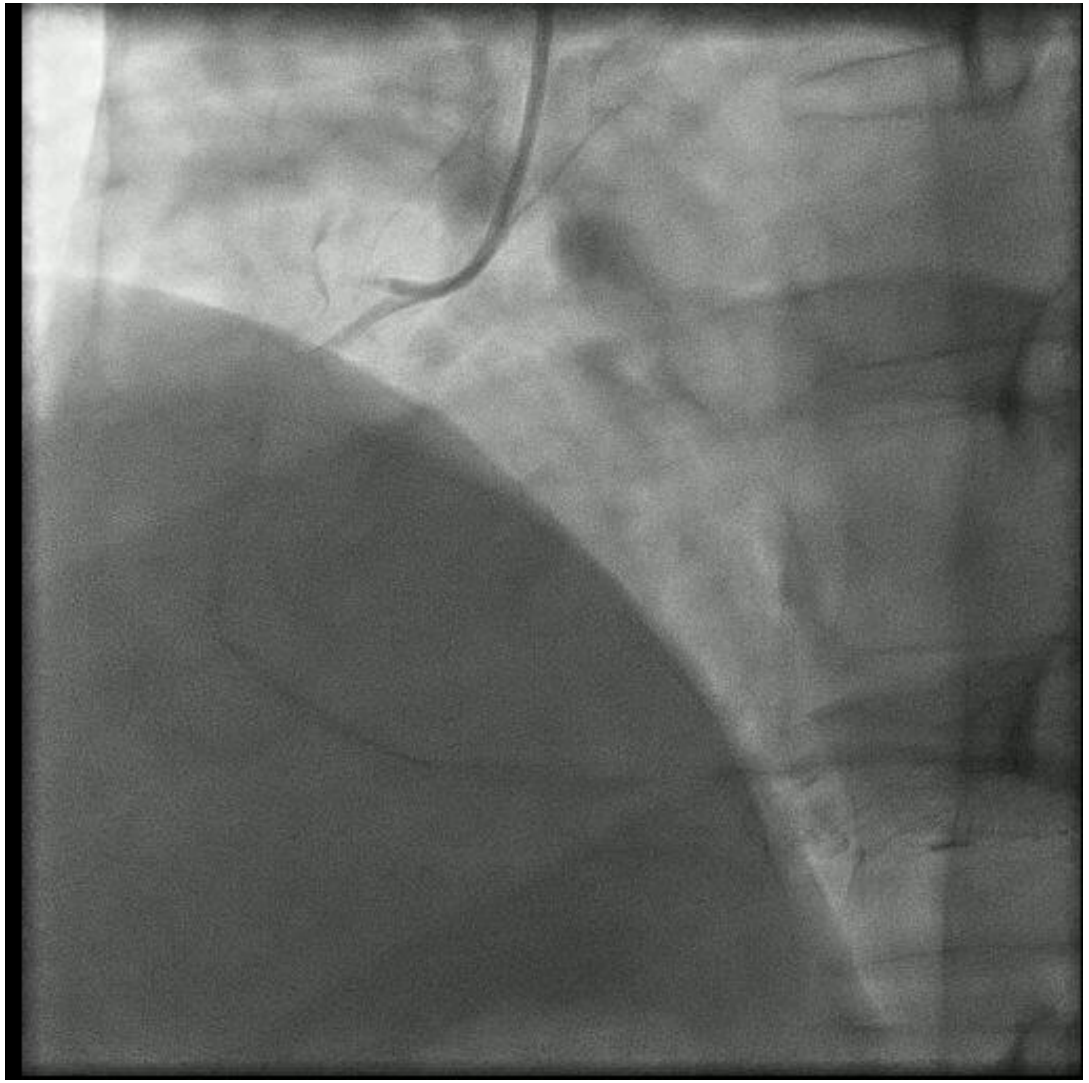
- Family hx. of early ASCVD

Brief History

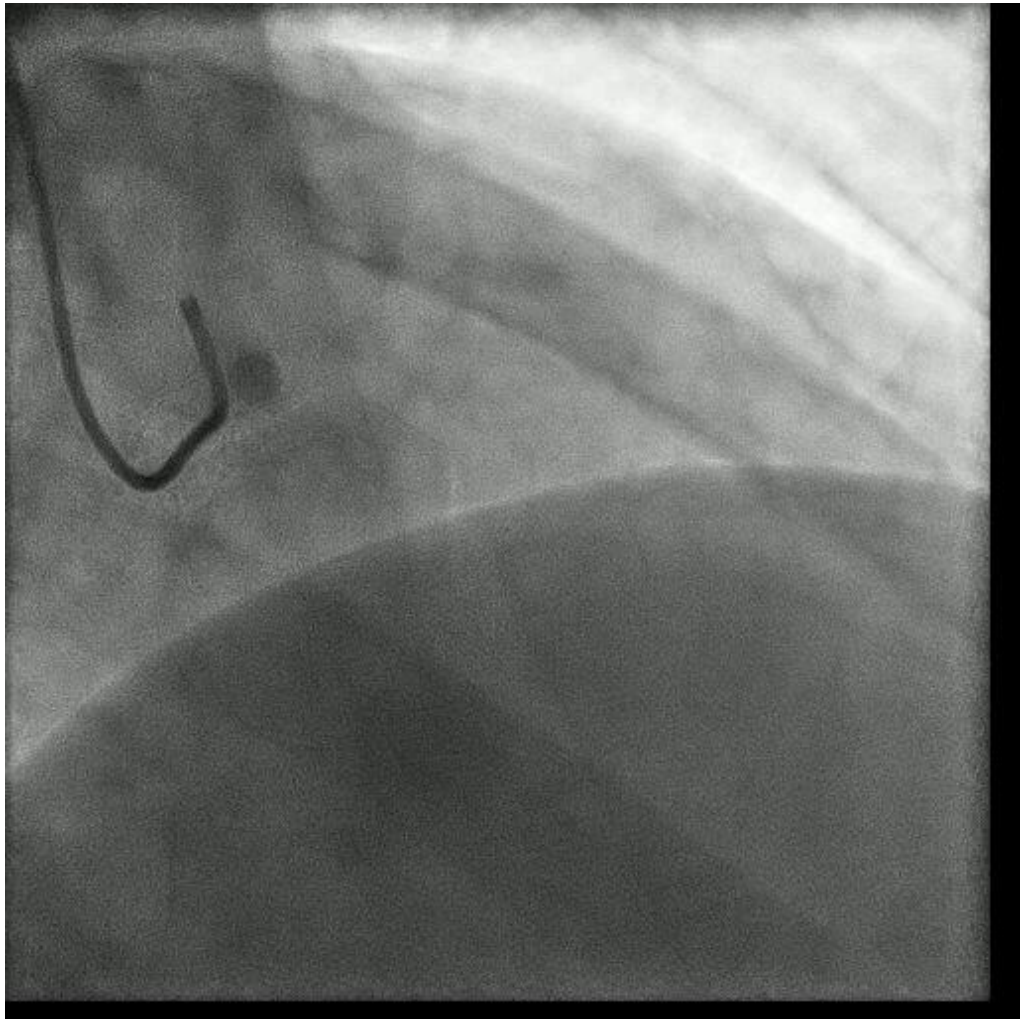
- Aggravated chest pain during exercise
- resting onset chest pain at morning



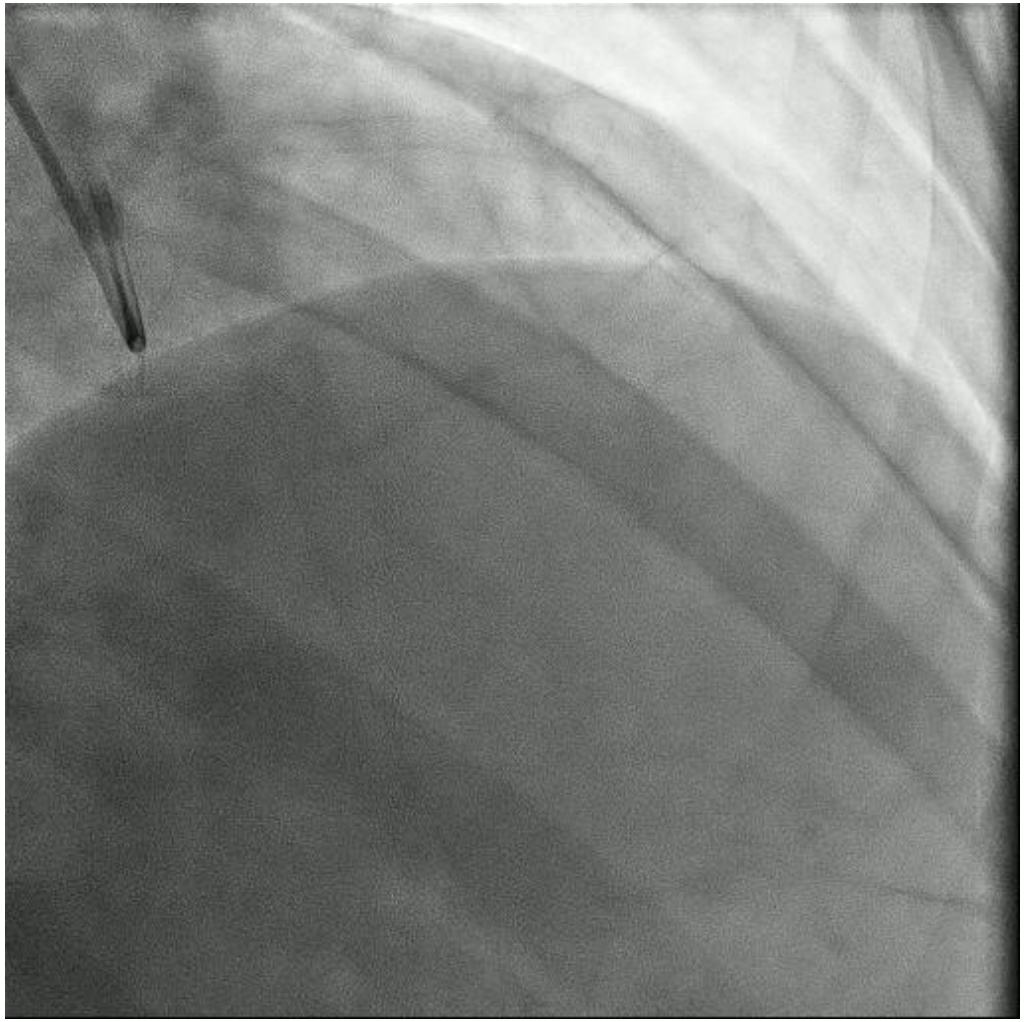
Case 1. Acute Coronary Syndrome



Case 1. Acute Coronary Syndrome



DES 3.5x28mm + 3.25x38mm



Case 1. Acute Coronary Syndrome

Case

- 46YR , Male, 184cm/95kg, BMI 28.0

Dx	LDL (mg/dL)	Medication
Unstable Angina	257	
1mo	115	Rosuva 20mg/Eze 10mg
3mo	36	**Alirocumab 150mg q 2wks**, Rosuva 20/Eze 10mg
12mo	40	**Alirocumab 150 mg q 4wks,** Rosuva 20/Eze 10mg
18mo	98	D/C Alirocumab Rosuva 20/Eze 10mg
24 mo	35	**Alirocumab 150 mg q 2wks,** Rosuva 20/Eze 10mg

Case 1. Acute Coronary Syndrome

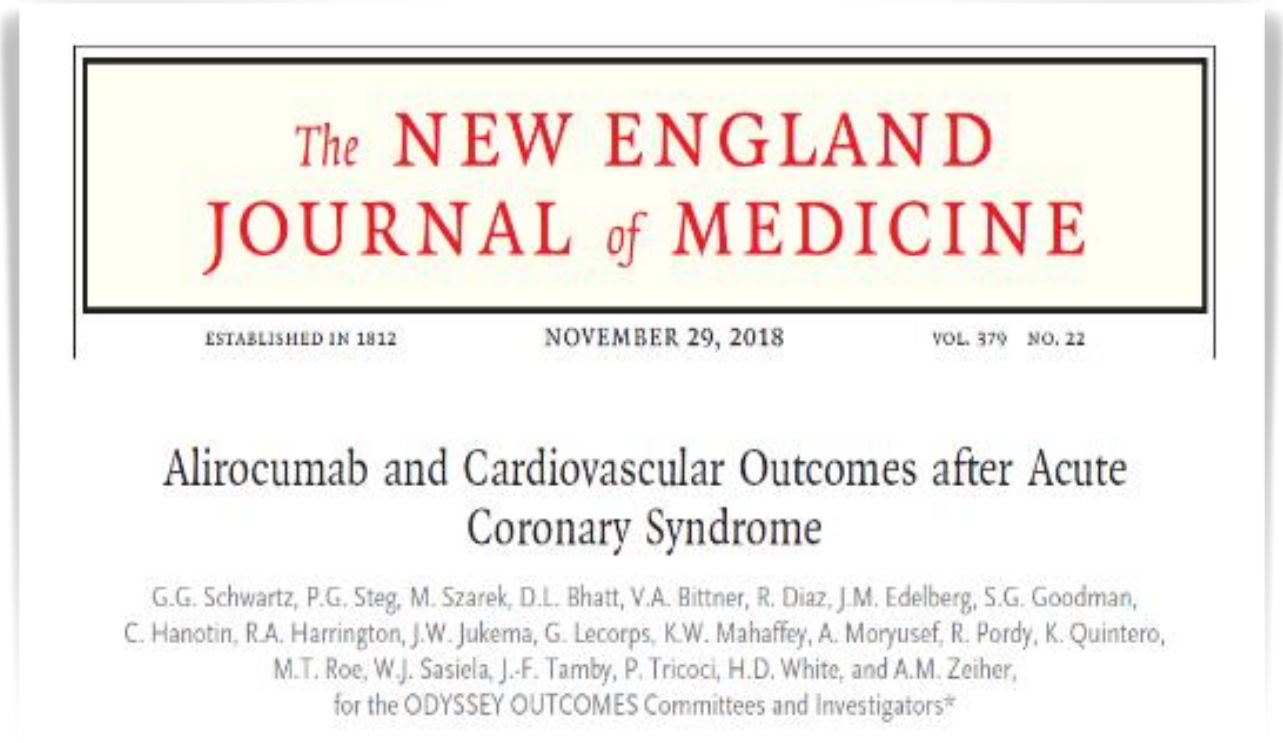
The Patient's Question?

1. What is the benefit of PCSK9i for me ?
2. Is it safe for long-term use, especially in Asian?

ODYSSEY OUTCOMES

Alirocumab and Cardiovascular Outcomes after Acute Coronary Syndrome
- Schwarz GG, et al. N Engl J Med. 2018;379:2097–107.

Praluent®
alirocumab



The NEW ENGLAND JOURNAL of MEDICINE

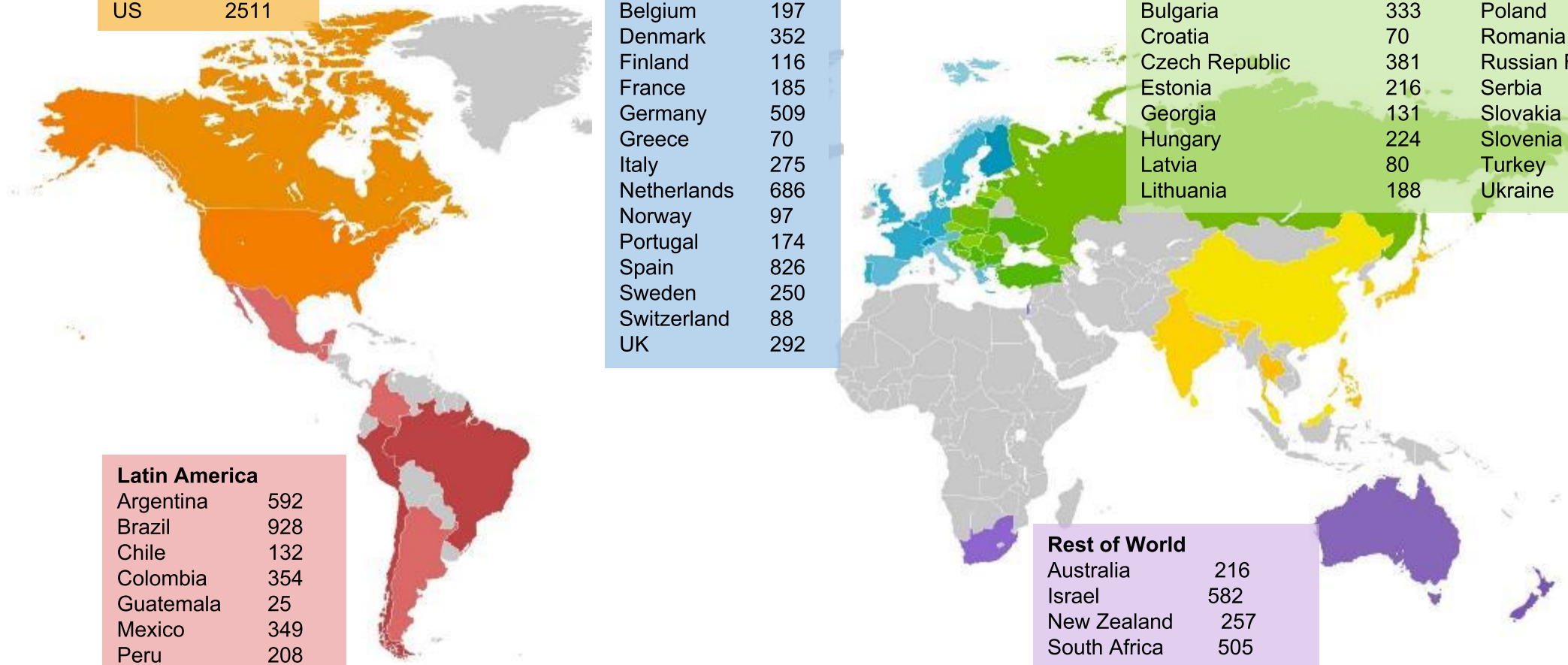
ESTABLISHED IN 1812 NOVEMBER 29, 2018 VOL. 379 NO. 22

Alirocumab and Cardiovascular Outcomes after Acute Coronary Syndrome

G.G. Schwartz, P.G. Steg, M. Szarek, D.L. Bhatt, V.A. Bittner, R. Diaz, J.M. Edelberg, S.G. Goodman, C. Hanotin, R.A. Harrington, J.W. Jukema, G. Lecorps, K.W. Mahaffey, A. Moryusef, R. Pordy, K. Quintero, M.T. Roe, W.J. Sasiela, J.-F. Tamby, P. Tricoci, H.D. White, and A.M. Zeiher, for the ODYSSEY OUTCOMES Committees and Investigators*

ODYSSEY OUTCOMES: 18,924 patients randomized at 1315 sites in 57 countries, Nov 2, 2012 – Nov 11, 2017

Praluent® alirocumab



Canada/USA	
Canada	361
US	2511

Western Europe	
Austria	58
Belgium	197
Denmark	352
Finland	116
France	185
Germany	509
Greece	70
Italy	275
Netherlands	686
Norway	97
Portugal	174
Spain	826
Sweden	250
Switzerland	88
UK	292

Central/Eastern Europe			
Bosnia–Herzegovina	156	Macedonia	132
Bulgaria	333	Poland	926
Croatia	70	Romania	145
Czech Republic	381	Russian Federation	1109
Estonia	216	Serbia	255
Georgia	131	Slovakia	340
Hungary	224	Slovenia	36
Latvia	80	Turkey	78
Lithuania	188	Ukraine	639

Asia	
China	614
Hong Kong	17
India	521
Japan	204
Korea	94
Malaysia	110
Philippines	116
Singapore	49
Sri Lanka	314
Taiwan	93
Thailand	161

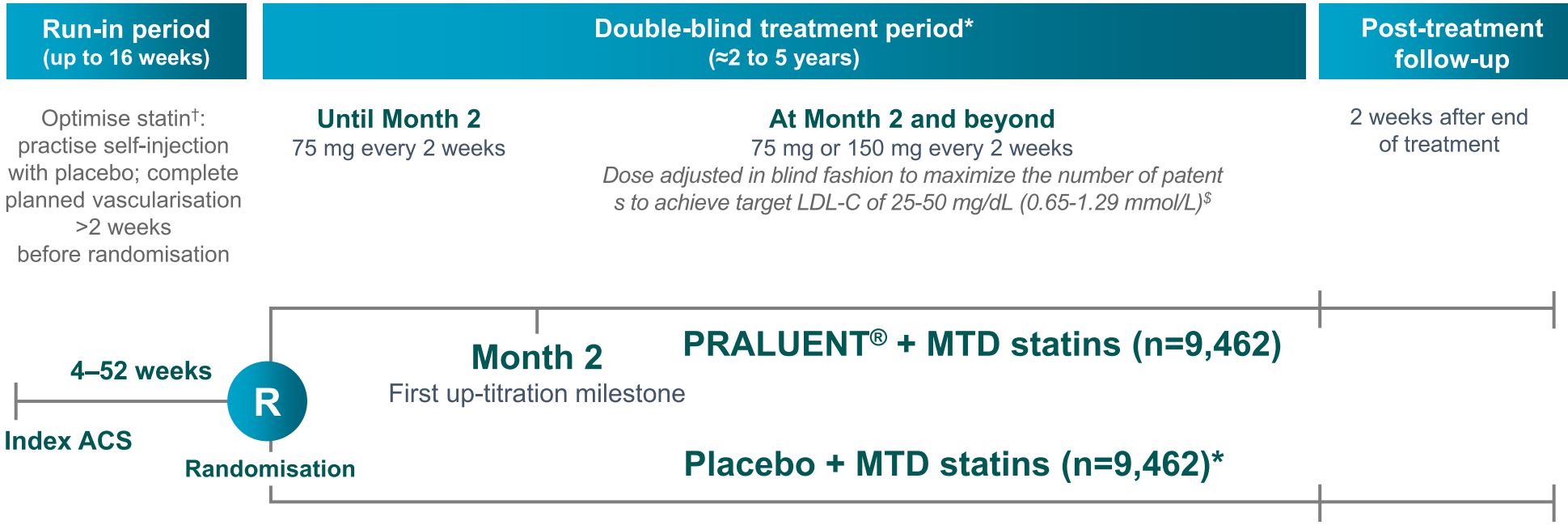
Latin America	
Argentina	592
Brazil	928
Chile	132
Colombia	354
Guatemala	25
Mexico	349
Peru	208

Rest of World	
Australia	216
Israel	582
New Zealand	257
South Africa	505

1. Schwartz GG, et al. Am Heart J. 2014;168:682–689

ODYSSEY OUTCOMES is a long-term study of CV outcomes in 18,924 patients[1,2]

Praluent® alirocumab



The only double-blind, randomized PCSK9i CV outcomes study with treat-to-target LDL-C approach, **2.8 years median follow-up**, and **44 %** of patients eligible to be followed for **3-5 years**.

Clinically stable **high-risk patients with prior CHD event of ACS**, likely to derive high absolute benefit

Patients with residual cardiovascular risk (despite moderate/intensive statins) **most likely to be modified** by further reduction of LDL-C lipoproteins‡

*Background therapy: 96% aspirin; 88% P2Y12 inhibitor; 85% beta blocker.

†Optimal statin treatment: atorvastatin 40 or 80 mg, rosuvastatin 20 or 40 mg, or maximal tolerated dose of one of these statins, with or without non-statin lipid treatments. NCEP-ATP III therapeutic lifestyle changes or equivalent throughout study. Other CV prevention therapies not excluded (other than PCI within 2 weeks of start of trial). ‡Inadequate control of atherogenic lipoproteins. At least one of the following: LDL-C ≥70 mg/dL (1.81 mmol/L), non HDL-C ≥100 mg/dL (2.59 mmol/L), or apo B ≥80 mg/dL.

$Dose was up-titrated from 75 mg Q2W to 150 mg Q2W at month 2 if LDL-C was ≥50 mg/dL at month 1. Dose was down-titrated from 150 mg Q2W to 75 mg Q2W if LDL-C was <25 mg/dL on 2 consecutive measures. Patients on the 75 mg Q2W dose were blindly switched to placebo if LDL-C was <15 mg/dL on 2 consecutive measures.

ACS, acute coronary syndrome; apo B, apolipoprotein B; HDL-C, high density lipoprotein cholesterol; MTD, maximally tolerated dose; NCEP-ATP III, National Cholesterol Education Program - Adult Treatment Panel III.

Reference. 1. Schwartz GG, et al. Am Heart J. 2014;168:682–689. 2. Schwartz GG, et al. N Engl J Med. 2018;379:2097–2b107.

ODYSSEY OUTCOMES studied the effect of PRALUENT® on CV outcomes[1,2]

Praluent® alirocumab

Endpoint	Further details
Primary endpoint (MACE)	
• CHD death • Nonfatal MI • Ischaemic stroke • UA	**Major CV events** Composite of CHD death, non-fatal MI, fatal or non-fatal ischaemic stroke, UA requiring hospitalisation Estimate of 1,613 primary endpoint events to provide 90% power to detect a 15% hazard reduction with PRALUENT® compared with placebo
Secondary endpoints (in order of hierarchical testing)	
• CHD event • Major CHD event • CV event • Composite of all-cause mortality, nonfatal MI, nonfatal is chaemic stroke • CHD death • CV death • All-cause mortality	**CHD event:** CHD death, non-fatal MI, unstable angina requiring hospitalisation, or ischaemia-driven coronary reva scularisation **Major CHD event:** CHD death or non-fatal MI **CV event:** CV death, non-fatal CHD event, or non-fatal ischaemic stroke
Other secondary endpoints	Components of the primary endpoint considered individually: CHD death, non-fatal MI, fatal and non-fatal ischaemi c stroke, unstable angina requiring hospitalisation Ischaemia-driven coronary revascularisation Congestive heart failure requiring hospitalisation
Safety data	Adverse events, laboratory tests
Other	Development of anti-alirocumab antibodies

*Major adverse cardiovascular events (MACE)=primary composite endpoint of CHD death, nonfatal myocardial infarction, fatal and nonfatal ischaemic stroke, or unstable angina requiring hospitalisation.

†With only nominal statistical significance by hierarchical testing (HR 0.85, 95% CI 0.73, 0.98; P=0.03, nominal P value); The hierarchical analysis was stopped after the first nonsignificant P value was observed, in accordance with the hierarchical testing plan. Therefore, the p-value for all-cause death was considered nominal because all-cause death followed CHD death and cardiovascular death in the prespecified hierarchy of main secondary end points1-4

‡From prespecified subgroup analysis according to baseline LDL-C ≥100 mg/dL (N=5,629). §Interaction P value to assess interaction between treatment and baseline LDL-C level.

‖In a post hoc analysis, death was examined in three predefined subgroups of baseline LDL-C level (<80 mg/dL, 80 to <100 mg/dL and ≥100 mg/dL). The HR for death was numerically lowest in the subgroup with baseline LDL-C ≥100 mg/dL (0.71; 95% CI, 0.56 to 0.90), but there was no significant heterogeneity of the effect of alirocumab on relative risk of death across categories of baseline LDL-C of (P interaction=0.12).

CHD, coronary heart disease; CV, cardiovascular; MI, myocardial infarction, UA, unstable angina.

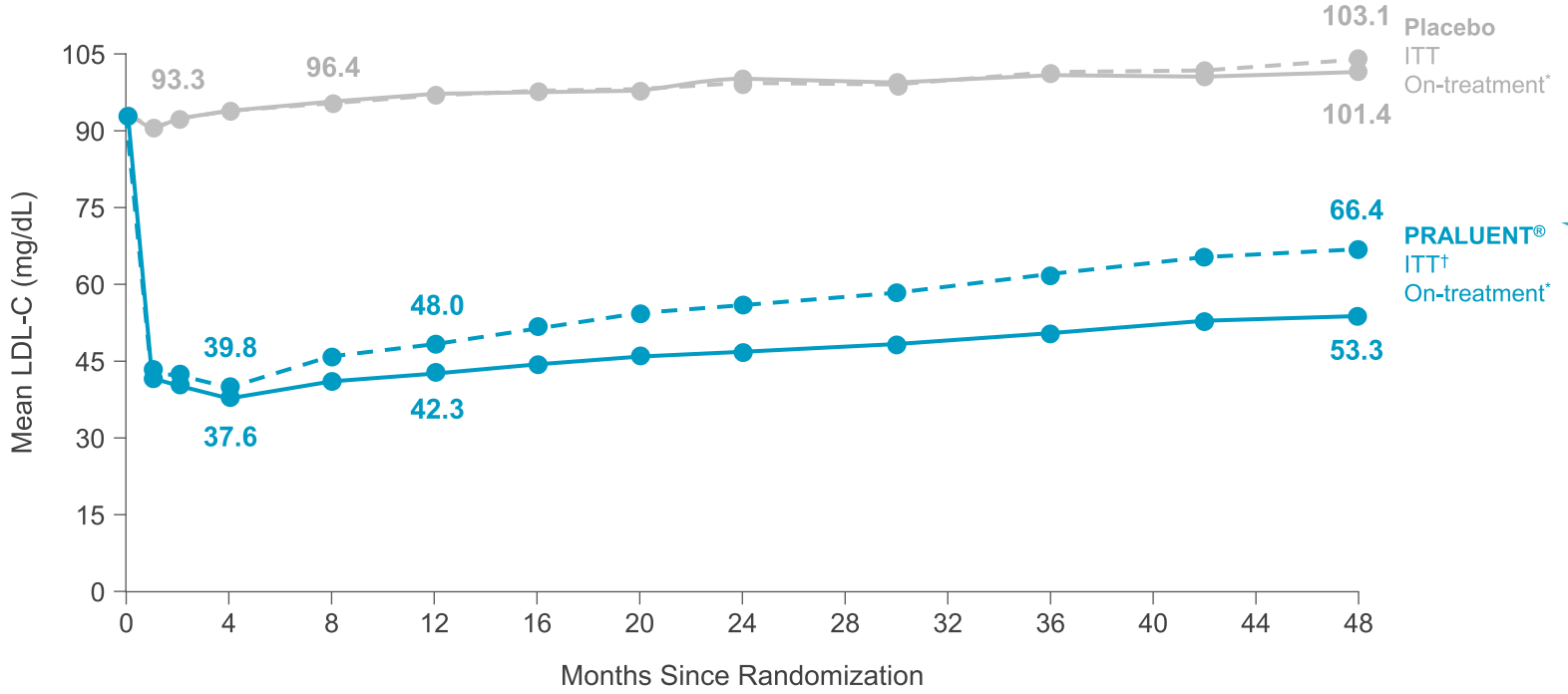
Reference. 1. Schwartz GG, et al. Am Heart J. 2014;168:682–689. 2. Schwartz GG, et al. N Engl J Med. 2018;379:2097–107.

ODYSSEY OUTCOMES: LDL-C by ITT & On-Treatment Analyses
LDL-C reduction for PRALUENT® vs placebo

Praluent® alirocumab

Rapid LDL-C reduction sustained over 48 months

LDL Cholesterol Levels during the Trial



54.7% mean LDL-C reduction at 4 years

*Excludes LDL-C values after premature treatment discontinuation or blinded switch to placebo
†All LDL-C values, including those after premature treatment discontinuation, blinded down titration, or blinded switch to placebo

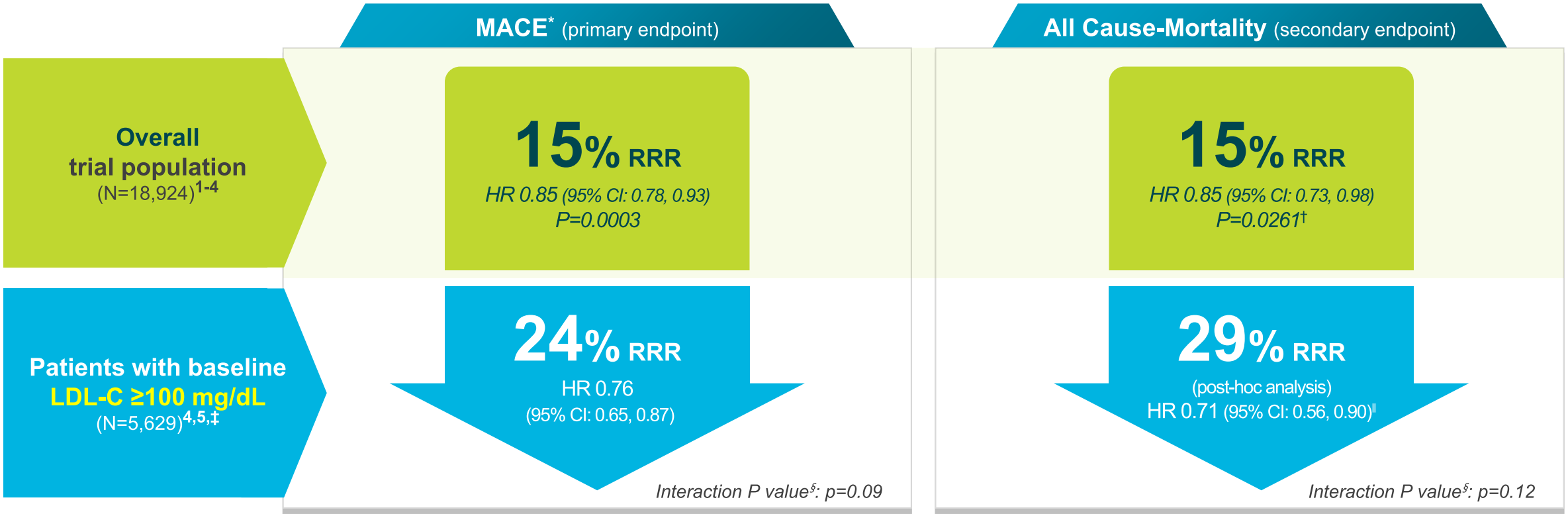
ITT, intention-to-treat; LDL-C, low-density lipoprotein cholesterol.

[Study Design[1]] ODYSSEY OUTCOMES was a randomised, double-blind, placebo-controlled phase 3 study. 18,924 Patients with a recent MI or unstable angina, and on high-intensity statin (40 or 80 mg atorvastatin or 20 or 40 mg rosuvastatin, or maximally tolerated dose of one of these agents) +/- other lipid-lowering therapy but not at predefined target LDL-C were enrolled. The primary end point was a composite of death from coronary heart disease, nonfatal myocardial infarction, fatal or nonfatal ischemic stroke, or unstable angina requiring hospitalization.

Reference. 1. Schwartz GG, et al. N Engl J Med. 2018;379:2097–107.

PRALUENT® reduced risk of MACE and was associated with a reduction of all-cause mortality which was observed in a CV outcomes trial

Praluent® alirocumab



*Major adverse cardiovascular events (MACE)=primary composite endpoint of CHD death, nonfatal myocardial infarction, fatal and nonfatal ischaemic stroke, or unstable angina requiring hospitalisation.
†With only nominal statistical significance by hierarchical testing (HR 0.85, 95% CI 0.73, 0.98; P=0.03, nominal P value); The hierarchical analysis was stopped after the first nonsignificant P value was observed, in accordance with the hierarchical testing plan. Therefore, the p-value for all-cause death was considered nominal because all-cause death followed CHD death and cardiovascular death in the prespecified hierarchy of main secondary end points[1-4]
‡From prespecified subgroup analysis according to baseline LDL-C ≥100 mg/dL (N=5,629). §Interaction *P* value to assess interaction between treatment and baseline LDL-C level.
‖In a post hoc analysis, death was examined in three predefined subgroups of baseline LDL-C level (<80 mg/dL, 80 to <100 mg/dL and ≥100 mg/dL). The HR for death was numerically lowest in the subgroup with baseline LDL-C ≥100 mg/dL (0.71; 95% CI, 0.56 to 0.90), but there was no significant heterogeneity of the effect of alirocumab on relative risk of death across categories of baseline LDL-C of (P interaction=0.12).

CV, cardiovascular; **MACE,** major adverse cardiovascular event.
[Study Design[1]] ODYSSEY OUTCOMES was a randomised, double-blind, placebo-controlled phase 3 study. 18,924 Patients with a recent MI or unstable angina, and on high-intensity statin (40 or 80 mg atorvastatin or 20 or 40 mg rosuvastatin, or maximally tolerated dose of one of these agents) +/- other lipid-lowering therapy but not at predefined target LDL-C were enrolled. The primary end point was a composite of death from coronary heart disease, nonfatal myocardial infarction, fatal or nonfatal ischemic stroke, or unstable angina requiring hospitalization.
[Study Design[2]] ODYSSEY OUTCOMES (Evaluation of Cardiovascular Outcomes After an Acute Coronary Syndrome During Treatment With Alirocumab) was a double-blind, randomized comparison of alirocumab or placebo in 18,924 patients who had an ACS 1 to 12 months previously and elevated atherogenic lipoproteins despite intensive statin therapy. Alirocumab dose was blindly titrated to target achieved low-density lipoprotein cholesterol (LDL-C) between 25 and 50 mg/dL. We examined the effects of treatment on all-cause death and its components, cardiovascular and noncardiovascular death, with log-rank testing. Joint semiparametric models tested associations between nonfatal cardiovascular events and cardiovascular or noncardiovascular death.
Reference 1. Schwartz GG, et al. N Engl J Med. 2018;379(22):2097-2107. **2.** Steg PG, et al. Circulation. 2019;140(2):103-112.**3.** 프랄런트®펜주 식약처 허가사항(75, 150 mg: 2022.12.20 / 300 mg: 2023.02.13). **4.** Praluent® Summary of Product Characteristics. 2023.

ODYSSEY KT

Koh KK, et al. J Clinical Lipidology. 2018;12(1):S1933-2874.
Nam CW, et al. Korean J Intern Med. 2019;34(6):1252-1262.

Praluent® alirocumab

A randomized trial evaluating the efficacy and safety of alirocumab in South Korea and Taiwan (ODYSSEY KT)

Check for updates

Kwang Kon Koh, MD, PhD, FACC, Chang Wook Nam, MD, PhD, FACC, Ting-Hsing Chao, MD, FACC, FESC, Ming-En Liu, MD, Chiung-Jen Wu, MD, Dong-Soo Kim, MD, PhD, Chong-Jin Kim, MD, PhD, Ivy Li, MSc, Jianyong Li, MD, Marie T. Baccara-Dinet, MD, MSc, Pi-Jung Hsiao, MD, MS*, Chern-En Chiang, MD, PhD, FACC

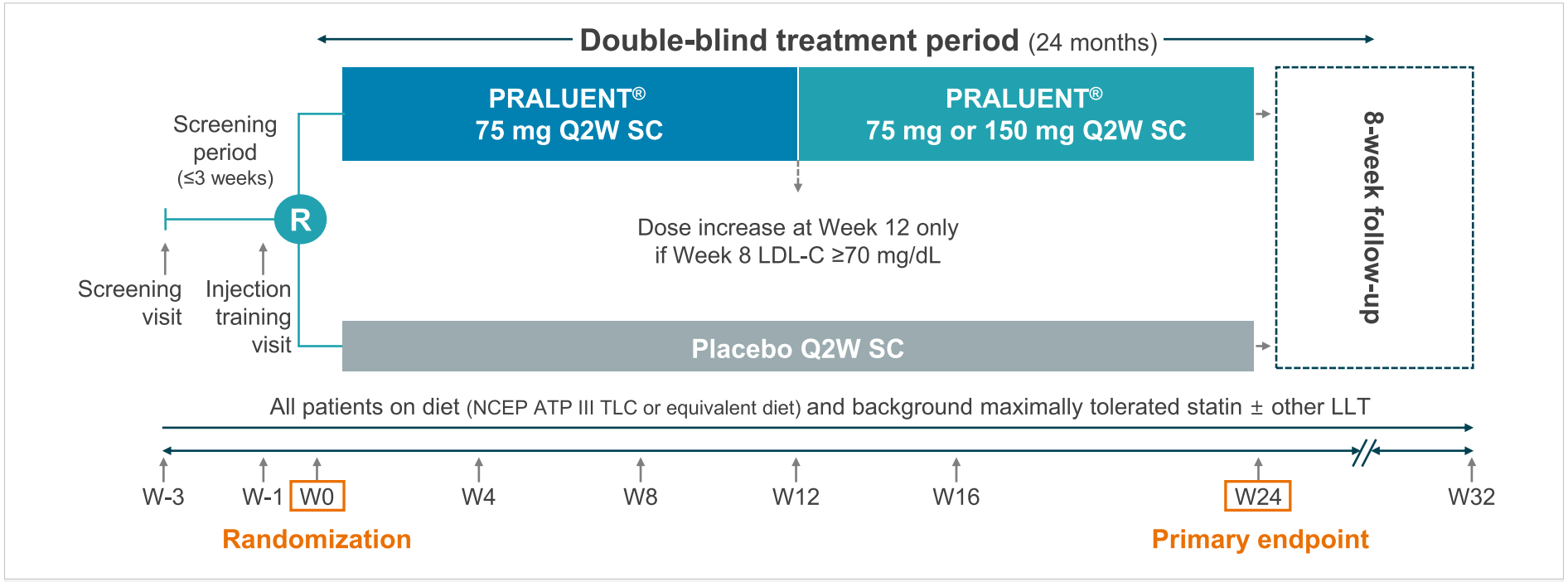
Efficacy and safety of alirocumab in Korean patients with hypercholesterolemia and high cardiovascular risk: subanalysis of the ODYSSEY-KT study

Chang-Wook Nam[1], Dong-Soo Kim[2], Jianyong Li[3], Marie T. Baccara-Dinet[4], Ivy Li[3], Ji-Hyun Kim[5], and Chong-Jin Kim[6]

ODYSSEY KT assessed the efficacy and safety of PRALUENT® in patients from South Korea and Taiwan

Praluent® alirocumab

- **Patients**: with hypercholesterolemia at **high cardiovascular risk** who were on maximally tolerated statin.
- **ODYSSEY KT** assessed the efficacy and safety of PRALUENT® in patients from **South Korea and Taiwan.**



LDL-C, low-density lipoprotein cholesterol; LLT, lipid-lowering therapy; NCEP ATP III, National Cholesterol Education Program Adult Treatment Panel III; Q2W, once every 2 weeks; SC, subcutaneous; TLC, therapeutic lifestyle changes; W,week.

[Study design[1]] ODYSSEY KT assessed the efficacy and safety of alirocumab in patients from South Korea and Taiwan. Randomized, double-blind, placebo-controlled, parallel-group, multicenter study conducted in 27 active centers (which screened at least 1 patient) from 16 study centers in South Korea and 11 in Taiwan enrolled patients (aged ≥18 years) with high CV risk who had inadequately controlled hypercholesterolemia on maximally tolerated statin therapy at a stable dose for at least 4 weeks before screening. In total, 199 patients were randomized to treatment with alirocumab 75 mg Q2W (n = 97) or placebo. The primary efficacy endpoint was the percent change in calculated LDL-C from baseline to week 24 analyzed with an intent-to-treat (ITT) approach.

Reference. 1. Koh KK, et al. J Clinical Lipidology. 2018;12(1):S1933-2874.

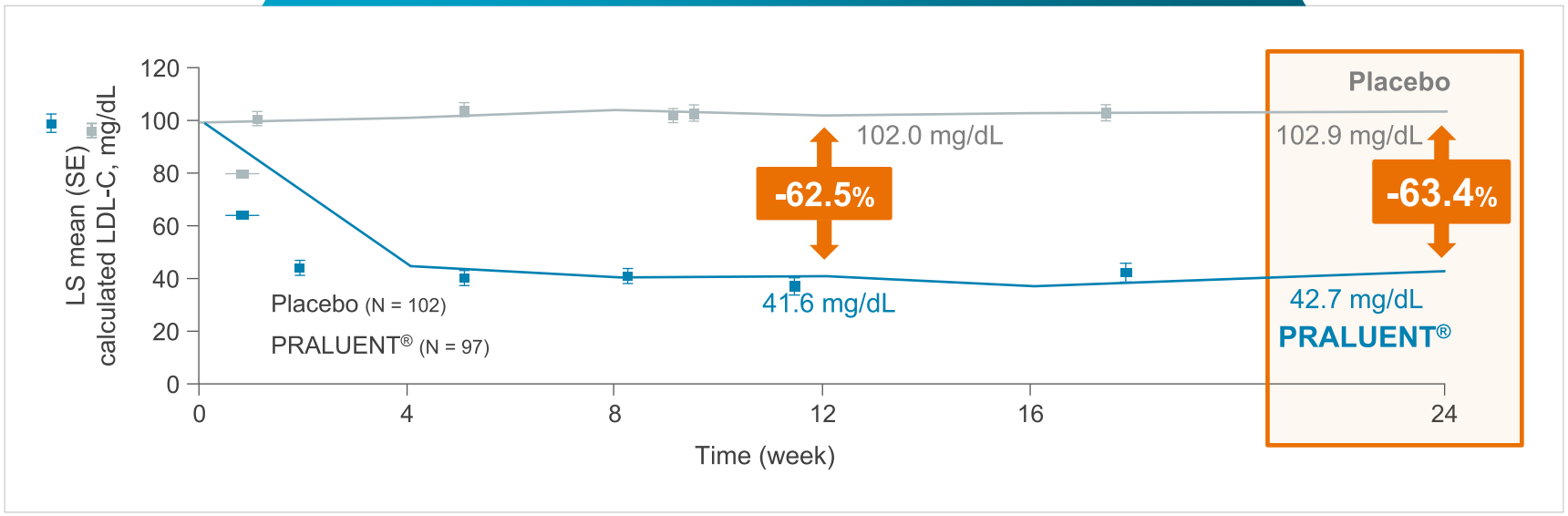
ODYSSEY KT

LDL-C reductions were observed from week 4 and maintained until week 24

Praluent® alirocumab

- The **difference in LDL-C levels from baseline** between two groups was statistically significant at week 24(-63.4%, *p*<0.0001)
- At week 24, **85.8% of patients in the PRALUENT® group reached LDL-C <70 mg/dL** (placebo: 14.2%; *p*<0.0001 vs. placebo)

Calculated LDL-C levels over time (ITT)



ITT, intent to treat; LDL-C, Low-density lipoprotein cholesterol; LS, least square; SE, standard error.

[Study design[1]] ODYSSEY KT assessed the efficacy and safety of alirocumab in patients from South Korea and Taiwan. Randomized, double-blind, placebo-controlled, parallel-group, multicenter study conducted in 27 active centers (which screened at least 1 patient) from 16 study centers in South Korea and 11 in Taiwan enrolled patients (aged ≥18 years) with high CV risk who had inadequately controlled hypercholesterolemia on maximally tolerated statin therapy at a stable dose for at least 4 weeks before screening. In total, 199 patients were randomized to treatment with alirocumab 75 mg Q2W (n = 97) or placebo. The primary efficacy endpoint was the percent change in calculated LDL-C from baseline to week 24 analyzed with an intent-to-treat (ITT) approach.

Reference. 1. Koh KK, *et al.* J Clinical Lipidology. 2018;12(1):S1933-2874.

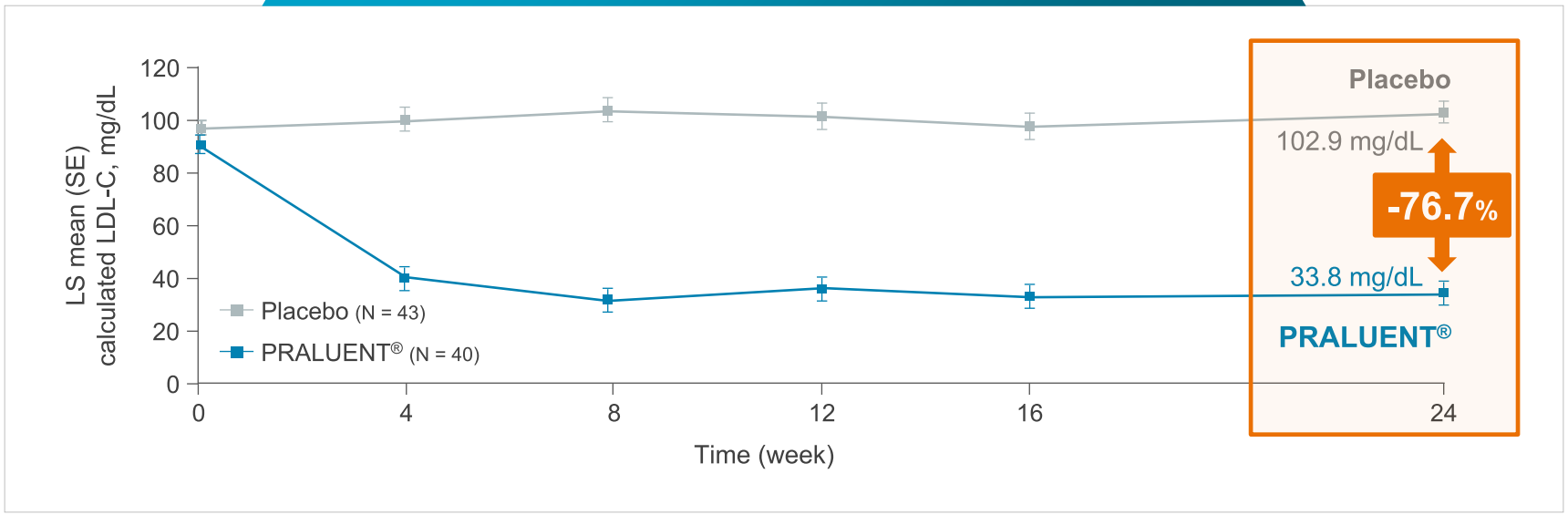
ODYSSEY KT

Results from Korean Sub-data : PRALUENT® has demonstrated to be effective in improvement of LDL-C level in Korean

Praluent® alirocumab

- The **difference in LDL-C levels from baseline** between two groups reached -76.7% at week 24 (p<0.0001)
- At week 24, **92.0% of patients in the PRALUENT® group reached LDL-C <70 mg/dL** (placebo: 12.7%; p<0.0001 vs. placebo)

Calculated LDL-C levels over time (ITT)



LDL-C, Low-density lipoprotein cholesterol; LS, least square

[Study Design[1]] In the ODYSSEY-KT study, South Korean and Taiwanese patients with hypercholesterolemia and high cardiovascular risks were randomized (1:1) to alirocumab or placebo. Alirocumab was self-administered subcutaneously at 75 mg every 2 weeks with a maximally tolerated statin dose with or without other lipid-modifying therapies. Alirocumab dose was increased to 150 mg every 2 weeks at week 12 if low density lipoprotein cholesterol (LDL-C) 70 mg/dL at week 8. Primary endpoint was percent change in LDL-C from baseline to week 24. Results from Korean cohort (n=83: 40 for alirocumab and 43 for placebo, respectively) analyses are reported here.

Reference. 1. Nam CW, *et al*. Korean J Intern Med. 2019;34(6):1252-1262.

ODYSSEY KT

Safety in Korean Sub-data : PRALUENT® was generally well tolerated with no significant safety signals

Praluent® alirocumab

PRALUENT® showed a comparable safety profile to placebo consistent with the whole KT population

n (%)	PRALUENT® (N=40)	Placebo (N=43)
TEAEs	18 (45.0%)	22 (51.2)
Treatment-emergent SAEs	5 (12.5)	5 (11.6)
TEAEs leading to death	0	0
TEAEs leading to treatment discontinuation	0	0
TEAEs occurring in ≥5% of patients		
Headache	4 (10.0)	0
Nasopharyngitis	3 (7.5)	2 (4.7)
Fall	2 (5.0)	0

SAE, serious adverse events; TEAE, treatment-emergent adverse events.

[Study Design[1]] In the ODYSSEY-KT study, South Korean and Taiwanese patients with hypercholesterolemia and high cardiovascular risks were randomized (1:1) to alirocumab or placebo. Alirocumab was self-administered subcutaneously at 75 mg every 2 weeks with a maximally tolerated statin dose with or without other lipid-modifying therapies. Alirocumab dose was increased to 150 mg every 2 weeks at week 12 if low density lipoprotein cholesterol (LDL-C) 70 mg/dL at week 8. Primary endpoint was percent change in LDL-C from baseline to week 24. Results from Korean cohort (n=83: 40 for alirocumab and 43 for placebo, respectively) analyses are reported here.

Reference 1. Nam CW, *et al.* Korean J Intern Med. 2019;34(6):1252-1262.

Case 2. Hx. of Multiple ASCVD

Case

- 62YR , Male, 169cm/79kg, BMI 27.66

Coronary Risk Factors

- IFG, smoking

Brief History

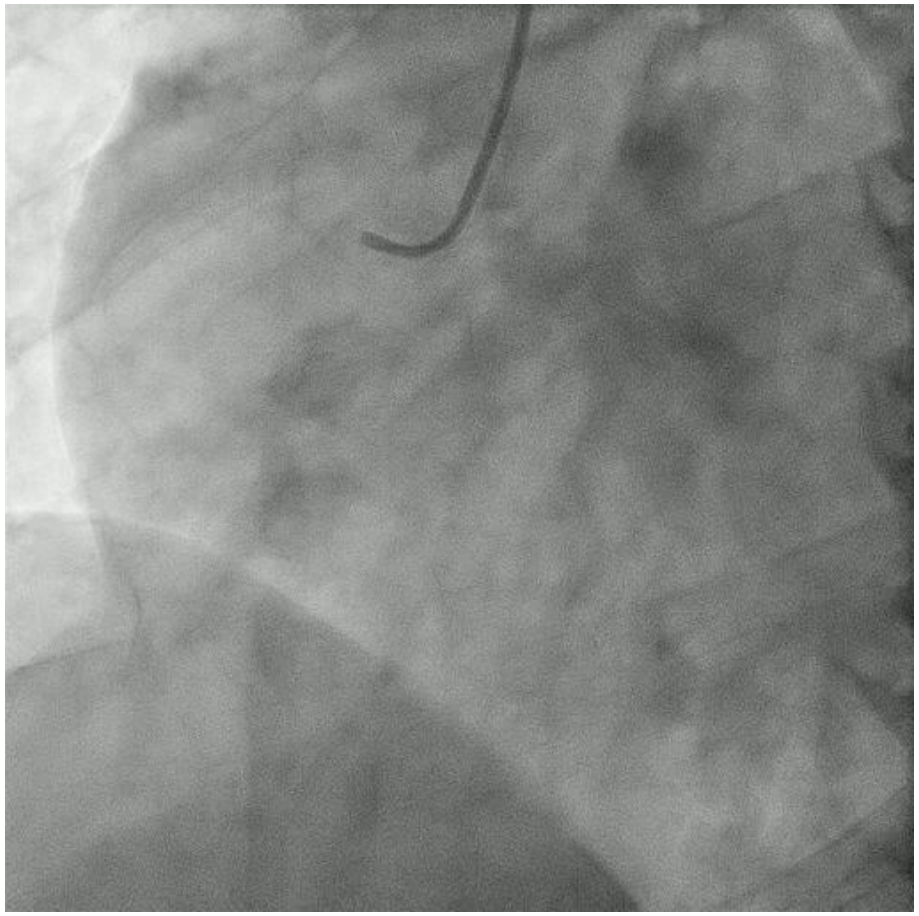
- Stroke developed at November 2020. - DAPT, **Atorvastatin 80mg**
- Resting onset chest pain developed at Jan 2021.

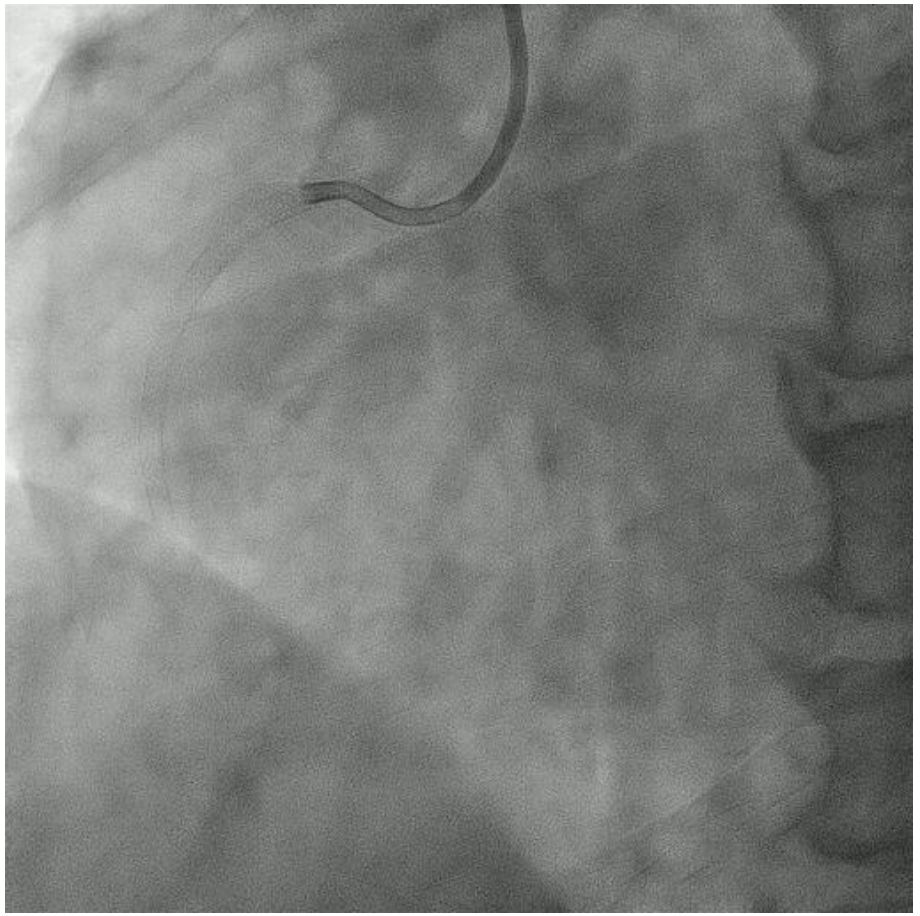
2020-12-09 06:07 [일반화학검	Glucose, fast	97
	Cholesterol, ·	257
	Triglyceride	159
	HDL-choleste	36
	LDL-choleste	204

Atova 80mg

Cholesterol, ·	127
Triglyceride	56
HDL-choleste	39
LDL-choleste	85

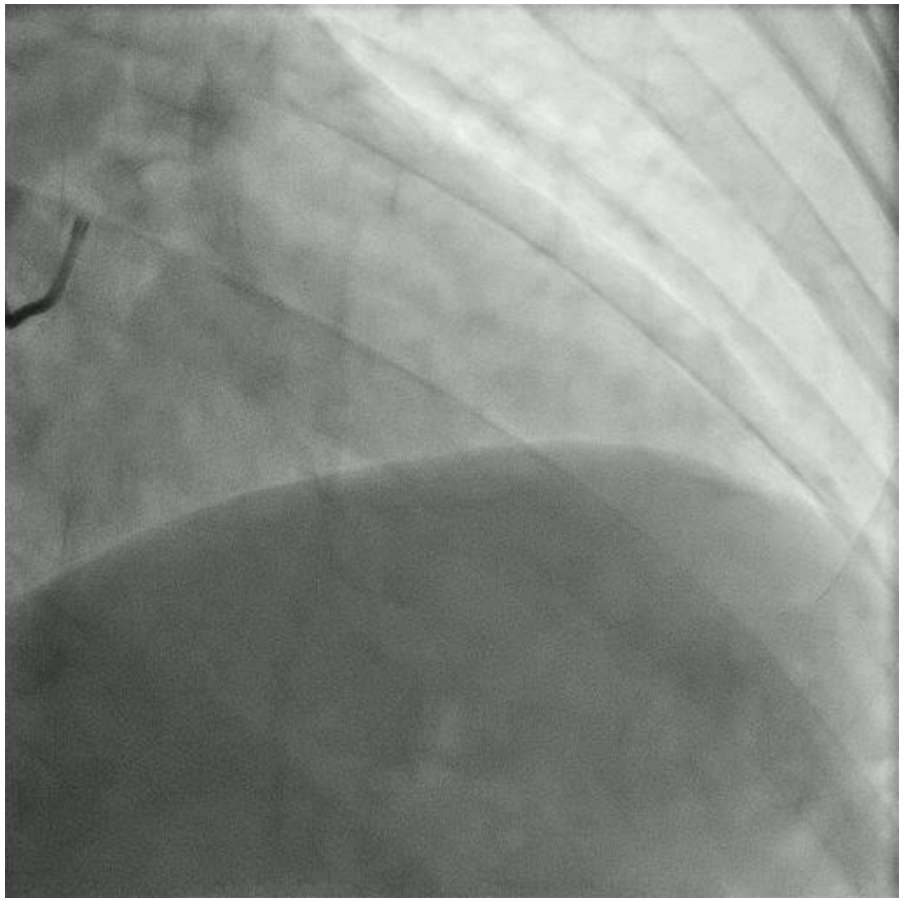
Case 2. Hx. of Multiple ASCVD

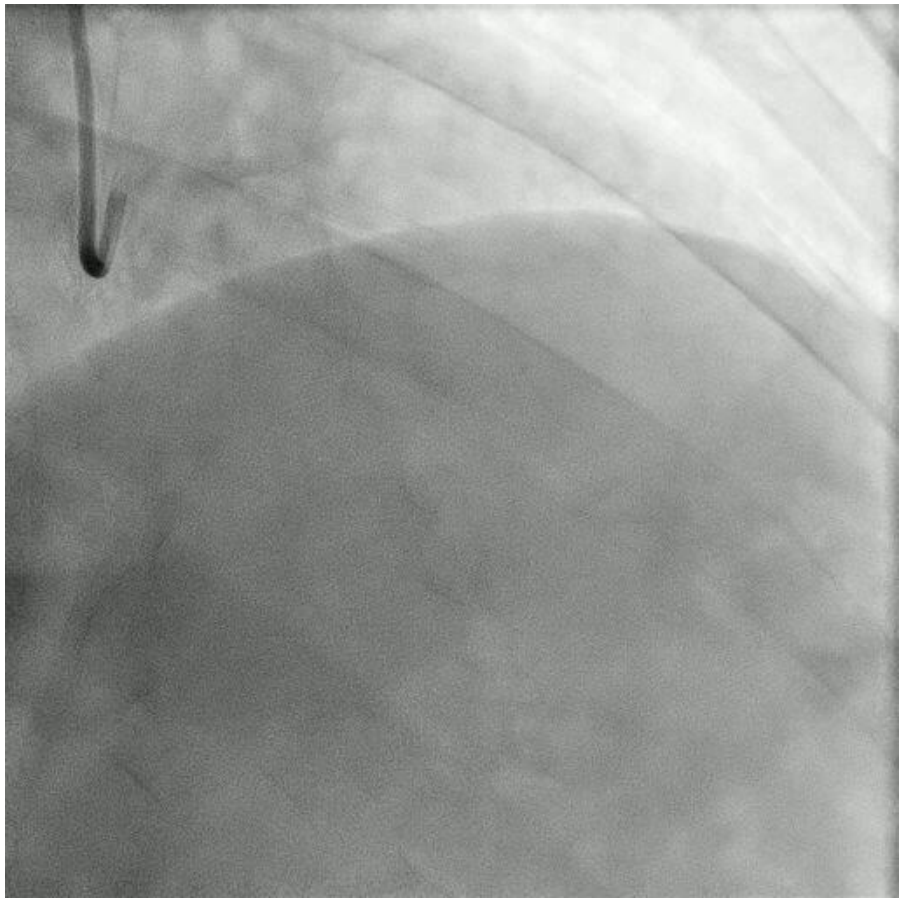




Ultimaster 3.0x18mm & 2.5x33mm

Case 2. Hx. of Multiple ASCVD





Ultimaster 3.0x33mm

Case 2. Hx. of Multiple ASCVD

Cholesterol,	127
Triglyceride	56
HDL-choleste	39
LDL-choleste	85

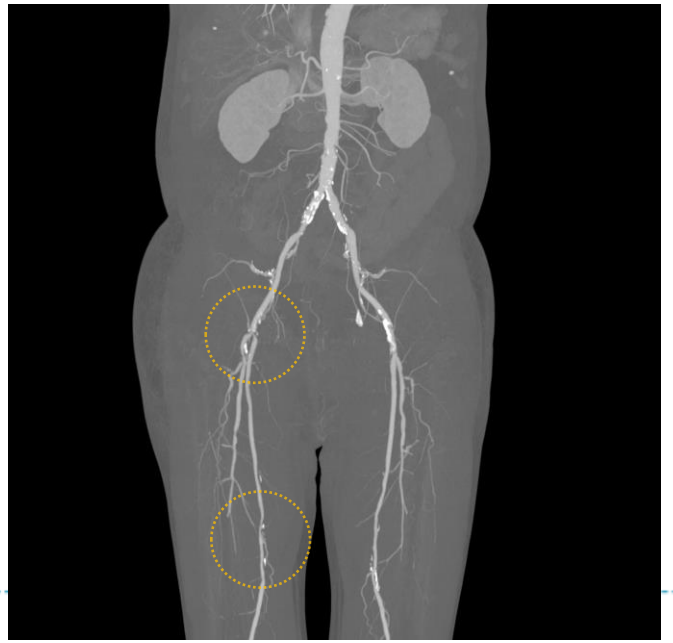
Atova 80mg

Eze 10mg

Cholesterol,	127
Triglyceride	80
HDL-choleste	44
LDL-choleste	72

Brief History

- **Stroke** developed at November 2020. - DAPT, Atorvastatin 80mg
- **Acute Coronary Syndrome** developed at Jan 2021. – Atorva/Eze 80/10mg
- **Leg pain after walking – ABI 0.75**



Case 2. Hx. of Multiple ASCVD

The Patient's Question?

1. Isn't an LDL of 72 low enough?
2. I already have multiple vessel disease; what good is it for me?

Praluent® demonstrated an absolute reduction in the risk of MACE, the primary endpoint in patients with ACS* and Polyvascular disease (PVD)[1] (vs One diseased bed : 1.4% ARR)

Praluent® alirocumab

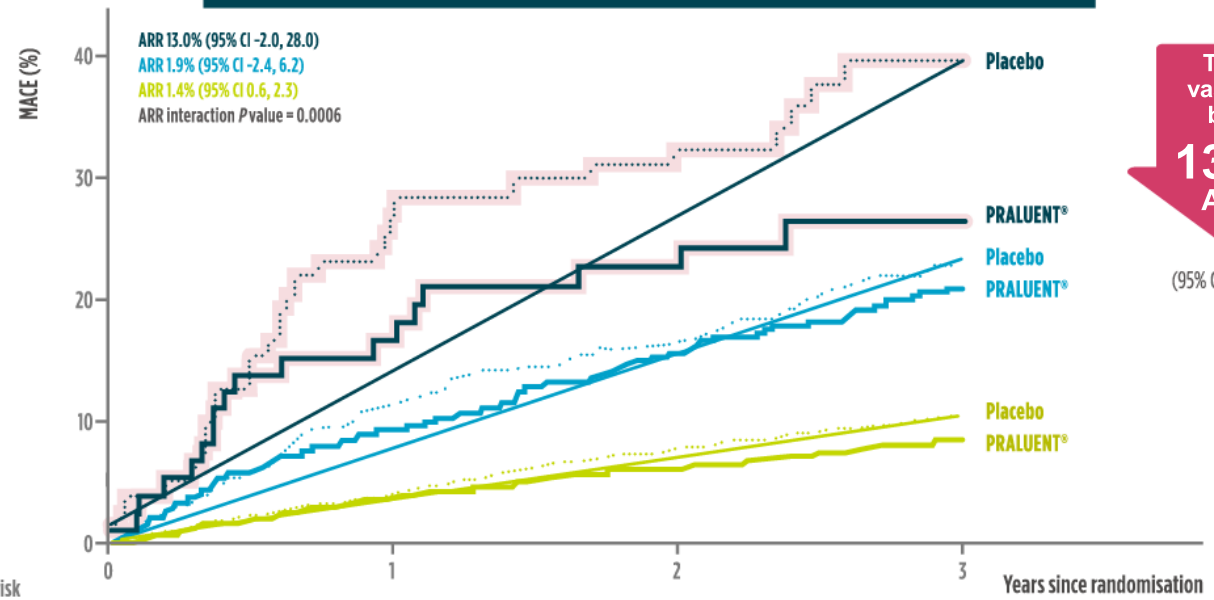
ODYSSEY OUTCOMES

Relative risk reduction in MACE and all-cause mortality for patients with a first or recurrent ACS with Praluent® vs placebo.

Primary Endpoint
MACE

Secondary Endpoint
All-Cause Mortality

Incidence of MACE† in the Praluent® vs. placebo in ACS*+PVD patients[1]



Three vascular beds
13 % RRR ARR
(95% CI -2.0, 28.0)

No. at risk				
PRALUENT®	8683	8167	7741	3304
Placebo	8687	8155	7612	3242
PRALUENT®	708	624	554	242
Placebo	697	594	541	206
PRALUENT®	71	56	51	29
Placebo	78	57	50	24

One vascular bed‡
Two vascular beds‡
Three vascular beds‡

* Defined as hospitalization due to ACS (Myocardial infarction or unstable angina); †Major adverse cardiovascular events (MACE) : primary composite endpoint of CHD death, nonfatal myocardial infarction, fatal and nonfatal ischaemic stroke, or unstable angina requiring; ‡One diseased bed = coronary artery disease (CAD) and no peripheral artery disease (PAD) or cerebrovascular disease (CeVD); 2 diseased beds = CAD and PAD or CeVD; 3 diseased beds = CAD and PAD and CeVD; §Atorvastatin 40 mg or 80 mg per day, Rosuvastatin 20 mg or 40 mg per day.
ACS, Acute Coronary Syndrome; ARR, Absolute Risk Reduction; CAD, Coronary Artery Disease; CeVD, Cerebrovascular Disease; CHD, Coronary Heart Disease CI, Confidence Interval; MACE, Major Adverse Cardiovascular Event; PAD, Peripheral Artery Disease; PVD, Polyvascular Disease; RRR, relative risk reduction.
[Study Design] This pre-specified analysis from ODYSSEY OUTCOMES (Evaluation of Cardiovascular Outcomes After an Acute Coronary Syndrome During Treatment With Alirocumab) determined whether polyvascular disease influenced risks of MACEs and death and their modification by alirocumab in patients with recent ACS and dyslipidemia despite intensive statin therapy ((n=18,924).
Reference. 1. Jukema JW, et al. J Am Coll Cardiol. 2019 Sep 3;74(9):1167-1176.

Praluent® demonstrated a relative risk reduction in the secondary endpoint, All-Cause Mortality* in patients with three polyvascular diseases[1]

Praluent® alirocumab

ODYSSEY OUTCOMES

Relative risk reduction in MACE and all-cause mortality for patients with a first or recurrent ACS with Praluent® vs placebo.

Secondary Endpoint

All-Cause Mortality

All-Cause Mortality* risk in Patients with ACS†+PVD patients[1]

		PRALUENT®	Placebo	HR (95% CI)	HR Interaction *p* Value	ARR (95% CI)
Monovascular disease (CAD without PAD or CeVD)		268/8,683 (3.1)	305/8,687 (3.5)	0.88 (0.75, 1.04)		0.4 (–0.1, 1.0)
Disease in 2 vascular beds	CAD and PAD	28/302 (9.3)	27/308 (8.8)	1.03 (0.60, 1.75)		–0.5 (–5.1, 4.0)
	CAD and CeVD	34/406 (8.4)	43/389 (11.1)	0.68 (0.44, 1.08)	0.06	2.7 (1.4, 6.8)
Disease in 3 vascular beds (CAD, PAD and CeVD)		**4/71 (5.6)**	**17/78 (21.8)**	**0.23 (0.08, 0.68)**		**16.2 (5.5, 26.8)**
All patients		334/9,462 (3.5)	392/9,462 (4.1)	0.85 (0.77, 0.98)		0.6 (0.1, 1.2)

※ With only nominal statistical significance by hierarchical testing (HR 0.23; 95% CI 0.08, 0.68)

Three vascular beds 16% ARR

Interaction *P* value: *P*=0.002

†Major adverse cardiovascular events (MACE) : primary composite endpoint of CHD death, nonfatal myocardial infarction, fatal and nonfatal ischaemic stroke, or unstable angina requiring; ‡One diseased bed = coronary artery disease (CAD) and no peripheral artery disease (PAD) or cerebrovascular disease (CeVD); 2 diseased beds = CAD and PAD or CeVD; 3 diseased beds = CAD and PAD and CeVD; §*Atorvastatin 40 mg or 80 mg per day, Rosuvastatin 20 mg or 40 mg per day.

*Atorvastatin 40 mg or 80 mg per day, Rosuvastatin 20 mg or 40 mg per day.

ACS, Acute Coronary Syndrome; ARR, Absolute Risk Reduction; CAD, Coronary Artery Disease; CeVD, Cerebrovascular Disease; CHD, Coronary Heart Disease; CI, Confidence Interval; HR, Hazard Ratio; MACE, Major Adverse Cardiovascular Event; PAD, Peripheral Artery Disease; PVD, Polyvascular Disease.

[Study Design] This pre-specified analysis from ODYSSEY OUTCOMES (Evaluation of Cardiovascular Outcomes After an Acute Coronary Syndrome During Treatment With Alirocumab) determined whether polyvascular disease influenced risks of MACEs and death and their modification by alirocumab in patients with recent ACS and dyslipidemia despite intensive statin therapy ((n=18,924).

Reference. 1. Jukema JW, et al. J Am Coll Cardiol. 2019 Sep 3;74(9):1167-1176.

Case 2. Hx. of Multiple ASCVD

Lipid History

Date	Dx	LDL (mg/dL)	Medication	LDL Goal	Ideal Strategy
2020.12	Stroke	204	Atorva 80mg	< 70	Aorva 80mg / Eze 10mg
2021.1	Stroke + NSTEMI	85	Atorva 80mg/Ezetimibe 10mg	< 55	Atorva / Eze + PCSK9i
2021.5	Stroke + NSTEMI + PAD	72	**PCSK9i** SC q 2wks,Atorva80/Ezetimibe 10mg	< 55 (< 40)	Atorva / Eze + PCSK9i
2021.10	Stroke + NSTEMI + PAD	12	**PCSK9i** SC q 2wks,Atorva80/Ezetimibe 10mg	< 55 (< 40)	Atorva / Eze +PCSK9i

Case 3. Young STEMI pt

Case

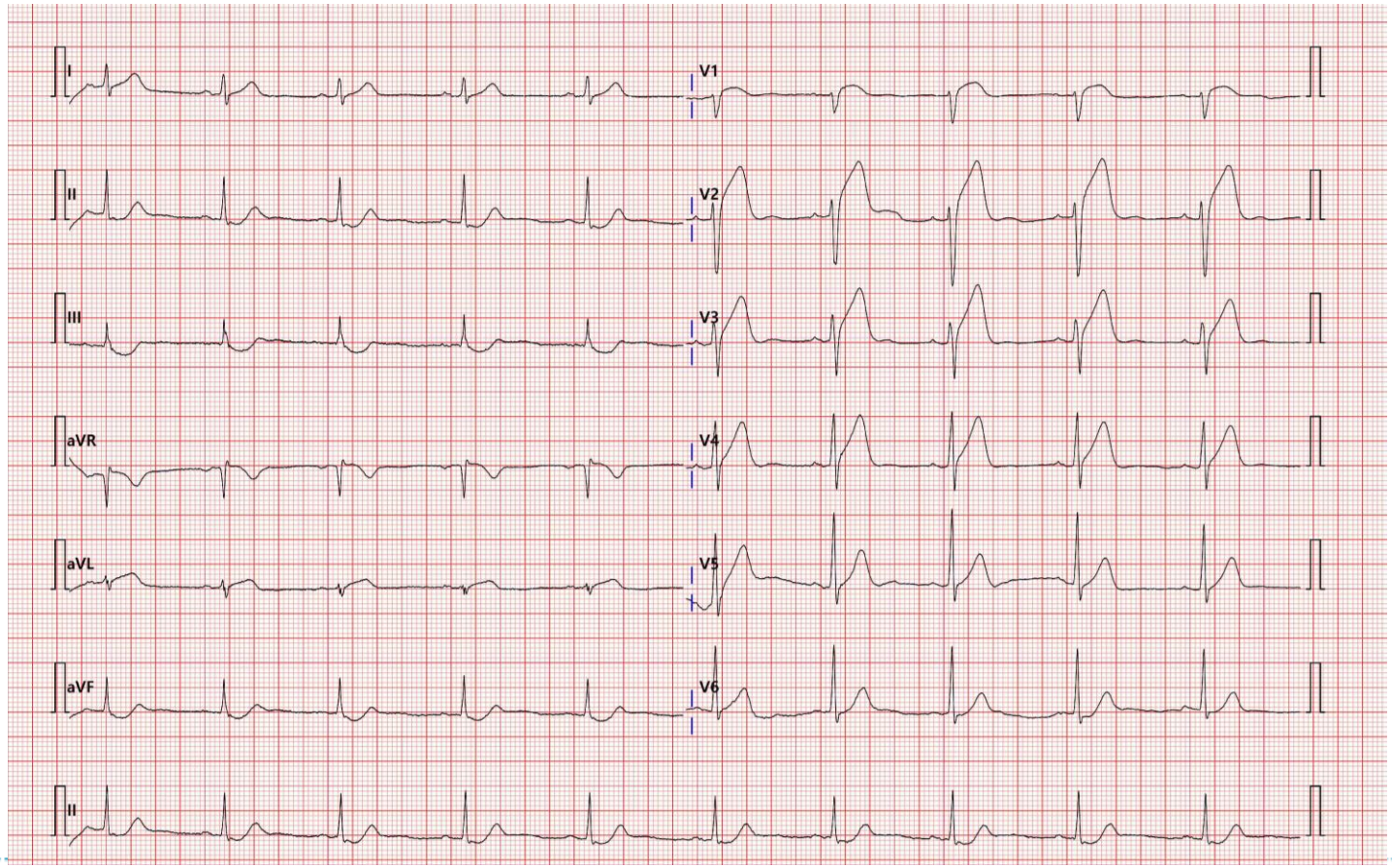
- 39YR , Male, 167cm/67kg, BMI 24.2, WC 88.5cm

Coronary Risk Factors

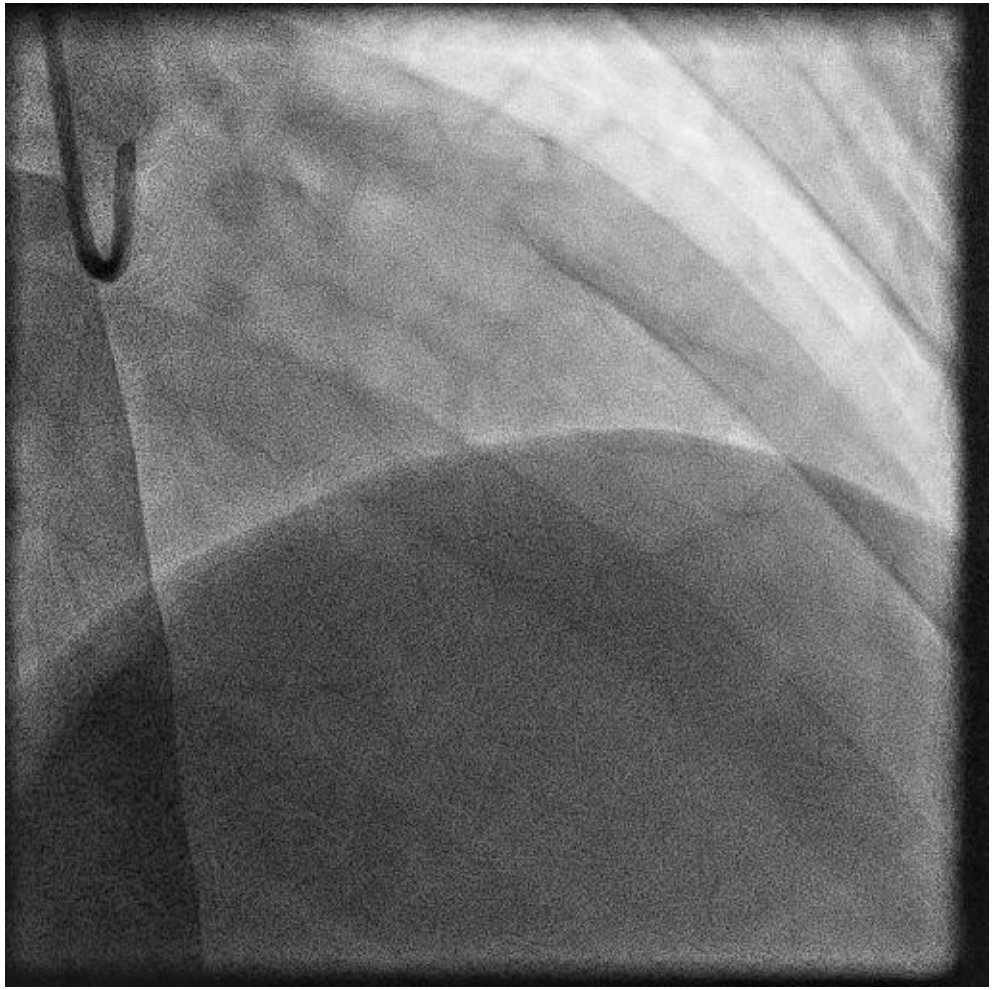
- Smoking

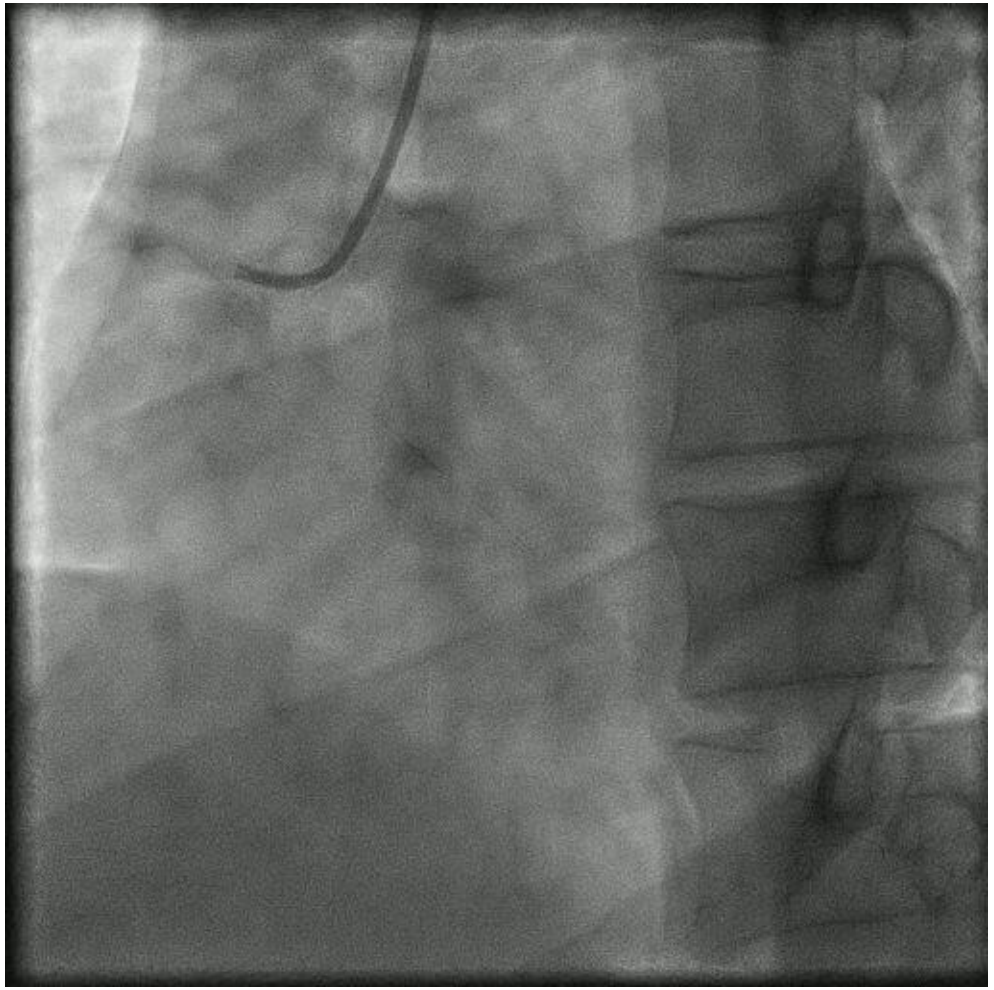
Brief History

- Resting onset chest pain



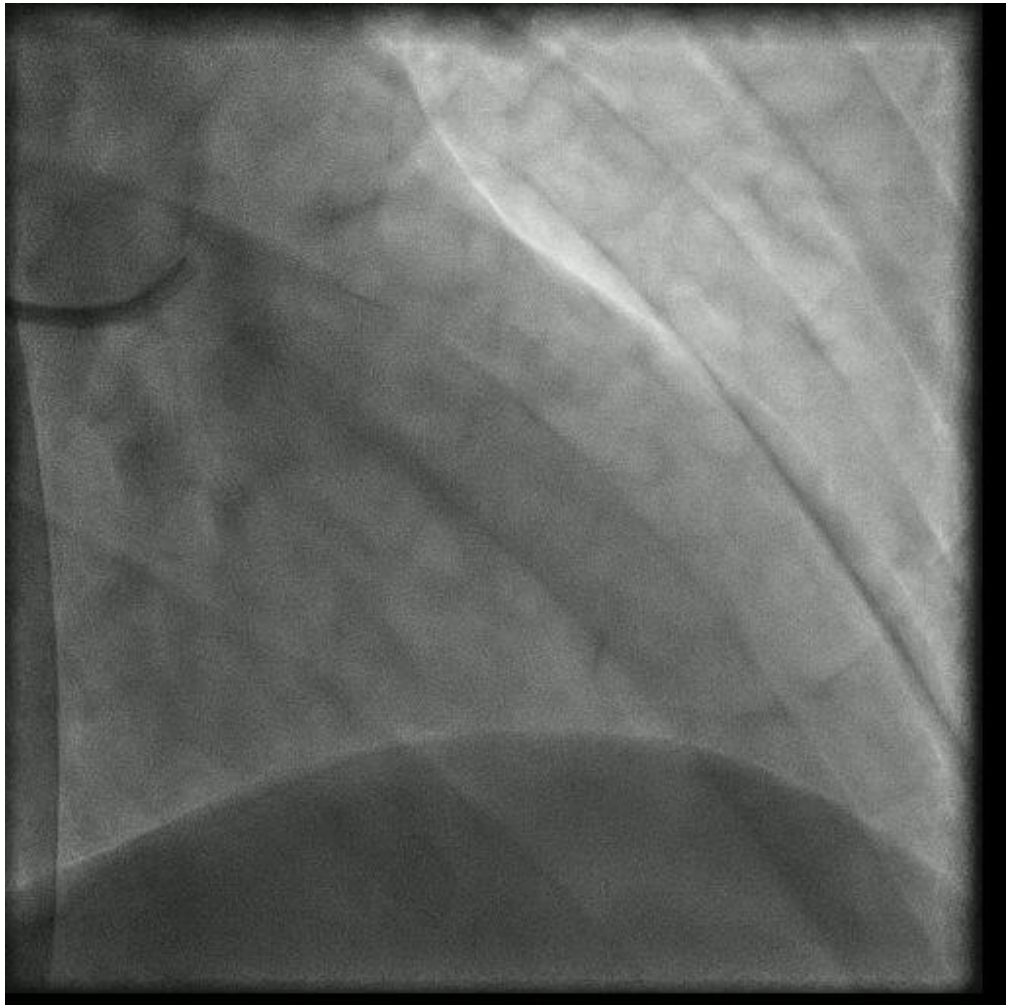
Case 3. Young STEMI pt

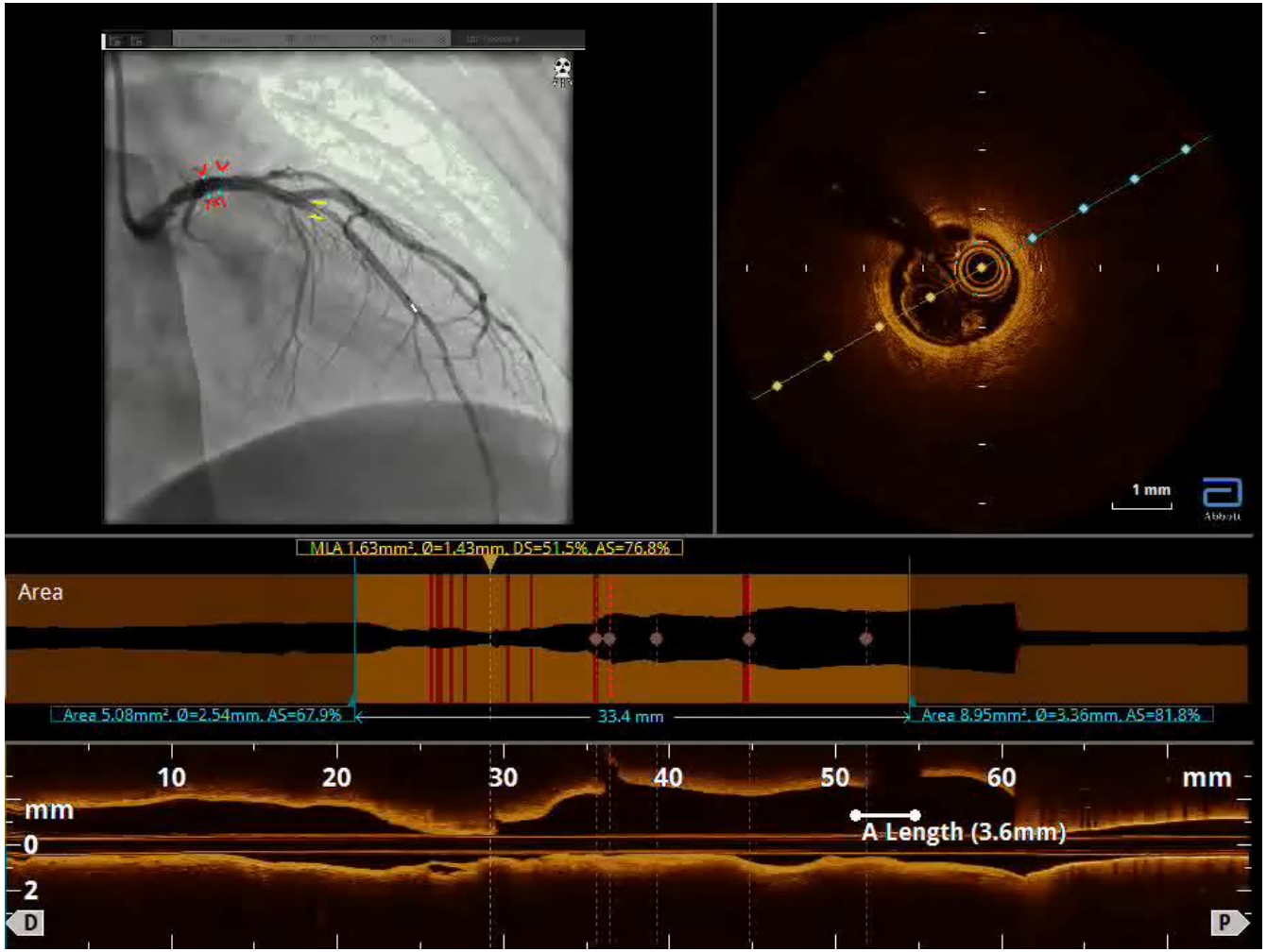




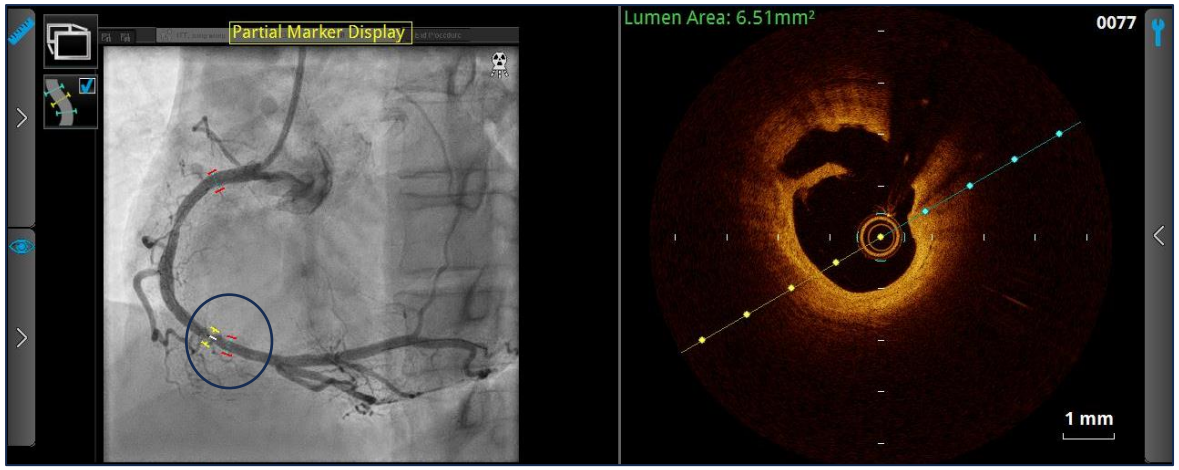
Case 3. Young STEMI pt

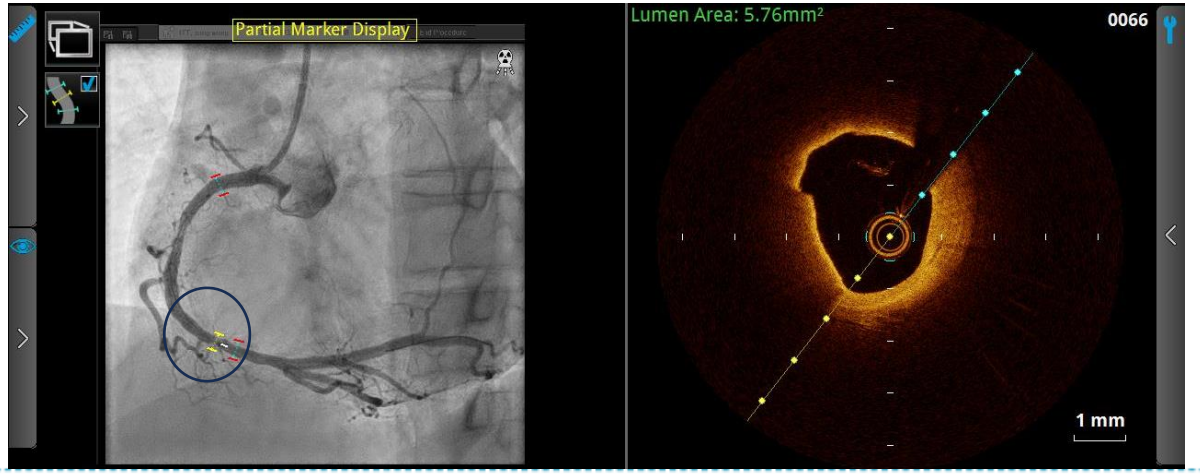
DES 2.75 x 28mm

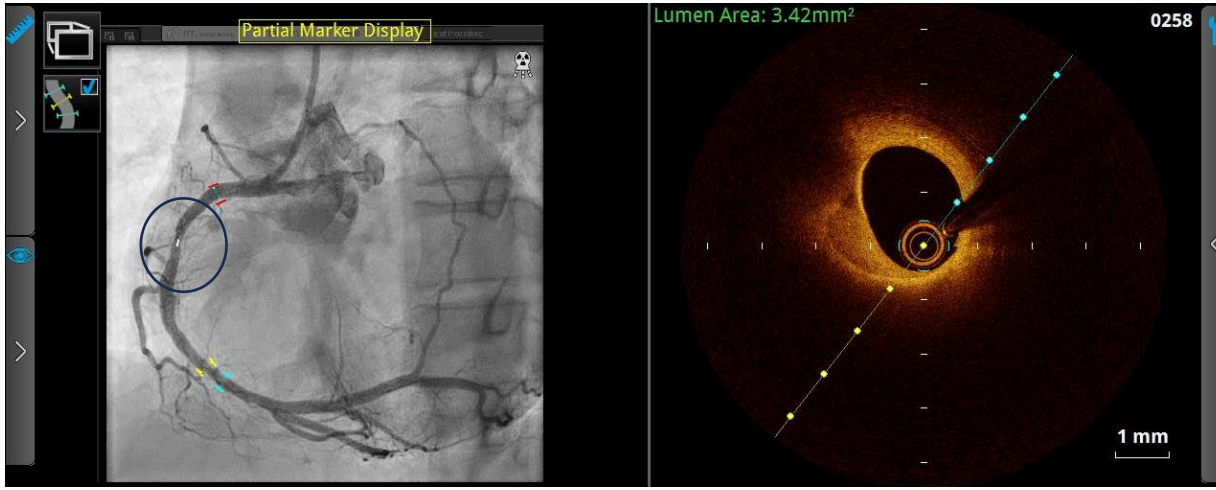




Case 3. Young STEMI pt.







Case 3. Young STEMI pt

Case

- 39YR , Male, 167cm/67kg, BMI 24.2, WC 88.5cm

Coronary Risk Factors

- Smoking

Brief History

- Resting onset chest pain

Cholester	405
Triglyceri	73
HDL-chol	48
LDL-chol	336
Apolipop	133
Apolipop	241

Case 3. Young STEMI pt

Case

- 39YR , Male, 167cm/67kg, BMI 24.2, WC 88.5cm

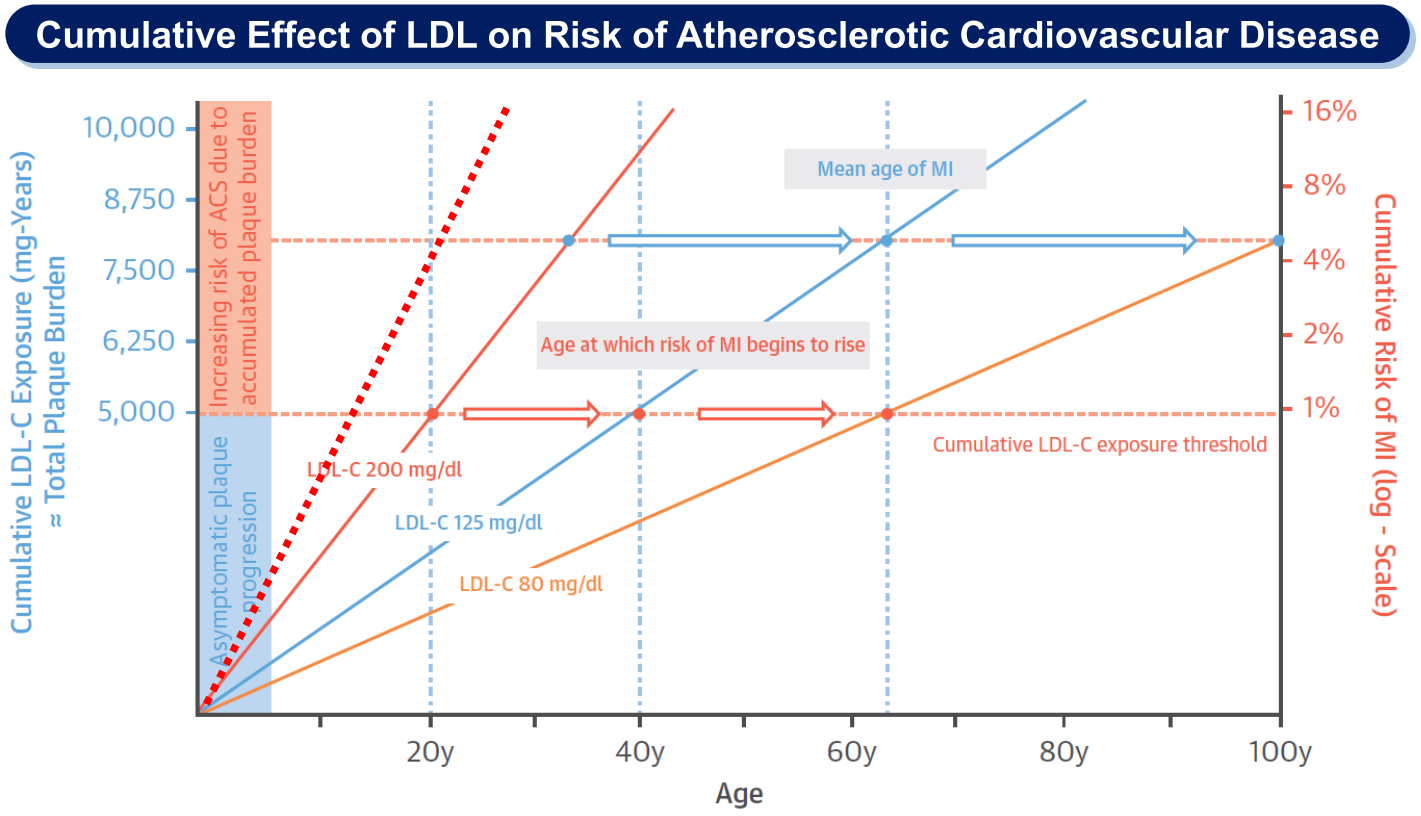
Coronary Risk Factors

- Smoking

Brief History

- Resting onset chest pain

Cholester	405
Triglyceri	73
HDL-chol	48
LDL-chol	336
Apolipop	133
Apolipop	241



Case 3. Young STEMI pt

Case

- 39YR , Male, 167cm/67kg, BMI 24.2, WC 88.5cm

Family History

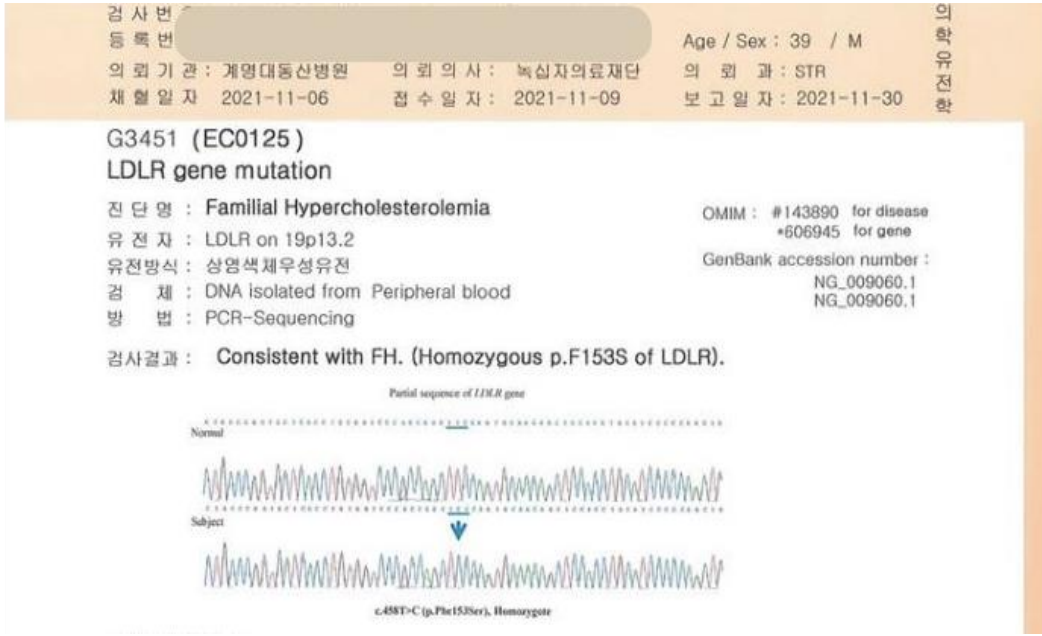
- Early Onset ASCVD (+)

Cholester	405
Triglyceri	73
HDL-chol	48
LDL-chol	336

Rosuva 20mg

Eze 10mg

Cholesterol,	157
Triglyceride	126
HDL-cholest	40
LDL-choleste	89



검사번 [redacted]
등록번
의뢰기관 : 계명대동산병원 의뢰의사 : 녹십자의료재단 Age / Sex : 39 / M
채혈일자 2021-11-06 접수일자 : 2021-11-09 의 뢰 과 : STR
보고일자 : 2021-11-30

G3451 (EC0125)
LDLR gene mutation

진단명 : Familial Hypercholesterolemia
유전자 : LDLR on 19p13.2
유전방식 : 상염색체우성유전
검 체 : DNA isolated from Peripheral blood
방 법 : PCR-Sequencing

OMIM : #143890 for disease
*606945 for gene
GenBank accession number :
NG_009060.1
NG_009060.1

검사결과 : Consistent with FH. (Homozygous p.F153S of LDLR).

Partial sequence of LDLR gene
Normal
Subject
c.458T>C (p.Phe153Ser), Homozygote

Case 3. Young STEMI pt

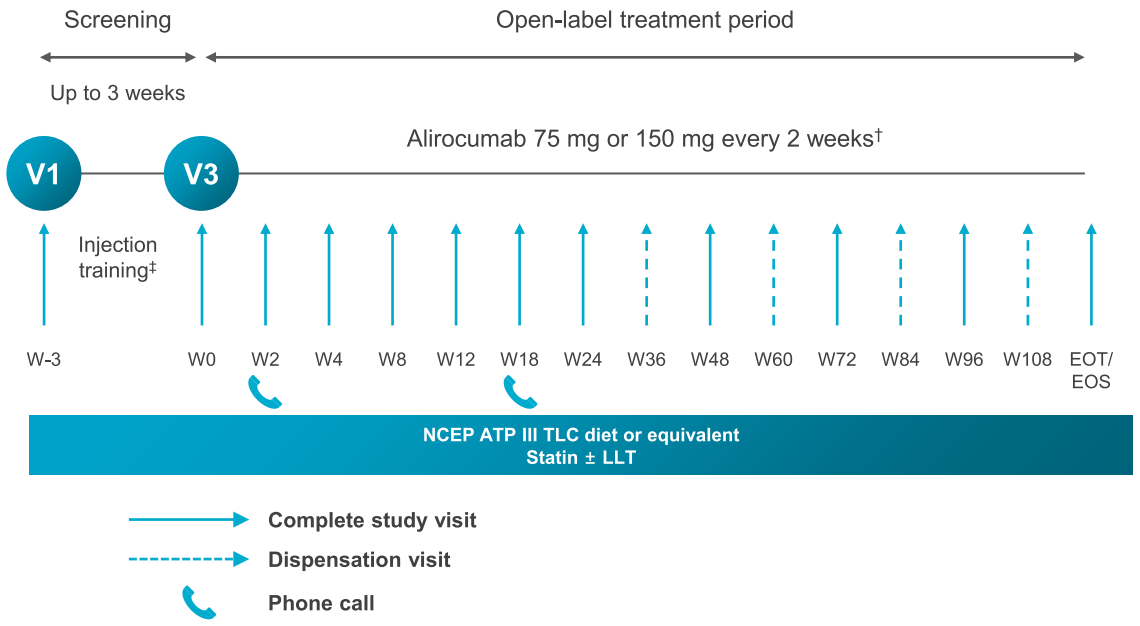
My Questions

1. Is PCSK9i still effective in patients with familial hyperlipidemia?
2. Can Potent LDL lowering with PCSK9i affect the fate of the Vulnerable Plaque? Evidence?

ODYSSEY APPRISE assessed the efficacy and safety of PRALUENT® in high CV risk and/or HeFH patients

Praluent® alirocumab

Patients: high CV risk patients with severe hypercholesterolaemia inadequately controlled with MTD ± other LLT (excluding PCSK9 inhibitors).



Primary endpoint: to assess safety parameters throughout the study, including AEs.

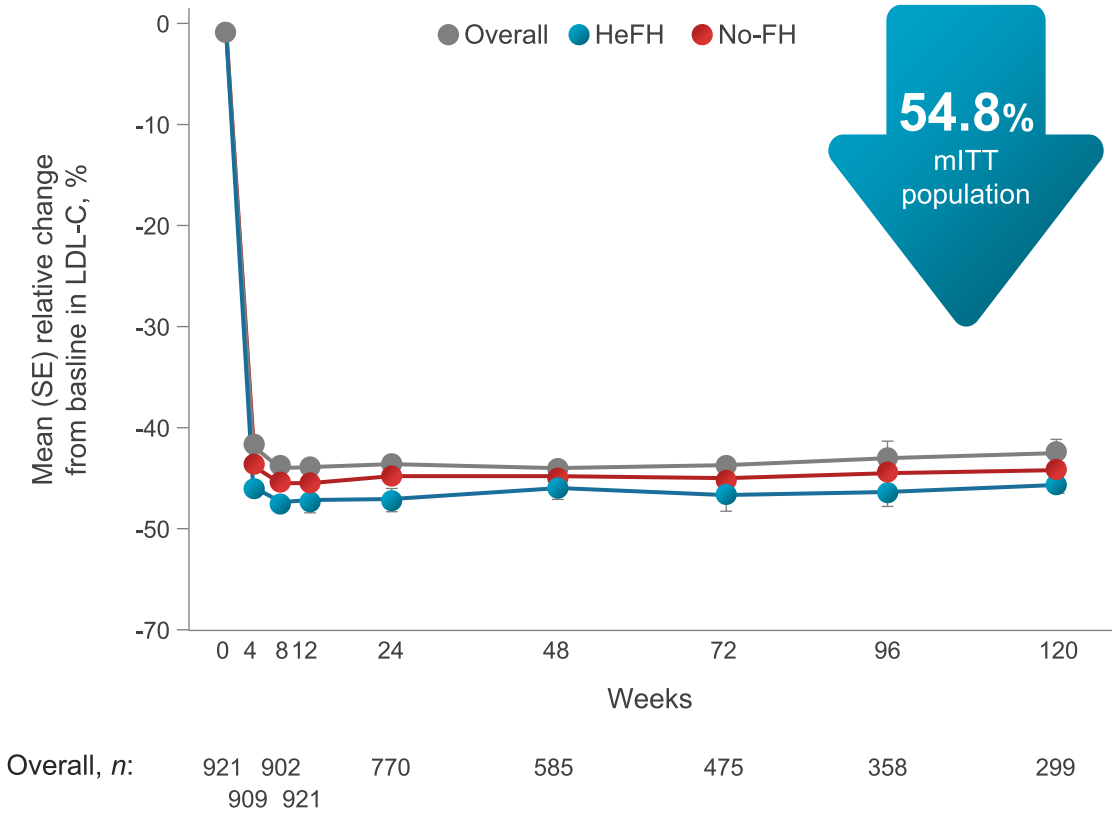
Secondary efficacy endpoints at Week 12: proportion of patients achieving predefined LDL-C goals (<100 mg/dL, <70 mg/dL, and <70 mg/dL and/or ≥50% reduction from baseline), and percent changes from baseline in LDL-C and other lipid parameters.

Safety and efficacy parameters: descriptive statistics for the overall population and according to FH status.

†Dose adjustment from alirocumab 75 mg to 150 mg, or vice versa, was possible based on physician's clinical judgement.
‡Injection training could be done either at a specific visit (visit 2), or alternatively at visit 1 or 3.
AE, adverse event; CV, cardiovascular; EOS, end of study; EOT, end of treatment; LDL-C, low-density lipoprotein cholesterol; LLT, lipid-lowering therapy; MTD, maximally tolerated dose; NCEP ATP III, National Cholesterol Education Program Adult Treatment Panel-III; PCSK9, proprotein convertase subtilisin/kexin type 9; V, visit; W, week.
[Study design[1]] ODYSSEY APPRISE (NCT02476006) was a single-arm, Phase 3b, open-label study designed to obtain safety, and efficacy data of alirocumab in a real-life setting among high CV risk patients with with heterozygous familial hypercholesterolaemia (HeFH) or very-high LDL-C levels despite MTD ± LLTs. Patients received subcutaneous alirocumab 75 mg or 150 mg every 2 weeks, with dose adjustment based on physician's judgment. The primary endpoint of the study was to assess safety parameters throughout the study, including adverse events.
Reference. 1. Gaudet D, et al. Eur J Prev Cardiol. 2022 Feb 3;28(17):1864-1872.

ODYSSEY APPRISE

PRALUENT® reduced LDL-C levels by over 50% from baseline to Week12[1]



PRALUENT® reduced the mean (SD) LDL-C decreased by 2.6 (1.2) mmol/L from baseline to Week 12.[1]

LDL-C was similar in the two hypercholesterolemia subgroups[1]
- HeFH: -53.4% - Non-FH: -57.6%

Reduction of LDL-C levels maintained for up to 2 years[1]

FH, familial hypercholesterolaemia; HeFH, heterozygous familial hypercholesterolaemia; LDL-C, low-density lipoprotein cholesterol; mITT, modified intention-to-treat; SE, standard error.

[Study design[1]] ODYSSEY APPRISE (NCT02476006) was a single-arm, Phase 3b, open-label study designed to obtain safety, and efficacy data of alirocumab in a real-life setting among high CV risk patients with with heterozygous familial hypercholesterolaemia (HeFH) or very-high LDL-C levels despite MTD ± LLTs. Patients received subcutaneous alirocumab 75 mg or 150 mg every 2 weeks, with dose adjustment based on physician's judgment. The primary endpoint of the study was to assess safety parameters throughout the study, including adverse events.

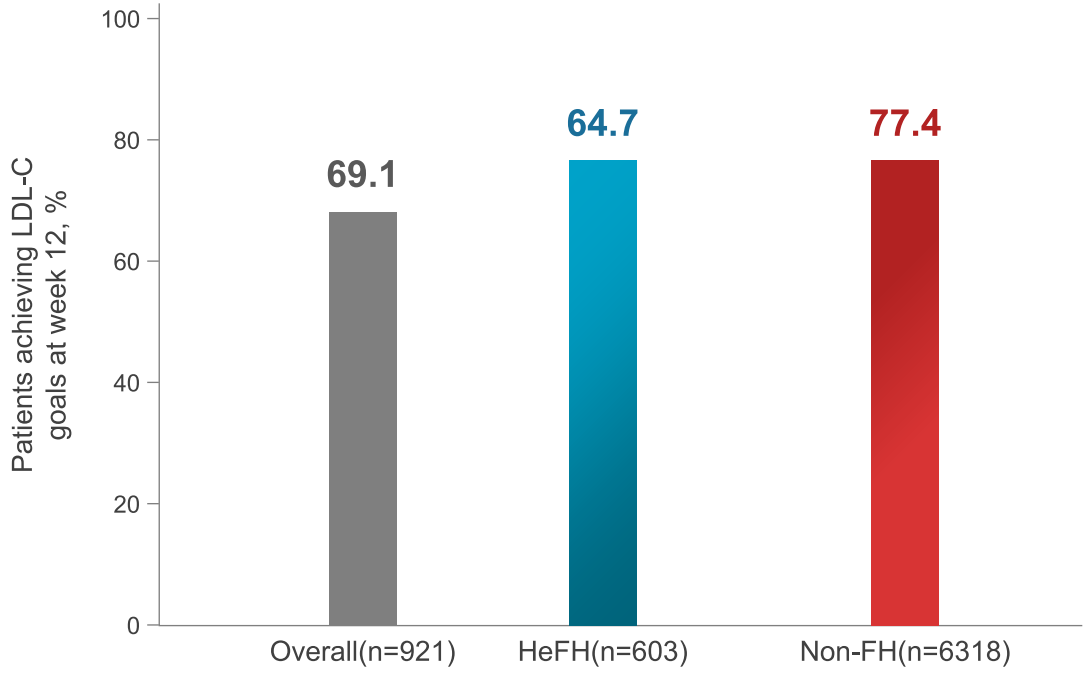
Reference. 1. Gaudet D, et al. Eur J Prev Cardiol. 2022 Feb 3;28(17):1864-1872

ODYSSEY APPRISE

Proportion of patients achieved LDL-C goals[1]

Praluent® alirocumab

LDL-C <1.8 mmol/L and/or ≥50% reduction form baseline



69.1%

PRALUENT® was of the general population achieved the therapeutic goal of reduced LDL-C levels <1.81 mmol/L (70 mg/dL) and/or ≥50% from baseline.[1]

FH, familial hypercholesterolaemia; HeFH, heterozygous familial hypercholesterolaemia; LDL-C, low-density lipoprotein cholesterol; mITT, modified intention-to-treat; SE, standard error.

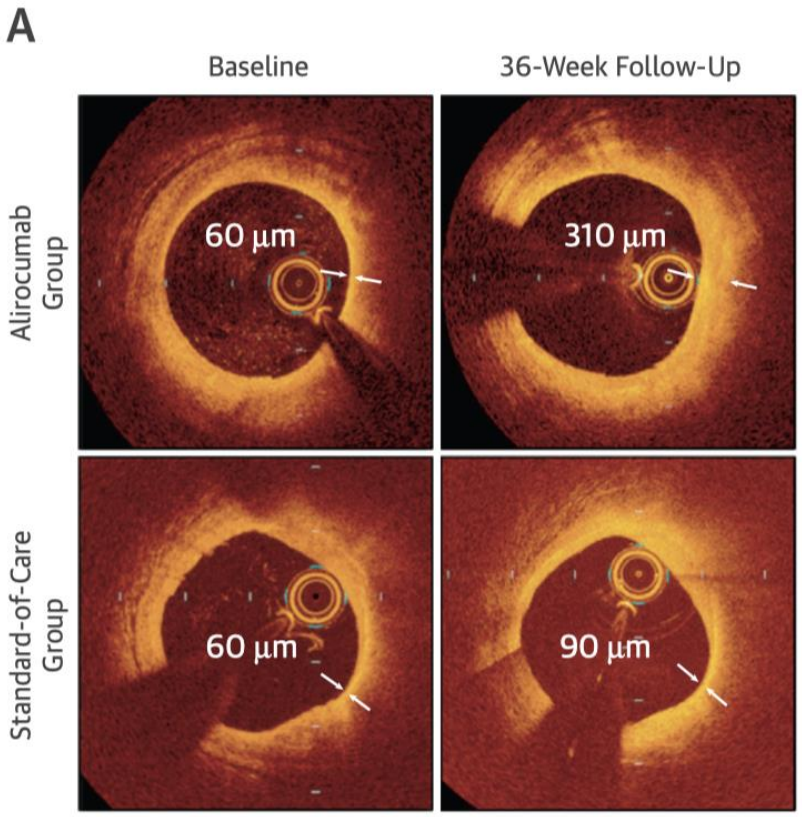
[Study design[1]] ODYSSEY APPRISE (NCT02476006) was a single-arm, Phase 3b, open-label study designed to obtain safety, and efficacy data of alirocumab in a real-life setting among high CV risk patients with with heterozygous familial hypercholesterolaemia (HeFH) or very-high LDL-C levels despite MTD ± LLTs. Patients received subcutaneous alirocumab 75 mg or 150 mg every 2 weeks, with dose adjustment based on physician's judgment. The primary endpoint of the study was to assess safety parameters throughout the study, including adverse events.

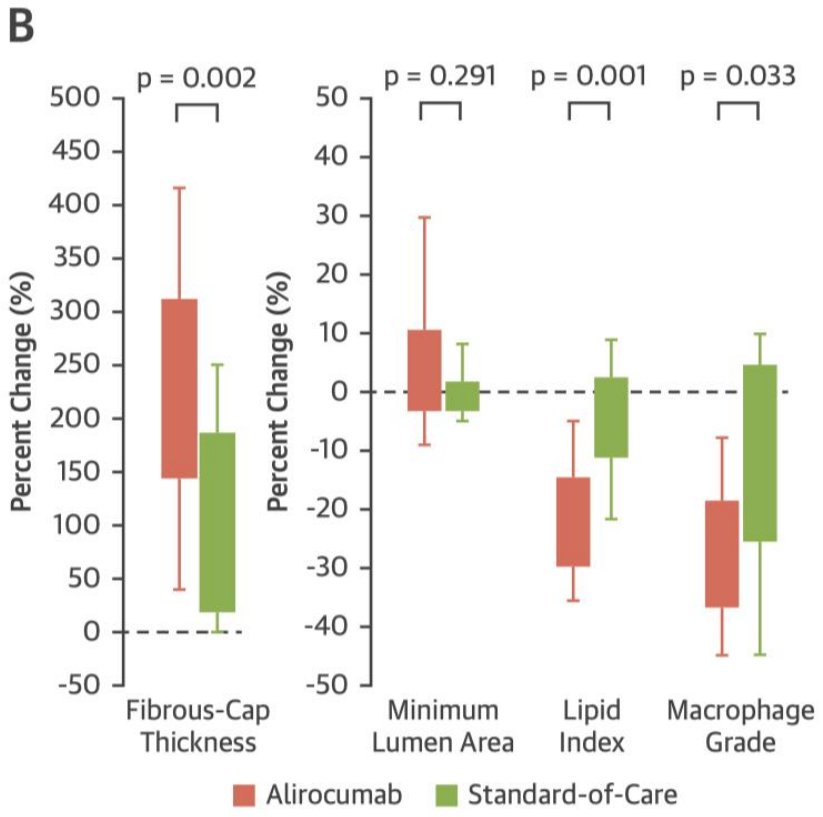
Reference. 1. Gaudet D, et al. Eur J Prev Cardiol. 2022 Feb 3;28(17):1864-1872

ALTAIR Trial

Open Label Prospective Single Center Study

Praluent® alirocumab





Adding Alirocumab to Rosuvastatin Helps Reduce the Vulnerability of Thin-Cap Fibroatheroma

JACC: CARDIOVASCULAR IMAGING, VOL. 13, NO. 6, 2020
JUNE 2020:1438-59

PACMAN - AMI Trial

Alirocumab + Statin in AMI patients

Patients with AMI (N-STEMI/STEMI) undergoing successful PCI of the infarct vessel &
2 non-infarct related arteries with non-obstructive lesions (diameter stenosis 20-50%)

Alirocumab PACMAN AMI

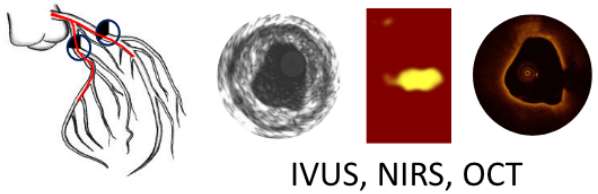
POC

No statin, LDL >125 mg/dL (>3.2 mmol/L)

On Statin, LDL >70 mg/dL (>1.8 mmol/L)

Enrollment of 300 Patients

Baseline



IVUS, NIRS, OCT

Baseline blood sampling

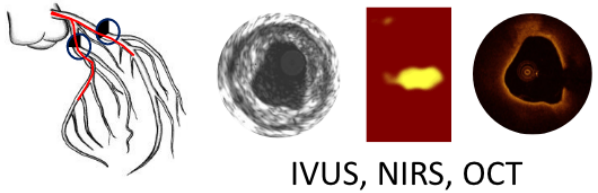
Alirocumab s.c. 150 mg / 2 weeks + Rosuvastatin 20 mg

R 1:1

Placebo s.c. / 2 weeks + Rosuvastatin 20 mg

Initiated <24 hrs after PCI

52 weeks

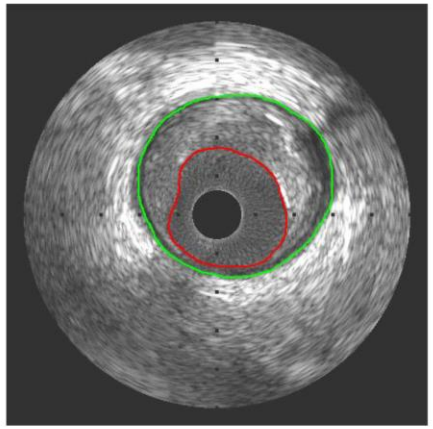


IVUS, NIRS, OCT

Blood sampling 4 weeks
3 visits, 4 phone calls
Blood sampling 52 weeks

PACMAN - AMI Trial

Primary Endpoint

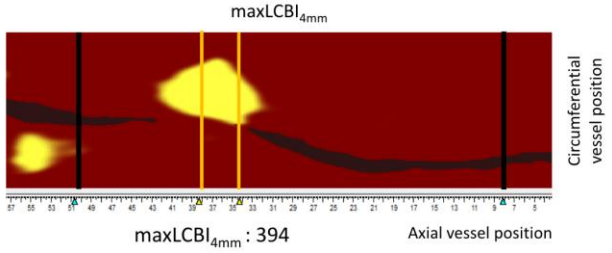


Analysis interval: 1 mm
Obtained by NIRS-IVUS catheter

$$PAV = \frac{\Sigma(EEM_{CSA} - LumenCSA)}{\Sigma EEM_{CSA}} \times 100$$

Change in **percent atheroma volume** (PAV) by **greyscale IVUS**

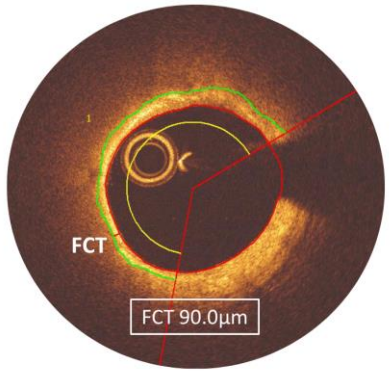
Powered Secondary Endpoint



maxLCBI$_{4mm}$=
a measure of lipid probability at the 4 mm with maximal lipid load of a vessel imaged by NIRS

Change in **maximal lipid-core burden index** (maxLCBI$_{4mm}$) by **NIRS**

Powered Secondary Endpoint

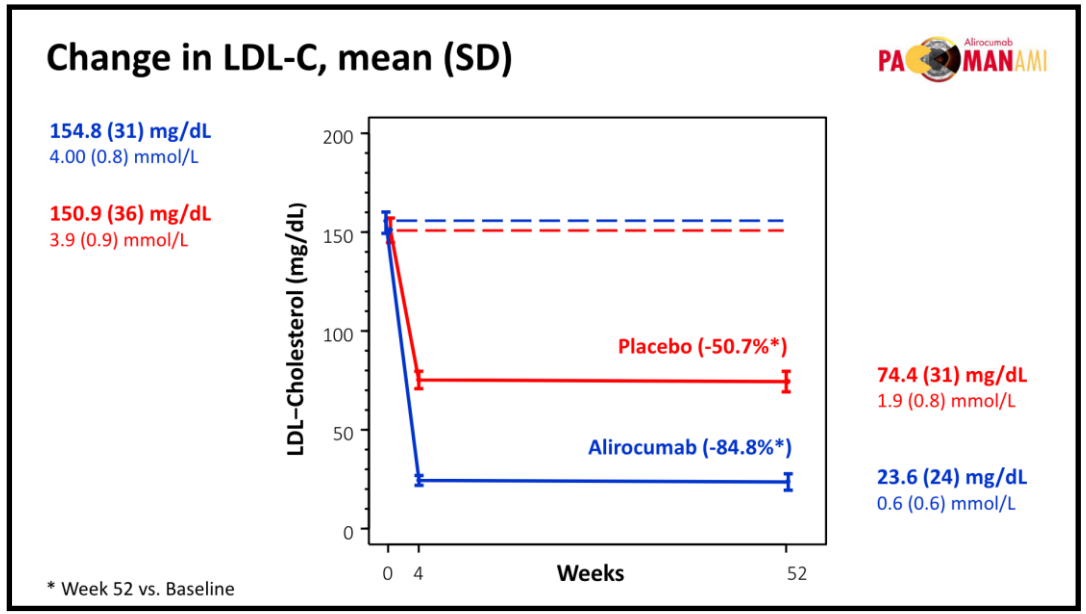


Analysis interval: 0.4 mm
Method: semiquantitative software assisted FCT tracing

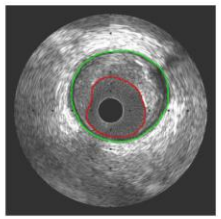
FCT$_{min}$ = minimal fibrous cap thickness anywhere in lipid rich plaques imaged by OCT

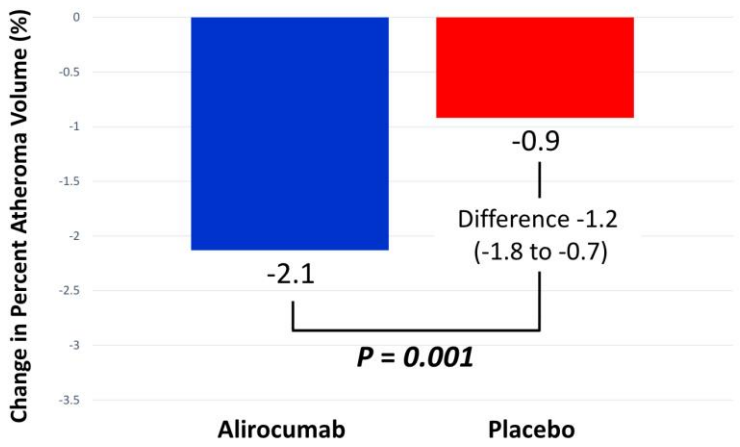
Change in **minimal fibrous cap thickness** (FCT$_{min}$) by **OCT**

Change in LDL-C, mean (SD)

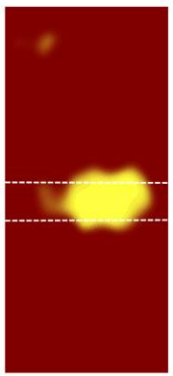


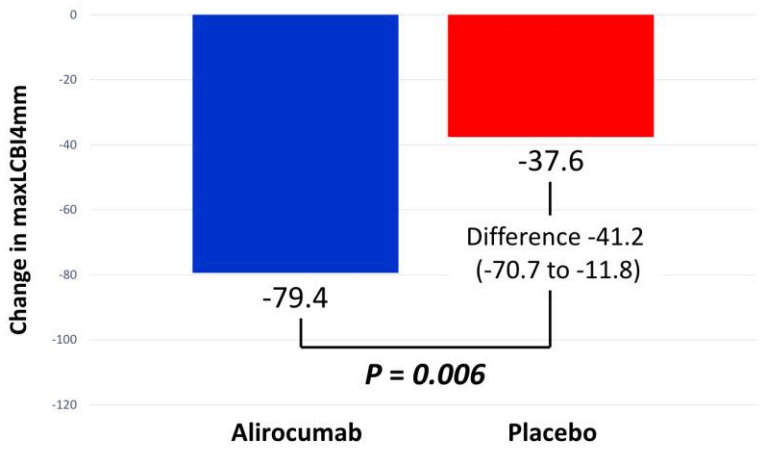
Primary EP:
Change in Percent Atheroma Volume (IVUS)



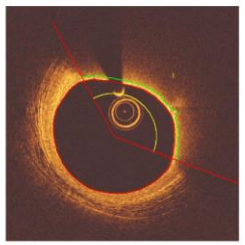


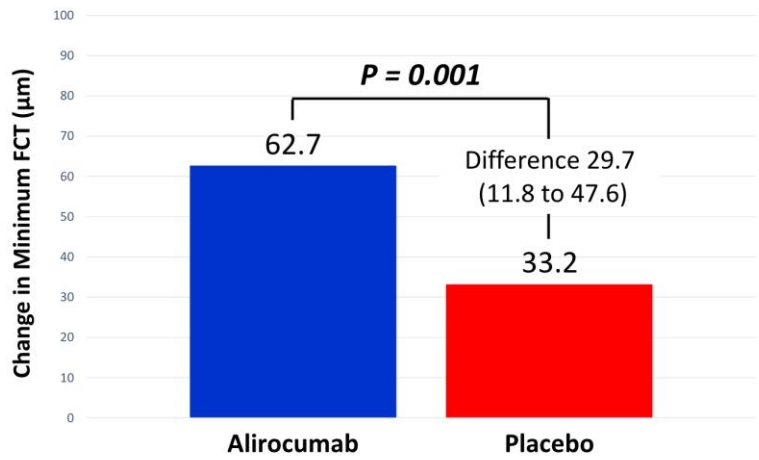
Powered Secondary EP:
Change in maxLCBI$_{4mm}$ (NIRS)





Powered Secondary EP:
Change in Minimum FCT (OCT)





PACMAN - AMI Trial

Conclusions

Compared with placebo, alirocumab initiated in the setting of acute AMI on top of high-intensity statin therapy resulted in greater decrease in PAV, larger reduction in lipid burden and higher increase in minimal fibrous cap thickness after 52 weeks of treatment.

These findings indicate **incremental coronary plaque regression, lipid core reduction and plaque stabilization with alirocumab** and provide a mechanistic rationale in favor of early initiation of very intensive LDL-C lowering in acute MI patients.

JAMA | Original Investigation

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

Lorenz Räber, MD, PhD; Yasushi Ueki, MD, PhD; Tatsuhiko Otsuka, MD; Sylvain Losdat, PhD; Jonas D. Häner, MD; Jacob Lonborg, MD; Gregor Fahrni, MD; Juan F. Iglesias, MD; Robert-Jan van Geuns, MD, PhD; Anna S. Ondracek, MSc; Maria D. Radu Juul Jensen, MD, PhD; Christian Zanchin, MD, PhD; Stefan Stortecky, MD; David Spirk, MD; George C. M. Siontis, MD, PhD; Lanja Saleh, PhD; Christian M. Matter, MD; Joost Daemen, MD, PhD; François Mach, MD; Dik Heg, PhD; Stephan Windecker, MD; Thomas Engstrøm, MD, PhD; Irene M. Lang, MD; Konstantinos C. Koskinas, MD, MSc; for the PACMAN-AMI collaborators

Raber el al.
JAMA . 2022: April

Case 3. Young STEMI pt

Case

- 39YR , Male, 167cm/67kg, BMI 24.2, WC 88.5cm

Family History

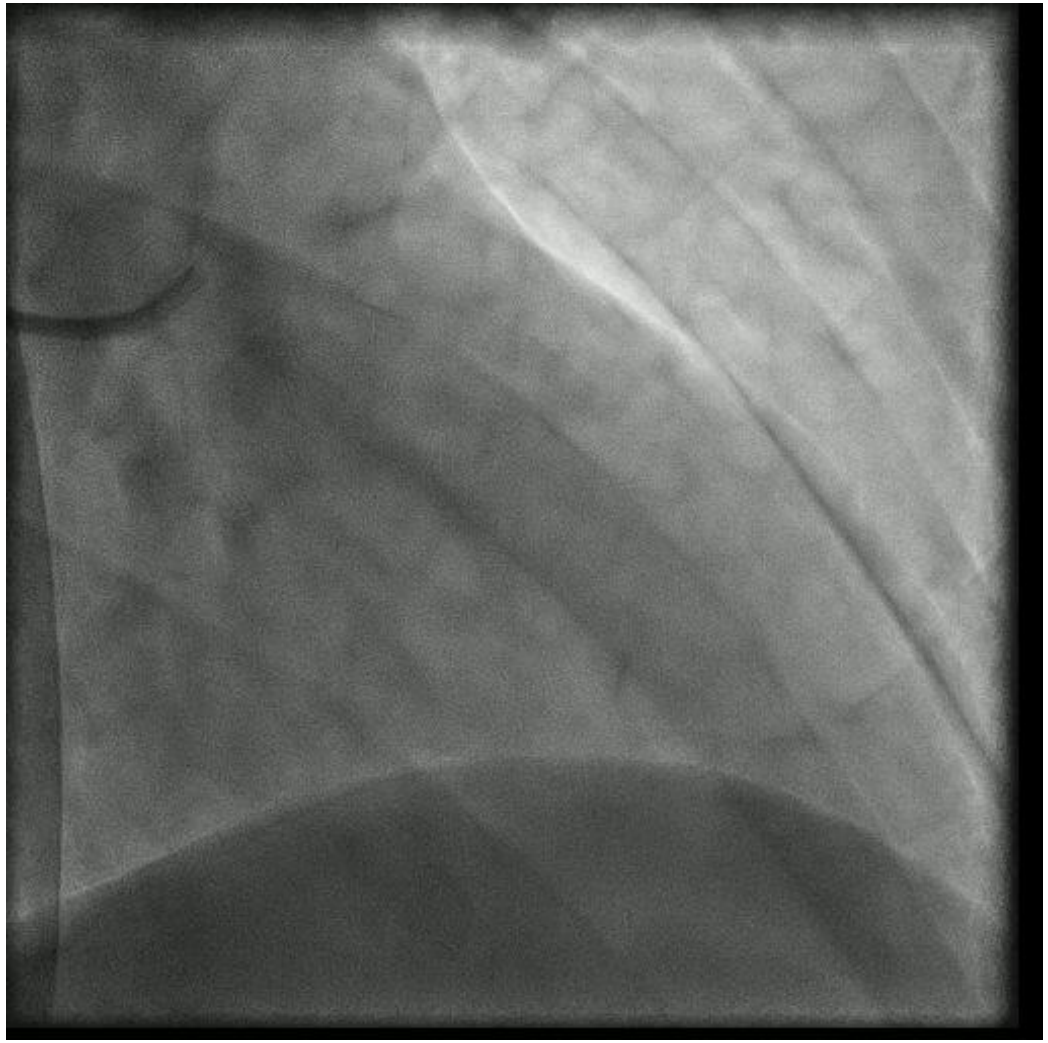
- Early Onset ASCVD (+)

Date	Dx	LDL (mg/dL)	AST / ALT	Medication
2021.11	STEMI (P-PCI)	336	62/62	Rosuva 20mg/Eze 10mg
2021.12	Familial HC	89	29/83	**PCSK9i q 2wks**,Rosuva 20/ Eze 10mg
2022.2		12	48/114	**PCSK9i q 2wks**, Rosuva 5/E ze 10mg
2022.4		20	23/53	**PCSK9i q 2wks**, Rosuva 5/E ze 10mg

Case 3. Young STEMI pt

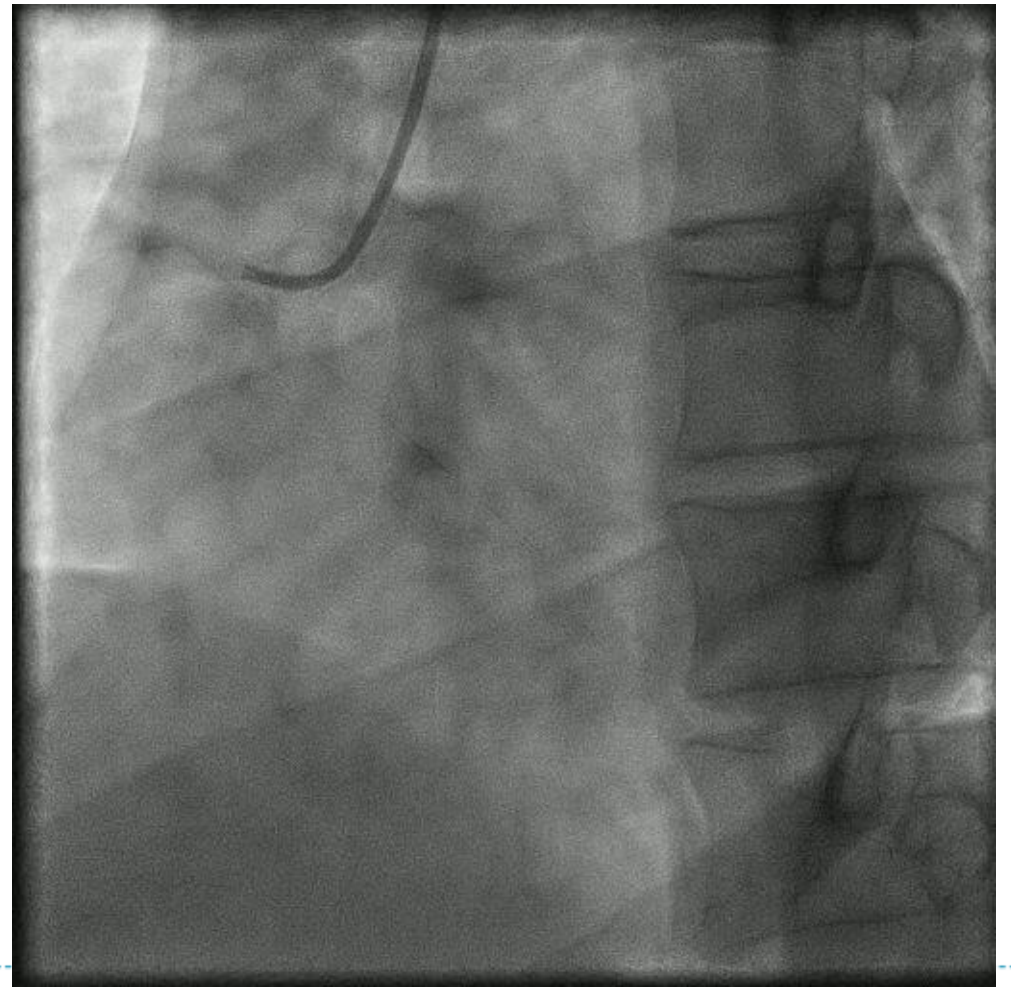
FU CAG

- 12Mo later

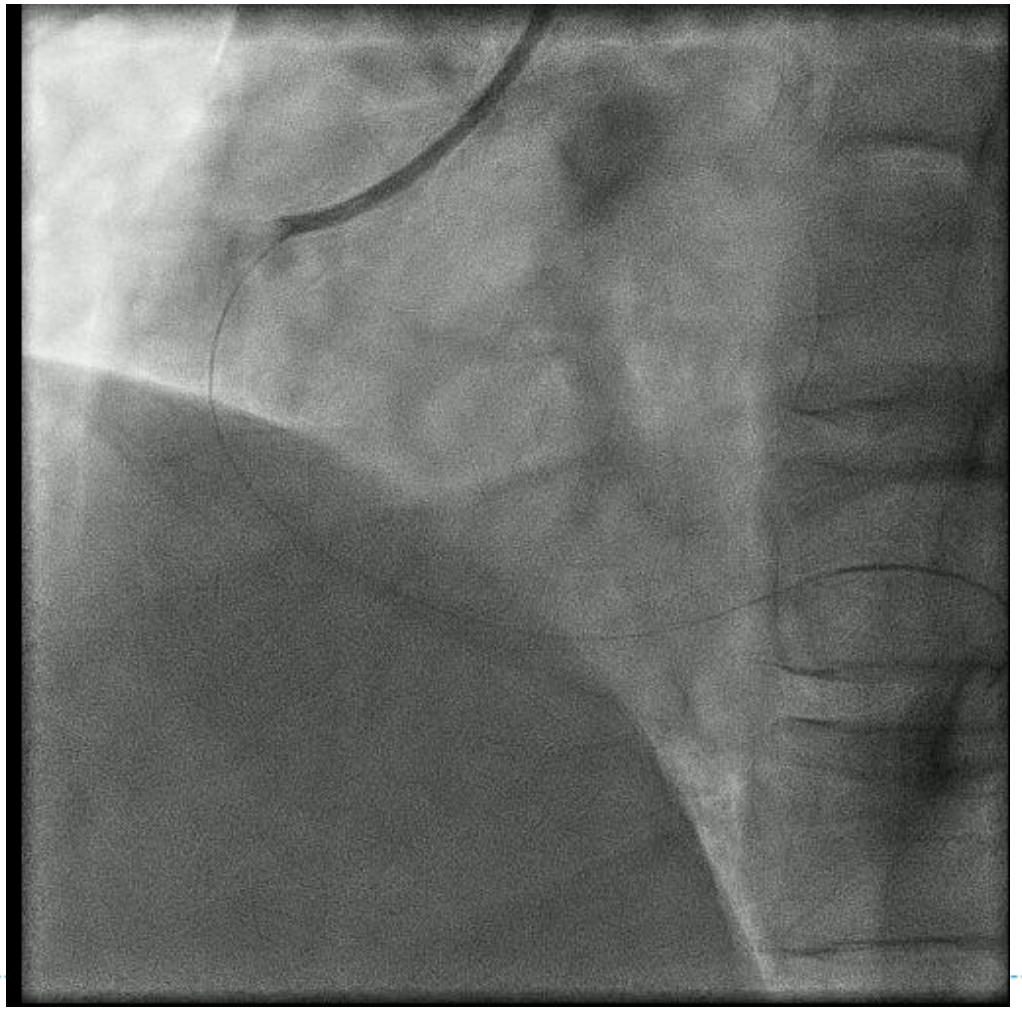


Case 3. Young STEMI pt

Index PCI



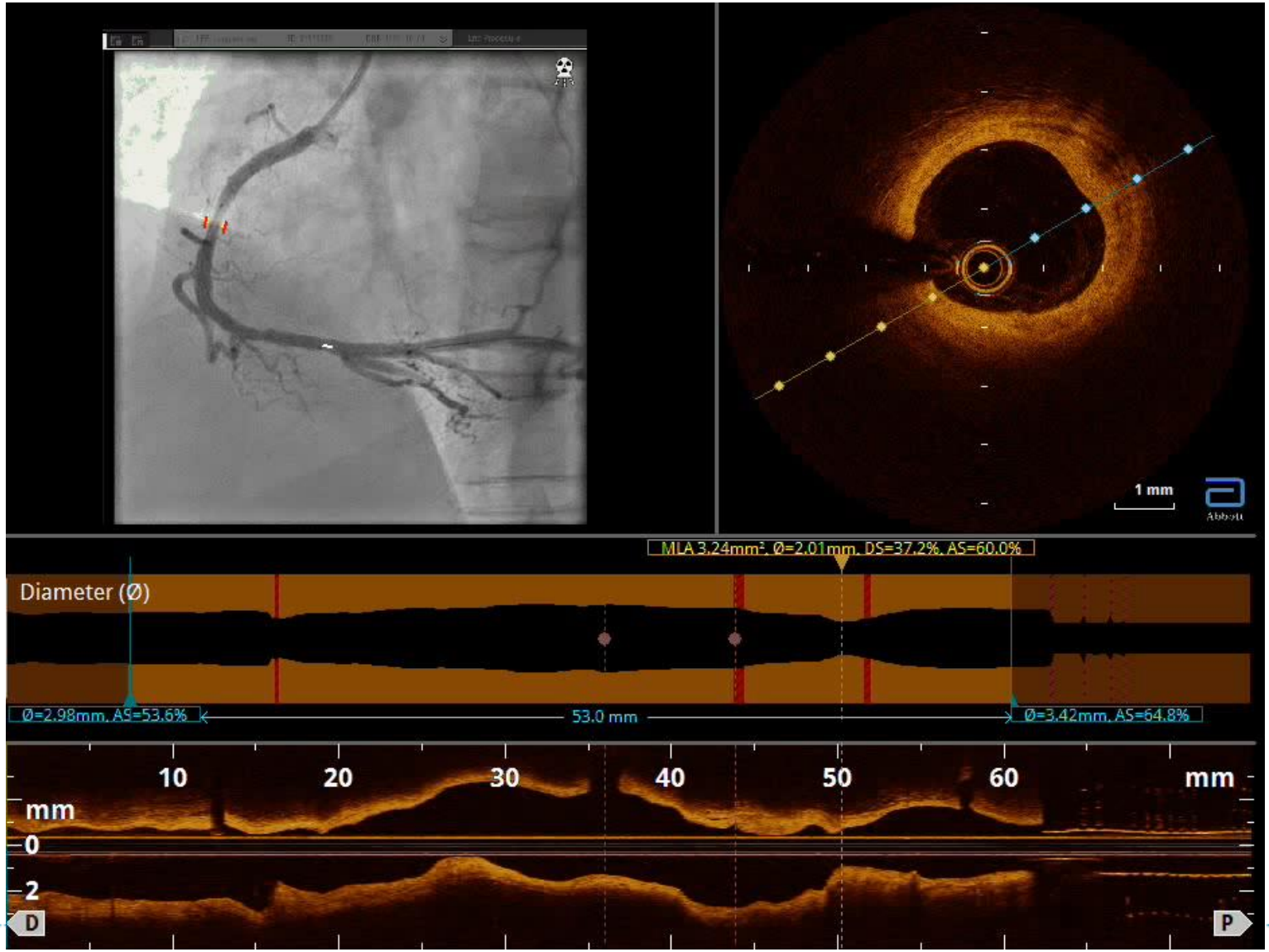
12 mo FU



Case 3. Young STEMI pt

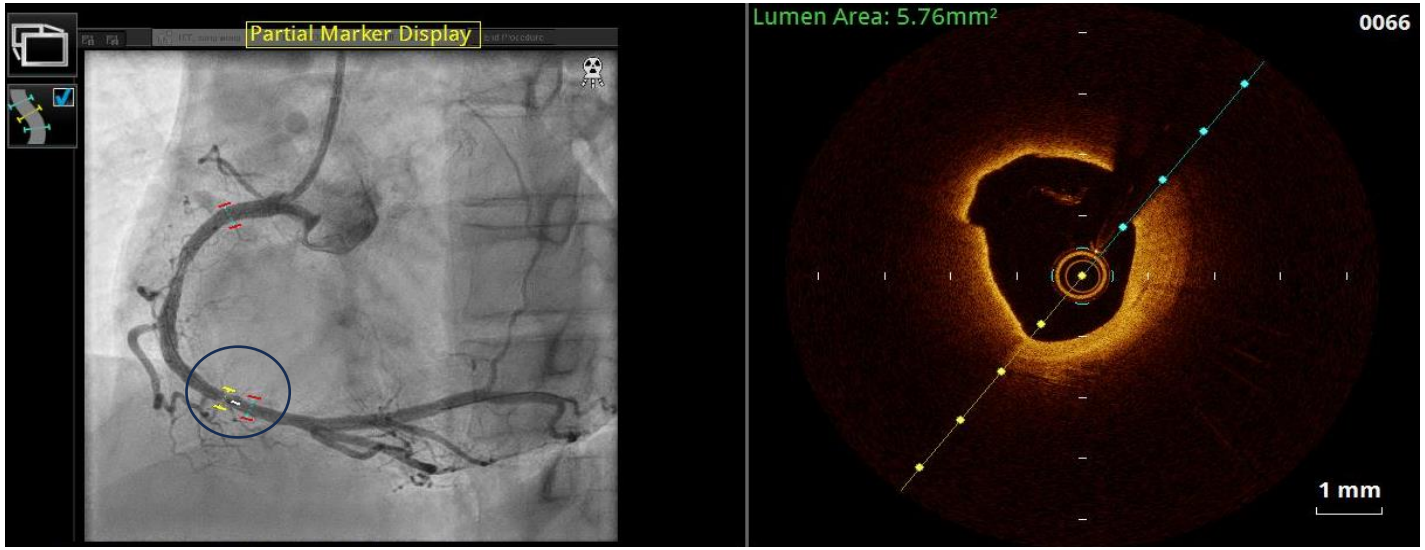
FU OCT

- 12Mo later

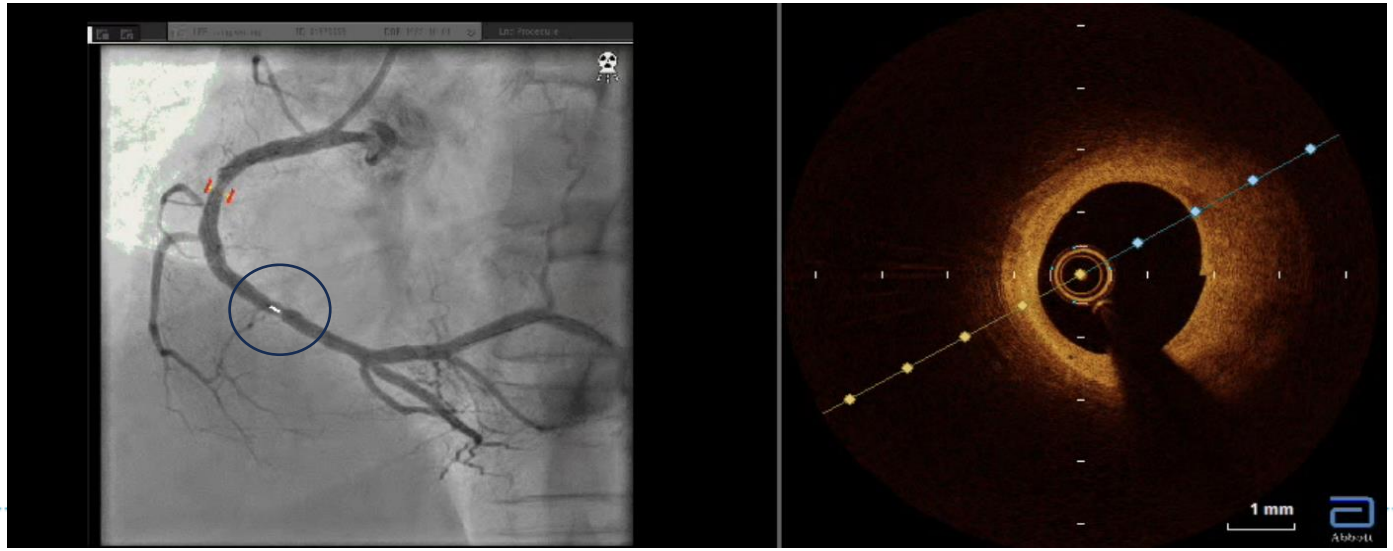


Case 3. Young STEMI pt

Baseline



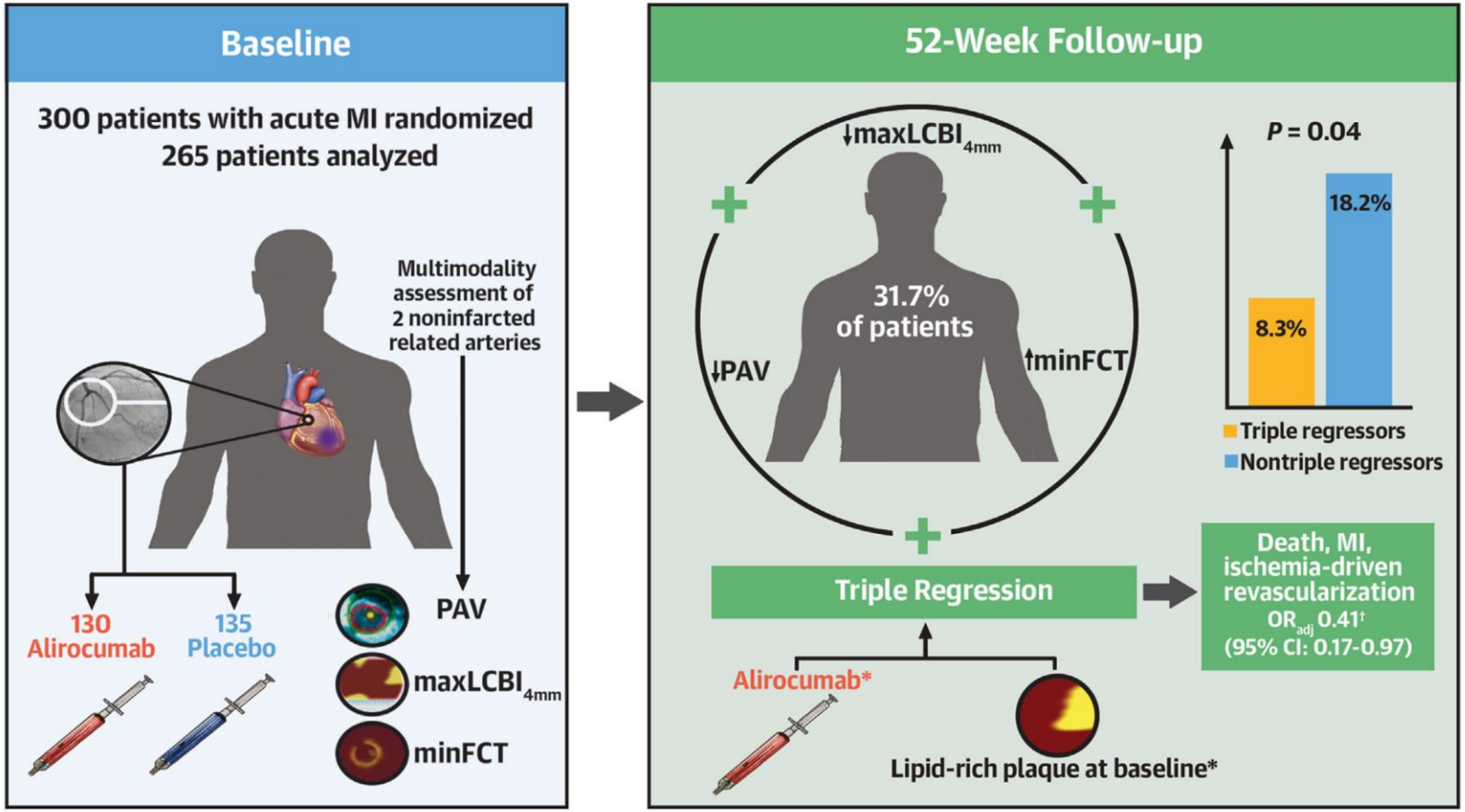
12months



PACMAN AMI sub-study

Coronary Atheroma Regression and Stabilization

Praluent® alirocumab



Biccirè FG, et al. J Am Coll Cardiol. 2023;82(18):1737-1747.

2019 ESC/EAS Guidelines

PCSK9i use is recommended to further lower LDL-C in very high-risk patients, including those with ACS.[1]

Praluent® alirocumab

"Adding a PCSK9i to maximally tolerated statins and ezetimibe is recommended by the 2019 ESC/EAS guidelines[1]"

Class	Level	CV risk category	Recommendation
I	A	In secondary prevention for patients at **very high-risk** not achieving their goal on a maximum tolerated statin and ezetimibe	A combination **with a PCSK9i** is recommended
I	C	In **very high-risk FH patients** (with ASCVD or another major risk factor) who do not achieve their goal on a maximum tolerated statin and ezetimibe	A combination **with a PCSK9i** is recommended

Class I: Evidence and/or general agreement that a given treatment or procedure is beneficial, useful and effective; **Level A:** Data derived from multiple randomised clinical trials or meta-analyses; **Level C:** Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

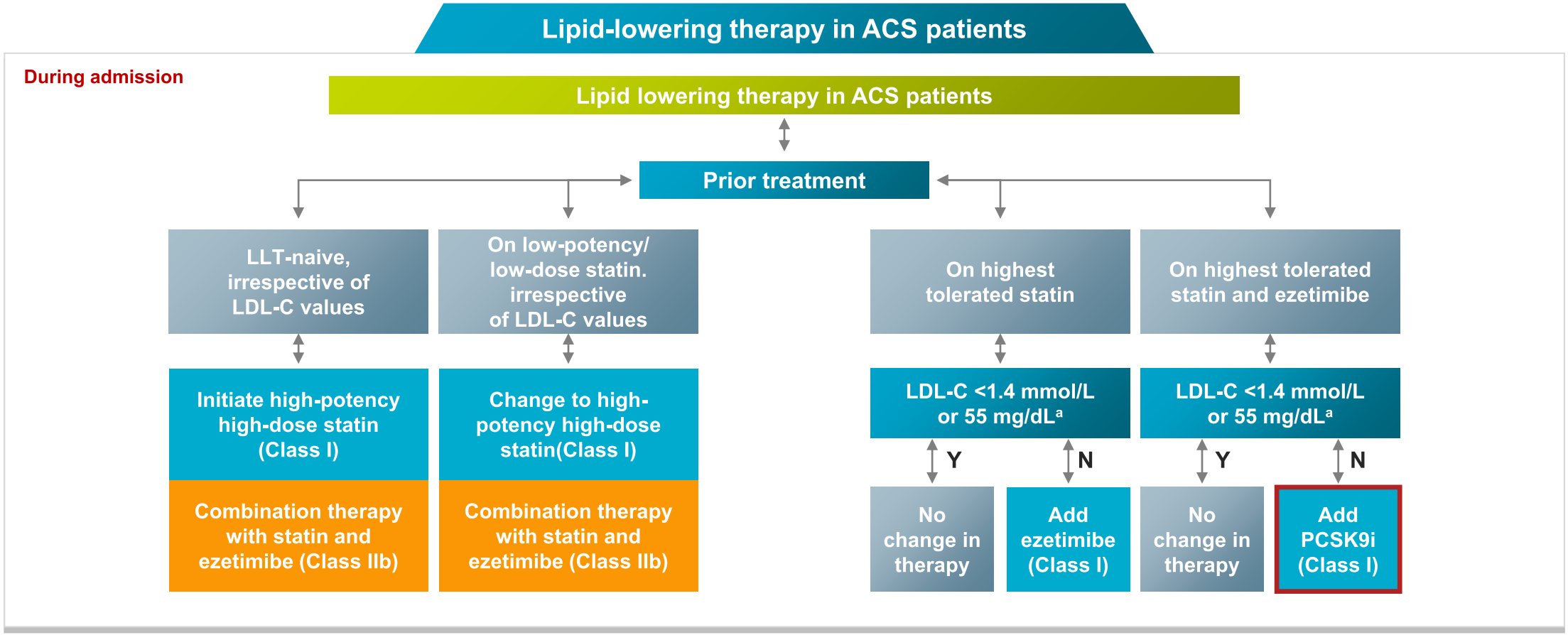
Very high-risk: People with any of the following: ① Documented ASCVD, either clinical or unequivocal on imaging. **Documented ASCVD includes previous ACS** (MI or unstable angina), stable angina, coronary revascularization (PCI, CABG, and other arterial revascularization procedures), stroke and TIA, and peripheral arterial disease. Unequivocally documented ASCVD on imaging includes those findings that are known to be predictive of clinical events, such as significant plaque on coronary angiography or CT scan (multivessel coronary disease with two major epicardial arteries having >50% stenosis), or on carotid ultrasound. ② DM with target organ damage, or at least three major risk factors, or early onset of T1DM of long duration (>20 years). ③ Severe CKD (eGFR <30 mL/min/1.73 m^2). ④ A calculated SCORE ≥10% for 10-year risk of fatal CVD. ⑤ FH with ASCVD or with another major risk factor.

ACS, acute coronary syndrome; ASCVD, atherosclerotic cardiovascular disease; BP, blood pressure; CKD, chronic kidney disease; DM, diabetes mellitus; EAS, European Atherosclerosis Society; eGFR, estimated glomerular filtration rate; ESC, European Society of Cardiology; FH, familial hypercholesterolaemia; LDL-C, low-density lipoprotein cholesterol; PCSK9i, proprotein convertase subtilisin/kexin type 9 inhibitors; SCORE, Systemic COronary Risk Evaluation; TC, total cholesterol.

Reference. 1. Mach F, *et al.* Eur Heart J. 2020 Jan 1;41(1):111-188.

PCSK9i treatment should be initiated during ACS hospitalization in patients who were not at their LDL-C goal despite being on statin and ezetimibe treatment

Praluent® alirocumab

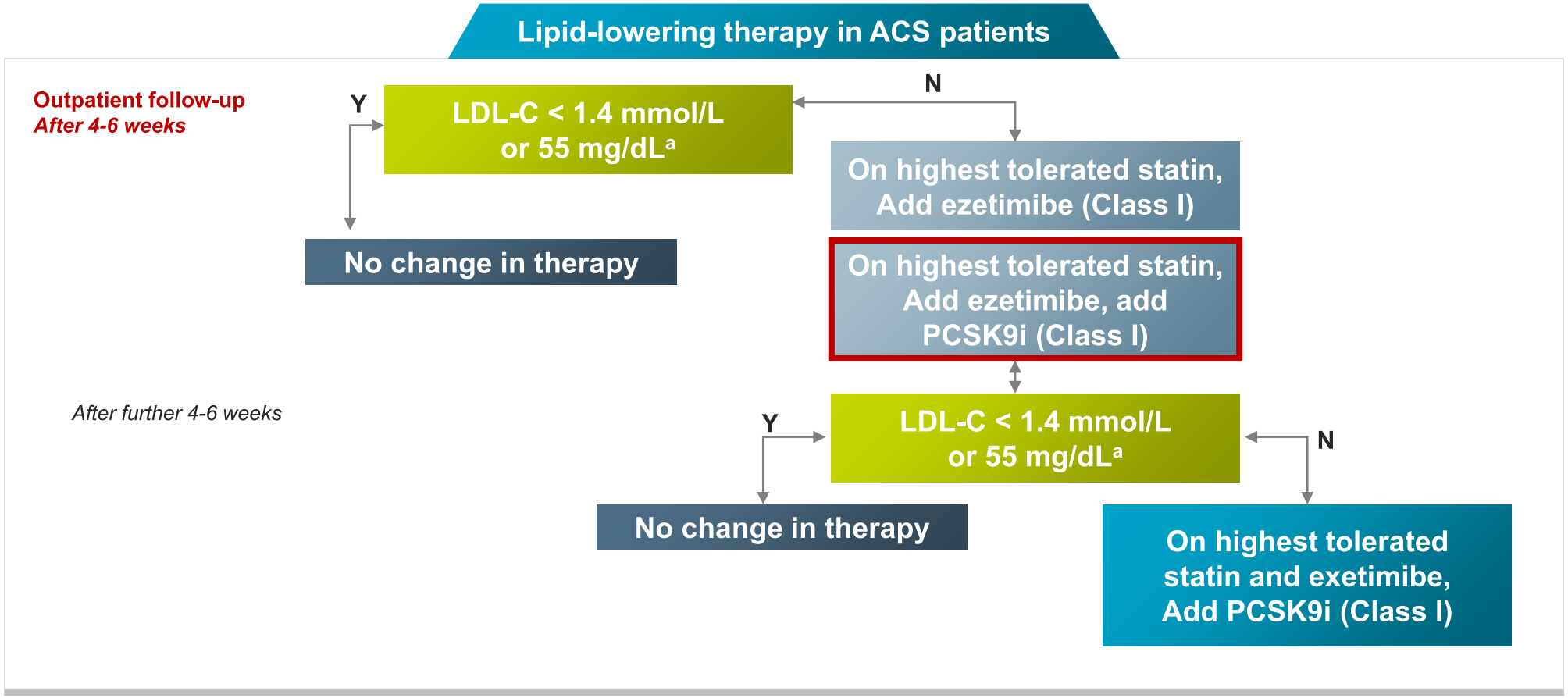


[a] Consider LDL-C <1.0 mmol/L if recurrent event.

ESC, European Society of Cardiology; EAS, European Atherosclerosis Society; ACS, acute coronary syndrome; LDL-C, low-density lipoprotein cholesterol; LLT, lipid-lowering therapy; PCSK9i, proprotein convertase subtilisin/kexin type 9 inhibitor

Reference. 1. Byrne RA, et al. Eur Heart J. 2023 Oct 12;44(38):3720-3826. .

Initiation of PCSK9i treatment is recommended in patients who do not reach their LDL-C goal despite maximum tolerated statin and ezetimibe therapy



a Consider LDL-C <1.0 mmol/L if recurrent event.

ESC, European Society of Cardiology; EAS, European Atherosclerosis Society; ACS, acute coronary syndrome; LDL-C, low-density lipoprotein cholesterol; LLT, lipid-lowering therapy; PCSK9i, proprotein convertase subtilisin/kexin type 9 inhibitor

Reference. 1. Byrne RA, et al. Eur Heart J. 2023 Oct 12;44(38):3720-3826.

Summary

1. The ODYSSEY OUTCOMES trial underscores Alirocumab's role in diminishing cardiovascular events post-ACS, complementing high-intensity statins.

2. Beyond Lipid-Lowering: Ongoing researches suggest Alirocumab's role might extend to plaque stabilization and vascular inflammation reduction, marking a potential advance in cardiovascular disease management.

3. The application of Alirocumab will expand to more high-risk patients earlier in their treatment course, and attention must be paid to the emerging data on improvements in cardiovascular outcomes as a result.