TRVALÁ ANTIKOAGULAČNÍ LÉČBA A PCI: CO VÍME V ROCE 2018?

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27. výroční sjezd České kardiologické společnosti

Brno, 8.5.2018

Trvalá antikoagulační léčba a PCI : 2018

Víme, že:

1. Po PCI je potřeba antikoagulační i protidestičková léčba
2. „Dual therapy“ je bezpečnější než „triple therapy“

Nevíme, zda:

1. Kyselina acetylsalicylová je nutnou součástí kombinace
2. Nové inhibitory P2Y12 jsou bezpečné v kombinaci s (N)OAC
3. „Dual therapy“ je stejně účinná jako „triple therapy“

Trvalá antikoagulační léčba a PCI : 2018

6-8% PCI má indikaci k trvalé antikoagulační terapii

fibrilace síní

mechanická chlopenní náhrada

žilní tromboembolická nemoc

A. Inhibitor P2Y12 (clopidogrel) je nezbytný pro prevenci trombózy stentu
B. OAC je nezbytný pro prevenci embolizační příhody (CMP)
C. Kyselina acetylsalicylová je nezbytná během PCI (úmrtí, IM)
D. Přidání (N)OAC k DAPT zvyšuje riziko vážného krvácení 3x

Trvalá antikoagulační léčba a PCI : 2018

The HAS-BLED bleeding risk score

Letter	Clinical characteristic*	Points awarded
H	Hypertension	1
A	Abnormal renal and liver function (1 point each)	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile INRs	1
E	Elderly (e.g. age > 65 years)	1
D	Drugs or alcohol (1 point each)	1 or 2
		Maximum 9 points

Modifiable bleeding risk factors
Hypertension (especially when systolic blood pressure is >160 mmHg)[a,b,c]
Labile INR or time in therapeutic range <60%[a] in patients on vitamin K antagonists
Medication predisposing to bleeding, such as antiplatelet drugs and non-steroidal anti-inflammatory drugs[a,d]
Excess alcohol (≥8 drinks/week)[a,b]
Potentially modifiable bleeding risk factors
Anaemia[b,c,d]
Impaired renal function[a,b,c,d]
Impaired liver function[a,b]
Reduced platelet count or function[b]
Non-modifiable bleeding risk factors
Age[e] (>65 years)[a] (≥75 years)[b,c,d]
History of major bleeding[a,b,c,d]
Previous stroke[a,b]

Trvalá antikoagulační léčba a PCI : 2018

PRECISE-DAPT

Tabulka 3 – Riziková skóre validovaná pro rozhodování o délce trvání duální protidestičkové léčby

	Skóre PRECISE-DAPT	Skóre DAPT
Doba uplatnění	V době koronárního stentingu	Po 12 měsících DAPT bez komplikací
Hodnocené strategie délky trvání DAPT	Krátkodobá DAPT (3–6 měsíců) oproti standardní/dlouhodobé DAPT (12–24 měsíců)	Standardní DAPT (12 měsíců) oproti dlouhodobé DAPT (30 měsíců)
Výpočet skóre[a]	Hb ≥12 11-5 11 10-5 ≤10 WBC ≤5 8 10 12 14 16 18 ≥20 Věk ≤50 60 70 80 ≥90 CrCl ≥100 80 60 40 20 0 Předchozí krvácení Ne Ano Body skóre 0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30	Věk ≥ 75 –2 body 65 až < 75 –1 bod < 65 0 bodů Kouření cigaret +1 bod Diabetes mellitus +1 bod IM vstupně +1 bod Předchozí PCI nebo předchozí IM +1 bod Stent uvolňující paclitaxel +1 bod Průměr stentu < 3 mm +1 bod CHF nebo EFLK < 30 % +2 body Stent z žilního štěpu +2 body
Rozmezí skóre	0 až 100 bodů	–2 až 10 bodů
Navrhovaná hraniční hodnota pro rozhodování	Skóre ≥ 25 → krátkodobá DAPT Skóre < 25 → standardní/dlouhodobá DAPT	Skóre ≥ 2 → dlouhodobá DAPT Skóre < 2 → standardní DAPT
Kalkulátor	www.precisedaptscore.com	www.daptstudy.org

PARIS

Parameter	Score				
Age, years	< 50	50-59	60-69	70-79	>80
	0	+1	+2	+3	+4
BMI, kg/m²	<25		25-34.9	> 35	
	+2		0	+2	
Current Smoking	Yes +2		No 0		
Anemia	Present +3		Absent 0		
CrCl <60 ml/min	Present +2		Absent 0		
TT* on discharge	Yes +2		No 0		

Trvalá antikoagulační léčba a PCI : 2018

Table 4 Strategies to avoid bleeding complications in patients treated with oral anticoagulant

• Assess ischaemic and bleeding risks using validated risk predictors (e.g. CHA_2DS_2-VASc, ABC, HAS-BLED) with a focus on modifiable risk factors.
• Keep triple therapy duration as short as possible; dual therapy after PCI (oral anticoagulant and clopidogrel) to be considered instead of triple therapy.
• Consider the use of NOACs instead of VKA.
• Consider a target INR in the lower part of the recommended target range and maximize time in therapeutic range (i.e. > 65–70%) when VKA is used.
• Consider the lower NOAC regimen tested in approval studies and apply other NOAC regimens based on drug-specific criteria for drug accumulation.[a]
• Clopidogrel is the $P2Y_{12}$ inhibitor of choice.
• Use low-dose (≤ 100 mg daily) aspirin.
• Routine use of PPIs.

1. Modifikovat ovlivnitelné rizikové faktory krvácení
2. „Triple therapy“ co nejkratší
3. Preferovat NOAC
4. OAC na dolní hranici
5. Preferovat clopidogrel
6. Vždy PPI

European Heart Journal (2017) **0**, 1–48
doi:10.1093/eurheartj/ehx419

Délka trojité léčby („triple therapy, TT“)

Delší

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

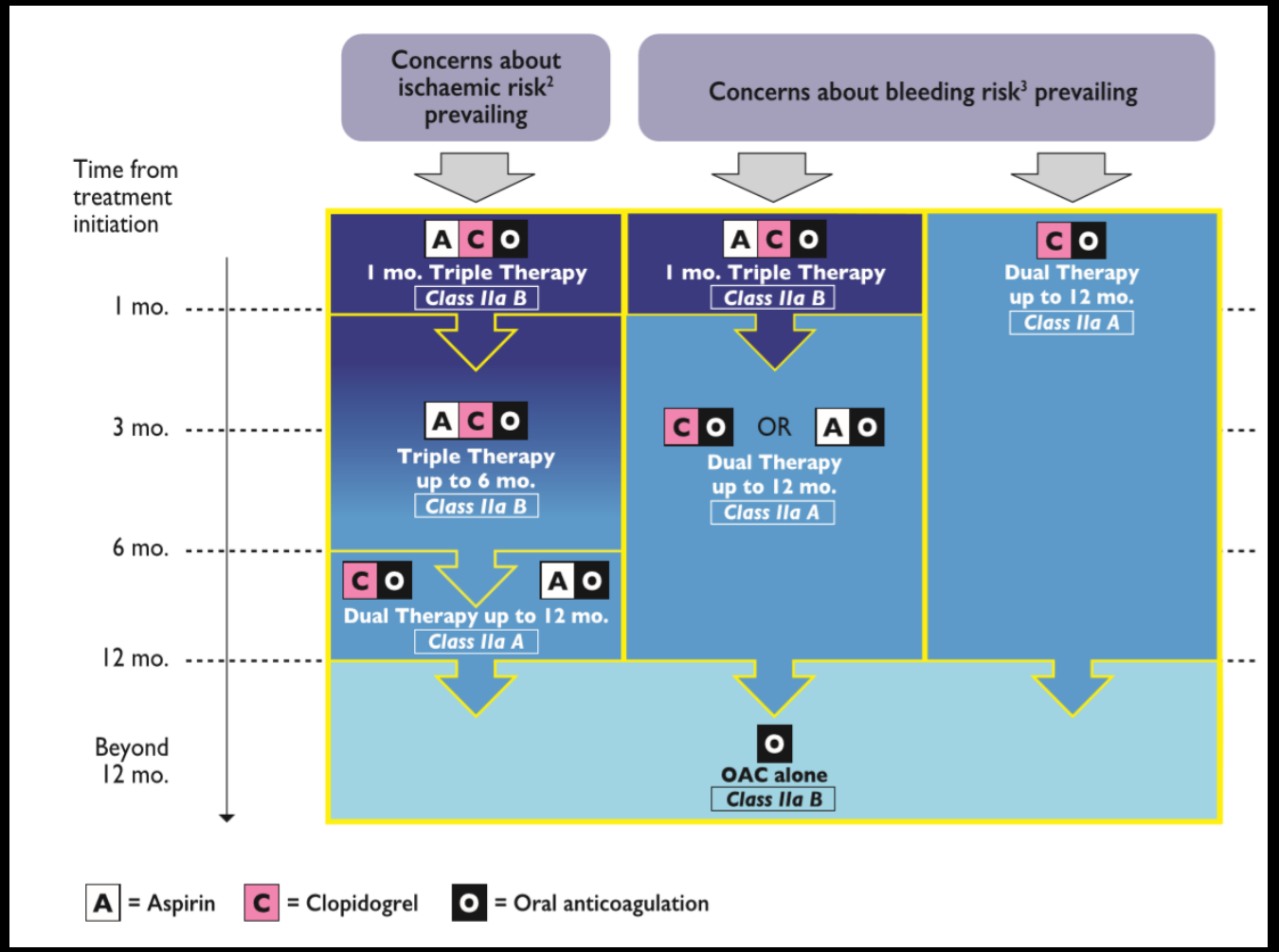
Kratší nebo DT

Table 6 Unfavourable patient profile for a combination of oral anticoagulant and antiplatelet therapy

• Short life expectancy
• Ongoing malignancy
• Poor expected adherence
• Poor mental status
• End stage renal failure
• Advanced age
• Prior major bleeding/prior haemorrhagic stroke
• Chronic alcohol abuse
• Anaemia
• Clinically significant bleeding on dual antithrombotic therapy

European Heart Journal (2017) **0**, 1–48
doi:10.1093/eurheartj/ehx419

Trvalá antikoagulační léčba a PCI : 2018



European Heart Journal (2017) **0**, 1–48
doi:10.1093/eurheartj/ehx419

WOEST: dual therapy vs triple therapy

WOEST

Study Design-1

Inclusion criteria:

1/ Indication for OAC for at least 1 year
2/ One coronary lesion eligible for PCI
3/ Age over 18

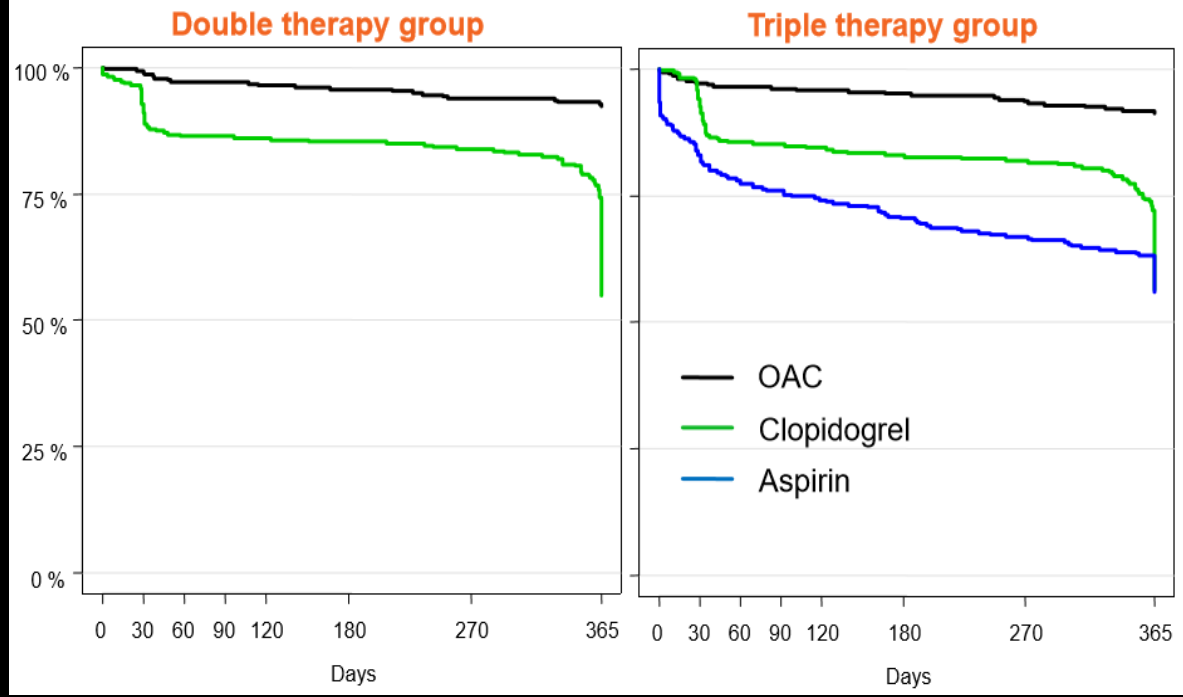
Exclusion criteria:

1/ History of intracranial bleeding
2/ Cardiogenic shock during hospitalisation
3/ Peptic ulcer in the previous 6 months
4/ TIMI major bleeding in the previous year
5/ Contra-indication for aspirin or clopidogrel
6/ Thrombocytopenia (platelet count less than 50,000 per ml)
7/ Pregnancy
8/ Age >80

ZIEKENHUIS ST ANTONIUS

WOEST

Compliance to OAC, aspirin and clopidogrel

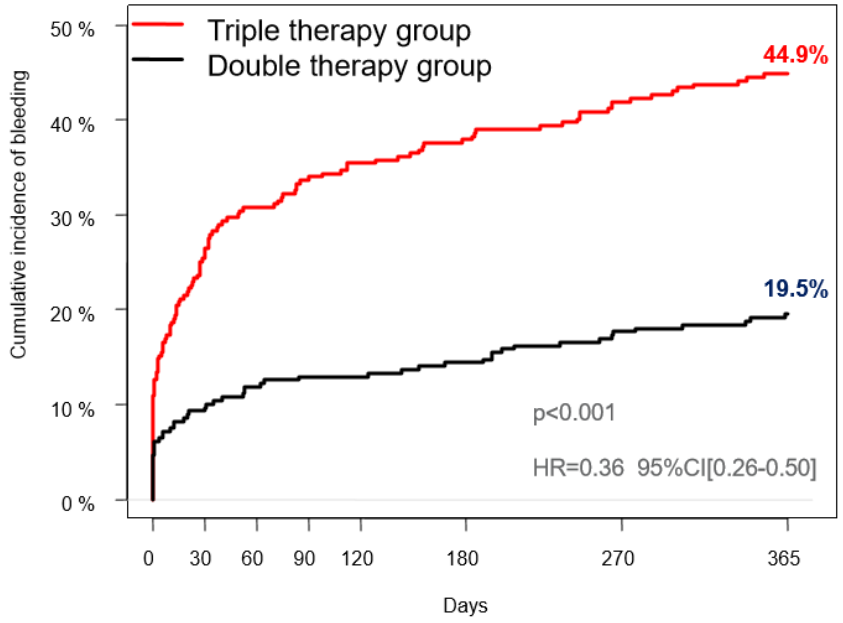


Lancet. 2013 Mar 30;381(9872):1107-15.

WOEST: dual therapy vs triple therapy

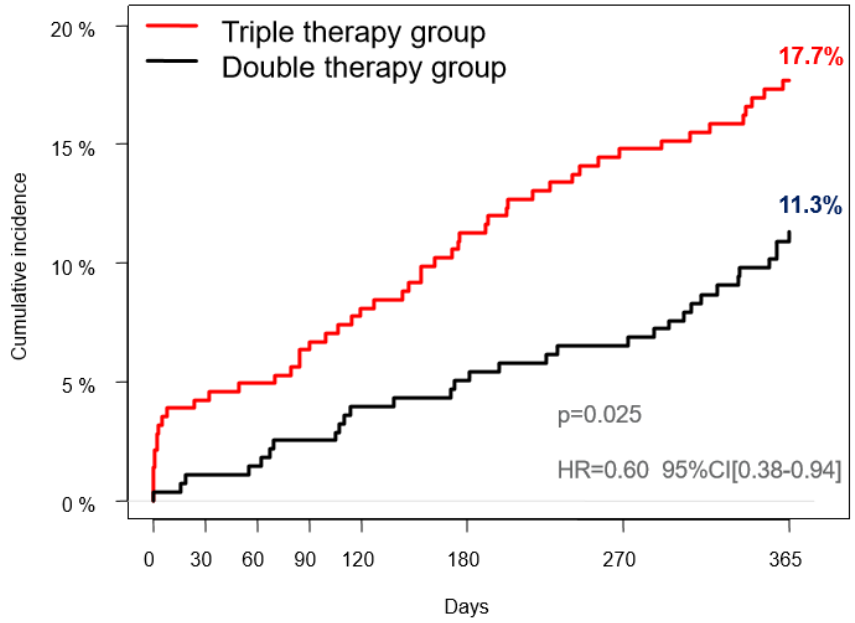
WOEST

Primary Endpoint: Total number of bleeding events (TIMI criteria)



WOEST

Secondary Endpoint (Death, MI,TVR, Stroke, ST)



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7/ Pregnancy
8/ Age >80

ZIEKENHUIS ST ANTONIUS

???

Dual therapy with clopidogrel 75 mg/day and OAC should be considered as an alternative to 1-month triple antithrombotic therapy in patients in whom the bleeding risk outweighs the ischaemic risk.[191,193]	IIa	A

Lancet. 2013 Mar 30;381(9872):1107-15.

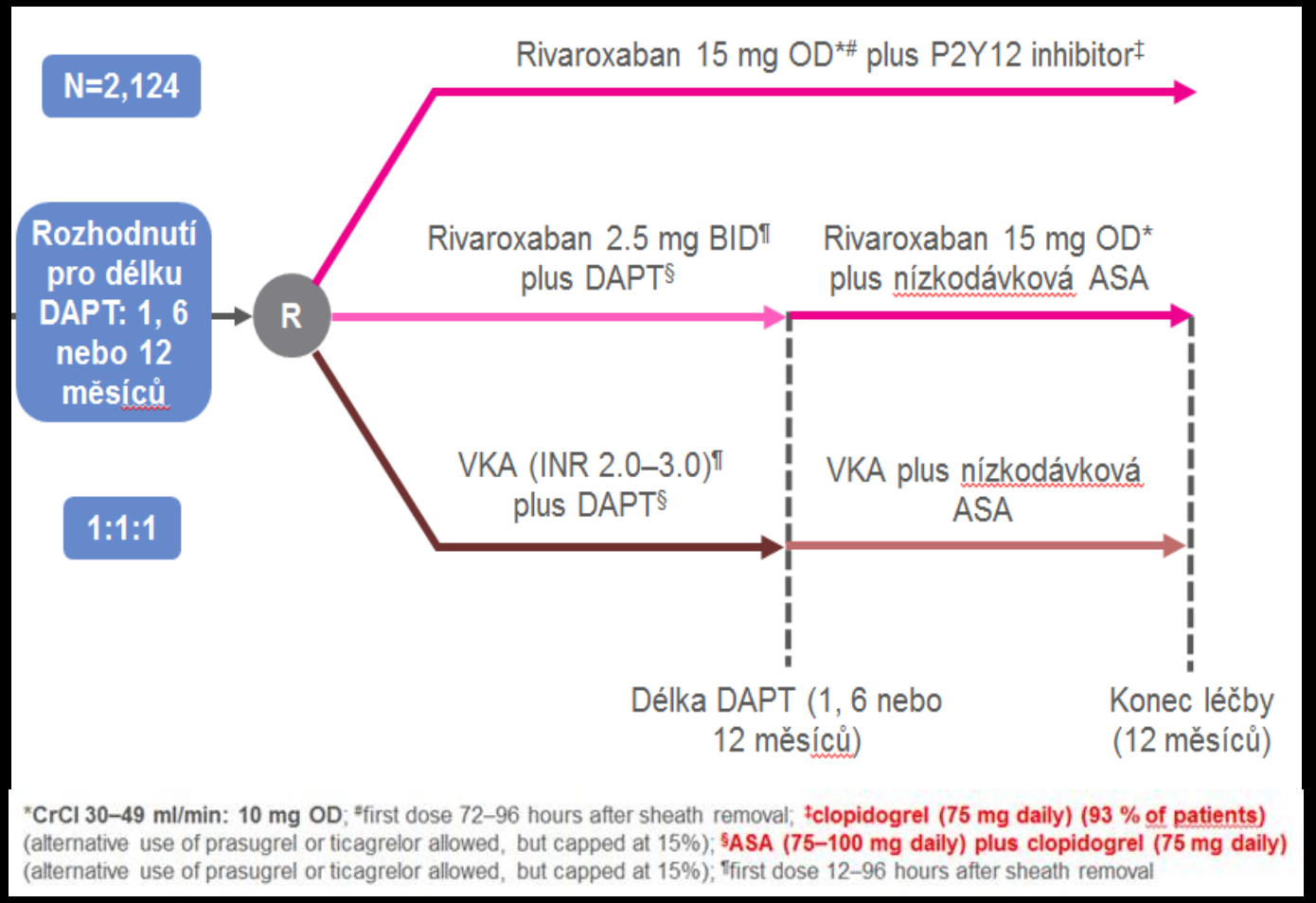
European Heart Journal (2017) **0**, 1–48
doi:10.1093/eurheartj/ehx419

PIONEER AF

Vstupní indikace:
PCI při fibrilace síní

Vylučující kriterium:
- anamnéza CMP/TIA
- krvácení GIT
- anémie
- CrCl <30 mL/min

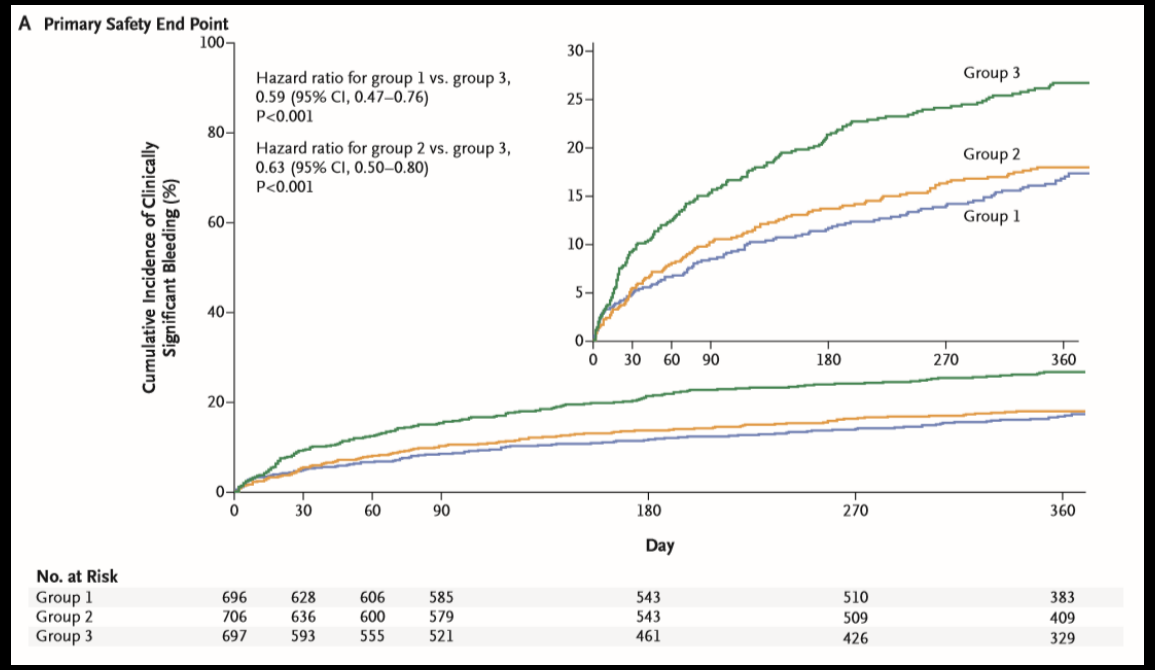
Randomizace 3 dny po PCI*

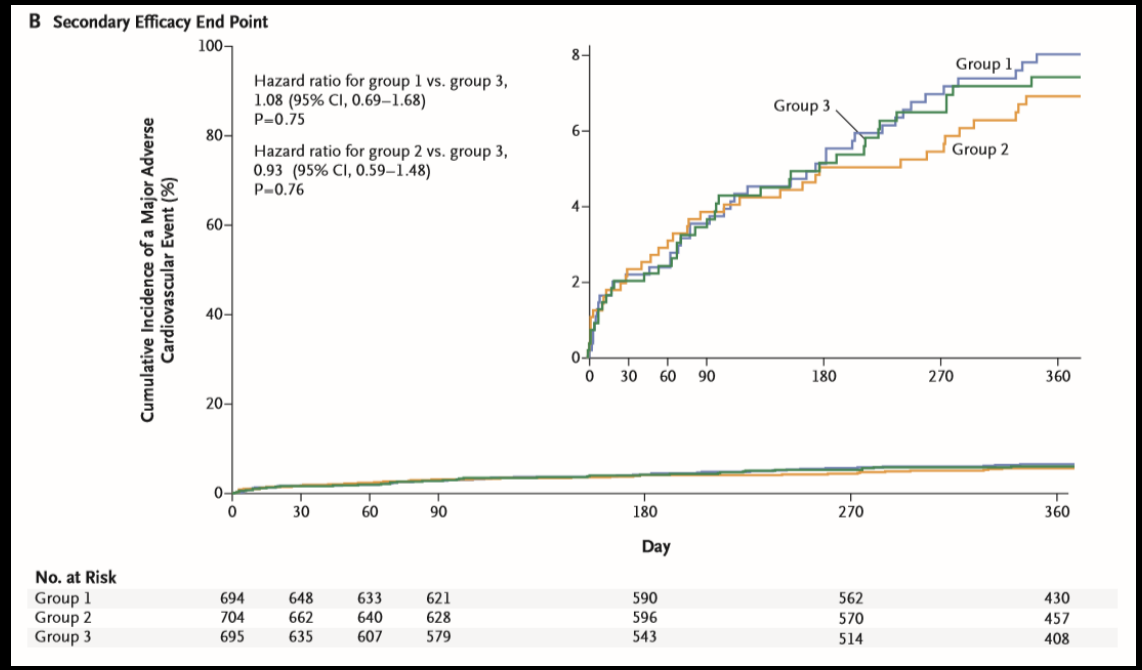


*platí pro studijní skupinu 1, # převážně clopidogrel – 93 % pacientů

N Engl J Med 2016;375:2423-34

PIONEER AF





N Engl J Med 2016;375:2423-34

PIONEER AF

	R	W		
Participants assigned to DAPT for 1 mo — no.	108	112		
Major adverse cardiovascular event	6 (5.8)	5 (5.2)	1.17 (0.36–3.84)	0.79
Death from cardiovascular causes	2 (2.1)	2 (2.2)	0.96 (0.13–6.80)	0.97
Myocardial infarction	3 (2.9)	1 (1.1)	2.93 (0.30–28.16)	0.33
Stroke	2 (1.9)	3 (3.1)	0.65 (0.11–3.91)	0.64
Stent thrombosis	2 (1.9)	1 (1.1)	1.97 (0.18–21.74)	0.57
Major adverse cardiovascular event or stent thrombosis	6 (5.9)	5 (5.2)	1.17 (0.36–3.84)	0.79
Participants assigned to DAPT for 6 mo — no.	248	243		
Major adverse cardiovascular event	16 (7.0)	9 (4.3)	1.72 (0.76–3.88)	0.19
Death from cardiovascular causes	6 (2.8)	4 (1.9)	1.45 (0.41–5.12)	0.57
Myocardial infarction	7 (3.0)	6 (2.9)	1.13 (0.38–3.37)	0.82
Stroke	6 (2.7)	0		0.02
Stent thrombosis	4 (1.7)	1 (0.4)	3.91 (0.44–35.02)	0.19
Major adverse cardiovascular event or stent thrombosis	16 (7.0)	9 (4.3)	1.72 (0.76–3.40)	0.19
Participants assigned to DAPT for 12 mo — no.	348	340		
Major adverse cardiovascular event	14 (4.5)	22 (7.4)	0.57 (0.29–1.11)	0.10
Death from cardiovascular causes	6 (1.9)	5 (1.7)	1.08 (0.33–3.55)	0.89
Myocardial infarction	7 (2.3)	14 (4.8)	0.44 (0.18–1.10)	0.07
Stroke	2 (0.6)	4 (1.3)	0.46 (0.08–2.51)	0.36
Stent thrombosis	0	2 (0.8)		0.10
Major adverse cardiovascular event or stent thrombosis	14 (4.5)	22 (7.4)	0.57 (0.29–1.11)	0.10

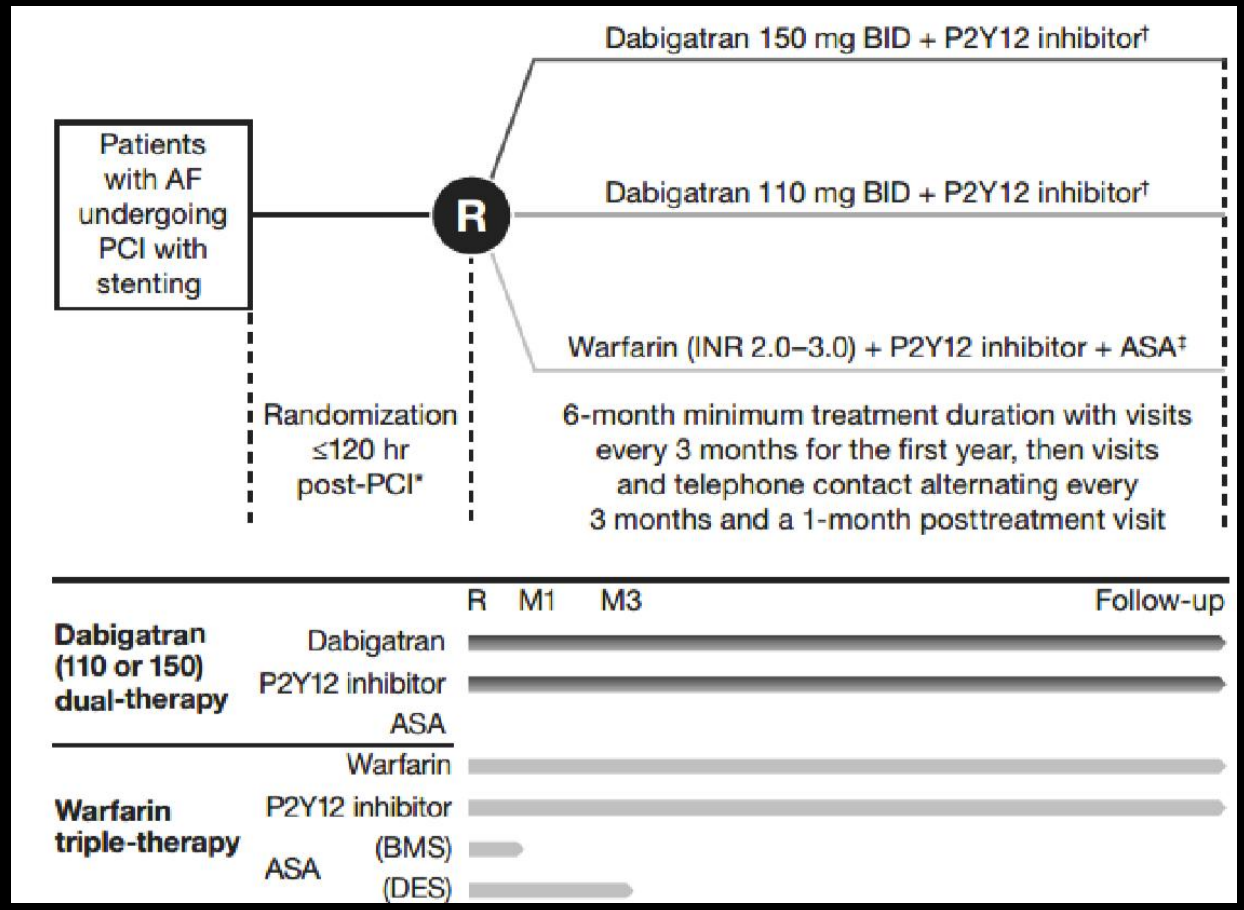
N Engl J Med 2016;375:2423-34

RE-DUAL

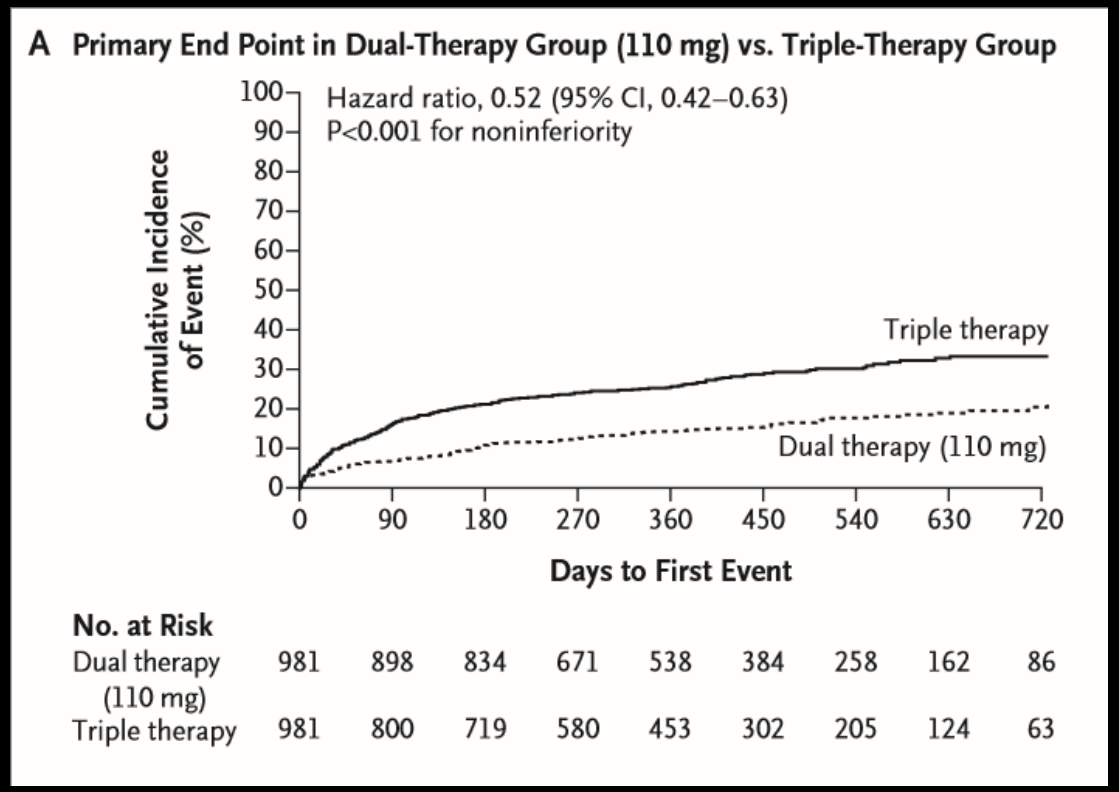
Vstupní indikace :
PCI při fibrilaci síní (ACS/stable)

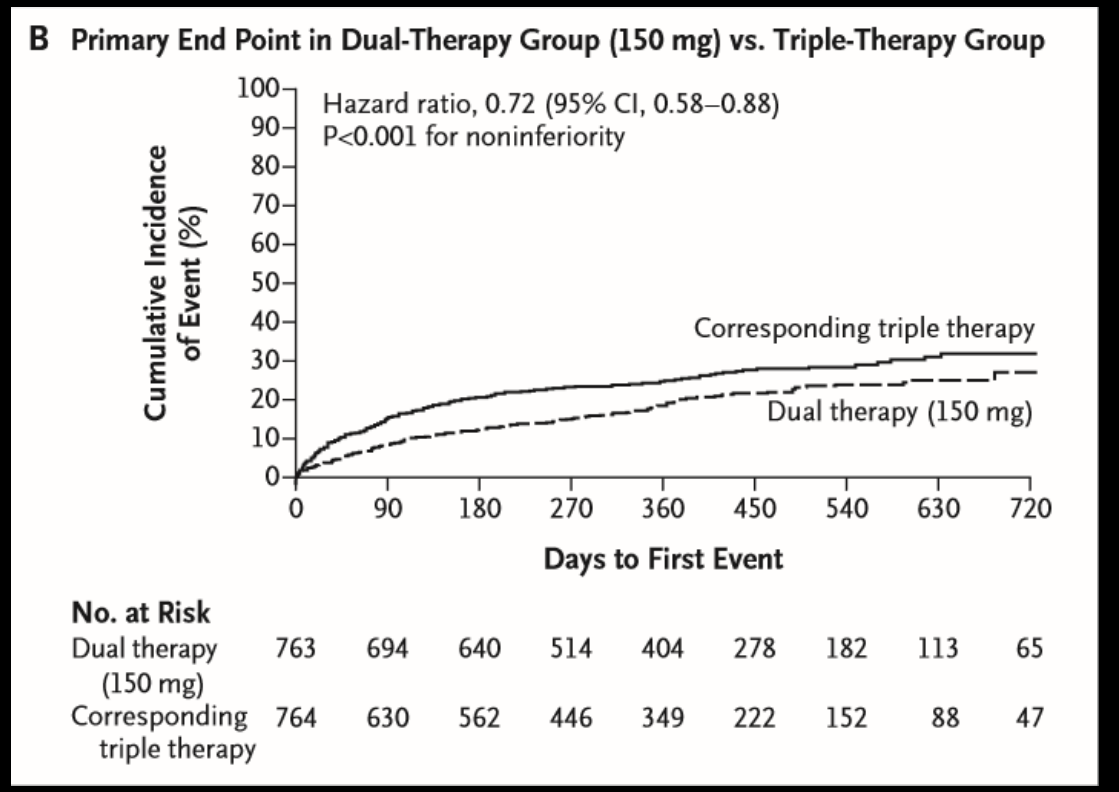
Vylučující kriteria :
anamnéza CMP/TIA (1m)
krvácení GIT (1m)
anémie
CrCl <30 mL/min

Randomizace : 5 dnů po PCI



RE-DUAL





N Engl J Med 2017; 377:1513-1524

RE-DUAL

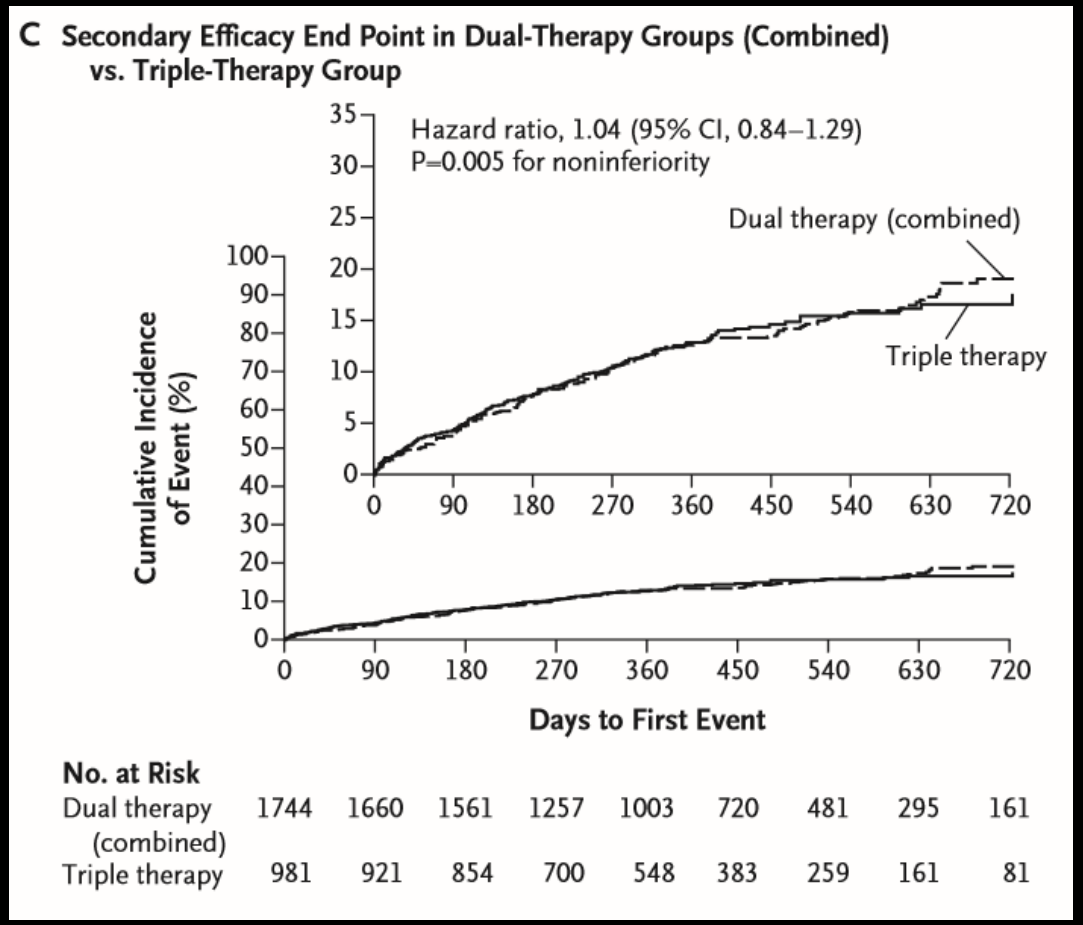
Table 2. Safety End Points.*

End Point	Dual Therapy with Dabigatran, 110 mg (N=981)	Triple Therapy with Warfarin (N=981)	Hazard Ratio (95% CI)	P Value†	Dual Therapy with Dabigatran, 150 mg (N=763)	Corresponding Triple Therapy with Warfarin (N=764)	Hazard Ratio (95% CI)	P Value†
	no. (%)				*no. (%)*			
Primary end point: ISTH major or clinically relevant nonmajor bleeding	151 (15.4)	264 (26.9)	0.52 (0.42–0.63)	<0.001 (<0.001 for noninferiority)	154 (20.2)	196 (25.7)	0.72 (0.58–0.88)	0.002 (<0.001 for noninferiority)
ISTH major bleeding	49 (5.0)	90 (9.2)	0.52 (0.37–0.74)	<0.001	43 (5.6)	64 (8.4)	0.64 (0.43–0.94)	0.02
Total bleeding	266 (27.1)	421 (42.9)	0.54 (0.46–0.63)	<0.001	254 (33.3)	316 (41.4)	0.72 (0.61–0.84)	<0.001
Intracranial hemorrhage	3 (0.3)	10 (1.0)	0.30 (0.08–1.07)	0.06	1 (0.1)	8 (1.0)	0.12 (0.02–0.98)	0.047
TIMI major bleeding	14 (1.4)	37 (3.8)	0.37 (0.20–0.68)	0.002	16 (2.1)	30 (3.9)	0.51 (0.28–0.93)	0.03
TIMI major or minor bleeding	29 (3.0)	69 (7.0)	0.41 (0.26–0.63)	<0.001	27 (3.5)	48 (6.3)	0.53 (0.33–0.85)	0.009

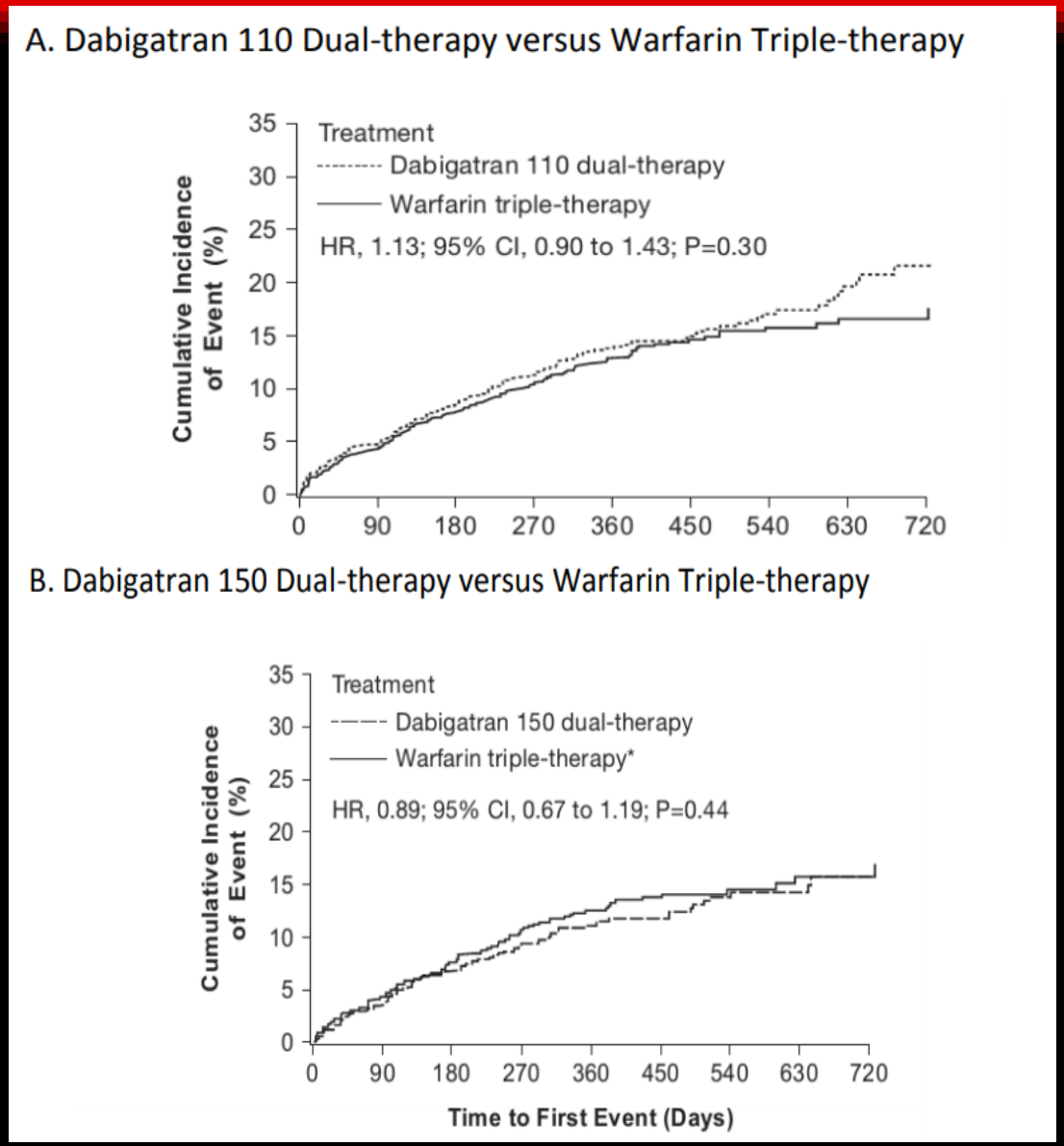
Characteristic	Dabigatran 110 Dual-therapy (n=981)	Warfarin Triple-therapy (n=981)	Dabigatran 150 Dual-therapy (n=763)	Warfarin Triple-therapy (n=764)§
Prior stroke/TIA, n (%)*	108 (11.0)	142 (14.5)	67 (8.8)	108 (14.1)
CHA_2DS_2-VASC score, n (%)				
≤2	230 (23.4)	193 (19.7)	247 (32.4)	184 (24.1)
>2	751 (76.6)	788 (80.3)	516 (67.6)	580 (75.9)
HAS-BLED score, n (%)				
<3	326 (33.2)	288 (29.4)	309 (40.5)	257 (33.6)
≥3	655 (66.8)	693 (70.6)	454 (59.5)	507 (66.4)

N Engl J Med 2017; 377:1513-1524

RE-DUAL



N Engl J Med 2017; 377:1513-1524



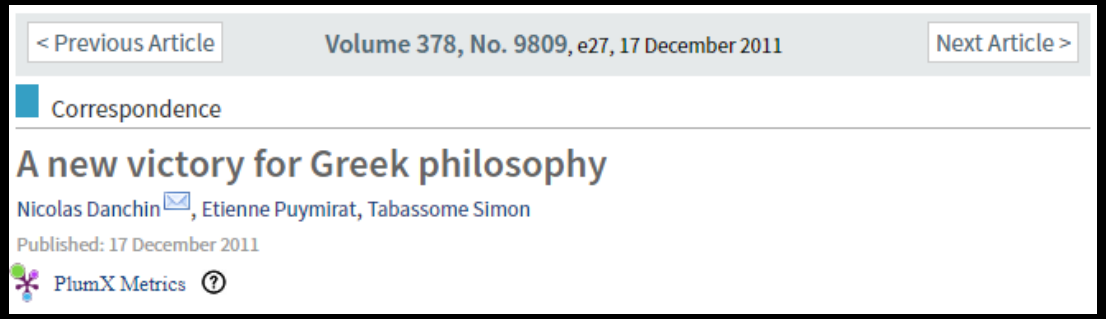
RE-DUAL

Table 3. Efficacy End Points.*

End Point	Dual Therapy with Dabigatran (Combined) vs. Triple Therapy with Warfarin				Dual Therapy with Dabigatran (110 mg) vs. Triple Therapy with Warfarin				Dual Therapy with Dabigatran (150 mg) vs. Triple Therapy with Warfarin			
	Combined Dual-Therapy Groups (N=1744)	Triple-Therapy Group (N=981)	Hazard Ratio (95% CI)	P Value†	110-mg Dual-Therapy Group (N=981)	Triple-Therapy Group (N=981)	Hazard Ratio (95% CI)	P Value†	150-mg Dual-Therapy Group (N=763)	Corresponding Triple-Therapy Group (N=764)	Hazard Ratio (95% CI)	P Value†
	no. (%)				*no. (%)*				*no. (%)*			
Composite efficacy end point: thromboembolic events, death, or unplanned revascularization	239 (13.7)	131 (13.4)	1.04 (0.84–1.29)	0.74 (0.005 for noninferiority)	149 (15.2)	131 (13.4)	1.13 (0.90–1.43)	0.30	90 (11.8)	98 (12.8)	0.89 (0.67–1.19)	0.44
Thromboembolic events or death	168 (9.6)	83 (8.5)	1.17 (0.90–1.53)	0.25 (0.11 for noninferiority)	108 (11.0)	83 (8.5)	1.30 (0.98–1.73)	0.07	60 (7.9)	60 (7.9)	0.97 (0.68–1.39)	0.88
Death					55 (5.6)	48 (4.9)	1.12 (0.76–1.65)	0.56	30 (3.9)	35 (4.6)	0.83 (0.51–1.34)	0.44
Myocardial infarction					44 (4.5)	29 (3.0)	1.51 (0.94–2.41)	0.09	26 (3.4)	22 (2.9)	1.16 (0.66–2.04)	0.61
Stroke					17 (1.7)	13 (1.3)	1.30 (0.63–2.67)	0.48	9 (1.2)	8 (1.0)	1.09 (0.42–2.83)	0.85
Definite stent thrombosis					15 (1.5)	8 (0.8)	1.86 (0.79–4.40)	0.15	7 (0.9)	7 (0.9)	0.99 (0.35–2.81)	0.98

N Engl J Med 2017; 377:1513-1524

Trvalá antikoagulační léčba a PCI : 2018



< Previous Article | Volume 378, No. 9809, e27, 17 December 2011 | Next Article >

Correspondence

A new victory for Greek philosophy

Nicolas Danchin, Etienne Puymirat, Tabassome Simon

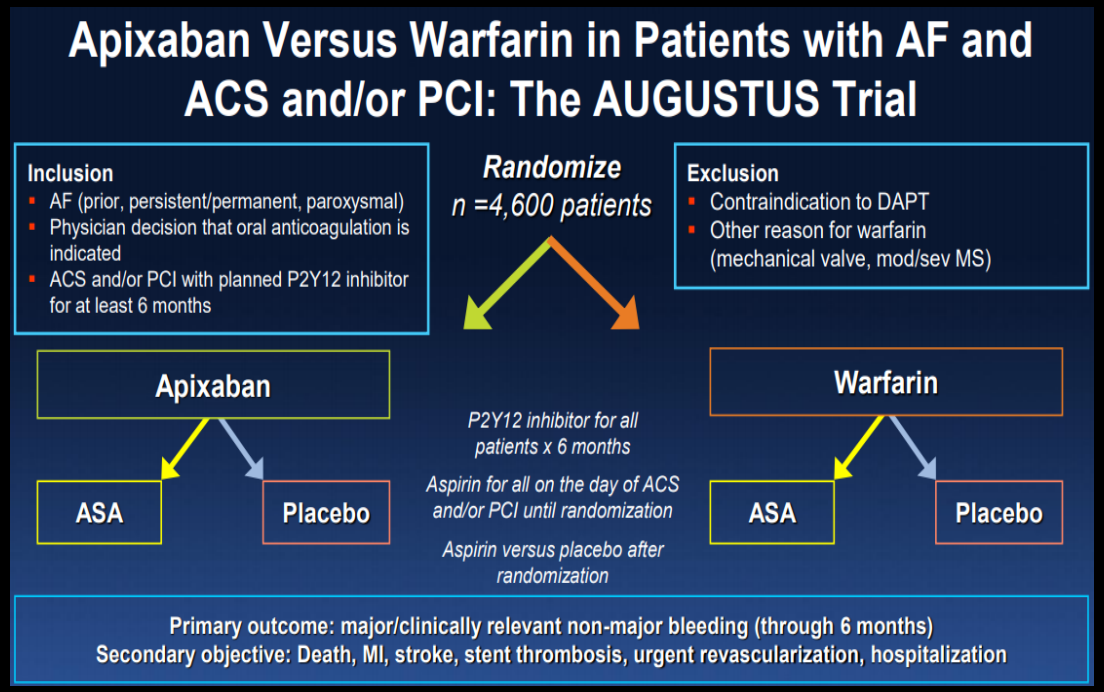
Published: 17 December 2011

PlumX Metrics

We found 149 trials that met our selection criteria (webappendix), 19 of which showed a significant reduction in total mortality: ARISTOTLE, PLATO, ADVANCE-BP, CARE-HF, COMET, COMMIT-clopidogrel, COPERNICUS, CREATE-ECLA-Reviparin, EMPHASIS, EPHESUS, GISSI-HF-PUFA, HOPE-ramipril, HPS-simvastatin, JUPITER, MADIT-2, OASIS-6, RAFT, SCD-Heft-ICD, and TAPAS. Overall, 100% of Greek philosopher trials showed a significant reduction in all-cause mortality, compared with 17 (12%) of 147 trials with any other kind of acronym (p=0·016, Fisher's exact test).

Trvalá antikoagulační léčba a PCI : 2018

AUGUSTUS



Actual Study Start Date :	June 4, 2015
Estimated Primary Completion Date :	December 27, 2018
Estimated Study Completion Date :	December 28, 2018

ENTRUST-AF

Am Heart J. 2018 Feb;196:105-112. doi: 10.1016/j.ahj.2017.10.009. Epub 2017 Oct 23.

Evaluation of the safety and efficacy of an edoxaban-based antithrombotic regimen in patients with atrial fibrillation following successful percutaneous coronary intervention (PCI) with stent placement: Rationale and design of the ENTRUST-AF PCI trial.

Vranckx P[1], Lewalter T[2], Valgimigli M[3], Tijssen JG[4], Reimitz PE[5], Eckardt L[6], Lanz HJ[5], Zierhut W[5], Smolnik R[5], Goette A[7].

Study Type :	Interventional (Clinical Trial)
Estimated Enrollment :	1500 participants
Allocation:	Randomized
Intervention Model:	Parallel Assignment
Masking:	None (Open Label)
Primary Purpose:	Treatment
Official Title:	Evaluation of the Safety and Efficacy of an Edoxaban- Placement.
Actual Study Start Date :	February 24, 2017
Estimated Primary Completion Date :	March 2019
Estimated Study Completion Date :	March 2019

Trvalá antikoagulační léčba a PCI : 2018

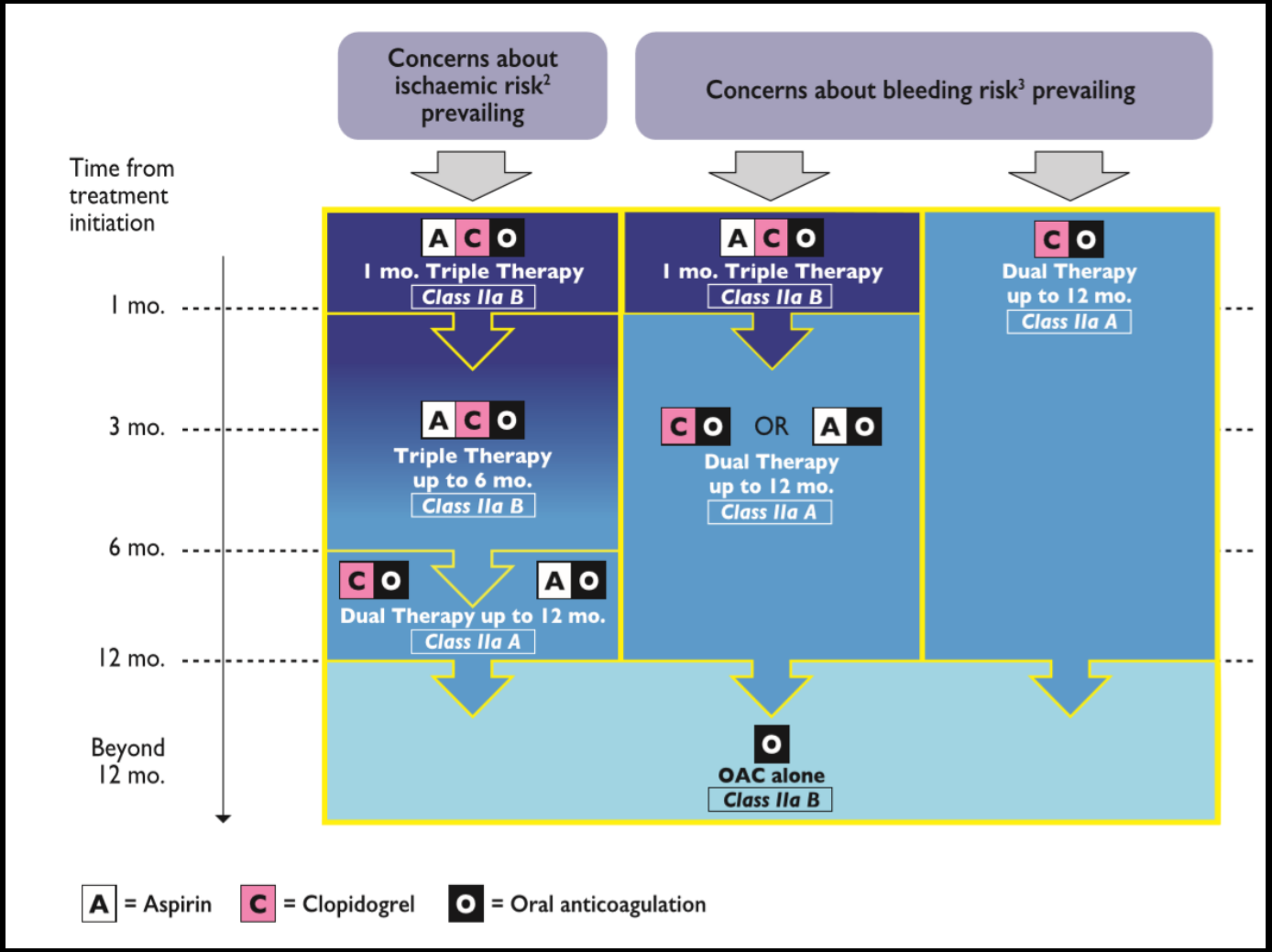
Víme, že:

1. Po PCI je potřeba antikoagulační i protidestičková léčba
2. „Dual therapy“ je bezpečnější než „triple therapy“

Nevíme, zda:

1. Kyselina acetylsalicylová je nutnou součástí kombinace (AUGUSTUS)
2. Nové inhibitory P2Y12 jsou bezpečné v kombinaci s (N)OAC
3. „Dual therapy“ je stejně účinná jako „triple therapy“ (metaanalýza?)

Trvalá antikoagulační léčba a PCI : 2018



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