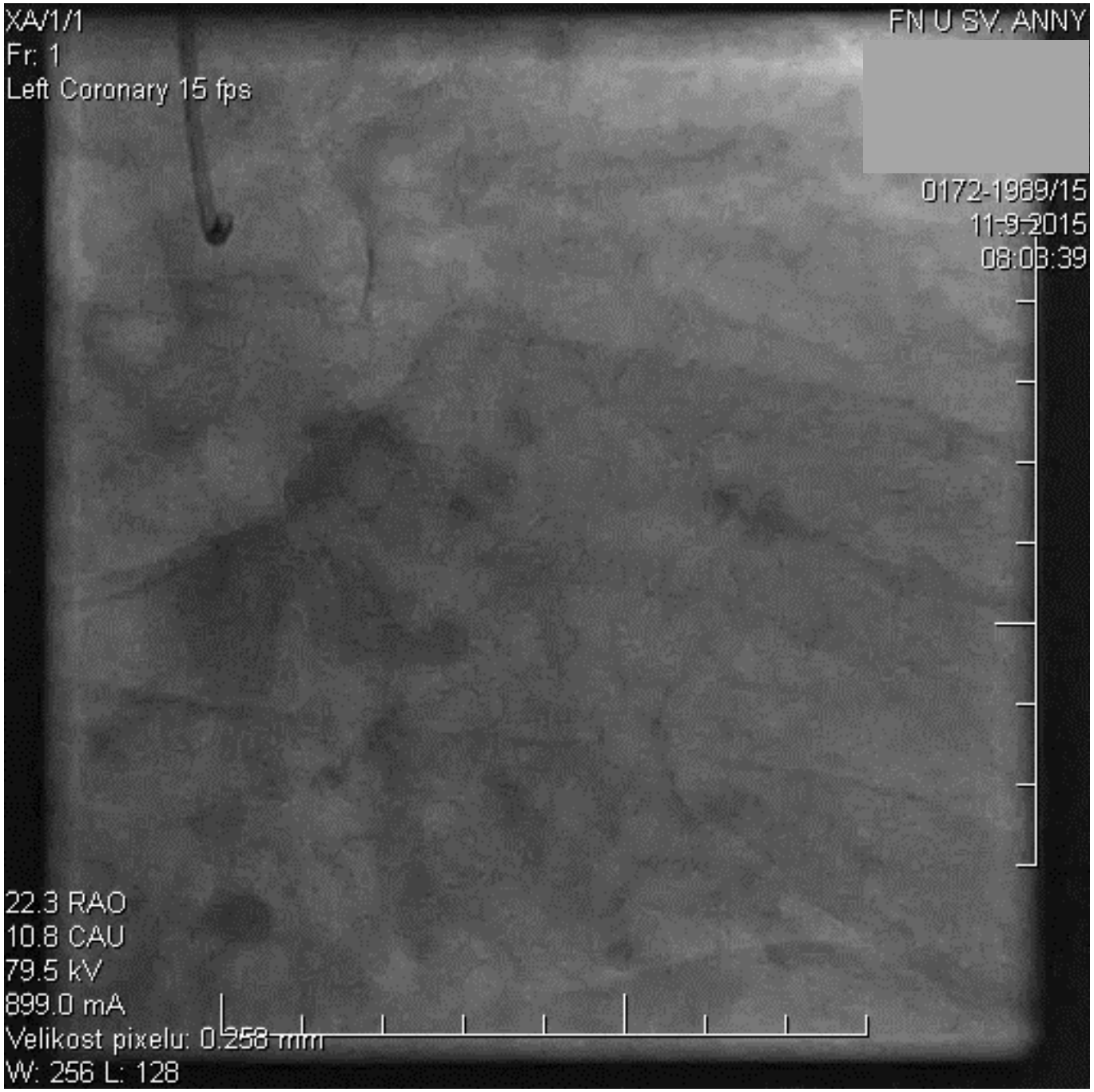
Aspirin po PCI je nezbytný

O. Hlinomaz

I. IKAK, ICRC, FN u sv. Anny, Brno
CINRE, Bratislava

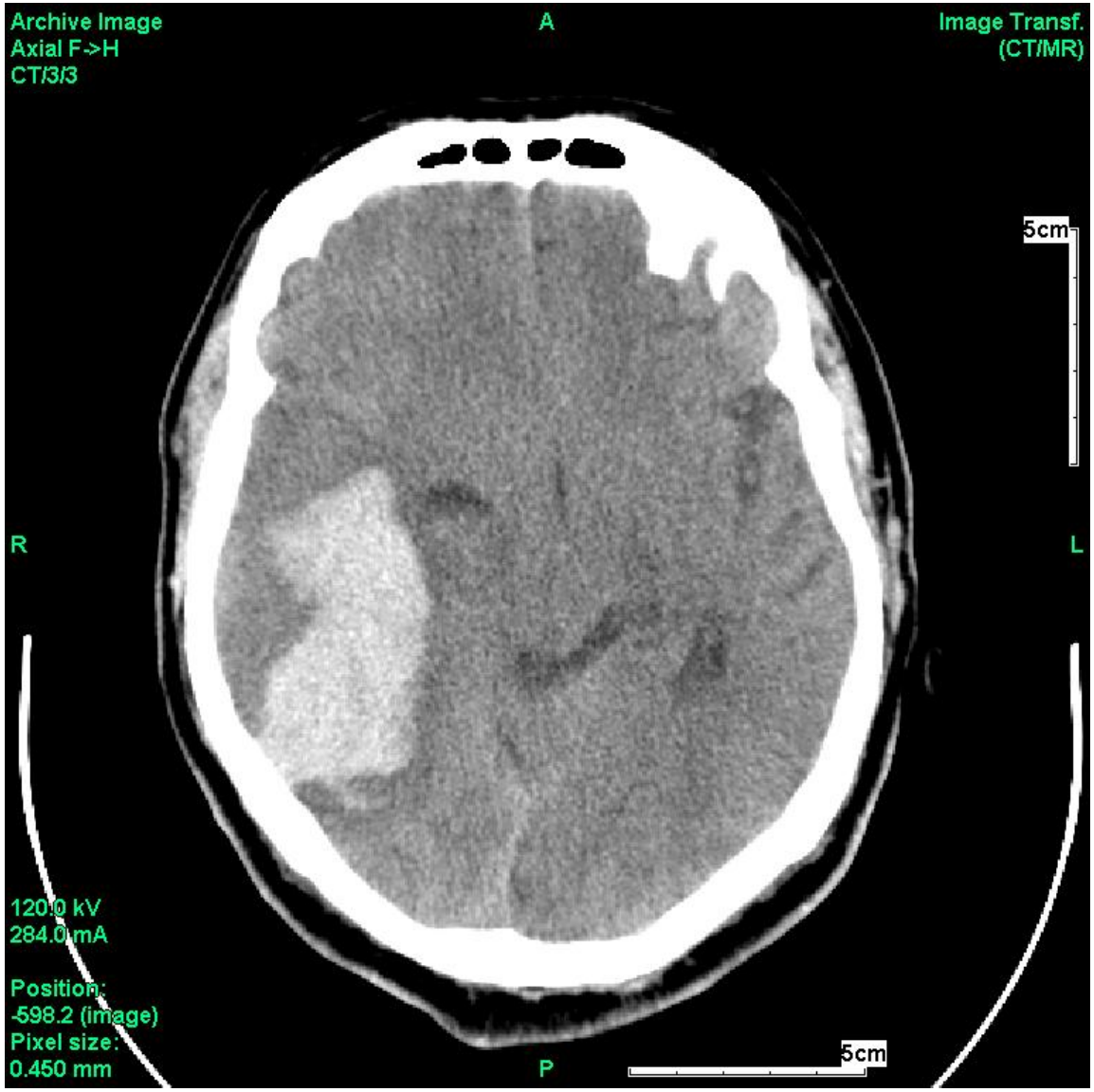


M, 69 let

NSTEMI
Preterminal neg. II,III,aVF,V4-6

DM II 5 let
Hypertenze
Obezita
Kolorektální Ca 2014- CH,R

Mozkové krvácení



Vol 6 September 2014 Clinical Pharmacist

Aspirin was one of the first drugs to come into common usage and is still one of the most researched drugs in the world, with an estimated 700 to 1,000 clinical trials conducted each year

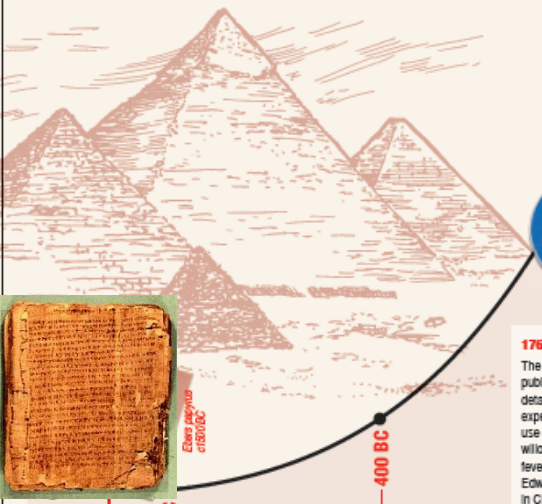
A history of aspirin

By **Dawn Connelly**

1899 Acetylsalicylic acid is named Aspirin by Bayer. The letter 'A' stands for acetyl, "spir" is derived from the plant known as *Spiraea ulmaria* (meadowsweet), which yields salicin, and "in" was a common suffix used for drugs at the time of the first stable synthesis of acetylsalicylic acid.

1974 Data from the first randomised controlled trial of aspirin in the secondary prevention of death from heart attack show a reduction in total mortality of 12% at 6 months and 25% at 12 months but the results are statistically inconclusive (*BMJ* 1974;1:436).

2014 A meta-analysis suggests that long-term prophylactic use of aspirin has a favourable benefit–harm profile and leads to a dramatic reduction in the incidence of bowel, stomach and oesophageal cancer (*Annals of Oncology*, online 5 August 2014).



Ebers papyrus c1500BC

3000 BC

1500 BC

400 BC

1763

1828

1830

1853

1876

1897

1950

1971

1991

1993

1997

1998

2005

2009

2011

2013

2015

2018

c3000 – 1500 BC Willow is used as a medicine by ancient civilisations like the Sumerians and Egyptians. The Ebers papyrus, an ancient Egyptian medical text, refers to willow as an anti-inflammatory or pain reliever for non-specific aches and pains.

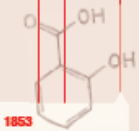
White Willow (Salix alba)

c400 BC In Greece, Hippocrates administers willow leaf tea, which contains the natural compound from which aspirin is derived, to women to ease the pain of childbirth.

Hippocrates admired Willow leaf tea in ancient Greece

1763 The Royal Society publishes a report detailing five years of experiments on the use of dried, powdered willow bark in curing fevers, submitted by Edward Stone, a vicar in Chipping Norton, Oxfordshire.

1828 Joseph Buchner, professor of pharmacy at Munich University, Germany, succeeds in extracting the active ingredient from willow, producing bitter tasting yellow crystals that he names salicin.



1853 French chemist Charles Frédéric Gerhardt determines the chemical structure of salicylic acid and chemically synthesises acetylsalicylic acid.

1830 Salicin is also found in the meadowsweet flower by Swiss pharmacist Johann Pagenstecher and later by German researcher Karl Jacob Löwig.

1876 The first rigorous clinical trial of salicin finds that it induces remission of fever and joint inflammation in patients with rheumatism (*Lancet* 1876;1:383).

1897 While working for pharmaceutical company Bayer, German chemist Felix Hoffmann, possibly under the direction of colleague Arthur Eichengrün, finds that adding an acetyl group to salicylic acid reduces its irritant properties and Bayer patents the process.

Bayer Pharmaceuticals was the first to produce the aspirin tablet

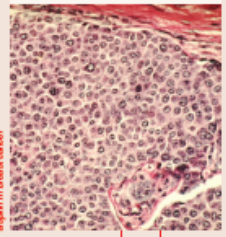
1950 Aspirin enters the Guinness World Records for being the most frequently sold painkiller.

1971 John Vane, professor of pharmacology at the University of London, publishes research describing aspirin's mechanism of action (dose-dependent inhibition of prostaglandin synthesis) (*Nature New Biology* 1971;231:232).

He later wins a Nobel prize (1982) for this work, along with Bengt Samuelsson and Sune Bergström.

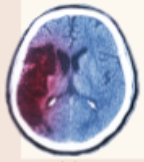
English pharmacologist Sir John Robert Vane 1927–2004

1991 & 1993 Results from the CPS (cancer prevention study)-II, a large US prospective cohort study, confirm the cancer benefits of aspirin seen in smaller observational studies (*NEJM* 1991;325:1593 and *Cancer Research* 1993;53:1322).



Study confirms benefit of aspirin in breast cancer

1997 Results from the CAST (Chinese acute stroke trial) study of early aspirin use in 20,000 patients with acute ischaemic stroke show that aspirin started early in hospital produces a small but definite net benefit (*Lancet* 1997; 349:1641).



Early aspirin in ischaemic stroke produces benefit

1998 Results from the HOT (hypertension optimal treatment) trial show that aspirin significantly reduces major cardiovascular events in hypertensive patients, with the greatest benefit seen in preventing heart attacks. The incidence of non-fatal major bleeds was twice as common (*Lancet* 1998;351;1755).

2005 Results from WHS (women's health study), a large, primary-prevention trial among women, suggest that aspirin lowers the risk of stroke without affecting the risk of heart attack or death from cardiovascular causes (*NEJM* 2005;352:1293). The WHS was conducted by investigators from Harvard Medical School.

2009 A meta-analysis by the ATT (antithrombotic trialists) collaboration suggests that aspirin has substantial overall benefit in secondary prevention but in primary prevention, aspirin is of uncertain net value as the reduction in occlusive events needs to be weighed against any increase in major bleeds (*Lancet* 2009;373:1849).

2011 A meta-analysis of eight clinical trials finds that, after five years of follow-up, trial participants who took aspirin daily for a mean of four years have a 44% reduced risk of dying from cancer compared with participants who took a placebo (*Lancet* 2011;377:31).

2013 Follow-up results of the WHS confirm that long-term use of alternate day low-dose aspirin results in a 42% reduction in colorectal cancer incidence, with benefits starting to appear after 10 years. The results also show increased risk of gastrointestinal bleeding and peptic ulcers (*Annals of Internal Medicine* 2013;159:77).

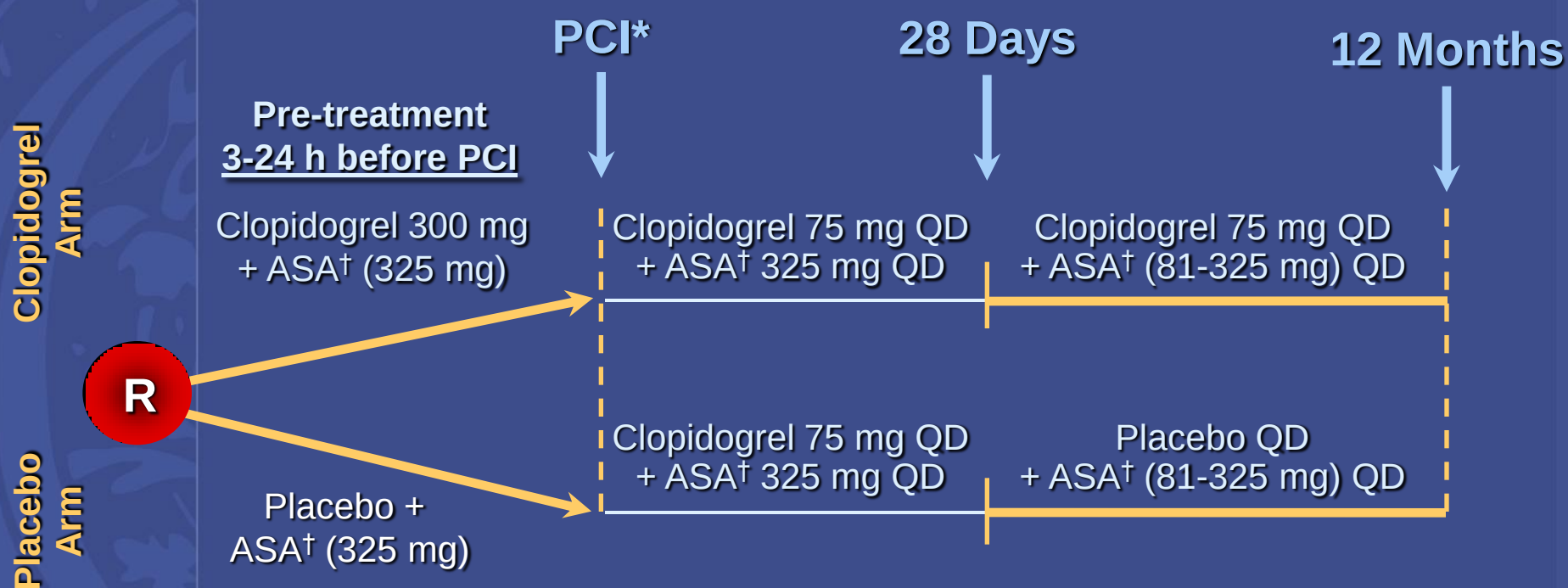
2015 Results expected from the ARRIVE (aspirin to reduce risk of initial vascular events) study.

2018 Results expected from the ASPREE (aspirin in reducing events in the elderly) study to determine whether the potential benefits of low-dose aspirin outweigh the risks in healthy people older than 70 years of age.

1. Aspirin je základ léčby

- ASA základem všech studií s DAPT po PCI
- P2Y12 inhibitory – vždy přidávány k ASA

Overall Study Design



† Plus other standard therapies
* Both groups received clopidogrel 75 mg + ASA 325 mg at time of procedure

Steinhubl S, Berger P, Tift Mann III J et al. *JAMA*. 2002;Vol 288,No 19:2411-2420.

Co-medication

PLATO Invasive

Medication	Ticagrelor (n=6,732)	Clopidogrel (n=6,676)
Anti-thrombotic treatment in hospital, %		
Aspirin	97.7	97.9
Unfractionated heparin	35.1	36.0
Low molecular weight heparin	41.1	40.9
Fondaparinux	1.6	1.8
Bivalirudin	1.2	1.3
GP IIb/IIIa inhibitor	19.7	20.3
Other medication in hospital or at discharge, %		
Beta-blockade	85.5	86.1
ACE /ARB	87.0	86.8
Cholesterol lowering (statin)	95.4	95.5
Proton pump inhibitor	54.4	53.7

TRÎTON TIMI·38
STENT ANALYSIS

Main Trial Design

ACS (STEMI or UA/NSTEMI) & Planned PCI

ASA ↓ **N= 13,608**

Double-blind

CLOPIDOGREL 300 mg LD/ 75 mg MD	**PRASUGREL** 60 mg LD/ 10 mg MD

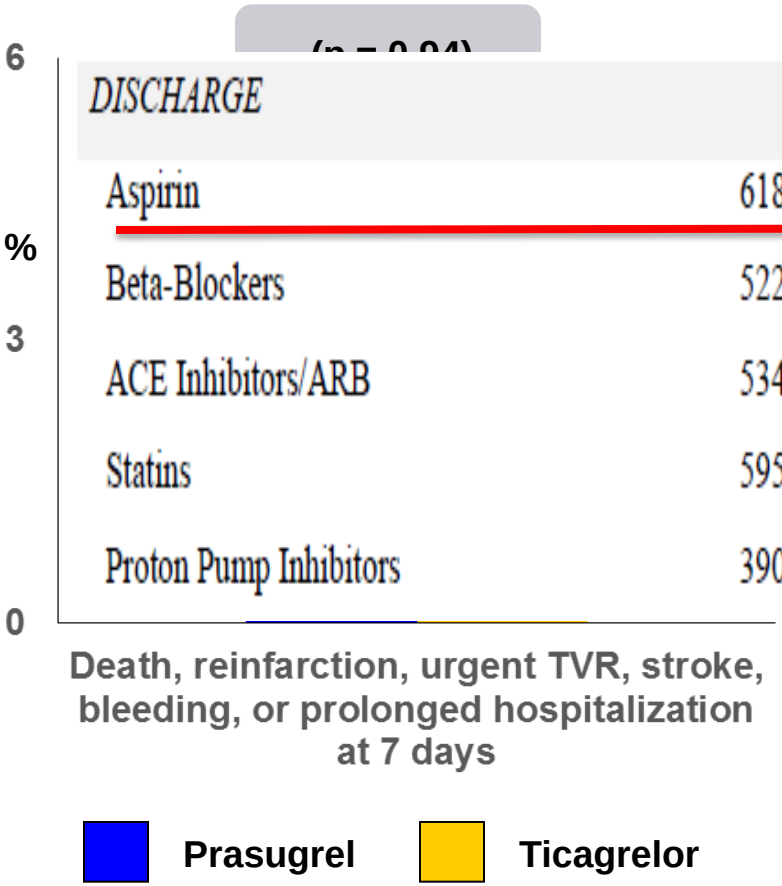
Duration of therapy: 6-15 months

1º endpoint:	CV death, MI, Stroke
2º endpoint:	Stent Thrombosis
Safety endpoints:	TIMI major bleeds, Life-threatening bleeds

Wiviott SD, Antman EM et al AHJ 2006

PRAGUE-18

Trial design: Patients with STEMI undergoing primary PCI were randomized to prasugrel (n = 634) versus ticagrelor (n = 596).



DISCHARGE			
Aspirin	618 (97.5%)	579 (97.1%)	0.721
Beta-Blockers	522 (82.3%)	486 (81.5%)	0.719
ACE Inhibitors/ARB	534 (84.2%)	496 (83.2%)	0.633
Statins	595 (93.8%)	558 (93.6%)	0.871
Proton Pump Inhibitors	390 (61.5%)	360 (60.4%)	0.690

Results

Conclusions

- Among patients with STEMI undergoing primary PCI, similar efficacy and bleeding was observed for either prasugrel or ticagrelor. Among such patients, the use of either agent is acceptable.

Motovska Z, et al. Circulation 2016;Aug 30:[Epub]

2. Různá délka DAPT

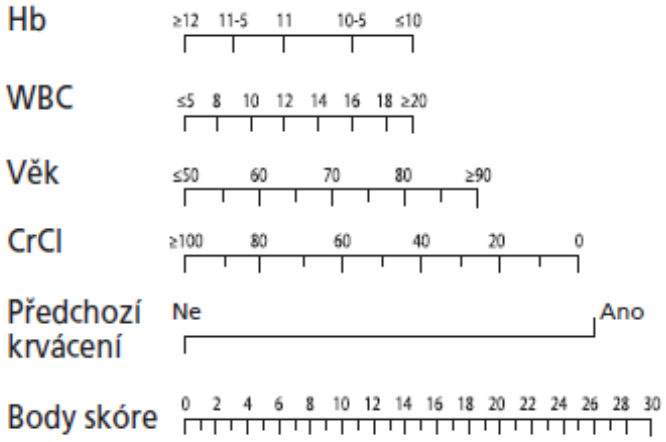
ASA trvale, P2Y12 dočasně

Table 1 Studies comparing different durations of dual antiplatelet therapy after PCI

Study (year)	Randomisation	Sample size	Primary endpoint	Design and randomisation	% ACS	Proportion with Newer-Generation DES (%)	Primary endpoint (short vs. long DAPT)
RESET (2012) [13]	3 vs. 12 months DAPT	2,117	Cardiac death, MI, ST, revasc. or bleeding	Non-inferiority Randomisation at time of PCI	55	85	4.7% in both arms (p_{NI} <0.001)
OPTIMIZE (2014) [14]	3 vs. 12 months DAPT	3,119	NACCE—death, MI, stroke, or bleed	Non-inferiority Randomisation at time of PCI	32	100	6.0% with 3 months DAPT vs. 5.8% with 1-year DAPT ($p_{NI}=0.002$)
EXCELLENT (2011) [15]	6 vs. 12 months DAPT	1,443	Cardiac Death, MI, or ischemia driven TVR	Non-inferiority Randomisation at time of PCI	51	75	4.8% with 6-months vs. 4.3% with 1-year DAPT ($p_{NI}=0.001$)
ISAR-SAFE (2014) [16]	6 vs. 12 months DAPT	4,000* (planned: 6,000)	Death, MI, stroke, or TIMI major bleed	Non-inferiority Randomisation at DAPT discontinuation	40	72	1.5% with 6 months DAPT vs. 1.6% with 1-year DAPT ($p_{NI}<0.001$)
SECURITY (2014) [17]	6 vs. 12 months DAPT	1,399* (planned: 2,740)	Cardiac death, MI, ST, or stroke	Non-inferiority Randomisation at time of PCI	38	100	4.5% with 6-months DAPT vs. 5.7% with 1-year DAPT ($p_{NI} \leq 0.05$)
PRODIGY (2012) [20]	6 vs. 24 months DAPT	1,970	Death, MI, stroke	Superiority Randomisation 1 month after PCI	75	50	10.0% with 6 months DAPT vs. 10.1% with 2-year DAPT ($p=0.91$)
ITALIC (2014) [21]	6 vs. 24 months DAPT	1,822* (planned: 2,475)	Death, MI, urgent TVR, stroke or bleeding	Non-inferiority Randomisation at time of PCI	24	100	1.6% with 6 months DAPT vs. 1.5% with 2-year DAPT
ARCTIC Interruption (2014) [22]	12 vs. 18–24 months	1,259	Death/MI/ST/CVA/TVR	Superiority Randomisation at DAPT discontinuation	26	63	4.0% in both arms (median 17 months FU) ($p=0.58$)
DAPT (2015) [23]	12 vs. 30 months	9,961	1 ST 2 MACE	Superiority Randomisation at DAPT discontinuation	43	59	ST: 1.4% vs. 0.4% and MACE 4.1 vs. 2.1% ($p<0.001$)
DES-LATE (2010) [24]	12 vs. 36 months	5,045	Cardiac death/MI/CVA	Superiority Randomisation at DAPT discontinuation	61	30	2.4% SAPT vs. 2.7% DAPT ($p=0.75$)
OPTIDUAL (2015) [25]	12 vs. 48 months	1,385* (planned: 1,966)	Death/MI/CVA/bleeding	Superiority Randomisation at DAPT discontinuation	36	59	7.5% SAPT vs. 5.8% DAPT ($p=0.17$)

PRECISE-DAPT a 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]		Věk ≥ 75 65 až < 75 < 65 Kouření cigaret Diabetes mellitus IM vstupně Předchozí PCI nebo předchozí IM Stent uvolňující paclitaxel Průměr stentu < 3 mm CHF nebo EFLK < 30 % Stent z žilního štěpu	 –2 body –1 bod 0 bodů +1 bod +1 bod +1 bod +1 bod +1 bod +1 bod +2 body +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	

DAPT ESC Guidelines 2017

3. Lze ASA někdy vysadit?

One-Month Dual Antiplatelet Therapy
Followed by Clopidogrel Monotherapy
versus
Standard 12-Month Dual Antiplatelet Therapy with Clopidogrel
After Drug-Eluting Stent Implantation:

STOPDAPT-2

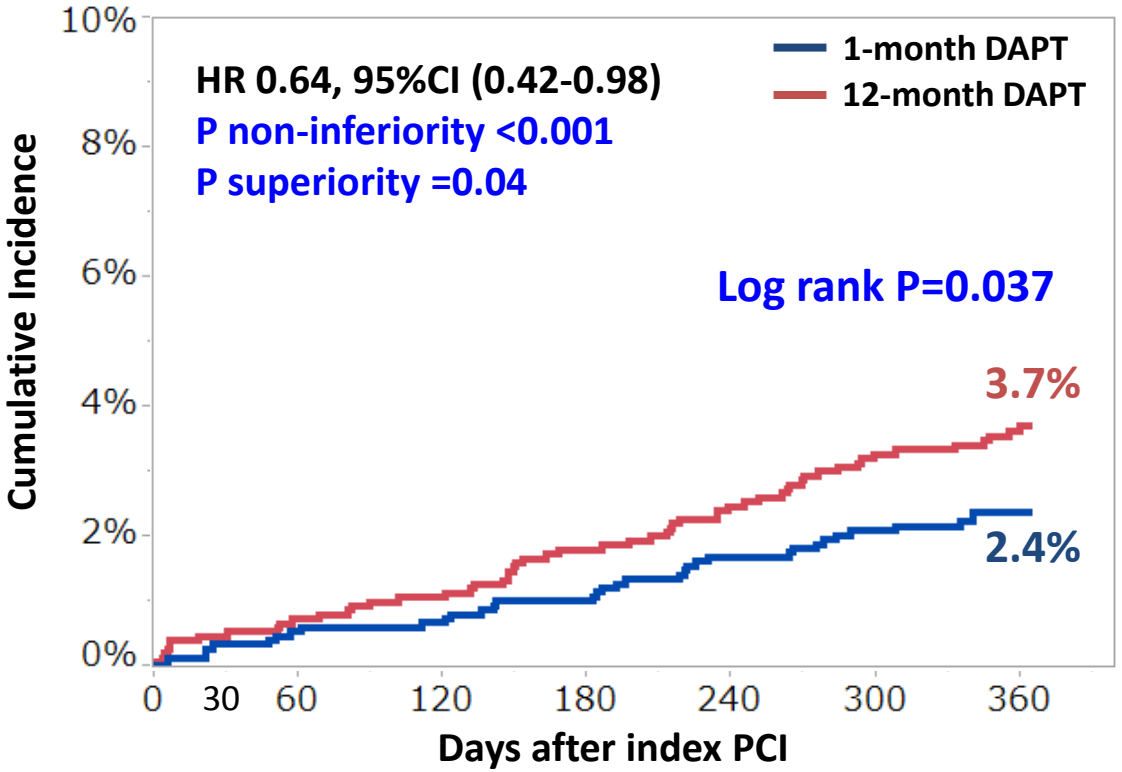
Hirotoshi Watanabe

Takenori Domei, Takeshi Morimoto, Hiroki Shiomi, Masahiro Natsuaki, Toshiaki Toyota, Kensuke Takagi, Yoshiki Hata, Satoru Suwa, Mamoru Nanasato, Masanobu Ohya, Masahiro Yagi, Takafumi Yokomatsu, Mitsuru Abe, Kenji Ando, Kazushige Kadota, Ken Kozuma, Yoshihiro Morino, Yuji Ikari, Kengo Tanabe, Koichi Nakao, Kazuya Kawai, Yoshihisa Nakagawa, and Takeshi Kimura, on behalf of STOPDAPT-2 investigators

ACC 2019

Primary Endpoint: Net clinical benefit

CV death/MI/ST/Stroke/TIMI major/minor bleeding

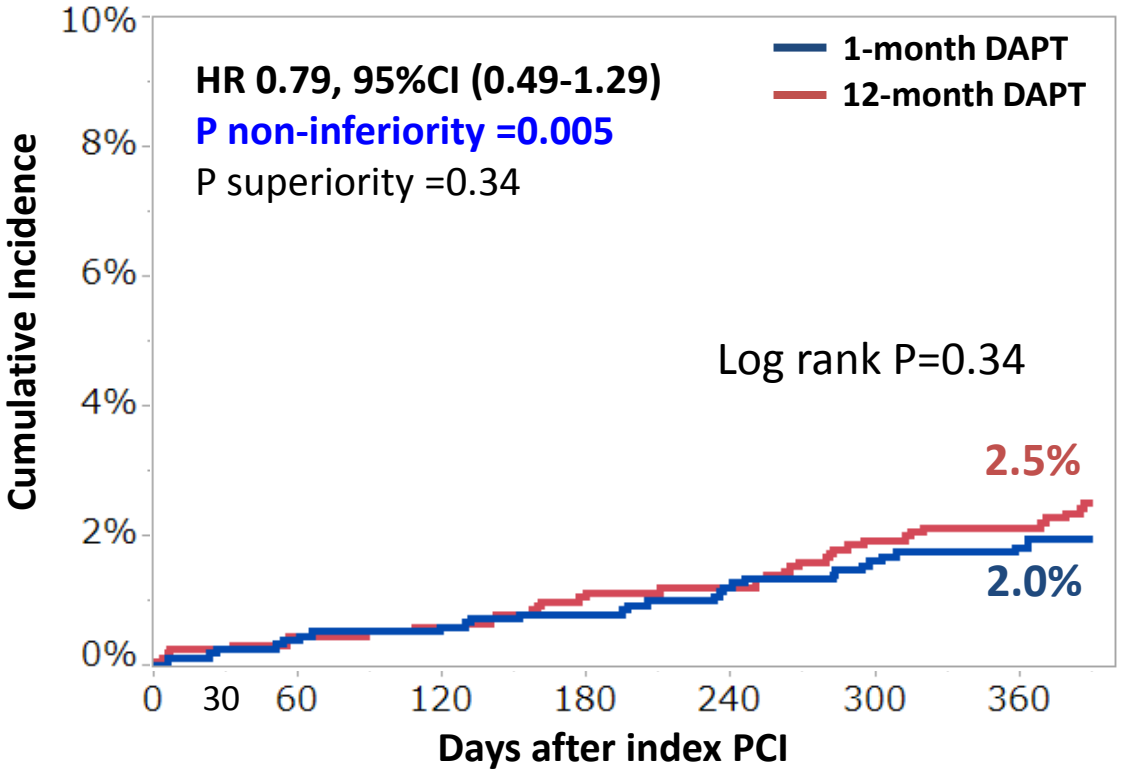


No. at risk								
12-month DAPT	1509	1501	1486	1481	1469	1458	1442	1159
1-month DAPT	1500	1494	1479	1475	1468	1453	1441	1151

ACS 38%

Major secondary ischemic endpoint

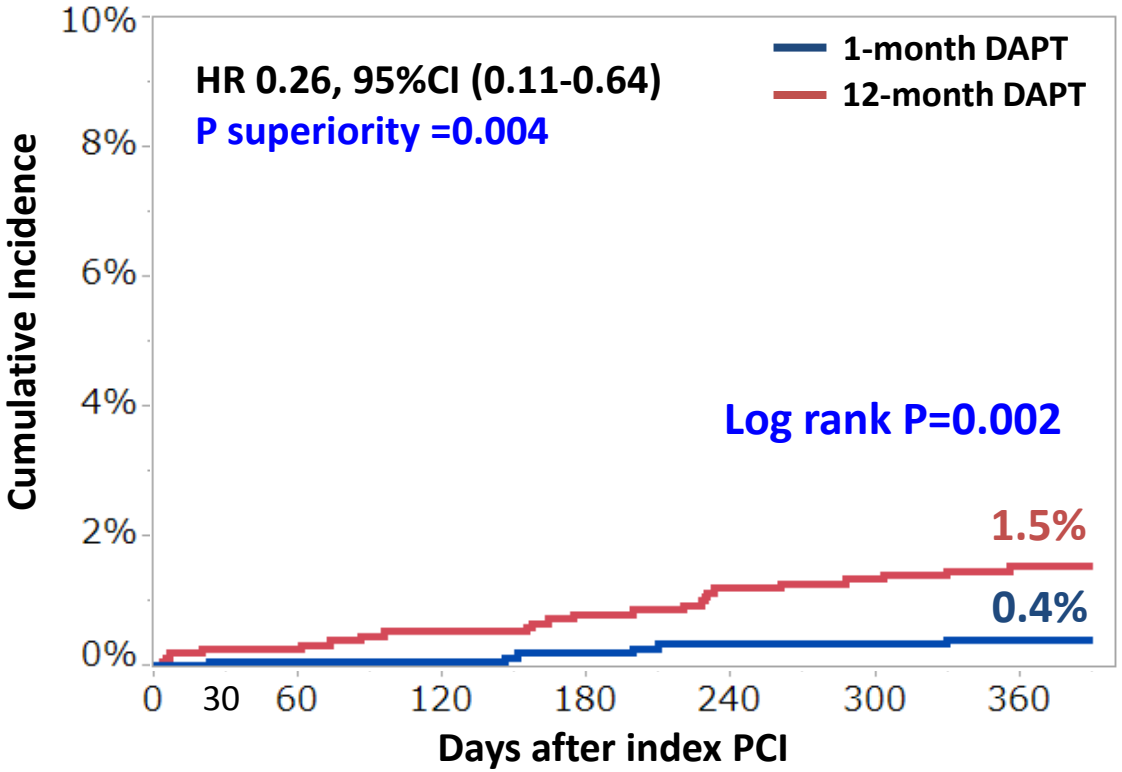
CV death/MI/ST/Stroke



No. at risk								
12-month DAPT	1509	1504	1490	1488	1479	1473	1458	1172
1-month DAPT	1500	1495	1480	1476	1471	1458	1446	1157

Major secondary bleeding endpoint

TIMI major/minor bleeding



No. at risk								
12-month DAPT	1509	1504	1491	1487	1480	1471	1462	1180
1-month DAPT	1500	1495	1483	1481	1477	1467	1457	1166

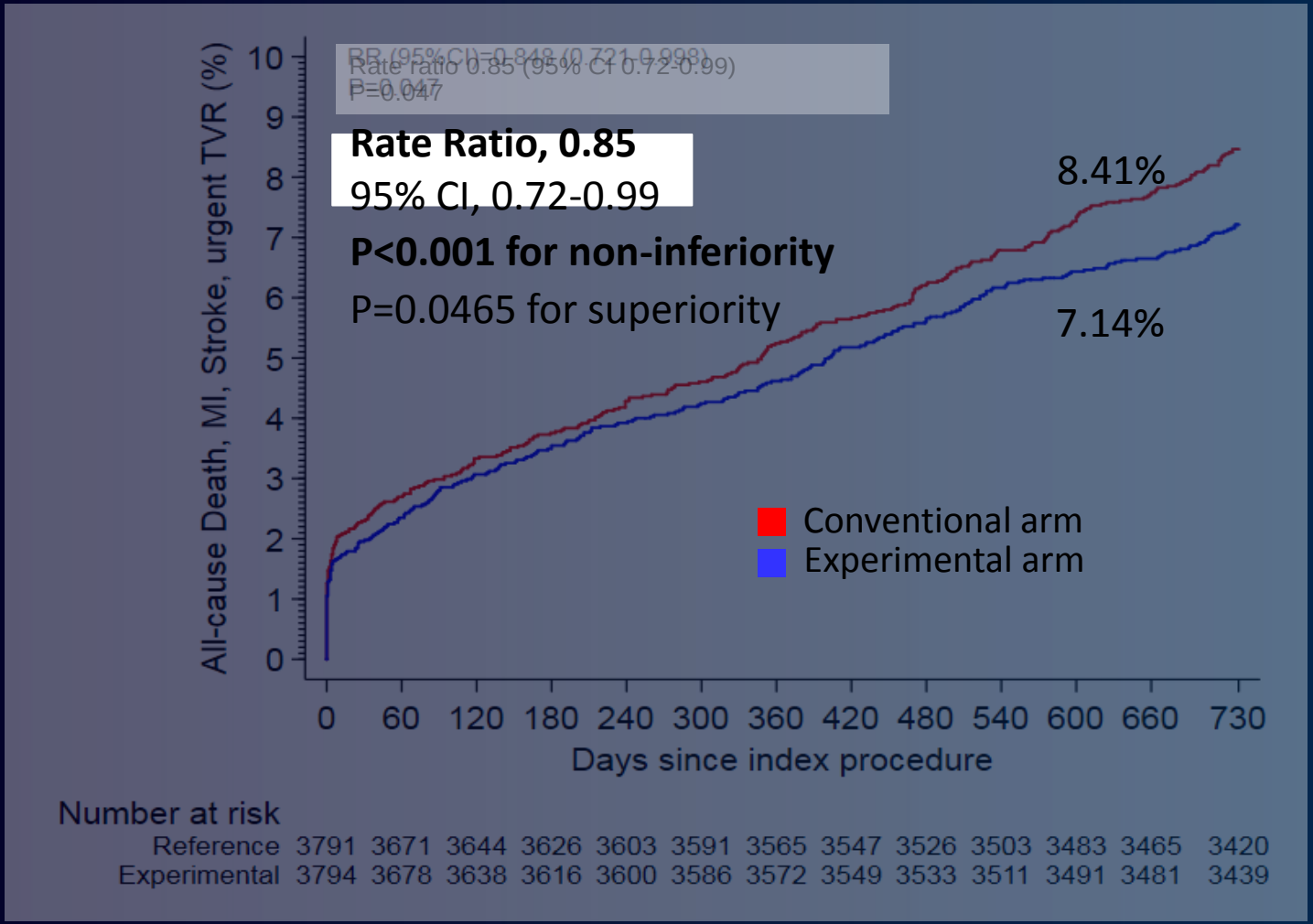
Ticagrelor Monotherapy Beyond One Month Versus Conventional Therapy On Adjudicated Ischemic And Bleeding Endpoints Following Drug Eluting Sent Implantation. Primary Results of the GLOBAL LEADERS Adjudication Sub-StudY (GLASSY)

NCT01813435

M. Valgimigli, MD, PhD
Swiss Cardiovascular Center Bern,
Inselspital, Bern, Switzerland
on behalf of GLASSY Investigators

GLASSY – Co-primary Efficacy EP

(celková mortalita, MI, CMP a urg. TVR po 2 letech)



ACS 51%

Žádný rozdíl v krvácení

ACC 2019

Trial Design

INCLUSION
- Atrial fibrillation (prior, persistent, >6 hr)
  - Physician decision for OAC
- Acute coronary syndrome or PCI
  - Planned $P2Y_{12}$ inhibitor for ≥6 months

Randomize
n=4600
patients

EXCLUSION
- Contraindication to DAPT
- Other reason for VKA (prosthetic valve, moderate / severe mitral stenosis)

Apixaban 5 mg BID
Apixaban 2.5 mg BID in selected patients

Open Label

VKA
(INR 2–3)

Aspirin for all on the day of ACS or PCI
Aspirin versus placebo after randomization

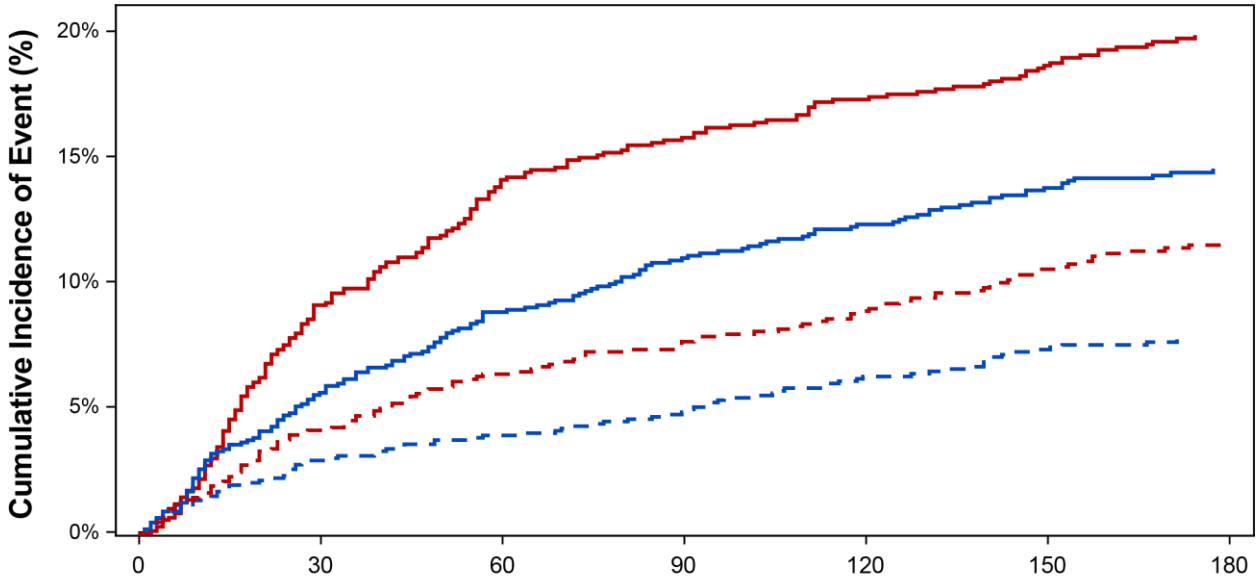
Aspirin — *Double Blind* — **Placebo**

Aspirin — *Double Blind* — **Placebo**

Primary outcome: ISTH major / CRNM bleeding
Secondary outcome(s): death / hospitalization, death / ischemic events

Lopes RD, et al. Am Heart J. 2018;200:17-23.

Major / CRNM Bleeding



Number at Risk							
Apixaban and Aspirin	1145	1036	975	937	903	880	485
Apixaban and Placebo	1143	1075	1044	1007	975	947	536
VKA and Aspirin	1123	962	881	838	800	776	467
VKA and Placebo	1126	1007	947	917	883	851	528

VKA + Aspirin (18.7%)

Apixaban + Aspirin (13.8%)

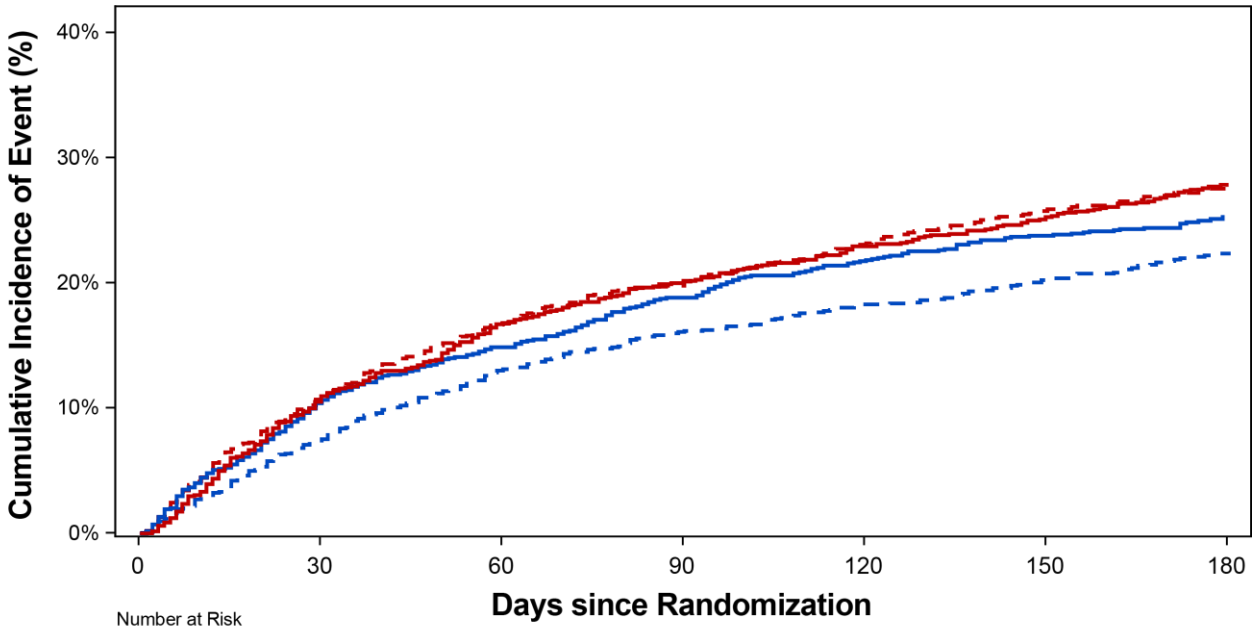
VKA + Placebo (10.9%)

Apixaban + Placebo (7.3%)

Apixaban + Placebo vs. VKA + Aspirin: 11.4% absolute risk reduction (NNT=9)

NEJM 2019

Death / Hospitalization



Number at Risk							
Apixaban and Aspirin	1153	1026	970	923	888	863	459
Apixaban and Placebo	1153	1064	995	958	933	909	488
VKA and Aspirin	1154	1016	939	899	864	836	492
VKA and Placebo	1154	1019	946	906	868	837	509

VKA + Aspirin (27.5%)
VKA + Placebo (27.3%)
Apixaban + Aspirin (24.9%)
Apixaban + Placebo (22.0%)

Apixaban + Placebo vs. VKA + Aspirin:
5.5% absolute risk reduction (NNT=18)

NEJM 2019

4. Co říkají Guidelines?

PCI s implantací DES: ASA vždy

- ACS: 12M
  - PreciseDapt ≥25 6M
- Stable CAD: 6M
  - PreciseDapt ≥25 3M
  - 1M
- DEB 6M

Individuální posouzení rizika ischémie vs krvácení

1 M vs celý život

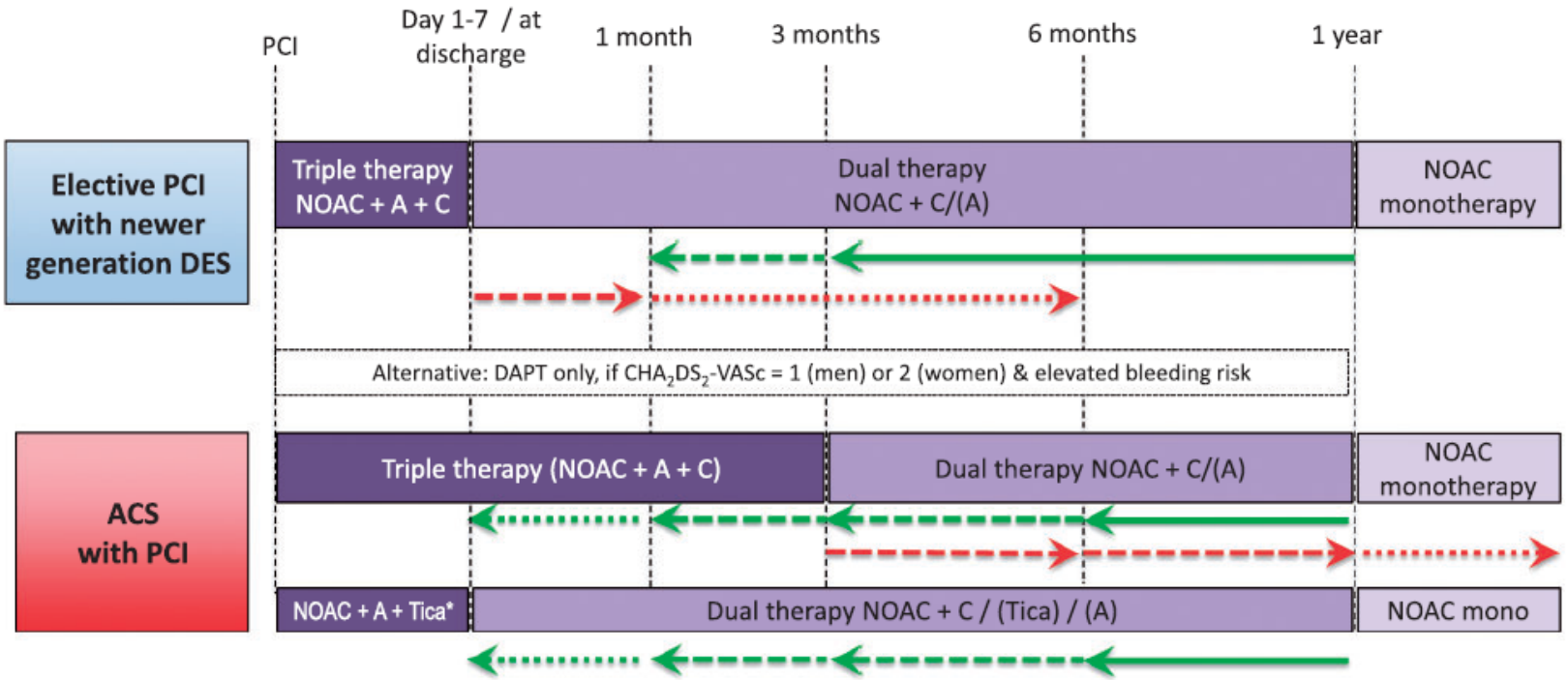
Souhrn dokumentu připravený ČKS

ČESKÁ KARDIOLOGICKÁ SPOLEČNOST
THE CZECH SOCIETY OF CARDIOLOGY

(2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS. Summary of the document prepared by the Czech Society of Cardiology)

Zuzana Moťovská[a], Ivo Varvařovský[b], Petr Ošťádal[c]

NOAK a PCI



Factors to shorten combination therapy

- (Uncorrectable) high bleeding risk
- Low atherothrombotic risk (by REACH or SYNTAX score if elective; GRACE ≥140 if ACS)

Factors to lengthen combination therapy

- First-generation DES
- High atherothrombotic risk (scores as above ; stenting of the left main, proximal LAD, proximal bifurcation; recurrent MIs; stent thrombosis etc.) and low bleeding risk

EHRA Guidelines, EHJ 2018

Aspirin po PCI je nezbytný !

(4000 let, levný, ověřený)

Jak dlouho po PCI?

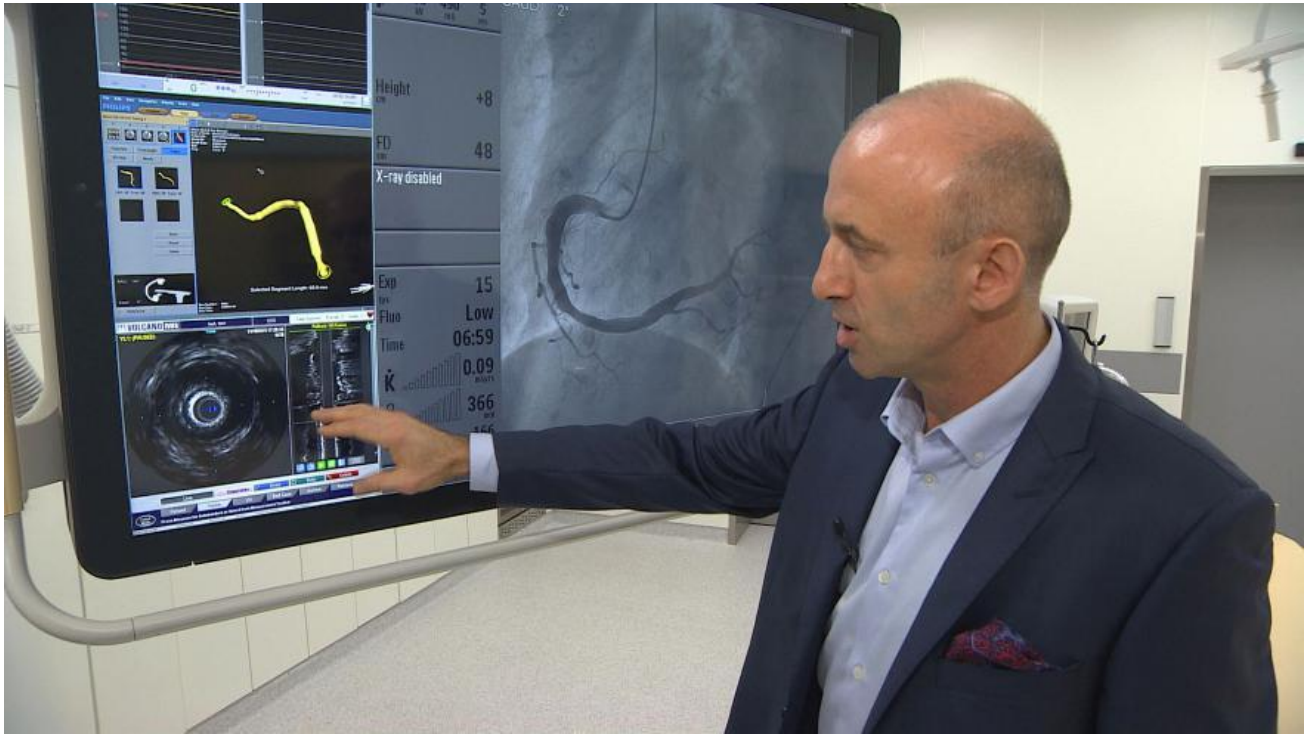
trvale – 12 – 6 – 3 – 1 M

Nové studie bez ASA

špičková kvalita PCI (OCT, IVUS)
málo rizikoví nem.
rozdíl jen v krvácení

ASA monoth. by vyšla podobně

PCI – kvalita (vysokotlaká PD)



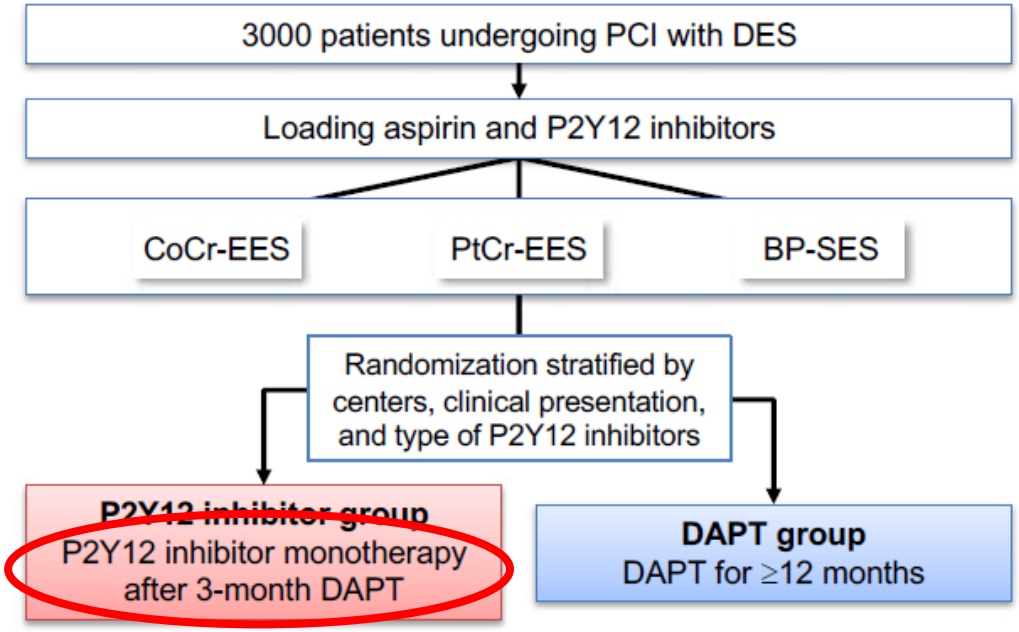
Net clinical benefit

SMART-CHOICE

SMART-CHOICE

Study design

A prospective, multicenter, randomized, open-label, noninferiority trial

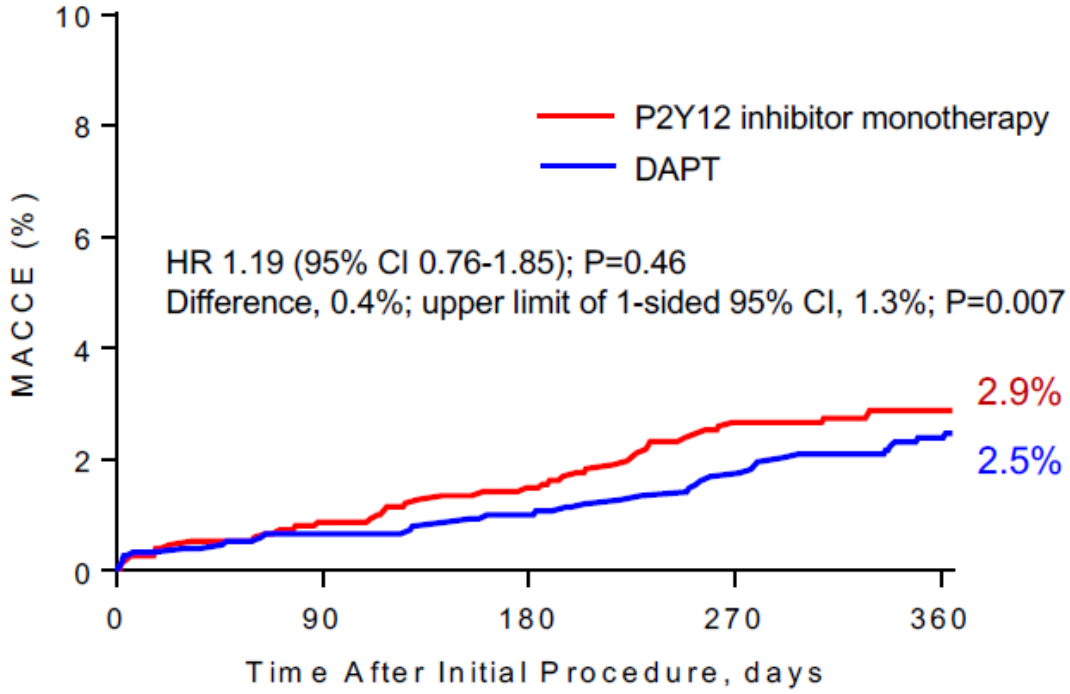


- CoCr-EES: cobalt-chromium everolimus eluting stent (Xience series)
- PtCr-EES: platinum-chromium everolimus-eluting stent (Promus series and Synergy)
- BP-SES: bioresorbable polymer- sirolimus-eluting stent (Orsiro)

Primary endpoint: 12-month MACCE

ClinicalTrials.gov NCT02079194

Primary end point (MACCE)



No. at risk					
DAPT	1498	1471	1454	1436	1220
P2Y12 inhibitor	1495	1456	1430	1402	1202

* MACCE = A composite of all-cause death, myocardial infarction, or stroke

Clinical outcomes at 12 months

Outcome	P2Y12 inhibitor monotherapy (n=1495)	Dual antiplatelet therapy (n=1498)	HR (95% CI)	P Value
MACCE	42 (2.9%)	36 (2.5%)	1.19 (0.76-1.85)	0.46
Death	21 (1.4%)	18 (1.2%)	1.18 (0.63-2.21)	0.61
Myocardial infarction	11 (0.8%)	17 (1.2%)	0.66 (0.31-1.40)	0.28
Cerebrovascular accident	11 (0.8%)	5 (0.3%)	2.23 (0.78-6.43)	0.14
Death or myocardial infarction	31 (2.1%)	32 (2.2%)	0.98 (0.60-1.61)	0.94
Cardiac death	11 (0.8%)	13 (0.9%)	0.86 (0.38-1.91)	0.70
Cardiac death or myocardial infarction	22 (1.5%)	27 (1.9%)	0.83 (0.47-1.45)	0.50
Stent thrombosis	3 (0.2%)	2 (0.1%)	1.51 (0.25-9.02)	0.65
Bleeding BARC type 2-5	28 (2.0%)	49 (3.4%)	0.58 (0.36-0.92)	0.02
Major bleeding	12 (0.8%)	14 (1.0%)	0.87 (0.40-1.88)	0.72
Net adverse clinical and cerebral events	65 (4.5%)	81 (5.6%)	0.81 (0.58-1.12)	0.20

Major bleeding was defined as BARC type 3-5 bleeding.
Net adverse clinical and cerebral events were defined as MACCE plus BARC type 2-5 bleeding.

Short DAPT study with new DES (n=12)+1 BMS

Study	Device	Population	DAPT Duration	Primary Endpoint
ASET - NCT03469856	Synergy	SCAD and stabilized ACS	**No aspirine**	Composite of cardiac death, TV-MI or def ST
SENIOR - NCT02099617	Synergy	**Age ≥75**	1 month (SCAD) 6 months (ACS)	MACCE (Death, MI, stroke, ID-TLR)
POEM - NCT03112707	Synergy	**HBR**	1 month	MACE (CD or MI, ARC def/prob ST)
EVOLVE Short DAPT NCT02605447	Synergy	**HBR**	3 months	Death or MI, def/prob ST
IDEAL LM NCT02303717	Synergy	LM disease	4 months	MACE (death, MI, ID-TVR)
STOP-DAPT2 NCT02619760	Xience	**After successful DES implantation**	1 month	CD, MI, ARC def ST, stroke and bleeding
XIENCE 28 NCT03355742	Xience	**HBR**	1 months	NACE (Death, MI, ST, stroke, bleeding (BARC2-5))
XIENCE 90 NCT03218787	Xience	**HBR**	3 months	Death or MI
MASTER-DAPT NCT03023020	Ultimaster	HBR	1 month	NACE (Death, MI, stroke and bleeding (BARC 3 or 5))
Onyx ONE NCT03344653	Resolute	**HBR**	1 month	Death or MI, ARC def/prob ST
TICO - NCT02494895	Orsiro	**ACS**	3 months	MACCE
COBRA REDUCE NCT02594501	Cobra PzF (non DES)	**OAC**	2 weeks	Death, MI, def/ prob ST or ischemic stroke
SMART-DATE NCT01701453	EES,ZES,BES	**ACS**	6 months	Death, MI, stroke

Very-low-dose twice-daily aspirin maintains platelet inhibition and improves haemostasis during dual-antiplatelet therapy for acute coronary syndrome

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Abstract

Higher aspirin doses may be inferior in ticagrelor-treated acute coronary syndrome (ACS) patients and reducing bleeding risk whilst maintaining antithrombotic benefits could improve outcomes. We characterized the pharmacodynamics of a novel dual-antiplatelet-therapy regimen consisting of very-low-dose twice-daily (BD) aspirin with standard-dose ticagrelor. A total of 20 ticagrelor-treated ACS patients entered a randomized crossover to take aspirin 20 mg BD (12-hourly) during one 14-day period and 75 mg once-daily (OD) in the other. After 14 days of treatment, serum thromboxane (TX)B_2 and light-transmittance aggregometry were assessed pre- and 2 h post-morning-dose, bleeding time was measured post-dose, and TXA_2 and prostacyclin stable metabolites were measured in urine collected 2 h post-morning-dose. Data are expressed as mean ± SD. After 14 days treatment, serum TXB_2 levels were significantly greater 2 h post-dosing with aspirin 20 mg BD vs. 75 mg OD (3.0 ± 3.6 ng/mL vs. 0.8 ± 1.9 ng/mL; $p = 0.018$) whereas pre-dosing levels were not significantly different (3.5 ± 4.1 ng/mL vs. 2.5 ± 3.1 ng/mL, $p = 0.23$). 1-mmol/L arachidonic acid-induced platelet aggregation was similarly inhibited by both regimens pre-dose (8.5 ± 14.3% vs. 5.1 ± 3.6%, $p = 0.24$) and post-dose (8.7 ± 14.2% vs. 6.6 ± 5.3%; $p = 0.41$). Post-dose bleeding time was shorter with 20 mg BD (680 ± 306 s vs. 834 ± 386 s, $p = 0.02$). Urinary prostacyclin and TX metabolite excretion were not significantly different. In conclusion, compared to aspirin 75 mg OD, aspirin 20 mg BD provided consistent inhibition of platelet TXA_2 release and aggregation, and improved post-dose hemostasis, in ticagrelor-treated ACS patients. Further studies are warranted to assess whether this regimen improves the balance of clinical efficacy and safety.

Keywords

Aspirin, bleeding, $P2Y_{12}$ inhibitors, thromboxane, ticagrelor

History

Received 9 December 2018
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Accepted 11 January 2019

Prasugrel monotherapy

EuroIntervention. 2019 Apr 23. pii: EIJ-D-19-00131. doi: 10.4244/EIJ-D-19-00131.

[Epub ahead of print]

Prasugrel monotherapy after PCI with the SYNERGY stent in patients with chronic stable angina or stabilized acute coronary syndromes: rationale and design of the ASET pilot study.

Kogame N(1), Modolo R, Tomaniak M, Cavalcante R, de Martino F, Tinoco J, Ribeiro EE, Mehran R, Campos CM, Onuma Y, Lemos PA, Serruys PW; Collaborators.

Collaborators: Morel MA, Piek JJ, Wykrzykowska JJ.

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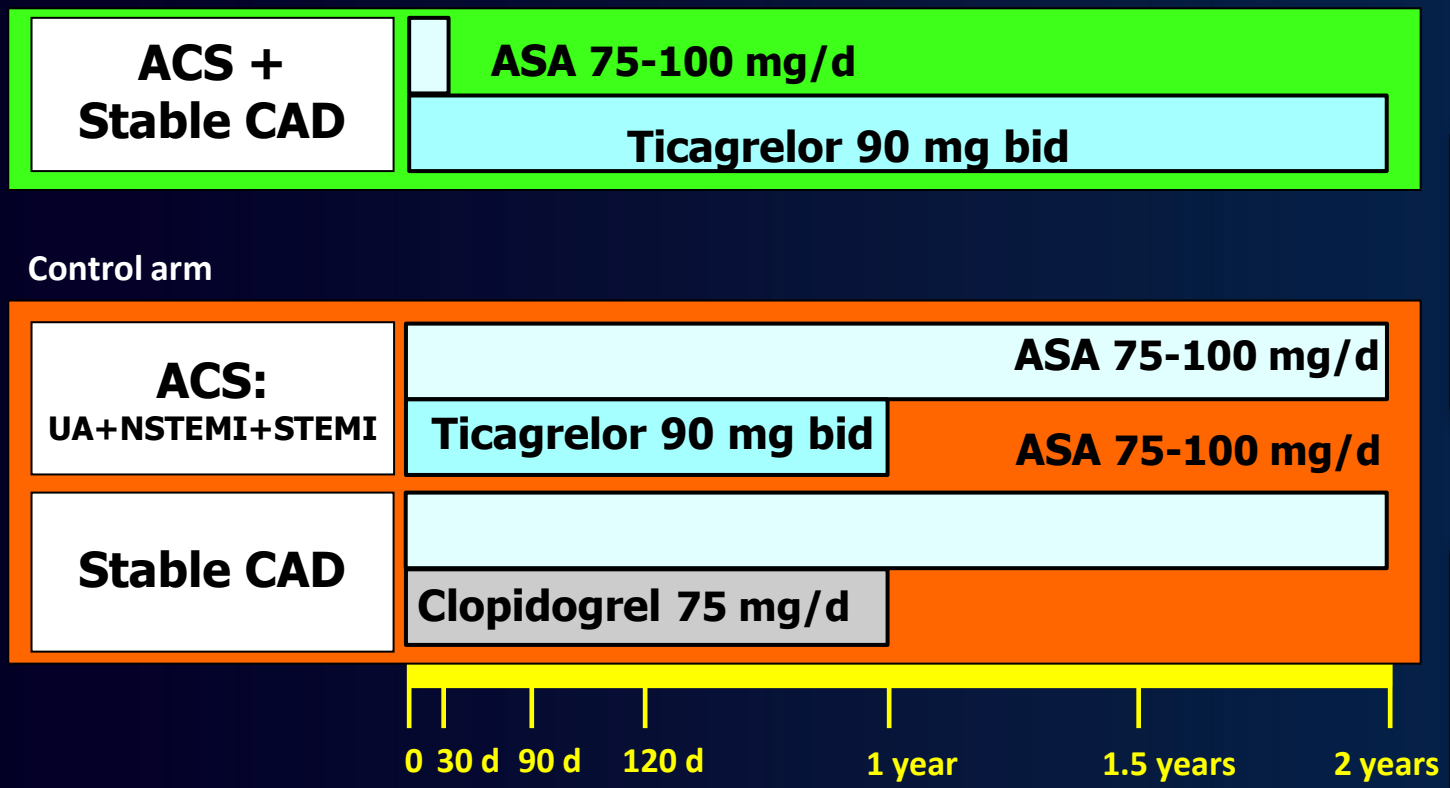
(1)Department of Cardiology, Amsterdam University Medical Center, Amsterdam, the Netherlands.

AIMS: To demonstrate the feasibility and safety of prasugrel monotherapy without aspirin post procedure in selected patients undergoing successful percutaneous coronary intervention (PCI) with the SYNERGY stent.

Limitations

- Lack of consensus on the use of the NACE as primary endpoint
- Open label design with its inherent limitations
- Limited enrollment of high ischemic risk patients
- Lower ischemic risk of Japanese versus US/European CAD patients
- Ticagrelor / Prasugrel (standard dose) not available in Japan
- No assessment of aspirin monotherapy after 1-month DAPT

GLOBAL LEADERS design



Randomization was also stratified by site

"All-comers" PCI population
N = 15,991
1:1 Randomisation, open-label design, 130 centers worldwide

Any type of lesions: Left main, SVG, CTO bifurcation, ISR, etc.

Unrestricted use of DES (number, length)

SMART-CHOICE trial

- In the SMART-CHOICE study, which was presented in the same late-breaking trials session by Joo-Yong Hahn, MD, PhD (Samsung Medical Center, Seoul, Korea), 2,993 patients receiving PCI with current-generation DES (Xience, Promus, Synergy, and Orsiro) at 33 Korean centers were randomized to keep or drop the aspirin after 3 months of DAPT and followed through 1 year.
- There was no difference between the short- and long-term DAPT patients regarding the primary endpoint of MACCE (all-cause death, MI, or stroke; 2.9% vs 2.5%; HR 1.19; 95% CI 0.76-1.85), and this was confirmed in a landmark analysis at 90 days.
- Clinical outcomes at 12 months were similar between the study groups, with the exception of a greater degree of BARC 2-5 bleeding observed in those receiving 12 months of DAPT (2.0% vs 3.4%; HR 0.36; 95% CI 0.36-0.92; *P* = 0.02). This was somewhat mediated in a landmark analysis at 90 days (HR 0.59; 95% CI 0.34-1.01; *P* = 0.053).
- All prespecified subgroups seemed to consistently benefit from either DAPT regimens, although patients who received prasugrel or ticagrelor as their P2Y12 inhibitor compared with clopidogrel tended to do better with 12 months of DAPT.

Conclusions

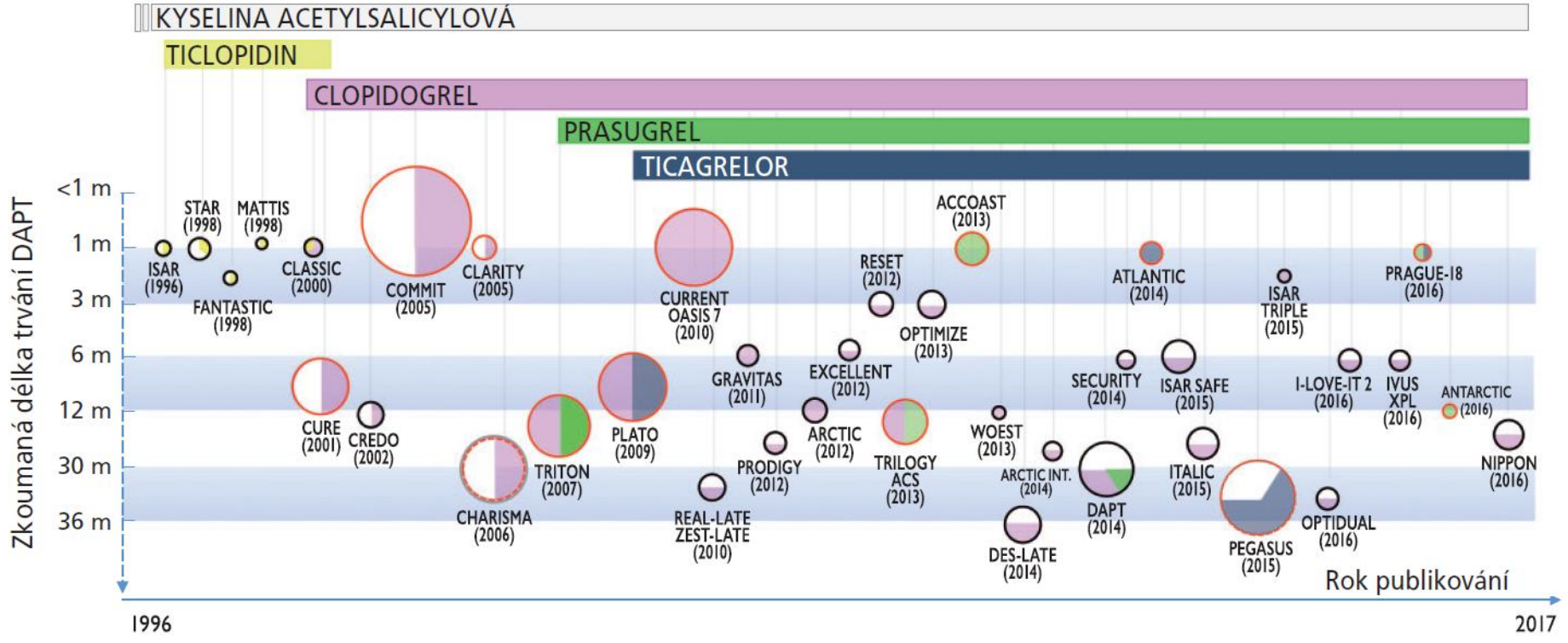
- In this prospective randomized trial, P2Y12 inhibitor monotherapy after 3-month DAPT was noninferior to 12-month DAPT for the primary end point of MACCE at 12 months after the index procedure.
- The 3-month landmark analysis and per-protocol analysis showed consistent results.
- Moreover, P2Y12 inhibitor monotherapy reduced the risk of bleeding compared with prolonged DAPT.
- P2Y12 inhibitor monotherapy after short duration of DAPT is a novel antiplatelet strategy balancing ischemic and bleeding risk in patients undergoing PCI.

Aspirin primary prevention trials

The ARRIVE trial (Aspirin to Reduce Risk of Initial Vascular Events)—published simultaneously in *The Lancet*—randomized >12 000 European and US primary care patients age 55 to 60 with moderate cardiovascular risk to 100 mg aspirin or placebo daily and followed them for 5 years. It found no reduction in the incidence of major cardiovascular events in the aspirin group. In fact,

The results of the ASPREE trial, published in the *New England Journal of Medicine* in September, raised further doubt about the benefits of aspirin for primary prevention. That

A second major trial presented at the meeting, the ASCEND trial (A Study of Cardiovascular Events iN Diabetes)—published simultaneously in the *New England Journal of Medicine*—randomly assigned >15 000 patients with diabetes mellitus to either 100 mg aspirin or placebo daily. Aspirin reduced the risk of a first vascular event, but at a cost of serious bleeding events requiring hospitalization, said principal investigator Jane Armitage, FRCP, FFPH,



Velikost kroužků odpovídá velikosti zkoumaných souborů

Barva ohraničení kroužků označuje typ pacientů zařazených do dané studie

Doporučení týkající se výběru a načasování podávání inhibitorů $P2Y_{12}$ *(Dokončení ze strany xx)*

U pacientů s AKS podstupujících PCI je vedle kyseliny acetylsalicylové doporučován prasugrel (nasycovací dávka 60 mg, denní dávka 10 mg), což se týká pacientů dosud neléčených inhibitory $P2Y_{12}$ s non-STE AKS nebo se zpočátku konzervativně léčenými STEMI, je-li potvrzena indikace PCI, případně u pacientů se STEMI podstupujících neodkladnou koronární katetrizaci,[c] není-li přítomno vysoké riziko život ohrožujícího krvácení nebo jiná kontraindikace.	I	B

Souhrn dokumentu připravený ČKS

ČESKÁ KARDIOLOGICKÁ SPOLEČNOST
THE CZECH SOCIETY OF CARDIOLOGY

(2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS. Summary of the document prepared by the Czech Society of Cardiology)

Zuzana Moťovská[a], Ivo Varvařovský[b], Petr Ošťádal[c]

Table 7 Doses of antiplatelet and anticoagulant drugs used during and after myocardial revascularization

Antiplatelet drugs	
Aspirin	Loading dose of 150–300 mg orally or 75–150 mg i.v. if oral ingestion is not possible, followed by a maintenance dose of 75–100 mg/day.
Clopidogrel	Loading dose of 600 mg orally, followed by a maintenance dose of 75 mg/day.
Prasugrel	Loading dose of 60 mg orally, followed by a maintenance dose of 10 mg/day. In patients with body weight <60 kg, a maintenance dose of 5 mg is recommended. In patients aged >75 years, prasugrel is generally not recommended, but a dose of 5 mg should be used if treatment is deemed necessary.
Ticagrelor	Loading dose of 180 mg orally, followed by a maintenance dose of 90 mg b.i.d.

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

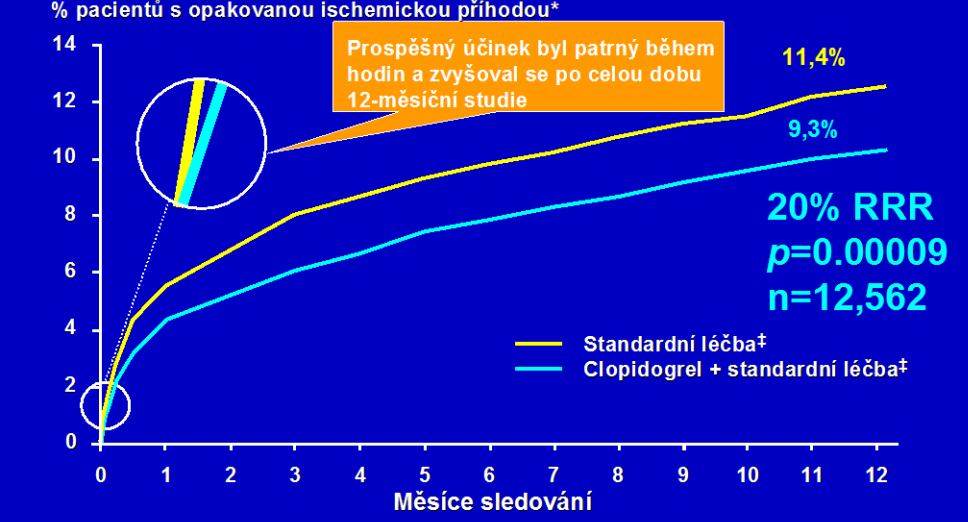
DAPT consisting of aspirin and a $P2Y_{12}$ receptor inhibitor represents the cornerstone of treatment in patients undergoing elective PCI.[665]

ESC Revascularization Guidelines 2018

CLOPIDOGREL

CURE – Hlavní výsledky účinnost

Primární endpoint (2)



‡včetně ASA

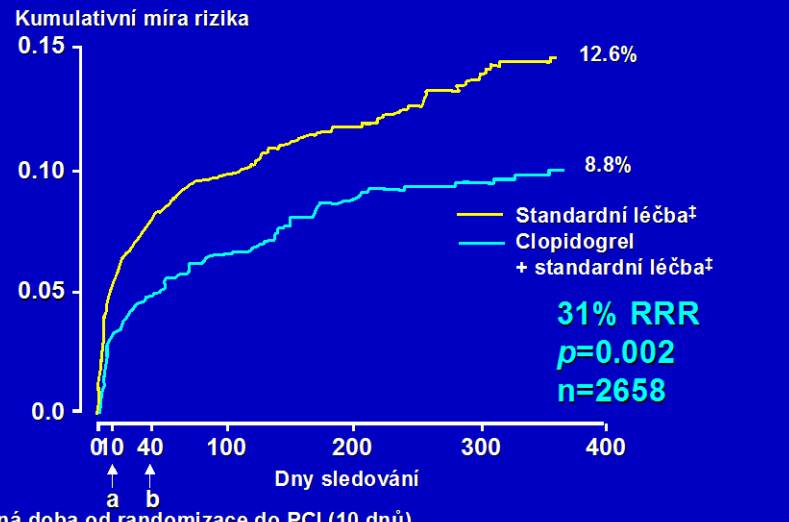
*kardiovaskulární smrt, IM, nebo CMP

The CURE Investigators. *N Eng J Med* August 2001

Data on file

PCI-CURE – Celkové dlouhodobé† výsledky

Složenina kardiovaskulární smrti a infarktu myokardu od randomizace do konce sledování†



a = průměrná doba od randomizace do PCI (10 dnů)

b = 30 dní po průměrné době PCI

†až 12 měsíců ‡včetně ASA

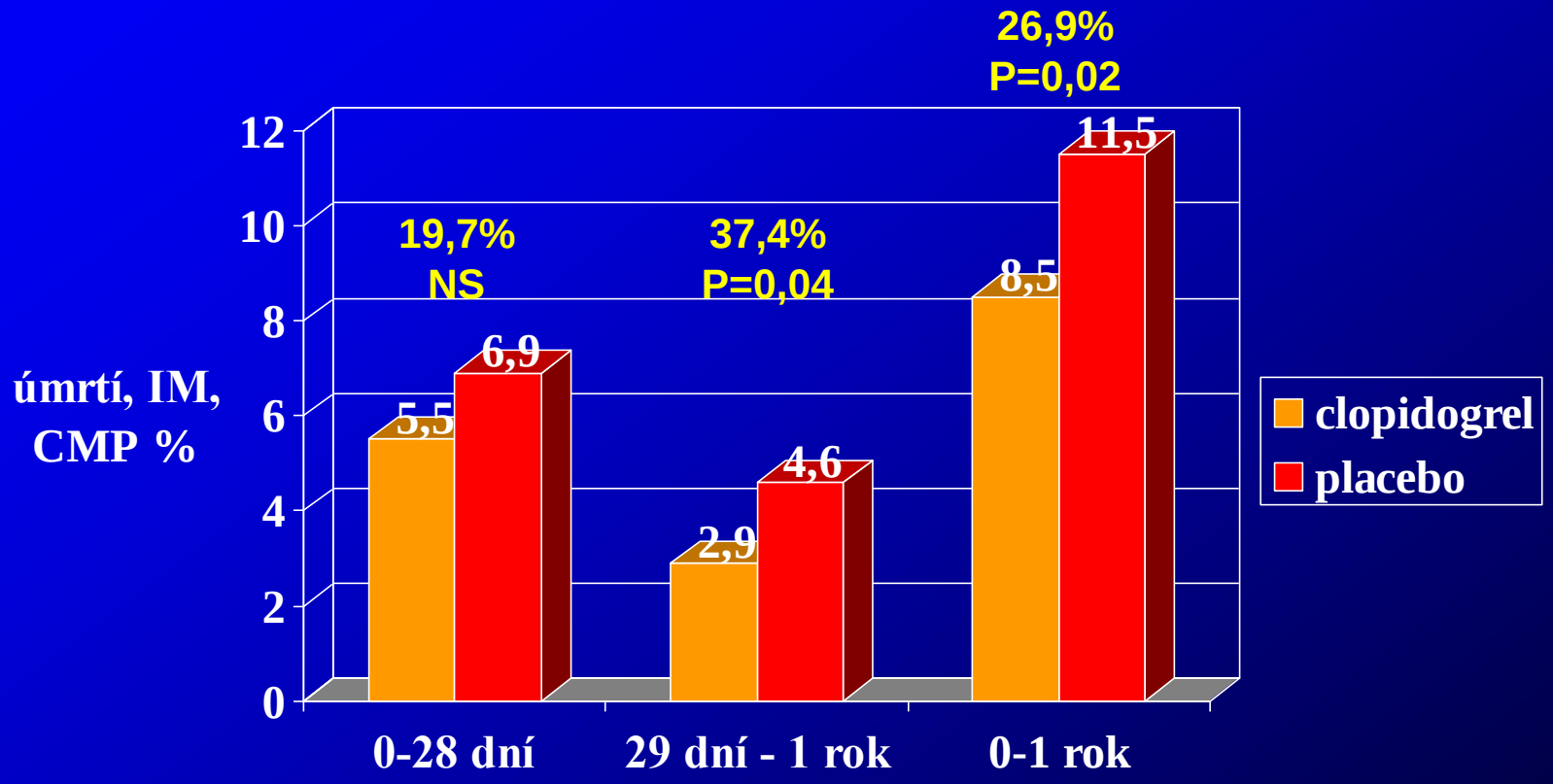
The CURE Investigators. *Lancet* August 2001

12 662 nem. s NSTE AKS do 24h

2 658 s PCI

CREDO

Clopidogrel for the Reduction of Events during Observation



3-24h před PCI; 2 116 nemocných