Antiagregační léčba akutní fáze infarktu myokardu

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ESC GUIDELINES

2023 ESC Guidelines for the management of acute coronary syndromes

Developed by the task force on the management of acute coronary syndromes of the European Society of Cardiology (ESC)

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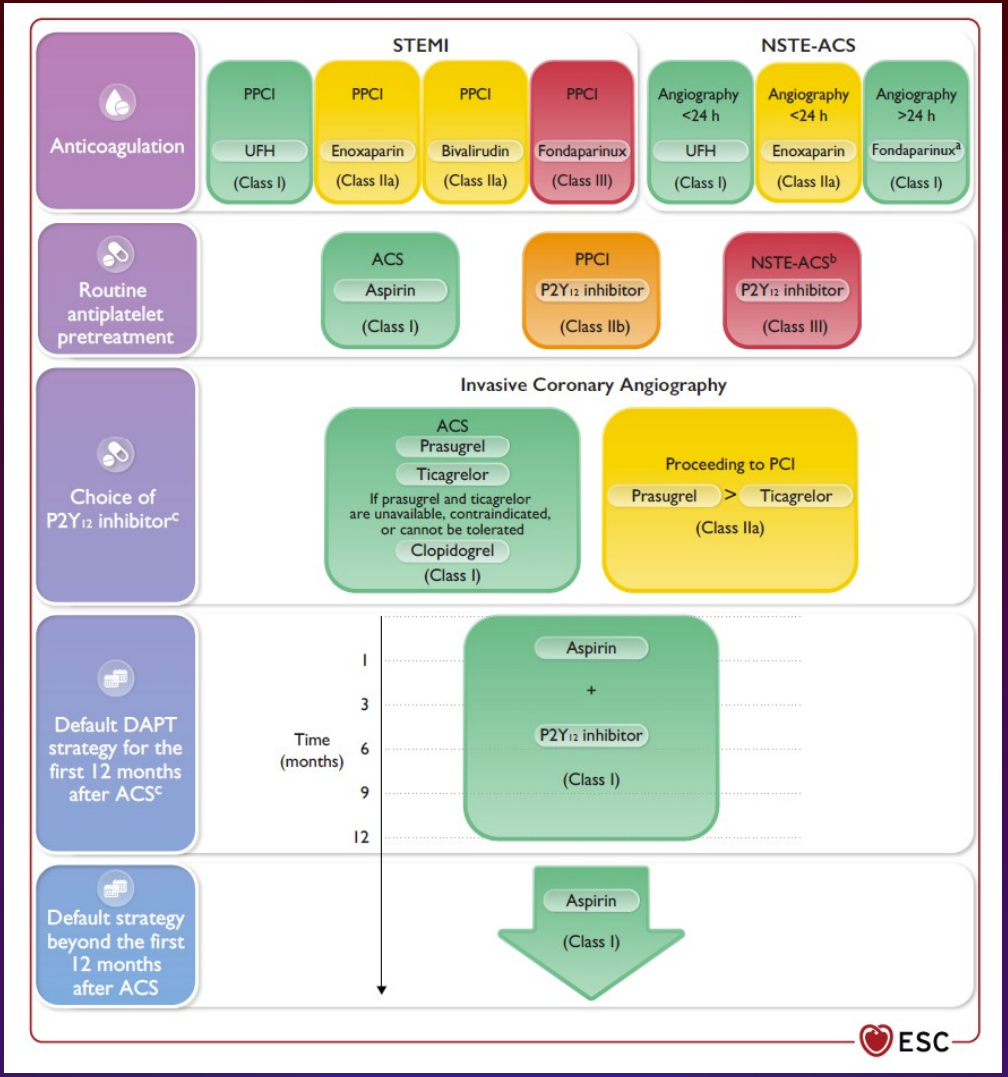
Antiagregační léčba akutní fáze infarktu myokardu

Table 6 **Dose regimen of antiplatelet and anticoagulant drugs in acute coronary syndrome patients**

I. Antiplatelet drugs	
Aspirin	LD of 150–300 mg orally or 75–250 mg i.v. if oral ingestion is not possible, followed by oral MD of 75–100 mg o.d.; no specific dose adjustment in CKD patients.
$P2Y_{12}$ receptor inhibitors (oral or i.v.)	
Clopidogrel	LD of 300–600 mg orally, followed by an MD of 75 mg o.d.; no specific dose adjustment in CKD patients. Fibrinolysis: at the time of fibrinolysis an initial dose of 300 mg (75 mg for patients older than 75 years of age).
Prasugrel	LD of 60 mg orally, followed by an MD of 10 mg o.d. In patients with body weight <60 kg, an MD of 5 mg o.d. is recommended. In patients aged ≥75 years, prasugrel should be used with caution, but a MD of 5 mg o.d. should be used if treatment is deemed necessary. No specific dose adjustment in CKD patients. Prior stroke is a contraindication for prasugrel.
Ticagrelor	LD of 180 mg orally, followed by an MD of 90 mg b.i.d.; no specific dose adjustment in CKD patients.
Cangrelor	Bolus of 30 mcg/kg i.v. followed by 4 mcg/kg/min infusion for at least 2 h or the duration of the procedure (whichever is longer). In the transition from cangrelor to a thienopyridine, the thienopyridine should be administered immediately after discontinuation of cangrelor with an LD (clopidogrel 600 mg or prasugrel 60 mg); to avoid a potential DDI, prasugrel may also be administered 30 min before the cangrelor infusion is stopped. Ticagrelor (LD 180 mg) should be administered at the time of PCI to minimize the potential gap in platelet inhibition during the transition phase.
GP IIb/IIIa receptor inhibitors (i.v.)	
Eptifibatide	Double bolus of 180 mcg/kg i.v. (given at a 10-min interval) followed by an infusion of 2.0 mcg/kg/min for up to 18 h. For CrCl 30–50 mL/min: first LD, 180 mcg/kg i.v. bolus (max 22.6 mg); maintenance infusion, 1 mcg/kg/min (max 7.5 mg/h). Second LD (if PCI), 180 mcg/kg i.v. bolus (max 22.6 mg) should be administered 10 min after the first bolus. Contraindicated in patients with end-stage renal disease and with prior ICH, ischaemic stroke within 30 days, fibrinolysis, or platelet count <100 000/mm^3.
Tirofiban	Bolus of 25 mcg/kg i.v. over 3 min, followed by an infusion of 0.15 mcg/kg/min for up to 18 h. For CrCl ≤60 mL/min: LD, 25 mcg/kg i.v. over 5 min followed by a maintenance infusion of 0.075 mcg/kg/min continued for up to 18 h. Contraindicated in patients with prior ICH, ischaemic stroke within 30 days, fibrinolysis, or platelet count <100 000/mm^3.

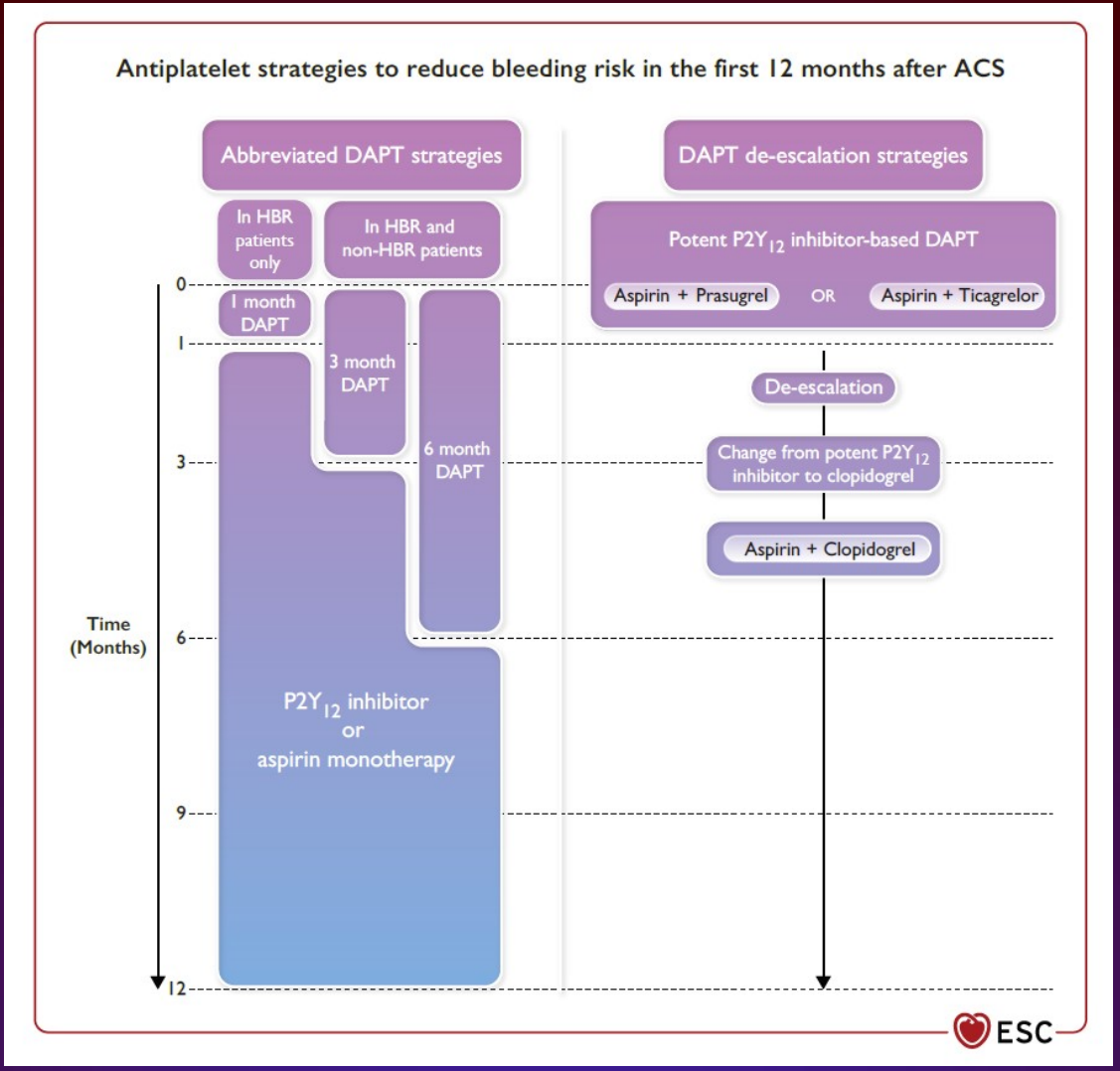
Antiagregační léčba akutní fáze infarktu myokardu



Antiagregační léčba akutní fáze infarktu myokardu : předléčení

PRE-TREATMENT IN ACS						
ACCOAST [7]	2013	4033 pts	Pre-treatment with prasugrel vs. placebo (NSTE-ACS)	30 days	death from CV causes, MI, stroke, urgent revascularization or GP IIb/IIIa bailout	HR 1.02; 95% CI, 0.84 to 1.25; $p = 0.81$
DUBIUS [8]	2020	1499 pts	Pre-treatment with ticagrelor vs. no pre-treatment (NSTE-ACS)	30 days	death due to vascular causes, non-fatal MI or non-fatal stroke	ARR: –0.46; 95% CI: –2.87 to 1.89
ATLANTIC [10]	2014	1862 pts	Pre-treatment with ticagrelor vs. in-hospital treatment with ticagrelor (STEMI)	30 days	70% or greater resolution of ST-elevation / no TIMI flow grade 3 in the IRA	ST-elevation: OR 0.93; 95% CI, 0.69 to 1.25; $p = 0.63$ TIMI flow: 0.97; 95% CI, 0.75 to 1.25; $p = 0.82$

Antiagregační léčba akutní fáze infarktu myokardu : zkrácení léčby a deeskalace léčby



Antiagregační léčba akutní fáze infarktu myokardu : zkrácení léčby a deeskalace léčby

RTENING OF DAPT						
WILIGHT [11]	2019	7119 pts	3 vs. 12 mo ticagrelor-based DAPT	15 mo	BARC type 2,3, or 5	HR 0.99; 95% CI, 0.78 to 1.25; $P_{\text{non-inferiority}}$ <
ICO [12]	2020	3056 pts	3 vs. 12 mo ticagrelor-based DAPT	12 mo	TIMI major bleeding, all-cause death, MI, ST, stroke, or TVR	HR 0.66; 95% CI, 0.48 to 0.92; $p = 0.01$
TOPDAPT-2 [13]	2019	3045 pts	1 vs. 12 mo clopidogrel-based DAPT	12 mo	CV death, MI, ST, stroke, or TIMI major or minor bleeding	HR 0.26, 95% CI, 0.11 to 0.64, $p = 0.004$
TOPDAPT2-ACS [14]	2022	4169 pts	1 vs. 12 mo clopidogrel-based DAPT	12 mo	CV death, MI, ST, stroke, or TIMI major or minor bleeding	HR 1.14; 95% CI, 0.80 to 1.6; $P_{\text{non-inferiority}}$ =
IASTER-DAPT [15]	2021	4434 pts	1 vs. $\geq$ 3 mo clopidogrel-based DAPT	11 mo	all-cause death, MI, stroke, or BARC type 3, or 5	−0.23 percentage points; 95% CI, −1.80 to $P_{\text{non-inferiority}} < 0.001$
SCALATION OF DAPT						
ROPICAL-ACS [16]	2017	2610 pts	de-escalation to clopidogrel-based DAPT at day 7–14 after discharge vs. standard DAPT	12 mo	CV death, MI, stroke, BARC type $\geq$ 2	HR 0.81; 95% CI, 0.62 to 1.06; $P_{\text{non-inferiority}}$ =
OPULAR GENETICS [17]	2019	2499 pts	de-escalation to clopidogrel-based DAPT at day 1 to 3 after PCI vs. standard DAPT	12 mo	all-cause death, MI, ST, stroke, or PLATO major bleeding	95% CI, 2.0 to 0.7; $P_{\text{non-inferiority}} < 0.001$
OPIC [18]	2017	646 pts	de-escalation 30 days after PCI to clopidogrel-based DAPT vs. standard DAPT	12 mo	CV death, TVR, stroke, BARC type $\geq$ 2	HR 0.48; 95% CI 0.34–0.68; $p < 0.01$
ALOS-AMI [19]	2021	2697 pts	de-escalation 30 days after PCI to clopidogrel-based DAPT vs. standard DAPT	12 mo	CV death, MI, stroke, BARC type 2,3, or 5	HR 0.55; 95% CI, 0.40 to 0.76; $P_{\text{non-inferiority}}$ <

Antiagregační léčba akutní fáze infarktu myokardu : zkrácení DAPT

JAMA Cardiology | Original Investigation

Ticagrelor or Clopidogrel Monotherapy vs Dual Antiplatelet Therapy After Percutaneous Coronary Intervention

A Systematic Review and Patient-Level Meta-Analysis

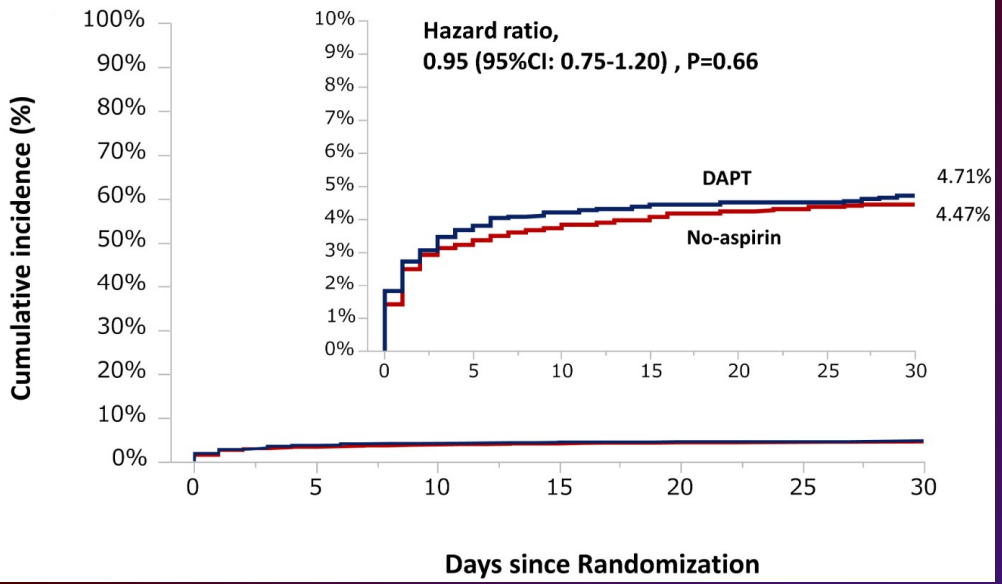
Marco Valgimigli, MD, PhD; Felice Gragnano, MD, PhD; Mattia Branca, PhD; Anna Franzone, MD, PhD; Bruno R. da Costa, PhD; Usman Baber, MD;

CONCLUSIONS AND RELEVANCE This systematic review and meta-analysis found that ticagrelor monotherapy was noninferior to DAPT for all-cause death, MI, or stroke and superior for major bleeding and NACE. Clopidogrel monotherapy was similarly associated with reduced bleeding but was not noninferior to DAPT for all-cause death, MI, or stroke, largely because of risk observed in 1 trial that exclusively included East Asian patients and a hazard that was driven by an excess of noncardiovascular death.

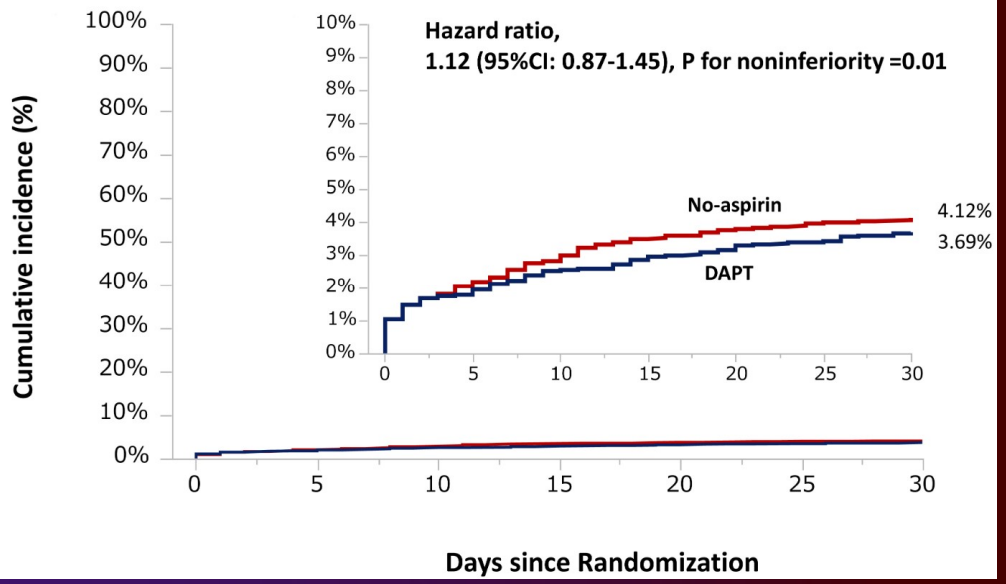
JAMA Cardiol. 2024;9(5):437-448. doi:10.1001/jamacardio.2024.0133
Published online March 20, 2024.

Antiagregační léčba akutní fáze infarktu myokardu: **STOPDAPT-3**

Co-primary bleeding endpoint



Co-primary cardiovascular endpoint



Circulation
Volume 149, Issue 8, 20 February 2024; Pages 585-600
https://doi.org/10.1161/CIRCULATIONAHA.123.066720

American Heart Association.

ORIGINAL RESEARCH ARTICLE

An Aspirin-Free Versus Dual Antiplatelet Strategy for Coronary Stenting: STOPDAPT-3 Randomized Trial

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Antiplatelet therapy		
Aspirin is recommended for all patients without contraindications at an initial oral LD of 150–300 mg (or 75–250 mg i.v.) and an MD of 75–100 mg o.d. for long-term treatment.[284,285]	I	A
In all ACS patients, a $P2Y_{12}$ receptor inhibitor is recommended in addition to aspirin, given as an initial oral LD followed by an MD for 12 months unless there is HBR[c].[238,239,263,286]	I	A
A proton pump inhibitor in combination with DAPT is recommended in patients at high risk of gastrointestinal bleeding.[287,288]	I	A
Prasugrel is recommended in $P2Y_{12}$ receptor inhibitor-naïve patients proceeding to PCI (60 mg LD, 10 mg o.d. MD, 5 mg o.d. MD for patients aged ≥75 years or with a body weight <60 kg).[239]	I	B
Ticagrelor is recommended irrespective of the treatment strategy (invasive or conservative) (180 mg LD, 90 mg b.i.d. MD).[238]	I	B
Clopidogrel (300–600 mg LD, 75 mg o.d. MD) is recommended when prasugrel or ticagrelor are not available, cannot be tolerated, or are contraindicated.[263,289]	I	C
If patients presenting with ACS stop DAPT to undergo CABG, it is recommended they resume DAPT after surgery for at least 12 months.	I	C
Prasugrel should be considered in preference to ticagrelor for ACS patients who proceed to PCI.[244,290]	IIa	B
GP IIb/IIIa receptor antagonists should be considered if there is evidence of no-reflow or a thrombotic complication during PCI.	IIa	C
In $P2Y_{12}$ receptor inhibitor-naïve patients undergoing PCI, cangrelor may be considered.[251–254]	IIb	A
In older ACS patients,[d] especially if HBR,[c] clopidogrel as the $P2Y_{12}$ receptor inhibitor may be considered.[242,243,291]	IIb	B

Antiagregační léčba akutní fáze infarktu myokardu : mikrovaskulární obstrukce

TABLE 1 Pathogenesis of coronary microvascular obstruction (MVO).

1a	Genetic predisposition and comorbidities	Ischaemic pre-conditioning can be a protective factor against MVO.
		Genetic factors that increase susceptibility to MVO include 1976T.C polyporphism of the adenosine 2A, genetic variations within defined regions of VEGFA and CDKN2B-AS1 genes, sex-specific allelic variants within MYH15, VEGFA and NT5E genes (Niccoli et al., 2016)
1b	Pre-existing coronary microvascular obstruction	Impaired coronary flow reserve can occur in patients with increased age and certain health conditions such as hypertension, diabetes, dyslipidaemia, insulin resistance and chronic inflammatory diseases (Crea et al., 2014)
2	Ischaemic Injury	Important clinical predictors of MVO are the ischaemia duration and extent confirmed on ECG by ST resolution, echocardiogram, CMR and invasive coronary indices to measure MVO (Niccoli et al., 2016)
3	Reperfusion Injury	Generally occurs when ischaemia lasts >3 h. MVO is caused by neutrophil-platelet aggregates that produce vasoconstrictors and inflammatory mediators, obliterating the vessel lumen (Thomas and Storey, 2015)
4	Distal Embolisation	Re-opening of blocked coronary arteries can cause distal embolisation of plaque material. The embolised material is thought to be biologically active and aggravates reperfusion injury even if the microcirculation is not mechanically obstructed. Myocardial perfusion generally falls when these embolised particles obstruct >50% of the coronary capillaries (Topol and Yadav, 2000)

Front. Mol. Biosci. 11:1287553.
doi: 10.3389/fmolb.2024.1287553

Antiagregační léčba akutní fáze infarktu myokardu : mikrovaskulární obstrukce

Nasycovací dávka aspirinu 500mg lepší než 250mg : menší mikrovaskulární obstrukce (MVO), lepší funkce LK.

Calvieri, C., Galea, N., Cilia, F., Pambianchi, G., Mancuso, G., Filomena, D., et al. (2022). Protective value of aspirin loading dose on left ventricular remodeling after ST-elevation myocardial infarction. Front. Cardiovasc. Med. 9, 786509. doi:10.3389/fcvm.2022.786509

Ticagrelor vede ke snížení MVO ve srovnání s clopidogrelem a má výslednou lepší funkci LK.

Wang, X., Li, X., Wu, H., Li, R., Liu, H., Wang, L., et al. (2019). Beneficial effect of ticagrelor on microvascular perfusion in patients with ST-segment elevation myocardial infarction undergoing a primary percutaneous coronary intervention. Coron. Artery Dis. 30 (5), 317–322.

Cangrelor je srovnatelný s ticagrelorem z hlediska rozsahu MVO.

Ubaid, S., Ford, T. J., Berry, C., Murray, H. M., Wrigley, B., Khan, N., et al. (2019). Cangrelor versus ticagrelor in patients treated with primary percutaneous coronary intervention: impact on platelet activity, myocardial microvascular function and infarct size: a randomized controlled trial. Thrombosis Haemostasis 119 (7), 1171–1181.

Front. Mol. Biosci. 11:1287553.
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Antiagregační léčba akutní fáze infarktu myokardu : mikrovaskulární obstrukce

Inhibitory GPVI (kolagenem aktivovaná destičková agregace)

Revacept, Glenzocimab

omezí interakci destička-neutrofil

Inhibitory komplexu GPI-IX-V-vWF (úvodní adheze na poraněný povrch)

Caplacizumab

léčba pacientů s TTP, brání mikrovaskulární obstrukci

Inhibitor P-selectinu (adhezní molekula destička-epitel-leukocyt)

Crizanlizumab

Front. Mol. Biosci. 11:1287553.
doi: 10.3389/fmolb.2024.1287553

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