Protidestičková léčba

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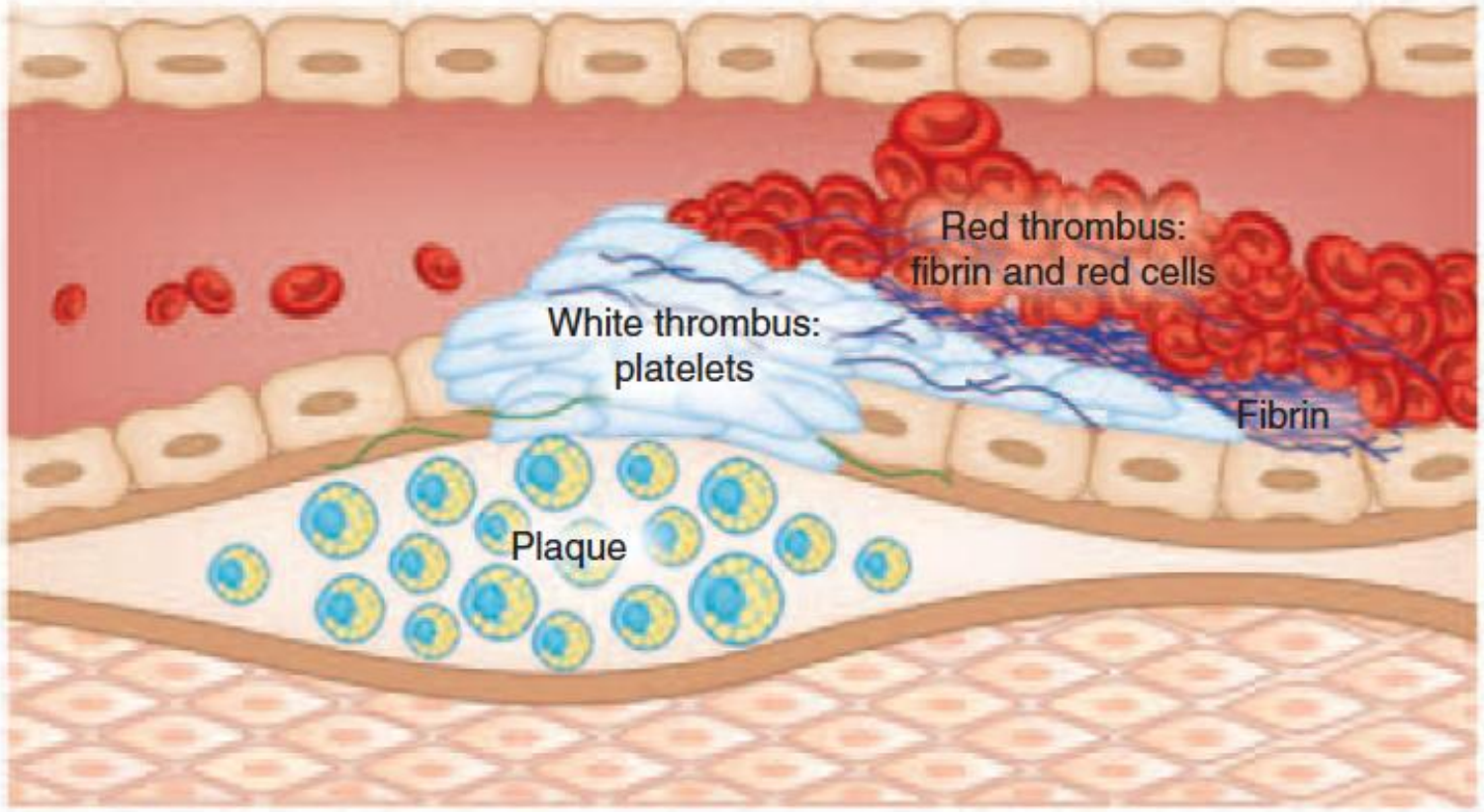
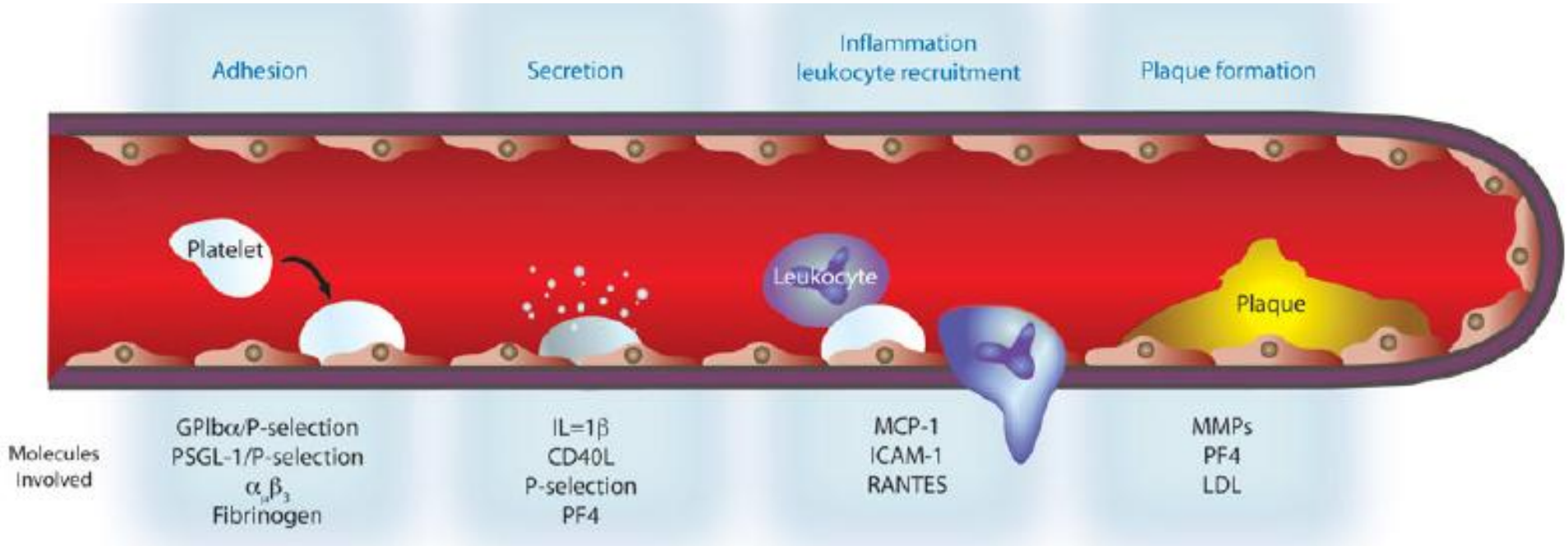
Destičky a Aterotrombóza



Nature Med 2011; 17: 1423

Destičky a Aterogenéza



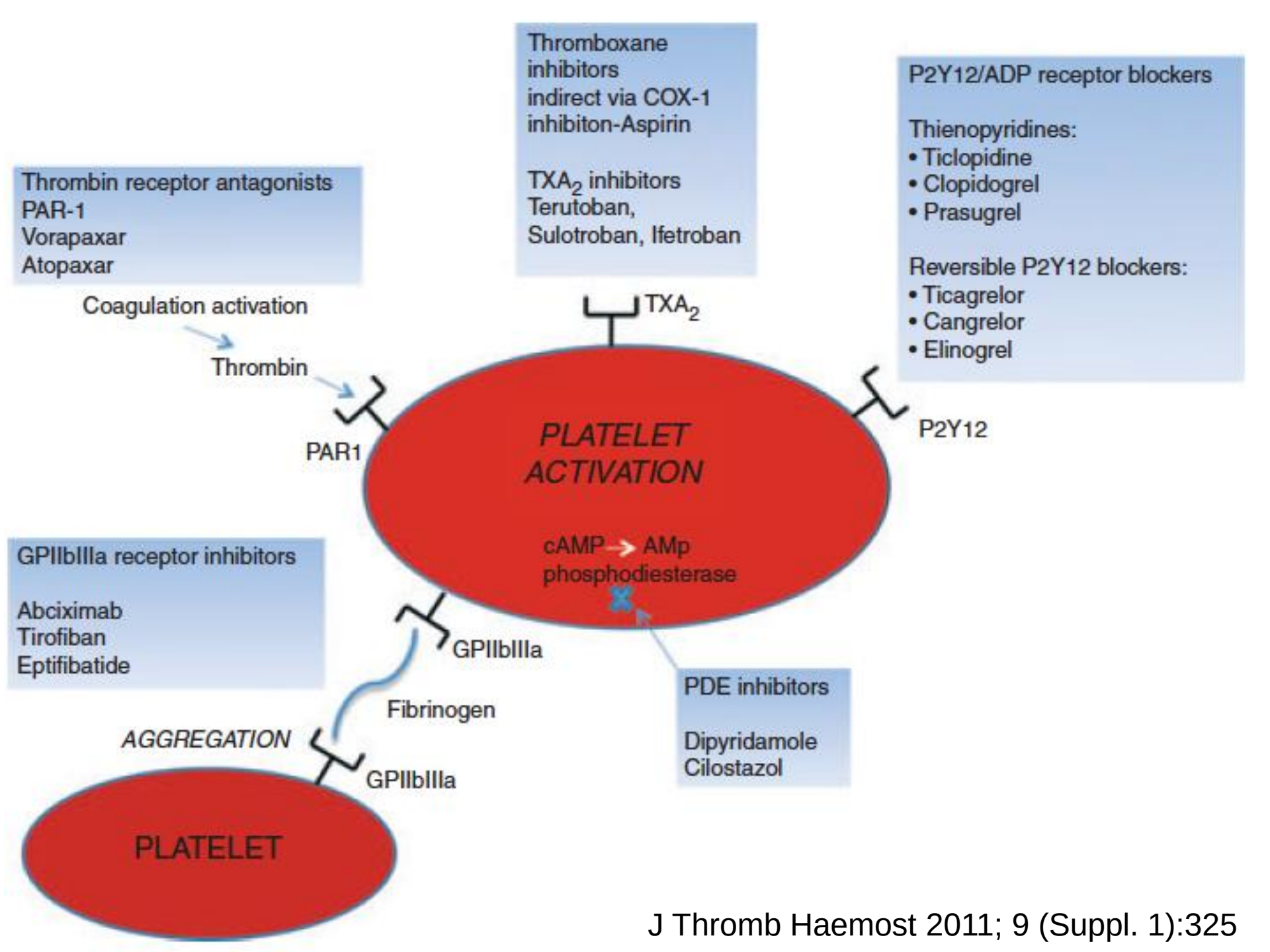
Destičky přispívají k iniciaci a progresy aterosklerotické léze:

- Adherují na místa s aktivovanými endotelovými bb.,
- Uvolňují adhesivní ligandy, které přitahují monocyty a makrofágy,
- Iniciují tvorbu agregátů destiček s monocyty,
- Lokálně uvolňují mediátory zánětu a mitogenéze.

Eur Heart J Suppl 2008; 10 (suppl I): I4.

Protidestičková léčba

- Akutní koronární syndrom,
- PCI s implantací stentu,
- Primární prevence kardiovaskulárních nemocí,
- Sekundární prevence kardiovaskulárních nemocí.



J Thromb Haemost 2011; 9 (Suppl. 1):325

KAS v primární a sekundární prevenci kardiovaskulárních nemocí

Clinical setting	Benefit[a]	Risk[b]	Benefit/risk ratio
	Number of patients in whom a major vascular event is avoided per 1000/year	Number of patients in whom a major GI bleeding event is caused per 1000/year	
Men and women at low-cardiovascular risk	1–2	1–2	1
Essential hypertension	1–2	1–2	1
Chronic stable angina	10	1–2	5–10
Prior stroke or TIA	10	1–2	5–10
Prior myocardial infarction	15	1–2	7.5–15
Unstable angina	50	1–2	25–50

Chest 2008;133:199S
Eur Heart J 2011; 32 (23): 2922

Primární prevence kardiovaskulárních onemocnění

4.10.1 Antiplatelet therapy in individuals without overt cardiovascular disease

Primary prevention in individuals without overt cardiovascular or cerebrovascular disease was investigated using long-term aspirin vs. control in a systematic review of six trials including 95 000 individuals.

- A risk reduction from 0.57% to 0.51% per year of serious vascular events was found by the Antithrombotic Trialists' Collaboration.
- Major gastrointestinal and extracranial bleeds increased by 0.03% per year.
- Risk of vascular mortality was not changed by treatment with aspirin.

Aspirin cannot be recommended in primary prevention due to its increased risk of major bleeding.

Eur Heart J 2012; 33: 1635–1701

Monoterapie Clopidogrelem v sekundární prevenci kardiovaskulárních nemocí

Studie “Clopidogrel versus Aspirin in Patients at Risk of Ischaemic Events” (CAPRIE)

Clopidogrel (75mg/d) vs. KAS (325mg/d) u pacientů po IM, CMP, s PAD; N = 19 185

- Výskyt IM/CMP/KV smrti:
  KAS 5.83%/rok; P=0.043
  Clopidogrel 5.32%/rok
- Výskyt intrakraniálního krvácení:
  KAS: 0.49%
  Clopidogrel 0.35% p=0.23

Lancet 1996; 348: 1329–39

Duální protidestičková léčba (DAT)

- KAS + inhibitor $P2Y_{12}$

Inhibitory receptoru $P2Y_{12}$

Tienopyridiny

– potřeba metabilizace na aktivní formu léku,

– ireverzibilní inhibice.

Clopidogrel – významná interindividuální variabilita účinku

Prasugrel – rychlý nástup účinku, vysoká efektrivita

Netienopyridiny

– přímá a reverzibilní inhibice;

Ticagrelor – p.o., biol. poločas ~12 h (2x/d);

Cangrelor – i.v., biol. poločas 3-5 min, odeznění inhibice 20min;

Elinogrel – i.v. + p.o., odeznění inhibice 24h;

Duální protidestičková léčba - Přínos

	Výskyt 1° EP (% pacientů)		
Sekundární prevence (?)			
CHARISMA (N = 15 603)	KAS	Clop + KAS	P value
Všichni pp (prim.+sek. prevence)	7.3	6.8	0.22
Stp MI, stroke, or PAD	8.8	7.3	0.01
Stent PCI			
CREDO(N = 2 116)	KAS	LD-Clop + KAS	
LD ≥ 15h	9.7	3.5	0.011
NSTE ACS	KAS	Clop + KAS	
CURE (N = 12 562)	11.4	9.3	<0.001
STEMI	KAS	Clop + KAS	
TLL CLARITY (N = 3 491)	21.7	15.0	<0.001
± TLL COMMIT (N = 45 852)	10.1	9.2	0.002

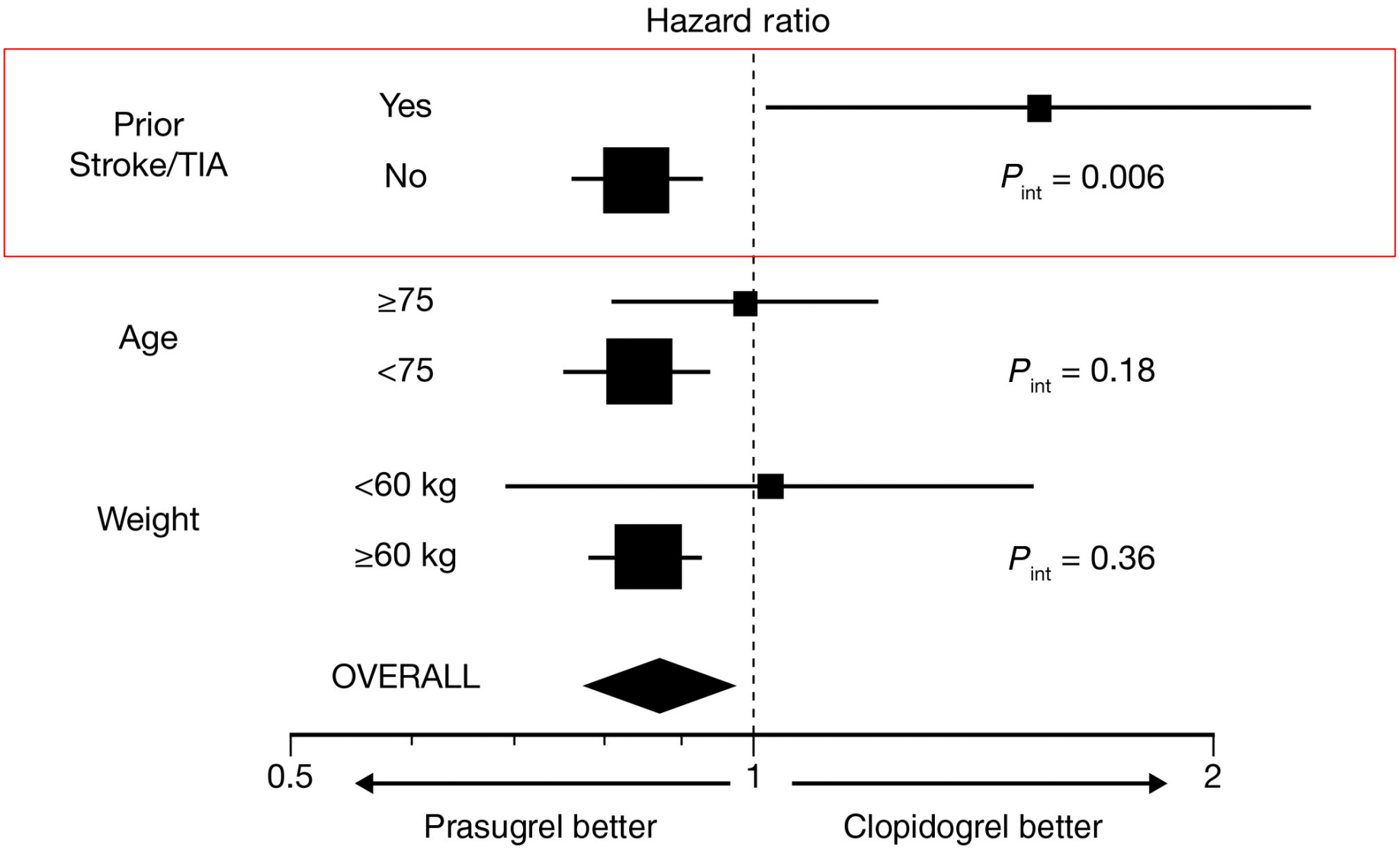
Duální protidestičková léčba - Přínos

	Výskyt 1° EP (% pacientů)		
AKS + PCI			
TRITON TIMI 38 (N = 13 608)	Clop + KAS	Prasugrel + KAS	P value
Všichni pacienti	12.7	9.9	<0.001
AKS ± PCI			
PLATO (N = 18 624)	Clop + KAS	Ticagrelor + KAS	
Všichni pacienti	11.7	9.8	<0.001

Duální protidestičková léčba - Riziko

Trial	Event rate (% of patients)		P
	Control arm	Active arm	
PCI			
CREDO	Aspirin	Clopidogrel + aspirin	
Modified TIMI major at 28 d	3.6	4.7	0.19
NSTE ACS			
CURE	Aspirin	Clopidogrel + aspirin	
Major	2.7	3.7	0.001
Patients undergoing PCI			
Major to 30 d	1.4	1.6	0.69
ACS			
TRITON	Clopidogrel + aspirin	Prasugrel + aspirin	
TIMI major, non-CABG	1.8	2.4	**0.03**
TIMI major, CABG	3.2	13.4	**0.001**
PLATO	Clopidogrel + aspirin	Ticagrelor + aspirin	
TIMI major, non–CABG-related	2.2	2.8	**0.03**
STEMI			
CLARITY	Aspirin	Clopidogrel + aspirin	
TIMI major at 30 d	1.7	1.9	0.80
COMMIT	Aspirin	Clopidogrel + aspirin	
Any	0.55	0.58	0.59

PRASUGREL „NE“



www.TIMI.org

Ticagrelor (180-mg loading dose, 90 mg twice daily) is recommended for all patients at moderate-to-high risk of ischaemic events (e.g. elevated troponins) , regardless of initial treatment strategy and including those pre-treated with clopidogrel (which should be discontinued when ticagrelor is commenced).	I
Prasugrel (60-mg loading dose, 10-mg daily dose) is recommended for $P2Y_{12}$-inhibitor-naïve patients (especially diabetics) in whom coronary anatomy is known and who are proceeding to PCI unless there is a high risk of life-threatening bleeding or other contraindications.[d]	I
Clopidogrel (300-mg loading dose, 75-mg daily dose) is recommended for patients who cannot receive ticagrelor or prasugrel.	I
A 600-mg loading dose of clopidogrel (or a supplementary 300-mg dose at PCI following an initial 300-mg loading dose) is recommended for patients scheduled for an invasive strategy when ticagrelor or prasugrel is not an option.	I

ESC Guidelines for NSTE ACS, 2011

Recommendations	Class	Level
Antiplatelet therapy		
Aspirin oral or i.v. (if unable to swallow) is recommended	I	B
An ADP-receptor blocker is recommended in addition to aspirin. Options are:	I	A
• Prasugrel in clopidogrel-naive patients, if no history of prior stroke/TIA, age < 75 years.	I	B
• Ticagrelor.	I	B
• Clopidogrel, preferably when prasugrel or ticagrelor are either not available or contraindicated.	I	C

ESC Guidelines for STE MI, 2012

ESC GUIDELINES „On myocardial recascularization“

(b) Recommended duration of dual antiplatelet therapy

After percutaneous coronary intervention

- 1 month after BMS implantation in stable angina;[55,60,94]
- 6–12 months after DES implantation in all patients;[60,94]
- 1 year in all patients after ACS, irrespective of revascularization strategy.

Eur Heart J 2010; 31: 2501

Triple protidestičková léčba

- KAS + inhibitor $P2Y_{12}$+ iGP IIb/IIIa

  selektivně u pacientů s AKS, kteří podstupují PCI