# Aspirin po PCI je zbytečný

Varvařovský Ivo

KCA Pardubice

27.sjezd ČKS, Brno 12.-15.5.2019

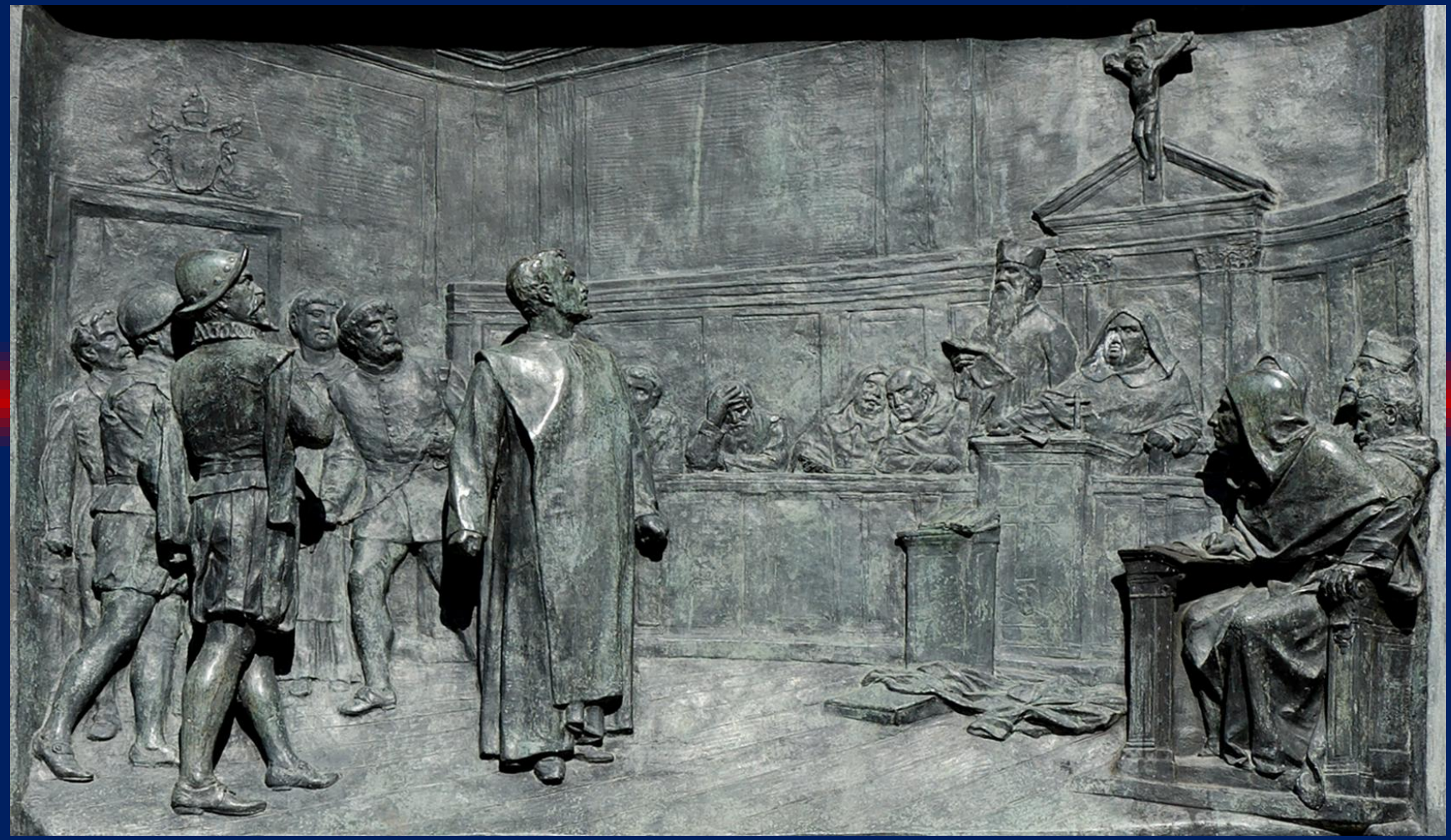
# 2018 ESC/EACTS Guidelines on myocardial revascularization

| Peri-interventional treatment | | |
|---|---|---|
| Aspirin is indicated before elective stenting.[681–683] | I | A |
| An oral loading dose of aspirin (150–300 mg p.o. or 75–250 mg i.v.) is recommended if the patient is not pre-treated. | I | C |

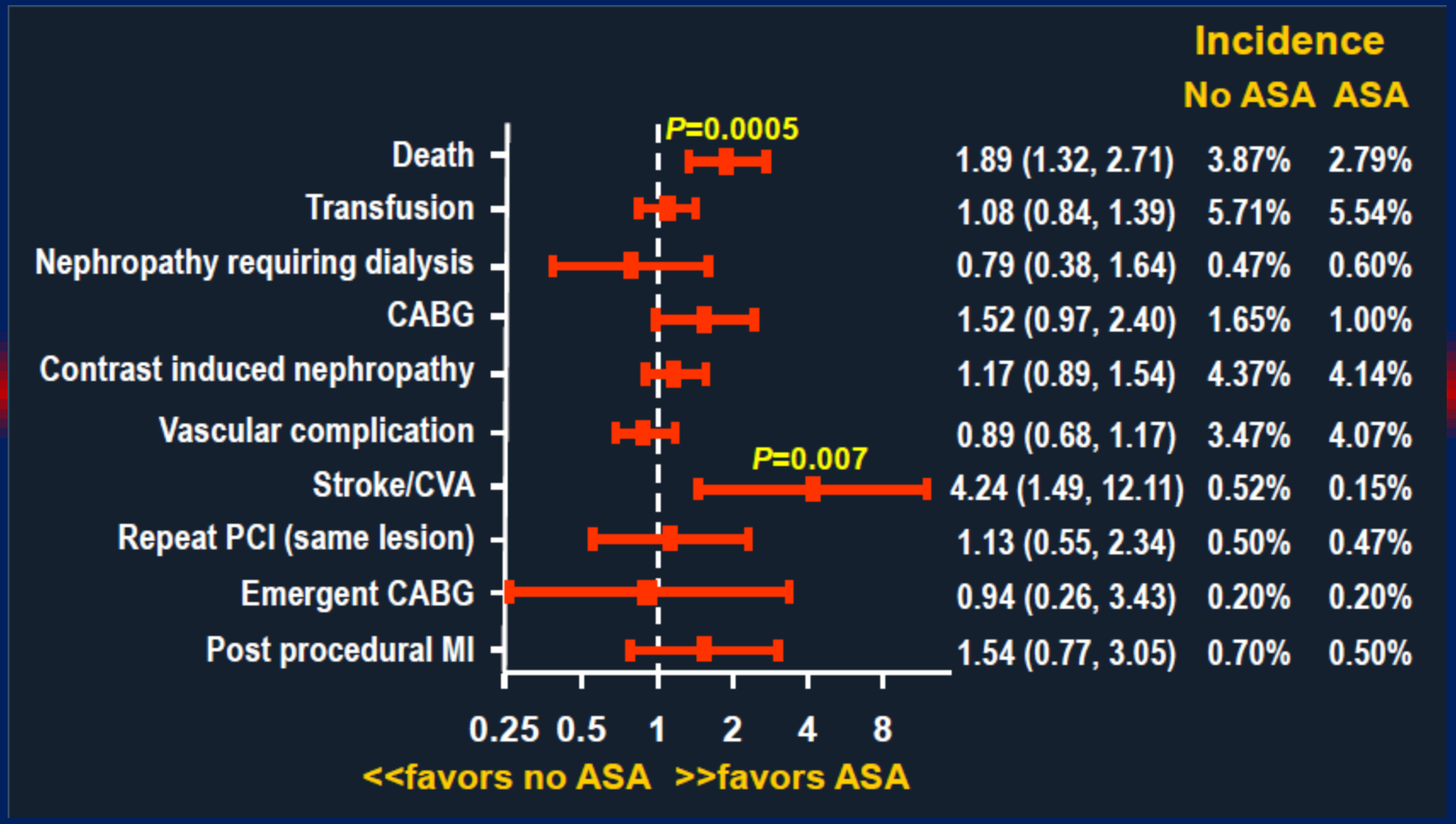
| Post-interventional and maintenance treatment | | |
|---|---|---|
| Life-long single antiplatelet therapy, usually aspirin, is recommended.[681,683] | I | A |
| Instruction of patients about the importance of complying with antiplatelet therapy is recommended. | I | C |

European Heart Journal (2019) **40**, 87–165

# Aspirin po PCI je zbytečný



# Aspirin při PCI je nezbytný




J Am Coll Cardiol 2013;62:2083–9

# Aspirin při PCI je nezbytný ???

**WOEST**

## Study Design-2

***1:1 Randomisation:***

| Double therapy group: | Triple therapy group |
|---|---|
| OAC + 75mg Clopidogrel qd | OAC + 75mg Clopidogrel qd + 80mg Aspirin qd |
| 1 month minimum after BMS | 1 month minimum after BMS |
| 1 year after DES | 1 year after DES |

***Follow up:*** 1 year

***Primary Endpoint:*** The occurence of all bleeding events (TIMI criteria)

***Secondary Endpoints:***
- Combination of stroke, death, myocardial infarction, stent thrombosis and target vessel revascularisation
- All individual components of primary and secondary endpoints

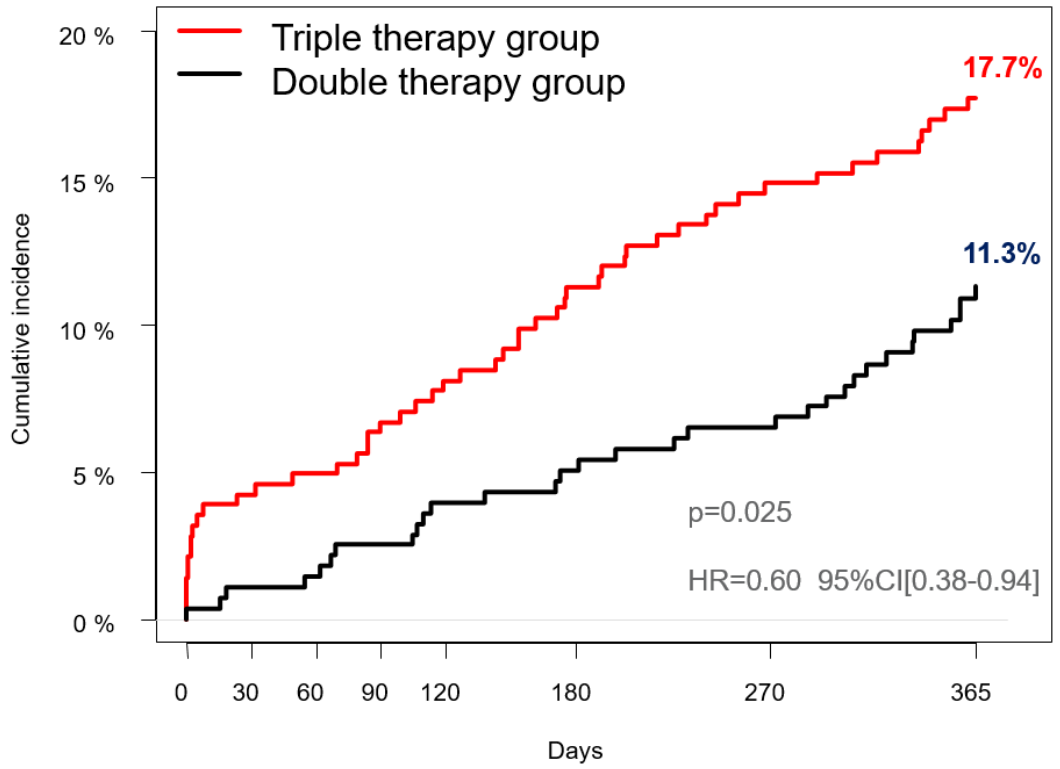
ZIEKENHUIS ST ANTONIUS

DeWilde W, et al. ESC Munich, August 28, 2012

# Aspirin při PCI je nezbytný ???

**WOEST**

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




DeWilde W, et al. ESC Munich, August 28, 2012

# GLOBAL LEADERS: schéma léčby

ECRI European Cardiovascular Research Institute

GLOBAL LEADERS

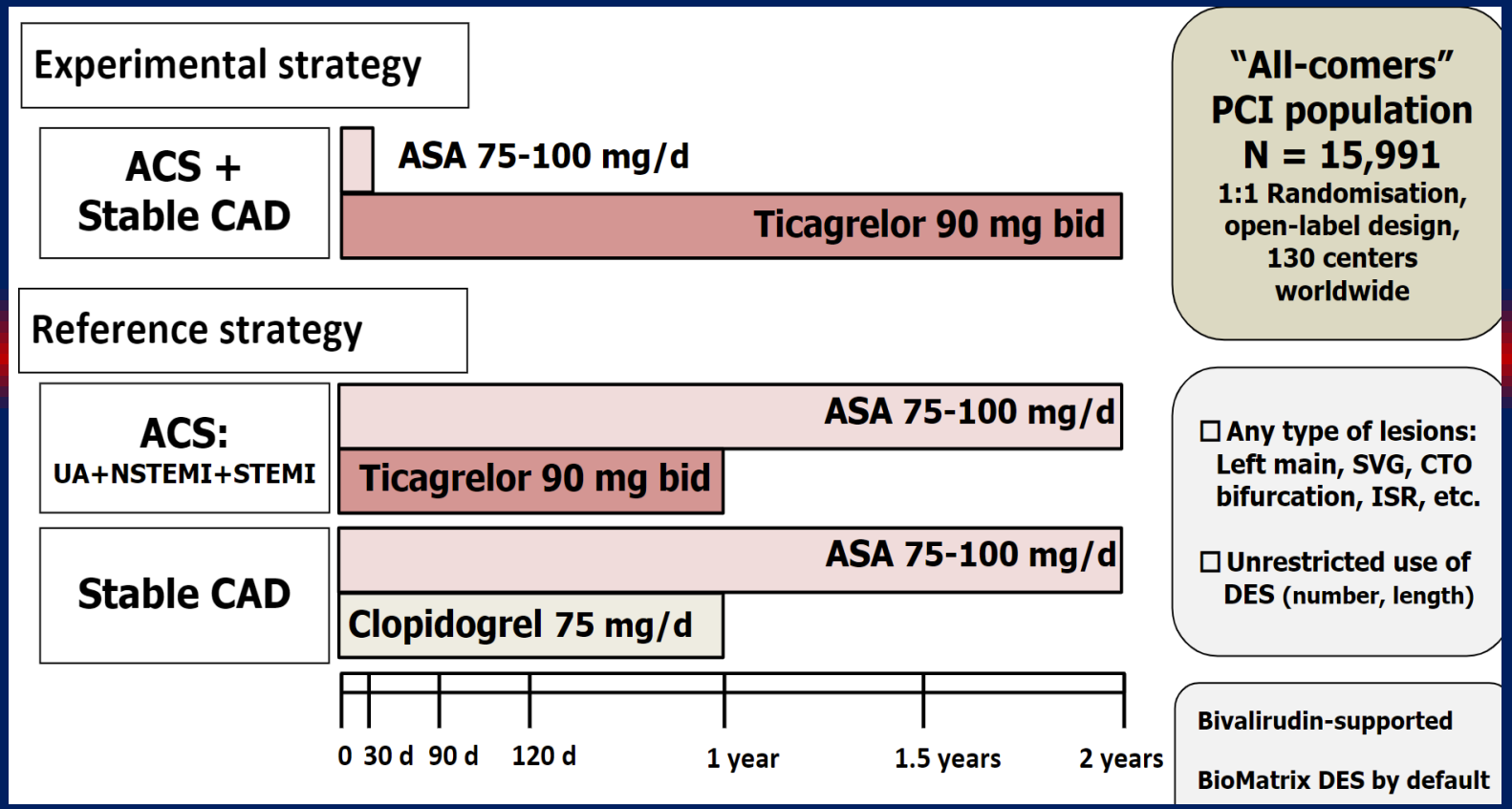
**Ticagrelor monotherapy beyond one month vs. standard dual antiplatelet therapy following drug eluting stent implantation: A randomised multicentre superiority trial.**

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

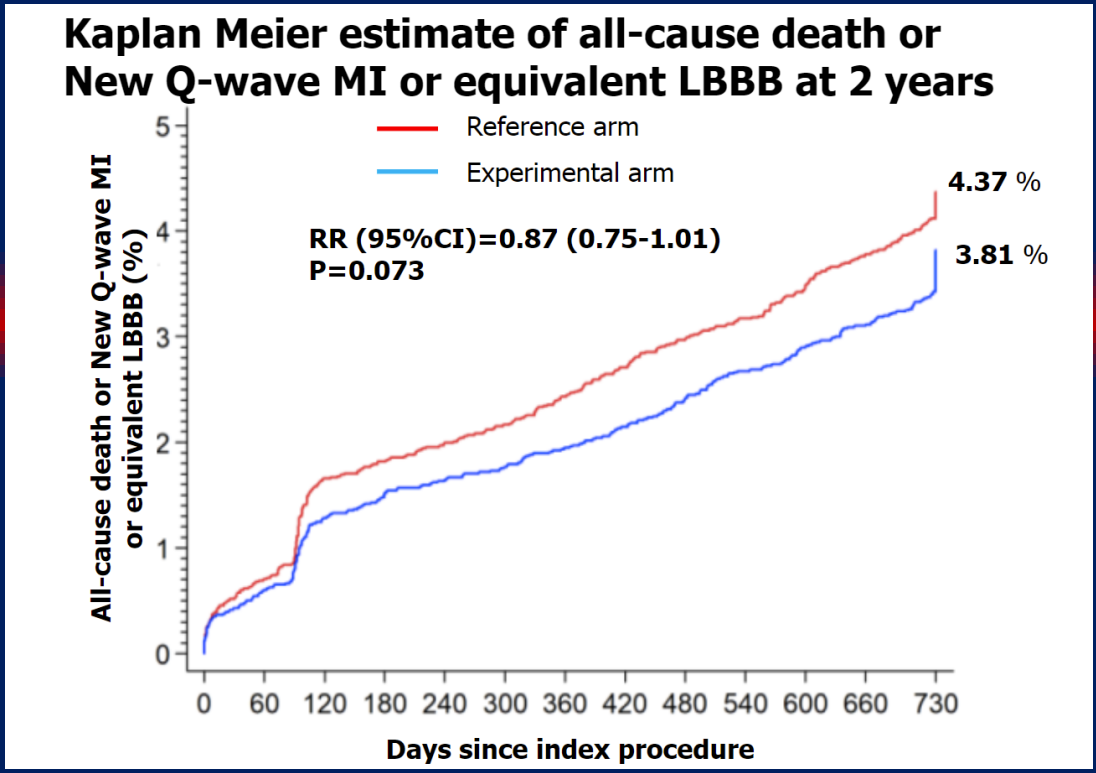
Pascal Vranckx, Marco Valgimigli, Stephan Windecker (PIs)
Christian W. Hamm, Peter Jüni, P. Gabriel Steg, Gerrit-Anne van Es (SC)

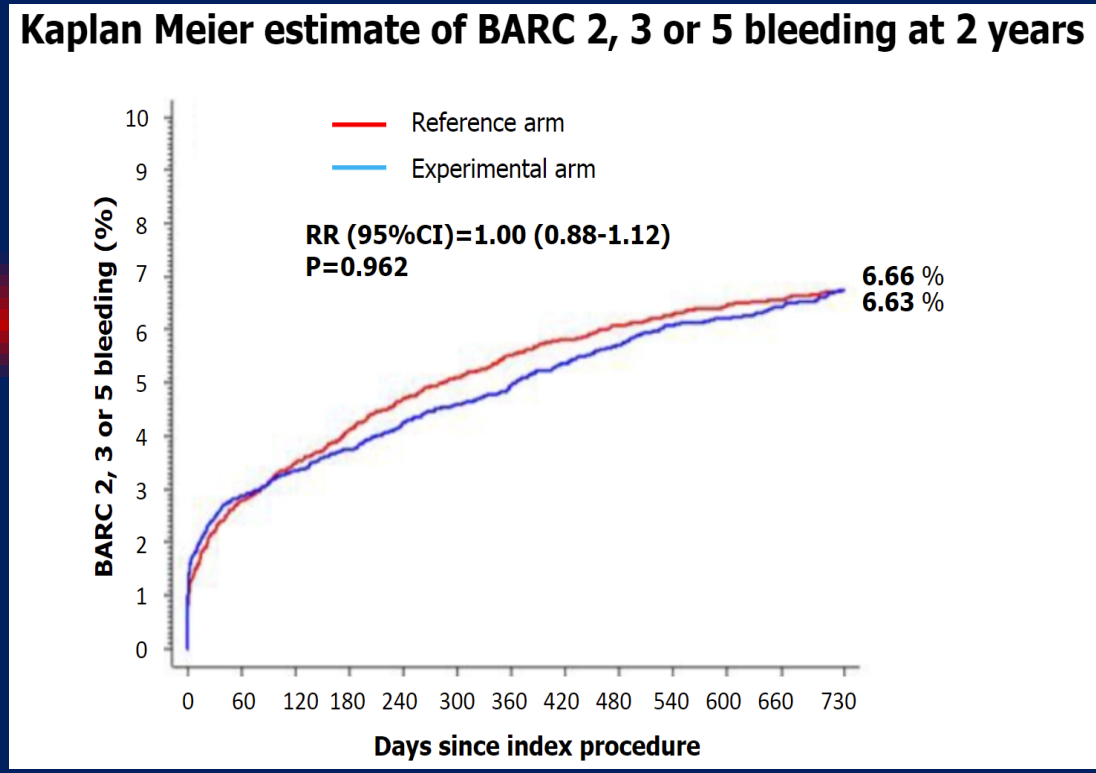
ESC Congress Munich 2018

Lancet. 2018 Sep 15;392(10151):940-949



# GLOBAL LEADERS: výsledky po 2 letech

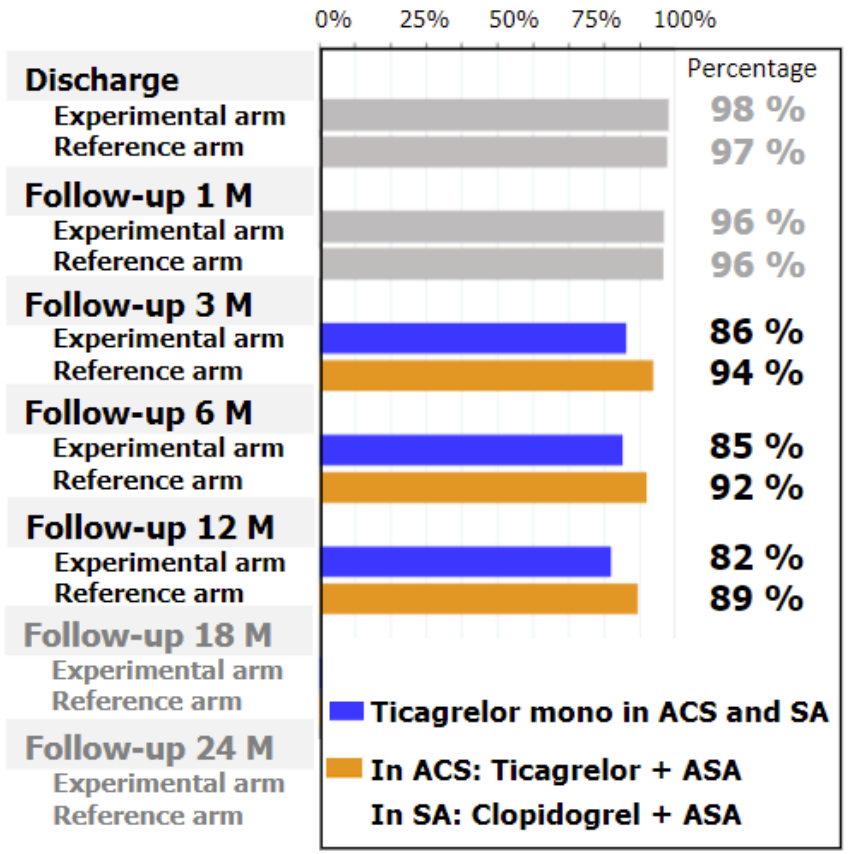



Lancet. 2018 Sep 15;392(10151):940-949

# GLOBAL LEADERS: compliance ve 1.roce vs klinické výsledky

## 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

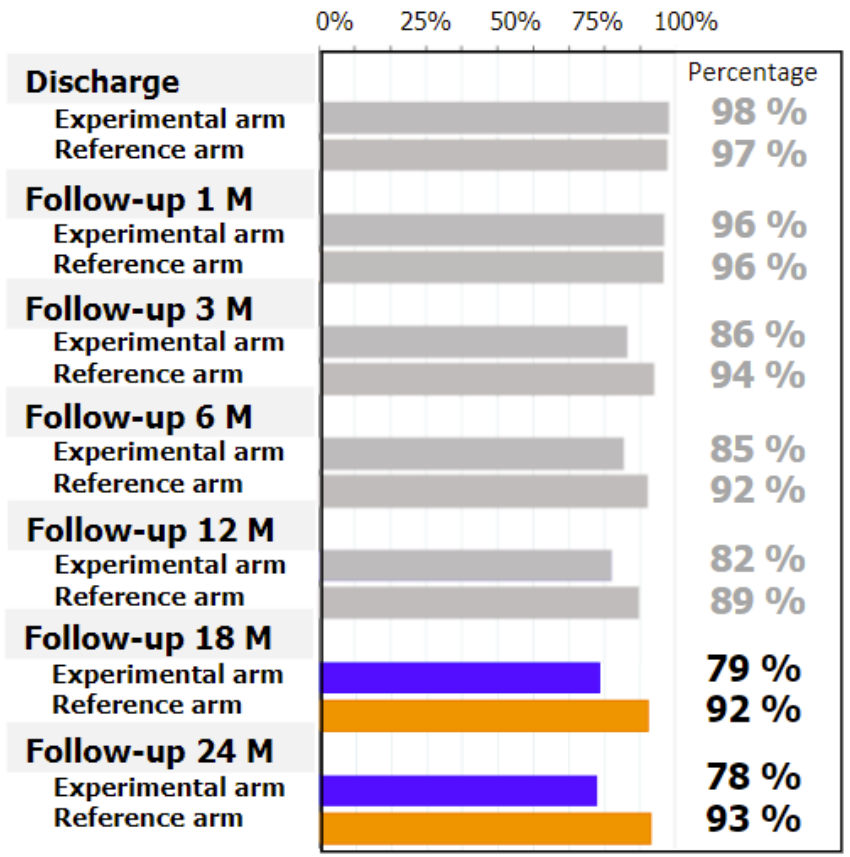
**Mantel-Cox log-rank method for secondary safety endpoints



Lancet. 2018 Sep 15;392(10151):940-949

# GLOBAL LEADERS: compliance ve 2.roce vs klinické výsledky

## 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

10

Lancet. 2018 Sep 15;392(10151):940-949

# Compliance při léčbě ticagrelorem: problém u pacienta nebo u lékaře ?

## 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<br>(28.7% (60mg | 21.40% | 36 months |
| **Socrates** | 17.50% | 14.70% | 90 days |
| **Euclid** | 30.10% | 25.90% | 30 months |

Lancet. 2018 Sep 15;392(10151):940-949

# DAPT po ACS 1 měsíc ???

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

Lekce z GLOBAL LEADERS:

# Aspirin zůstává základním lékem pro dlouhodobou monoterapii nemocných po PCI

(celkový výsledek na konci studie neprokázal statisticky významnou převahu monoterapie ticagrelorem)

**…ale ticagrelor bez aspirinu byl v 1.roce významně lepší !**

Lekce z GLOBAL LEADERS:

Vysazování ticagreloru při podezření na nežádoucí účinky léčby je v 75% případů nepřiměřené

**1-měsíční DAPT po ACS, následovaná monoterapií ticagrelorem**

významně snižuje vážné krvácení proti 12-měsíční DAPT při srovnatelné účinnosti

ESC
European Society of Cardiology

# 2018 ESC/EACTS Guidelines on myocardial revascularization

## Dual antiplatelet therapy duration in patients with indication for oral anticoagulation

| | | |
|---|---|---|
| It is recommended that periprocedural aspirin and clopidogrel are administered to patients undergoing coronary stent implantation. | I | C |
| In patients treated with coronary stent implantation, triple therapy with aspirin, clopidogrel, and an OAC should be considered for 1 month, irrespective of the type of stent used.[755] | IIa | B |
| Triple therapy with aspirin, clopidogrel, and an OAC for longer than 1 month and up to 6 months should be considered in patients with high ischaemic risk due to ACS or other anatomical/procedural characteristics, which outweigh the bleeding risk.[755] | IIa | B |

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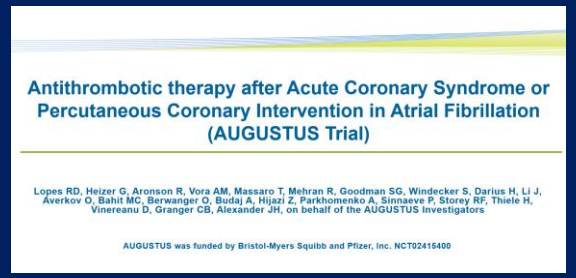



# Aspirin po PCI je zbytečný : AUGUSTUS

## 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)

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

***Anticoagulant 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***

***Antiplatelet Comparison***
*(n =4,614)*

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***

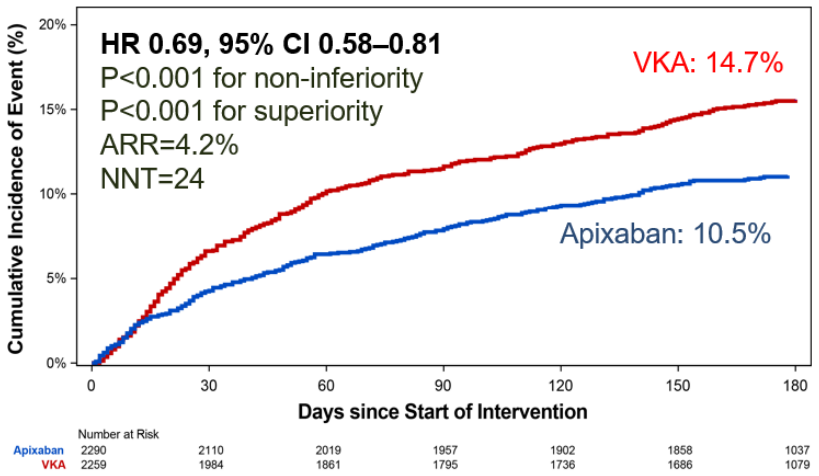
Adapted from: Lopes RD, et al. *Am Heart J*. 2018;200:17-23. Lopes RD, Heizer G, Aronson R, et al. *N Engl J Med*. 2019;doi: 10.1056/NEJMoa1817083

N Engl J Med 2019; 380:1509-1524

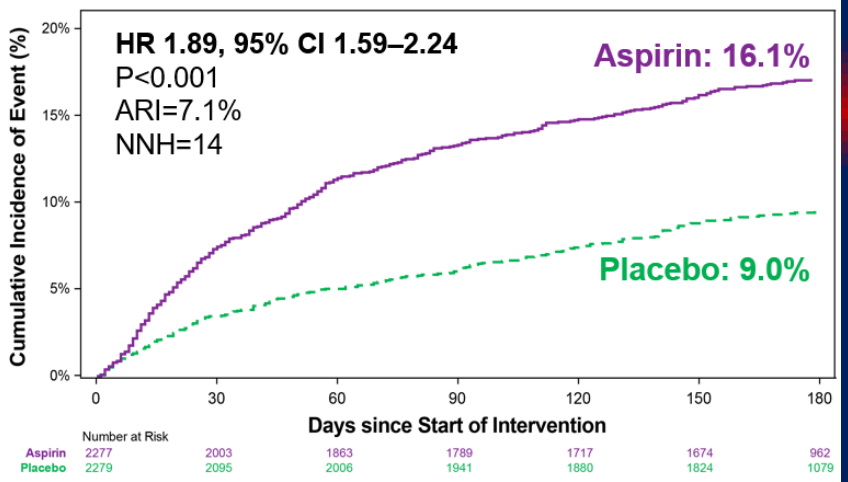
# Aspirin po PCI je zbytečný : AUGUSTUS

## Primary Outcome: ISTH major or CRNM bleeding

Apixaban vs VKA




Aspirin vs Aspirin Placebo




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

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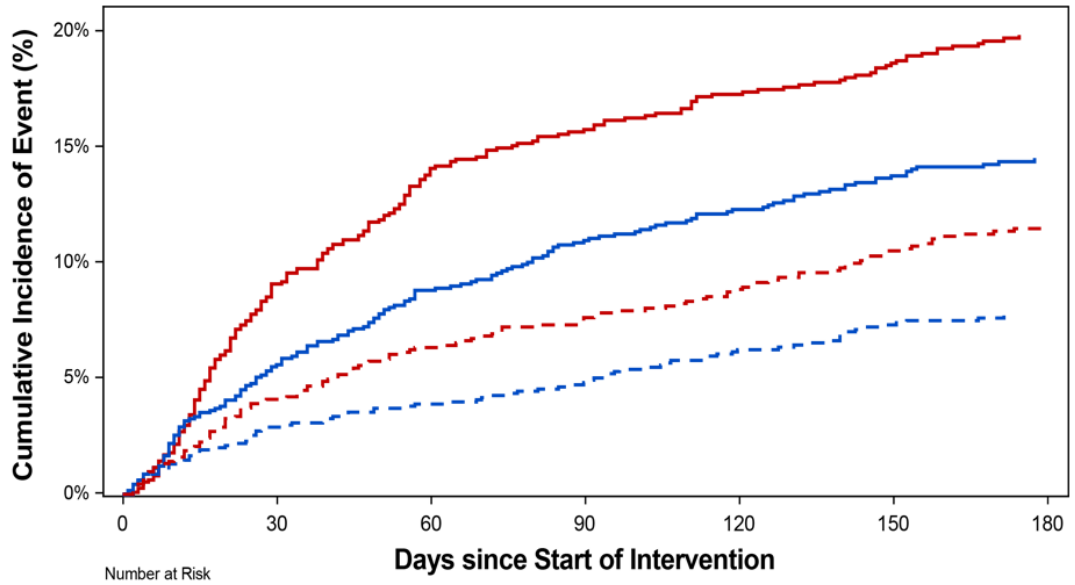
# Aspirin po PCI je zbytečný : AUGUSTUS

## ISTH or CRNM Bleeding, According to Intervention Combination




| 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 |

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

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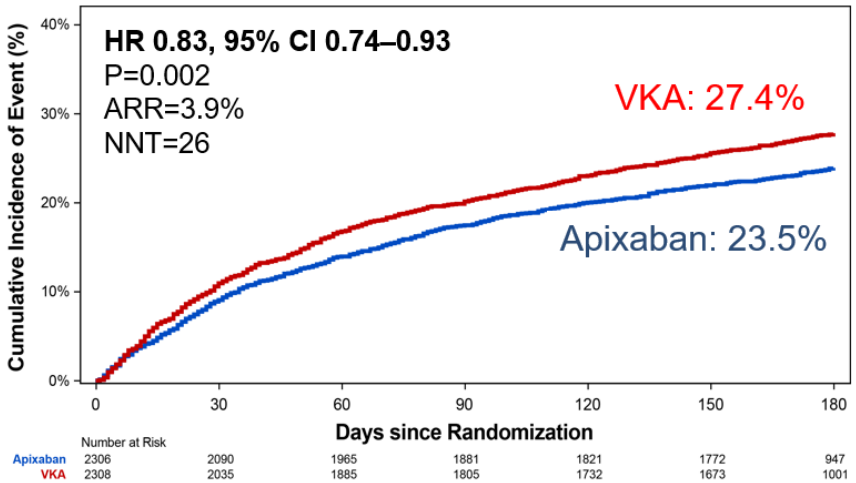
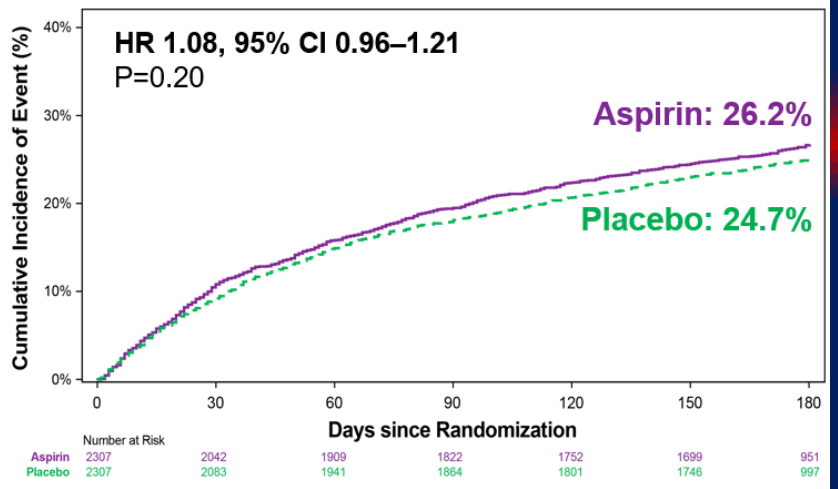
# Aspirin po PCI je zbytečný : AUGUSTUS

## Secondary Outcome: Death or Hospitalization

Apixaban vs VKA




Aspirin vs Aspirin Placebo

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# Aspirin po PCI je zbytečný : AUGUSTUS

1. Dual therapy bezpečnější triple therapy
2. Apixaban je bezpečnější (NNT=24) a účinnější (NNT=26) než VKA
3. Aspirin výrazně zvyšuje riziko krvácení (NNH=14)
4. Aspirin nesnižuje významně riziko ischemických příhod

# Aspirin je po PCI rozhodně zbytečný, protože:

- Po PCI (stabilní, ACS) *budou* výhodnější $P2Y_{12}$ inhibitory (=budoucnost)

- Po PCI u nemocných s fibrilací síní přidání aspirinu zvyšuje riziko krvácení a nepřináší významný prospěch (= žhavá současnost)

# Aspirin po PCI je zbytečný