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LDL the lower the Better

THE CLINICAL BENEFITS OF PCSK9 INHIBITORS

FROM CLINICAL DATA TO REAL WORLD EXPERIENCE

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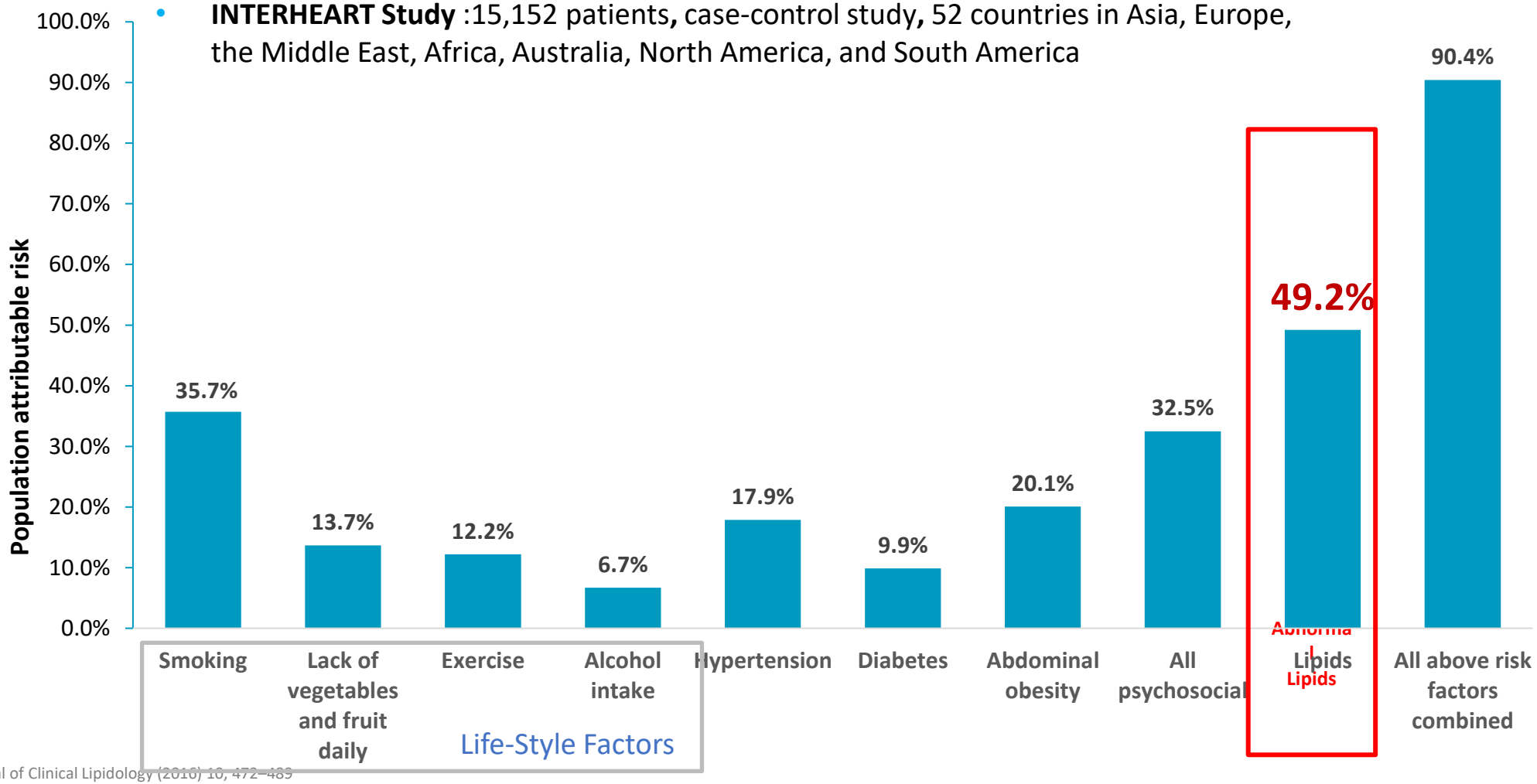
6th Dec. 2020

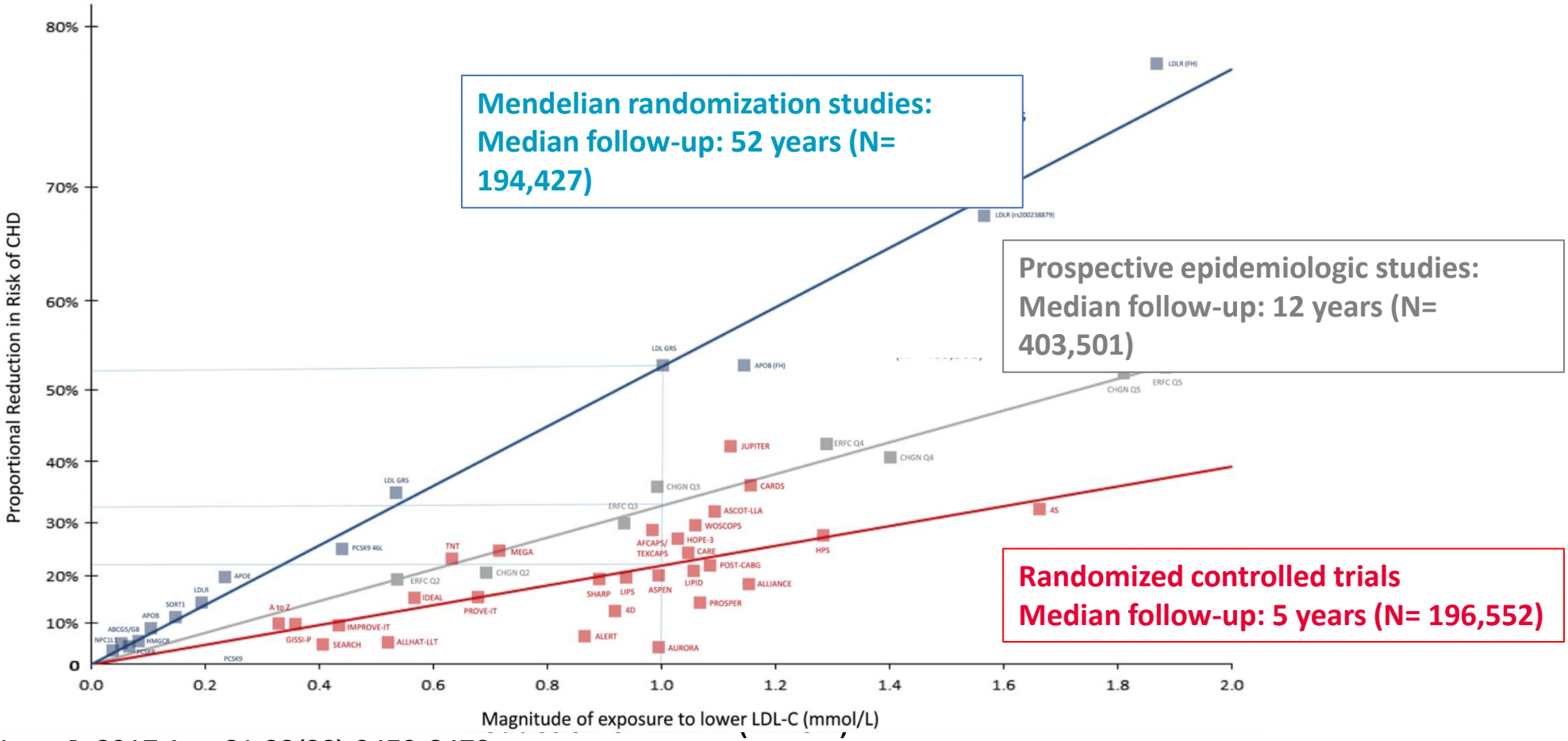
Abnormal lipids : the most risk factor for myocardial infarction

- **INTERHEART Study** :15,152 patients, case-control study, 52 countries in Asia, Europe, the Middle East, Africa, Australia, North America, and South America



Journal of Clinical Lipidology (2010) 10, 472–489

LDL cause atherosclerotic cardiovascular disease (ASCVD) : Evidence from genetic, epidemiologic, and clinical studies

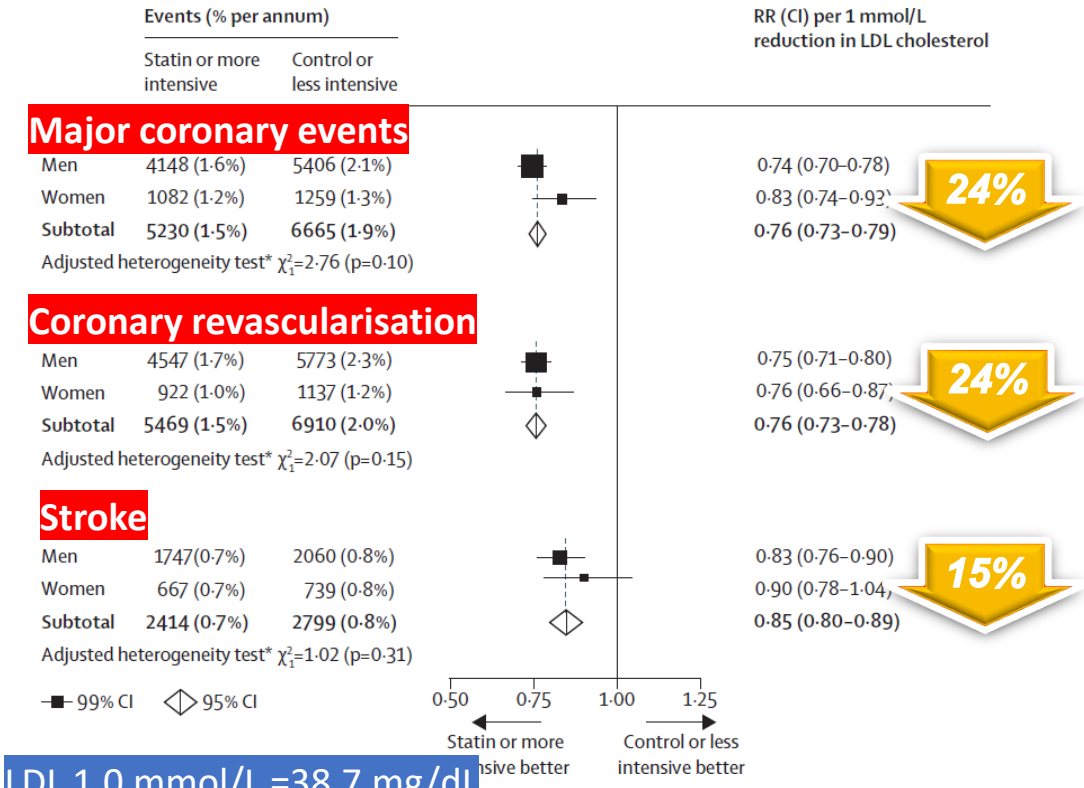


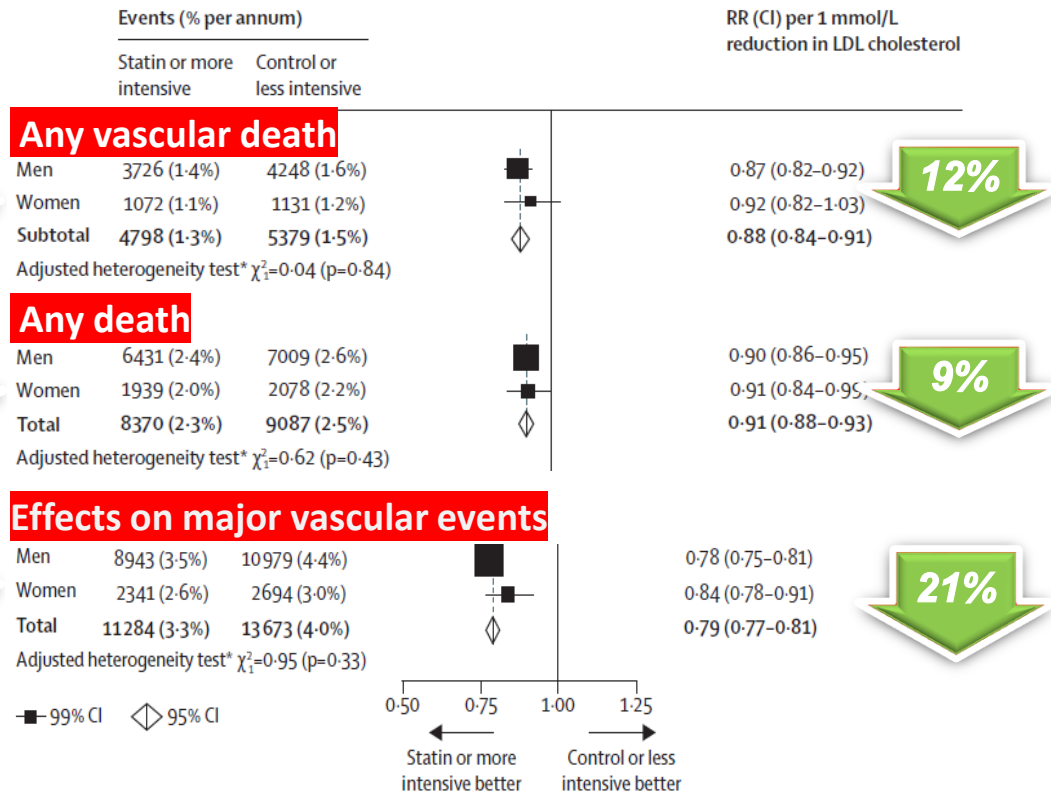
<u>Eur Heart J.</u> 2017 Aug 21;38(32):2459-2472.

Reduce 1 mmol/L LDL by statin: reduce 21% risk of major vascular events

Cholesterol Treatment Trialists' (CTT) Collaboration

174 000 participants, meta-analysis, **27 randomized trials**



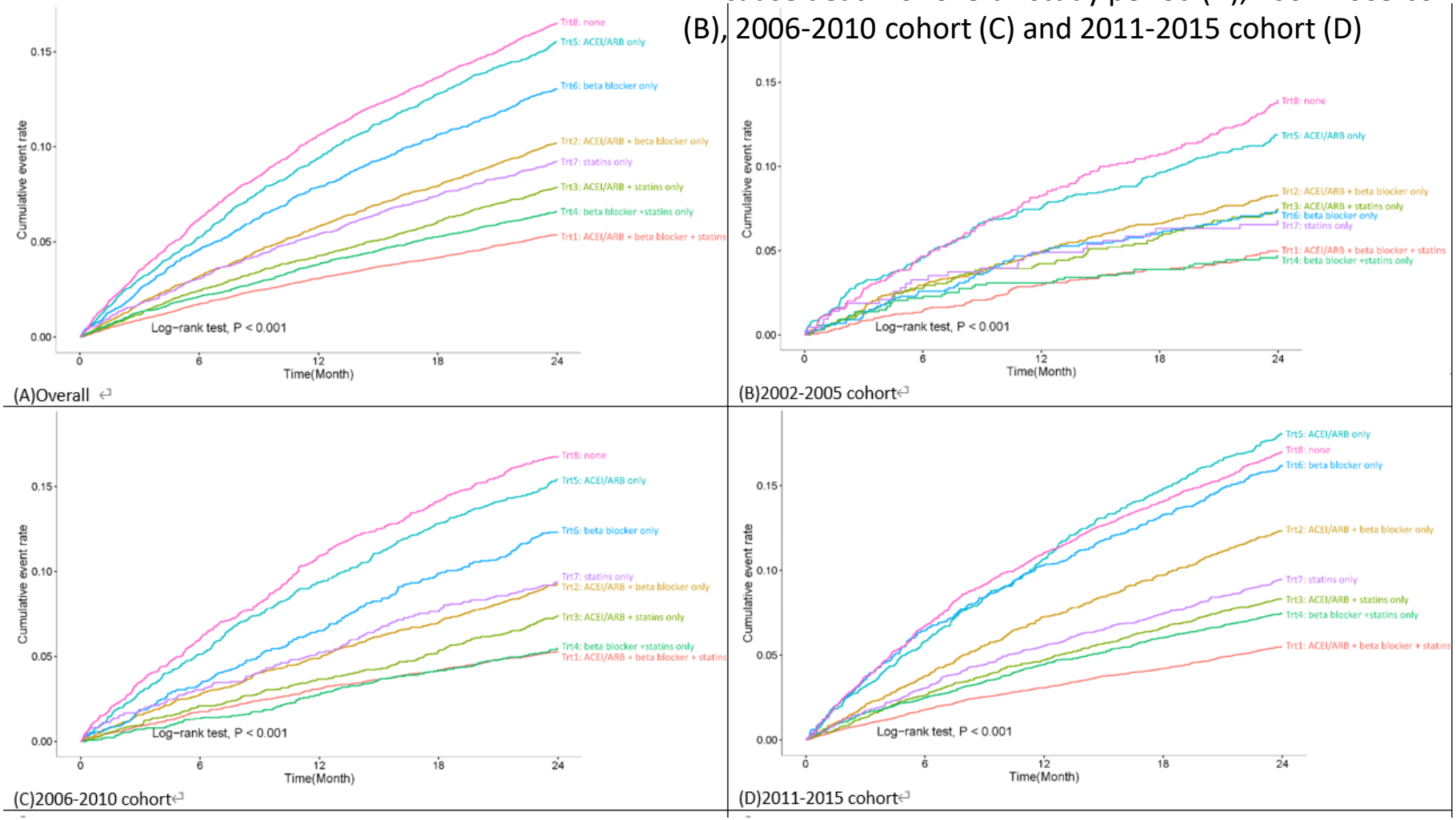


LDL 1.0 mmol/L =38.7 mg/dL

Lancet. 2015 Apr 11;385(9976):1397-405

Association with post discharge adherence to guideline-directed medical therapy (GDMT) and long-term health outcomes after AMI in Taiwan

All cause death for overall study period (A), 2002-2005 cohort (B), 2006-2010 cohort (C) and 2011-2015 cohort (D)



Chen CW, Huang CY 2020 submission

Association with post discharge adherence to guideline-directed medical therapy (GDMT) and long-term health outcomes after AMI in Taiwan

(A)The percent of event rate(no. of events/ no. of patients) and hazard risk of all cause death (A) and MACE (B) in 12months and 24 months follow up

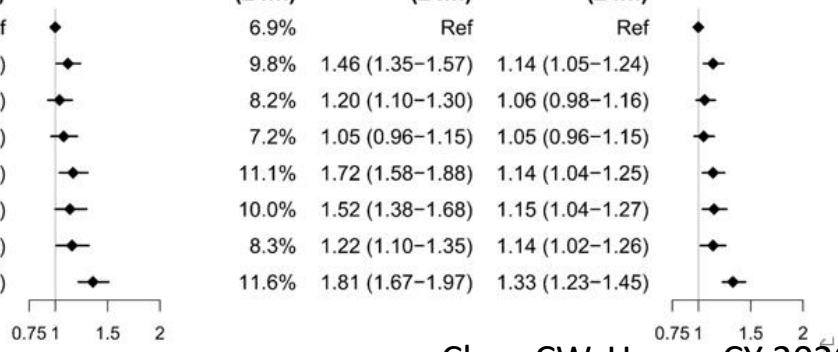
(A)

Group	Event rate (12m)	Crude HR (12m)	Adjusted HR (12m)	Event rate (24m)	Crude HR (24m)	Adjusted HR (24m)
Trt1: ACEI/ARB + beta blocker + statin	3.1%	Ref	Ref	5.4%	Ref	Ref
Trt2: ACEI/ARB + beta blocker only	5.8%	1.92 (1.73−2.14)	1.25 (1.12−1.40)	10.2%	1.94 (1.79−2.11)	1.29 (1.19−1.41)
Trt3: ACEI/ARB + statin only	4.3%	1.40 (1.24−1.58)	1.07 (0.95−1.21)	7.9%	1.48 (1.35−1.62)	1.13 (1.04−1.24)
Trt4: beta blocker +statin only	3.8%	1.25 (1.10−1.42)	1.15 (1.01−1.31)	6.6%	1.23 (1.12−1.36)	1.16 (1.05−1.27)

In addition to follow GDMT (Statin + RAAI + BB)
Using Statin treatment is the most Important prognostic predictor for patients with ACS in Taiwan

(B)

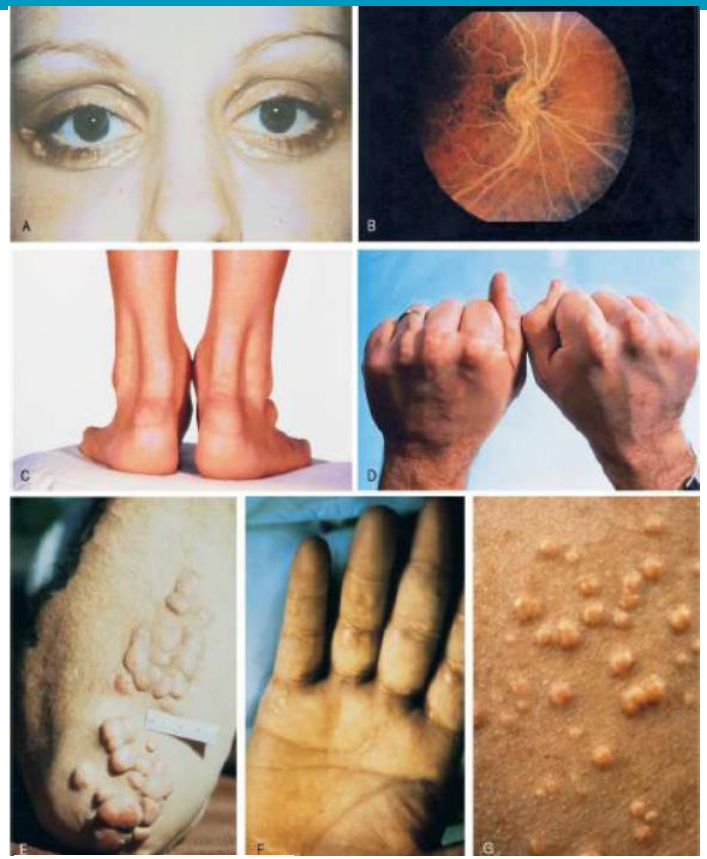
Group	Event rate (12m)	Crude HR (12m)	Adjusted HR (12m)	Event rate (24m)	Crude HR (24m)	Adjusted HR (24m)
Trt1: ACEI/ARB + beta blocker + statin	4.4%	Ref	Ref	6.9%	Ref	Ref
Trt2: ACEI/ARB + beta blocker only	6.2%	1.44 (1.31−1.59)	1.12 (1.01−1.24)	9.8%	1.46 (1.35−1.57)	1.14 (1.05−1.24)
Trt3: ACEI/ARB + statin only	5.1%	1.17 (1.05−1.31)	1.04 (0.93−1.16)	8.2%	1.20 (1.10−1.30)	1.06 (0.98−1.16)
Trt4: beta blocker +statin only	4.7%	1.08 (0.97−1.21)	1.08 (0.96−1.21)	7.2%	1.05 (0.96−1.15)	1.05 (0.96−1.15)
Trt5: ACEI/ARB only	7.5%	1.78 (1.60−1.98)	1.17 (1.04−1.31)	11.1%	1.72 (1.58−1.88)	1.14 (1.04−1.25)
Trt6: beta blocker only	6.5%	1.54 (1.36−1.74)	1.14 (1.00−1.30)	10.0%	1.52 (1.38−1.68)	1.15 (1.04−1.27)
Trt7: statin only	5.4%	1.26 (1.11−1.43)	1.16 (1.01−1.32)	8.3%	1.22 (1.10−1.35)	1.14 (1.02−1.26)
Trt8: none	7.9%	1.88 (1.70−2.08)	1.36 (1.22−1.51)	11.6%	1.81 (1.67−1.97)	1.33 (1.23−1.45)



Chen CW, Huang CY 2020 submission

01 UNMET NEEDS AND UPCOMING CHALLENGES IN TAIWAN

The recognition of more frequent incidence of FH and more strict treatment goals for FH



A- Xanthelasma

B – Corneal arcus (Arcus senilis)

C - Achilles tendon xanthomas

D - Tendon xanthomas

E - Tuberous xanthomas

F - Palmar xanthomas

Recommendations for the detection and treatment of patients with heterozygous familial hypercholesterolaemia

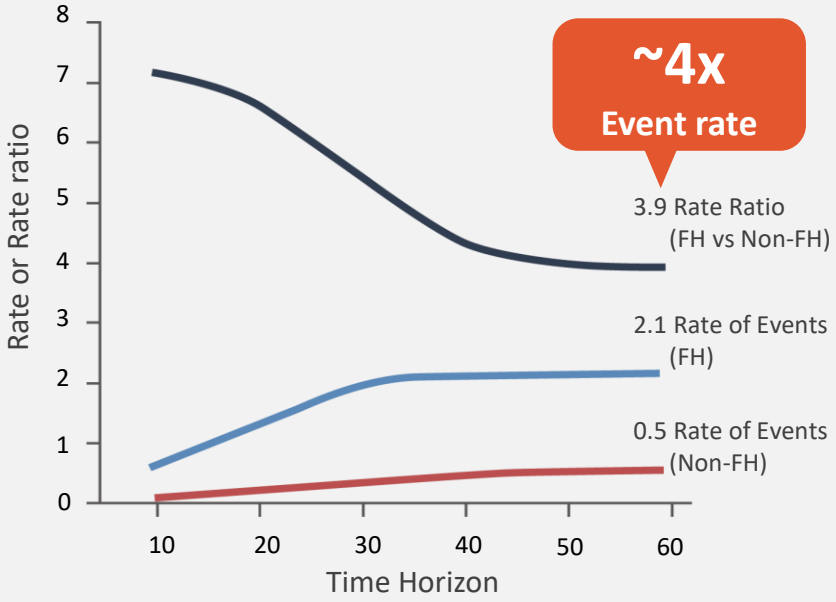
Recommendations	Class[a]	Level[b]
It is recommended that a diagnosis of FH is considered in patients with CHD aged <55 years for men and <60 years for women, in people with relatives with premature fatal or non-fatal CVD, in people with relatives who have tendon xanthomas, in people with severely elevated LDL-C [in adults >5 mmol/L (>190 mg/dL), in children >4 mmol/L (>150 mg/dL)], and in first-degree relatives of FH patients.	I	C
It is recommended that FH should be diagnosed using clinical criteria and confirmed, when possible, via DNA analysis.	I	C
Once the index case is diagnosed, family cascade screening is recommended.	I	C
It is recommended that FH patients with ASCVD or who have another major risk factor are treated as very-high-risk, and that those with no prior ASCVD or other risk factors are treated as high-risk.	I	C
In primary prevention, for individuals with FH at very-high risk, an LDL-C reduction of ≥50% from baseline and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) should be considered.	IIa	C
Treatment with a PCSK9 inhibitor is recommended in very-high-risk FH patients if the treatment goal is not achieved on maximal tolerated statin plus ezetimibe.	I	C
In children, testing for FH is recommended from the age of 5 years, or earlier if HoFH is suspected.	I	C
Children with FH should be educated to adopt a proper diet and treated with a statin from 8–10 years of age. Goals for treatment should be LDL-C <3.5 mmol/L (<135 mg/dL) at >10 years of age.	IIa	C

家族性高胆固醇血症病人治療標準已和一般病人標準接軌

ESC 2019 Guideline for dyslipidemia

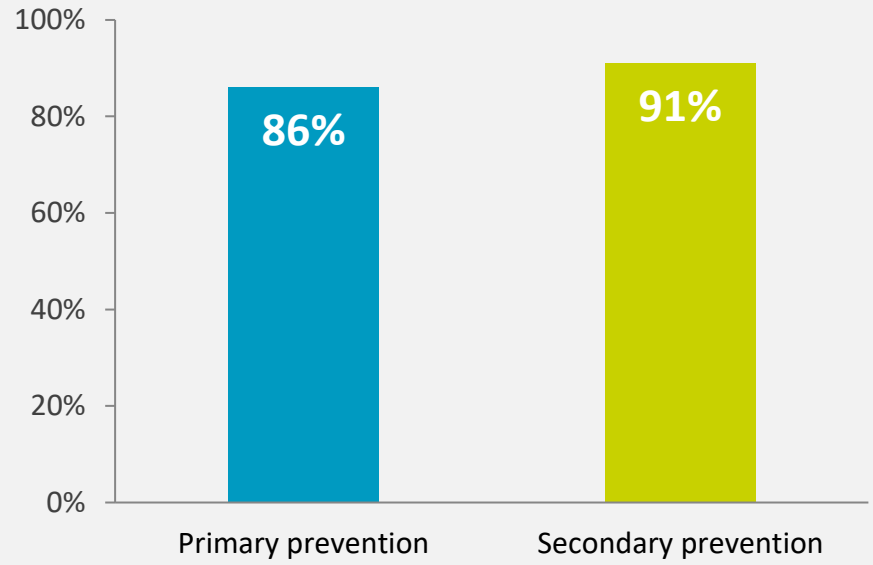
FH patients treated with current therapies will almost certainly experience an event in their life

Prediction of Lifetime Events Rates in FH and Non-FH Patients



FH patients were predicted to have **3.9 times** more CV events over a lifetime horizon than non-FH patients with a similar risk profile.

Prediction of lifetime CV risk* in FH patients†

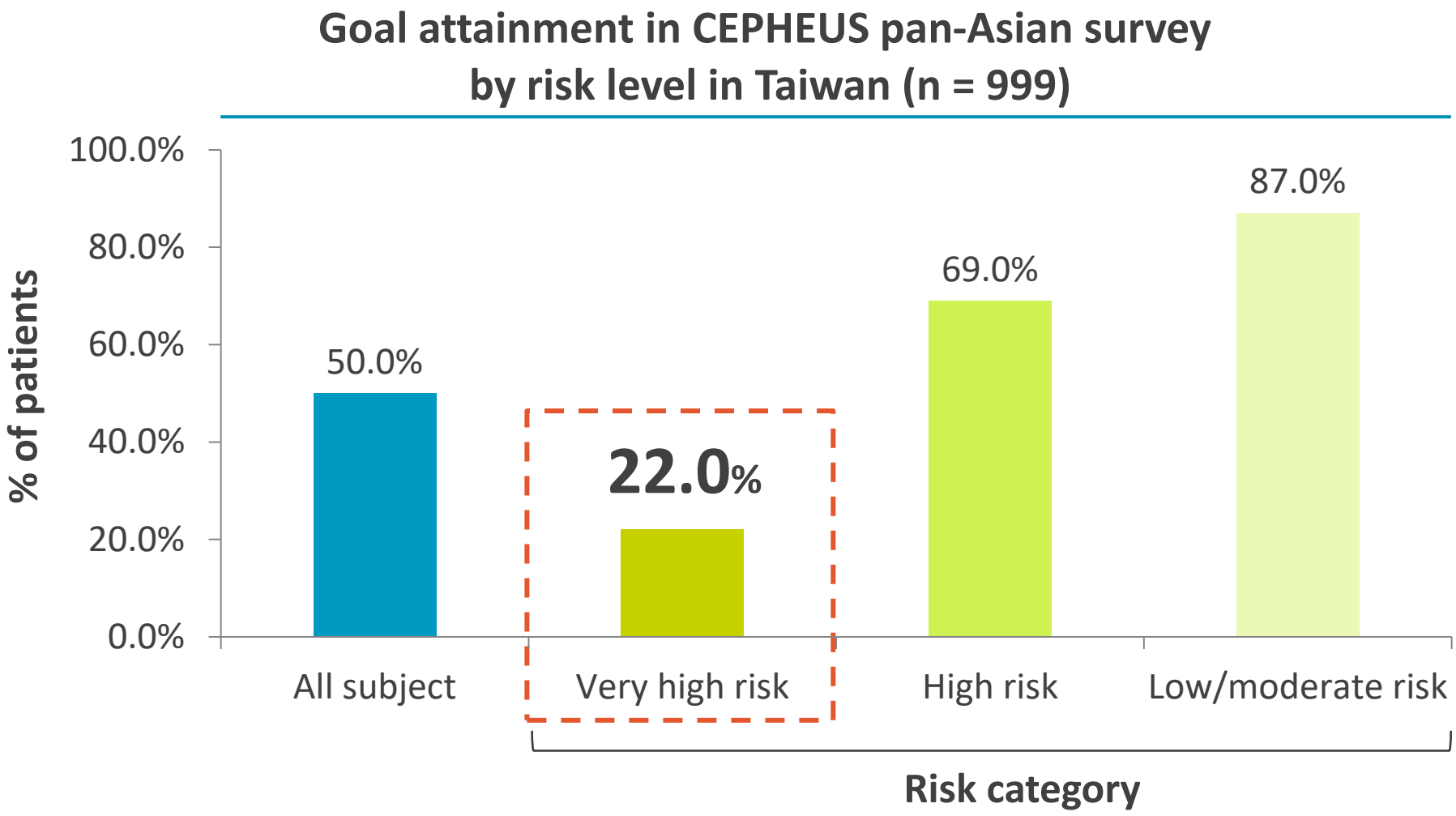


Lifetime CV risks were similar in the different scenarios, as primary prevention patients will eventually become secondary prevention.

*Risk of 1 or more CV events.
†CV risk calculations based on Benn et al. were used on patient characteristics from RUTHERFORD-2 clinical trail population.
CV, cardiovascular; FH, familial hypercholesterolemia.

Villa G, et al. Eur Heart J Qual Care Clin Outcomes. 2017;3(4):274–80.

CEPHEUS Pan-Asian Survey in Taiwan

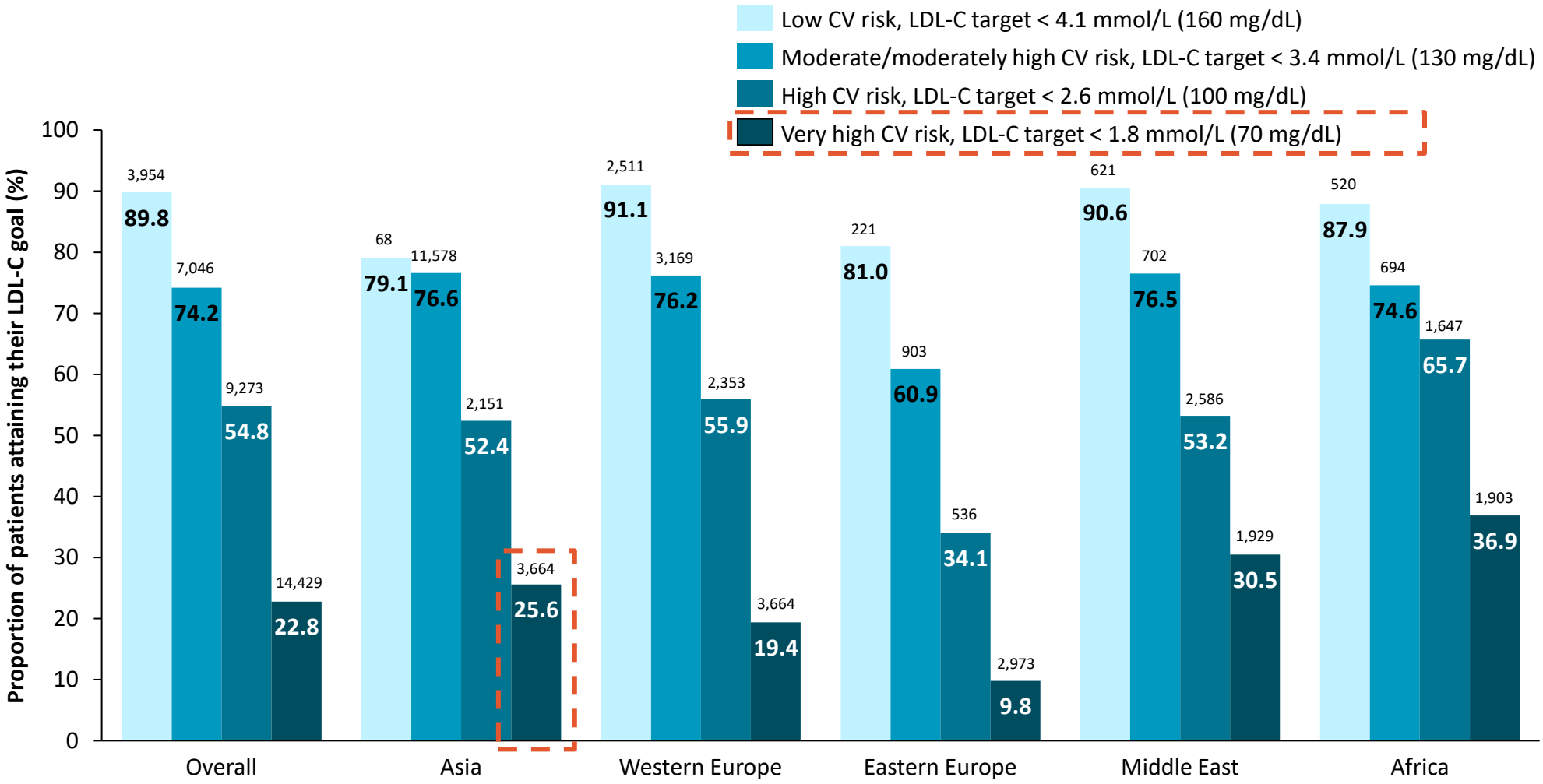


Wang KF, et al. J Chin Med Assoc. 2014;77(2):61–7.

Pan-CEPHEUS Trial

Goal-attainment by Risk Group

Multicenter, cross-sectional CEPHEUS were conducted across Asia, Western Europe, Eastern Europe, the Middle East, and Africa; Adult patients who had been receiving LDLs for at least 3 months without dose changes for at least 6 weeks were included



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

Chiang CE, et al. J Atheroscler Thromb. 2016;23(5):567–87.

T-SPARCLE Trial

ORIGINAL ARTICLE

Guideline-adherent therapy in patients with cardiovascular diseases in Taiwan

- A multicenter observational registry
- Taiwanese secondary prevention for patients with atherosclerotic disease **(T-SPARCLE)**
- Data from 14 teaching hospitals in Taiwan
- Adult patients who had stable symptomatic atherosclerotic diseases, including CAD and CVD, were recruited

CAD, coronary artery disease; CVD, cerebrovascular disease.

Jeng JS, et al. J Formos Med Assoc. 2015;114(10):1000-7.

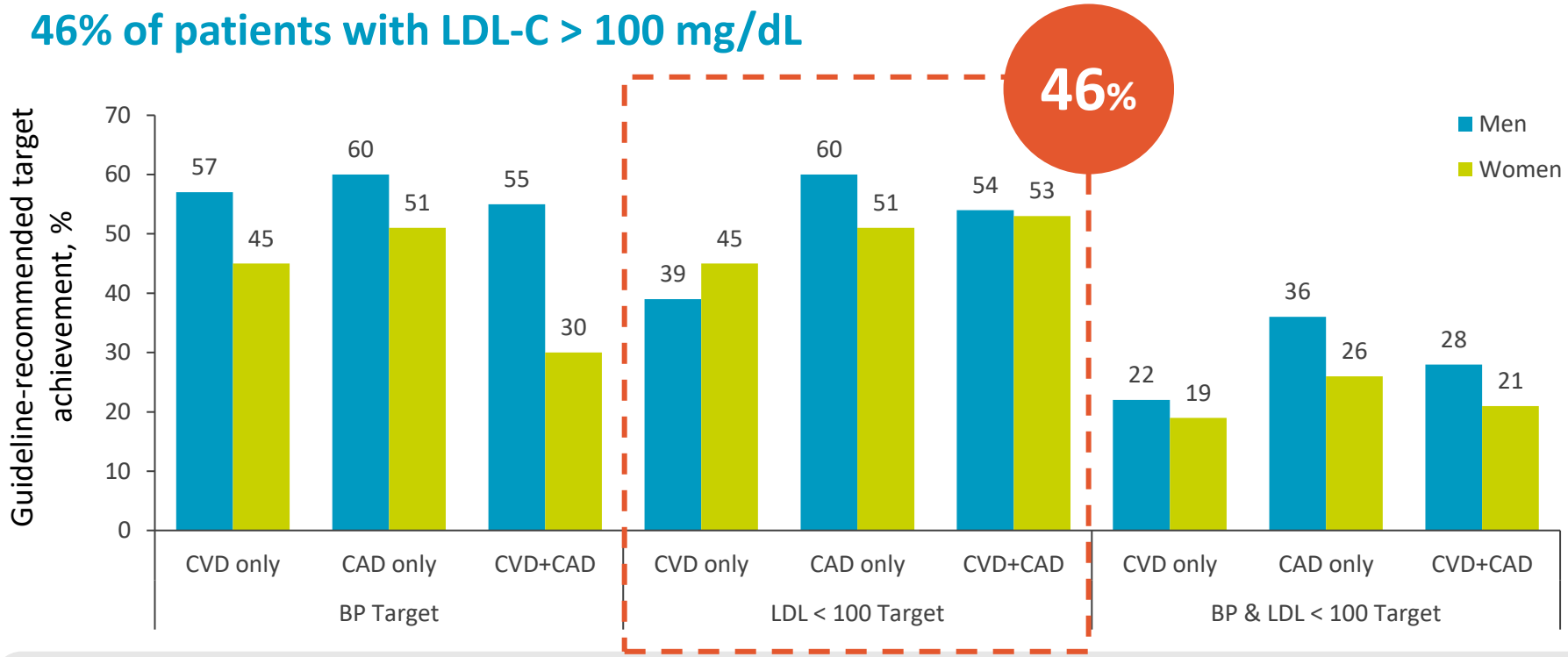
T-SPARCLE

Suboptimal LDL-C Control in Patients with Cardiovascular Diseases

ORIGINAL ARTICLE

Guideline-adherent therapy in patients with cardiovascular diseases in Taiwan

- 73% of patients with CVD and/or CAD used lipid-lowering drugs and **46% of patients with LDL-C > 100 mg/dL**



- Lipid treatment guideline adherence needs to be improved
- Even high dose statin + ezetimibe could not meet current need for patients with hypercholesterolemia in Taiwan

BP, blood pressure; CAD, coronary artery disease; CVD, cerebrovascular disease; LDL-C, low-density lipoprotein cholesterol.

Jeng JS, et al. J Formos Med Assoc. 2015;114(10):1000-7.

Key patient populations may need additional LDL-C lowering therapies (新世代/新挑戰)

Patients who could benefit from additional lipid lowering therapy	Magnitude of impact
High-risk patients with poorly controlled LDL-C despite treatment with standard of care[1]	Up to **76%** of high risk patients fail to reach their LDL-C goal of less than 70mg/dL[1]
Those who cannot or will not take statins due to **adverse effects**[2,3]	**10 - 20%** of patients treated with high dose statins show some degree of statin intolerance[2,7,8] **40 - 50%** of patients are non-adherent at 1 year[9,10]
Familial hypercholesterolemia at high risk of premature coronary disease[4] and who fail to reach their LDL-C goal[5,6]	Approximately **80% of patients** with familial hypercholesterolemia failed to reach an LDL-C target < 100mg/dL[11]

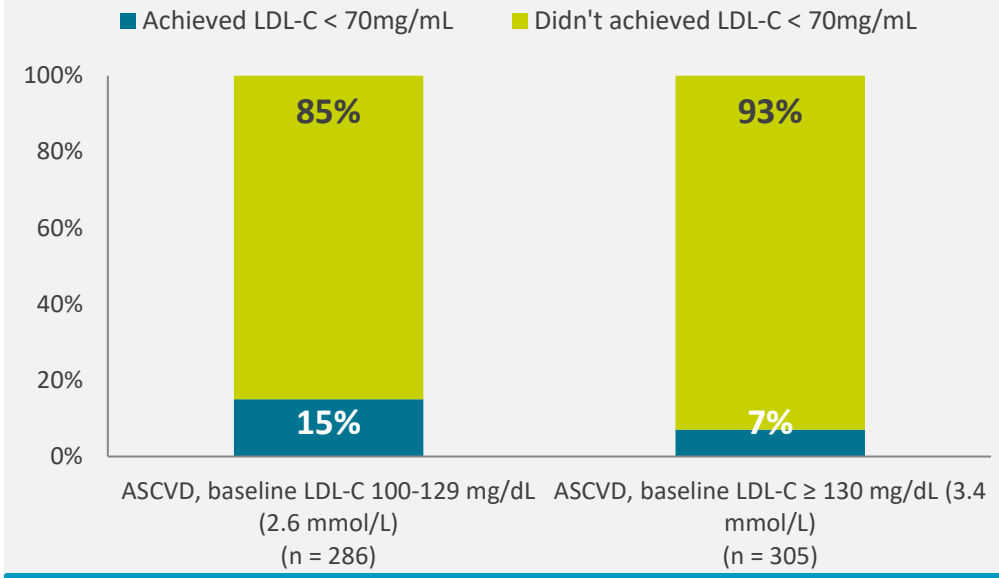
更嚴格的LDL下降標準!

LDL-C, low-density lipoprotein cholesterol.

1. Jones PH, et al. J Am Heart Assoc. 2012;1:e001800.
2. Bruckert E, et al. Cardiovasc Drugs Ther. 2005;19(6):403–14.
3. Cohen JD, et al. J Clin Lipidol. 2012;6:208–15.
4. Rees A. Eur Heart J. 2008;29:2583–4.
5. Stein EA, et al. Am J Cardiol. 2003;92:1287–93.
6. Pijlman AH, et al. Atherosclerosis. 2010;209:189–94.
7. Arca M, et al. Diabetes Metab Syndr Obes. 2011;4:155–66.
8. Betteridge DJ, et al. Nat Rev Endocrinol. 2013;9:76-8.
9. Avorn J, et al. JAMA. 1998;279(18):1458–62.
10. Casula M, et al. Patient Prefer and Adherence. 2012;6:805–14.
11. Stein E, et al. Am Heart J. 2004;148:447–55.

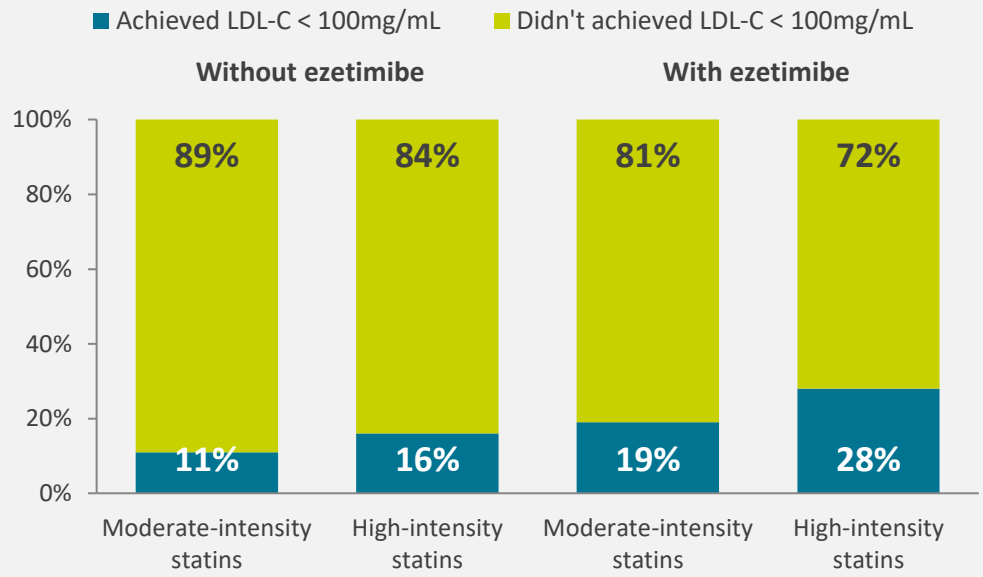
Significant patients are still not at goal even with statin + ezetimibe

ASCVD patients reached LDL-C target with statins + ezetimibe†



Routine use of ezetimibe before advancing to more efficacious lipid-lowering therapy would still **leave many ASCVD and/or probable HeFH patients with elevated LDL-C levels.**

HeFH Patients reached LDL-C target with and without ezetimibe



Based on observed LDL-C levels and expected maximal LDL-C reductions with current LMT options (including HIST), **many HeFH patients are unlikely to reach their treatment goal.**

†The extent to which patients were receiving maximally tolerated statin therapy was not available in the data.
ASCVD, atherosclerotic cardiovascular diseases; HeFH, heterozygous familial hypercholesterolemia; HIST, high-intensity statin therapy; LDL-C, low-density lipoprotein cholesterol; LMT, lipid-modifying therapy.

1. Mentin J, et al. J Manag Care Spec Pharm. 2017;23(12):1270–6.
2. Harthers ML, et al. Atherosclerosis. 2016;252:e203.

Updated treatment thresholds in the 2019 ESC/EAS clinical practice guidelines expand indications for lipid-lowering treatment at population level

Insights from the population-based Rotterdam Study

7262 participants, aged **45-75** years, enrolled **1997-2008** The Rotterdam Study

Without history of atherosclerotic CVD

Calculated **10-year CVD mortality risk** using the SCORE for ESC 2016 and 2019 guidelines

Statin treatment indication was defined as either:

- 'treatment recommended' – provide lifestyle intervention and concomitant drug
- 'treatment considered' – provide lifestyle intervention and consider adding drug
- 'no treatment' – provide lifestyle advice

- Updated treatment recommendations in the 2019 ESC/EAS dyslipidaemia clinical practice guideline primarily extend statin treatment to asymptomatic individuals aged 45-55 at low risk, and individuals aged 65-75 years.

- Whether the broadening of statin indications in asymptomatic low-risk individuals and those aged 65-75 years will lead to greater uptake of primary prevention efforts and thereby long-term lowering of the burden of CVD in Europe, remains to be investigated.

02 GUIDELINE RECOMMENDATION

2018 ACC/AHA Guideline Recommendations for Statin Therapy

Statin Benefit Groups

Heart healthy lifestyle habits are the foundation of ASCVD prevention

1. *Secondary ASCVD Prevention*

- ≤ 75 yrs : High-intensity statin (Goal: ↓LDL-C ≧ 50 %) (Class I)
- >75yrs : Initiation of moderate or high-intensity statin is reasonable (Class IIa)

2. *Primary Prevention:* Severe Hypercholesterolemia *(LDL-C ≥190)*

- 20 to 75 years of age : High-intensity statin (Class I)
- 20 to 75 years of age : Reduce ≧ 50% reduction in LDL-C (Class IIa)

3. *Primary Prevention: Diabetes Mellitus with 40-75 Years*

- Moderate-intensity statin (Class I)
- For those who achieve less than 50% reduction while receiving maximally tolerated statin, ezetimibe therapy is reasonable (Class IIb)

4. *Primary Prevention: assess ASCVD Risk in Each Age Group*

- High risk(≥20%): statin to reduce LDL-C ≧ 50% (Class I)
- Intermediate risk(7.5-20 %): moderate-intensity statin to reduce LDL-C by 30- 49% (Class I)
- Borderline risk (5-7.5%): moderate-intensity statin(Class IIb)
- Low risk (<5%): Healthy Lifestyle (Class I)

Circulation. 2018 Nov 10:CIR0000000000000625

2017 AACE/ACE Guidelines for Management of Dyslipidemia and Prevention of CV Disease

Lipid parameter	Goal (mg/dL)
TC	< 200
LDL-C	< 130 (low risk) < 100 (moderate risk) < 100 (high risk) < 70 (very high risk) < 55 (extreme risk)
Non–HDL-C	30 above LDL-C goal; 25 above LDL-C goal (extreme risk individuals)
TG	< 150
Apo B	< 90 (individuals at high risk of ASCVD, including those with diabetes) < 80 (individuals at very high risk with established ASCVD or diabetes plus ≥1 additional risk factor) < 70 (individuals at extreme risk)

極端危險

Apo, apolipoprotein; AACE, American Association of Clinical Endocrinologists; ACE, American College of Endocrinology; ASCVD, atherosclerotic cardiovascular diseases; CV, cardiovascular; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglycerides..

1. AACE/ACE 2017;epub ahead of print.
2. Baigent C, et al. Lancet. 2010;376:1670-81.
3. Boekholdt SM, et al. J Am Coll Cardiol. 2014;64(5):485-94.
4. Brunzell JD, et al. Diabetes Care. 2008;31:811-22.
5. Cannon CP, et al. N Engl J Med. 2015;372(25):2387-97.
6. Heart Protection Study Collaborative Group. Lancet. 2002;360:7-22.
7. Jellinger PS, et al. Endocr Pract. 2017;23(4):479-97.
8. Ridker PM, J Am Coll Cardiol. 2005;45:1644-8.
9. Sever PS, et al. Lancet. 2003;361:1149-58.
10. Shepherd J, et al. Lancet. 2002;360:1623-30.
11. Weiner DE, et al. J Am Soc Nephrol. 2004;15(5):1307-15.

2019 ESC/EAS Guidelines for the management of dyslipidaemias: *lipid modification to reduce cardiovascular risk*

Task Force Members:

François Mach (ESC Chairperson) (Switzerland), Colin Baigent (ESC Chaiperson) (United Kingdom), Alberico L. Catapano (EAS Chairperson) (Italy), Konstantinos C. Koskinas (Switzerland), Manuela Casula[1] (Italy), Lina Badimon (Spain), M. John Chapman[1] (France), Guy G. De Backer (Belgium), Victoria Delgado (Netherlands), Brian A. Ference (United Kingdom), Ian M. Graham (Ireland), Alison Halliday (United Kingdom), Ulf Landmesser (Germany), Borislava Mihaylova (United Kingdom), Terje R. Pedersen (Norway), Gabriele Riccardi[1] (Italy), Dimitrios J. Richter (Greece), Marc S. Sabatine (United States of America), Marja-Riitta Taskinen[1] (Finland), Lale Tokgozoglu[1] (Turkey), Olov Wiklund[1] (Sweden).

[1]Representing the European Atherosclerosis Society (EAS)

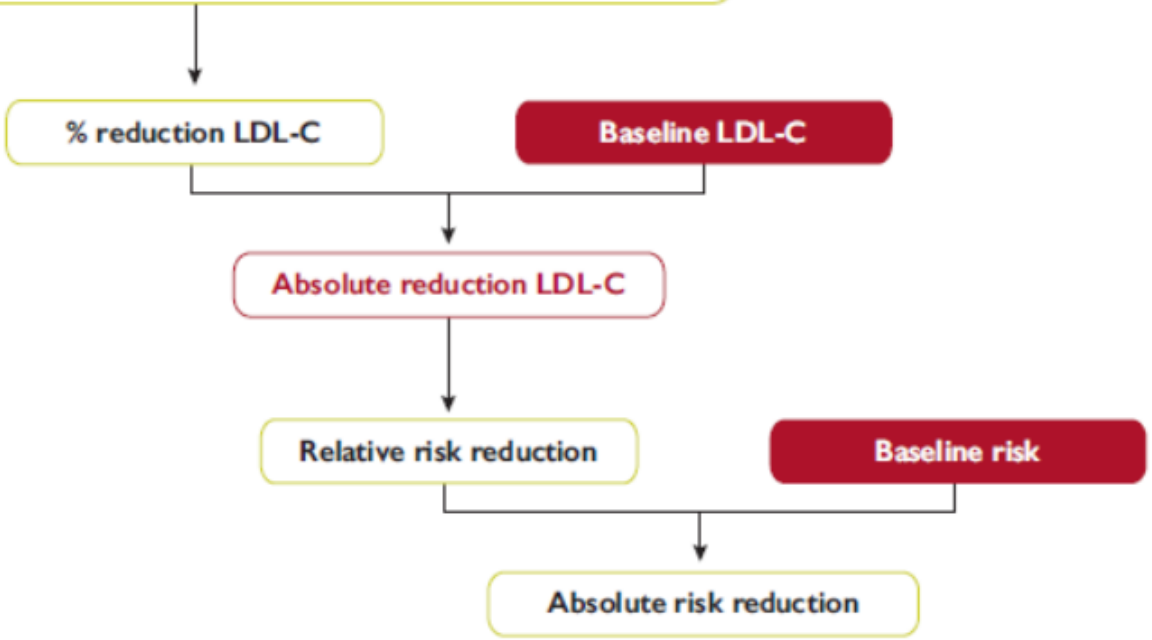
European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455

ESC European Society of Cardiology

EAS

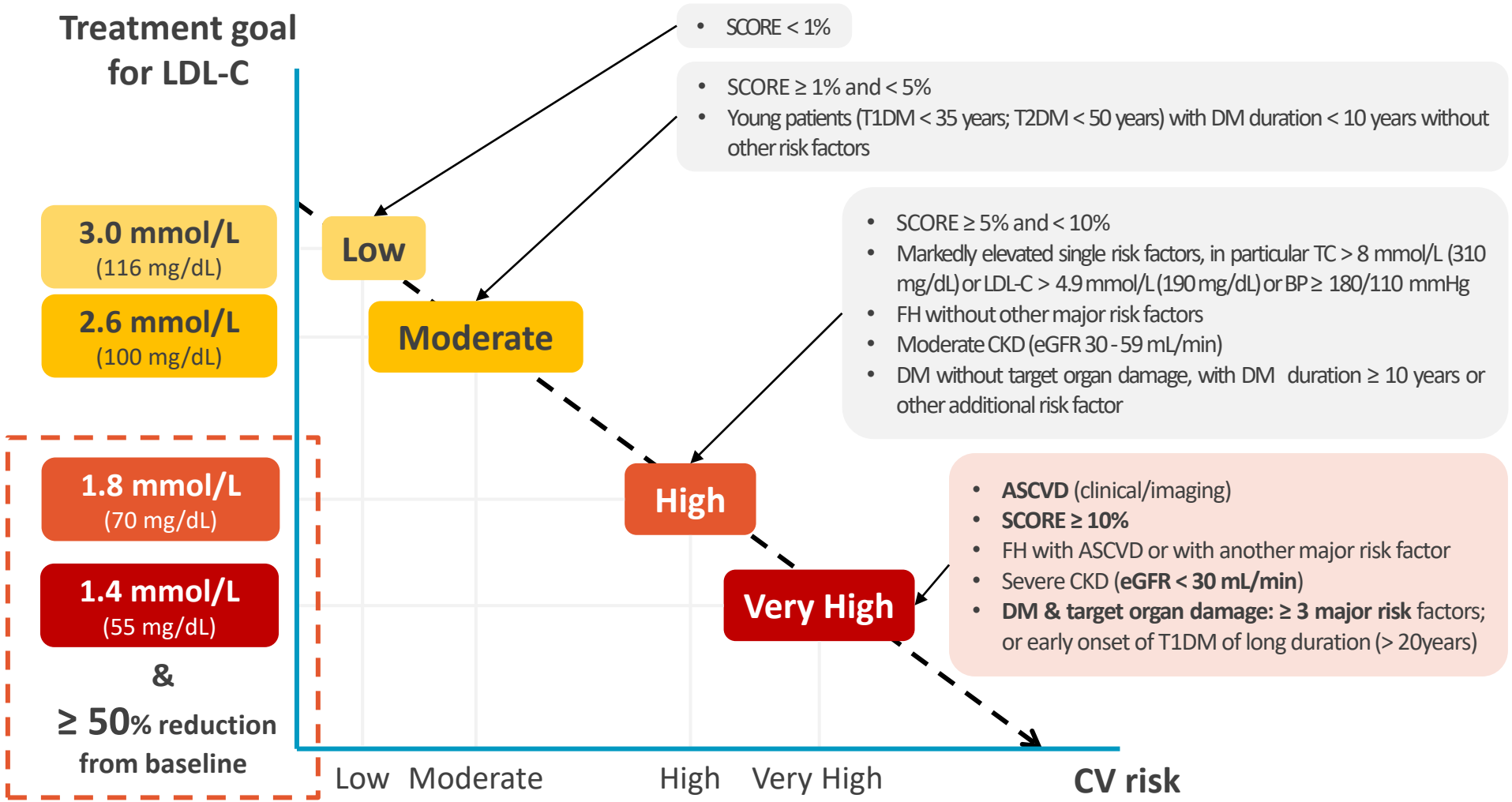
Intensity of lipid lowering treatment

Treatment	Average LDL-C reduction
Moderate intensity statin	= 30%
High intensity statin	= 50%
High intensity statin plus ezetimibe	= 65%
PCSK9 inhibitor	= 60%
PCSK9 inhibitor plus high intensity statin	= 75%
PCSK9 inhibitor plus high intensity statin plus ezetimibe	= 85%



ESC 2019 Guideline for dyslipidemia

Treatment goals for LDL-C across categories of total cardiovascular disease risk



ASCVD, atherosclerotic cardiovascular disease; BP, blood pressure; CKD, chronic kidney disease; CV, cardiovascular; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; FH, familial hypercholesterolaemia; LDL-C, low-density lipoprotein cholesterol; SCORE, Systematic Coronary Risk Estimation; T1DM, type 1 DM; T2DM, type 2 DM; TC, total cholesterol.

Mach F, et al. Eur Heart J. 2020;41(1):111-88.

ESC 2019 Guideline for dyslipidemia

Table 4 Cardiovascular risk categories

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

ESC 2019 Guideline for dyslipidemia

2019 ESC/EAS guideline:
For very-high risk patients, LDL-C target has changed from 70 mg/dL to 55 mg/dL

Recommendations	Class	Level
In secondary prevention for patients at **very-high risk**, an **LDL-C reduction of ≥50%** from baselined **and** an **LDL-C goal of <1.4 mmol/L (<55 mg/dL)** are recommended.	I	A
For patients with ASCVD who **experience a second vascular event within 2 years** (not necessarily of the same type as the first event) while taking maximally tolerated statin-based therapy, an **LDL-C goal of <1.0 mmol/L (<40 mg/dL)** may be considered.	IIb	B

The rationale for the revised, lower LDL-C goals across CV risk categories is discussed, based on a critical synthesis of available evidence from lipid-modifying interventions resulting in reductions in CV risk.

Very-high risk definition

- Documented ASCVD, either clinical or unequivocal on imaging. Documented ASCVD includes **previous ACS (MI or unstable angina), stable angina, coronary revascularization (PCI, CABG, and other arterial revascularization procedures), stroke and TIA, and peripheral arterial disease.** Unequivocally documented ASCVD on imaging includes those findings that are known to be predictive of clinical events, such as **significant plaque** on coronary angiography or CT scan (multivessel coronary disease with two major epicardial arteries having >50% stenosis), or on carotid ultrasound.
- **DM with target organ damage***, or at least three major risk factors, or early onset of T1DM of long duration (>20 years).
- **Severe CKD (eGFR <30 mL/min/1.73 m2)**.
- A calculated SCORE ≥10% for 10-year risk of fatal CVD.
- FH with ASCVD or with another major risk factor.

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

European Heart Journal (2019) 00, 1-78

TREATMENT GOALS

ESC European Society of Cardiology
EAS

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

New/Revised Concepts → Targets changed depending on CV risk :

- Secondary prevention:
  ≥50% reduction **AND** target < 55mg/dL (1.4 mmol/L) (1A) & 40mg/dL (< 1.0 mmol/L) ASCVD with second vascular event in 2 years on (IIb)
- Primary prevention very high risk (w/o FH or w/o ASCVD):
  ≥50% reduction **AND** target < 55mg/dL (1.4 mmol/L) (1C)

ESC European Society of Cardiology
EAS

Recommendations	Class[a]	Level[b]
It is recommended that a high-intensity statin is prescribed up to the highest tolerated dose to reach the goals set for the specific level of risk.[32,34,38]	I	A
If the goals[c] are not achieved with the maximum tolerated dose of a statin, combination with ezetimibe is recommended.[33]	I	B
For primary prevention patients at very-high risk, but without FH, if the LDL-C goal is not achieved on a maximum tolerated dose of a statin and ezetimibe, a combination with a PCSK9 inhibitor may be considered.	IIb	C
For secondary prevention, patients at very-high risk not achieving their goal[c] on a maximum tolerated dose of a statin and ezetimibe, a combination with a PCSK9 inhibitor is recommended.[119,120]	I	A
For very-high-risk FH patients (that is, with ASCVD or with another major risk factor) who do not achieve their goal[c] on a maximum tolerated dose of a statin and ezetimibe, a combination with a PCSK9 inhibitor is recommended.	I	C
If a statin-based regimen is not tolerated at any dosage (even after rechallenge), ezetimibe should be considered.[197,265,353]	IIa	C
If a statin-based regimen is not tolerated at any dosage (even after rechallenge), a PCSK9 inhibitor added to ezetimibe may also be considered.[197,265,353]	IIb	C
If the goal[c] is not achieved, statin combination with a bile acid sequestrant may be considered.	IIb	C

www.escardio.org/guidelines

✓ 針對極高風險患者的次級預防，若使用最大劑量的Statin再加上Ezetimide仍然無法達到治療目標，應考慮併用PCSK9i。(IA)

2017 Taiwan Lipid Guidelines for High Risk Patients

LDL-C targets in ACS, CAD, and PAD

Disease category	LDL-C target
Primary target	
ACS	**LDL-C < 70 mg/dL**
ACS + DM	LDL-C < 55 mg/dL can be considered
Stable CAD	**LDL-C < 70 mg/dL**
PAD	LDL-C < 100 mg/dL
PAD + CAD	LDL-C < 70 mg/dL
Secondary target	
ACS, stable CAD, PAD with TG > 200 mg/dL	Non-HDL-C < 100 mg/dL

ACS, acute coronary syndrome; CAD, coronary artery disease; DM, diabetes mellitus; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; PAD, peripheral arterial disease; TG, triglyceride.

Li YH, et al. J Formos Med Assoc. 2017 Apr;116(4):217–48.

2017 Taiwan Lipid Guidelines for High Risk Patients

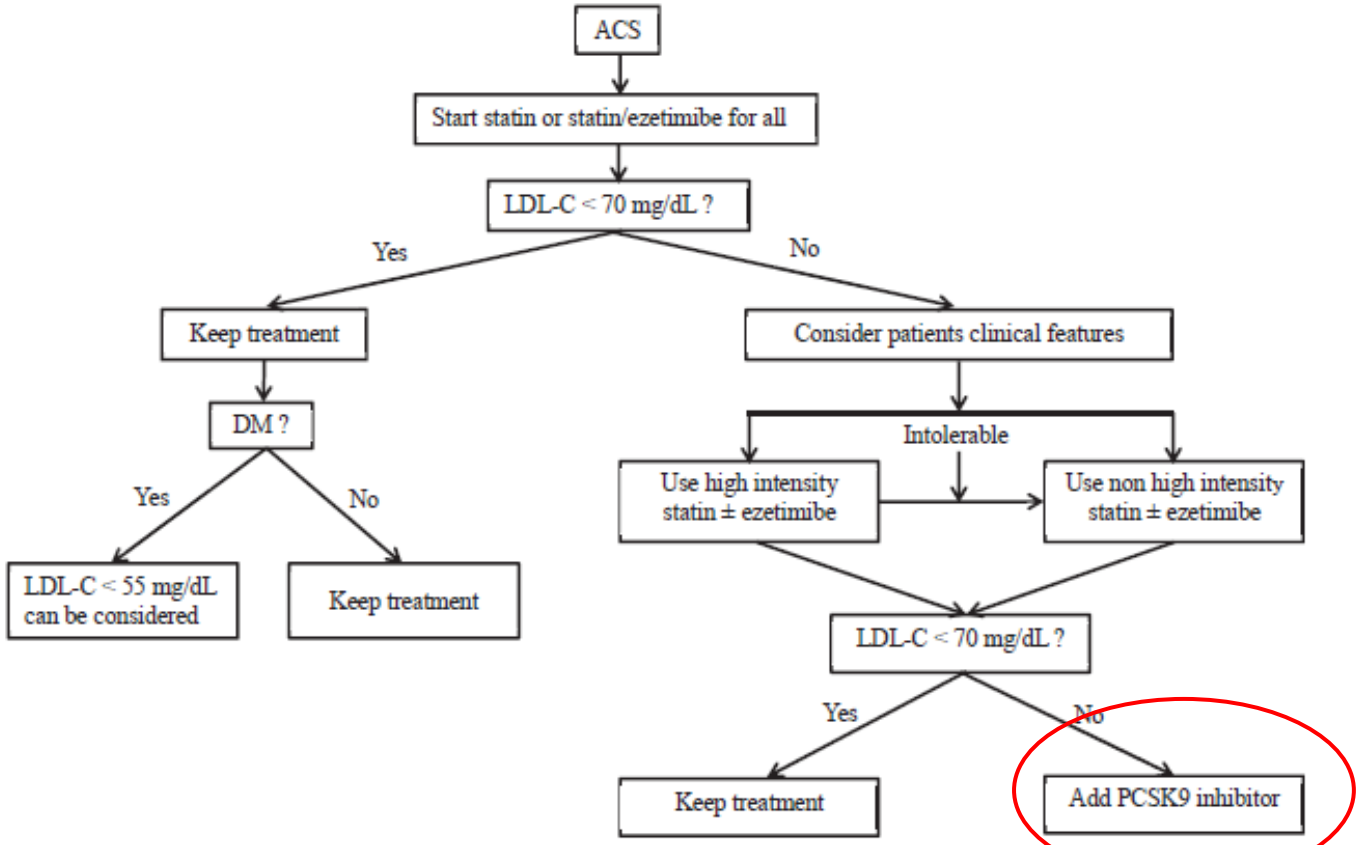
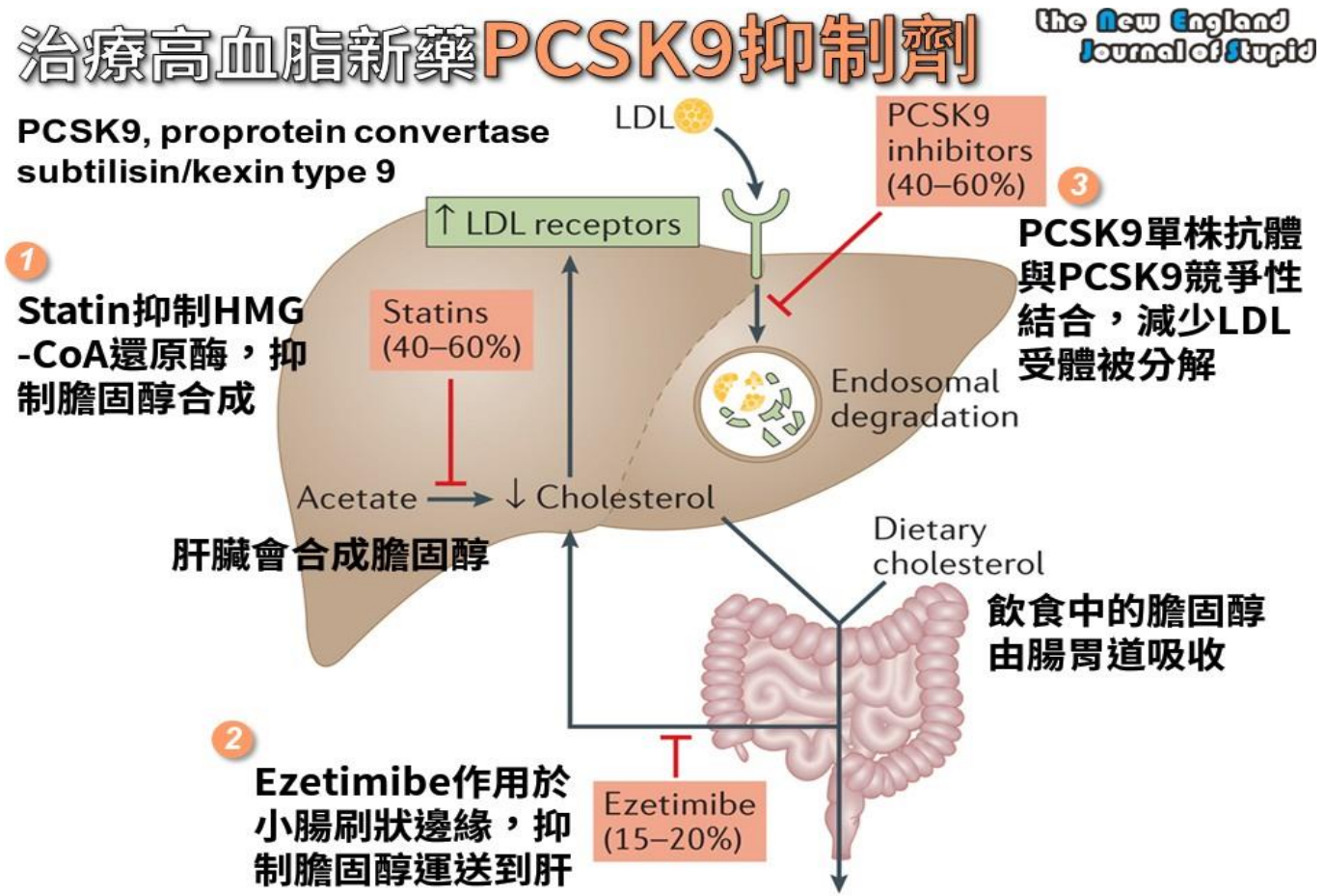


Figure 2 LDL-C treatment algorithm for ACS patients. ACS = acute coronary syndrome; DM = diabetes mellitus; LDL-C = low-density lipoprotein cholesterol; PCSK9 = proprotein convertase subtilisin kexin 9.

03 新一類降血脂用藥

Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor



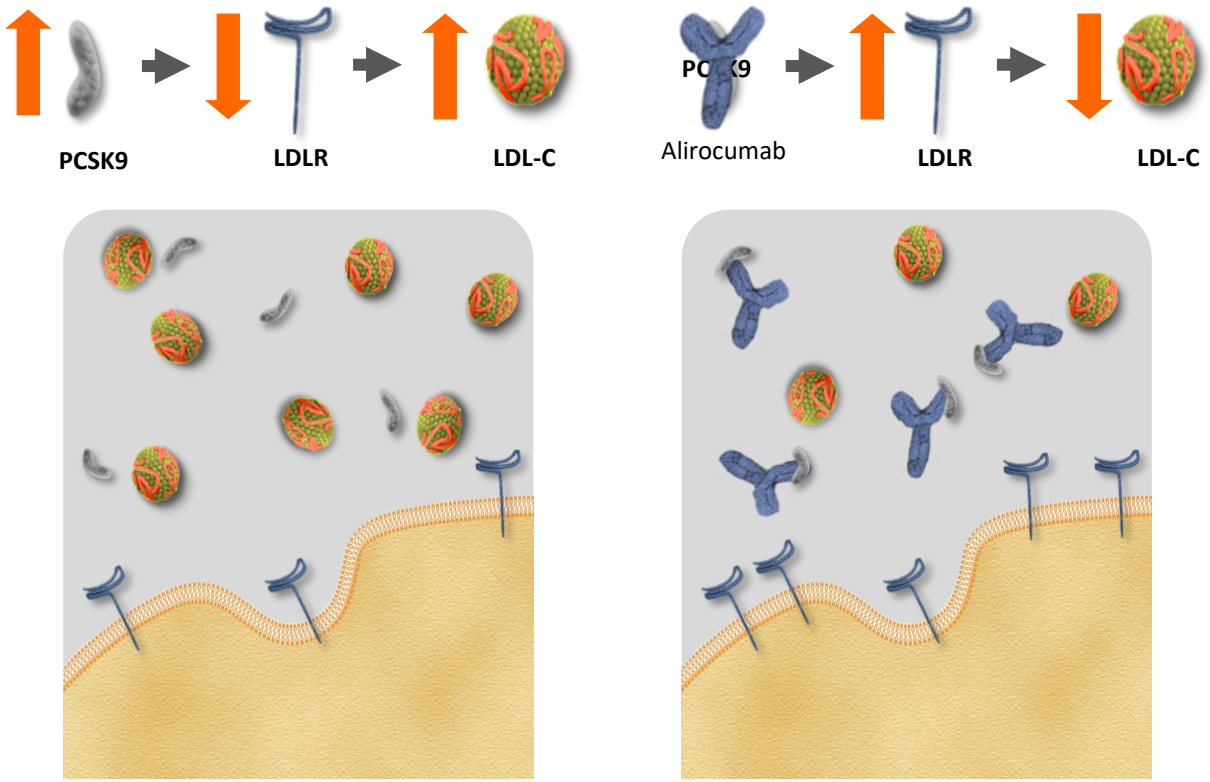
人類單株抗體PCSK9抑制劑，目標鎖定於血脂未獲控制的族群

SANOFI REGENERON

MAT-TW-2000572-2.0-10/2020

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

PCSK9 Physiology and Inhibition by Alirocumab (PCSK9mAb)



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

Praluent (Alirocumab) 75mg 適應症

1) 預防心血管事件
對於已確診心血管疾病的成年病人，Praluent可用於降低心肌梗塞、 中風以及需住院治療的不穩定心絞痛之風險。

2) 原發性高血脂症（包含異合子家族性高膽固醇血症） Praluent可單獨使用或併用其他降血脂藥物（例如：Statin類藥物、ezetimibe）,作為飲食外的輔助治療以降低原發性高血脂症成年病人 之低密度脂蛋白膽固醇 (LDL-C)。

給藥方式:
皮下注射使用。
Praluent 可皮下注射於大腿、腹部或上臂。
建議每次注射都更換注射部位。

SANOFI REGENERON
MAT-TW-2000572-2.0-10/2020
Praluent® (alirocumab) Injection 75mg/mL 150mg/mL

Praluent (Alirocumab) 75mg 用法用量

1) Praluent開始給藥前，應先排除高血脂症或混合型血脂異常之次要病因 (例如，腎病症候 群、甲狀腺功能低下)
2) Praluent的建議起始劑量為75 mg，每2週皮下注射一次，因為大多數的患者在此 劑量下能使LDL-C充分下降。若LDL-C的反應不足，則可增加至最高劑量150 mg，每2 週注射一次
3) Praluent之劑量可依個別病患之特性調整，如：LDL-C基期濃度、治療目標及反應。 血脂濃度可於治療開始或調整後4-8週進行評估 (此時LDL-C通常已達到穩定狀態) 並 隨之調整劑量 (增加劑量或減少劑量)。病患應給予最低必要劑量，以達到LDL-C所希 望之降低程度。
4) 若漏打一次劑量，病患應儘快於漏打後七天內補打該次藥物，並依原注射時程繼續　治療。若未能於漏打後七天內補打該次注射藥物，則不須補打，依原注射時程繼續治療。

SANOFI REGENERON
MAT-TW-2000572-2.0-10/2020
Praluent® (alirocumab) Injection 75mg/mL 150mg/mL

04 | PCSK-9 I OUTCOMES

PCSK9 Inhibitor CV Outcomes Trials

	Evolocumab (AMG 145)	Alirocumab (SAR236553/REGN727)
Sponsor	Amgen	Sanofi/ Regeron
Trial	FOURIER[1]	ODYSSEY Outcomes[2]
Sample size	22,500	18,000
Patients	MI, Stroke, or PAD	4 - 52 weeks post ACS
Statin	Maximally tolerated dose of statin	Maximally tolerated dose of statin
LDL-C, mg/dL (mmol/L)	≥ 70 (≥ 1.8)	≥ 70 (≥ 1.8)
PCSK9 inhibitor dosing	Q2W or Q4W	Q2W
Endpoint	Cardiovascular death, Myocardial infarction, Stroke, hospitalization for unstable angina, or coronary revascularization	Death from coronary heart disease, nonfatal myocardial infarction, fatal or nonfatal ischemic stroke, or unstable angina requiring hospitalization
Completion	November 2016	December 2017

ACS, acute coronary syndrome; MI, myocardial infarction; Stroke, nonhemorrhagic stroke; PAD, peripheral artery disease; PCSK9, proprotein convertase subtilisin/kexin type 9; Q2W, every two week; Q4W, every four week; LDL-C, low-density, lipoprotein cholesterol

1. ClinicalTrials.gov.NCT01764633, https://clinicaltrials.gov/ct2/show/NCT01764633.
2. ClinicalTrials.gov. NCT01663402, https://clinicaltrials.gov/ct2/show/NCT01663402.

ODYSSEY OUTCOMES Trial

18,000 patients

- Age > 40 years
- 4 - 52 weeks post-ACS
- On evidence-based medical therapy
- LDL-C ≥ 70 mg/dL or non-HDL-C ≥ 100mg/dL or apolipoprotein B ≥ 80mg/dL
- 64 months randomized treatment period and 2-month follow-up period

Randomization
(N = 18,924) 1:1

Alirocumab SQ
(n = 9,462)

Placebo SQ
(n = 9,462)

- Expected LDL-C level: **30 - 40** mg/dL
- Finished in December, 2017

Primary endpoint:

- CHD death
- Nonfatal MI
- Ischemic stroke
- UA requiring hospitalization

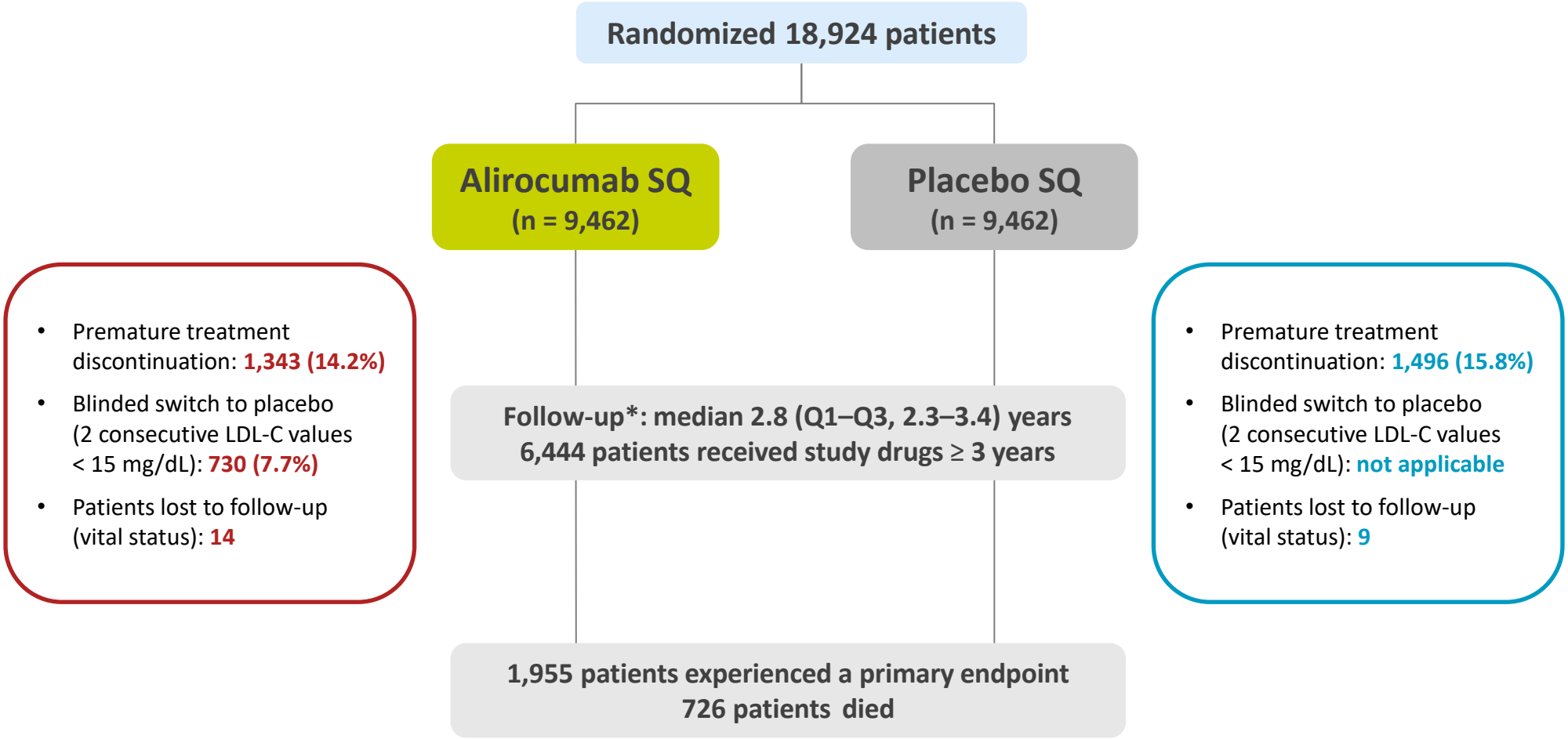
Secondary endpoint:

- Any CHD event
- Major CHD event
- Any CV event
- Composite of all-cause mortality, nonfatal MI or stroke
- All cause mortality

ACS, acute coronary syndrome; CHD, coronary heart disease; CV, cardiovascular; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; MI, myocardial infarction; UA, unstable angina.

ClinicalTrials.gov. NCT01663402, https://clinicaltrials.gov/ct2/show/NCT01663402.

Patient Disposition



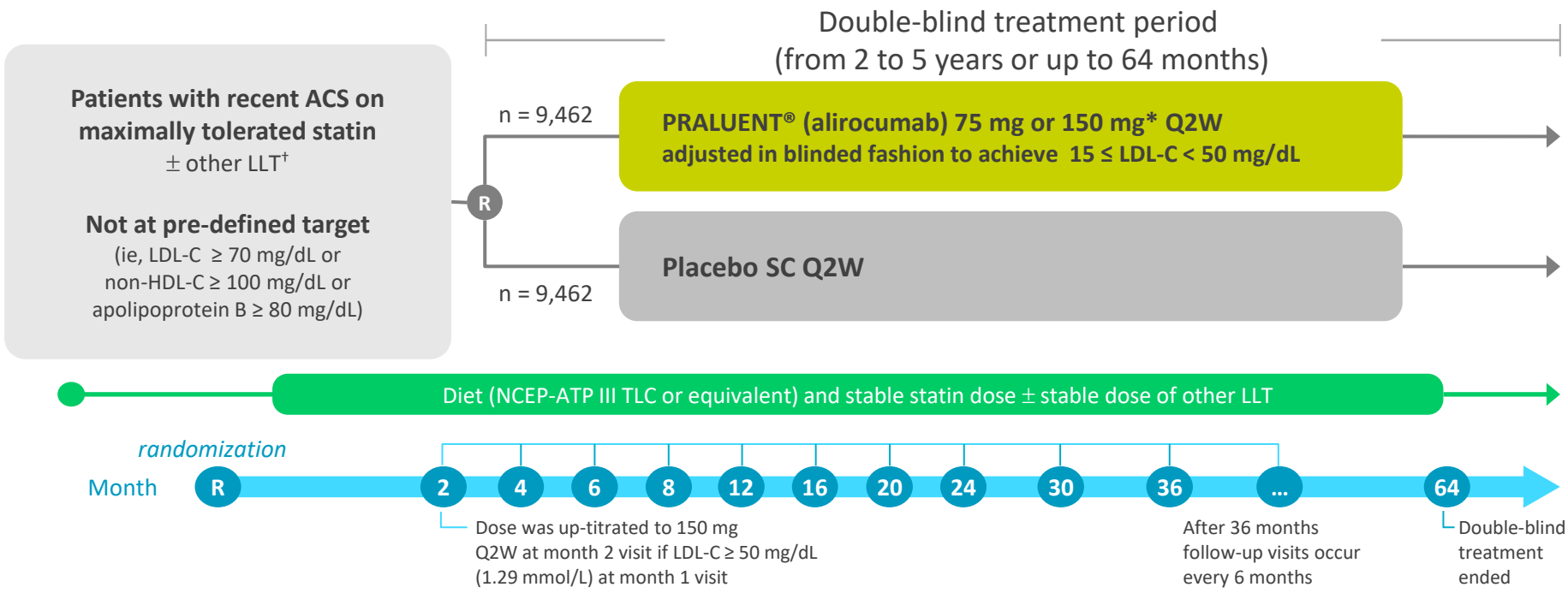
*Ascertainment was complete for 99.1% and 99.8% of potential patient-years of follow-up for the primary endpoint and all-cause death, respectively

LDL-C, low-density lipoprotein cholesterol; Q2W, every two weeks; SC, subcutaneous.

Schwartz GG, et al. N Engl J Med. 2018;379(22):2097–107.

ODYSSEY Outcomes - Study Design

A randomized, double-blind, placebo-controlled study



*Dose titrated up to 150 mg Q2W at month 2 if LDL-C ≥ 50 mg/dL (1.29 mmol/L) at month 1 visit.
†Atorvastatin 40-80 mg or rosuvastatin 20-40 mg OR maximally tolerated dose of statin (can be 0 mg).

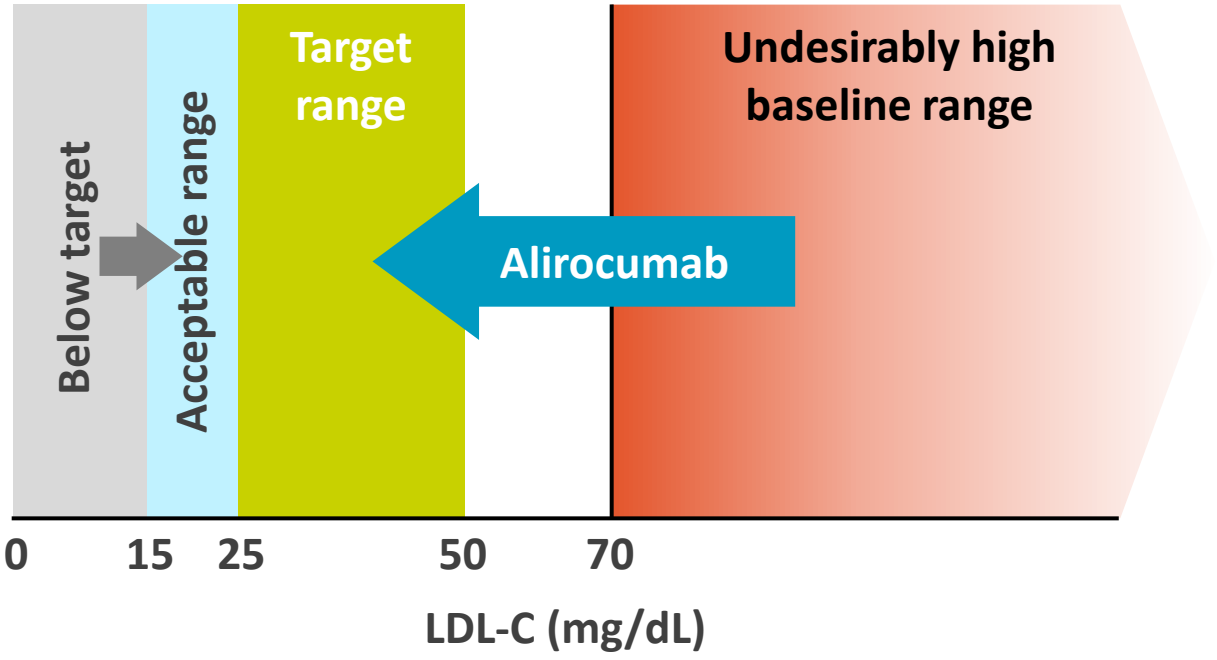
If LDL-C < 25 mg/dL on any 2 consecutive measurements on alirocumab 150 mg, the dose is reduced to 75 mg.
If LDL-C < 15 mg/dL on 2 consecutive measurements with alirocumab 75 mg, active treatment is discontinued at the next study visit and substituted with placebo.

ACS, acute coronary syndromes; LDL-C, low-density lipoprotein cholesterol; LLT, lipid-lowering therapy; NCEP-ATP III TLC, national cholesterol education program adult treatment panel III therapeutic lifestyle change; Q2W, every two weeks; SC, subcutaneous.

Schwartz GG, et al. Am Heart J. 2014;168:682–9.

LDL-C Target Range

- The investigators attempted to maximize the number of patients in the target range and minimize the number below target by blindly
  - ✓ titrating alirocumab (75 or 150 mg SC Q2W)
  - ✓ or switching to placebo



LDL-C, low-density lipoprotein cholesterol; Q2W, every two weeks; SC, subcutaneous.

Schwartz GG, et al. N Engl J Med. 2018;379(22):2097–107.

Baseline characteristics*

Characteristic	Alirocumab (N = 9,462)	Placebo (N = 9,462)
Age, years	58.5 ± 9.3	58.6 ± 9.4
Female sex, no. (%)	2,390 (25.3)	2,372 (25.1)
Race, no. (%)†		
White	7,500 (79.3)	7,524 (79.5)
Asian	1,251 (13.2)	1,247 (13.2)
Black	235 (2.5)	238 (2.5)
Other	475 (5.0)	451 (4.8)
Region of enrollment, no. (%)		
Central and Eastern Europe	2,719 (28.7)	2,718 (28.7)
Western Europe	2,084 (22.0)	2,091 (22.1)
Canada or United States	1,435 (15.2)	1,436 (15.2)
Latin America	1,293 (13.7)	1,293 (13.7)
Asia	1,150 (12.2)	1,143 (12.1)
Rest of world	781 (8.3)	779 (8.2)

(Continued from previous column) Characteristic	Alirocumab (N = 9,462)	Placebo (N = 9,462)
Medical history before index acute coronary syndrome, no. (%)		
Hypertension	6,205 (65.6)	6,044 (63.9)
Diabetes mellitus	2,693 (28.5)	2,751 (29.1)
Current tobacco smoker	2,282 (24.1)	2,278 (24.1)
Family history of premature coronary heart disease	3,408 (36.0)	3,365 (35.6)
Myocardial infarction	1,790 (18.9)	1,843 (19.5)
Percutaneous coronary intervention	1,626 (17.2)	1,615 (17.1)
Coronary-artery bypass graft	521 (5.5)	526 (5.6)
Stroke	306 (3.2)	305 (3.2)
Peripheral artery disease	373 (3.9)	386 (4.1)
Congestive heart failure	1,365 (14.4)	1,449 (15.3)
Body-mass index‡	28.5 ± 4.9	28.5 ± 4.8

*Plus–minus values are means ±SD. There were no significant differences between the two groups in demographic or baseline characteristics.
†Race was reported by the patient.
‡The body-mass index is the weight in kilograms divided by the square of the height in meters.

Schwartz GG, et al. N Engl J Med. 2018;379(22):2097–107.

Baseline Index Events

All Randomized Patients

% (n)	Alirocumab (N = 9,462)	Placebo (N = 9,462)
Index ACS, % (n)		
STEMI	**34.9 (3,301)**	**34.2 (3,235)**
NSTEMI	**48.3 (4,574)**	**48.6 (4,601)**
Unstable angina	16.6 (1,568)	17.1 (1,614)
Percutaneous coronary intervention or coronary-artery bypass grafting for index ACS, % (n)	71.8 (6,798)	72.7 (6,878)
Median time from index ACS to randomization, months, IQR	**2.6 (1.7 - 4.4)**	**2.6 (1.7 - 4.3)**

ACS, acute coronary syndromes; IQR, interquartile range; NSTEMI, non- ST-Elevation Myocardial Infarction; STEMI, ST-Elevation Myocardial Infarction.

Schwartz GG, et al. N Engl J Med. 2018;379(22):2097–107.

Medications Use at Randomization

% (n)	Alirocumab (N = 9,462)	Placebo (N = 9,462)
High-intensity atorvastatin or rosuvastatin†	**88.6 (8,380)**	**89.1 (8,431)**
Atorvastatin 80 mg or rosuvastatin 40 mg	27.6 (2,607)	27.2 (2,572)
Atorvastatin 40 mg or rosuvastatin 20 mg	61.0 (5,773)	61.9 (5,859)
Low- or moderate-intensity atorvastatin or rosuvastatin	8.8 (830)	8.2 (777)
Other statin	0.2 (19)	0.3 (27)
No statin	2.4 (227)	2.5 (233)
Ezetimibe	2.8 (269)	3.0 (285)
Antiplatelet agent	**98.8 (9,350)**	**98.9 (9,354)**
Aspirin	95.6 (9,050)	95.5 (9,036)
$P2Y_{12}$ inhibitor	87.7 (8,296)	87.1 (8,245)
Vitamin K antagonist or other oral anticoagulant	4.1 (378)	4.3 (403)
Beta-blocker	84.5 (7,998)	84.5 (7,992)
ACE inhibitor or ARB	77.7 (7,356)	77.8 (7,360)

After 1 year of follow-up, 84.7% of the patients in the alirocumab group and 86.2% in the placebo group were receiving high-intensity atorvastatin or rosuvastatin; after 3 years of follow-up, the percentages were 82.8% in the alirocumab group and 86.6% in the placebo group.

ACE, angiotensin converting enzyme; ARB, angiotensin II receptor blocker.

Schwartz GG, et al. N Engl J Med. 2018;379(22):2097–107.

Lipid Levels at Randomization

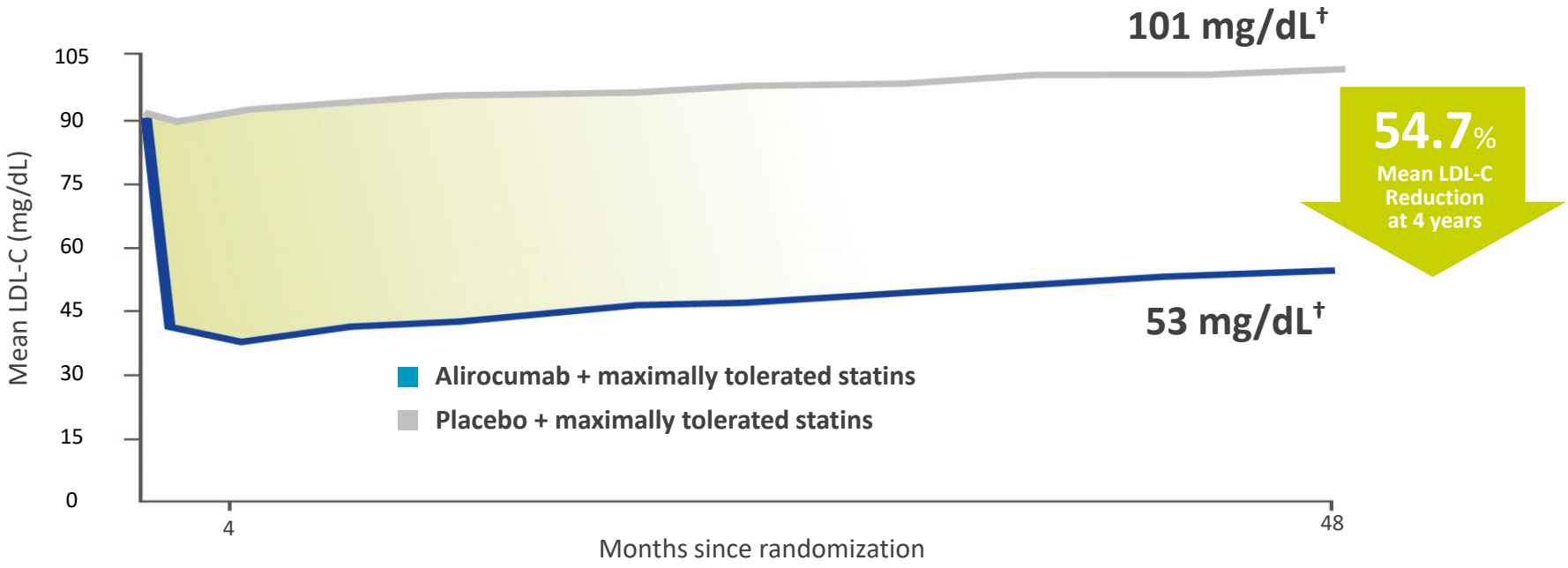
Lipids, mg/dL, median (IQR)†	Alirocumab (N = 9,462)	Placebo (N = 9,462)
LDL-C	**87 (73 – 104)**	**87 (73 – 104)**
LDL-C, mean (SD)	**92 (31)**	**92 (31)**
Non-HDL-C	115 (99 – 136)	115 (99 – 137)
Non-HDL-C, mean (SD)	122 (35)	123 (36)
Apolipoprotein B	79 (69 – 93)	80 (69 – 93)
Apolipoprotein B, mean (SD)	83 (21)	83 (22)
HDL-C	43 (37 – 50)	42 (36 – 50)
Apolipoprotein A1	131 (118 – 148)	132 (117 – 147)
Triglycerides	129 (94 – 181)	129 (95 – 183)
Lipoprotein(a)	21 (7 – 59)	22 (7 – 60)

†Unless where shown as mean (SD).
HDL-C, high-density lipoprotein cholesterol; IQR, interquartile range; LDL-C, low-density lipoprotein cholesterol; non-HDL-C, non-high-density lipoprotein cholesterol; SD, standard deviation.

Schwartz GG, et al. N Engl J Med. 2018;379(22):2097–107.

LDL-C Levels Over Time (On-Treatment Analysis*)

LDL-C reduction within CV outcomes



In the on-treatment analysis, at 4, 12, and 48 months, average LDL-C levels in patients treated with alirocumab were 62.7%, 61.0%, and 54.7% **lower than** the respective levels in the placebo group.

Earliest down-titration of alirocumab (including placebo substitution) could not occur before the Month 4 visit

*Excluded LDL-C levels measured after premature discontinuation or after blinded substitution of placebo but included LDL-C measured after dose adjustments of Alirocumab under blinded conditions between the 75 mg dose and the 150 mg dose.

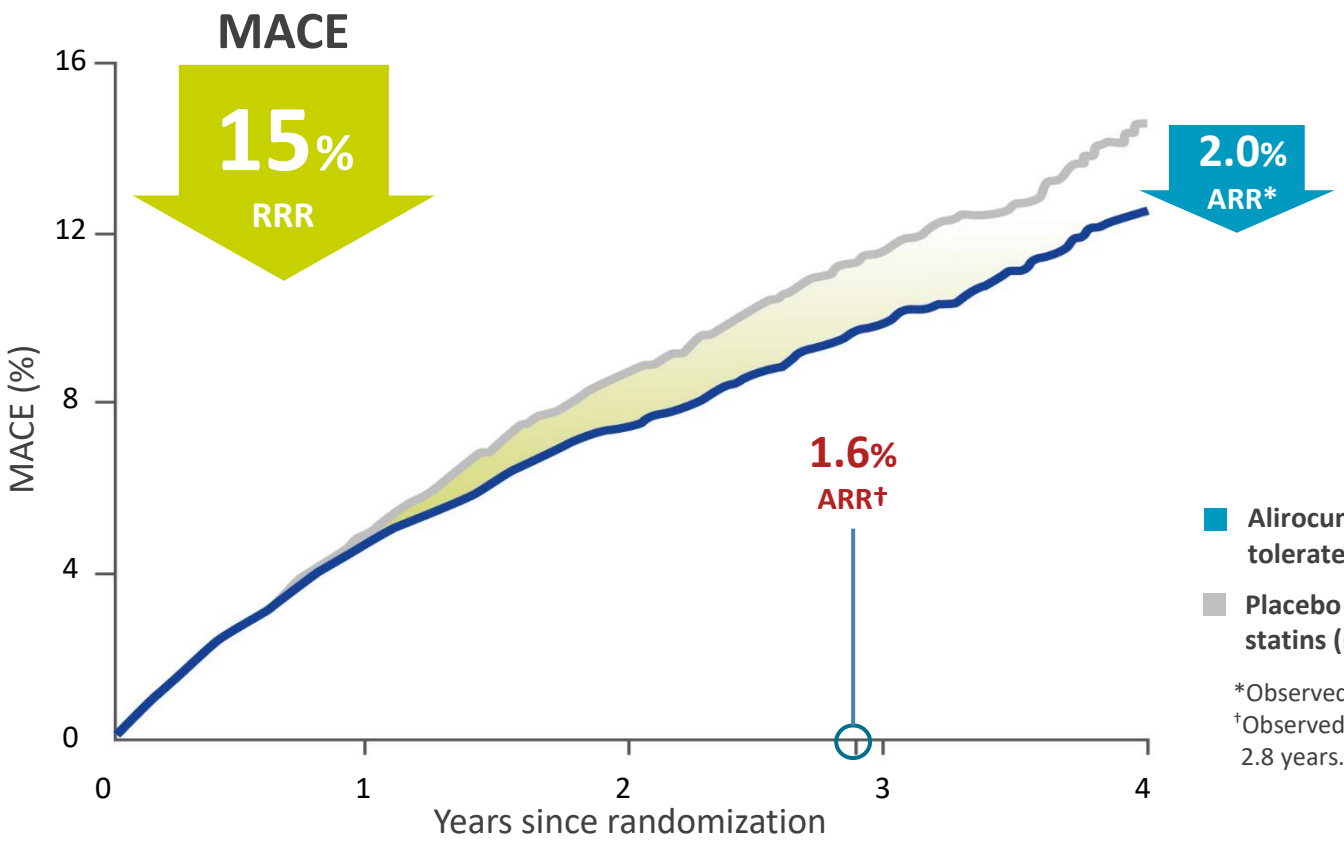
†101 mg/dL = 2.6 mmol/L, 53mg/dL = 1.4 mmol/L.

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

Schwartz GG, et al. N Engl J Med. 2018;379(22):2097–107.

Cumulative Incidence of the Composite Primary Endpoint

Primary efficacy endpoint: MACE over all trial population



- NNT = 49, to prevent the occurrence of one primary end-point event, 49 patients would need to be treated for 4 years.

Alirocumab + maximally tolerated statins (n = 9,462)

Placebo + maximally tolerated statins (n = 9,462)

*Observed cumulative incidence of events over 4 years.
†Observed cumulative incidence of events over a median of 2.8 years.

ARR, absolute risk reduction; CI, confidence interval; CY, cardiovascular; HR, hazard ratio; LDL-C, low-density lipoprotein cholesterol; MACE, major adverse cardiovascular event; NNT, number needed to treat; RRR, relative risk reduction.

Schwartz GG, et al. N Engl J Med. 2018;379(22):2097–107.

Composite Primary Endpoint and Secondary Endpoints (ITT Population)

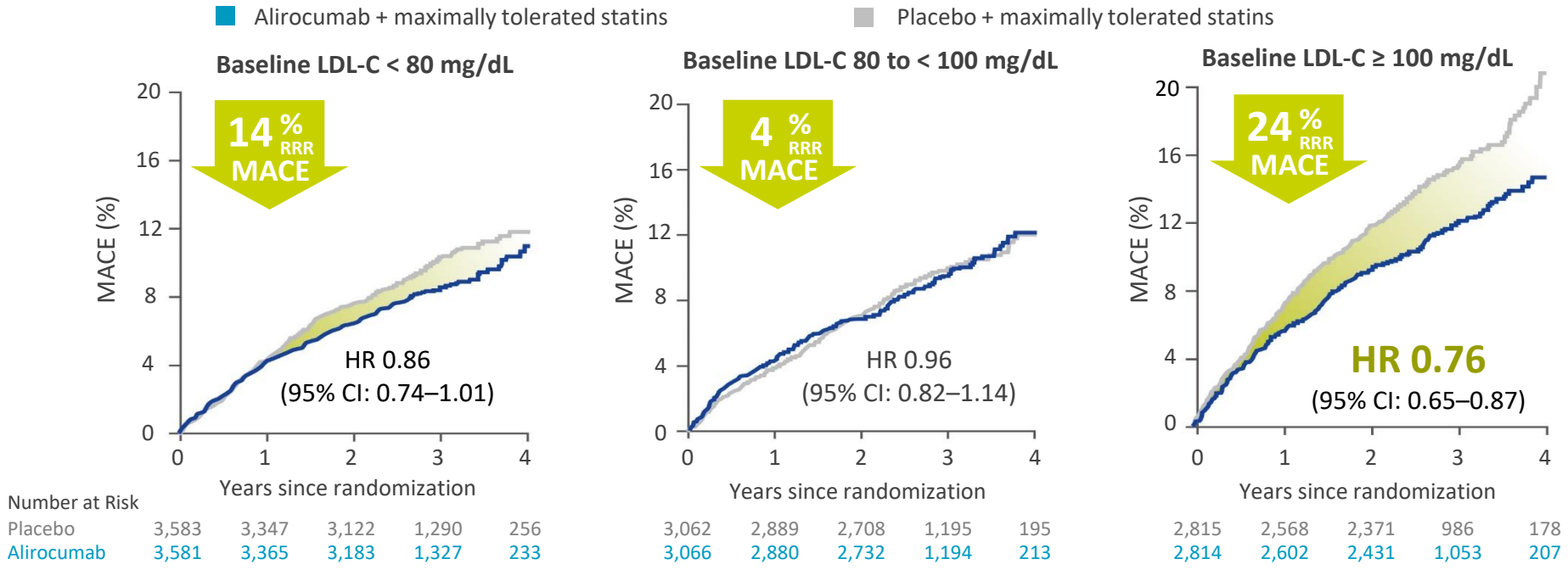
Endpoint, % (n)	Alirocumab (N=9462)	Placebo (N=9462)	HR (95% CI)	Log-rank P-value
Primary endpoint	9.5 (903)	11.1 (1052)	**0.85 (0.78–0.93)**	<0.001
Main secondary endpoints, in order of hierarchical testing				
Any CHD event	12.7 (1199)	14.3 (1349)	0.88 (0.81–0.95)	0.001
Major CHD event	8.4 (793)	9.5 (899)	0.88 (0.80–0.96)	0.006
Any cardiovascular event	13.7 (1301)	15.6 (1474)	0.87 (0.81–0.94)	<0.001
Composite of death from any cause, nonfatal MI, or nonfatal ischemic stroke[†]	10.3 (973)	11.9 (1126)	0.86 (0.79–0.93)	<0.001
Death from CHD	2.2 (205)	2.3 (222)	0.92 (0.76–1.11)	0.38[‡]
Death from cardiovascular causes	2.5 (240)	2.9 (271)	0.88 (0.74–1.05)	
Death from any cause	3.5 (334)	4.1 (392)	**0.85 (0.73–0.98)**	
Other Endpoints[§]				
Nonfatal MI	6.6 (626)	7.6 (722)	0.86 (0.77–0.96)	
Fatal or nonfatal ischemic stroke	1.2 (111)	1.6 (152)	0.73 (0.57–0.93)	
Unstable angina requiring hospitalization	0.4 (37)	0.6 (60)	0.61 (0.41–0.92)	
Ischemia-driven coronary revascularization procedure	7.7 (731)	8.8 (828)	0.88 (0.79–0.97)	
Hospitalization for congestive heart failure	1.9 (176)	1.9 (179)	0.98 (0.79–1.20)	

[‡]The hierarchical analysis was stopped after the first nonsignificant P value was observed, in accordance with the hierarchical testing plan. [§]The analysis was not adjusted for multiplicity; therefore, no *P* values are reported.

Schwartz GG et al. *N Engl J Med 2018;379:2097-107.*

Primary Endpoint by Baseline LDL-C Levels (ITT Population)

MACE incidence rate during 4-year follow-up



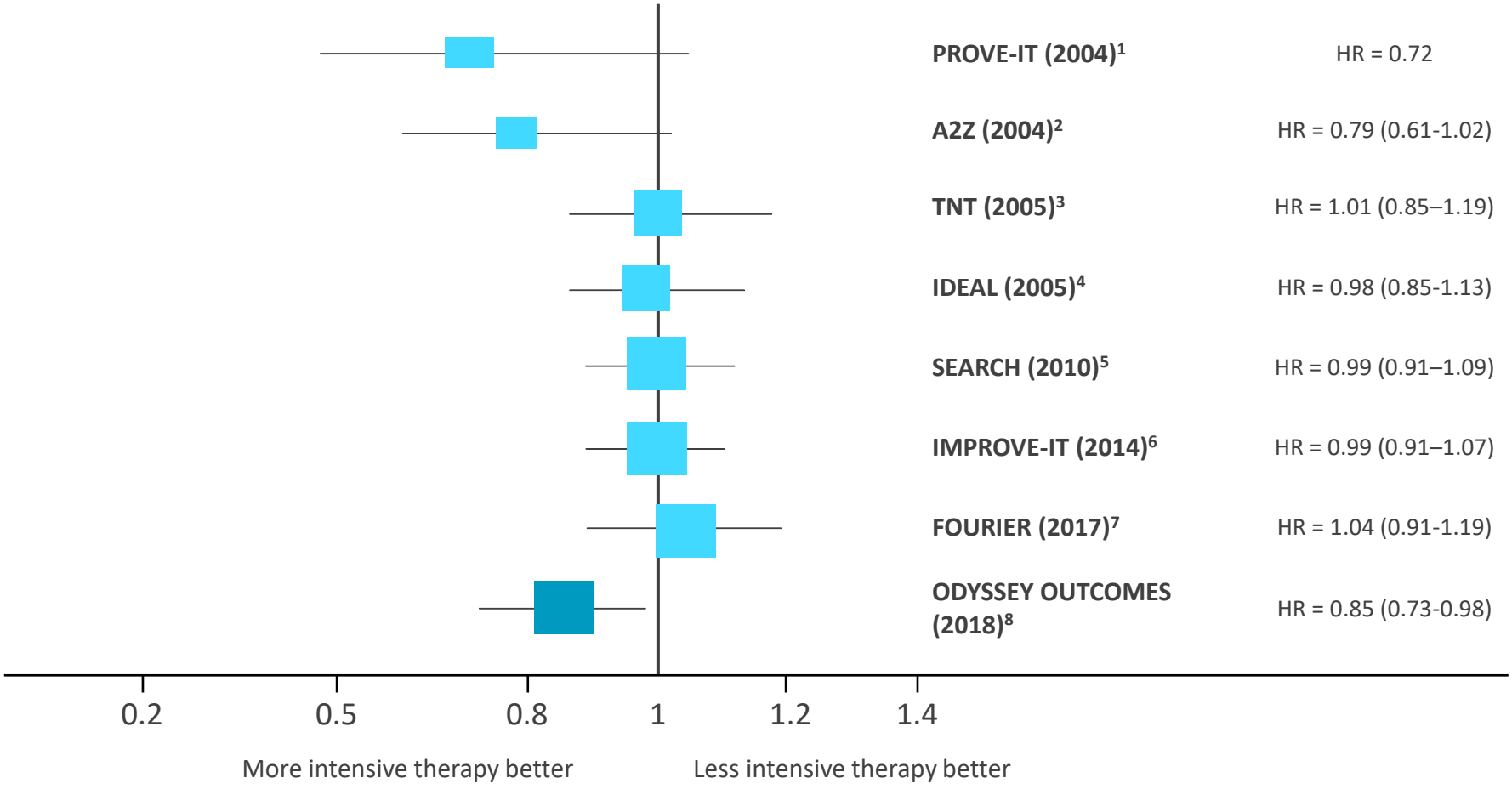
- **No significant interaction** of treatment and baseline LDL-C category on the relative risk of the primary endpoint (*P* = 0.09).
- **Absolute reduction** in the risk of the primary endpoint with alirocumab was **greatest in** the group of patients with **baseline LDL-C ≥ 100 mg/dL** (*P* < 0.0001).

CI, confidence interval; HR, hazard ratio; LDL-C, low-density lipoprotein cholesterol; MACE, major adverse cardiac events; RRR, relative risk reduction.

Schwartz GG, et al. N Engl J Med. 2018;379(22):2097–107.

All Cause Death in 2ndry prevention LLT trials

More intensive vs less intensive regimen



1. Cannon CP, et al. N Engl J Med 2004;350:1495-504.
2. De Lemos, et al. JAMA. 2004;292:1307-16.
3. LaRosa JC, et al. N Engl J Med 2005;352:1425-35.
4. Pedersen, TR, et al. JAMA. 2005;294:2437-45.
5. SEARCH collaborative group. Lancet 2010; 376:1658–69.
6. Cannon CP, et al. N Engl J Med 2015;372:2387-97.
7. Sabatine MS, et al. N Engl J Med 2017;376:1713-22.
8. Schwartz GG, et al. N Engl J Med. 2018;379:2097-107.

Summary of ODYSSEY Outcomes Study

試驗中收納約一萬九千位曾經發生過急性冠心症 (90%已在使用Statin)的患者，隨機分派至使用Praluent組或安慰組，探討Praluent對此病患群長期的療效及安全性：

- 整體的MACE風險降低15% (HR 0.85; 95% CI: 0.78–0.93; *P*<0.001)
- 全因性死亡率降低15% (HR 0.85; 95% CI: 0.73–0.98)
- 獲益最大的是原先LDL-C ≥ 100 mg/dL 的患者，MACE風險減少24% (HR 0.76; 95% CI: 0.65–0.87)

之
部分規定（自109年1月1日生效）

修訂後給付規定	原給付規定
2.6.4.PCSK9 血脂調節劑 2.6.4.1.Evolocumab (如Repatha)：(107/3/1、108/5/1)(略) 2.6.4.2 Alirocumab(如Praluent) (109/1/1)： 限使用於發生重大心血管事件之病人： 1.須經事前審查核准後使用，每次申請得核准使用 6 個月，再次申請須檢附評估報告，若血中 LDL-C較本藥物開始使用前下降程度未達 30%，即屬療效不佳，則不再給付。 2.限給付於發生重大心血管事件之後一年內且使用最大耐受劑量statin之病人，如心肌梗塞、接受冠狀動脈或其他動脈血管再通術 (revascularization)、動脈硬化相關之缺血性腦中風等之動脈粥狀硬化心血管疾病之成人病人，且符合下列條件之一者： (1)經使用高強度statin (如 rosuvastatin 20mg 或atorvastatin 40 mg(含)以上)或病人可耐受之最大劑量的statin三個月(含)以上且之後再合併使用ezetimibe 10 mg 三個月(含)以上，LDL-C 仍高於135 mg/dL者。 (2)對statin有禁忌症或確診為對statin不耐受之病人，經其他降血脂藥物(至少需有ezetimibe 10 mg)持續治療3個月，LDL-C仍高於135 mg/dL者。 3.最高劑量為每兩週使用 1 支。 4.不可同時使用其他PCSK9 血脂調節劑。	2.6.4.Evolocumab (如Repatha)：(107/3/1、108/5/1) (略)

05 | REAL WORLD EXPERIENCE

Case : A Patient presenting as ACS

- **Name: Mrs. 李**
- **Gender: Male**
- **Age: 60-Years-old**
- **Chief complaint: Chest discomfort on exertion visited ER on Sep. 2016**

- **Diagnosis: Non-STEMI**

Case : A Patient with ACS

Comorbid illness:

1. Hypertension history (Norvasc 5mg bid, Diovan 160 mg qd, Fluitran 4 mg qd) for 8 years
2. Hyperlipidemia (Lipitor 20 mg qd and ezetrol) for 8 years
3. Diabetes (Metformin 500mg bid, Actos 1 tab qd, Amaryl 1 tab qd) for 10 years
4. Smoker (Try to quit for times but in vain)
5. CAD with BRS stent implantation (3.0X18 Abbot) on Oct. 2013 (Aspirin 100 mg qd)

Laboratory data in ER

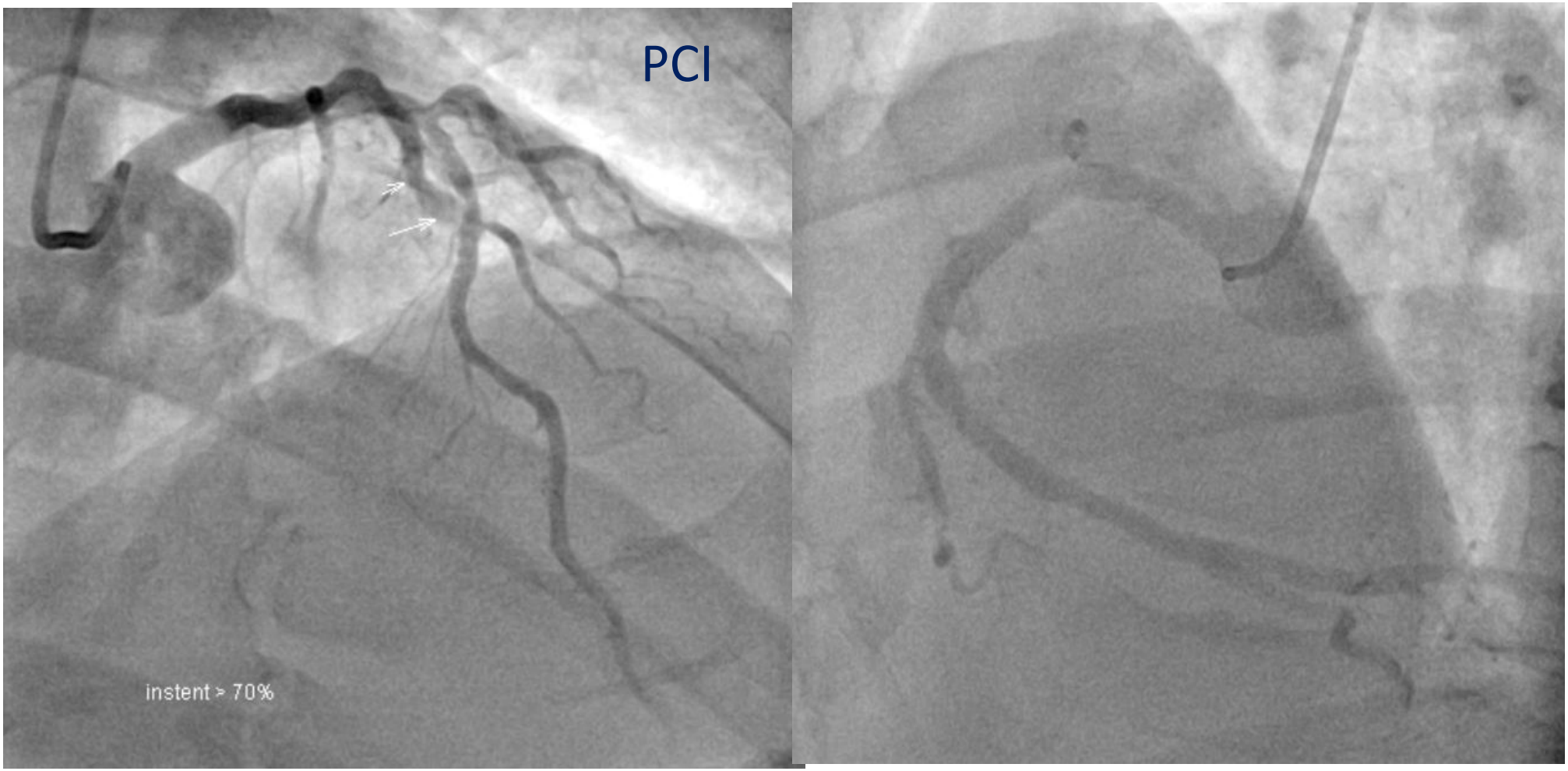
CPK 210 ↑, CK-MB 30 ↑, Troponin T 0.12 ↑↑, Cr 0.8 mg/dl, GPT 30 U

FBS 78 mg/dL ↓, HbA1C 6.7% ↓

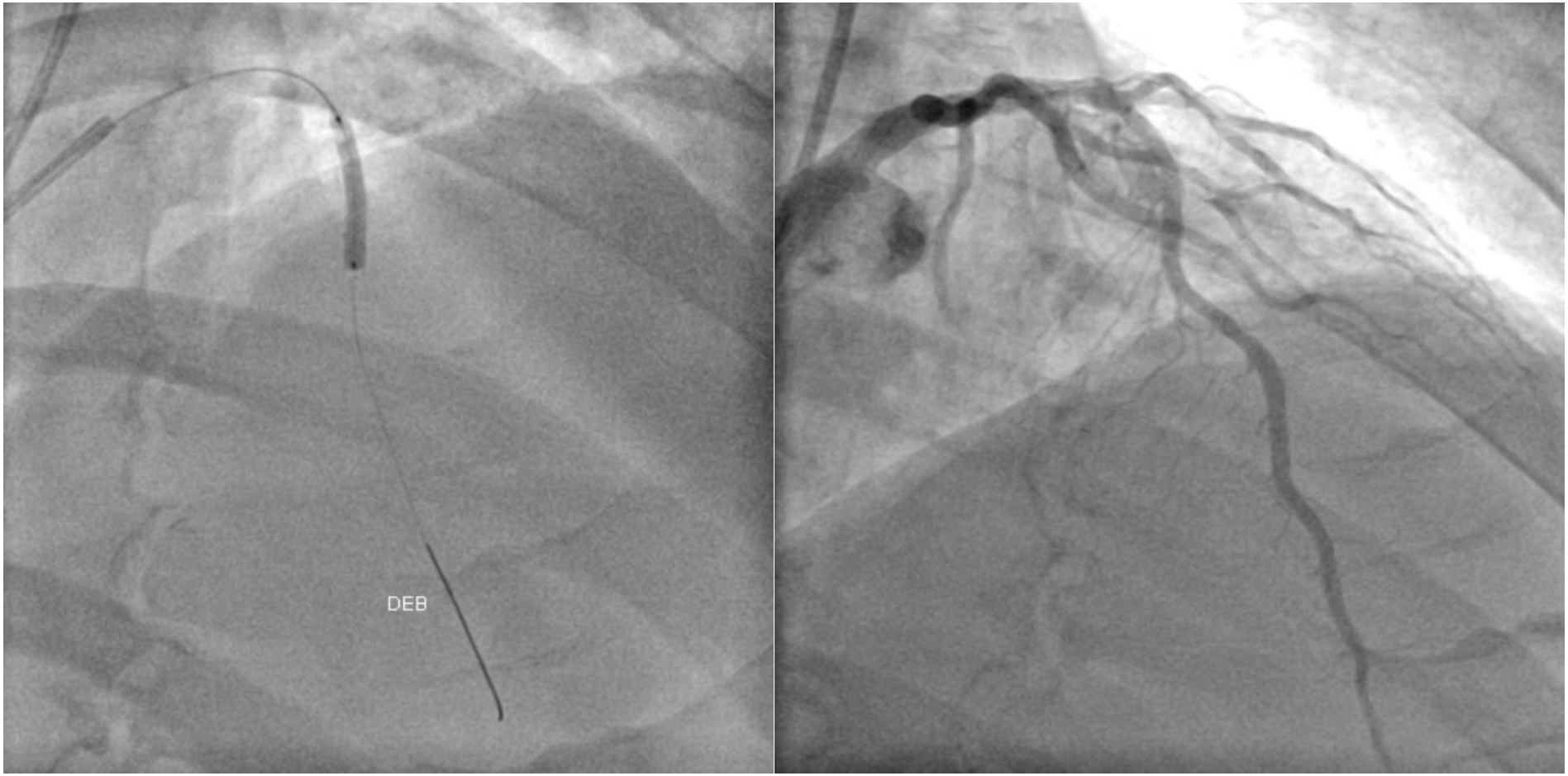
Lipid profiles:

TC 133 mg/dl; LDL 70 mg/dl ↓; TG 115 mg/dl ↓ ; HDL 53 mg/dl ↑;
Non-HDL-C 80 mg/dl ↓

Coronary Angiography and intervention



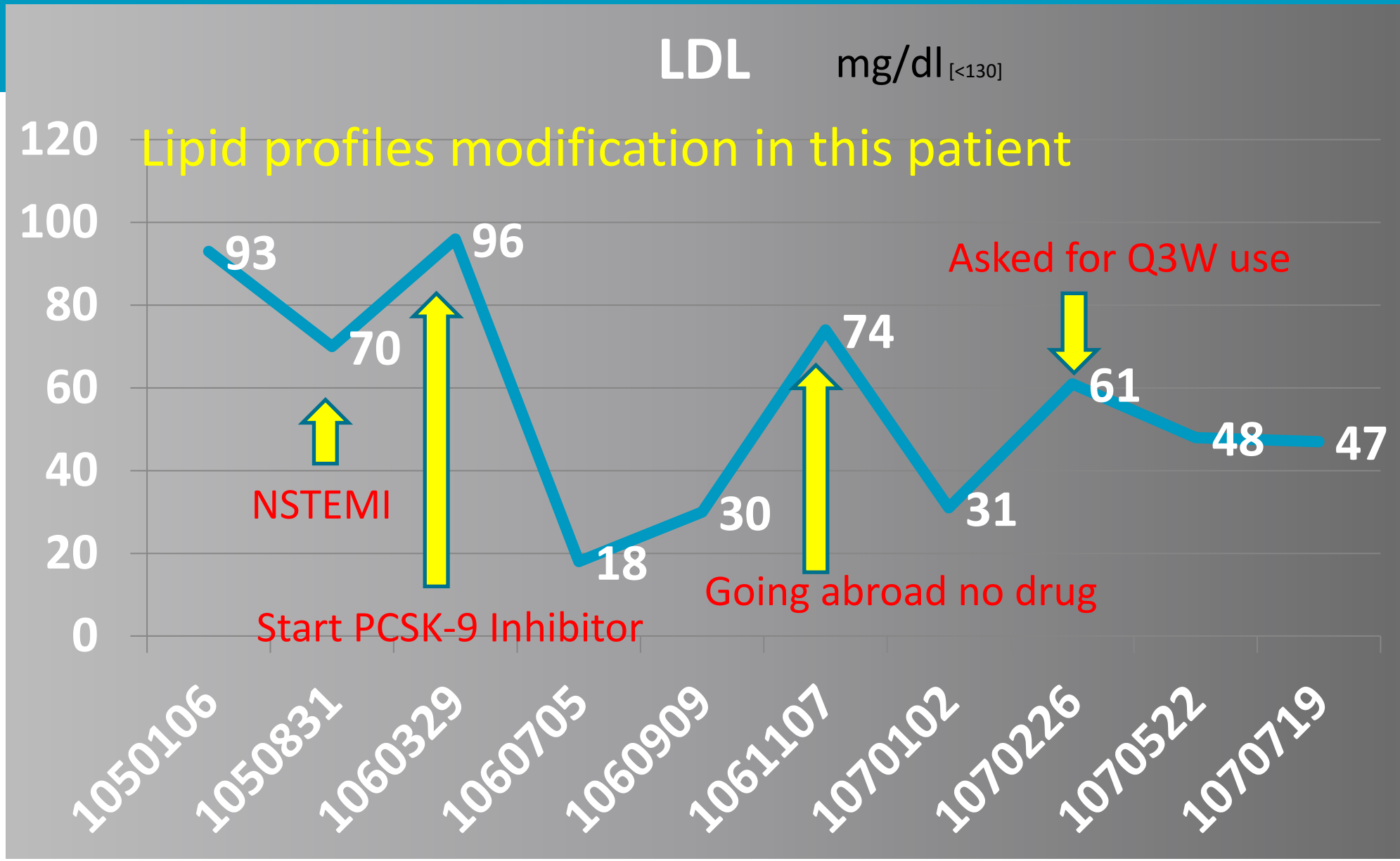
Coronary Angiography and intervention

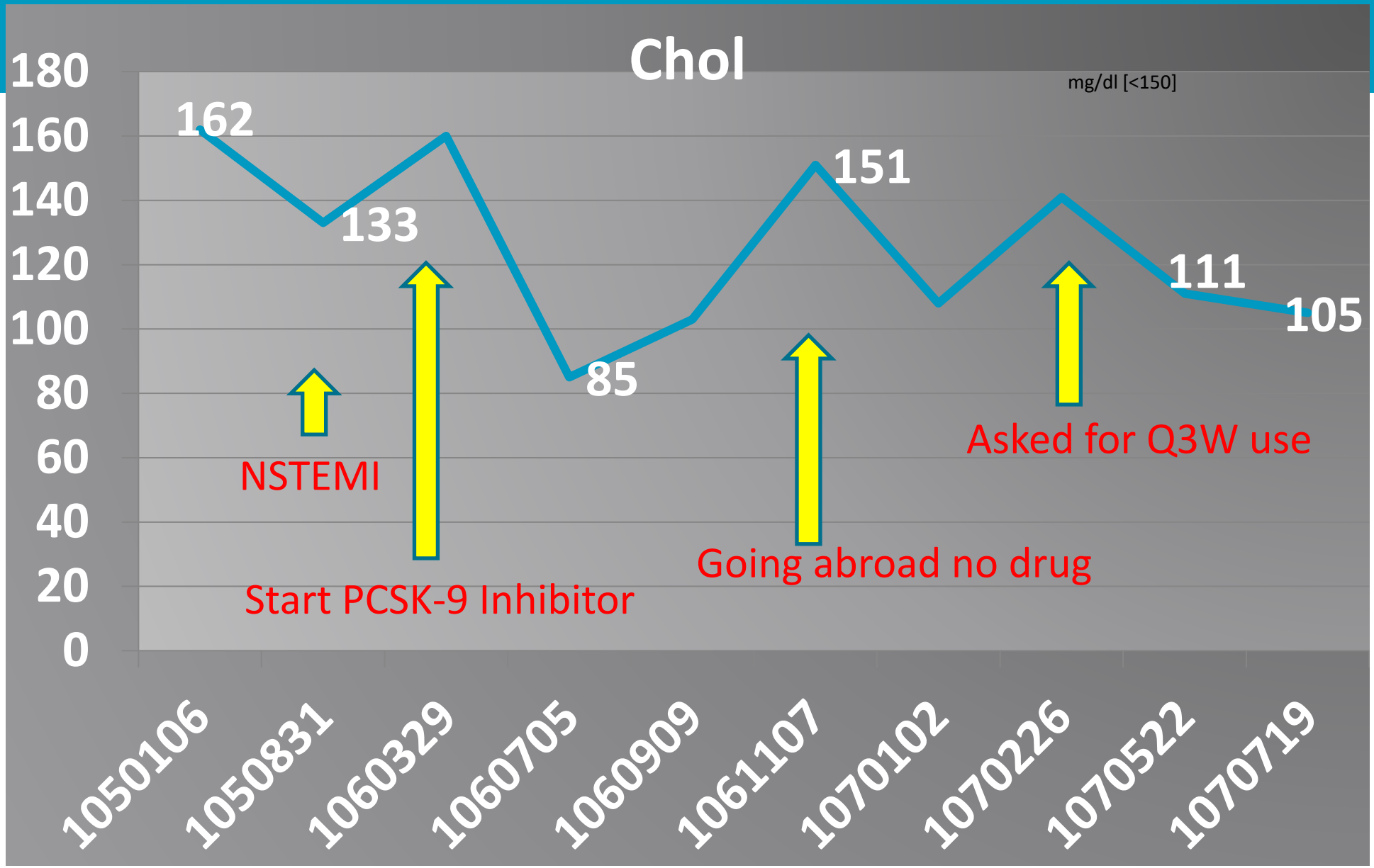


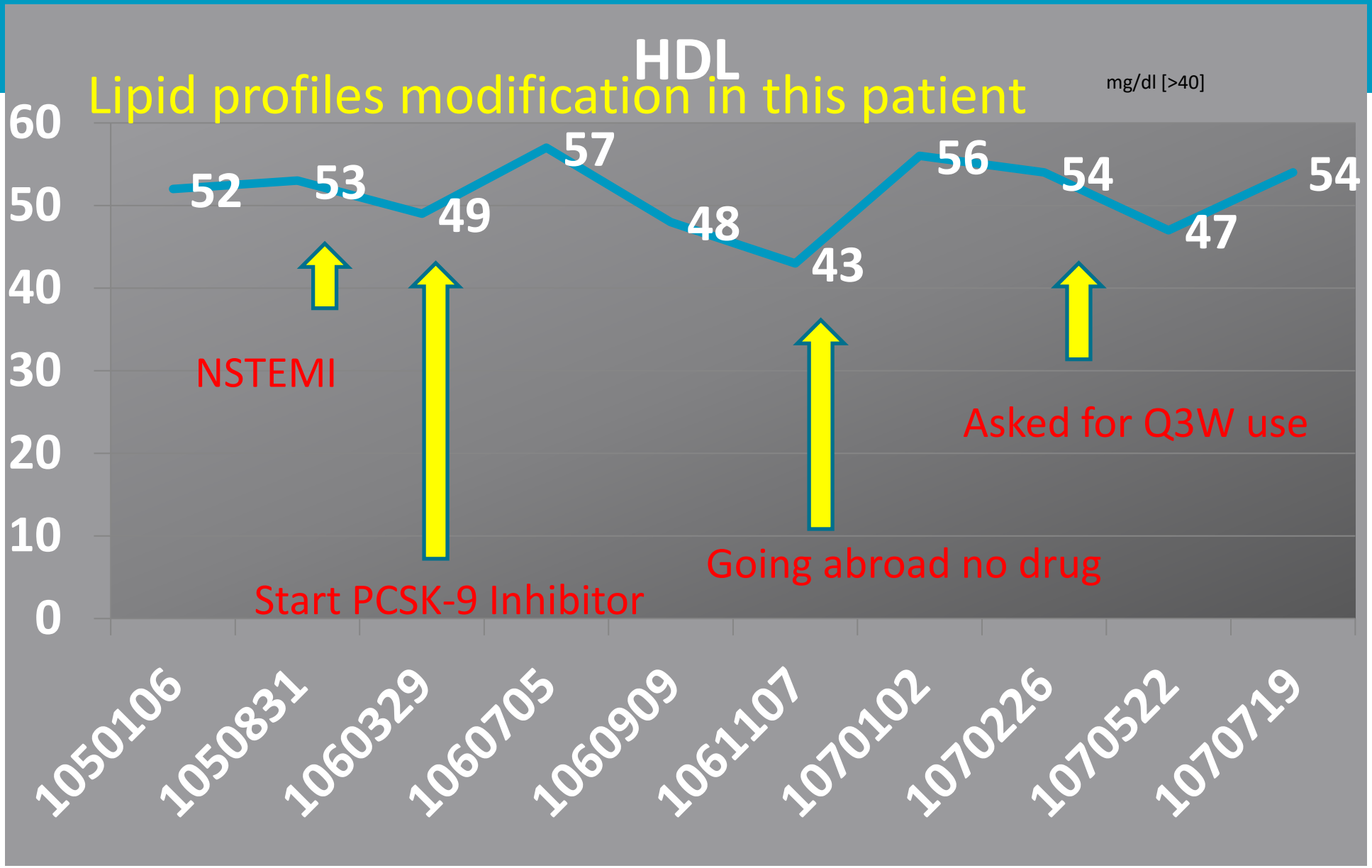
Why NSTEMI?

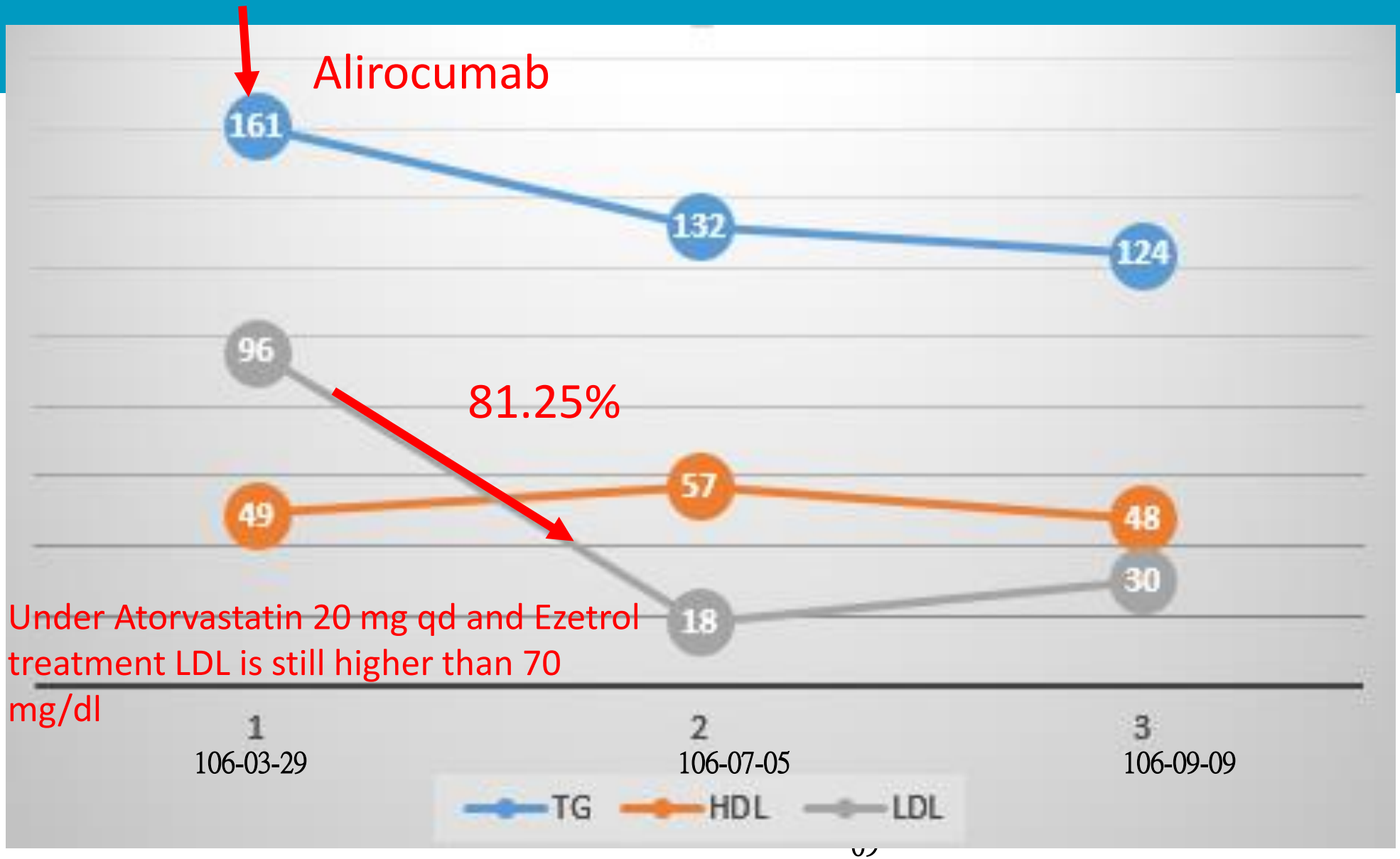
How to improve and prevent further events?

- Too tight blood sugar control and inappropriate drug use (FBS 78 mg/dl, HbA1C 6.7%, Metformin, Actos, Amaryl) ?
- Inadequate Blood pressure control (home BP 130/80 mmHg)?
- Keep on smoking and failed cessation process ?
- BVS late thrombosis related (IVUS showing remaining scaffold and negative remodeling of vessels) ?
- Lipid goal not achieved (LDL 70 mg/dl in ER) ?


LDL mg/dl [<130]
Lipid profiles modification in this patient
120
100
80
60
40
20
0
93
70
96
18
30
74
31
61
48
47
NSTEMI
Start PCSK-9 Inhibitor
Going abroad no drug
Asked for Q3W use
10501061
10508311
10603291
10607051
10609091
10611071
10701021
10702261
10705221
10707191

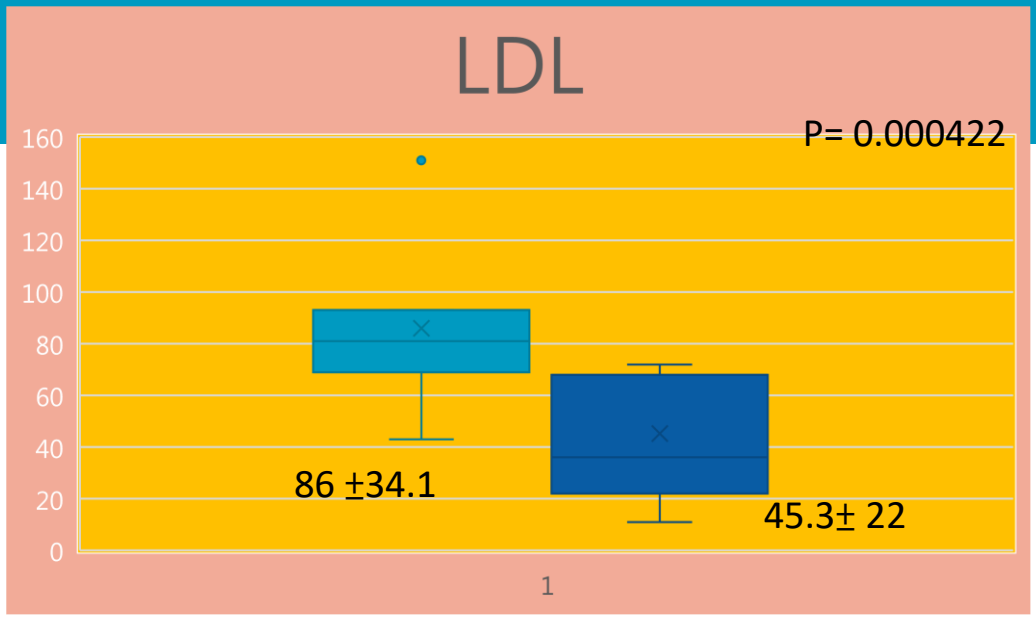

Chol
mg/dl [<150]
180
160
140
120
100
80
60
40
20
0
162
133
85
151
111
105
NSTEMI
Start PCSK-9 Inhibitor
Going abroad no drug
Asked for Q3W use
1050106
1050831
1060329
1060705
1060909
1061107
1070102
1070226
1070522
1070719


HDL
Lipid profiles modification in this patient
mg/dl [>40]
60
50
40
30
20
10
0
52
53
49
57
48
43
56
54
47
54
NSTEMI
Start PCSK-9 Inhibitor
Going abroad no drug
Asked for Q3W use
1050106
1050831
1060329
1060705
1060909
1061107
1070102
1070226
1070522
1070719



Under Atorvastatin 20 mg qd and Ezetrol treatment LDL is still higher than 70 mg/dl

Any side effects?



- **Injection-site reaction: no;**
- **Allergic reaction : no**
- **Muscle-related event: no**
- **Rhabdomyolysis: no;**
- **Cataract ?**
- **Adjudicated case of new-onset diabetes† ?**
- **Neurocognitive event: no (Case 1 complained of mild tired feeling)**
- **ALT/AST/CK Abnormality: no**
- **ICH: No**

Does evolocumab use in Europe match the 2019 ESC/EAS lipid guidelines? Results from the HEYMANS study

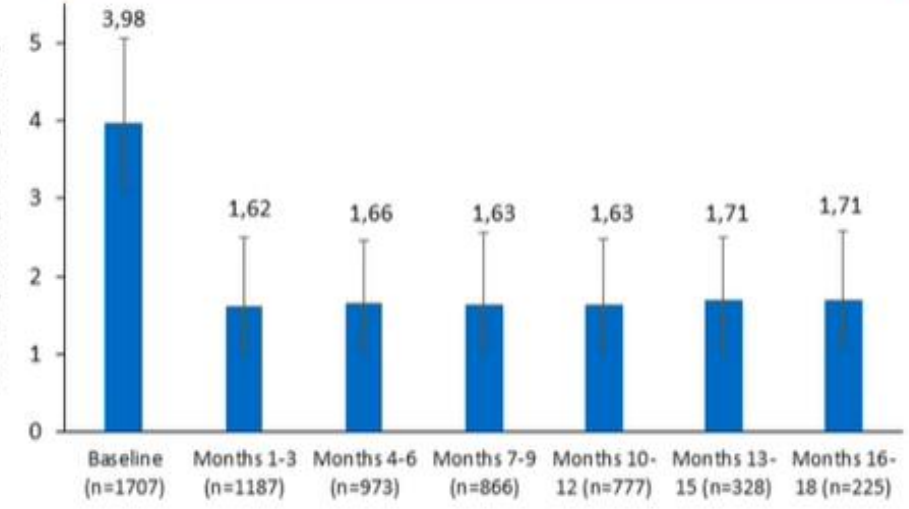
Characteristics of patients initiating evolocumab and treatment patterns across 12 European countries: the HEYMANS* study

K K Ray[1], E Bruckert[2], B Van Hout[3], M Feudjo Tepie[4], I Bridges[4], M Sibartie[6]

[1]Imperial College, London, UK; [2]Hôpital Pitié Salpêtrière, Paris, France; [3]Sheffield University, UK; [4]Amgen UK Ltd, Uxbridge, UK; [5]Amgen (Europe) GmbH, Rotkreuz, Switzerland

LLT use and LDL-C target achievement

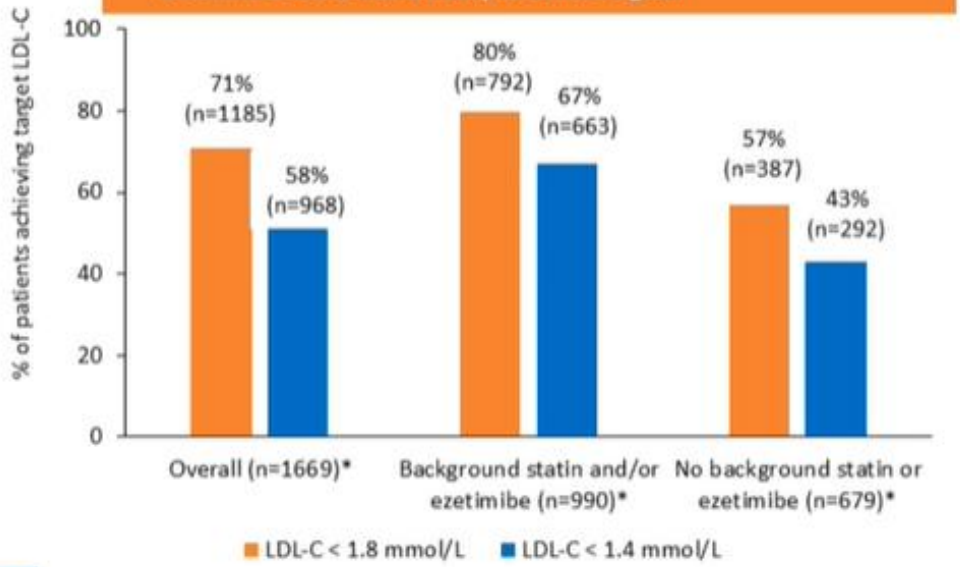
- LDL-C levels decreased by 58% within three months of evolocumab initiation
- This reduction was maintained over 12-18 months



Median (Q1, Q3) reduction from baseline (%)

Months 1–3	Months 4–6	Months 7–9	Months 10–12	Months 13–15	Months 16–18
↓ 58.10%	↓ 57.39%	↓ 56.95%	↓ 57.59%	↓ 56.00%	↓ 57.76%
(−70.98, −40.92)	(−69.91, −41.38)	(−70.70, −42.00)	(−68.90 −40.55)	(−69.78, −39.83)	(−71.43, −39.53)

- Most patients achieved an LDL-C level of < 1.8 mmol/L; 58% achieved an LDL-C level of < 1.4 mmol/L
- Patients receiving evolocumab in combination with statins ± ezetimibe were more likely to achieve goal†



*n=number of patients with at least one LDL-C value post evolocumab initiation. †Compared with patients receiving evolocumab

Conclusions

Unmet need

- Significant patients are still not at goal of LDL-C even with statin + ezetimibe therapy.[1,2]

- The risk of MACE was **lower** among patients who were treated with alirocumab than among those who received placebo, while the incidence of adverse events and of laboratory abnormalities was **similar**.[3]
- In the on-treatment analysis, average LDL-C levels were **lower** than the respective levels in the placebo group. [3]
- In subgroups of **statin intolerance**, **very low LDL-C**, **diabetes**, **prior CABG** and **PVD**, patients who received alirocumab had great risk reduction of MACE.[4-8]

ODYSSEY OUTCOMES

CABG, coronary artery bypass graft; LDL-C, low-density lipoprotein cholesterol; MACE, major adverse cardiovascular event; PVD, polyvascular disease.

1. Menzin J, et al. J Manag Care Spec Pharm. 2017;23(12):1270–6.
2. Harthers ML, et al. Atherosclerosis. 2016;252:e203.
3. Schwartz GG, et al. N Engl J Med. 2018;379(22):2097–107.
4. Diaz R, et al. Eur. Heart J. 2019;40(Suppl 1):ehz745.0119.
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6. Ray KK, et al. Lancet Diabetes Endocrinol. 2019;7:618-28.
7. Goodman SG, et al. J Am Coll Cardiol. 2019; 74:1177-86.
8. Jukema JW, et al. J Am Coll Cardiol. 2019;74:1167-76.

感謝聆聽