Antitrombotika při PCI: update 2019

Varvařovský Ivo
KCA Pardubice
Workshop ČAIK, 11.4.2019, Plzeň

Antitrombotika při PCI: update 2019

1. PCI na trvalé antikoagulační léčbě (AUGUSTUS)
2. Monoterapie P2Y12 (GLOBAL LEADERS)
3. Individualizace délky DAPT po PCI

Antitrombotika při PCI: update 2019

What is new in the 2018 Guidelines?

- Calculation of the Syntax Score, if left main or multivessel revascularization is considered
- Radial access as standard approach for coronary angiography and PCI
- DES for any PCI
- Systematic re-evaluation of patients after myocardial revascularization
- Stabilised NSTE-ACS patients: revascularization strategy according to principles for SCAD
- Use of the radial artery grafts over saphenous vein grafts in patients with high-degree stenosis
- Myocardial revascularization in patients with CAD, heart failure, and LVEF ≤35%
  - CABG preferred
  - PCI as alternative to CABG

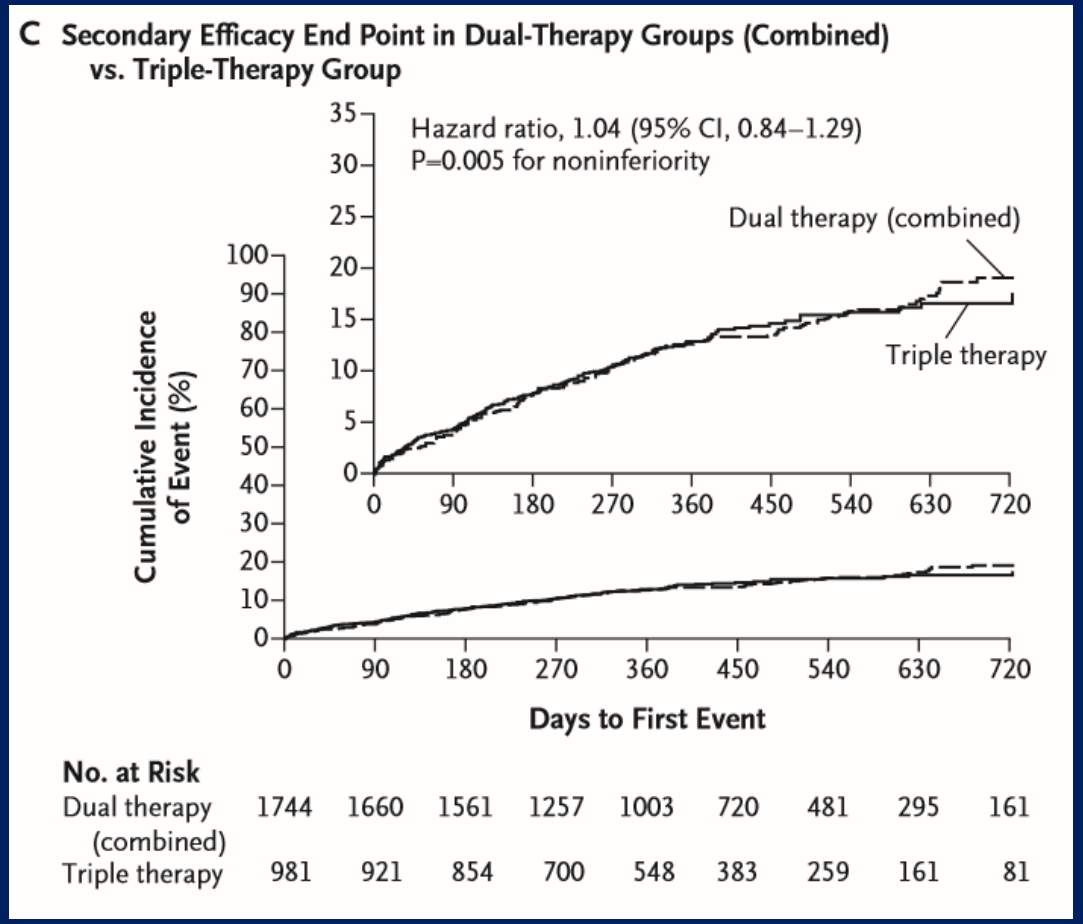
- Completeness of revascularization prioritized, when considering CABG vs PCI
- NOAC preferred over VKA in patients with non-valvular AF requiring anticoagulation and antiplatelet treatment
- No-touch vein technique, if open vein harvesting for CABG
- Annual operator volume for left main PCI of at least 25 cases per year
- Pre- and post-hydration with isotonic saline in patients with moderate or severe CKD if the expected contrast volume is >100 mL

DOWNGRADES

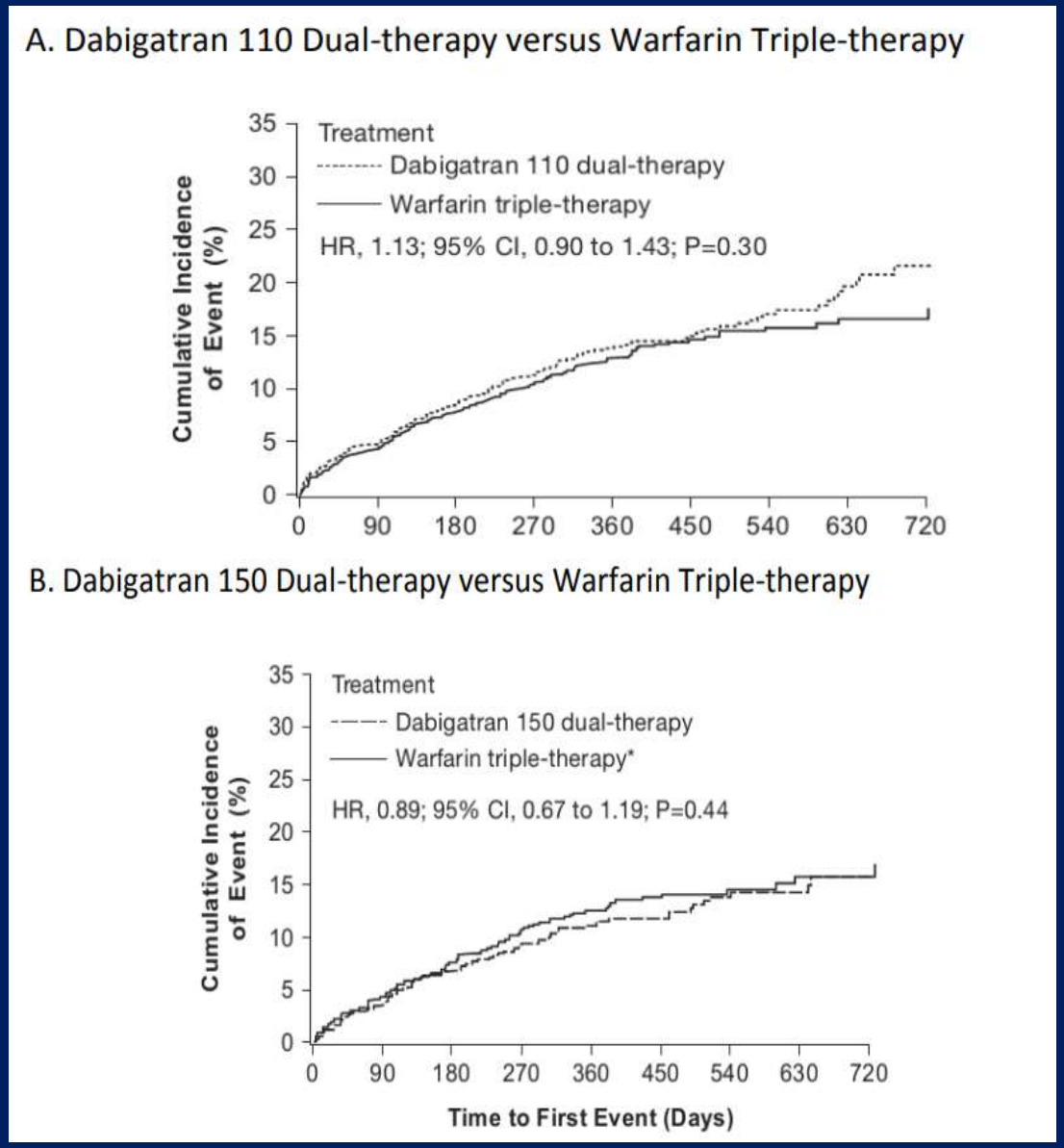
- Distal protection devices for PCI of SVG lesions
- Bivalirudin for PCI in NSTE-ACS
- Bivalirudin for PCI in STEMI
- PCI for MVD with diabetes and SYNTAX score <23
- Platelet function testing to guide antiplatelet therapy interruption in patients undergoing cardiac surgery

- Routine non-invasive imaging surveillance in high-risk patients 6 months after revascularization
- Double-kissing crush technique preferred over provisional T-stenting in true left main bifurcations.
- Cangrelor in $P2Y_{12}$-inhibitor naïve patients undergoing PCI
- GP IIb/IIIa inhibitors for PCI in $P2Y_{12}$-inhibitor naïve patients with ACS undergoing PCI
- Dabigatran 150-mg dose preferred over 110-mg dose when combined with single antiplatelet therapy after PCI
- De-escalation of $P2Y_{12}$ inhibitor guided by platelet function testing in ACS patients
- Routine revascularization of non-IRA lesions in myocardial infarction with cardiogenic shock
- Current generation BRS for clinical use outside clinical studies

RE-DUAL

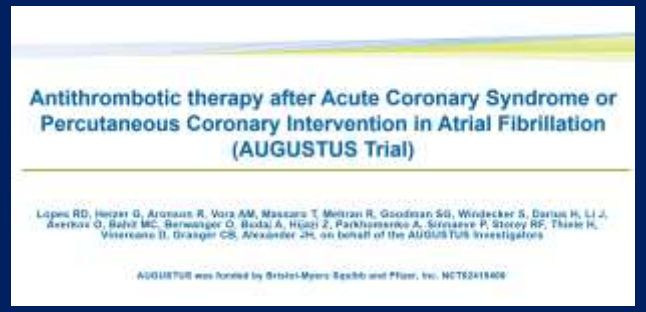


N Engl J Med 2017; 377:1513-1524



Antitrombotika při PCI: trvalá OAC + DAPT 2019

- Dosud testován pouze warfarin + DAPT vs NOAC + SAPT
- NOAC + clopidogrel bezpečnější pro krvácení, není ale jistota o bezpečné eliminaci ischemických příhod
- Randomizace 3.-5. den po PCI = triple po PCI na počátku vždy



Antitrombotika při PCI: trvalá OAC + DAPT 2019

The AUGUSTUS Trial: Apixaban vs VKA or Aspirin vs Placebo in Patients with Atrial Fibrillation and Acute Coronary Syndrome and/or Percutaneous Coronary Intervention:

NVAF (prior, persistent/permanent, paroxysmal)
- Physician decision that oral anticoag is indicated
- ACS and/or PCI with planned $P2Y_{12}$ inhibitor for at least 6 months

Exclusion
- Contraindication to Dual Antiplatelet Therapy
- Other reason for VKA (mechanical valve, moderate/severe Mitral valve stenosis)

Anticoagulant Comparison
(n =4,614)

2x2 Factorial Design
1:1:1:1 Randomization to four treatment Regimens

Antiplatelet Comparison
(n =4,614)

Open Label

Apixaban 5 mg BID
2.5 mg BID if criteria met

VKA
(INR 2.0-3.0)

Double blind

Double blind

ASA | **Placebo** | **ASA** | **Placebo**

A $P2Y_{12}$ inhibitor for all patients x 6 months

Double blind

ASA 81 mg QD

Placebo

Open Label

Open Label

Apixaban | **VKA** | **Apixaban** | **VKA**

A $P2Y_{12}$ inhibitor for all patients x 6 months

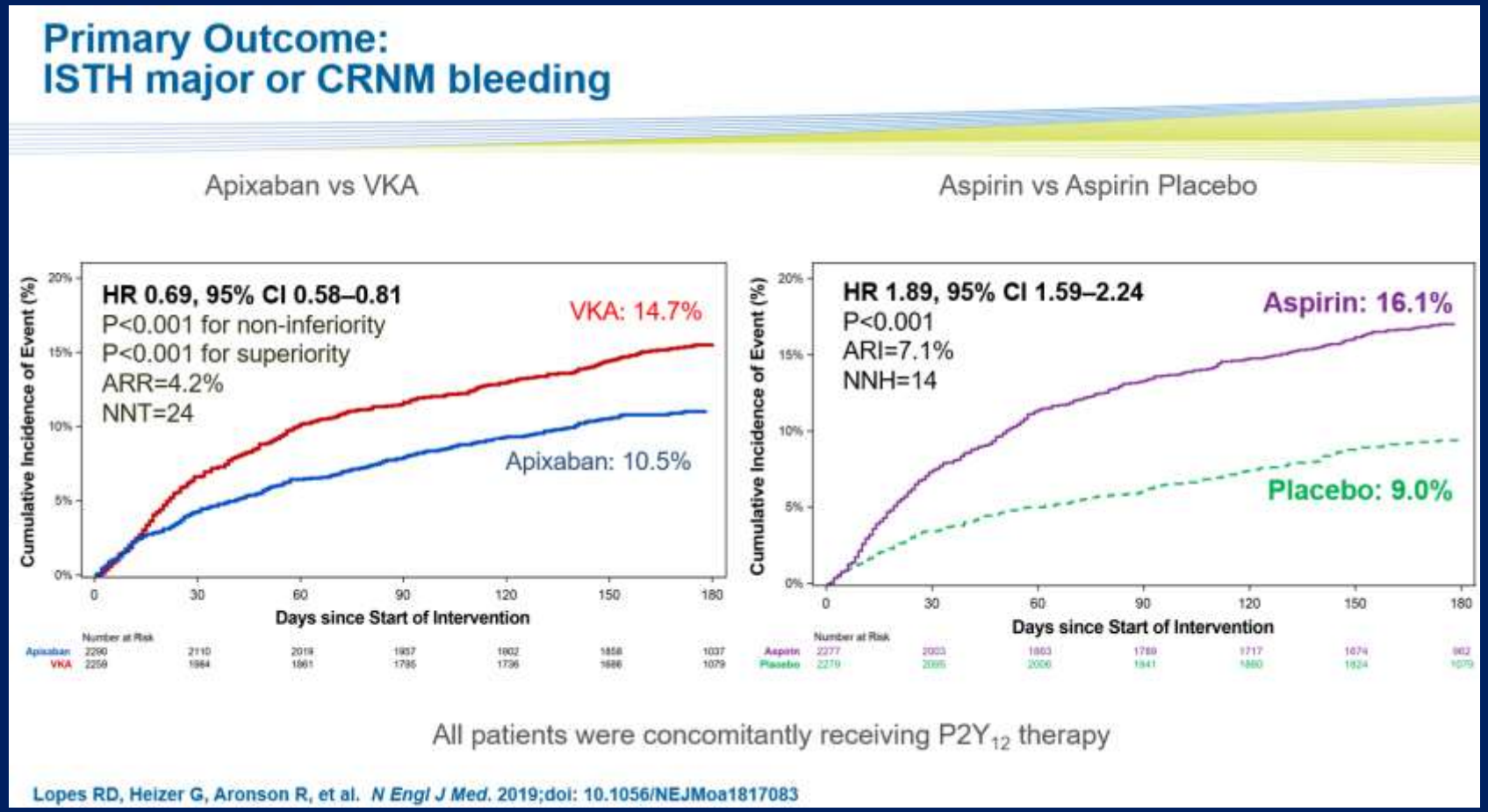
Adapted from: Lopes RD, et al. *Am Heart J.* 2018;200:17-23. Lopes RD, Heizer G, Aronson R, et al. *N Engl J Med.* 2019;doi: 10.1056/NEJMoa1817083

Antitrombotika při PCI: trvalá OAC + DAPT 2019

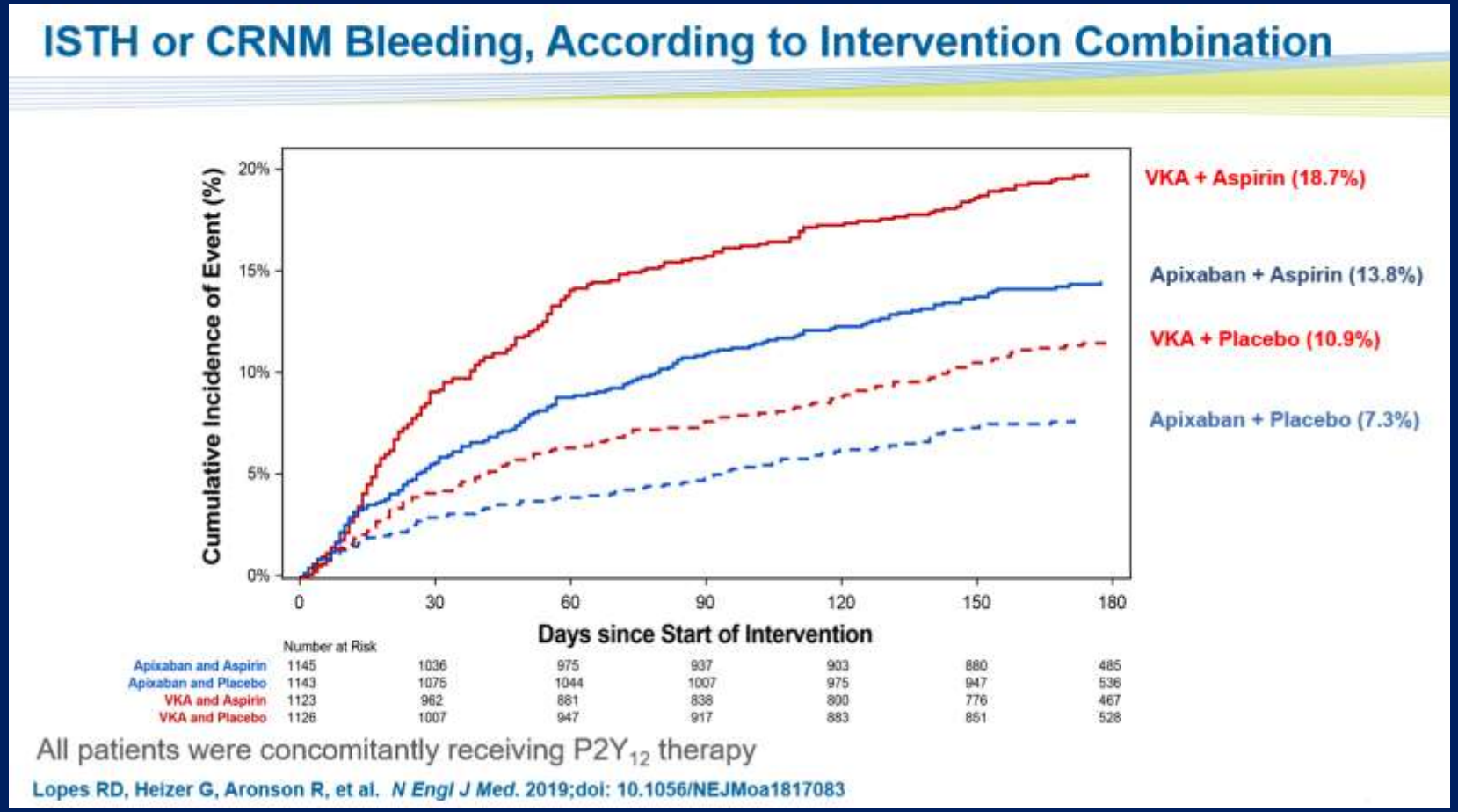
Baseline Characteristics

	Total (N=4614)
Age, median (25th, 75th), years	70.7 (64.2, 77.2)
Female, %	29.0
CHA_2DS_2-VASc score, mean (SD)	3.9 (1.6)
HAS-BLED score, mean (SD)	2.9 (0.9)
Prior OAC, %	49.0
$P2Y_{12}$ inhibitor, %	
Clopidogrel	92.6
Prasugrel	1.1
Ticagrelor	6.2
Number of days from ACS/PCI to randomization, mean (SD)	6.6 (4.2)
Qualifying index event, %	
ACS and PCI	37.3
ACS and no PCI	23.9
Elective PCI	38.8

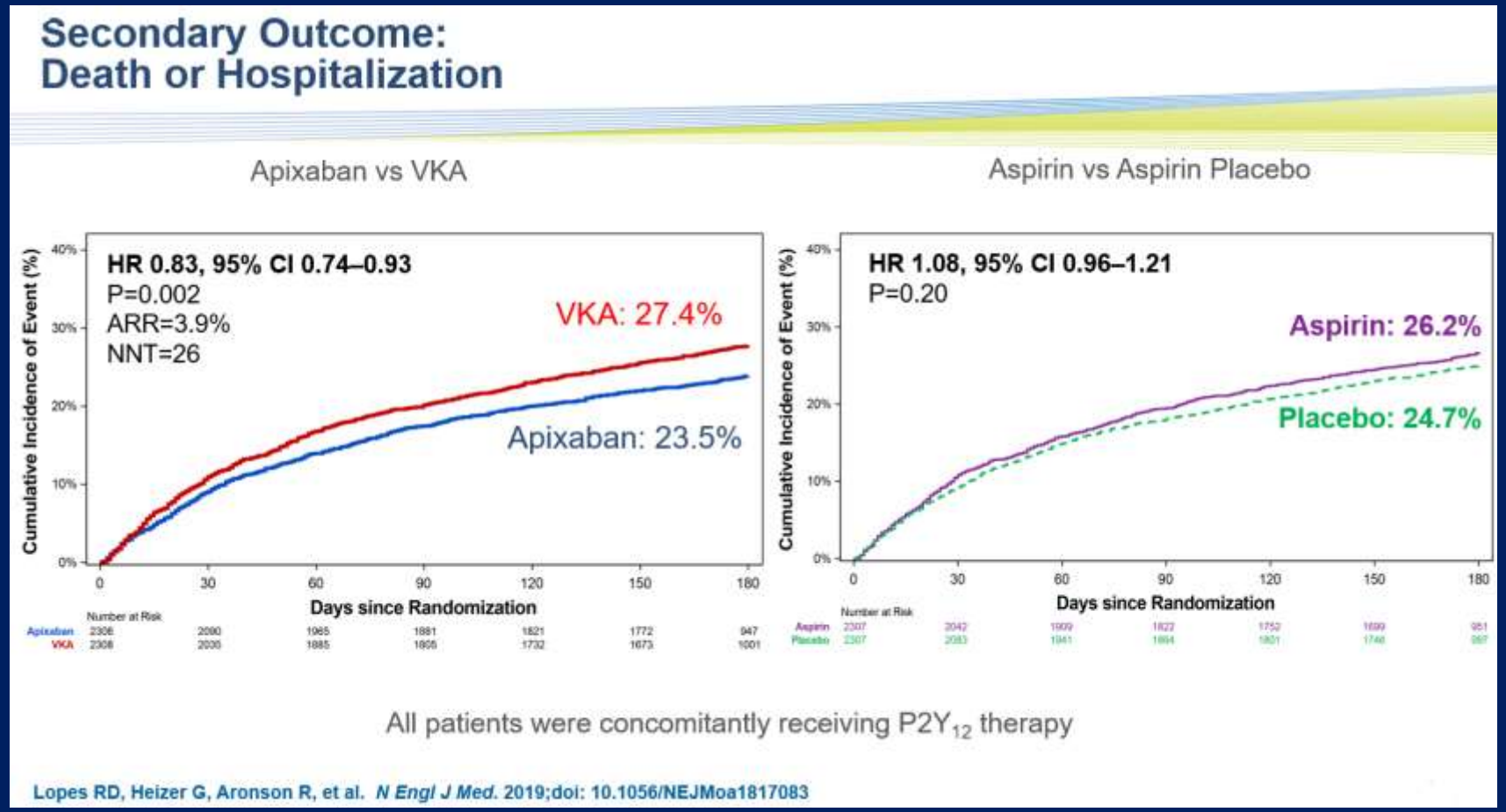
Antitrombotika při PCI: trvalá OAC + DAPT 2019



Antitrombotika při PCI: trvalá OAC + DAPT 2019



Antitrombotika při PCI: trvalá OAC + DAPT 2019



Antitrombotika při PCI: trvalá OAC + DAPT 2019

Secondary Outcomes: Death or Ischemic event
Apixaban vs VKA and Aspirin vs Placebo

Endpoint	Apixaban (N=2306)	VKA (N=2308)	Hazard Ratio (95%CI)	Aspirin (N=2307)	Placebo (N=2307)	Hazard Ratio (95%CI)
Death / Ischemic Events (%)	6.7	7.1	0.93 (0.75-1.16)	6.5	7.3	0.89 (0.71-1.11)
Death (%)	3.3	3.2	1.03 (0.75-1.42)	3.1	3.4	0.91 (0.66-1.26)
CV Death (%)	2.5	2.3	1.05 (0.72-1.52)	2.3	2.5	0.92 (0.63-1.33)
Stroke (%)	0.6	1.1	0.50 (0.26-0.97)	0.9	0.8	1.06 (0.56-1.98)
Myocardial Infarction (%)	3.1	3.5	0.89 (0.65-1.23)	2.9	3.6	0.81 (0.59-1.12)
Definite or Probable Stent Thrombosis (%)	0.6	0.8	0.77 (0.38-1.56)	0.5	0.9	0.52 (0.25-1.08)
Urgent Revascularization (%)	1.7	1.9	0.90 (0.59-1.38)	1.6	2.0	0.79 (0.51-1.21)
Hospitalization (%)	22.5	26.3	0.83 (0.74-0.93)	25.4	23.4	1.10 (0.98-1.24)

All patients were concomitantly receiving $P2Y_{12}$ therapy

Lopes RD, Heizer G, Aronson R, et al. *N Engl J Med.* 2019;doi: 10.1056/NEJMoa1817083

Antitrombotika při PCI: update 2019

AUGUSTUS

1. První studie, srovnávající NOAC vs VKA při PCI + AF
2. Dual therapy bezpečnější triple therapy
3. Aspirin výrazně zvyšuje riziko krvácení (NNH=14)
4. Apixaban je bezpečnější (NNT=24) a účinnější (NNT=26) než VKA

Apixaban v dávce pro prevenci CMP při fibrilaci síní má v současnosti nejlepší data při ACS+PCI, ACS bez PCI a při elektivní PCI.

Antitrombotika při PCI: update 2019

4. **Antikoagulační léčba pacientů s FS indikovaných k PCI (na základě nových klinických hodnocení) – na žádost OS od 1.1.2018**
   - Jde o pacienty s FS a ICHS – stabilní anginou pectoris (vyloučeni jsou pacienti s akutním koronárním syndromem) s vysokým rizikem krvácení po elektivní PCI (vysoké riziko krvácení = skóre PRECIDE-DAPT ≥25)
   - Léčba dabigatran etexilátem 150 mg nebo 110 mg 2x denně nebo rivaroxabanem 15 nebo 10 mg 1x denně v kombinaci s P2Y12 inhibitorem po dobu 12 měsíců od provedení elektivní PCI.

- VZP bude dále akceptovat jako důvod k preskripci NOAC souběžné užívání Warfarinu a LP s významným rizikem potenciálních lékových interakcí za situace, kdy léčbu nelze změnit. Takové situace je nutné řádně a jednoznačně zdokumentovat.

Za odborné společnosti:

Prof. MUDr. Miloš Táborský, CSc., FESC, MBA

MUDr. Robert Čihák, CSc.

MUDr. Hana Skalická, CSc., FESC

Antitrombotika při PCI: monoterapie ticagrelorem

Post-interventional and maintenance treatment		
Life-long single antiplatelet therapy, usually aspirin, is recommended.[681,683]	I	A
Instruction of patients about the importance of complying with antiplatelet therapy is recommended.	I	C
In patients with SCAD treated with coronary stent implantation, DAPT consisting of clopidogrel in addition to aspirin is generally recommended for 6 months, irrespective of the stent type.[c 690–694]	I	A
In patients with SCAD considered at high bleeding risk (e.g. PRECISE-DAPT ≥25), DAPT should be considered for 3 months.[d 695,696]	IIa	A
In patients with SCAD who have tolerated DAPT without a bleeding complication and who are at low bleeding risk but high thrombotic risk, continuation of DAPT with clopidogrel for >6 months and up to 30 months may be considered.[697–700]	IIb	A
In patients with SCAD in whom 3 month DAPT poses safety concerns, DAPT may be considered for 1 month.	IIb	C

Antitrombotika při PCI: monoterapie ticagrelorem

ECRI European Cardiovascular Research Institute

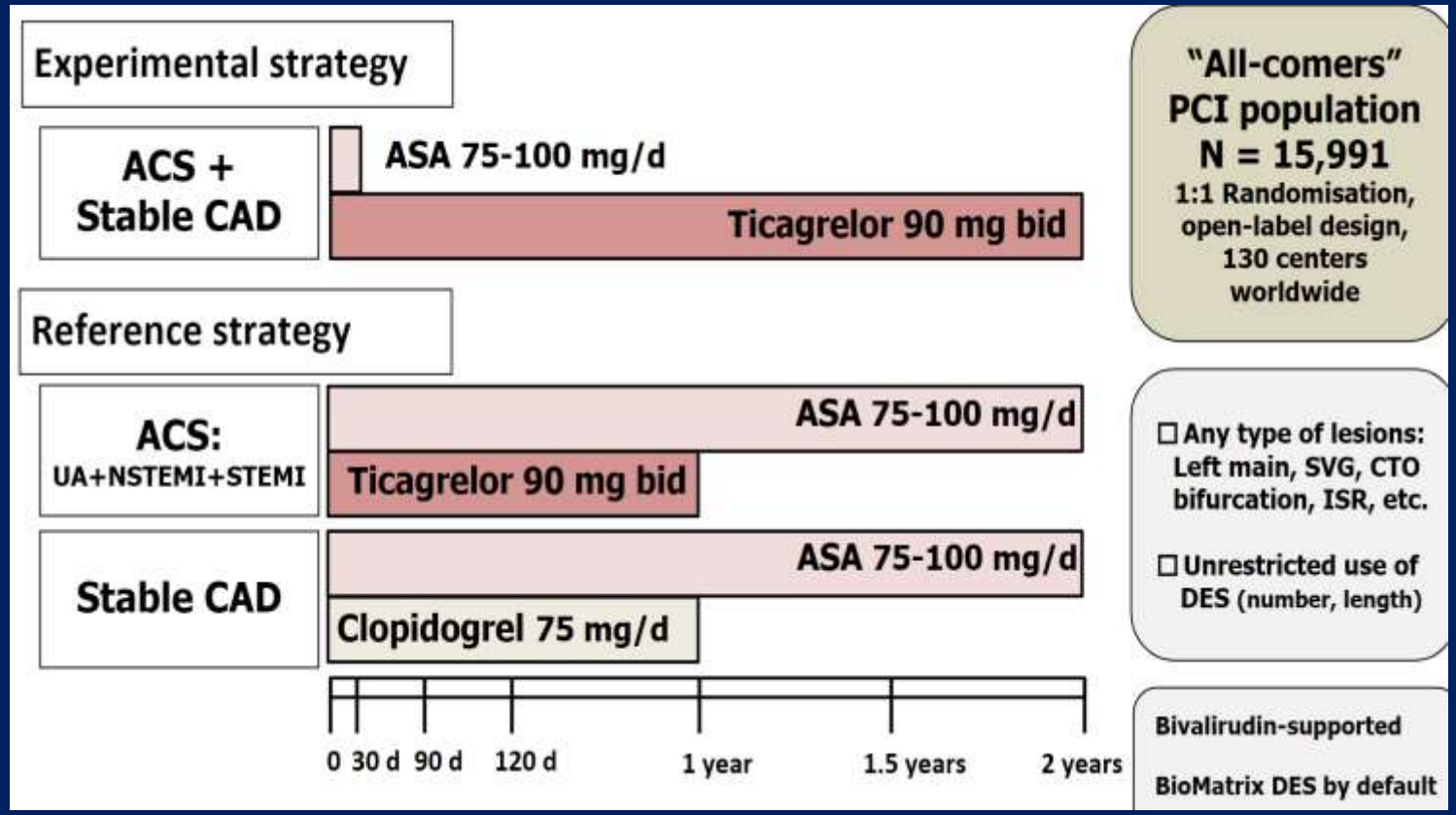
GLOBAL LEADERS

Ticagrelor monotherapy beyond one month vs. standard dual antiplatelet therapy following drug eluting stent implantation: A randomised multicentre superiority trial.

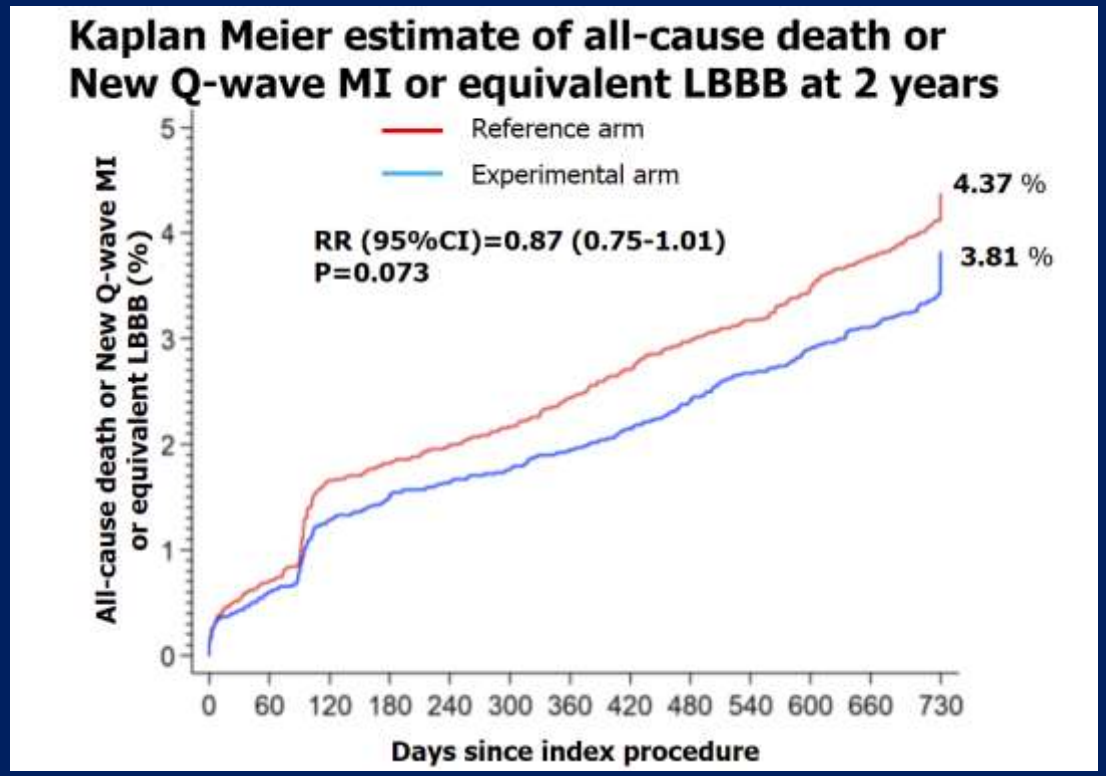
Patrick W. Serruys MD PhD
Erasmus University, Rotterdam, Netherlands

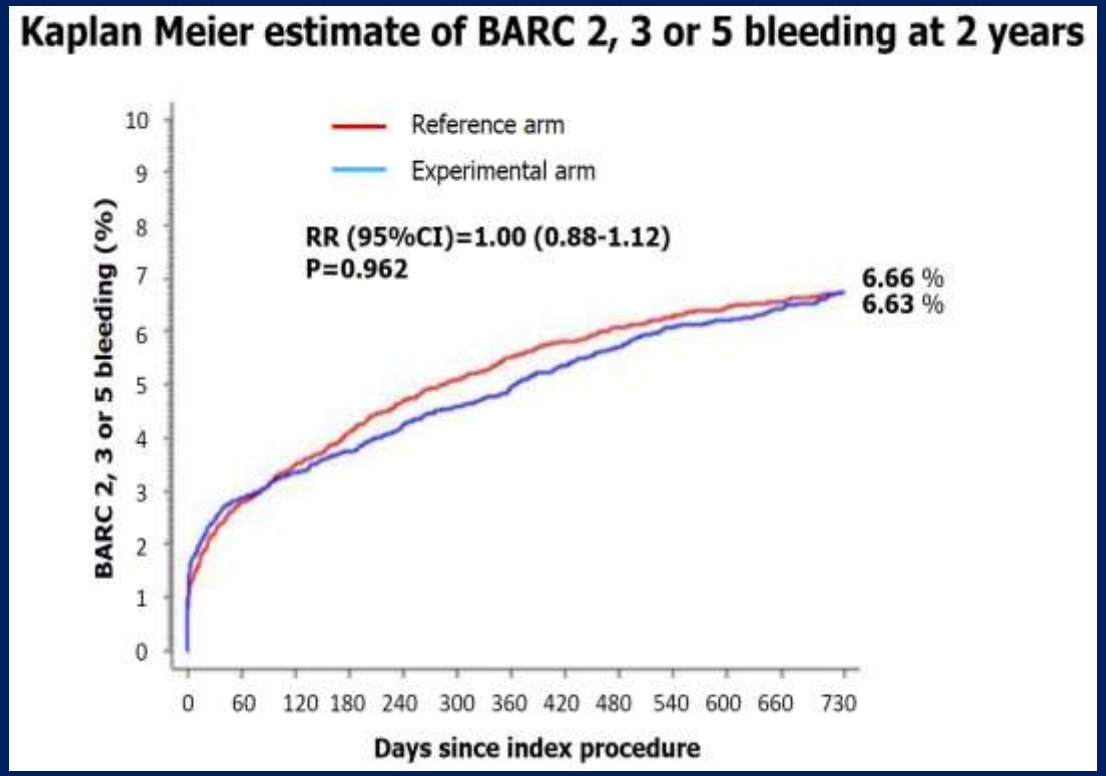
Pascal Vranckx, Marco Valgimigli, Stephan Windecker (PIs)
Christian W. Hamm, Peter Jüni, P. Gabriel Steg, Gerrit-Anne van Es (SC)

ESC Congress Munich 2018



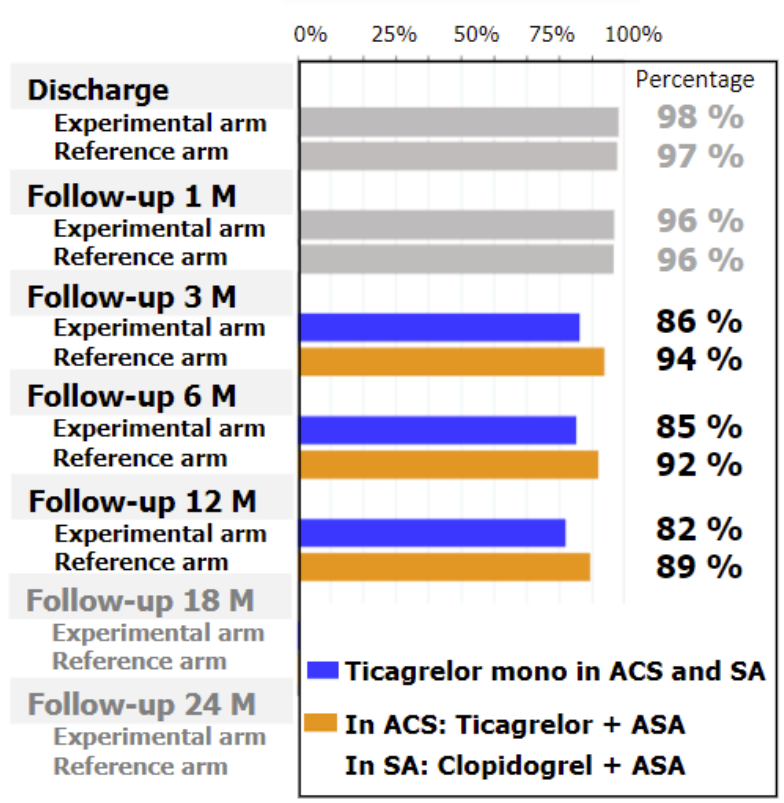
Antitrombotika při PCI: monoterapie ticagrelorem





Antitrombotika při PCI: monoterapie ticagrelorem

Adherence to treatment strategies



Primary and secondary outcomes at 12 months (Intention to treat)

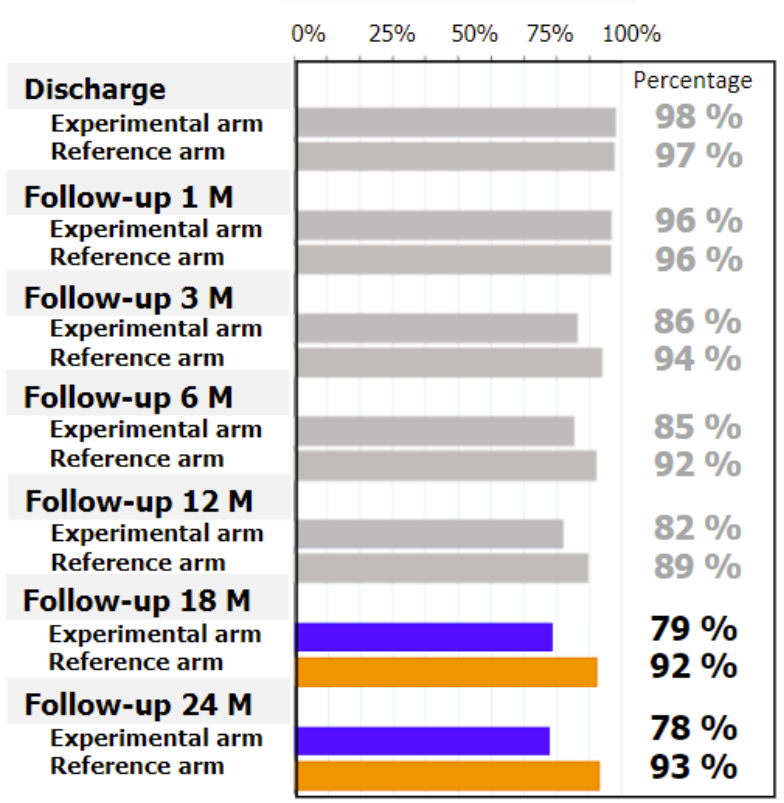
	Experimental group	Reference group	Risk Ratio (95% CI)	p-value
Number of pts.	N=7980	N=7988		
All-cause mortality or new Q-wave MI*	**1.95 %,** (156)	**2.47 %,** (197)	**0.79** (0.64-0.98)	**0.028**
All-cause mortality	**1.35 %** (108)	**1.64 %** (131)	**0.82** (0.64-1.06)	0.138
New Q-wave MI	**0.60 %** (48)	**0.86 %** (69)	**0.70** (0.48-1.00)	0.052

*Mantel-Cox method based on time of death or diagnosis of new Q wave MI

**Mantel-Cox log-rank method for secondary safety endpoints

Antitrombotika při PCI: monoterapie ticagrelorem

Adherence to treatment strategies



Primary and secondary outcomes at 24 months (Intention to treat)

	Experimental group	Reference group	Risk Ratio (95% CI)	p-value
Number of pts.	N=7980	N=7988		
All-cause mortality or new Q-wave MI	3.81 %, (304)	4.37 %, (349)	0.87 (0.75-1.01)	0.073
All-cause mortality	2.81 % (224)	3.17 % (253)	0.88 (0.74-1.06)	0.18
New Q-wave MI	1.04 % (83)	1.29 % (103)	0.80 (0.60-1.07)	0.14

Ticagrelor monotherapy in ACS and SA

ASA monotherapy in ACS and SA

Antitrombotika při PCI: monoterapie ticagrelorem

Study drug/strategy non-adherence in published ticagrelor trials

Study	Experimental Treatment Group	Reference treatment Group	Follow up
Global Leaders	27.40%	6.90%	2 years
Plato	23.40%	23.10%	1 year
Plato invasive	23.10%	21.80%	1 year
Pegasus	(32.0% (90mg (28.7% (60mg	21.40%	36 months
Socrates	17.50%	14.70%	90 days
Euclid	30.10%	25.90%	30 months

Antitrombotika při PCI: monoterapie ticagrelorem

ACS	ASA+ticagrelor do 1m Ticagrelor 2-24m	ASA+ ticagrelor do 12m ASA 13-24 m	RR (95% CI)
Úmrtí + infarkt myokardu	147	169	0,86 (0,69-1,08)
Krvácení BARC 3,5	73	100	0,73 (0,54-0,98)

Antitrombotika při PCI: monoterapie ticagrelorem

Stable CAD	**ASA+ticagrelor do 1m Ticagrelor 2-24m**	**ASA+ clopidogrel do 12m ASA 13-24 m**	**RR (95% CI)**
Úmrtí + infarkt myokardu	157	180	0,87 (0,71-1,08)
Krvácení BARC 3,5	90	69	1,32 (0,97-1,81)

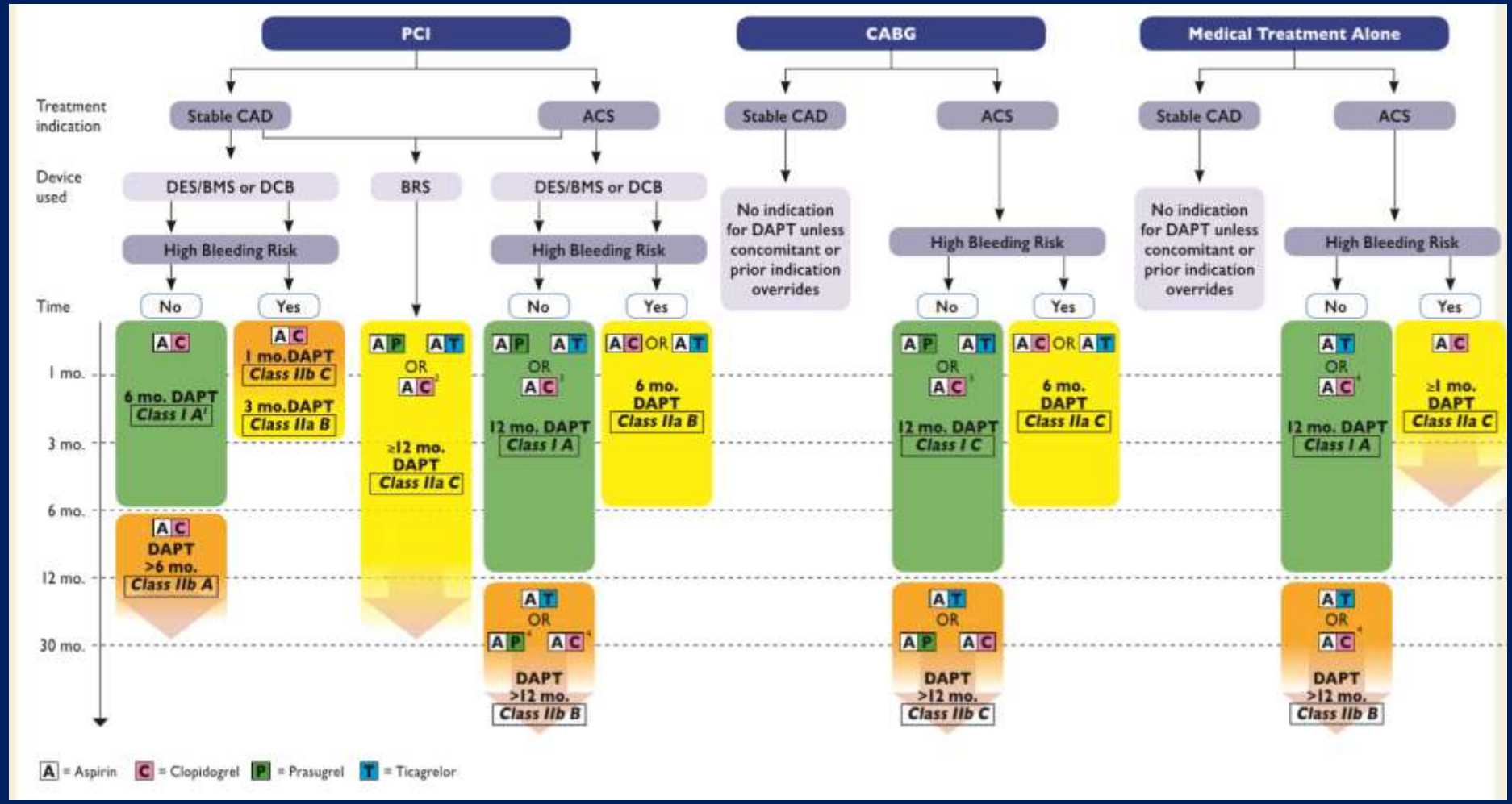
Antitrombotika při PCI: update 2019

1. **Monoterapie ticagrelorem po 1 měsíci** od PCI pro **ACS** je přinejmenším stejně účinná a rozhodně bezpečnější než DAPT (ASA+ticagrelor) po dobu 12 měsíců

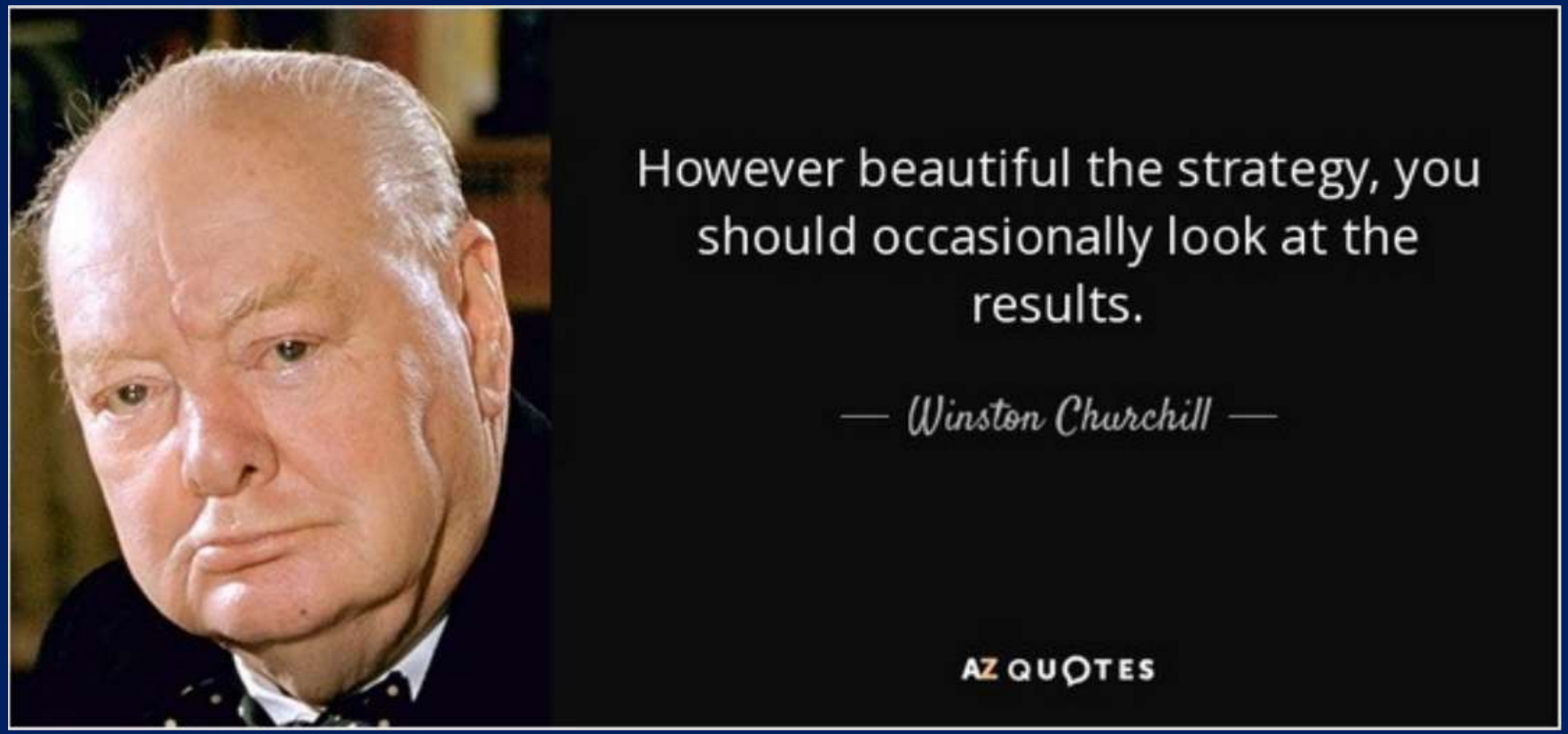
2. Dlouhodobá monoterapie inhibitorem P2Y12 po PCI může být účinnější aspirinu – bude-li tolerována (další studie?)

3. Vysazení ticagreloru pro dušnost by mělo být provedeno až po důkladném vyloučení jiných příčin obtíží

Antitrombotika při PCI: individualizace DAPT



Antitrombotika při PCI: individualizace DAPT



Duální protidestičková léčba (DAPT): rozlišení podle ACS ???

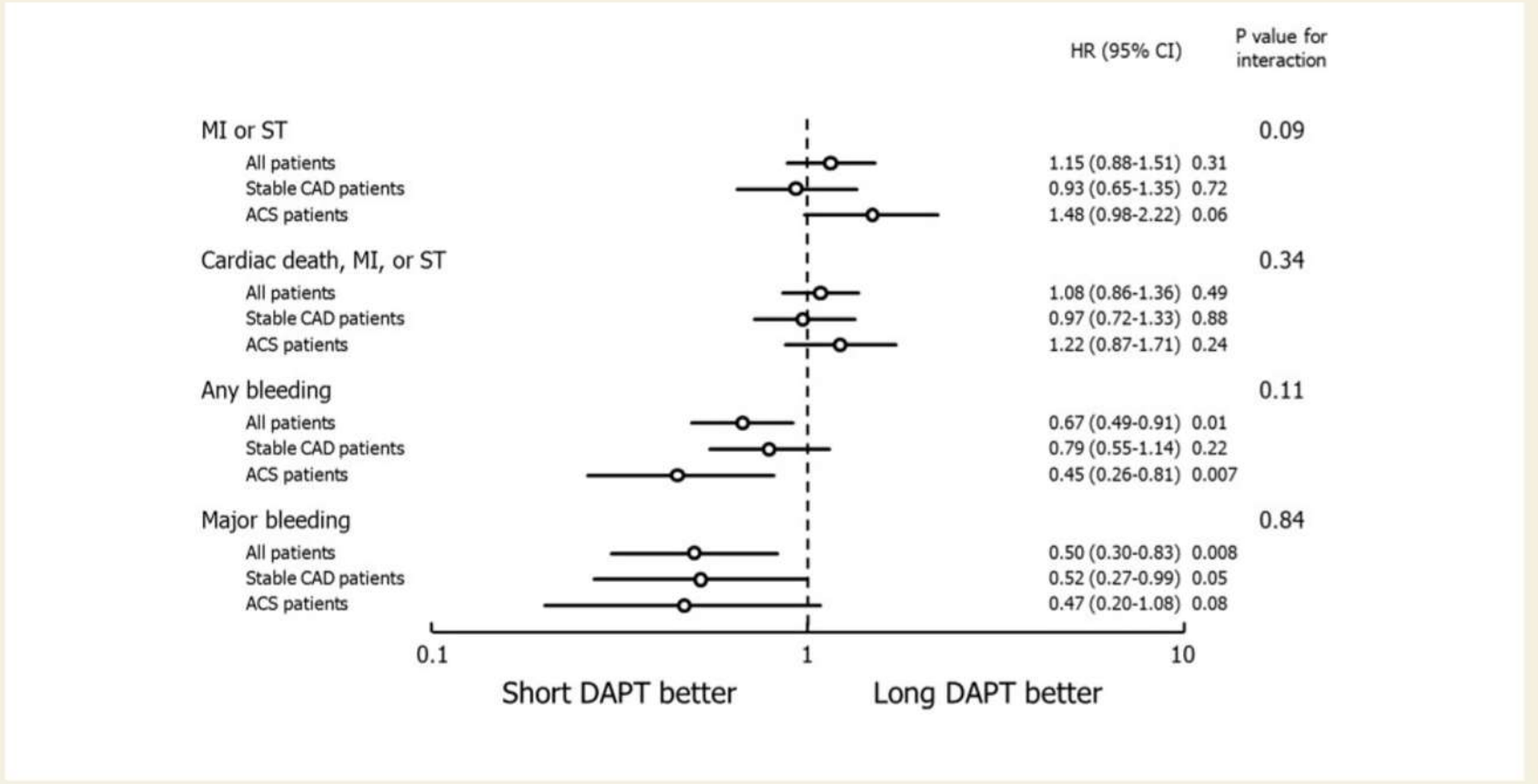


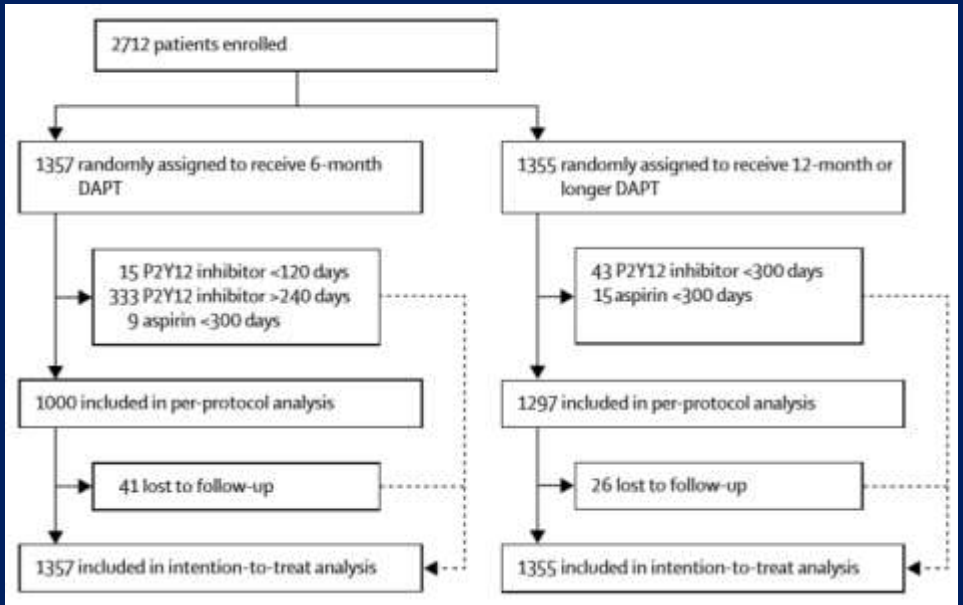
Figure 1 Main clinical outcomes and interaction analysis between dual antiplatelet therapy (DAPT) duration and clinical presentation in the intention-to-treat population. MI, myocardial infarction; ST, definite/probable stent thrombosis; CAD, coronary artery disease; ACS, acute coronary syndrome; HR, hazard ratio; CI, confidence interval.

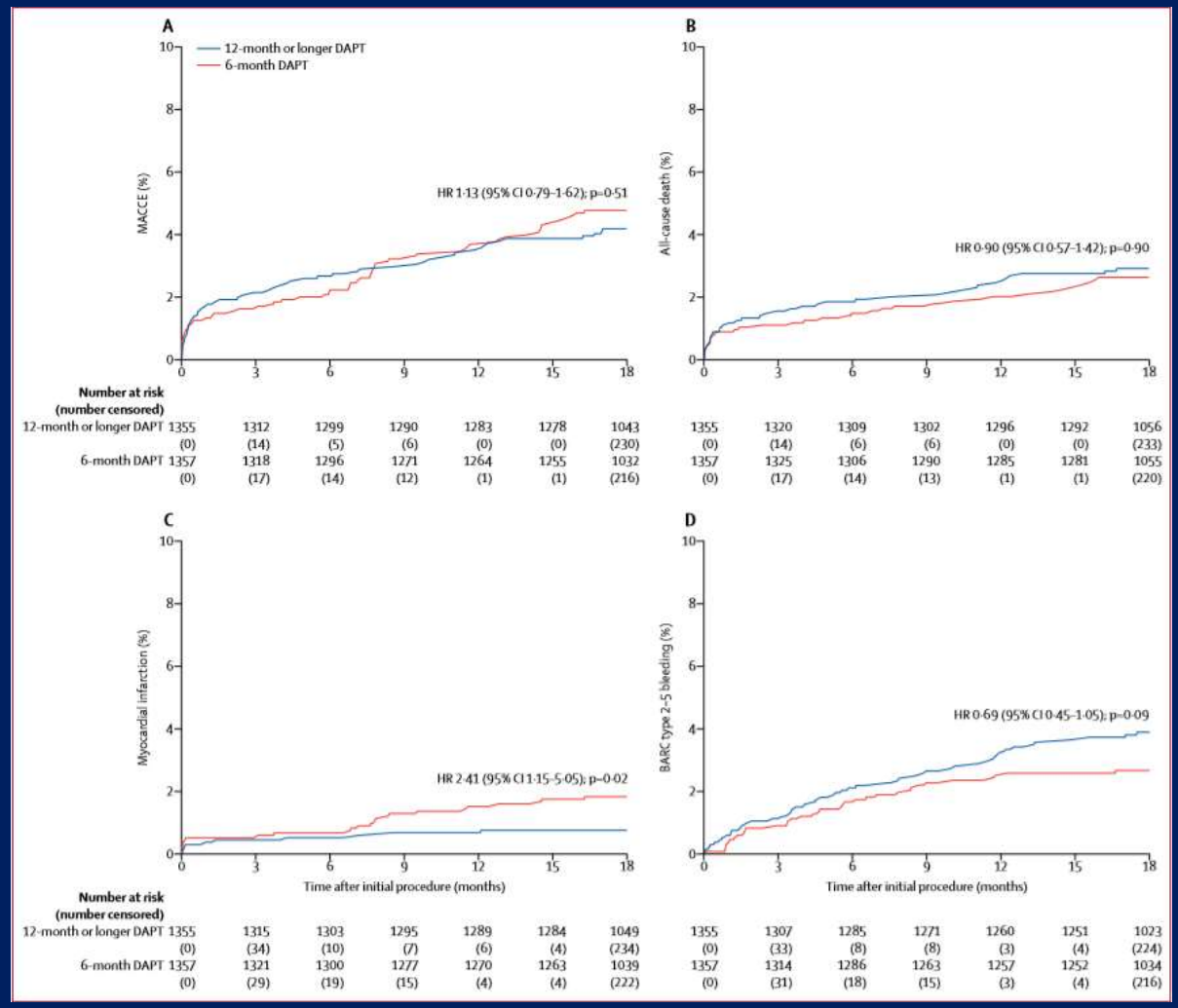
European Heart Journal (2017) **38**, 1034–1043

Duální protidestičková léčba (DAPT): rozlišení podle ACS ???

6-month versus 12-month or longer dual antiplatelet therapy after percutaneous coronary intervention in patients with acute coronary syndrome (SMART-DATE): a randomised, open-label, non-inferiority trial

Joo-Yong Hahn, Young Bin Song*, Ju-Hyeon Oh, Deok-Kyu Cho, Jin Bae Lee, Joon-Hyung Doh, Sang-Hyun Kim, Jin-Ok Jeong, Jang-Ho Bae, Byung-Ok Kim, Jang Hyun Cho, Il-Woo Suh, Doo-il Kim, Hoon-Ki Park, Jong-Seon Park, Woong Gil Choi, Wang Soo Lee, Jihoon Kim, Ki Hong Choi, Taek Kyu Park, Joo Myung Lee, Jeong Hoon Yang, Jin-Ho Choi, Seung-Hyuk Choi, Hyeon-Cheol Gwon, for the SMART-DATE investigators†*





www.thelancet.com March 12, 2018 http://dx.doi.org/10.1016/ S0140-6736(18)30493-8

Antitrombotika při PCI: individualizace DAPT

Table 5 High-risk features of stent-driven recurrent ischaemic events

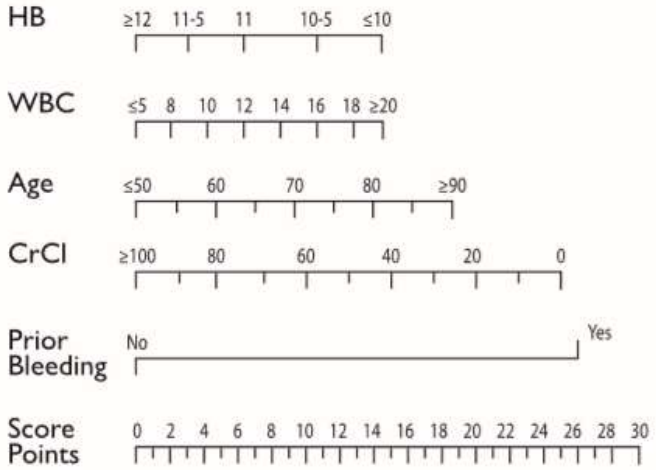
• Prior stent thrombosis on adequate antiplatelet therapy
• Stenting of the last remaining patent coronary artery
• Diffuse multivessel disease especially in diabetic patients
• Chronic kidney disease (i.e. creatinine clearance <60 mL/min)
• At least three stents implanted
• At least three lesions treated
• Bifurcation with two stents implanted
• Total stent length >60 mm
• Treatment of a chronic total occlusion

Costa *et al.*
PRECISE-DAPT Score and Complex PCI

PRECISE-DAPT score[18]

At the time of coronary stenting

Short DAPT (3–6 months)
vs.
Standard/long DAPT (12–24 months)



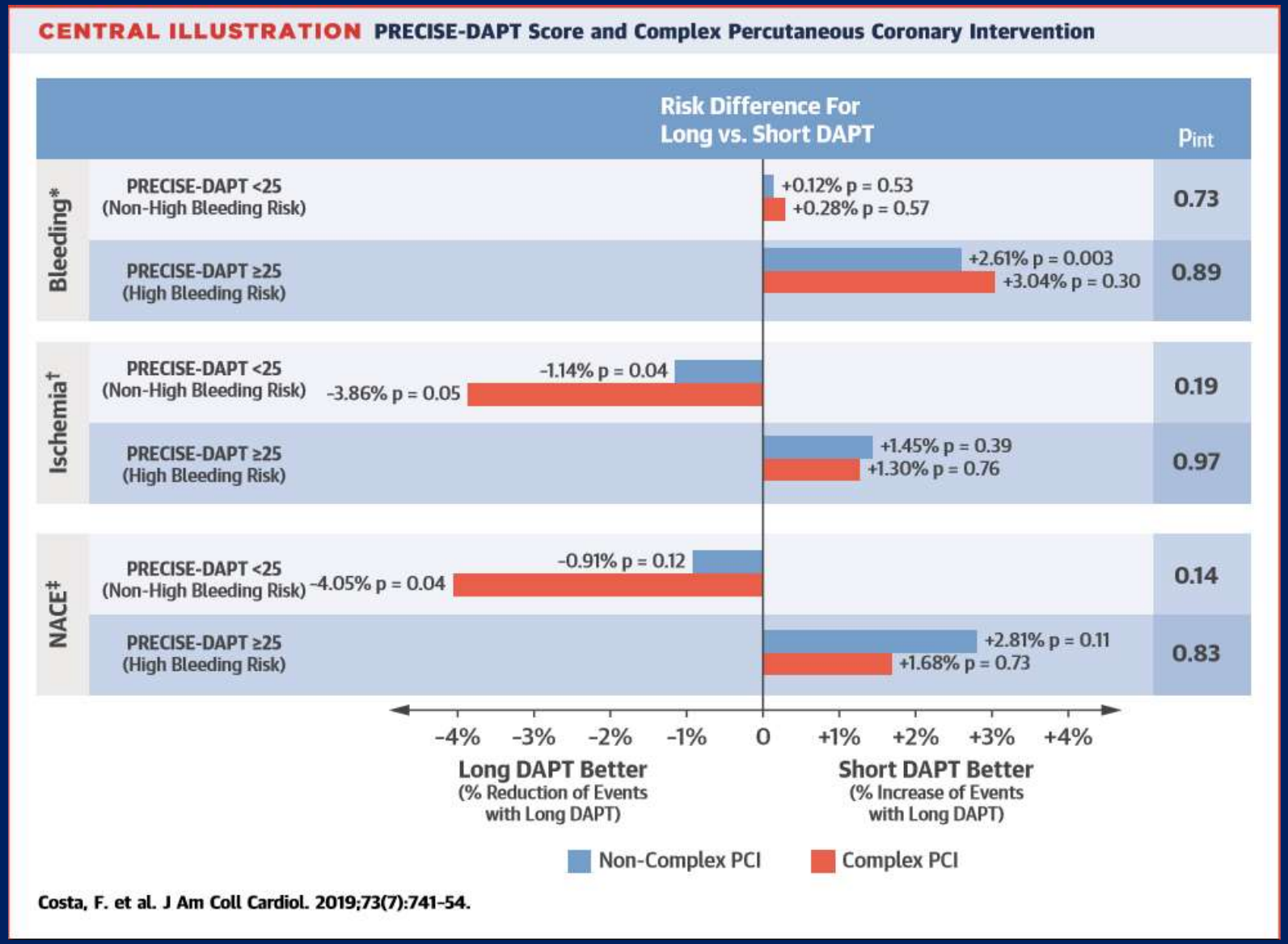
0 to 100 points

Score ≥25 → Short DAPT
Score <25 → Standard/long DAPT

www.precisedaptscore.com

JACC VOL. 73, NO. 7, 2019
FEBRUARY 26, 2019:741–54

Antitrombotika při PCI: individualizace DAPT



Costa, F. et al. J Am Coll Cardiol. 2019;73(7):741-54.


BLEEDING
FIRST

Duální protidestičková léčba (DAPT): individuální přístup

Riziko ischémie / Riziko krvácení	**nízké**	**vysoké**
nízké	DAPT 12 m	DAPT 12-36 m
vysoké	Zkrácená DAPT 1-3 m	Zkrácená DAPT 1-6m

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