

# Krónikus koszorúér szindróma (CCS) diagnosztikája és kezelése'24

Prof. Dr. Tóth Kálmán

PTE KK I.sz. Belgyógyászati Klinika Kardiológiai Tanszék



## Stabil angina/SCAD/CCS ajánlás ESC'2006-13-19-24



European Heart Journal doi:10.1093/eurheartj/ehl002 **ESC Guidelines** 

Guidelines on the management of stable angina pectoris: full text<sup>‡</sup>

SCAD

**CCS** 

The Task Force on the Management of Stable Angina Pectoris of the European Society of Cardiology

Authors/Task Force Members, Kim Fox, Chairperson, London (UK)\*, Maria Angeles Alonso Garcia, Madrid (Spain), Diego Ardissino, Parma (Italy), Pawel Buszman, Katowice (Poland), Paolo G. Camici, London (UK), Filippo Crea, Roma (Italy), Caroline Daly, London (UK), Guy De Backer, Ghent (Belgium), Paul Hjemdahl, Stockholm (Sweden), José Lopez-Sendon, Madrid (Spain), Jean Marco, Toulouse (France), João Morais, Leiria (Portugal), John Pepper, London (UK), Udo Sechtem, Stuttgart (Germany), Maarten Simoons, Rotterdam (The Netherlands), Kristian Thygesen, Aarhus (Denmark)



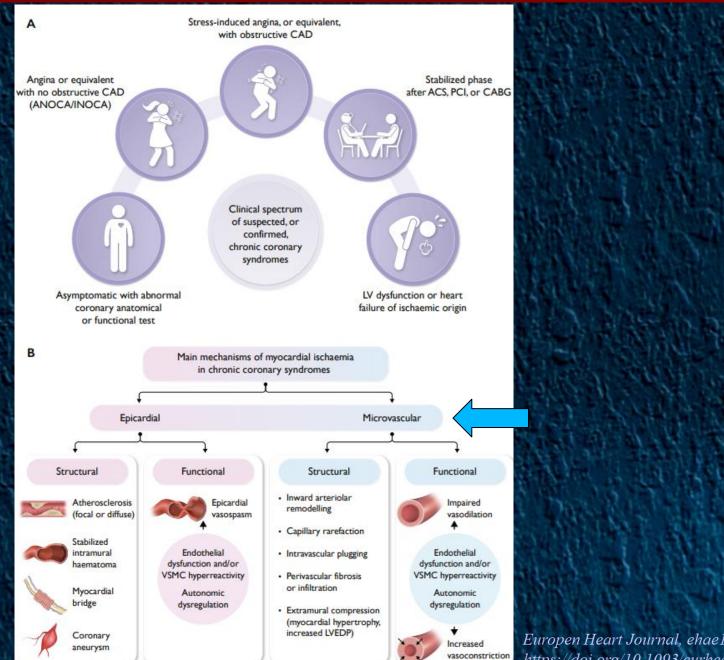
# Stabil angina/SCAD/CCS fogalmak

Stabil angina – klinikai tünetegyüttes

Stabil koszorúér betegség – kibővített fogalom: stabil angina, stabil állapotú post-MI, post-PCI, post-CABG betegek

CCS – minden, ami nem ACS

## Krónikus koronária szindróma típusai - ESC'24



Europen Heart Journal, ehae177, https://doi.org/10.1093/eurheartj/ehae177

#### Krónikus koronária szindróma ellátása - ESC'24

#### Step | Initial evaluation



Non-cardiac reason for symptoms identified: treat underlying cause

symptoms, physical examination

Resting ECG. Biochemistry

Pulmonary function test<sup>a</sup> Chest X-ray<sup>a</sup>

Unstable cardiac symptoms with angina, heart failure or arrhythmia: acute assessment by the ED

#### Családorvosi szint

#### Step 2 Further evaluation



Very low clinical likelihood of obstructive CAD (≤5%): consider deferring further testingb

Assess clinical likelihood of obstructive CAD

Echocardiography at rest Exercise ECG<sup>2</sup>

Severe comorbidities or low quality of life: consider no further testing and treat medically

#### Szakorvosi szint

Centrum szint

#### Step 3 Confirming diagnosis and estimating event-risk



Consider ANOCA/INOCA



CCTA: obstructive CAD?

 In individuals with low and moderate (>5-50%) clinical likelihood

Further non-invasive testing recommended based on clinical likelihood, availability. local expertise, patient characteristics and

preferenceb

Selective second-line imaging to increase post-test likelihood

#### Invasive angiography if:

- Very high clinical likelihood (>85%)
- Suspicion of high-risk obstructive CAD
- · Severe myocardial ischaemia



Functional imaging: myocardial ischaemia?

 In individuals with moderate and high (>15-85%) clinical likelihood

#### Step 4 Treatment



Lifestyle and risk factor modification

To improve prognosis



Disease-modifying medical treatment

To improve prognosis

#### Revascularization if:

· high risk of adverse events · GDMT fails to relieve symptoms



#### Revascularization

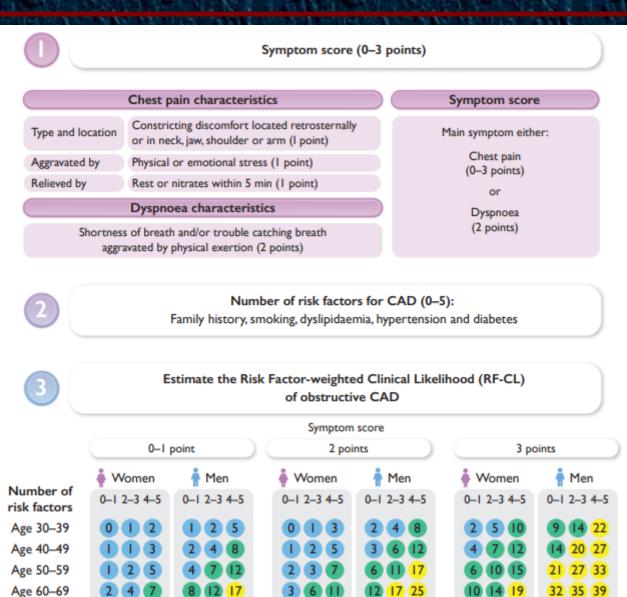
- To reduce symptoms
- To improve prognosis in patients with obstructive CAD who are at high risk of adverse events

#### Antianginal medical treatment

To reduce symptoms

Europen Heart Journal, ehae177, https://doi.org/10.1093/eurheartj/ehae177

#### Rizikó felmérés



Very low

22 27 34

Moderate

Age 70-80

Clinical likelihood:

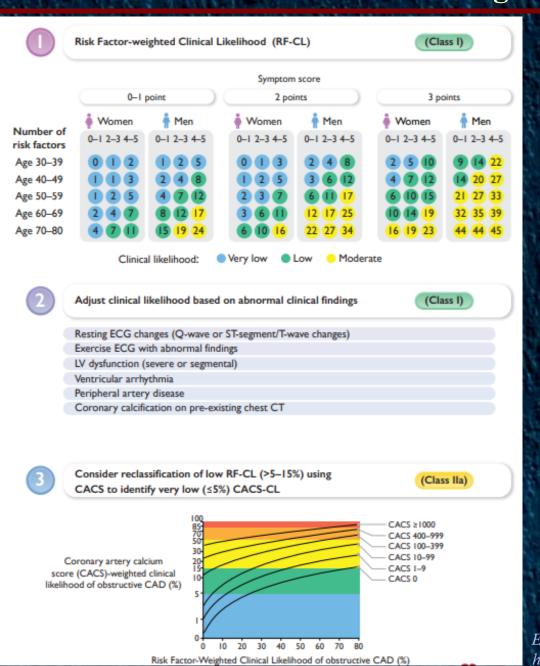
Europen Heart Journal, ehae177, https://doi.org/10.1093/eurheartj/ehae177

44 44 45

**ESC** 

16 19 23

### CCS klinikai valószínűsége



Europen Heart Journal, ehae177, https://doi.org/10.1093/eurheartj/ehae177

### Terheléses EKG

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>	
Exercise ECG is recommended in selected patients <sup>c</sup> for the assessment of exercise tolerance, symptoms, arrhythmias, BP response, and event risk.	1	С	
Exercise ECG may be considered as an alternative test to rule in and rule out CAD when non-invasive imaging tests are unavailable. 148,166,188,190,191	IIb	В	
An exercise ECG may be considered to refine risk stratification and treatment. 188	ПР	В	
In individuals with a low (>5%–15%) pre-test likelihood of obstructive CAD, an exercise ECG may be considered to identify patients in whom further testing can be deferred. <sup>144</sup>	ШЬ	c	
Exercise ECG is not recommended for diagnostic purposes in patients with ≥0.1 mV ST-segment depression on resting ECG, left bundle branch block or who are being treated with digitalis.	Ш	c	
In individuals with a low or moderate (>5%–50%) pre-test likelihood of obstructive CAD, an exercise ECG is not recommended to rule out CAD if CCTA or functional imaging tests are available. 148	m	С	© ESC 2024

BP, blood pressure; CAD, coronary artery disease; CCTA, coronary computed tomography angiography; ECG, electrocardiogram.

Europen Heart Journal, ehae177, https://doi.org/10.1093/eurheartj/ehae177

<sup>&</sup>lt;sup>a</sup>Class of recommendation.

<sup>&</sup>lt;sup>b</sup>Level of evidence.

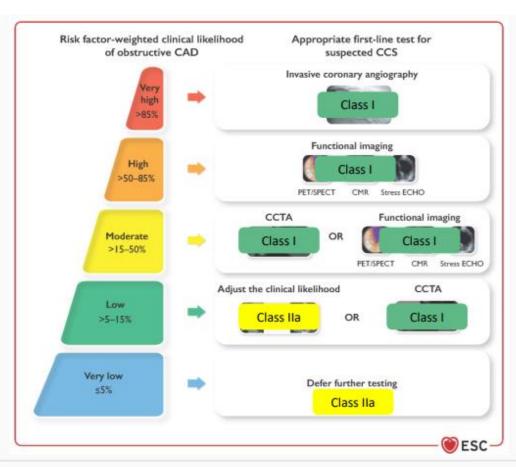
<sup>&</sup>lt;sup>c</sup>When this information will have an impact on diagnostic strategy or management.

### CCS diagnosztika I.

#### Summary



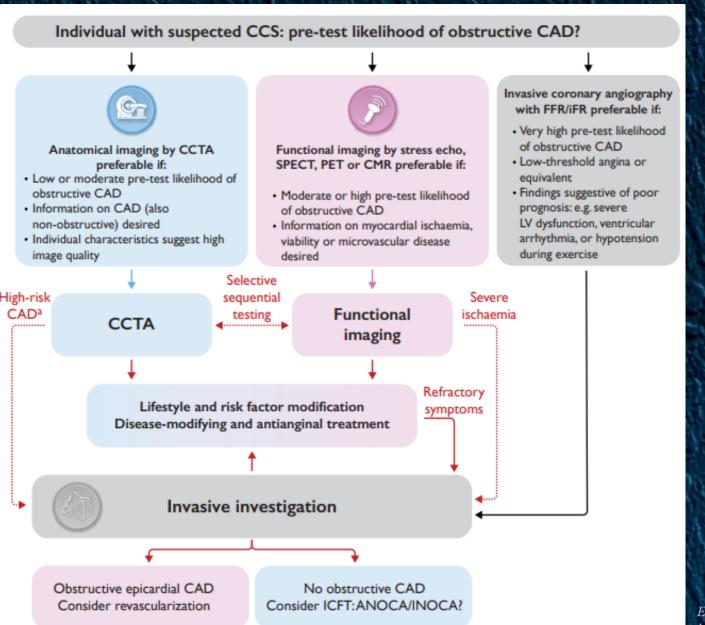
Appropriate first-line testing in symptomatic patients with suspected CCS



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2024 ESC Guidelines for the management of chronic coronary syndromes (European Heart Journal; 2024 – doi: 10.1093/eurheartj/ehae177)

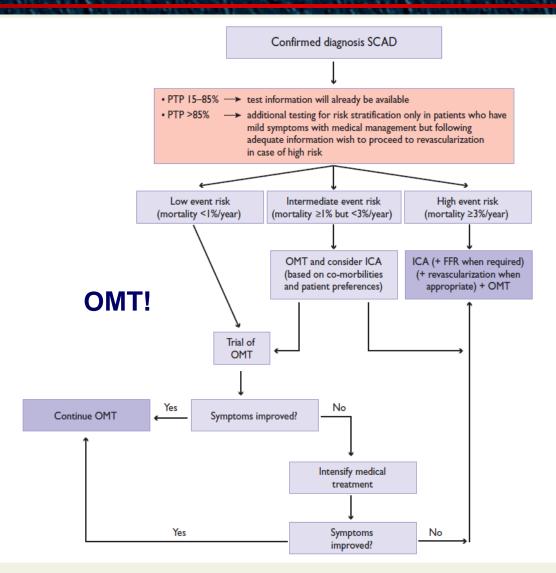
### CCS diagnosztika II.



Europen Heart Journal, ehae177, https://doi.org/10.1093/eurheartj/ehae177

## Kezelési stratégiák (13)





**Figure 3** Management based on risk determination for prognosis in patients with chest pain and suspected SCAD (for choice of test see Fig. 2, for definitions of event risk see Table 17). ICA = invasive coronary angiography; OMT = optimal medical therapy; PTP = pre-test probability; SCAD = stable coronary artery disease.

## Prognózis javítás: a "mágikus" négyes újra? (hármas/kettes)

# TCT aggr. gátló

(rezisztencia, dózis, kombináció, Gl vérzés, új szerek?)

ACE-inhibitor (ARB?)

**GLP1-agonista** 



Béta-blockoló

Kolhicin

Statin (új szerek!)

### **ABYSS**

#### ABYSS trial **#ESCCongress** Interruption vs. continuation of beta-blockers post-MI Conclusion The CV safety of interrupting vs. continuing beta-blockers could not be shown in patients with a history of myocardial infarction (MI) and there was no benefit to patients' quality of life (QoL). Impact on clinical practice The increase in hospitalisation for CV reasons and a negative effect on blood pressure levels, together with the absence of QoL improvement do not support beta-blocker interruption. Study objectives The ABYSS non-inferiority trial compared the effects of beta-blocker interruption vs. continuation on CV events and QoL in post-MI patients. Study population Primary endpoint Patients with prior MI taking Death, non-fatal MI, non-fatal stroke or hospitalisation for CV reasons long-term beta-blockers at longest follow-up LVEF ≥40% No CV events in the previous Median follow-up 3 years 6 months Interrupting O 23.8% beta-blocker Hazard ratio 1.16: 95% CI 1.01-1.33: Who and what? Continuing p=0.44 for non-inferiority 0 21.1% beta-blocker patients randomised Secondary endpoints 1:1 Interrupting Continuing beta-blocker beta-blocker Hospitalisation Blood pressure and for CV reasons QoL heart rate at 6 months Interrupting 0 18.9% beta-blocker No Increased Improvement (p<0.001) Where? Continuing 0 16.6% beta-blocker 49 sites in France

https://www.escardio.org/ Congresses-Events/

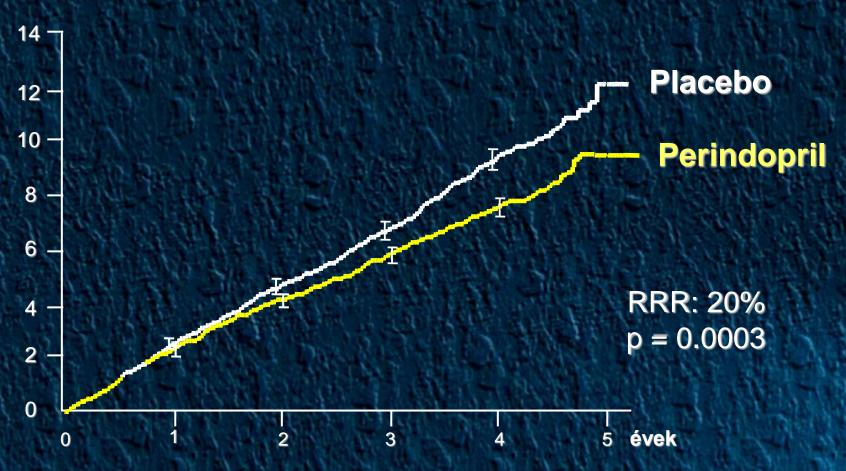
ESC-Congress/ Congress-resources

ESC



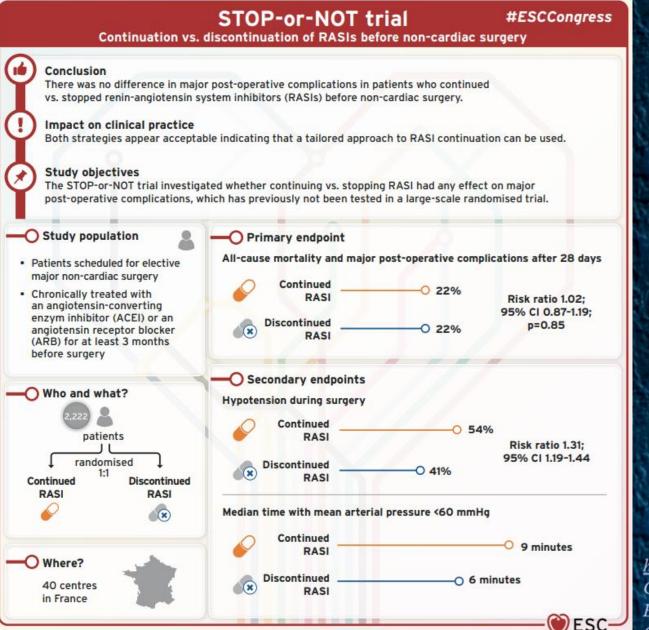
## Elsődleges végpont

## % CV halálozás, MI vagy szívmegállás



Placebo csoport, éves eseményráta: 2.4%

## STOP-or-NOT



https://www.escardio.org/ Congresses-Events/ ESC-Congress/ Congress-resources

## Terápia: Prognózist javító szerek - TAG

# Recommendations for antithrombotic therapy in patients with **©**ESC chronic coronary syndrome (1)

Long-term antithrombotic therapy in patients with chronic coronary syndrome and no clear indication for OAC

2019 Guidelines	Class	Level	2024 Guidelines	Class	Level
Antithrombotic therapy in patients wi	th chro	onic co	ronary syndrome		
Aspirin 75–100 mg daily is recommended in patients with a previous MI or revascularization.	1	Α	In CCS patients with a prior MI or remote PCI, aspirin 75–100 mg daily is recommended lifelong after an		•
Clopidogrel 75 mg daily is recommended as an alternative to aspirin in patients with aspirin intolerance.	initial period of DAPT.  B			^	
Clopidogrel 75 mg daily may be considered in preference to aspirin in symptomatic and asymptomatic patients with either PAD or a history of ischaemic stroke or transient ischaemic attack.	IIb	В	In CCS patients with a prior MI or remote PCI, clopidogrel 75 mg daily is recommended as a safe and effective alternative to aspirin monotherapy.	ı	Α

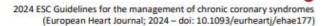
2024 ESC Guidelines for the management of chronic coronary syndromes (European Heart Journal; 2024 – doi: 10.1093/eurheartj/ehae177)

## Prognózist javító szerek - TAG

# Recommendations for antithrombotic therapy in patients with **©**ESC chronic coronary syndrome (2)

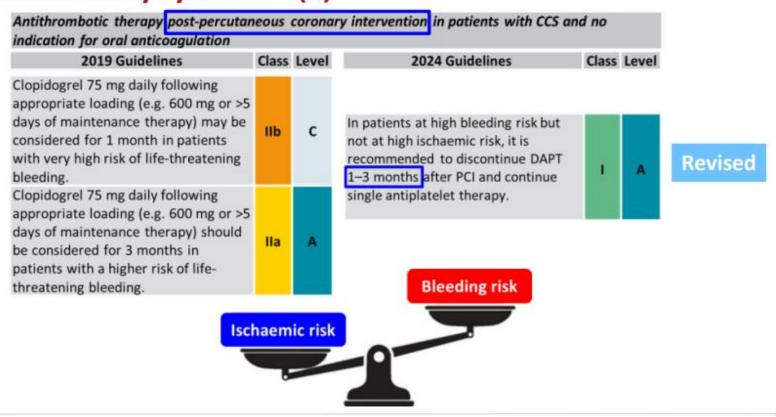
Long-term antithrombotic therapy in patients with chronic coronary syndrome and no clear indication for OAC

2019 Guidelines	Class	Level	2024 Guidelines	Class	Level
Antithrombotic therapy in patients wi	th chr	onic co	oronary syndrome cont.		
Aspirin 75–100 mg daily may be considered in patients without a history of MI or revascularization, but with definitive evidence of CAD on imaging.	IIb	С	In patients without prior MI or revascularization but with evidence of significant obstructive CAD aspirin 75–100 mg daily is recommended lifelong.	Ţ	В



#### TAG PCI után

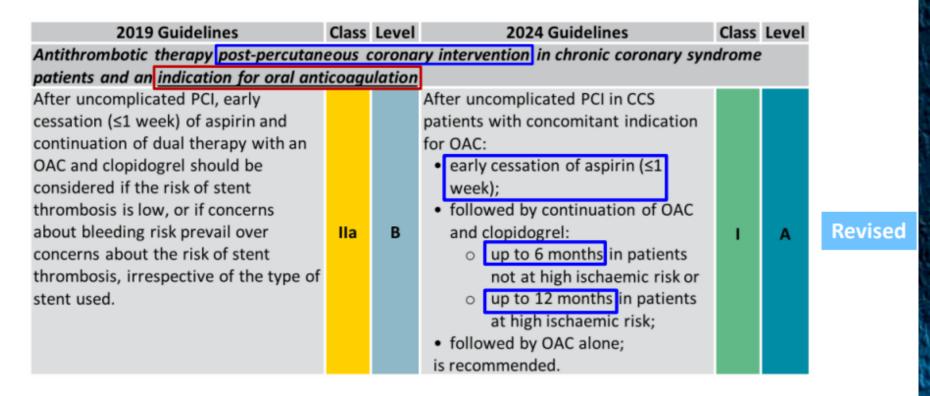
# Recommendations for antithrombotic therapy in patients with **WESC** chronic coronary syndrome (6)



2024 ESC Guidelines for the management of chronic coronary syndromes (European Heart Journal; 2024 – doi: 10.1093/eurheartj/ehae177)

#### TAG + OAC PCI után

# Recommendations for antithrombotic therapy in patients with **©**ESC chronic coronary syndrome (7)



2024 ESC Guidelines for the management of chronic coronary syndromes (European Heart Journal; 2024 – doi: 10.1093/eurhearti/ehae177)

### Rizikó besorolás

#### Magas ischaemiás kockázat meghatározása:

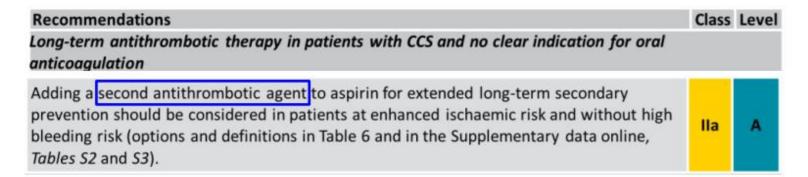
- Diffúz, több eret érintő CAD és az alábbiak közül legalább 1:
  - Diabetes mellitus, amely gyógyszeres kezelést igényel
  - Ismétlődő MI
  - PAD
  - CKD, ha az eGFR 15–59 ml/min/1.73 m<sup>2</sup>

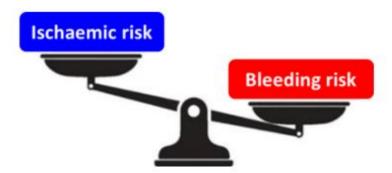
#### Mérsékelten magas ischaemiás kockázat meghatározása:

- Legalább 1 az alábbiak közül:
  - Több eret érintő/diffúz CAD
  - Diabetes mellitus, amely gyógyszeres kezelést igényel
  - Ismétlődő MI
  - PAD
  - HE
  - CKD, ha az eGFR 15–59 ml/min/1.73 m²

### TAG + magas ischaemiás rizikóban

# Recommendations for antithrombotic therapy in patients with **ESC** chronic coronary syndrome (4)





2024 ESC Guidelines for the management of chronic coronary syndromes (European Heart Journal; 2024 – doi: 10.1093/eurheartj/ehae177)

#### TAG + szerek

### Options for extended intensified antithrombotic therapy



Drug	Dose	Clinical setting	NNT (ischaemic outcomes)	NNH (bleeding outcomes)
Co-administered with a	aspirin 100 mg o.d.			
Rivaroxaban (COMPASS trial; vs. placebo)	2.5 mg b.i.d.	Patients with CAD or symptomatic PAD at high risk of ischaemic events	77	84 (modified-ISTH major bleeding)
Co-administered with I	ow-dose aspirin 75–162	? mg o.d.		
Clopidogrel, (6505/9961 of DAPT trial; vs. placebo)	75 mg/day	Post MI in patients who have tolerated DAPT for 1 year (25% ACS, 22% previous MI)	63	105 (moderate and severe GUSTO bleeds, or BARC 2, 3, and 5 bleeds)
Prasugrel, (3456/9961 of DAPT trial; vs. placebo)	10 mg/day (5 mg/day if body weight <60 kg or age ≥75 years)	Post PCI for MI in patients who have tolerated DAPT for 1 year	63	105 (as above)
Ticagrelor (PEGASUS- TIMI 54; vs. placebo)	60/90 mg b.i.d.	Post-MI in patients who have tolerated DAPT for 1 year	84	81 (TIMI major bleeds)

2024 ESC Guidelines for the management of chronic coronary syndromes (European Heart Journal; 2024 – doi: 10.1093/eurheartj/ehae177)

#### PPI használat

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
Use of proton pump inhibitors		
Concomitant use of a proton pump inhibitor is recommended in patients receiving aspirin monotherapy, DAPT, or OAC	1	Α
monotherapy who are at high risk of gastrointestinal bleeding.		

AF = atrial fibrillation; b.i.d. = bis in die (twice a day); CAD = coronary artery disease; CCS = chronic coronary syndromes; CHA2DS2-VASc = Cardiac failure, Hypertension, Age >\_75 [Doubled], Diabetes, Stroke [Doubled] Vascular disease, Age 6574 and Sex category [Female]; CKD = chronic kidney disease; DAPT = dual antiplatelet therapy; eGFR = estimated glomerular filtration rate; HF = heart failure; MI = myocardial infarction; NOAC = non-vitamin K antagonist oral anticoagulant; OAC = oral anticoagulant; o.d. = omni die (once a day); PAD = peripheral artery disease; PCI = percutaneous coronary intervention; VKA = vitamin K antagonist.

aClass of recommendation.

bLevel of evidence.

°Diffuse multivessel CAD with at least one of the following: diabetes mellitus requiring medication, recurrent MI, PAD, or CKD with eGFR 1559 mL/min/1.73 m2.

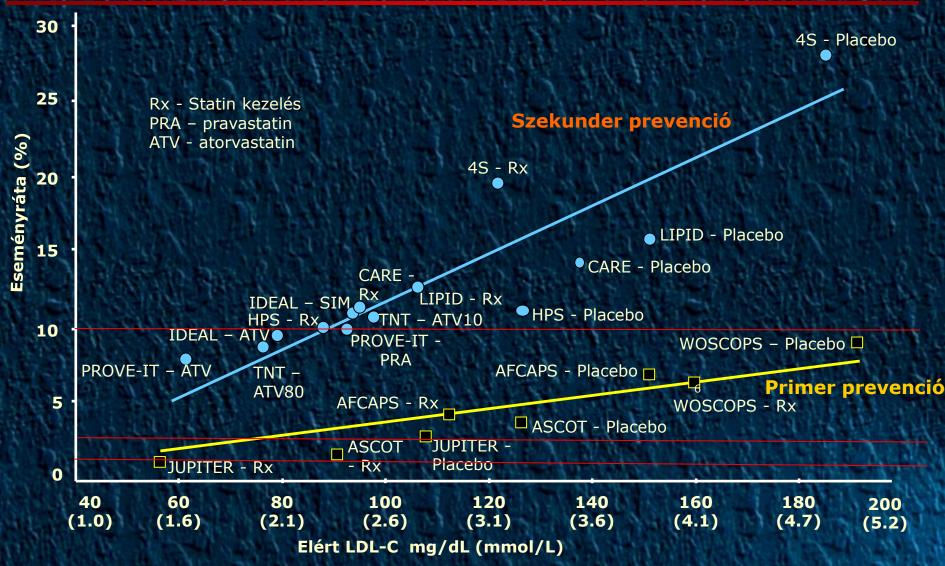
description intracerebral haemorrhage or ischaemic stroke, history of other intracranial pathology, recent gastrointestinal bleeding or anaemia due to possible gastrointestinal blood loss, other gastrointestinal pathology associated with increased bleeding risk, liver failure, bleeding diathesis or coagulopathy, extreme old age or frailty, or renal failure requiring dialysis or with eGFR <15 mL/min/1.73 m2.

eAt least one of the following: multivessel/diffuse CAD, diabetes mellitus requiring medication, recurrent MI, PAD, HF, or CKD with eGFR 1559 mL/min/1.73 m2. See summary of product characteristics for reduced doses or contraindications for each NOAC in patients with CKD, body weight <60 kg, age >7580 years, and/or drug interactions.

<sup>9</sup>Congestive HF, hypertension, age >\_75 years (2 points), diabetes, prior stroke/transient ischaemic attack/embolus (2 points), vascular disease (CAD on imaging or angiography, 312 prior MI, PAD, or aortic plaque), age 6574 years, and female sex.

<sup>h</sup>Risk of stent thrombosis encompasses (i) the risk of thrombosis occurring and (ii) the risk of death should stent thrombosis occur, both of which relate to anatomical, procedural, and clinical characteristics. Risk factors for CCS patients include stenting of left main stem, proximal LAD, or last remaining patent artery; suboptimal stent deployment; stent length >60 mm; diabetes mellitus; CKD; bifurcation with two stents implanted; treatment of chronic total occlusion; and previous stent thrombosis on adequate antithrombotic therapy.

# Az LDL-koleszterin és az 5 éves major koszorúér események kockázatának kapcsolata



Rosensen RS. Exp Opin Emerg Drugs 2004;9(2):269-, LaRosa JC et al. N Engl J Med 2005;352:e-version, Ridker PM, N Engl J Med 2008;359:2195- alapján

## **IMPROVE-IT - HIJ-PROPER**

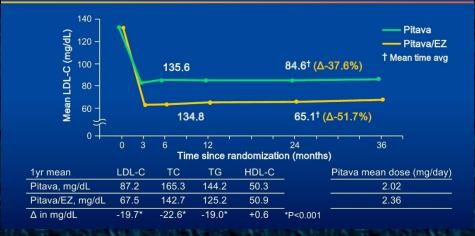
#### **LDL-C and Lipid Changes**





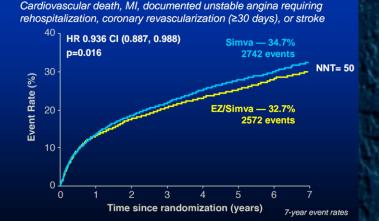
#### LDL-C and Lipid Changes





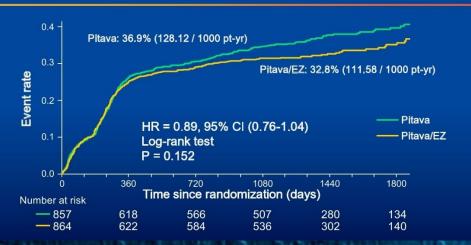
#### **Primary Endpoint — ITT**



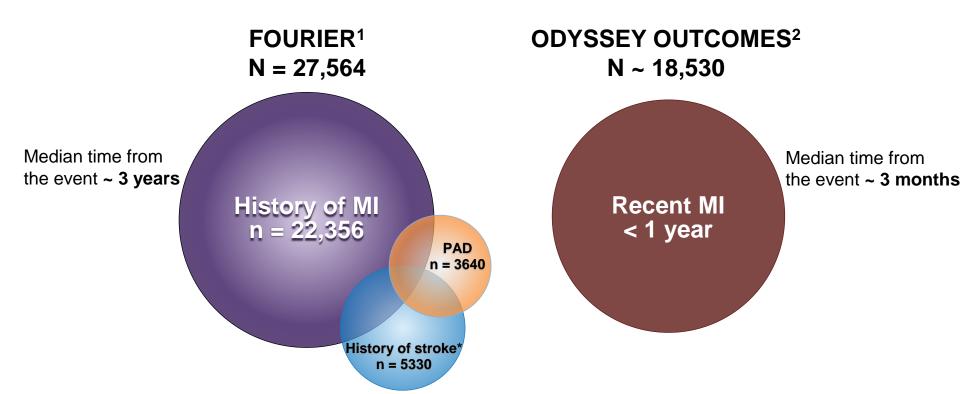


#### Primary Endpoint (composite)





# PCSK9 - FOURIER és ODYSSEY tanulmányok



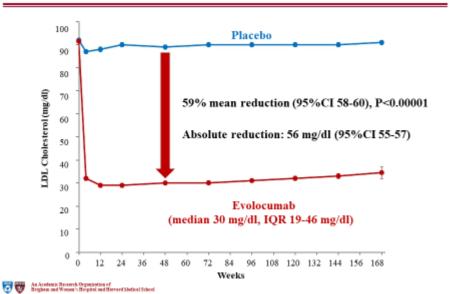
 <sup>\*</sup>Non-haemorrhagic stroke.

<sup>1.</sup> Sabatine MS, et al. Am Heart J 2016;173:94-101. 2. Schwartz GG, et al. Am Heart J 2014;168:682-9.



#### **LDL Cholesterol**



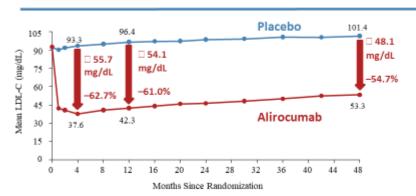






ACC.18

#### LDL-C: On-Treatment Analysis



Excludes LDL-C values after premature treatment discontinuation or blinded switch to placebo Approximately 75% of months of active treatment were at the 75 mg dose



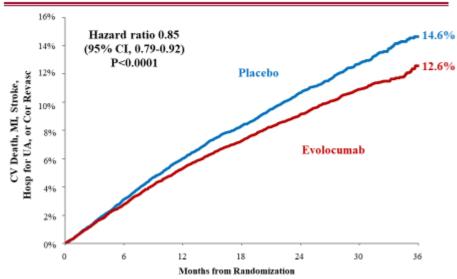






#### **Primary Endpoint**







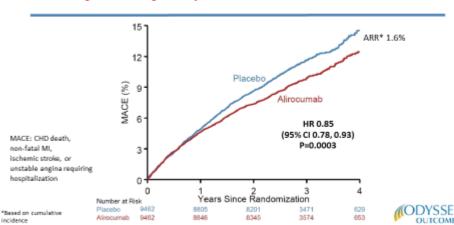
ACC.18



An Acrefornic Serverch Organization of Brighton and Women's Hospital and Harvard Medical School



#### Primary Efficacy Endpoint: MACE

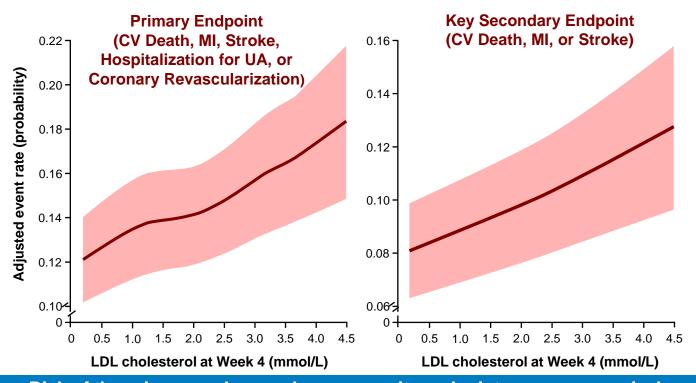








# Relationship Between Achieved LDL-C Level at Week 4 and Risk for the Primary and Key Secondary Efficacy Composite Endpoints



Risk of the primary and secondary composite endpoints was progressively lower as the achieved LDL-C at week 4 was reduced

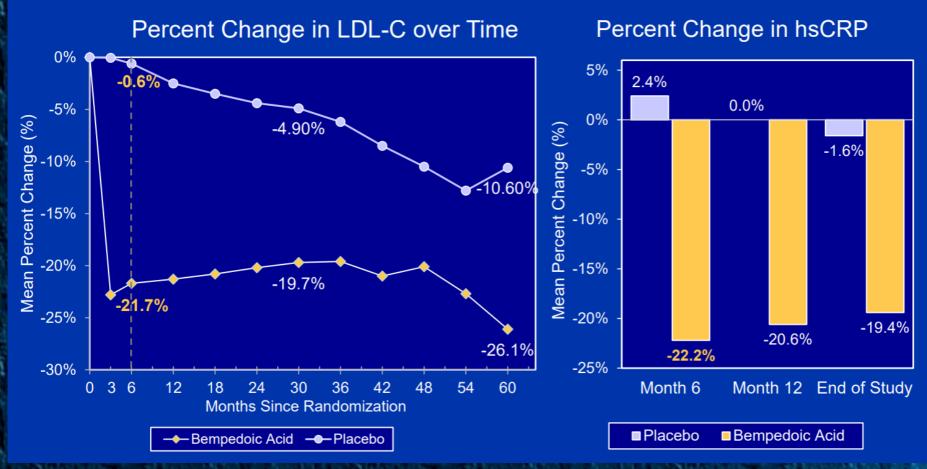
For the primary endpoint p = 0.0012 for the β coefficient. For the secondary endpoint p = 0.0001 for the β coefficient.

CV = cardiovascular, MI = myocardial infarction, UA = unstable angina. The blue line represents the hazard ratio and shaded areas are the 95% CIs of the regression model estimate. Giugliano RP, et al. *Lancet*. [published online ahead of print August 28, 2017]. doi: 10.1016/ S0140-6736(17)32290-0



#### A CLEAR vizsgálat - Bempedonsav

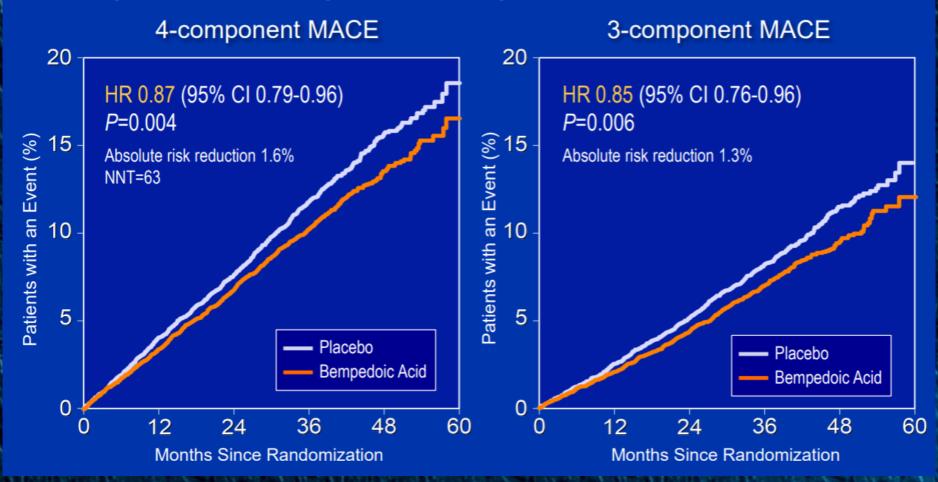
## Effect of Trial Regimens on LDL-C and hsCRP



13.970 statin intoleráns beteg

### A CLEAR vizsgálat

## Primary and First Key Secondary Cardiovascular End Points



### Prognózist javító szerek - lipidcsökkentés

# Recommendations for <u>lipid-lowering drugs</u> in patients with chronic coronary syndrome



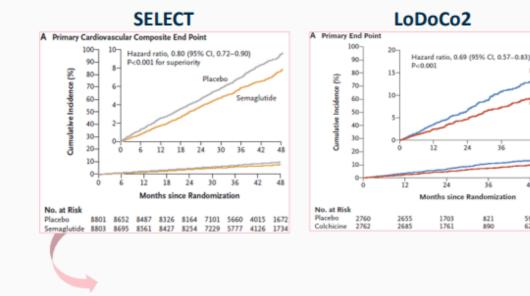
	Recommendations	Class	Level	
	Lipid-lowering treatment with an LDL-C goal of <1.4 mmol/L (55 mg/dL) and a ≥50% reduction in LDL-C vs. baseline is recommended.	1	Α	
	A high-intensity statin up to the highest tolerated dose to reach the LDL-C goals is recommended for all patients with CCS.	1	Α	
	If a patient's goal is not achieved with the maximum tolerated dose of statin, combination with ezetimibe is recommended.	1	В	
	For patients who are statin intolerant and do not achieve their goal on ezetimibe, combination with bempedoic acid is recommended.	1	В	New
>	For patients who do not achieve their goal on a maximum tolerated dose of statin and ezetimibe, combination with a PCSK9 inhibitor is recommended.	1	Α	
	For patients who do not achieve their goal on a maximum tolerated dose of statin and ezetimibe, combination with bempedoic acid should be considered.	lla	С	New
	For patients with a recurrent atherothrombotic event (not necessarily of the same type as the first event) while taking maximally tolerated statin therapy, an LDL-C goal of <1.0 mmol/L (<40 mg/dL) may be considered.	IIb	В	

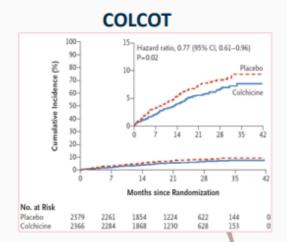
<sup>\*</sup> Nissen SE, at al. N Engl J Med 2023;388:1353-1364

2024 ESC Guidelines for the management of chronic coronary syndromes (European Heart Journal; 2024 – doi: 10.1093/eurheartj/ehae177)

### Prognózist javító új szerek

#### Event-Preventing Metabolic & Anti-inflammatory Drugs





New

The GLP-1 receptor agonist semaglutide should be considered in overweight (BMI >27 kg/m2) or obese CCS patients without diabetes to reduce CV mortality, MI, or stroke.

IIa B

In CCS patients with atherosclerotic CAD, low-dose colchicine (0.5 mg daily) should be considered to reduce myocardial infarction, stroke, and need for revascularization.

IIa A Revised

For lipid-lowering, antidiabetic, antihypertensive, HF and AF therapies please refer to guidelines and other congress 2024 sessions

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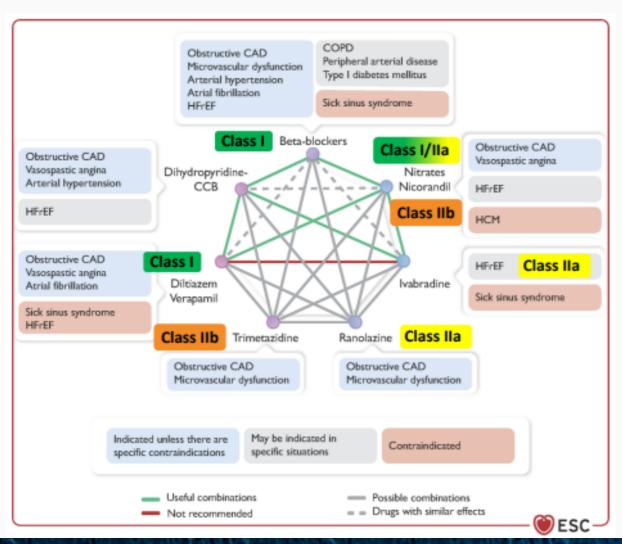
2024 ESC Guidelines for the management of chronic coronary syndromes (European Heart Journal; 2024 – doi: 10.1093/eurheartj/ehae177)

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## CCS gyógyszeres kezelése

# **Antianginal Drugs and Combinations**



## Antianginás gyógyszerek

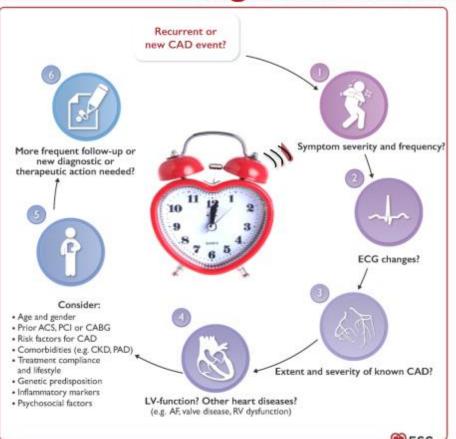
Recommendations	Class <sup>a</sup>	Levelb
General strategy		
It is recommended to tailor the selection of antianginal drugs to the patient's characteristics, comorbidities, concomitant medications, treatment tolerability, and underlying pathophysiology of angina, also considering local drug availability and cost.	1	с
Selection of antianginal medication		
Short-acting nitrates are recommended for immediate relief of angina. 536,537	1	В
Initial treatment with beta-blockers and/or CCBs to control heart rate and symptoms is recommended for most patients with CCS. <sup>c</sup> 518,538	1	В
If anginal symptoms are not successfully controlled by initial treatment with a beta-blocker or a CCB alone, the combination of a beta-blocker and a DHP-CCB should be considered, unless contraindicated. <sup>505,538,539</sup>	lla	В
Long-acting nitrates or ranolazine should be considered as add-on therapy in patients with inadequate control of symptoms while on treatment with beta-blockers and/or CCBs, or as part of initial treatment in properly selected patients. <sup>d</sup> 513,540	lla	В

When long-acting nitrates are prescribed, a nitrate-free or low-nitrate interval should be considered to reduce tolerance. 540	lla	В
Ivabradine should be considered as add-on antianginal therapy in patients with left ventricular systolic dysfunction (LVEF <40%) and inadequate control of symptoms, or as part of initial treatment in properly selected patients. 541,542	lla	В
Nicorandil or trimetazidine may be considered as add-on therapy in patients with inadequate control of symptoms while on treatment with beta-blockers and/or CCBs, or as part of initial treatment in properly selected patients. 543–550	ШЬ	В
Ivabradine is not recommended as add-on therapy in patients with CCS, LVEF >40%, and no clinical heart failure. <sup>509</sup>	Ш	В
Combination of ivabradine with non-DHP-CCB or other strong CYP3A4 inhibitors is not recommended. 551	III	В
Nitrates are not recommended in patients with hypertrophic cardiomyopathy or in co-administration with phosphodiesterase inhibitors. 552,553	Ш	В

Europen Heart Journal, ehae177, https://doi.org/10.1093/eurheartj/ehae177

### CCS gondozása

## Long-term Follow-up of CCS Patients



The use of one or more of the following test results is recommended to identify individuals at high risk of adverse events:

- exercise ECG: Duke Treadmill Score ≤ -10;
- stress SPECT or PET perfusion imaging: area of ischaemia ≥10% of the LV myocardium;
- stress echocardiography: ≥3 of 16 segments with stress-induced hypokinesia or akinesia;
- stress CMR: ≥2 of 16 segments with stress perfusion defects or ≥3 dobutamine-induced dysfunctional segments;
- CCTA: left main disease with ≥50% stenosis, three-vessel disease with ≥70 stenosis or twovessel disease with ≥70% stenosis, including the proximal LAD or one-vessel disease of the proximal LAD with ≥70% stenosis and FFR-CT <0.8</li>

In individuals at high risk of adverse events (regardless of symptoms), ICA—complemented by invasive coronary pressure (FFR/iFR) when appropriate—is recommended, with the aim of refining risk stratification and improving symptoms and cardiovascular outcomes by revascularization.

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# Köszönöm a figyelmet!

