FAKULTNÍ NEMOCNICE BRNO

Intervenční kardiologie
IKK FN Brno

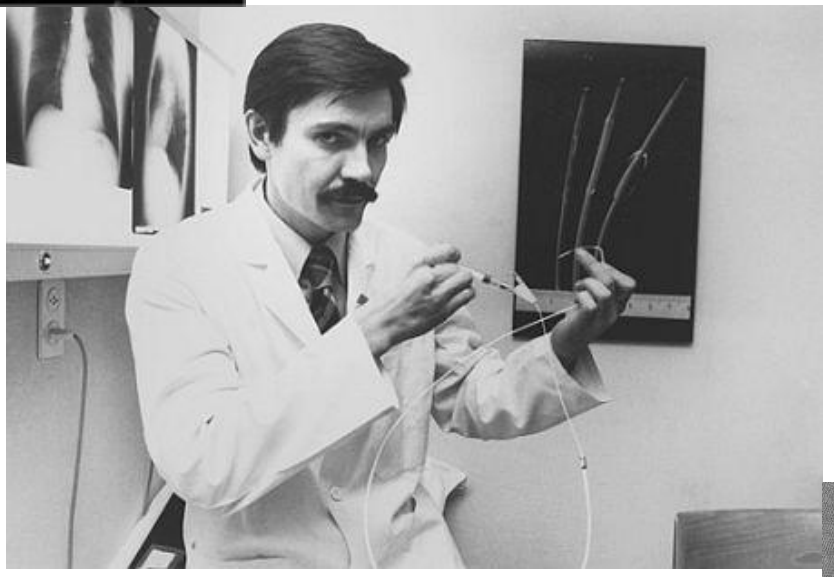
NOVINKY Z ACC
TRVALE ANTIKOAGULOVANÝ PACIENT PO PCI

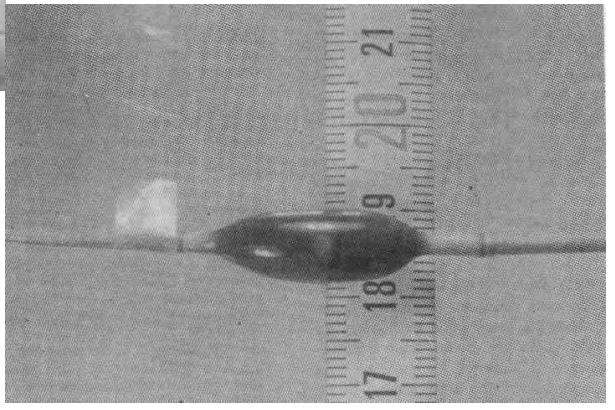
PCI u pacientů na antikoagulační léčbě – praktický návod

Doc. MUDr. Petr Kala, Ph.D., FESC, FSCAI

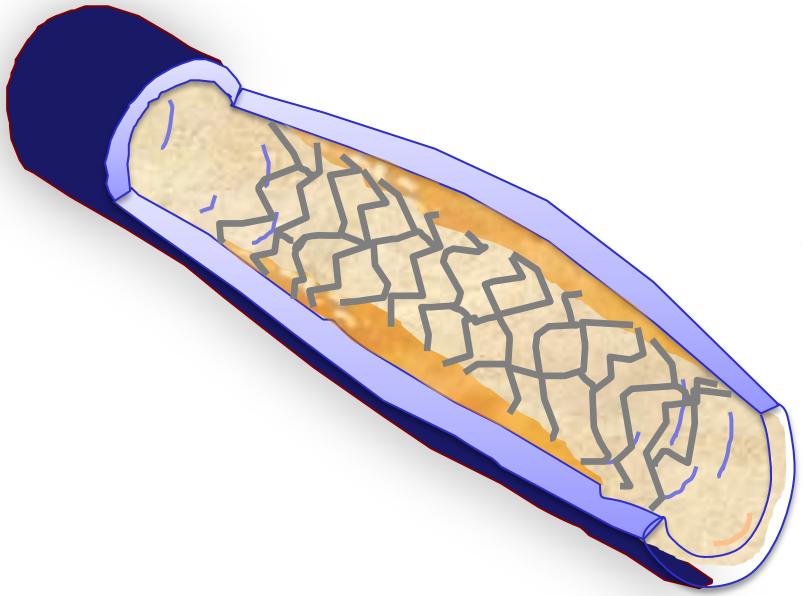
IKK FN Brno a LF MU

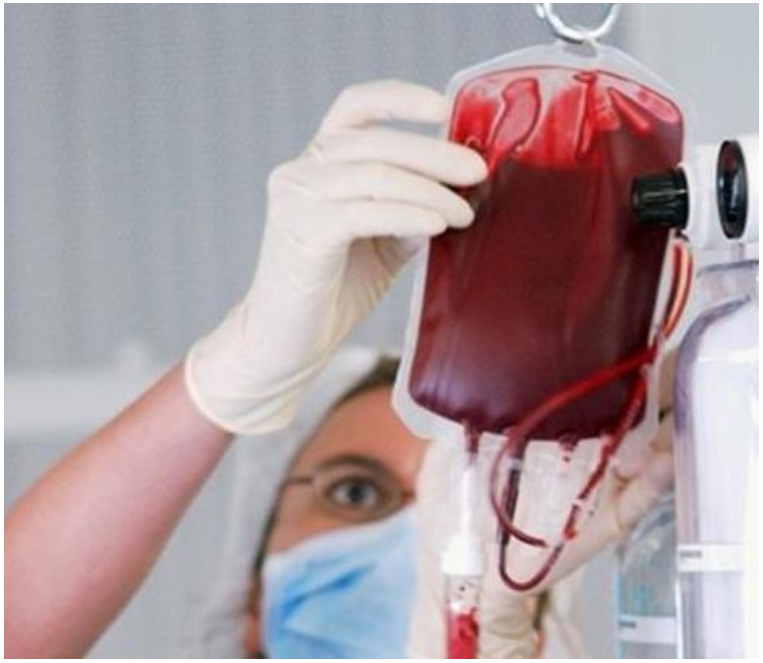
>40 let od první PCI



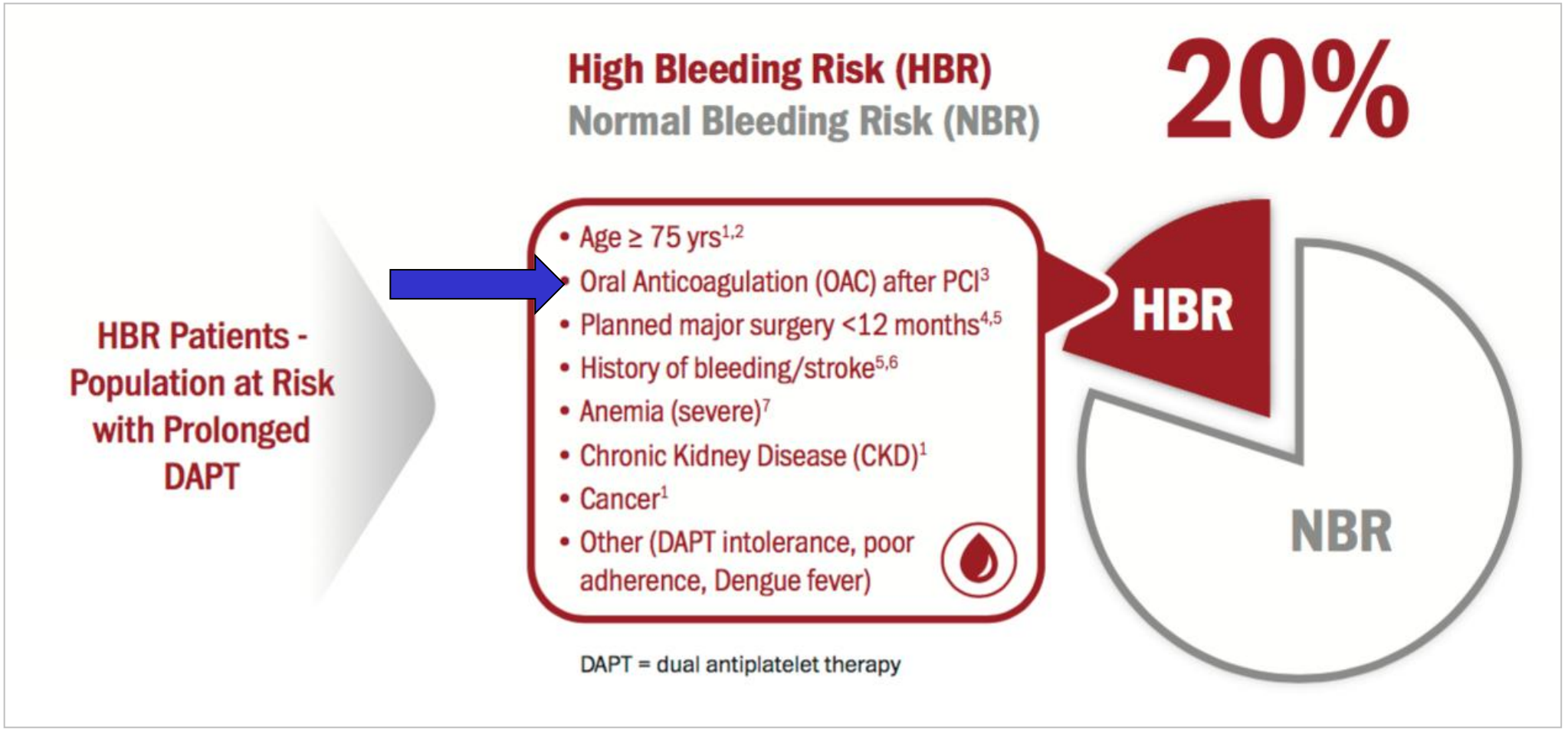


Trombóza stentu vs. krvácení





PCI a vysoké riziko krvácení



Kdy dochází ke krvácivým komplikacím?

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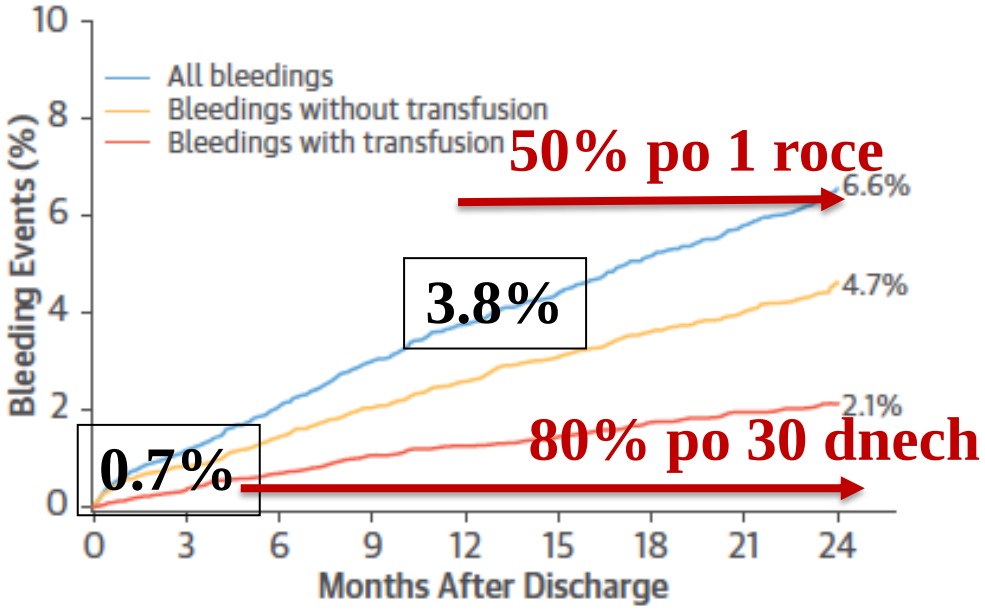
Incidence, Predictors, and Impact of Post-Discharge Bleeding After Percutaneous Coronary Intervention

Philippe Généreux, MD,*†‡ Gennaro Giustino, MD,§ Bernhard Witzenbichler, MD,‖ Giora Weisz, MD,*†¶ Thomas D. Stuckey, MD,# Michael J. Rinaldi, MD,** Franz-Josef Neumann, MD,†† D. Christopher Metzger, MD,‡‡ Timothy D. Henry, MD,§§‖‖ David A. Cox, MD,¶¶ Peter L. Duffy, MD, MMM,## Ernest Mazzaferri, MD,*** Mayank Yadav, MD,* Dominic P. Francese, MPH,* Tullio Palmerini, MD,††† Ajay J. Kirtane, MD, SM,*† Claire Litherland, MS,* Roxana Mehran, MD,*§ Gregg W. Stone, MD*†

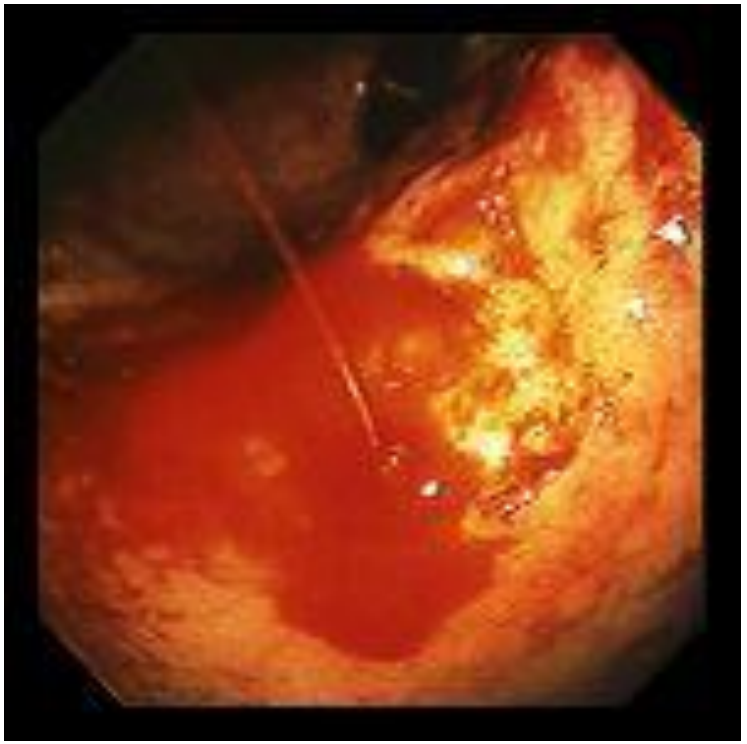
FIGURE 1 Bleeding Rates After Percutaneous Coronary Intervention

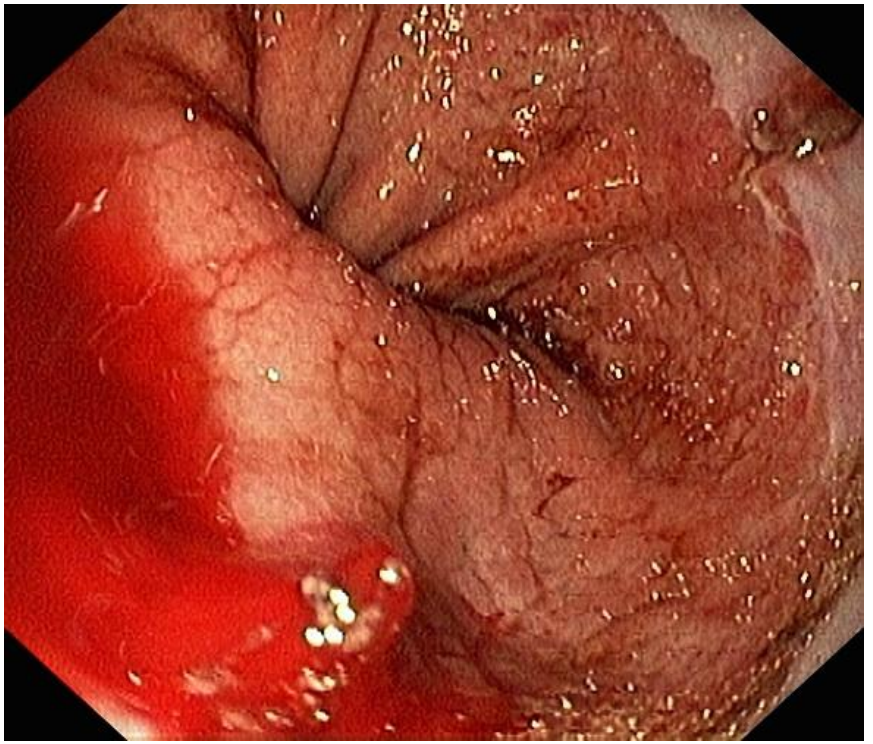


Cumulative rates of first post-discharge bleeding event increased over time in all patients; a similar pattern was seen when patients were stratified according to requirement for blood transfusion.

ADAPT-DES Trial

GI krvácení…nejen..





Místo krvácení a riziko ischémie po implantaci stentu

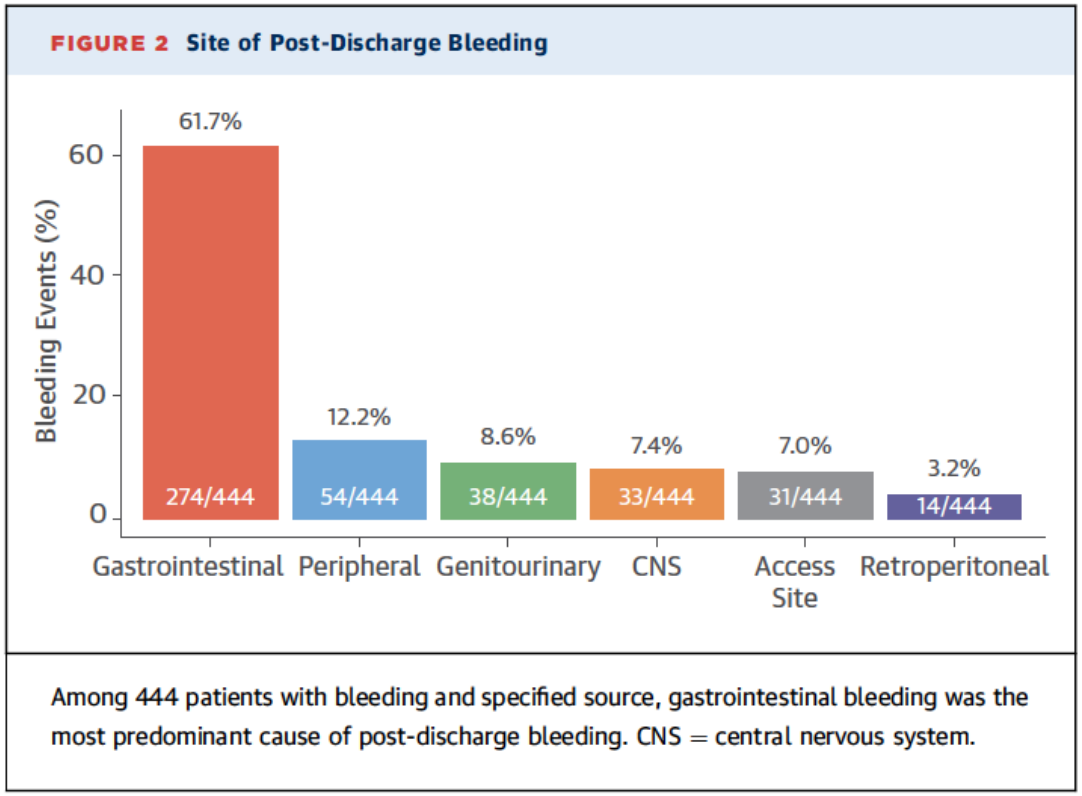


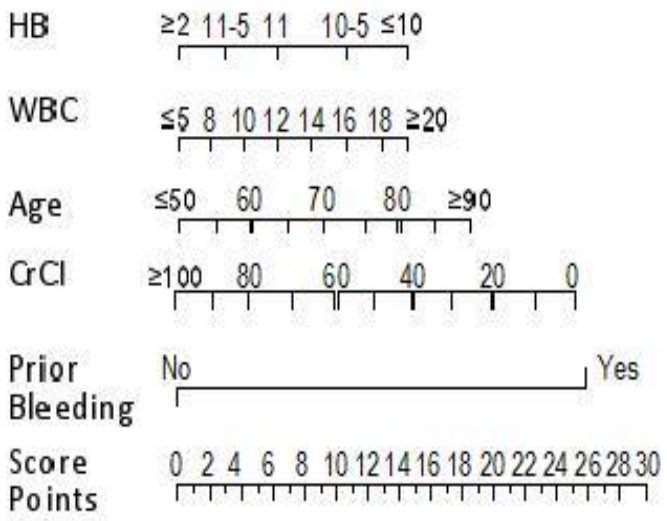
Table 5 High-risk features of stent-driven recurrent ischaemic events

• 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

ESC Guidelines

Risk scores validated for dual antiplatelet therapy duration decision-making

ESC European Society of Cardiology

	PRECISE-DAPT score	DAPT score	
Time of use	At the time of coronary stenting	After 12 months of uneventful DAPT	
DAPT duration strategies assessed	Short DAPT (3–6 months) vs. Standard/long DAPT (12–24 months)	Standard DAPT (12 months) vs. Long DAPT (30 months)	
Score calculation		Age ≥75 65 to <75 <65 Cigarette smoking Diabetes mellitus MI at presentation Prior PCI or prior MI Paclitaxel-eluting stent Stent diameter <3 mm CHF or LVEF <30% Vein graft stent	 −2 pt −1 pt 0 pt +1 pt +1 pt +1 pt +1 pt +1 pt +1 pt +2 pt +2 pt
Score range	0 to 100 points	−2 to 10 points	
Decision making cut-off suggested	Score ≥25 → Short DAPT Score <25 → Standard/long DAPT	Score ≥2 → Long DAPT Score <2 → Standard DAPT	
Calculator	www.precisedaptscore.com	www.daptstudy.org	

2017 ESC Focused Update on DAPT in Coronary Artery Disease, developed in collaboration with EACTS (European Heart Journal 2017 - doi:10.1093/eurheartj/ehx419)

Riziko CMP/TIA u pacientů s FiS

CHADS2 – VASc Score		
C	Congestive Heart Failure	1
H	Hypertension (>140/90 mmHg)	1
A	Age ≥ 75	2
D	Diabetes Mellitus	1
S_2	Prior TIA or stroke	2
V	Vascular disease (MI, aortic plaque etc)	1
A	Age 65-74	1
Sc	Sex category (Female = 1 pt)	1

Riziko krvácivých komplikací u pacientů s FiS

HAS-BLED

Letter	Clinical Characteristic	Points
H	Hypertension	1
A	Abnormal Liver or Renal Function	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile INR	1
E	Elderly (age > 65)	1
D	Drugs or Alcohol	1 or 2
Maximum Score		9

Measures to minimize bleeding while on dual antiplatelet therapy

ESC
European Society of Cardiology

Recommendations	Class	Level
Radial over femoral access is recommended for coronary angiography and PCI if performed by an expert radial operator.	I	A
In patients treated with DAPT, a daily aspirin dose of 75–100 mg is recommended.	I	A
A PPI in combination with DAPT is recommended.	I	B
Routine platelet function testing to adjust antiplatelet therapy before or after elective stenting is not recommended.	III	A

2017 ESC Focused Update on DAPT in Coronary Artery Disease, developed in collaboration with EACTS
(European Heart Journal 2017 - doi:10.1093/eurheartj/ehx419)

Co je nového v ESC Guidelines pro revaskularizace myokardu 2018?

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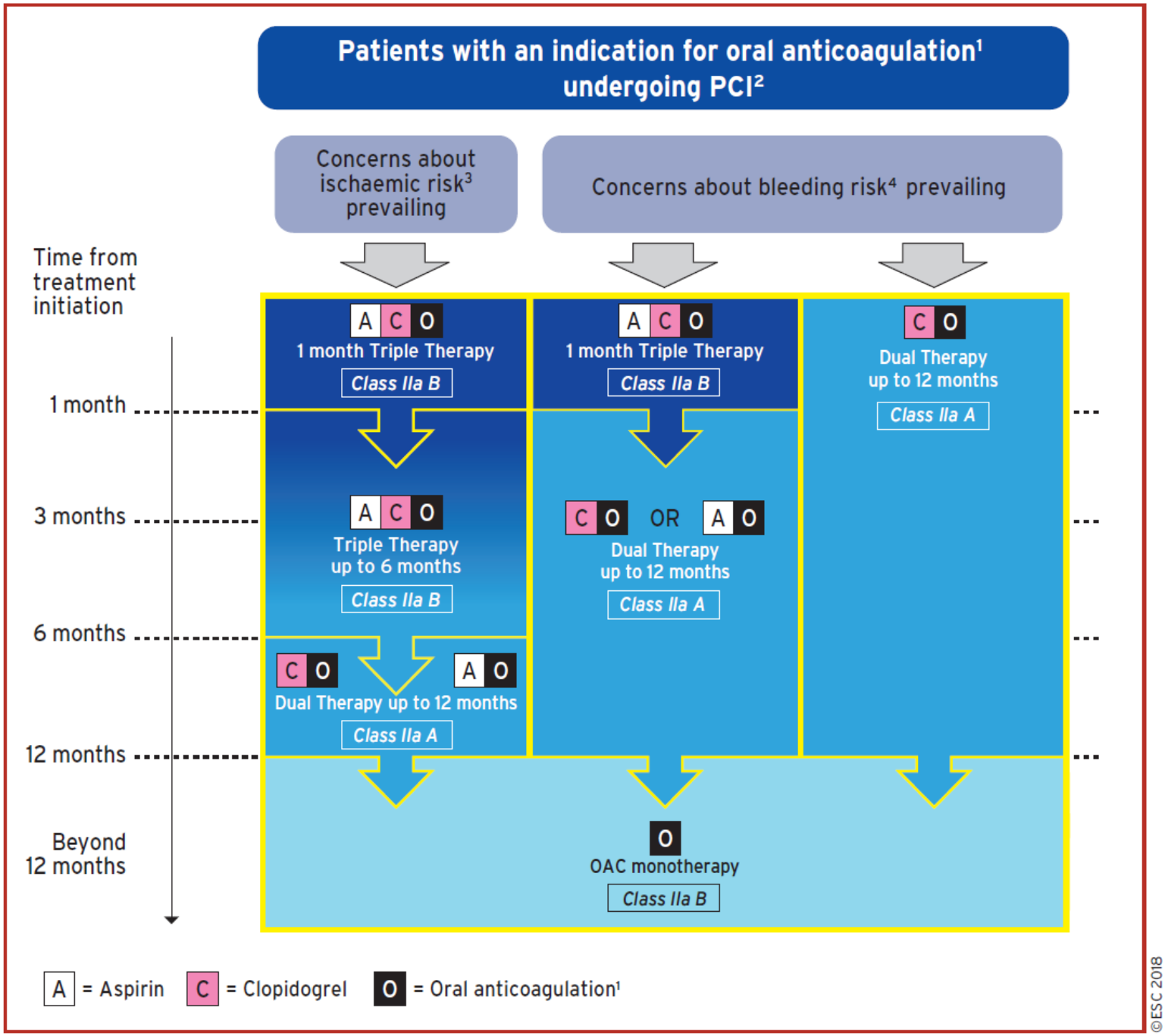
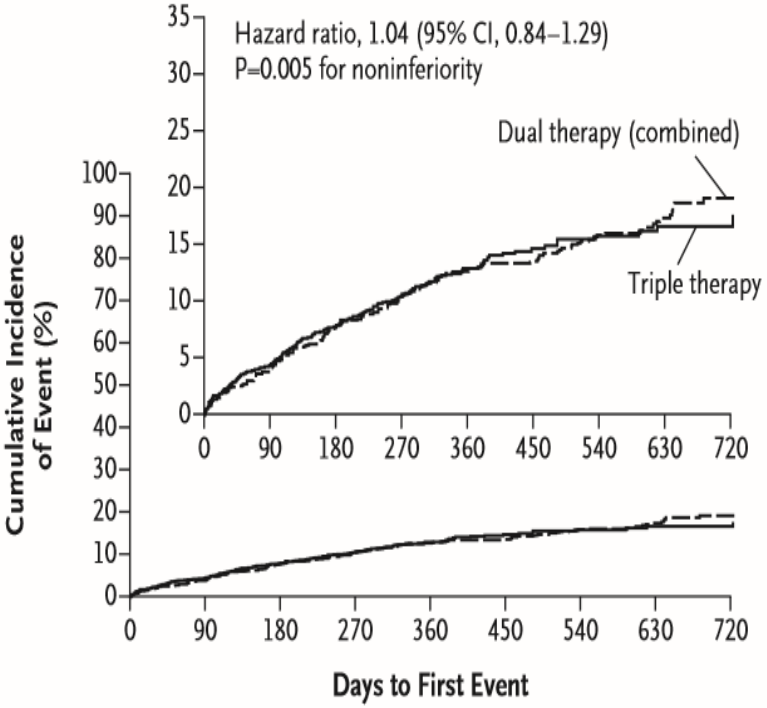
Calculation of the Syntax Score, if left main or multivessel revascularization is considered	Completeness of revascularization prioritized, when considering CABG vs PCI	Routine non-invasive imaging surveillance in high-risk patients 6 months after revascularization
Radial access as standard approach for coronary angiography and PCI	NOAC preferred over VKA in patients with non-valvular AF requiring anticoagulation and antiplatelet treatment	Double-kissing crush technique preferred over provisional T-stenting in true left main bifurcations.
DES for any PCI	No-touch vein technique, if open vein harvesting for CABG	Cangrelor in $P2Y_{12}$-inhibitor naïve patients undergoing PCI
Systematic re-evaluation of patients after myocardial revascularization	Annual operator volume for left main PCI of at least 25 cases per year	GP IIb/IIIa inhibitors for PCI in $P2Y_{12}$-inhibitor naïve patients with ACS undergoing PCI
Stabilised NSTE-ACS patients: revascularization strategy according to principles for SCAD	Pre- and post-hydration with isotonic saline in patients with moderate or severe CKD if the expected contrast volume is >100 mL	Dabigatran 150-mg dose preferred over 110-mg dose when combined with single antiplatelet therapy after PCI
Use of the radial artery grafts over saphenous vein grafts in patients with high-degree stenosis		De-escalation of $P2Y_{12}$ inhibitor guided by platelet function testing in ACS patients
Myocardial revascularization in patients with CAD, heart failure, and LVEF ≤35% CABG preferred PCI as alternative to CABG		Routine revascularization of non-IRA lesions in myocardial infarction with cardiogenic shock
		Current generation BRS for clinical use outside clinical studies

	Class I		Class IIa
	Class IIb		Class III

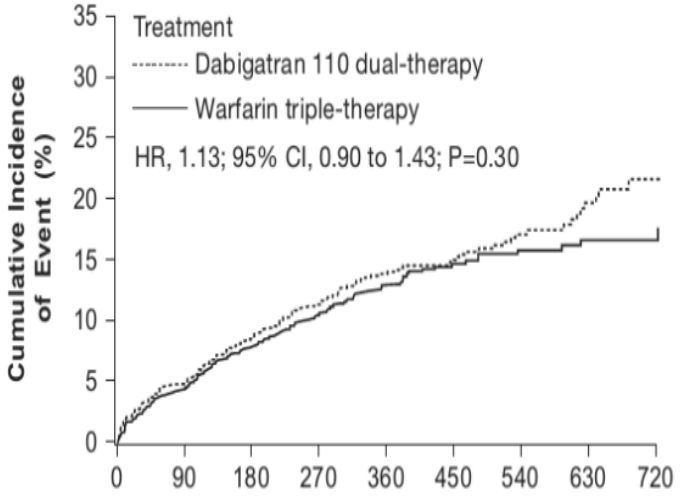

Patients with an indication for oral anticoagulation[1] undergoing PCI[2]
Concerns about ischaemic risk[3] prevailing
Concerns about bleeding risk[4] prevailing
Time from treatment initiation
1 month
3 months
6 months
12 months
Beyond 12 months
A C O
1 month Triple Therapy
Class IIa B
A C O
1 month Triple Therapy
Class IIa B
C O
Dual Therapy up to 12 months
Class IIa A
A C O
Triple Therapy up to 6 months
Class IIa B
C O OR A O
Dual Therapy up to 12 months
Class IIa A
C O
A O
Dual Therapy up to 12 months
Class IIa A
O
OAC monotherapy
Class IIa B
A = Aspirin
C = Clopidogrel
O = Oral anticoagulation[1]
©ESC 2018

Studie RE-DUAL

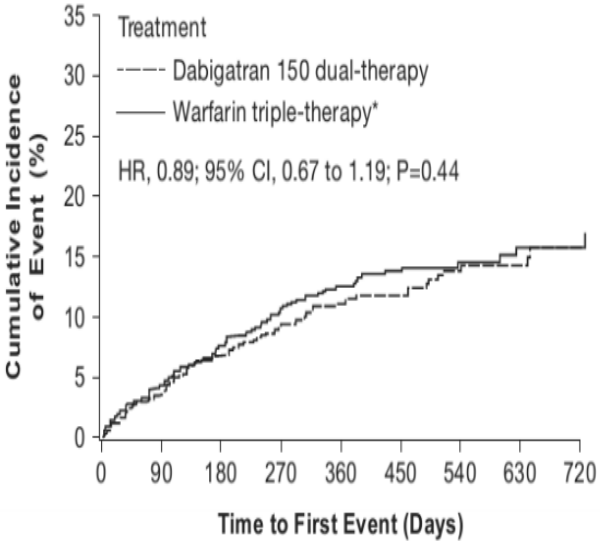


N Engl J Med 2017; 377:1513-1524

A. Dabigatran 110 Dual-therapy versus Warfarin Triple-therapy



B. Dabigatran 150 Dual-therapy versus Warfarin Triple-therapy



Studie AUGUSTUS
Krvácení a Úmrtí/hospitalizace

Intervenční kardiologie
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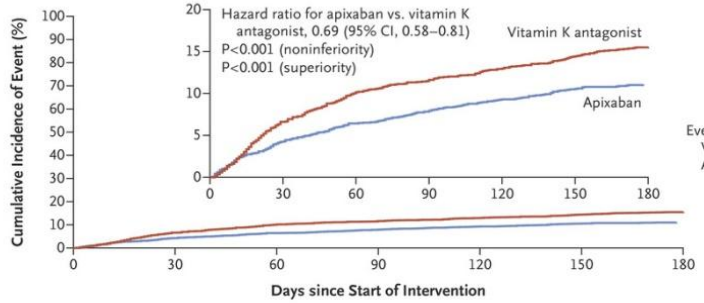
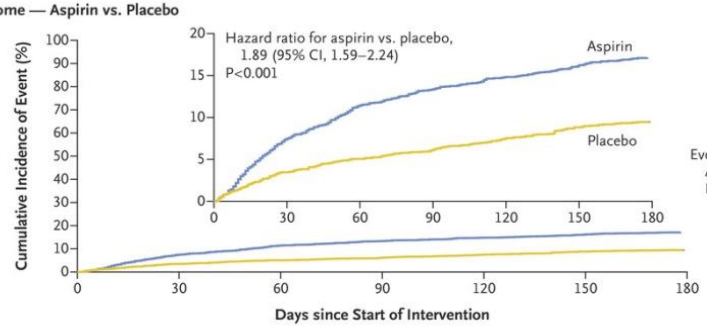
A Primary Outcome — Apixaban vs. Vitamin K Antagonist



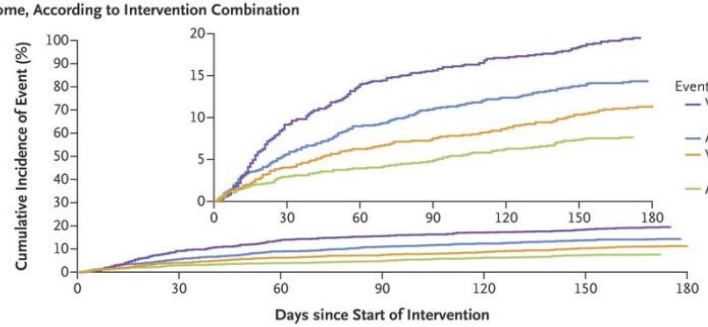
No. at Risk							
Vitamin K antagonist	2259	1984	1861	1795	1736	1686	1079
Apixaban	2290	2110	2019	1957	1902	1858	1037

B Primary Outcome — Aspirin vs. Placebo



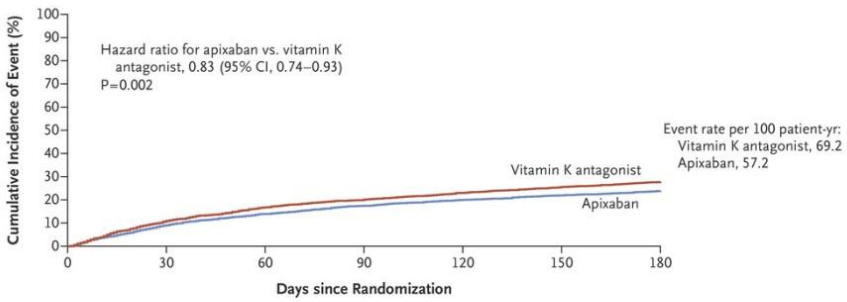
No. at Risk							
Aspirin	2277	2003	1863	1789	1717	1674	962
Placebo	2279	2095	2006	1941	1880	1824	1079

C Primary Outcome, According to Intervention Combination



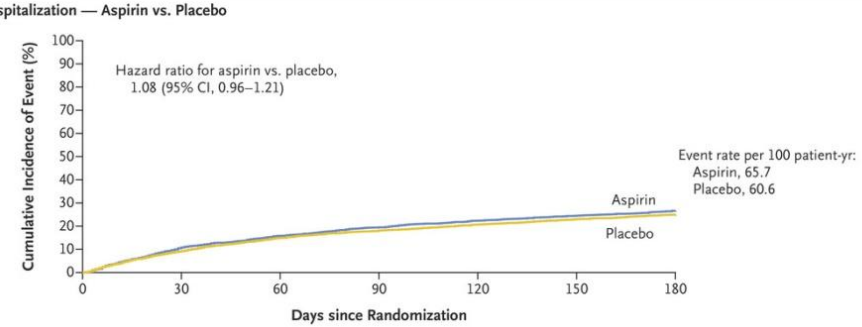
No. at Risk							
Vitamin K antagonist and aspirin	1123	962	881	838	800	776	467
Apixaban and aspirin	1145	1036	975	937	903	880	485
Vitamin K antagonist and placebo	1126	1007	947	917	883	851	528
Apixaban and placebo	1143	1075	1044	1007	975	947	536

A Death or Hospitalization — Apixaban vs. Vitamin K Antagonist



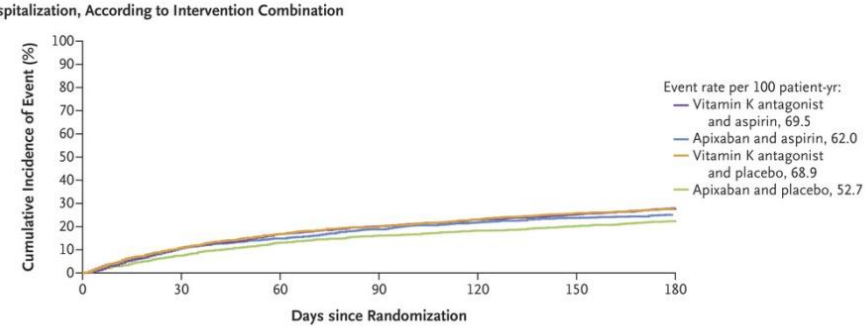
No. at Risk							
Vitamin K antagonist	2308	2035	1885	1805	1732	1673	1001
Apixaban	2306	2090	1965	1881	1821	1772	947

B Death or Hospitalization — Aspirin vs. Placebo



No. at Risk							
Aspirin	2307	2042	1909	1822	1752	1699	951
Placebo	2307	2083	1941	1864	1801	1746	997

C Death or Hospitalization, According to Intervention Combination



No. at Risk							
Vitamin K antagonist and aspirin	1154	1016	939	899	864	836	492
Apixaban and aspirin	1153	1026	970	923	888	863	459
Vitamin K antagonist and placebo	1154	1019	946	906	868	837	509
Apixaban and placebo	1153	1064	995	958	933	909	488

RD Lopes et al. N Engl J Med 2019;380:1509-1524.

ARISTOPHANES study

(Anticoagulants for Reduction in Stroke: Observational Pooled Analysis on Health Outcomes and Experience of Patients)

US retrospektivní observační studie s „matched“ populacís FiS

- **285.292 pacientů** - 6 skupin: 57 929 apixaban-warfarin, 26 838 dabigatran-warfarin, 83 007 rivaroxaban-warfarin, 27 096 apixaban-dabigatran, 62 619 apixaban-rivaroxaban, and 27 538 dabigatran-rivaroxaban

- *Riziko CMP/SE oproti warfarinu*: **apixaban (hazard ratio [HR], 0.61**; 95% CI, 0.54–0.69), **dabigatran (HR, 0.80**; 95% CI, 0.68–0.94), and **rivaroxaban (HR, 0.75**; 95% CI, 0.69–0.82)

- *Velké krvácení oproti warfarinu*: **apixaban (HR, 0.58**; 95% CI, 0.54–0.62) a **dabigatran (HR, 0.73**; 95% CI, 0.66–0.81), **rivaroxaban (HR, 1.07**; 95% CI,1.02–1.13)

Lip G. Stroke. 2018;49:2933-2944

DES se zkrácenou dobou DAPT

LEADERS FREE Trial Design

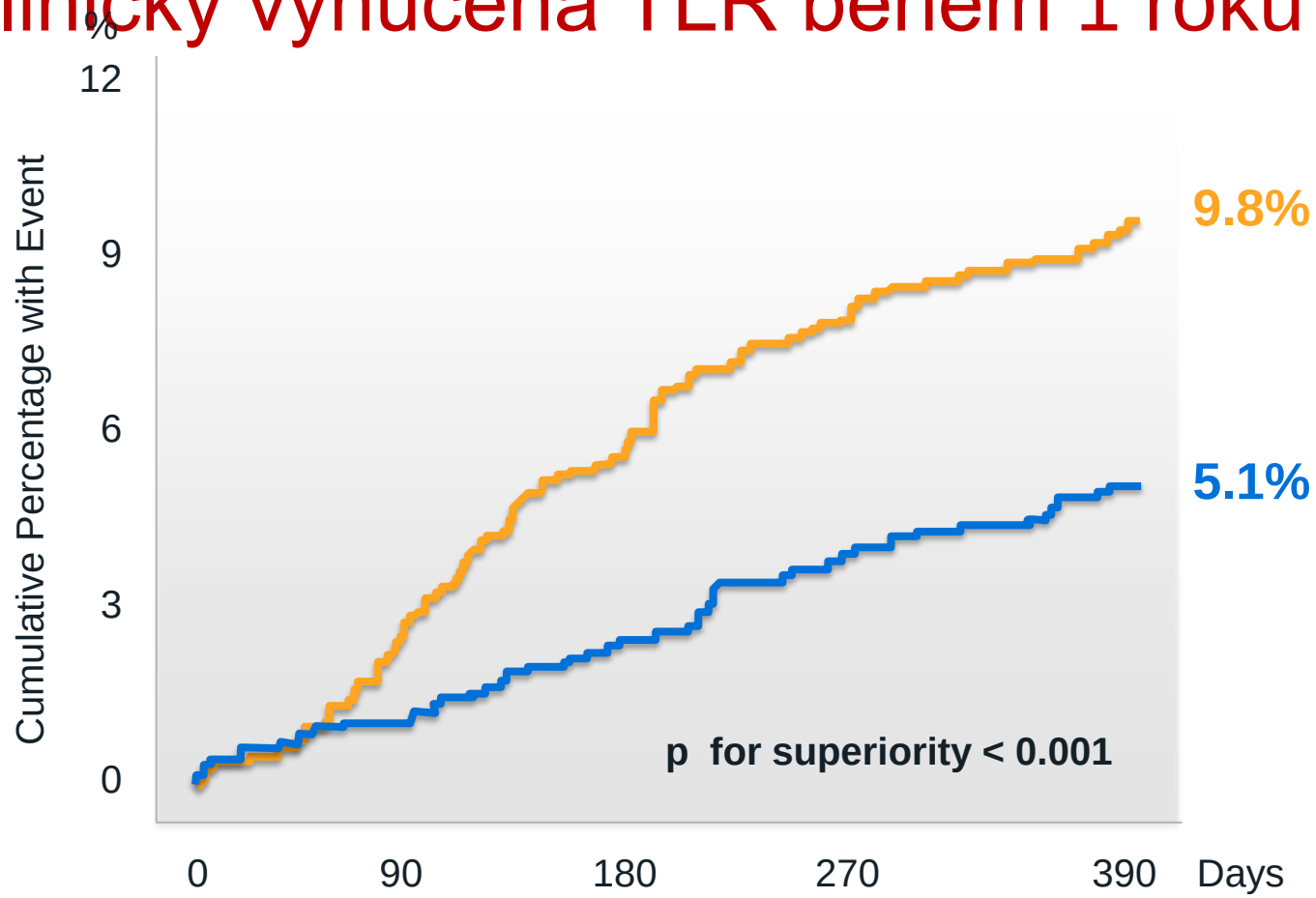
Prospektivní, dvojitě slepá randomizovaná studie (1:1)
2466 pacientů s vysokým rizikem krvácení a PCI
(High bleeding risk – HBR)

BioFreedom™ DCS **VS.** **Gazelle™ BMS**

DAPT vždy pouze 1 měsíc, poté dlouhodobá SAPT

- **Primární bezpečnostní ukazatel:**
  Kombinovaný – kardiální úmrtí, IM, trombóza stentu (potvrzená/pravděpodobná) během 1 roku
- **Primární ukazatel účinnosti:**
  Klinicky vynucená TLR během 1 roku (superiorita)

Primární ukazatel účinnosti:
Klinicky vynucená TLR během 1 roku

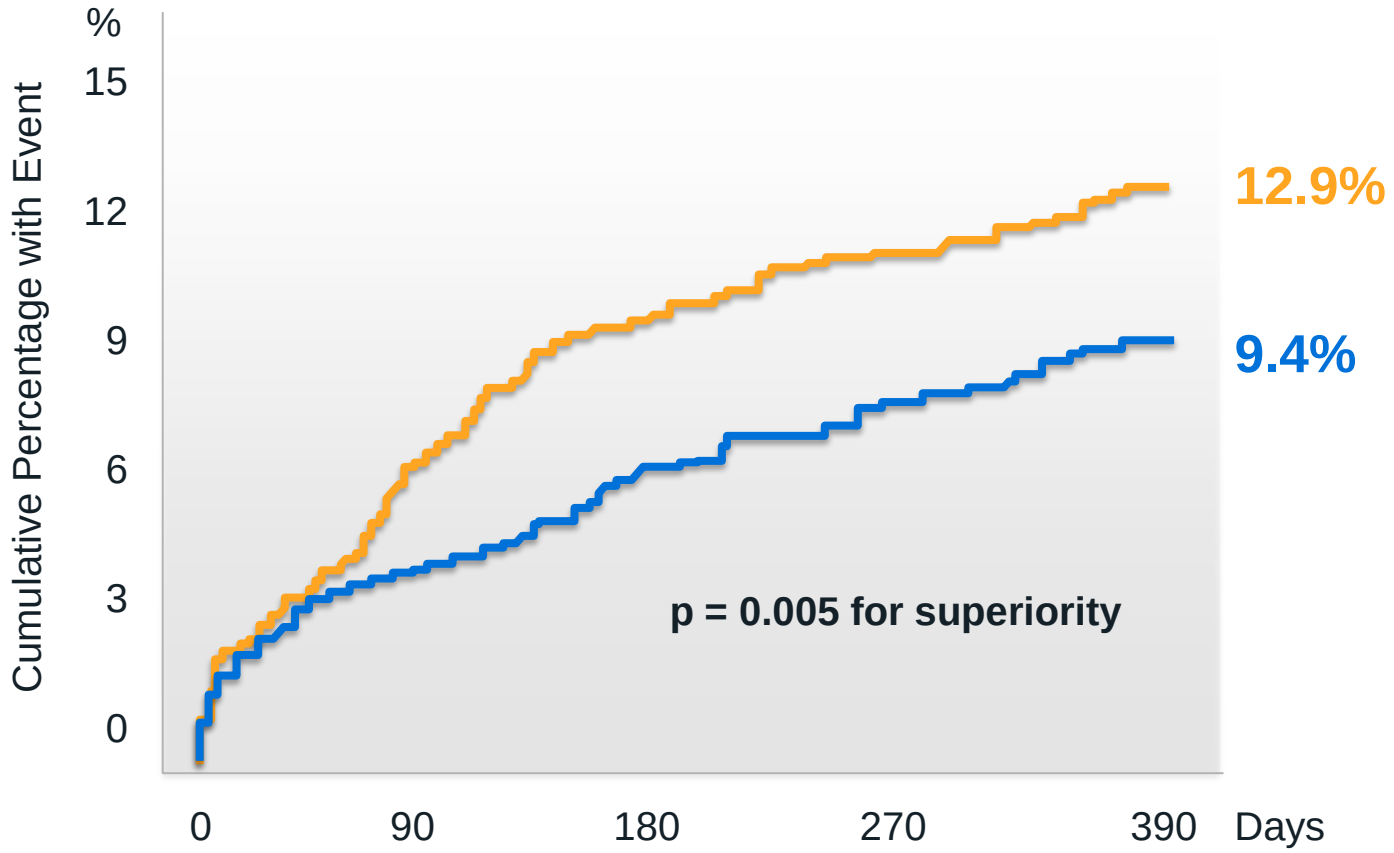


Number at Risk

DCS	1221	1167	1130	1098	1053
BMS	1211	1131	1072	1034	984

390 days chosen for assessing primary EP to capture potential evens driven by the 360 day FU contact

Primární bezpečnostní ukazatel:
Kombinovaný – kardiální úmrtí, IM, trombóza stentu



Number at Risk

DCS	1221	1146	1105	1081	1045
BMS	1211	1115	1066	1037	1000

390 days chosen for assessing primary EP to capture potential events driven by the 360 day FU contact

Studie MASTER-DAPT - design

Patient selection
- Site
- History of MI
- OAC

4300 patients from >100 international sites

1 month mandatory DAPT*

Randomisation

Abbreviated DAPT
SAPT ≥11 months

Prolonged DAPT
ASA 11 months + P2Y12 inhibitor for ≥5 months†

Primary endpoints
- NACE
- MACCE
- MCB

Eligibility after index procedure
- High bleeding risk
- All lesions treated with Ultimaster
- No further PCI planned

Eligibility at 30 days randomisation visit
- High bleeding risk at baseline or actionable non-access site-related bleeding episode post-PCI
- Free from MI, symptomatic restenosis, stroke, and any revascularisation
- No active bleeding within 7 days before randomisation
- Patient stable on DAPT for at least 7 days before randomisation

*DAPT duration is counted from the day of the last implanted stent; staging has to be pre-specified at the time of screening and cannot be planned later than 2 months after index PCI. †Patients receiving OAC can stop DAPT 2 months after confirmed randomisation.
ASA, acetylsalicylic acid; DAPT, dual antiplatelet therapy; MACCE, major adverse cardiac and cerebral events; MCB, major or clinically relevant non-major bleeding; MI, myocardial infarction; NACE, net adverse clinical endpoints; OAC, oral anticoagulant therapy; PCI, percutaneous coronary intervention; SAPT, single antiplatelet therapy.
Terumo. Ultimaster Drug Eluting Stent Instructions for Use, version 0.1-2018; MASTER DAPT trial. Available at https://clinicaltrials.gov/ct2/show/NCT03023020?term=master+dapt&rank=1 (accessed April 2018).

Pacient na (N)OAC k/s PCI
Základní otázky

1. **Základní klinické scénáře při přijetí pacienta**
   1. AKS s klinickou nutností katetrizace ihned – do 24hod
   2. AKS s klinickou možností odložení katetrizace o >24hod
   3. Stabilní ICHS
2. **Typ antikokagulace**
   1. Warfarin *(ponechání, INR 2-3 při radiálním přístupu)*
   2. NOAK – apixaban, dabigatran, edoxaban, rivaroxaban *(vysazení NOAK minim. 24-48hod)*
3. **Hospitalizace + propuštění**
   1. NOAK preferenčně (antidotum?)
   2. Duální vs triple terapie
4. **Při přijetí a v průběhu hospitalizace**
   1. Baseline stanovení rizika ischemie/krvácení + opakovaně v případě závažné změny (krvácení, reIM, trombóza)

STRATEGIE
k prevenci krvácení/ishemie u pacientů s PCI na OAK

- **Zhodnotit** (přehodnotit) **ischemické a krvácivé riziko** pomocí ověřených skórovacích systémů (tzn. CHA_2DS_2-VASc, HAS-BLED) a PRECISE-DAPT a hodnocení v čase (obecné doporučení monoth (N)OAK po 12 měs.) a **compliance** pacienta včetně **komorbidit**.

- Ponechat **triple terapii minimálně po dobu nezbytně nutnou** 5-7 dnů; **duální terapie** po PCI – (N)OAK a clopidogrel by měla být zvážena místo triple terapie.

- Je třeba zvážit použití **NOAK místo warfarinu** (dávka NOAK ke snížení rizika CMP/SE, v případě warfarinu INR 2-2,5).

STRATEGIE
k prevenci krvácení/ishemie u pacientů s PCI na OAK

- **Clopidogrel** je $P2Y_{12}$ inhibitor volby.
- Používat nízkou (**≤100 mg** denně) dávku **ASA**.
- **Rutinně PPI** po dobu kombinované léčby, při PCI **radiální přístup, funkční revaskularizace** (snížení počtu stentů), **DES se zkrácenou dobou DAPT.**
- **SPOLUPRÁCE** ošetřujících lékařů s nezastupitelnou rolí invazivního kardiologa, **optimalizace individualizované léčby**.

Děkuji za pozornost.