



Aggiornamenti in tema di **TERAPIA CARDIOVASCOLARE**



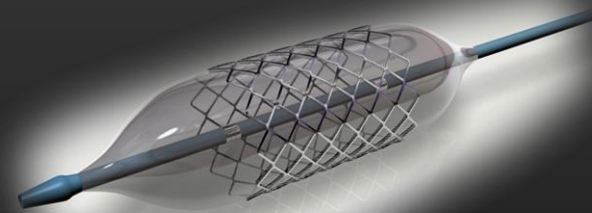
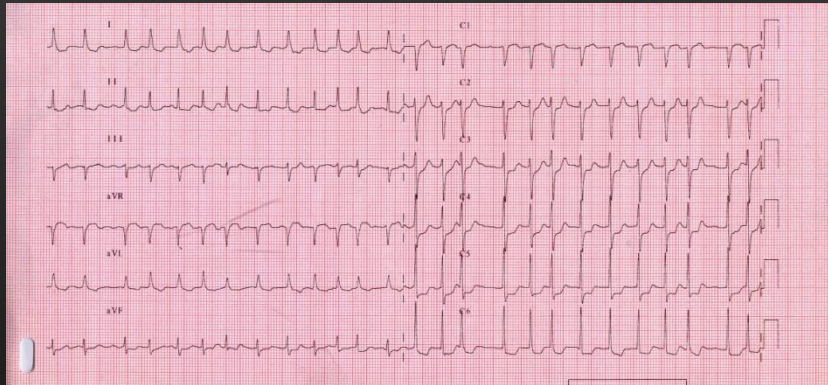
# LA TRIPLICE TERAPIA

**Dr. Federico Costa**

**Unità di Cura Coronarica  
ASST SPEDALI CIVILI BRESCIA**

# Epidemiologia FA e CAD

AF and CAD spesso sovrapposte a causa della forte associazione tra tali condizioni e l'età oltre che per la sovrapposizione di fattori di rischio



- **US ed Europa:**
- **20 Millions affetti da AF (1-2% of population)<sup>1,2</sup>**
- **di cui 16 Millions con indicazione a TAO (80%)<sup>1,2</sup>**
- **di cui 4.8 Millions con CAD (20%-45%)<sup>1,2</sup>**
- **e 1- 2 Millions con potenziale rivascolarizzazione (20%-25%)<sup>3,4</sup>**

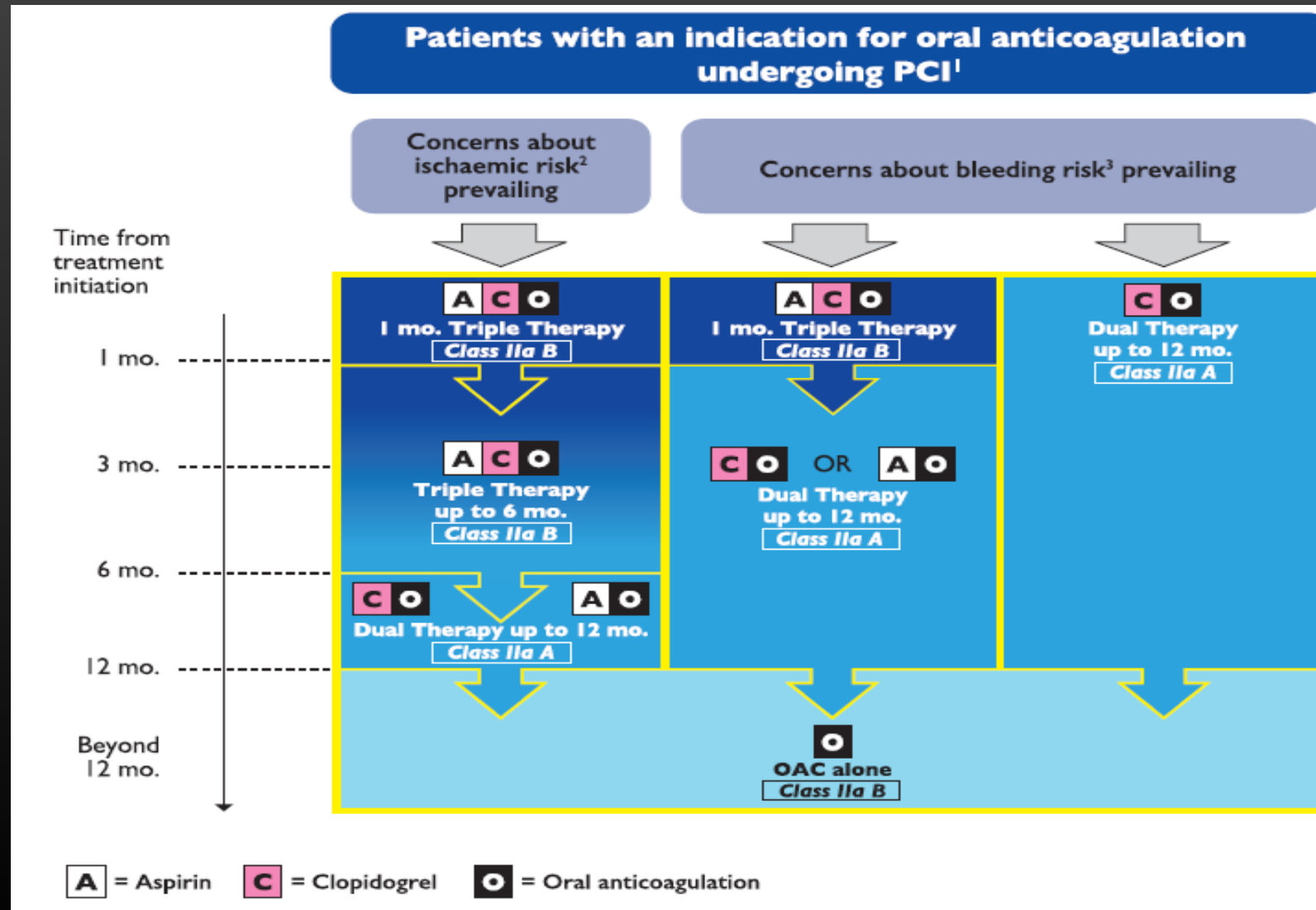
1. The AFFIRM Investigators. *Am Heart J* 2002;143:991–1001;

2. Carpodanno D *et al*, *Circ Cardiovasc Interv* 2014;7:113–124;

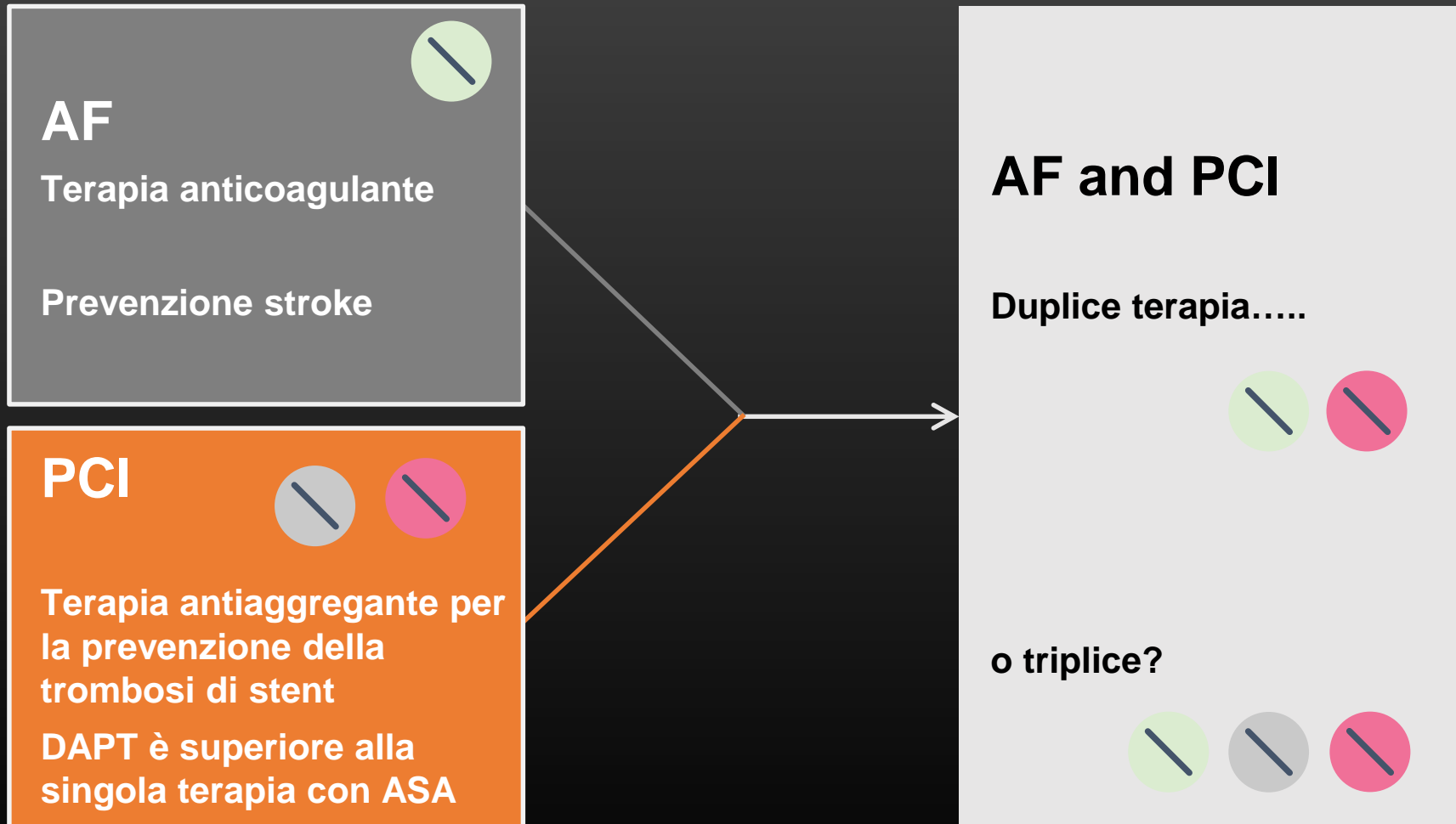
3. Kralev S *et al*, *PLoS One* 2011;6:e24964;

4. Bahit MC *et al*, *Int J Cardiol* 2013;170:215–220

# 2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS



# Quale combinazione di terapie nei pazienti affetti da FA a seguito di PTCA?



# La gestione ottimale della terapia di fibrillazione atriale e coronaropatia differisce

## Fibrillazione atriale (ACTIVE W)<sup>1</sup>:

La combinazione di ASA e clopidogrel non è efficace quanto il *warfarin* nei pazienti con AF<sup>1</sup>

*Tuttavia*

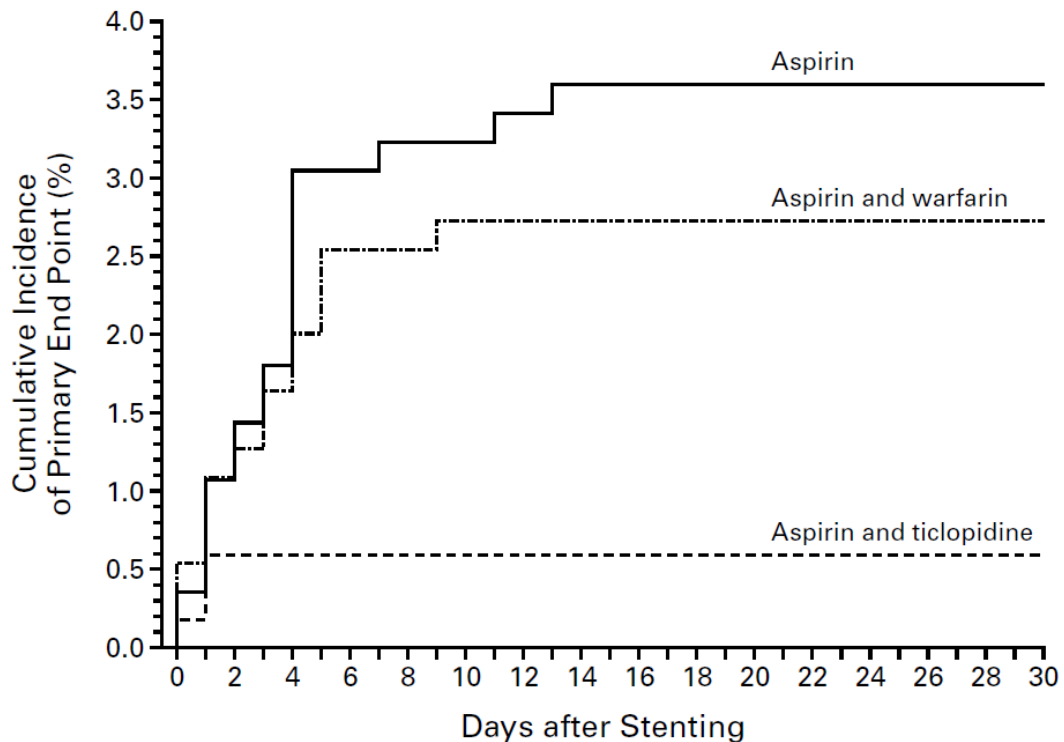
## Posizionamento di stent (STARS)<sup>2</sup>:

La combinazione di ASA e tienopiridine è più efficace del warfarin nei pazienti con stents coronarica <sup>2</sup>



# Il trial STARS

Dato ormai associato da tempo:



A CLINICAL TRIAL COMPARING THREE ANTITHROMBOTIC-DRUG REGIMENS AFTER CORONARY-ARTERY STENTING

A CLINICAL TRIAL COMPARING THREE ANTITHROMBOTIC-DRUG REGIMENS  
AFTER CORONARY-ARTERY STENTING

MARTIN B. LEON, M.D., DONALD S. BAIM, M.D., JEFFREY J. POPMA, M.D., PAUL C. GORDON, M.D.,  
DONALD E. CUTLIP, M.D., KALON K.L. HO, M.D., ALEX GIAMBARTOLOMEI, M.D., DANIEL J. DIVER, M.D.,  
DAVID M. LASORDA, D.O., DAVID O. WILLIAMS, M.D., STUART J. POCOCK, PH.D., AND RICHARD E. KUNTZ, M.D.,  
FOR THE STENT ANTICOAGULATION RESTENOSIS STUDY INVESTIGATORS\*

**Efficacia nettamente  
superiore della DAPT  
rispetto a ASA+TAO dopo 1  
stent coronarico**

The New England Journal of Medicine

Volume 339 Number 23 • 1665

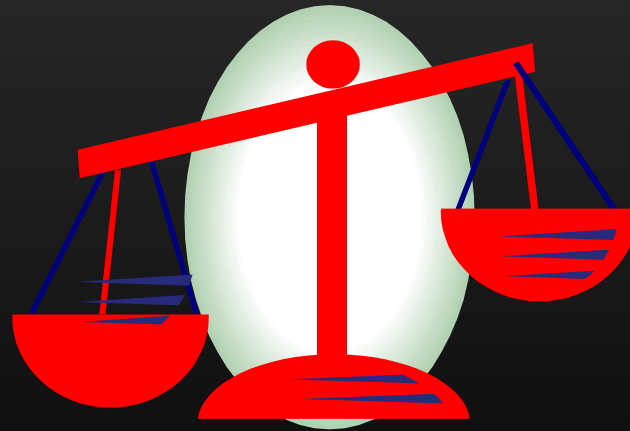
December 3, 1998

# La combinazione VKA + antiplagiarinici

Potenzialmente riduce il rischio tromboembolico

**ma**

Incrementa il rischio di sanguinamento di 3-5 volte



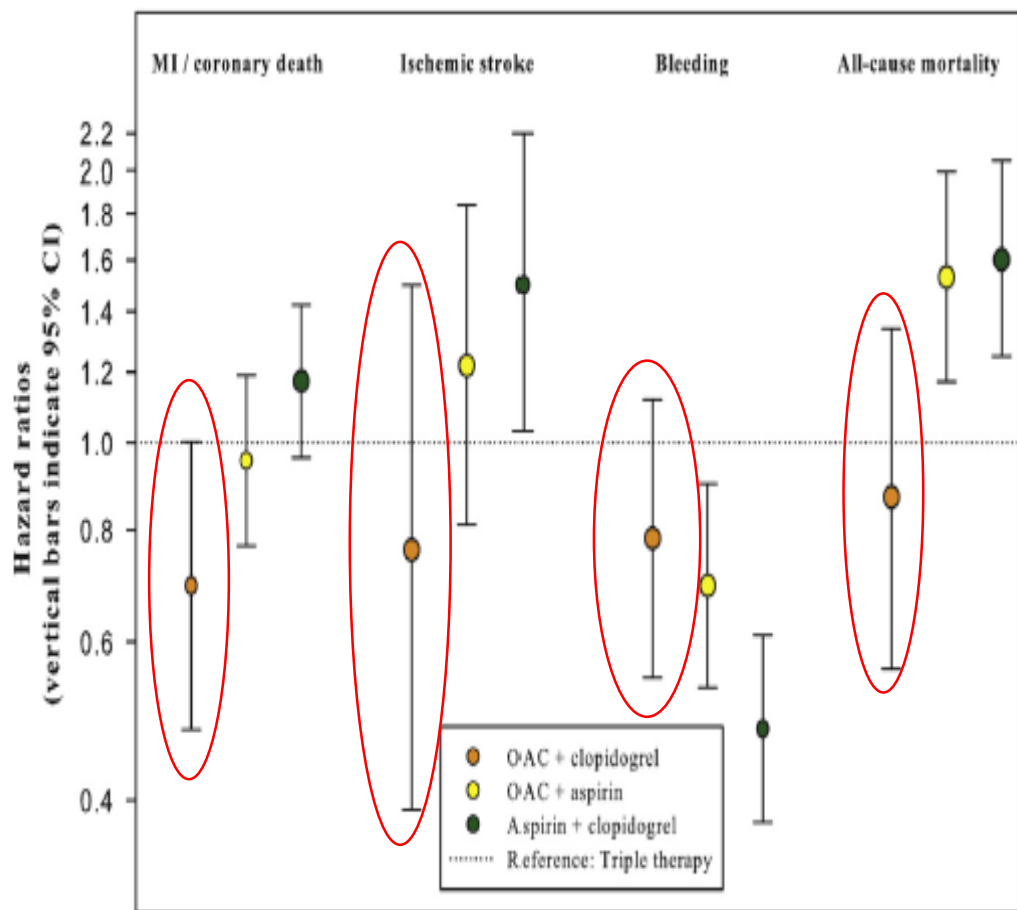
Haemorrhagic risk

Thrombotic risk

## Oral Anticoagulation and Antiplatelets in Atrial Fibrillation Patients After Myocardial Infarction and Coronary Intervention

Morten Lamberts, MD,\*† Gunnar H. Gislason, MD, PhD,\*‡§ Jonas Bjerring Olesen, MD,\*  
Søren Lund Kristensen, MD,\* Anne-Marie Schjerning Olsen, MD,\* Anders Mikkelsen, MB,\*  
Christine Benn Christensen, MD,\* Gregory Y. H. Lip, MD,† Lars Køber, MD, DMS,||  
Christian Torp-Pedersen, MD, DMS,\*¶ Morten Lock Hansen, MD, PhD\*

United Kingdom



In una popolazione reale di  
pazienti in FA con  
indicazione a terapia  
antiaggregante post SCA o  
PTCA:  
**OAC + clopidogrel** superiore  
sia per efficacia che per  
sicurezza rispetto a  
**OAC + clopidogrel + asa**  
(triplice terapia).

**L'ASA NON è  
INDISPENSABILE !!**



# *Il bravo Cardiologo tra Scilla e Cariddi*



**Scilla**  
*Trombosi*



**Cariddi**  
*Emorragia*

# L'ASA è necessaria nella triplice terapia? The WOEST



Use of clopidogrel with or without aspirin in patients taking oral anticoagulant therapy and undergoing percutaneous coronary intervention: an open-label, randomised, controlled trial

Willem J M Dewilde, Tom Oirbans, Freek W A Verhaugt, Johannes C Kelder, Bart J G L De Smet, Jean-Paul Herrman, Tom Adriaenssens, Mathias Vrolix, Antonius A C M Heestermans, Marjke M Vis, Jan G P Tijssen, Arnoud W van 't Hof, Jurrrien M ten Berg, for the WOEST study investigators

## Dual therapy:

OAC  
+ 75 mg clopidogrel

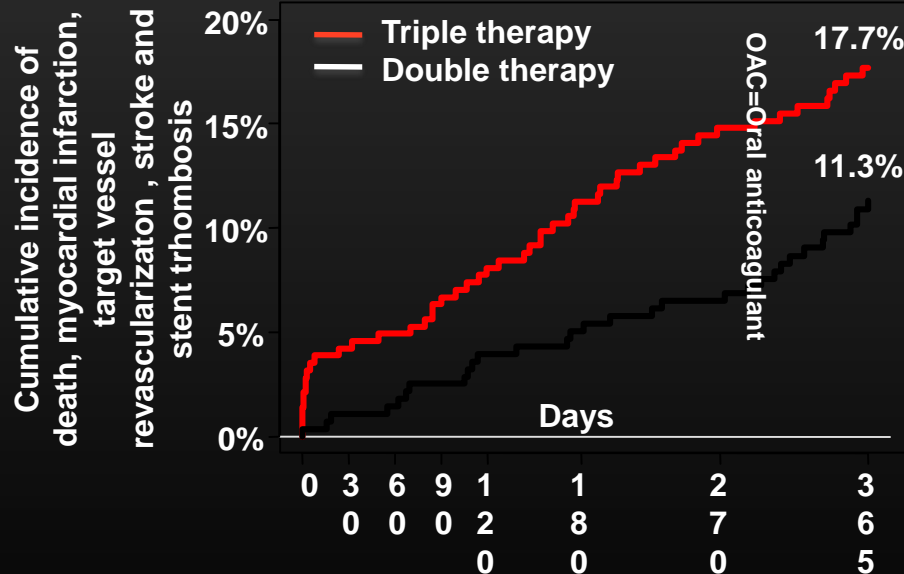
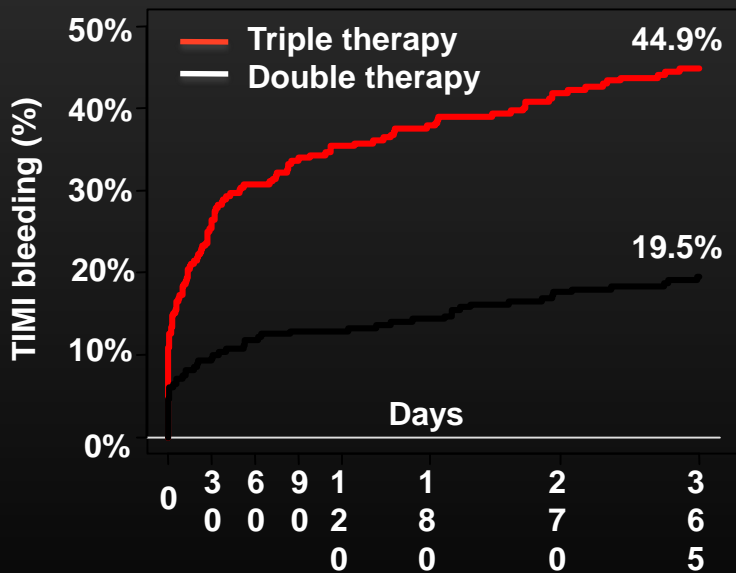
1Month minimum after BMS  
1Year minimum after DES

## Triple therapy:

OAC  
+ 75 mg clopidogrel  
+ 80mg acetylsalicyl acid **OR**  
100mg carbasylate calcium

1Month Min. after BMS  
1Year Min. after DES

573 pazienti sottoposti a PCI con indicazione ad anticoagulante orale randomizzati a doppia vs triplice regime antitrombotico\*



Il doppio regime riduceva significativamente il rischio CV ed i sanguinamenti

**Inibitori di P2Y12**  
**Quale ruolo nella triplice terapia?**

**Sia nel PLATO (ticagrelor)**

**che nel**

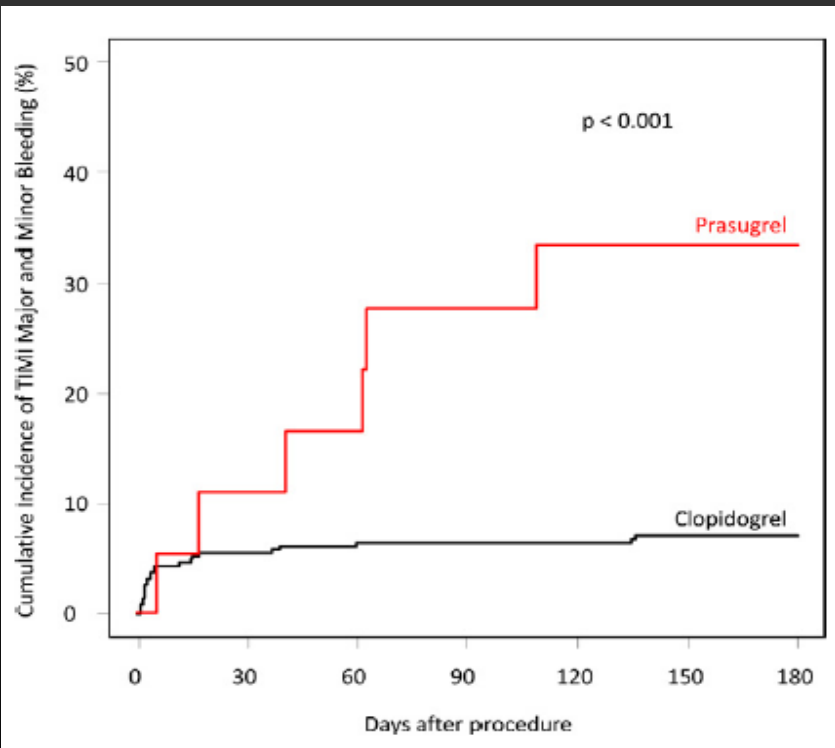
**TRITON-TIMI 38 (prasugrel)**

**Erano esclusi** dall'arruolamento i pazienti  
**in terapia con VKA**

# Triple Therapy With Aspirin, Prasugrel, and Vitamin K Antagonists in Patients With Drug-Eluting Stent Implantation and an Indication for Oral Anticoagulation

Nikolaus Sarafoff, MD,\* Amadea Martischinig, MD,† Jill Wealer, MS,† Katharina Mayer, MD,†  
Julinda Mehilli, MD,\* Dirk Sibbing, MD,\* Adnan Kastrati, MD†  
*Munich, Germany*

(J Am Coll Cardiol 2013;61:2060-6)

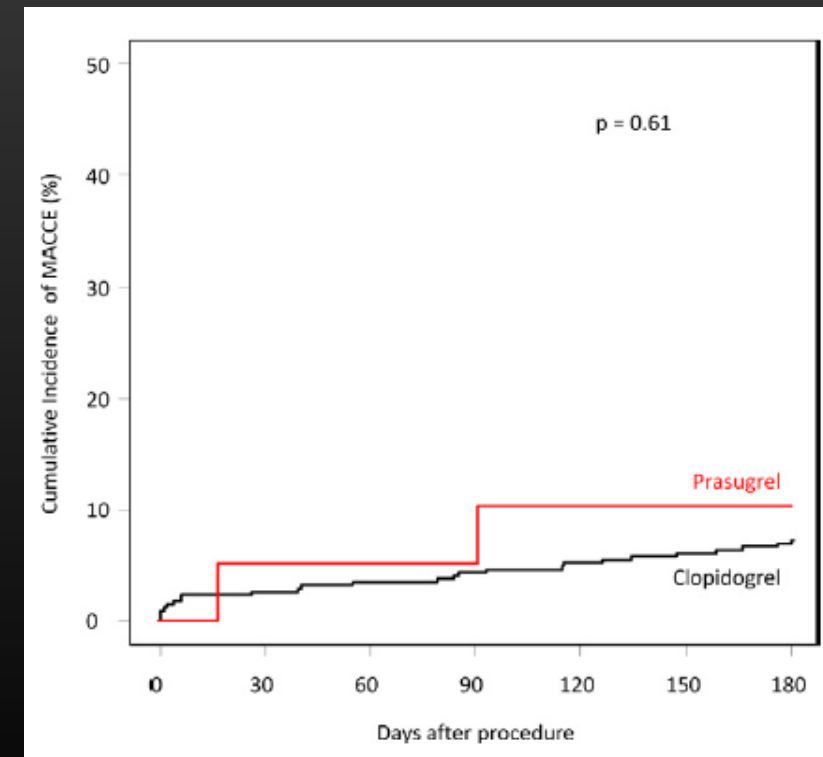


377 pazienti

Prasugrel + ASA + VKA  
Clopidogrel + ASA + VKA

incremento  
sanguinamenti

Non migliora l'efficacia



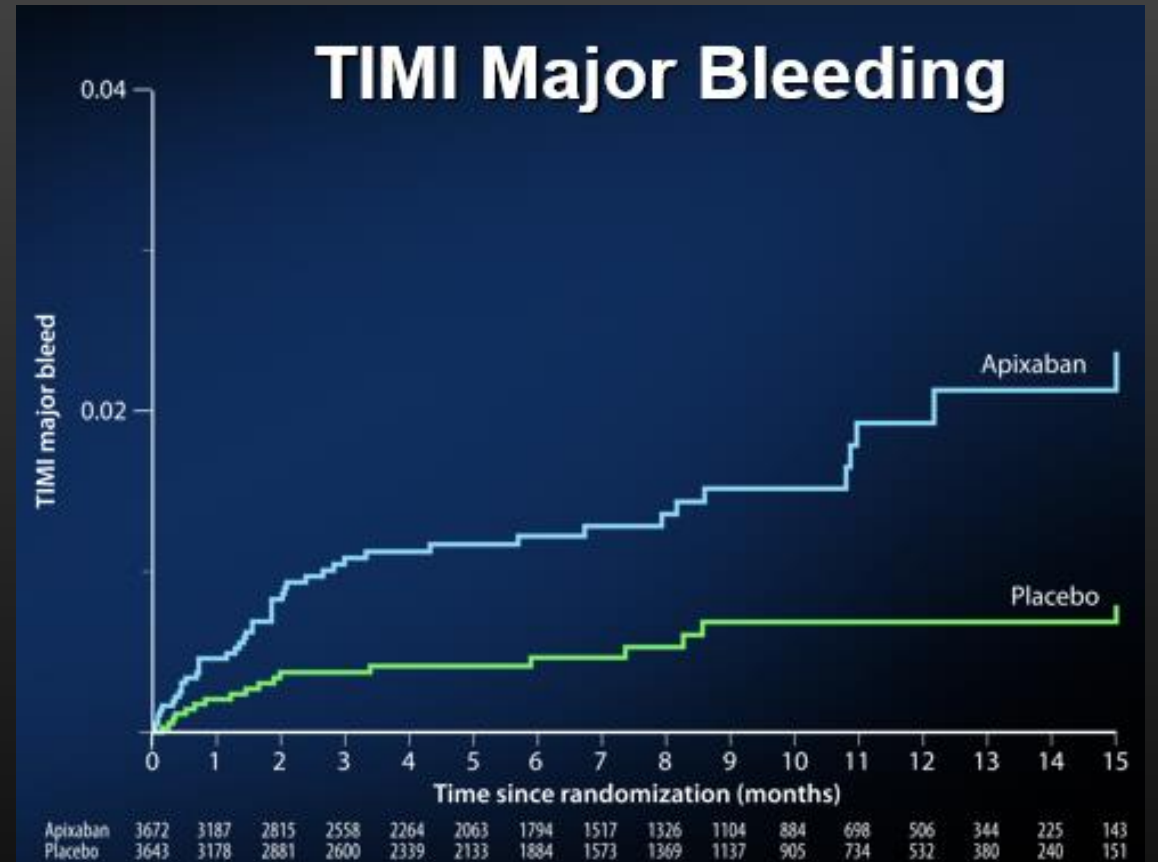
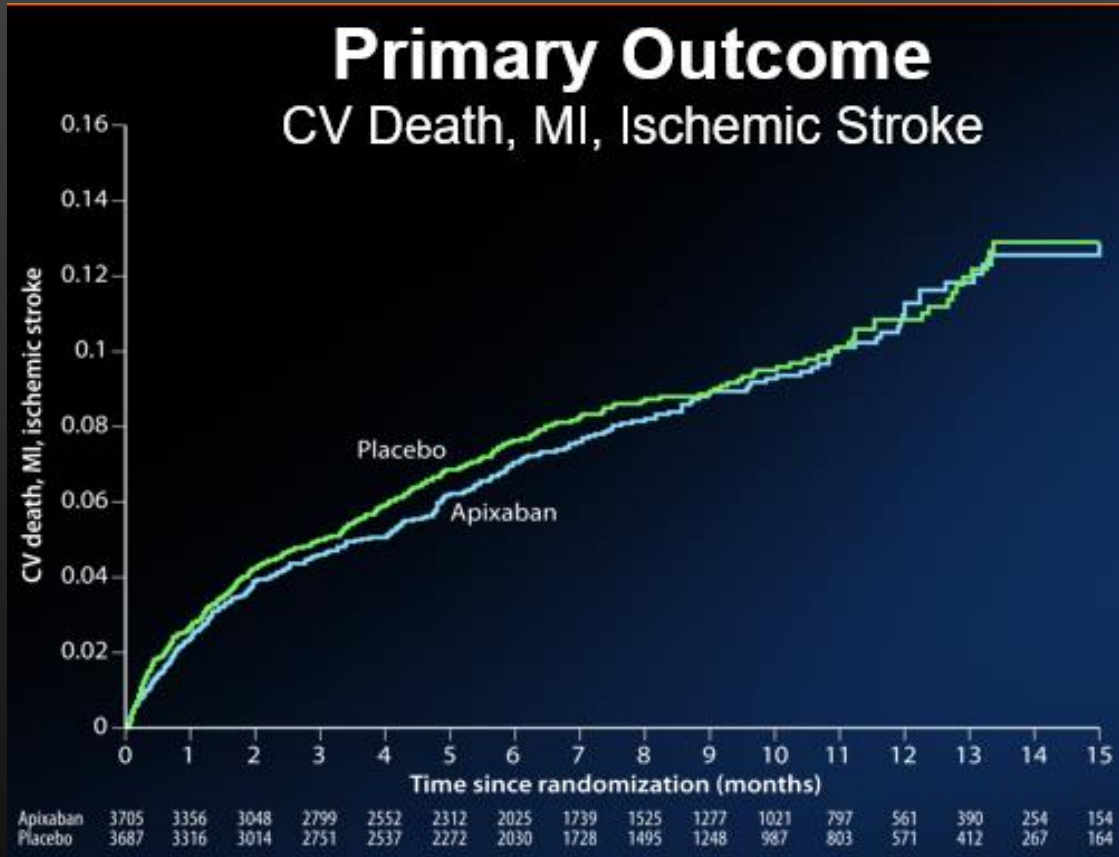
## La terapia anticoagulante è necessaria nella triplice terapia?

### APPRAISE 2 trial

- I pazienti affetti da SCA presentano eventi ricorrenti ischemici nonostante la rivascolarizzazione e la terapia antiaggregante.
  - Gli antagonisti della vitamina K si sono dimostrati efficaci nel ridurre **ULTERIORMENTE** tali eventi se associati ad aspirina.
- 
- Per determinare se apixaban 5 mg bid riduce il rischio composito di morte cardiovascolare, IMA o ictus con un rischio emorragico accettabile in pazienti ad alto rischio per eventi ischemici ricorrenti che ricevono terapia antiaggregante a seguito di una sindrome coronarica acuta

# La terapia anticoagulante è necessaria nella triplice terapia?

## APPRAISE 2 trial



**Il 15 novembre 2010 il Comitato di monitoraggio dei dati ha raccomandato di arrestare il trial a causa di un eccesso di emorragie clinicamente importanti nel braccio apixaban senza una riduzione controbilanciata negli eventi ischemici.**

**LA RIDUZIONE DEL DOSAGGIO DELL'ANTICOAGULANTE?**  
The ATLAS trial



**Recente ACS: STEMI, NSTEMI, UA**  
No increased bleeding risk, No warfarin, No ICH, No prior stroke if on ASA + Thienopyridine  
Stabilized 1-7 Days Post-Index Event

Stratified by Thienopyridine use at MD Discretion

+ ASA 75 to 100 mg/day

**Placebo**

N=5,176  
ASA + Thieno, n=4,821  
ASA, n=355

**RIVAROXABAN**

2.5 mg BID  
n=5,174  
ASA + Thieno, n=4,825  
ASA, n=349

**RIVAROXABAN**

5.0 mg BID  
N=5,176  
ASA + Thieno, n=4,827  
ASA, n=349

**PRIMARY ENDPOINT:**

**EFFICACY: CV Death, MI, Stroke\* (Ischemic + Hemg.)**  
**SAFETY: TIMI major bleeding not associated with CABG**  
Event driven trial of 1,002 events in 15,342 patients\*\*

\* Stroke includes ischemic stroke, hemorrhagic stroke, and uncertain stroke

\*\* 184 subjects were excluded from the efficacy analyses prior to unblinding

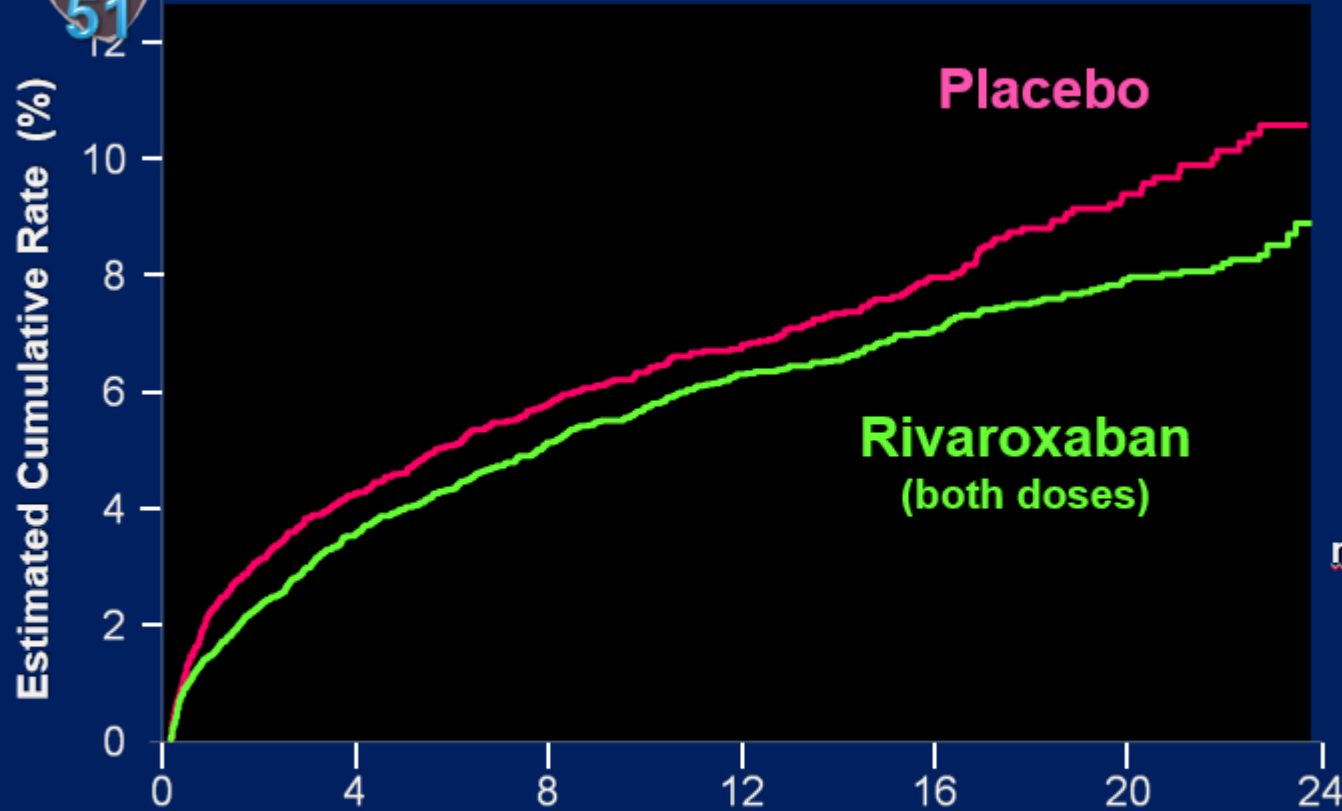
ATLAS ACS 2

**TIMI**

51

# PRIMARY EFFICACY ENDPOINT:

CV Death / MI / Stroke\* (Ischemic + Hemg.)



2 Yr KM Estimate

**10.7%**

**8.9%**

HR 0.84  
(0.74-0.96)

ARR 1.7%

mITT p = 0.008

ITT p = 0.002

**NNT = 59**

No. at Risk

|             | 0     | 4    | 8    | 12   | 16   | 20   | 24  |
|-------------|-------|------|------|------|------|------|-----|
| Placebo     | 5113  | 4307 | 3470 | 2664 | 1831 | 1079 | 421 |
| Rivaroxaban | 10229 | 8502 | 6753 | 5137 | 3554 | 2084 | 831 |

\*: First occurrence of cardiovascular death, MI, stroke (ischemic, hemorrhagic, and uncertain) as adjudicated by the CEC across thienopyridine use strata  
 Two year Kaplan-Meier estimates, HR and 95% confidence interval estimates from Cox model stratified by thienopyridine use are provided per mITT  
 approach; Stratified log-rank p-values are provided for both mITT and ITT approaches; ARR=Absolute Relative Reduction; NNT=Number needed to treat;  
Rivaroxaban=Pooled Rivaroxaban 2.5 mg BID and 5 mg BID.



# SAFETY ENDPOINTS

Treatment-Emergent Non CABG TIMI Major Bleeding\*

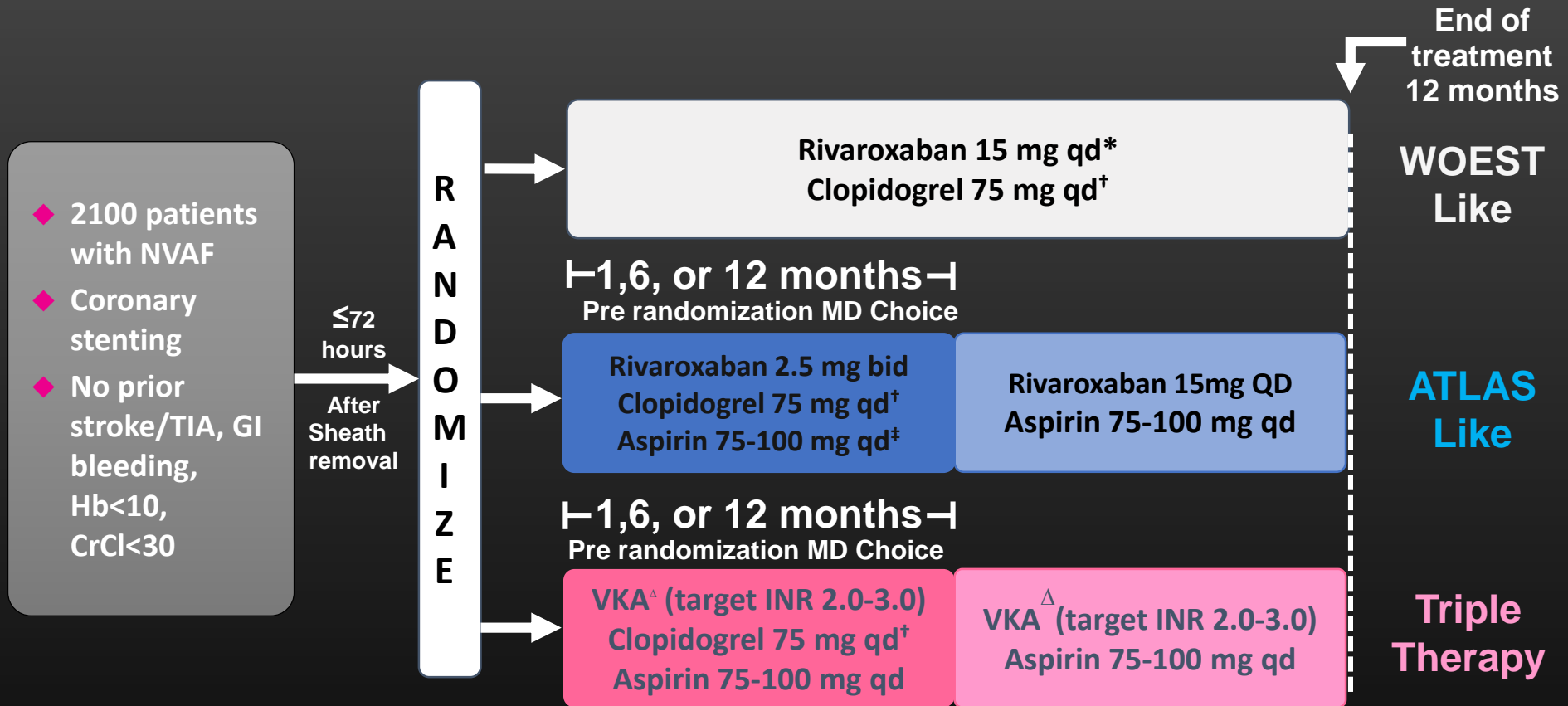
| Analysis         | Placebo | 2.5 mg Rivaroxaban | 5.0 mg Rivaroxaban |
|------------------|---------|--------------------|--------------------|
| 2 Yr KM Estimate | 0.6%    | 1.8%<br>HR 3.46    | 2.4%<br>HR 4.47    |

$p < 0.001$  (comparing Placebo to 2.5 mg Rivaroxaban)  
 $p < 0.001$  (comparing 2.5 mg Rivaroxaban to 5.0 mg Rivaroxaban)

There was no excess of either combined ALT > 3x ULN and Total Bilirubin > 2x ULN cases among patients treated with Rivaroxaban, or SAEs.

\*: First occurrence of Non-CABG TIMI major bleeding events occurred between first dose to 2 days post last dose as adjudicated by the CEC across thienopyridine use strata; Two year Kaplan-Meier estimates, HR and 95% confidence interval estimates from Cox model stratified by thienopyridine are provided; Stratified log-rank p-values are provided; #: Raw percentage for CV death/MI/stroke (ischemic, hemorrhagic, uncertain) ; ##: Raw percentage of subjects with abnormal value measured between first dose to 2 days post last dose among subjects with normal baseline measurement.

## Pazienti con FA e stenting coronarico



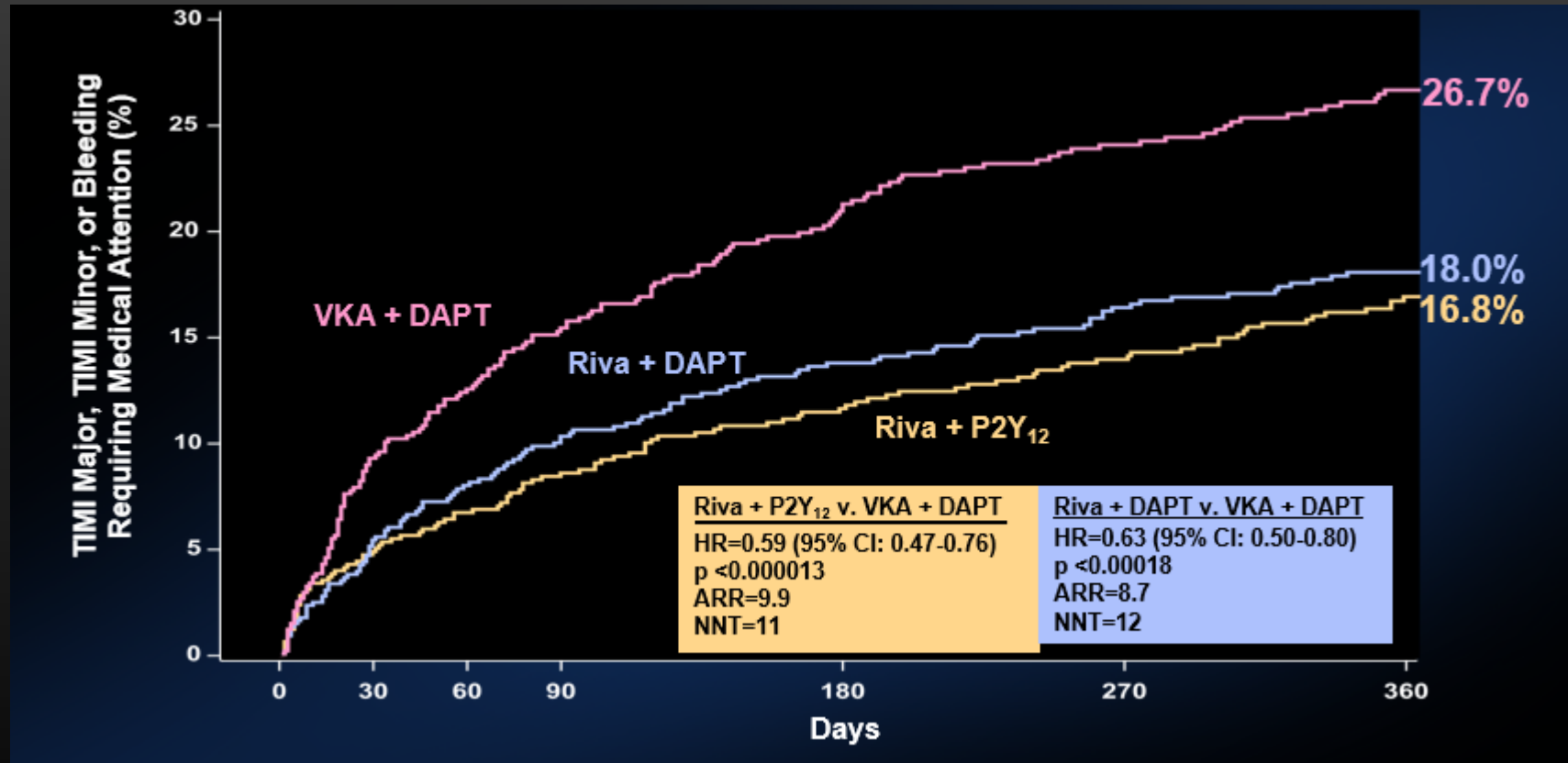
- Primary endpoint: TIMI major + minor + bleeding requiring medical attention
- Secondary endpoint: CV death, MI, and stroke (Ischemic, Hemorrhagic, or Uncertain Origin)

\*Rivaroxaban dosed at 10 mg once daily in patients with CrCl of 30 to <50 mL/min.

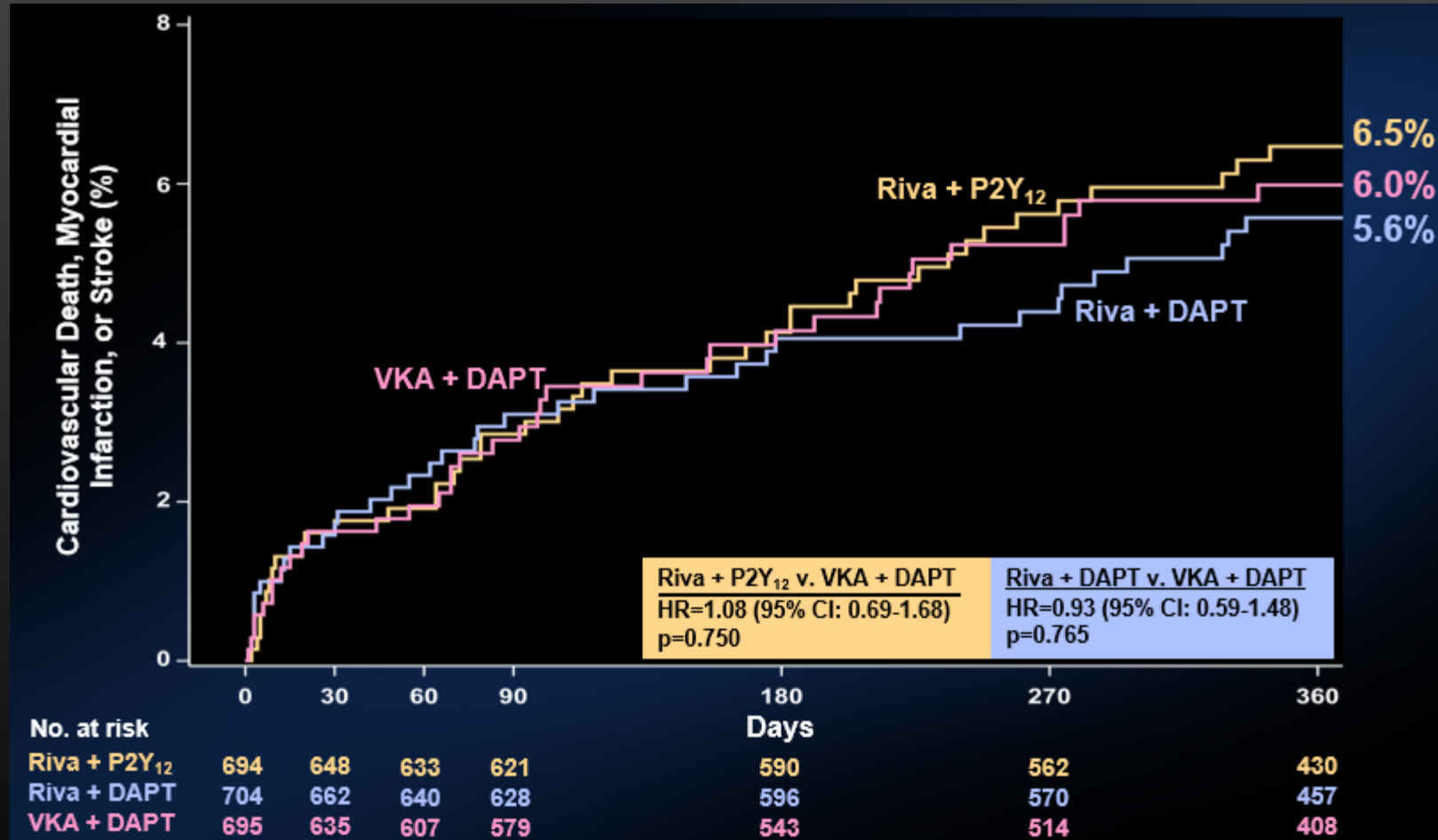
<sup>†</sup>Alternative P2Y<sub>12</sub> inhibitors: 10 mg once-daily prasugrel or 90 mg twice-daily ticagrelor.

<sup>‡</sup>Low-dose aspirin (75-100 mg/d). <sup>Δ</sup> Open label VKA

## Primo sanguinamento clinicamente significativo



# CV Death, MI or Stroke



\* La numerosità dello studio lo rendeva UNDERPOWERED per questo end-point

# Ospedalizzazioni ricorrenti per eventi avversi

## ORIGINAL RESEARCH ARTICLE

### Recurrent Hospitalization Among Patients With Atrial Fibrillation Undergoing Intracoronary Stenting Treated With 2 Treatment Strategies of Rivaroxaban or a Dose-Adjusted Oral Vitamin K Antagonist Treatment Strategy

**BACKGROUND:** Patients with atrial fibrillation who undergo intracoronary stenting traditionally are treated with a vitamin K antagonist (VKA) plus dual antiplatelet therapy (DAPT), yet this treatment leads to high risks of bleeding. We hypothesized that a regimen of rivaroxaban plus a P2Y<sub>12</sub> inhibitor monotherapy or rivaroxaban plus DAPT could reduce bleeding and thereby have a favorable impact on all-cause mortality and the need for rehospitalization.

**METHODS:** Stented subjects with nonvalvular atrial fibrillation (n=2124) were randomized 1:1:1 to administration of reduced-dose rivaroxaban 15 mg daily plus a P2Y<sub>12</sub> inhibitor for 12 months (group 1); rivaroxaban 2.5 mg twice daily with stratification to a prespecified duration of DAPT of 1, 6, or 12 months (group 2); or the reference arm of dose-adjusted VKA daily with a similar DAPT stratification (group 3). The present post hoc analysis assessed the end point of all-cause mortality or recurrent hospitalization for an adverse event, which was further classified as the result of bleeding, a cardiovascular, or another cause blinded to treatment assignment.

**RESULTS:** The risk of all-cause mortality or recurrent hospitalization was 34.9% in group 1 (hazard ratio=0.79; 95% confidence interval, 0.66-0.94; P=0.008 versus group 3; number needed to treat=15), 31.9% in group 2 (hazard ratio=0.75; 95% confidence interval, 0.62-0.90; P=0.002 versus group 3; number needed to treat=10), and 41.9% in group 3 (VKA+DAPT). Both all-cause death plus hospitalization potentially resulting from bleeding (group 1=8.6% [P=0.032 versus group 3], group 2=8.0% [P=0.012 versus group 3], and group 3=12.4%) and all-cause death plus hospitalization potentially resulting from a cardiovascular cause (group 1=21.4% [P=0.001 versus group 3], group 2=21.7% [P=0.011 versus group 3], and group 3=29.3%) were reduced in the rivaroxaban arms compared with the VKA arm, but other forms of rehospitalization were not.

**CONCLUSIONS:** Among patients with atrial fibrillation undergoing intracoronary stenting, administration of either rivaroxaban 15 mg daily plus P2Y<sub>12</sub> inhibitor monotherapy or 2.5 mg rivaroxaban twice daily plus DAPT was associated with a reduced risk of all-cause mortality or recurrent hospitalization for adverse events compared with standard-of-care VKA plus DAPT.

**CLINICAL TRIAL REGISTRATION:** URL: <https://clinicaltrials.gov>. Unique identifier: NCT01830543.

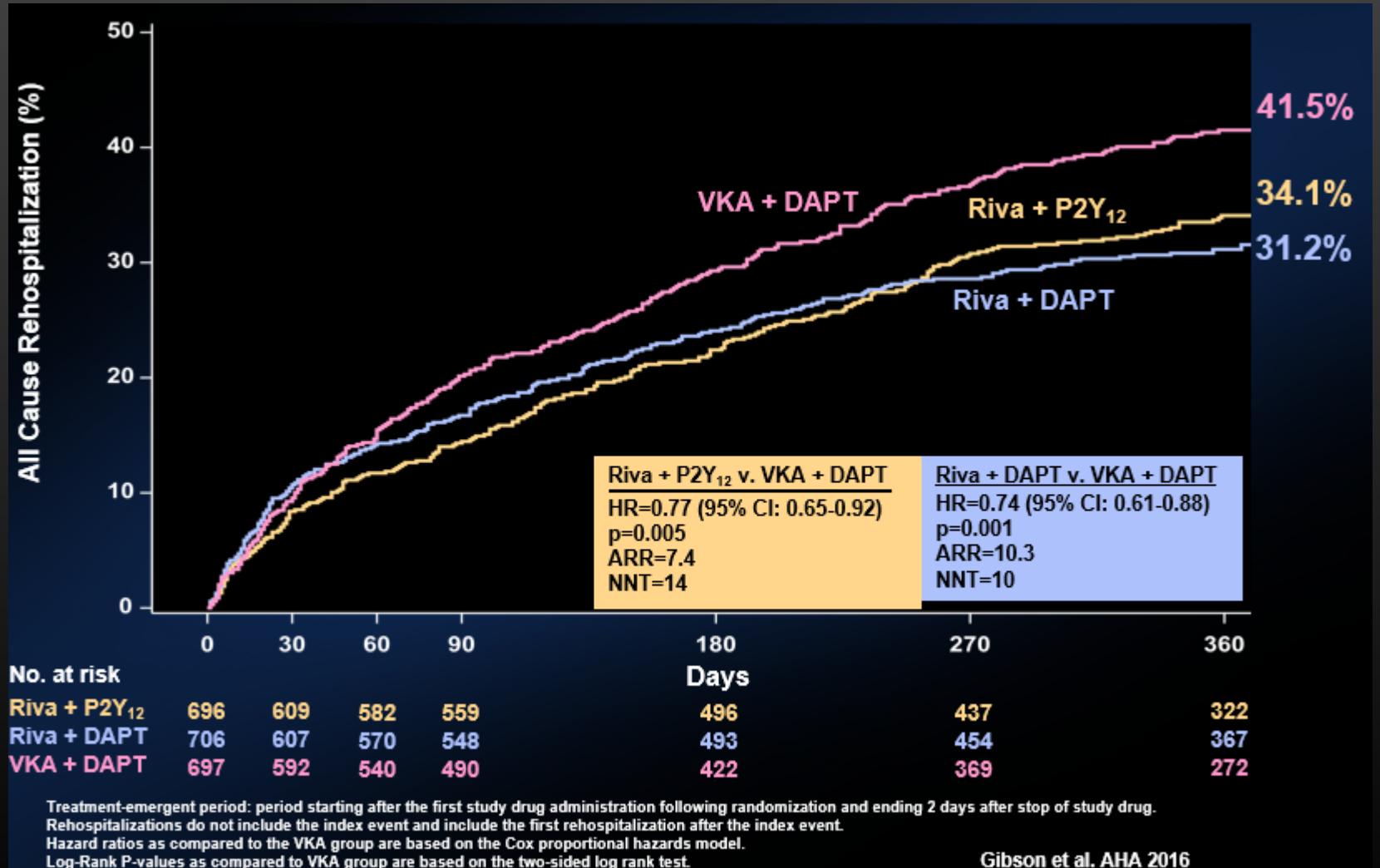
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Source of Funding, see page XXX

**Key Words:** atrial fibrillation  
percutaneous coronary intervention  
rivaroxaban  
vitamin K

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Gibson et al. AHA 2016

*...et voilà, il problema è risolto!*



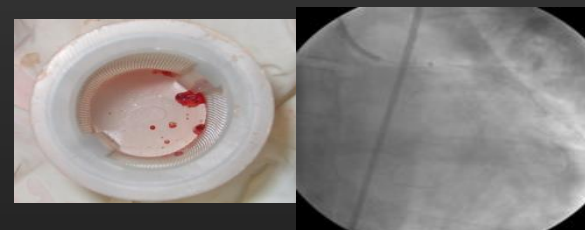
# RAPPORTO RISCHIO-BENEFICIO DEL SINGOLO PAZIENTE



## Caratteristiche cliniche

età avanzata, IRA, sesso femminile, basso peso, diabete mellito, arteriopatia periferica, scompenso cardiaco, ipertensione arteriosa, anemia preesistente, precedenti cerebrovascolari

## Esecuzione di procedure invasive (vie di accesso arteriose)



## Utilizzo di farmaci anticoagulanti



*The* NEW ENGLAND  
JOURNAL *of* MEDICINE

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Dual Antithrombotic Therapy with Dabigatran after PCI  
in Atrial Fibrillation

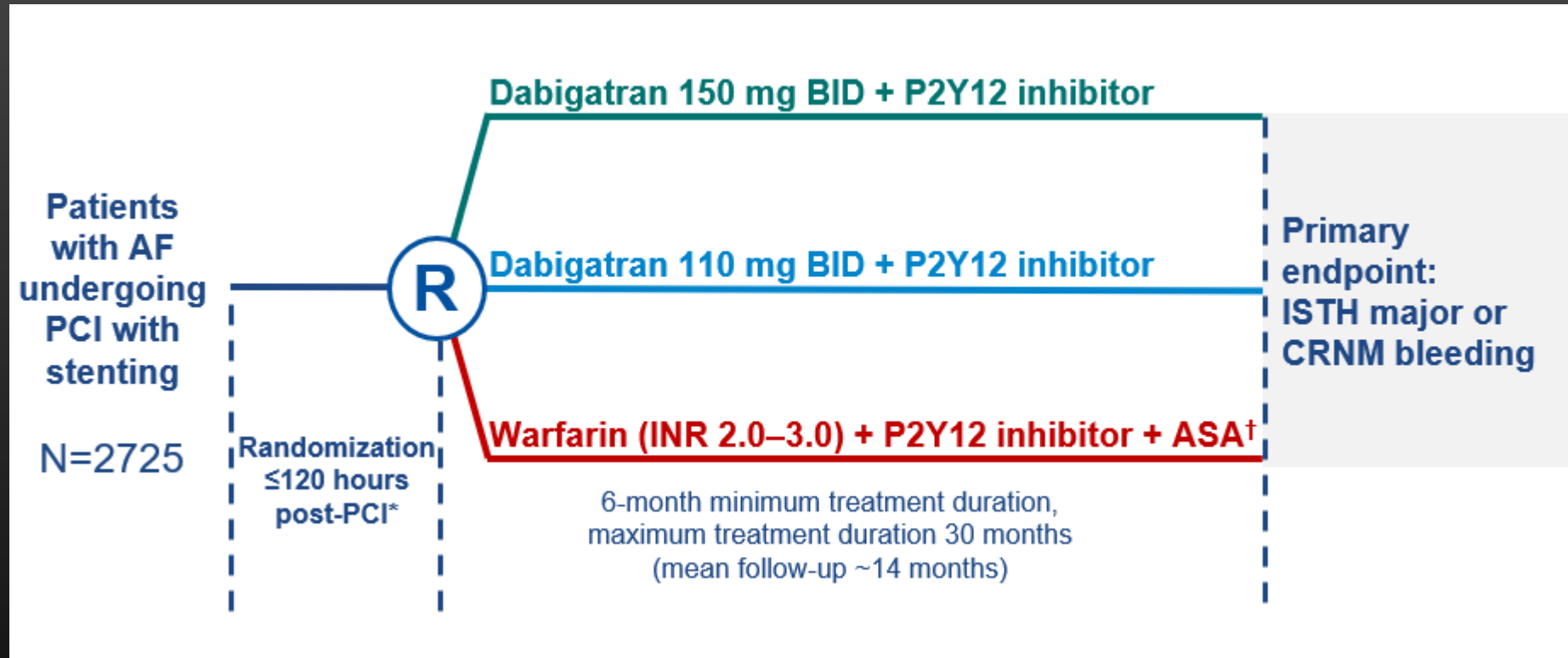
Christopher P. Cannon, M.D., Deepak L. Bhatt, M.D., M.P.H., Jonas Oldgren, M.D., Ph.D., Gregory Y.H. Lip, M.D.,  
Stephen G. Ellis, M.D., Takeshi Kimura, M.D., Michael Maeng, M.D., Ph.D., Bela Merkely, M.D.,  
Uwe Zeymer, M.D., Savion Gropper, M.D., Ph.D., Matias Nordaby, M.D., Eva Kleine, M.Sc., Ruth Harper, Ph.D.,  
Jenny Manassie, B.Med.Sc., James L. Januzzi, M.D., Jurrien M. ten Berg, M.D., Ph.D., P. Gabriel Steg, M.D.,  
and Stefan H. Hohnloser, M.D., for the RE-DUAL PCI Steering Committee and Investigators\*



# The RE-DUAL PCI trial

- **Studio randomizzato**
- **Duplica terapia (P2Y12 inib. + Dabigatran) vs triplice terapia con Warfarin nei pazienti con NVAF che hanno subito PTCA + stent**
- **Dabigatran (150 mg o 110 mg bid) + singolo antiaggregante vs Warfarin + DAPT**
- **Emorragie clinicamente rilevanti ed eventi trombotici (tasso combinato di morte, infarto miocardico e ictus)**

## RE-DUAL PCI tested the safety and efficacy of two regimens of dual therapy with dabigatran without ASA vs triple therapy with warfarin



- The primary endpoint was time to first ISTH major or clinically relevant non-major bleeding event
- Formally tested endpoints included:
  - non-inferiority and superiority of 110 mg and 150 mg dual therapy in time to first ISTH major bleeding event or clinically relevant non-major bleeding event
  - time to first event of death, thromboembolic event (MI, stroke, systemic embolism) with and without unplanned revascularization
- 100% of outcome events were independently adjudicated by blinded external committee

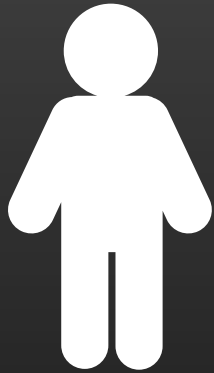
# Baseline characteristics

|  | Dabigatran 110 mg dual therapy (n=981) | Warfarin triple therapy (n=981) | Dabigatran 150 mg dual therapy (n=763) | Warfarin triple therapy (n=764) |
|--|--|---------------------------------|--|---------------------------------|
| <b>Age, years, mean</b>                                | 71.5                                   | 71.7                            | 68.6                                   | 68.8                            |
| ≥80 (USA, ROW), ≥70 (Japan), %                         | 22.9                                   | 22.9                            | 1.0                                    | 1.0                             |
| <80 (USA, ROW), <70 (Japan), %                         | 77.1                                   | 77.1                            | 99.0                                   | 99.0                            |
| <b>Male, %</b>   | 74.2                                   | 76.5                            | 77.6                                   | 77.7                            |
| <b>Baseline CrCl, mL/min, mean</b>                     | 76.3                                   | 75.4                            | 83.7                                   | 81.3                            |
| <b>Diabetes mellitus, %</b>                            | 36.9                                   | 37.9                            | 34.1                                   | 39.7                            |
| <b>CHA<sub>2</sub>DS<sub>2</sub>-VASc score (mean)</b> | 3.7                                    | 3.8                             | 3.3                                    | 3.6                             |
| <b>Modified HAS-BLED score at baseline (mean)</b>      | 2.7                                    | 2.8                             | 2.6                                    | 2.7                             |
| <b>ACS indication for PCI, %</b>                       | 51.9                                   | 48.4                            | 51.2                                   | 48.3                            |
| <b>DES placed only, %</b>                              | 82.0                                   | 84.2                            | 81.4                                   | 83.5                            |

ROW, rest of world; ACS, acute coronary syndrome; DES, drug-eluting stent; PCI, percutaneous coronary intervention;

Cannon et al. N Engl J Med 2017; Cannon et al. ESC 2017

## RE-DUAL PCI key inclusion and exclusion criteria



**Patients aged  $\geq 18$  years with paroxysmal, persistent or permanent NVAF**

**ACS successfully treated by PCI and stenting (BMS or DES)**

**Stable CAD with  $\geq 1$  lesion eligible for PCI that was successfully treated by elective PCI and stenting (BMS or DES)**



### Exclusion

- × Cardiogenic shock during current hospitalization**
- × Use of fibrinolytics within 24 hours of randomization that, in the investigator's opinion, will put patient at high risk of bleeding**
- × Stroke or major bleeding event within 1 month prior to screening visit**
- × Severe renal impairment (CrCl  $< 30$  mL/min)**

# RE-DUAL PCI primary endpoint

**RE-DUAL PCI  
primary safety  
endpoint:  
time  
to first...**

## **...ISTH major bleeding event**

- Symptomatic bleeding in a critical area or organ\*, and/or
- Bleeding associated with reduced haemoglobin  $\geq 2$  g/dL (1.24 mmol/L) or transfusion of  $\geq 2$  units of blood or packed cells<sup>†</sup> and/or
- Fatal bleed

**OR**

## **...ISTH CRNM bleeding event**

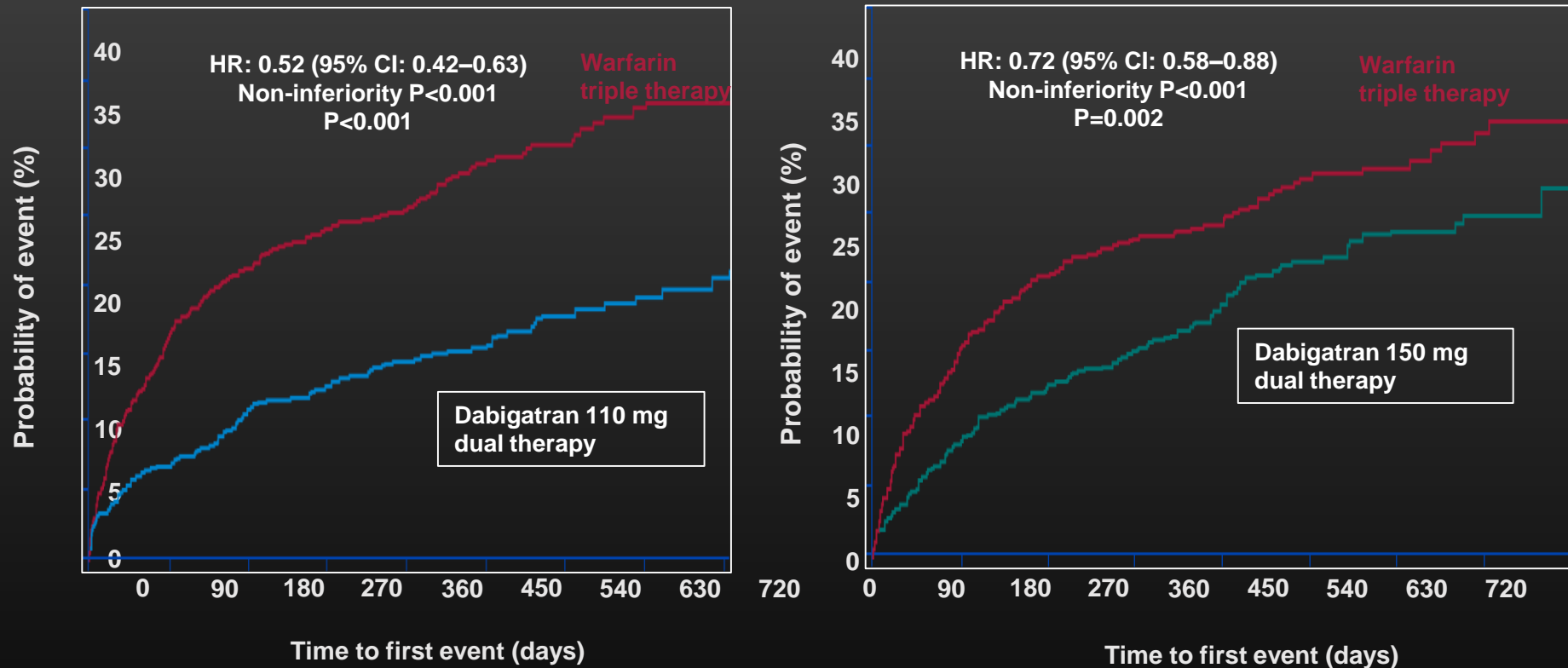
Not meeting criteria for a major bleed but prompts  $\geq 1$  of:

- Hospital admission
- Physician-guided medical or surgical treatment
- Physician-guided change, interruption ( $\geq 1$  dose) or discontinuation of study drug

**All primary and secondary endpoints were adjudicated  
by a treatment-blinded independent central committee**

\*E.g. intracranial, intraspinal, intra-ocular, retroperitoneal, intra-articular or pericardial, or intramuscular with compartment syndrome; <sup>†</sup>Bleeding should be overt and haemoglobin drop should be considered due to and temporally related to bleeding event. CRNM, clinically relevant non-major; ISTH, International Society on Thrombosis and Haemostasis; Cannon et al. Clin Cardiol 2016; Kaatz et al. J Thromb Haemost 2015; Schulman et al. J Thromb Haemost 2005

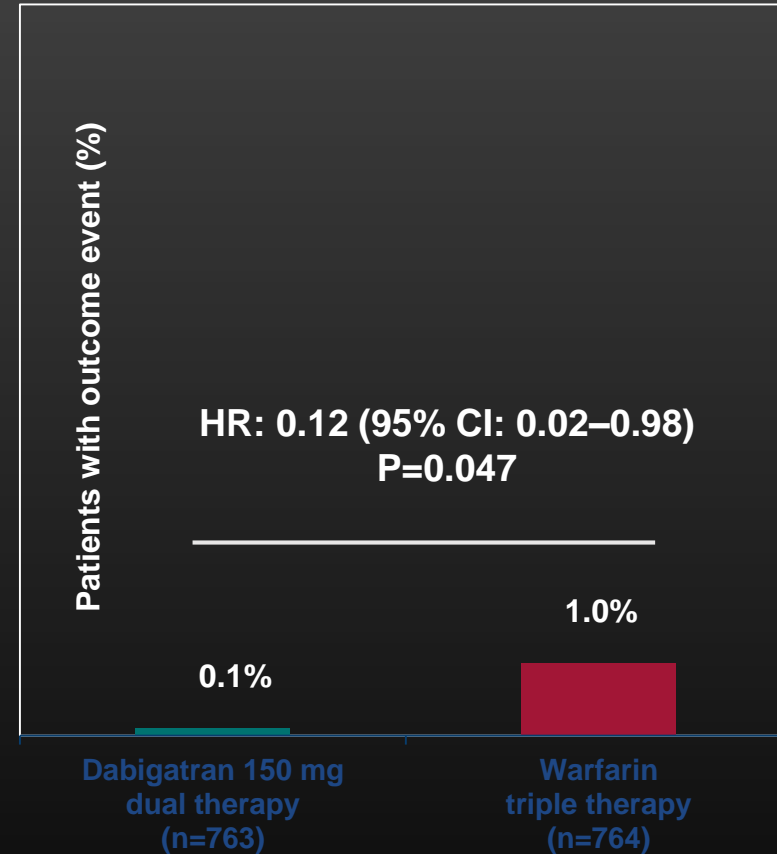
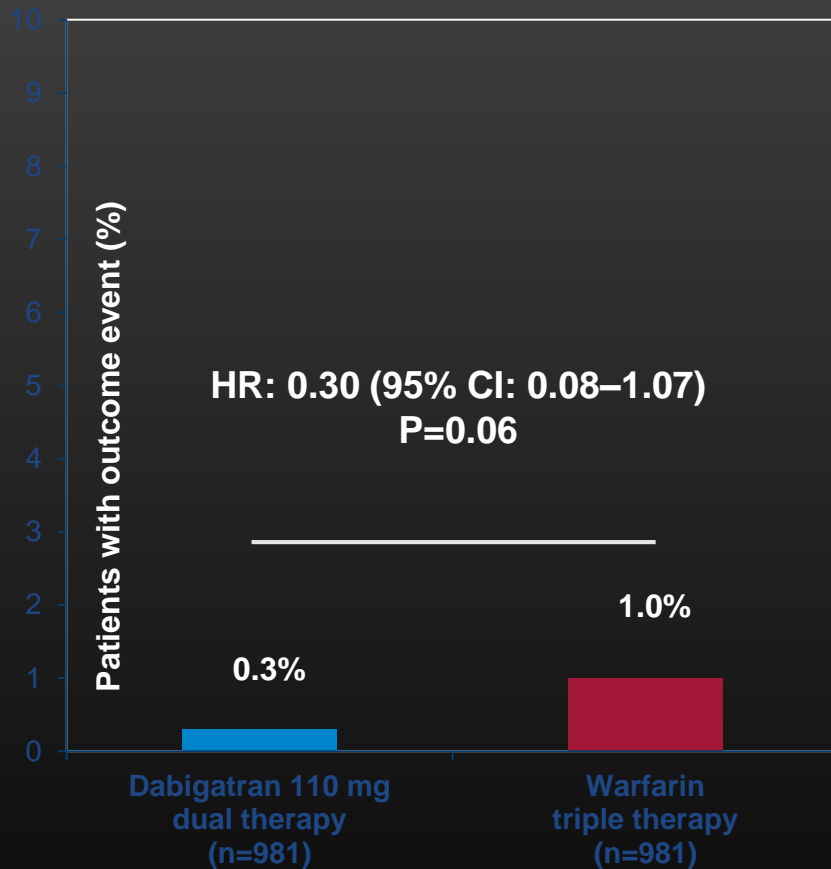
# La duplice terapia con Dabigatran + Clopidogrel (o altra tienopidirina) riduce significativamente l'incidenza di sanguinamenti (maggiori e clinicamente rilevanti)



For the dabigatran 150 mg vs warfarin comparison, elderly patients outside the USA ( $\geq 80$  years) and Japan ( $\geq 70$  years) are excluded. Full analysis set presented

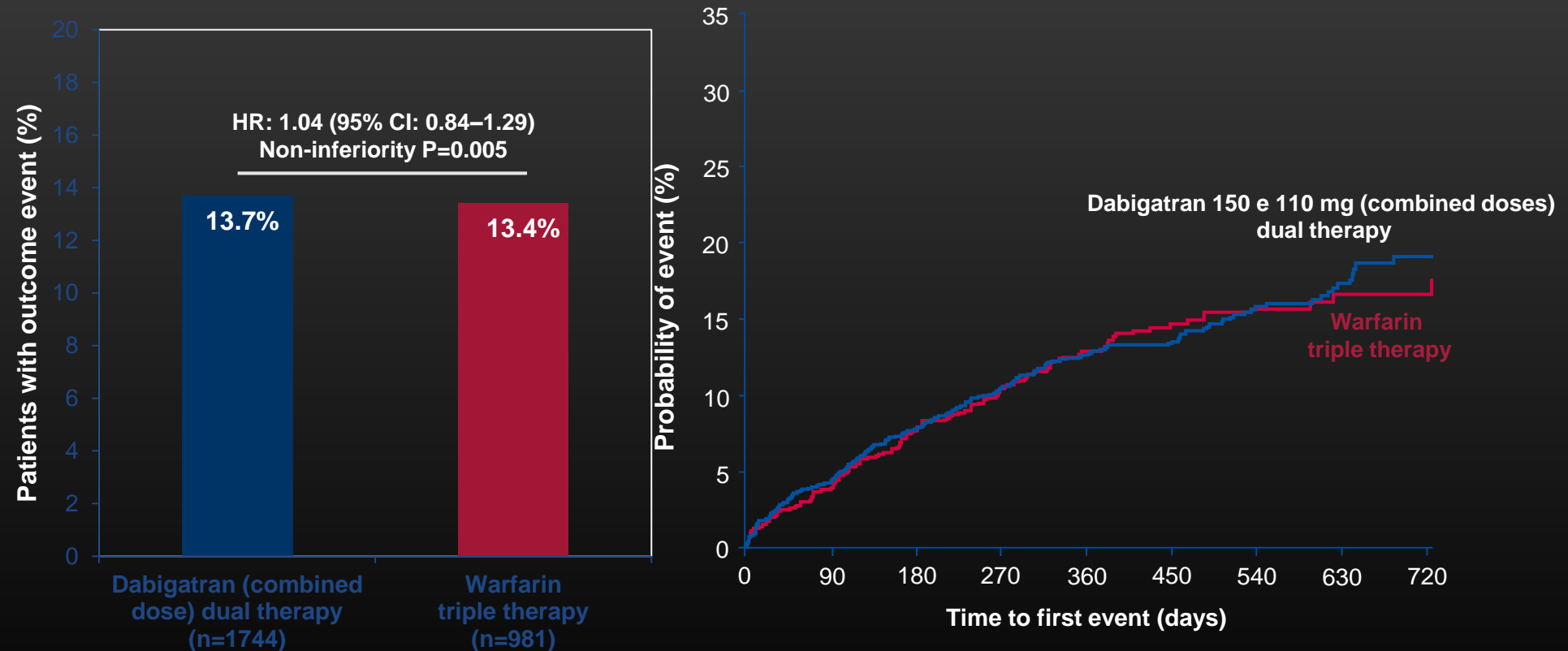
CRNMBE, clinically relevant non-major bleeding event; ISTH, International Society on Thrombosis and Haemostasis;  
Cannon et al. ESC 2017; Cannon et al. N Engl J Med 2017

# Emorragie intracraniche



# Non inferiorità della duplice con Dabigatran + tienopiridine rispetto a triplice con VKA nel ridurre gli eventi ischemici coronarici e stroke embolico

Composite endpoint of death or thromboembolic event (MI, stroke or systemic embolism) or unplanned revascularization (PCI/CABG)





# RE-DUAL PCI key points

**1**

Duplica terapia con Dabigatran + tienopiridina riduce il rischio di sanguinamenti rispetto alla triplice con Warfarin risultando non inferiore per tutti gli eventi tromboembolici

**2**

Il rischio di sanguinamento è ridotto sia nel braccio 110 mg, sia nel braccio 150 mg

**3**

La duplica terapia con dabigatran + tienopiridina è un'alternativa da considerare nei pazienti con FA non valvolare sottoposti ad impianto di stent coronarico

# The AUGUSTUS Trial: la prova dell'Apixaban

## Inclusion

- AF (prior, persistent, or >6 hrs duration)
- Physician decision that oral anticoag is indicated
- ACS and/or PCI with planned P2Y12 inhibitor for 6 months

Randomize  
 $n = 4,600$   
Patients

## Exclusion

- Contraindication to DAPT
- Other reason for warfarin (prosthetic valve, mod/sev MS)

Apixaban

Warfarin

*P2Y12 inhibitor for all patients x 6 months*  
*Aspirin for all on the day of ACS or PCI*  
*Aspirin versus placebo after randomization*

ASA

placebo

ASA

placebo

**Primary outcome: major/clinically relevant bleeding  
(through 6 months)**

**Secondary objective: Death, MI, stroke, stent thrombosis**

# Il Trial ENTRUST: la prova dell'Edoxaban

ENTRUST-AF PCI

## ENTRUST-AF-PCI Study Design

**PROBE design: prospective, randomized, open label, blinded evaluation edoxaban based regimen vs VKA based regimen in N ≈ 1500 AF patients**

12 months:  
end of treatment

**Inclusion Criteria:**

- OAC indication for AF for at least 12 months
- Successful PCI with stent placement (goal of at least 25% ACS)

4 hours  
– 5 days  
after  
sheath  
removal

**R  
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E**

**Edoxaban 60 mg/day\***

**P2Y<sub>12</sub> antagonist\*\*  
(without ASA)**

**Vitamin K Antagonist\*\*\***

**P2Y<sub>12</sub> antagonist  
(ASA 1 - 12 months)\*\*\*\***

\*Edoxaban dose reduction to 30 mg OD  
•if CrCL ≤ 50 ml/min  
•BW ≤ 60 kg  
•certain P-gp inhibitors

\*\*Clopidogrel 75mg once-daily or if documented need prasugrel 5 or 10mg once-daily or ticagrelor 90mg twice-daily .  
Predeclared at randomization

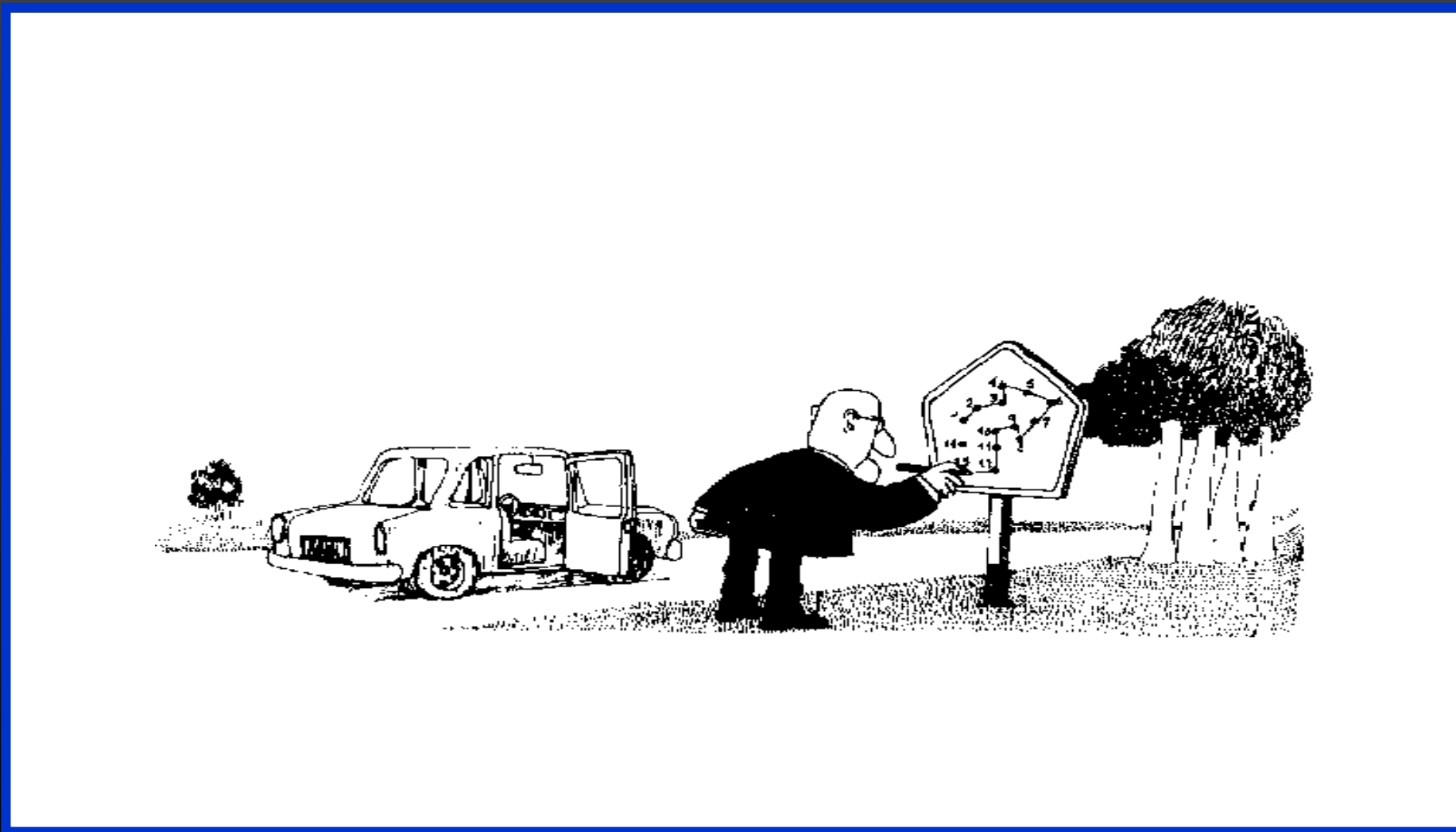
\*\*\* VKA, target INR 2-3

\*\*\*\*ASA 100mg OD for 1-12 months guided by clinical presentation (ACS or stable CAD), CHA<sub>2</sub>DS-VASc<sub>2</sub> and HAS\_BLED

**Primary outcome:  
ISTH major and clinically relevant non-major bleeding**

ClinicalTrials.gov Identifier: NCT02866175

*Qual è la direzione giusta?*



*dare il giusto peso alle cose...*



# Cosa rappresentano i sanguinamenti ?

**Associazione diretta tra morte e sanguinamenti fatali o intracranici**

**Associazione con interruzione parziale o completa delle varie componenti del regime antitrombotico. A volte altri farmaci, come statine e beta-bloccanti, possono anche essere sospesi e poi non ripresi.**

**A causa dei sanguinamenti maggiori possono essere necessari ricoveri che portano ad una serie di test e procedure, aumento del rischio di infezioni nosocomiali, o altre sequele avverse**

# Strategie per ridurre i sanguinamenti :

1. Ridurre il rischio di sanguinamenti periprocedurali: approccio radiale
2. Ridurre intensità anticoagulazione (warfarin) INR 2-2.5
3. Evitare i nuovi inibitori P2Y<sub>12</sub> (i.e., prasugrel, ticagrelor) nella triplice terapia
4. Limitare la durata della triplice terapia
5. Eliminare asa dalla triplice terapia

**Ma oggi, in un mondo in cui si dà troppo credito all'apparenza,  
forse vale ricordare che...l'apparenza inganna !**





# ***IL PAZIENTE REALE***

- **Alto rischio trombotico (CHADS<sub>2</sub>VASC<sub>2</sub> > 3)**
- **Alto rischio emorragico (HAS-BLED > 3)**
- **Insufficienza renale ed epatica**
- **Età avanzata (>80 anni)**
- **Cardiopatía ischemica**
- **Fibrillazione atriale persistente**
- **Scarsa compliance**

# IL PAZIENTE REALE

## CHA2DS2-VASc

| Stroke Risk Factor                        | Score |
|---|-------|
| Congestive Heart Failure / LV Dysfunction | 1     |
| Hypertension                              | 1     |
| Age ( $\geq 75$ years)                    | 2     |
| Diabetes                                  | 1     |
| Prior Stroke / TIA / thrombo-embolism     | 2     |
| Vascular Disease <sup>1</sup>             | 1     |
| Age 65-74                                 | 1     |
| Sex Category (female)                     | 1     |
| Max Score                                 | 9     |

| HAS-BLED risk criteria                             | Score  |
|--|--------|
| Hypertension                                       | 1      |
| Abnormal renal or liver function<br>(1 point each) | 1 or 2 |
| Stroke   | 1      |
| Bleeding   | 1      |
| Labile INRs  | 1      |
| Elderly<br>(e.g. age >65 yrs)                      | 1      |
| Drugs or alcohol<br>(1 point each)                 | 1 or 2 |

**Necessità di valutazione del profilo di rischio trombotico ed emorragico**

# Take Home Messages

## Nel paziente con fibrillazione atriale sottoposto a PCI:

- Il regime antitrombotico attualmente raccomandato è la triplice terapia  
→ warfarin/NAO + aspirina + clopidogrel (**ESC 2017**)
- Durante la triplice terapia, vanno attuate misure per contenere rischio emorragico
- Si attendono i risultati dei trial non completati e degli studi in corso circa possibili ulteriori regimi antitrombotici
- Va presa ora in considerazione la duplice terapia con DOACs + clopidogrel

E' importante la durata della vita,  
ma anche la sua qualità...

