Azienda Ospedaliera
G. Rummo - Benevento

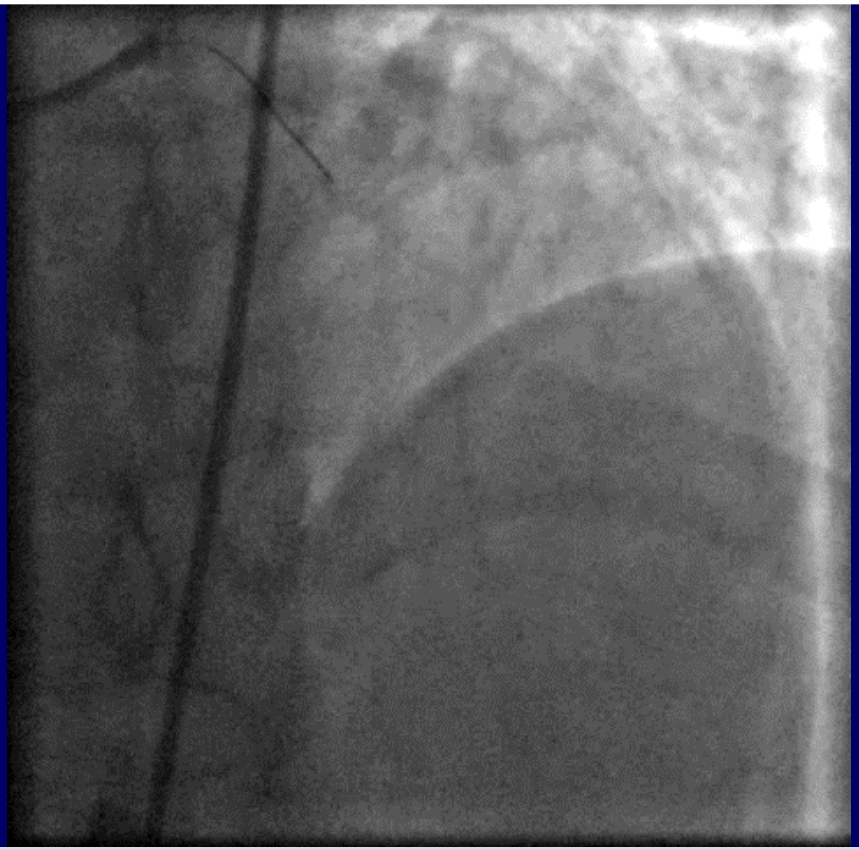
Dipartimento di CardioScienze
Unità Operativa Complessa
Cardiologia Interventistica e UTIC
Direttore : Dr Marino Scherillo

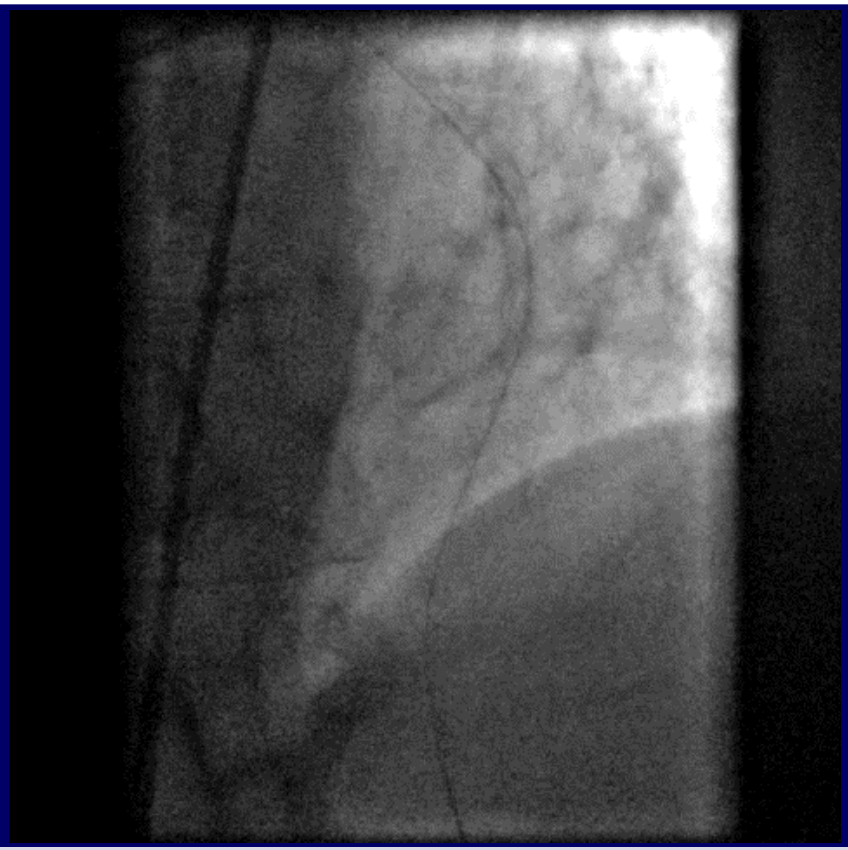
NOA Choice in clinical practice a personalized approach : THE COMPLEX PATIENT

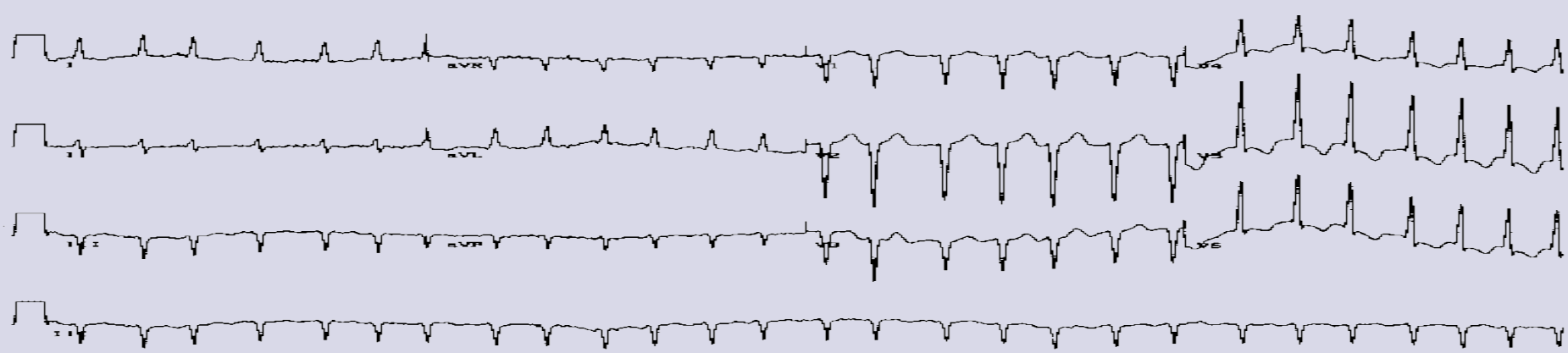
Marino Scherillo

Torino, 25 ottobre 2014

ANTONIO, 68 a : NSTEMI, T+, Diabete







Qual è la Migliore Trapia Antitrombotica nel Paziente con FA e SCA ?

1. Warfarin + ASA + CLO
2. Warfarin + CLO
3. ASA + CLO
4. Chiedo al Primario !

Fibrillazione Atriale e Coronaropatia

La fibrillazione atriale è presente fino al:

12.5 % dei pazienti con stable CAD

Goto S et al, on behalf of the REACH Registry Investigators.
Am Heart J 2008;156:855-863.

10 % dei pazienti con SCA

Al Khdair D et al, on behalf of the GRACE/GRACE2 and CANRACE Registry Investigators.
Can J Cardiol 2012;28:443-9.

Caratteristiche basali

6.394 pazienti arruolati

2.858 (44.7%)
STEMI/BBS

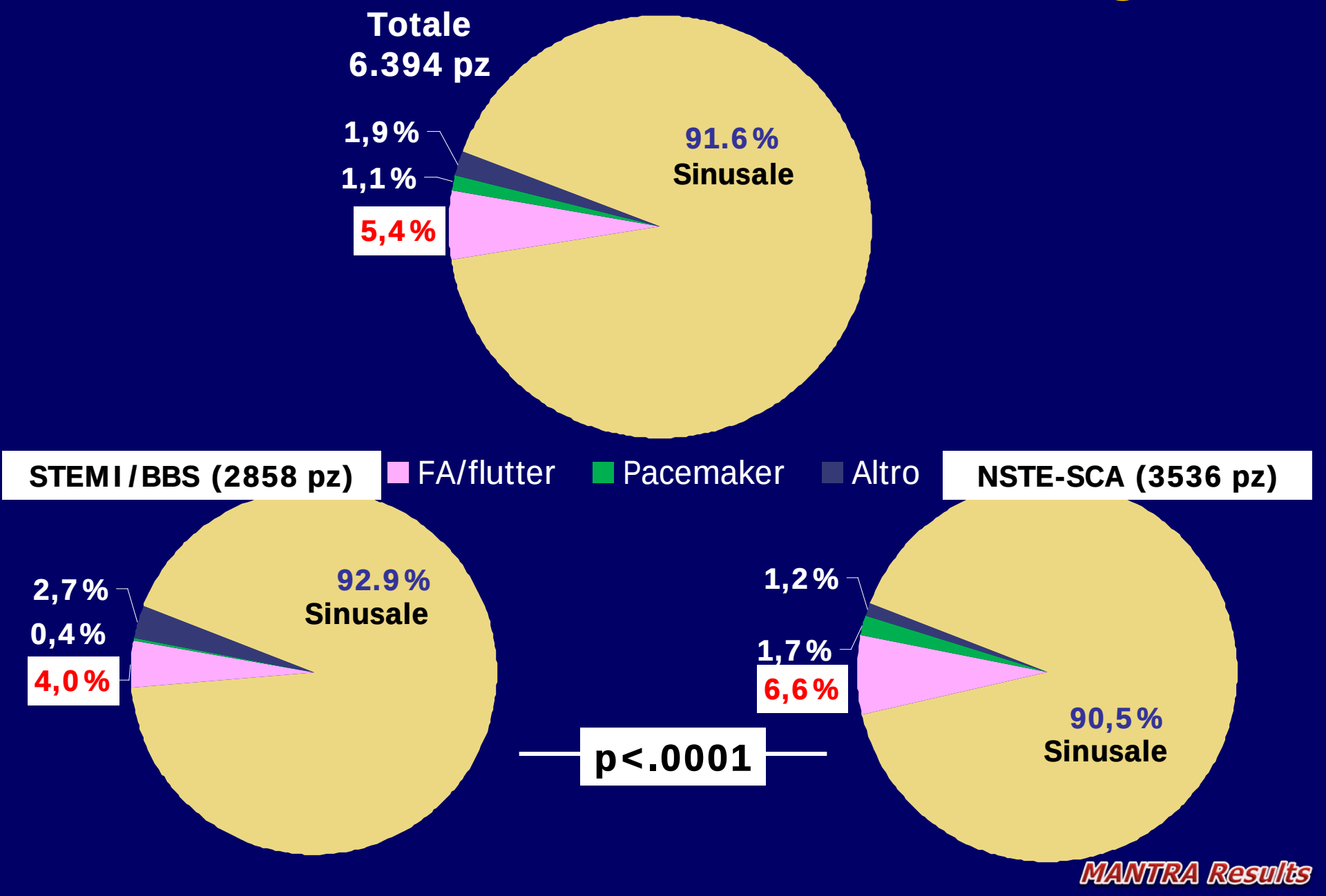
3.536 (55.3%)
NSTE-SCA

MANTRA Caratteristiche della popolazione

	Pazienti STEMI/BBS n. 2858	Pazienti NSTE-SCA n. 3536	p
Femmine, %	26.8	31.9	<.0001
Età ≥75aa, %	26.6	35.2	<.0001
Età, anni, **mediana** [25%-75%]	**65** [55-75]	**70** [60-77]	<.0001
BMI			0.30
≤25, %	38.5	37.0	
26-30, %	44.5	46.4	
>30, %	17.0	16.6	
BMI, mediana [25-75]	26 [24-29]	27 [24-29]	0.44
Fumo	(n. 2731)	(n. 3317)	<.0001
Attuale, %	42.1	29.7	
Ex fumatore, %	20.5	26.7	
Non fumatore, %	37.4	43.6	
Dislipidemia, %	42.3 (n. 2607)	49.0 (n. 3221)	<.0001
Diabete, %	21.6	30.8	<.0001
Ipertensione, %	58.3 (n. 2807)	70.2 (n. 3479)	<.0001
Familiarità, %	26.6 (n. 2628)	23.9 (n. 3232)	0.02

MANTRA

ECG all'ingresso



Guidelines on myocardial revascularization

The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

(b) Recommended duration of dual antiplatelet therapy

After percutaneous coronary intervention

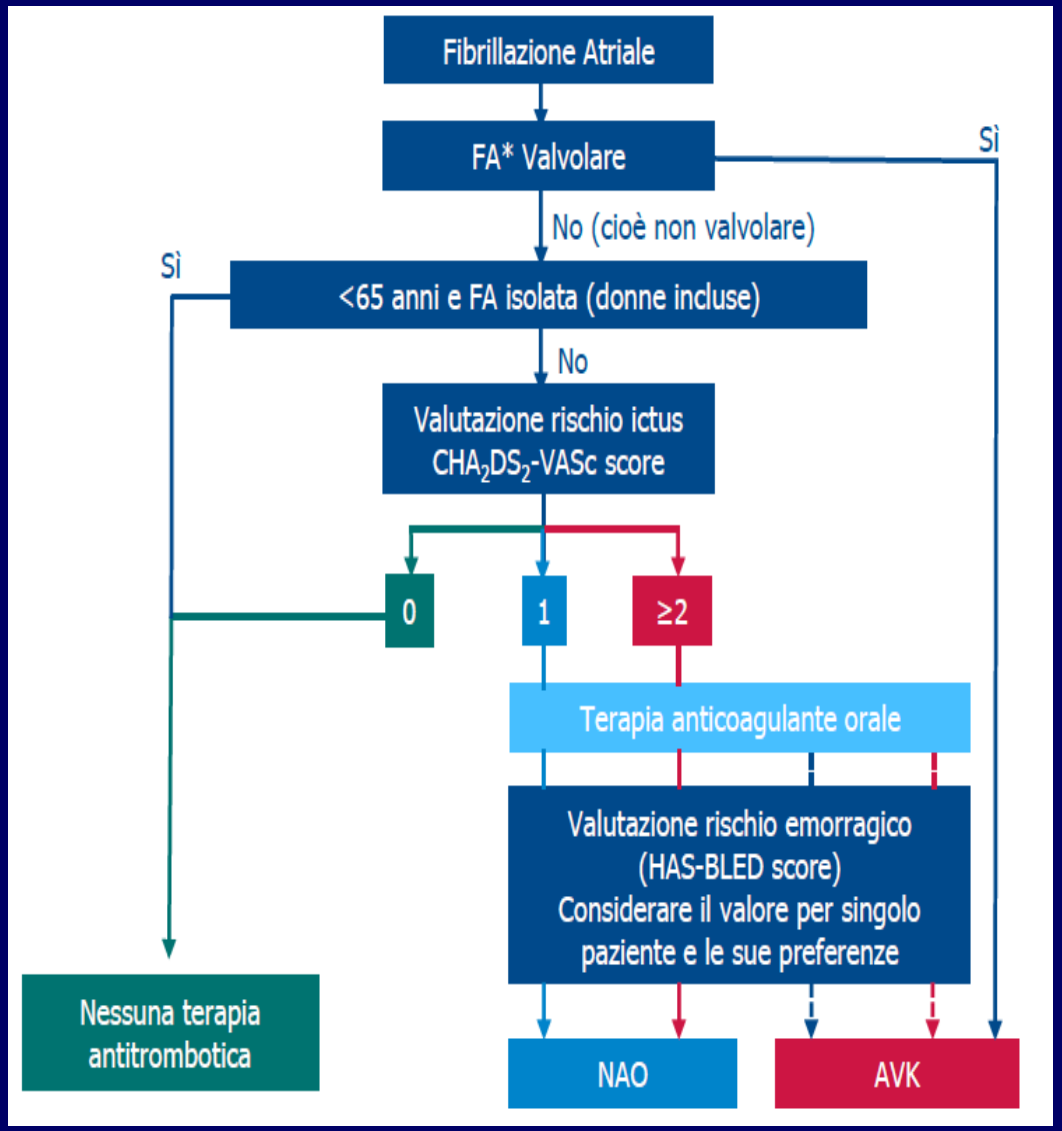
- 1 month after BMS implantation in stable angina;[55,60,94]
- 6–12 months after DES implantation in all patients;[60,94]
- 1 year in all patients after ACS, irrespective of revascularization strategy.

ESC Guideline :2014

Algoritmo di trattamento del paziente con fibrillazione atriale

"… per i pazienti con fibrillazione atriale che hanno uno o più fattori di rischio per ictus si raccomanda una adeguata terapia di prevenzione dell'ictus, che essenzialmente è la terapia con un anticoagulante orale, sia la terapia con AVK ben controllato (INR 2÷3 con un'alta percentuale di TTR, almeno il 70%) sia con uno dei NOA."

I NAO* rappresentano la migliore opzione terapeutica.



AF AND ORAL ANTICOAGULATION (OAC)

Risk factor	Score
Congestive heart failure/LV dysfunction	1
Hypertension	1
Age ≥75	2
Diabetes mellitus	1
Stroke/TIA/thrombo-embolism	2
Vascular disease[a]	1
Age 65–74	1
Sex category (i.e. female sex)	1
Maximum score	**9**

The CHA_2DS_2-VASc score

Risk category	CHA_2DS_2-VASc score	Recommended antithrombotic therapy
One 'major' risk factor or ≥2 'clinically relevant non-major' risk factors	≥ 2	OAC[a]
One 'clinically relevant non-major' risk factor	1	Either OAC[a] or aspirin 75–325 mg daily. Preferred: OAC rather than aspirin.
No risk factors	0	Either aspirin 75–325 mg daily or no antithrombotic therapy. Preferred: no antithrombotic therapy rather than aspirin.

about 90% of AF patients

Camm AJ et al. Eur Heart J 2010;31:2369-429

FOLLOWING PCI + STENT in patients with AF

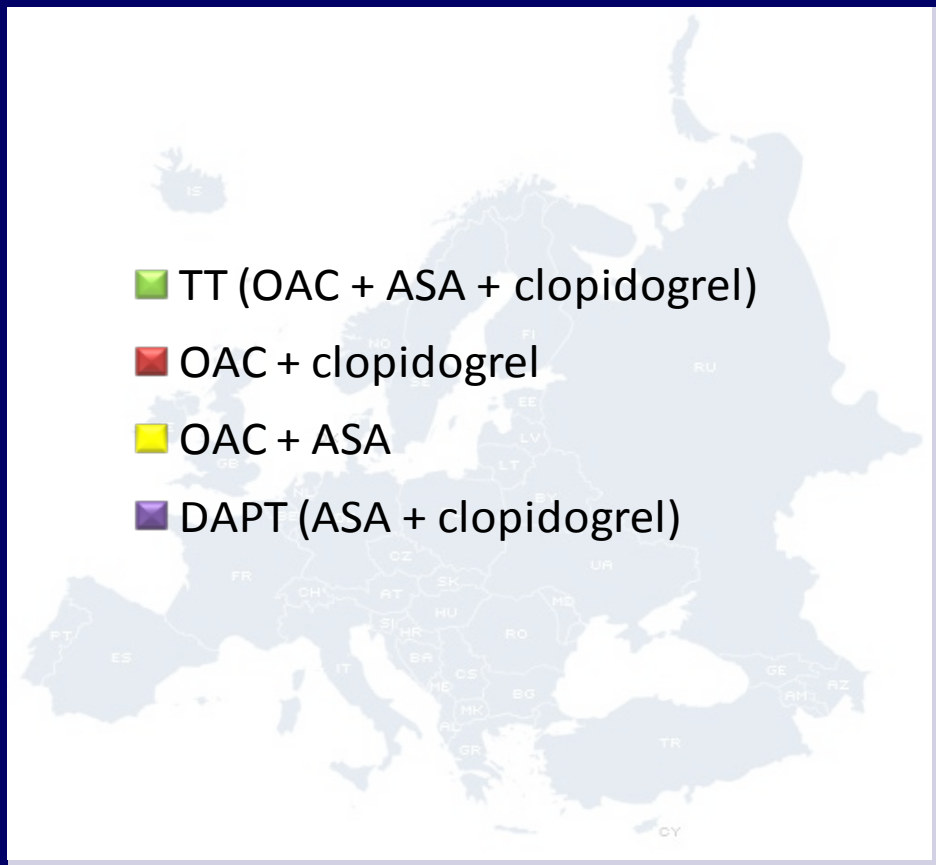
OAC

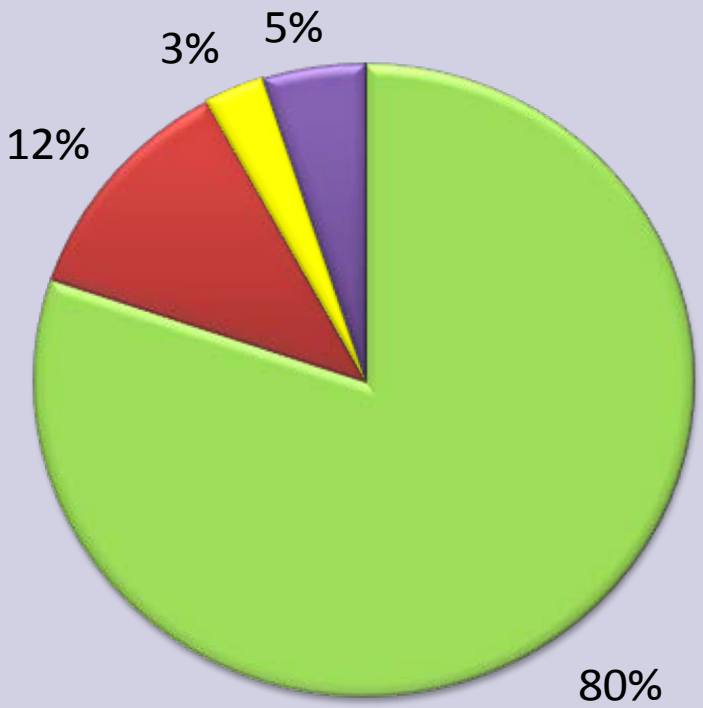
+

1 **antiplatelet agent**	***2*** **antiplatelet agents**
(ASA *or* clopidogrel)	**(ASA *and* clopidogrel)**

The Management of Patients on Oral Anticoagulation Undergoing Coronary Stent Implantation: A Survey among Interventional Cardiologists from Eight European Countries

ANDREA RUBBOLI, M.D., F.E.S.C.[1], WILLEM DEWILDE, M.D.[2], KURT HUBER, M.D., F.E.S.C., F.A.C.C.[3], ERIC EECKHOUT, M.D., F.E.S.C.[4], ISTVAN HERZFELD, M.D.[5], JOSE' VALENCIA, M.D.[6], STEPHAN WINDECKER, M.D., F.E.S.C.[7], K.E. JUHANI AIRAKSINEN, M.D., F.E.S.C.[8], and GREGORY Y. H. LIP, M.D., F.E.S.C., F.A.C.C.[9]





Rubboli A et al. J Interv Cardiol 2011

Antithrombotic therapy in patients treated with oral anticoagulation undergoing coronary artery stenting. An expert consensus document with focus on atrial fibrillation

ANDREA RUBBOLI[1], JONATHAN L. HALPERIN[2], K.E. JUHANI AIRAKSINEN[3], MICHAEL BUERKE[4], ERIC EECKHOUT[5], SAUL B. FREEDMAN[6], ANTHONY H. GERSHLICK[7], AXEL SCHLITT[4], HUNG-FAT TSE[8], FREEK W.A. VERHEUGT[9] & GREGORY Y.H. LIP[10]

1. Orford JL et al. Am J Cardiol (2004)
2. Mattichak SL et al. J Interven Cardiol (2005)
3. Khurram Z et al. J Invasive Cardiol (2006)
4. Porter A et al. Catheter Cardiovasc Interv (2006)
5. Lip GYH & Karpha M. Chest (2006)
6. Karjalainen PP et al. Eur Heart J (2007)
7. DeEugenio D et al. Pharmacotherapy (2007)
8. Rubboli A et al. Coron Artery Dis (2007)
9. Nguyen MC et al. Eur Heart J (2007)
10. Wang TY et al. Am Heart J (2008)
11. Ruiz-Nodar JM et al. J Am Coll Cardiol (2008)
12. Rogacka R et al. J Am Coll Cardiol Intv (2008)

Triple Therapy (OAC+ASA+thienopyridine) =

less stroke & more (major) bleeding

(increasing as treatment prolongs)

Rubboli A et al. Ann Med 2008;40:428-36

The WOEST Trial

What is the Optimal antiplatElet and anticoagulant therapy in patients with oral anticoagulation and coronary StenTing

Aim of the study

To test the hypothesis that in patients on OAC undergoing PCI, clopidogrel alone is superior to the combination aspirin and clopidogrel with respect to bleeding but is not increasing thrombotic risk in a multicentre two-country study (The Netherlands and Belgium)

The WOEST trial: Study Design

573 pazienti: dual terapy 284 pts. Triple terapy 289 pts.

1:1 Randomisation:

Dual 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

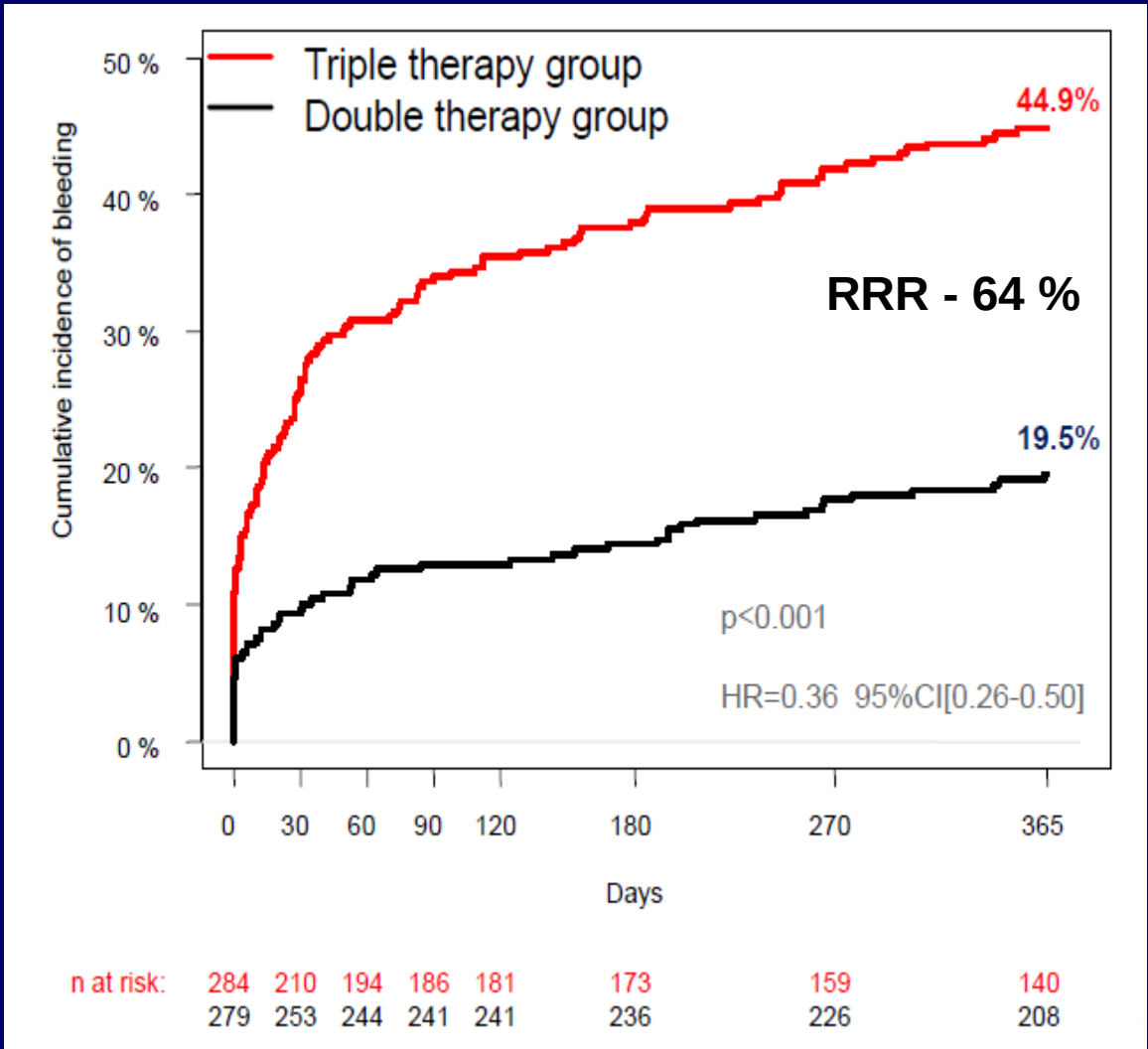
Follow up: 1 year

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

Secondary Endpoints:

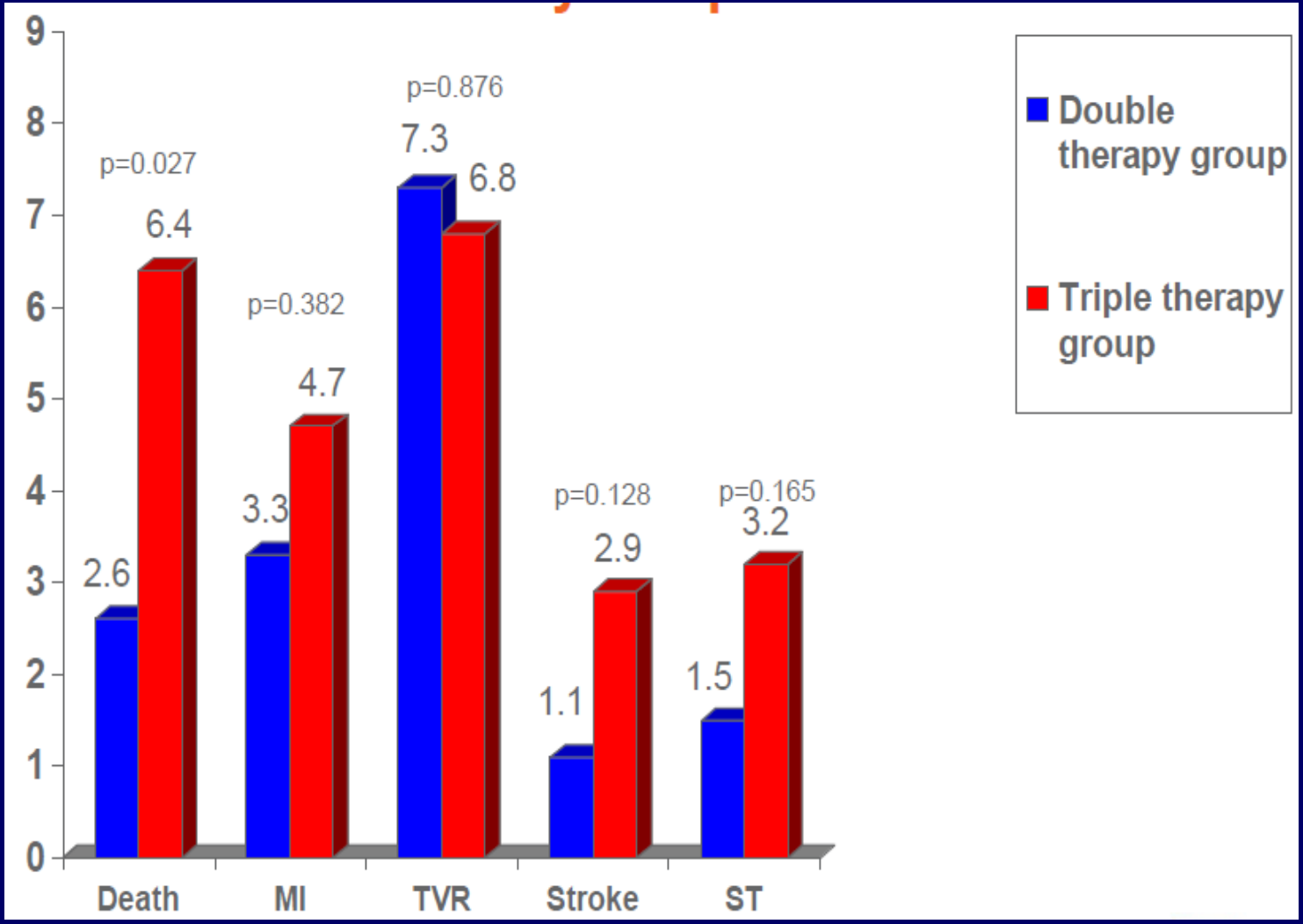
- Combination of stroke, death, myocardial infarction, stent thrombosis and target vessel revascularisation
- All individual components of primary and secondary endpoints

The WOEST trial: Primary Endpoint



ESC Congress 2012 Hot Line

The WOEST trial: Secondary Endpoint



ESC Congress 2012 Hot Line

The WOEST trial: Implication

A strategy of oral anticoagulants plus clopidogrel, but without aspirin could be applied in this group of high-risk patients on OAC when undergoing PCI

SCENARI CLINICI COMPLESSI IN PAZIENTI CORONAROPATICI SOTTOPOSTI A PCI :

il Paziente con FA in TAO

Che cosa è utile fare nella pratica clinica quotidiana ?

Action # 1: Bleeding Risk Stratification

The HAS-BLED score

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

... whereby a score of ≥ 3 indicates 'high risk', and some caution and regular review of the patient is needed following the initiation of antithrombotic therapy, …

Camm AJ et al. Eur Heart J 2010;31:2369-429

European Heart Journal Advance Access published August 25, 2014

European Heart Journal
doi:10.1093/eurheartj/ehu298

CURRENT OPINION

Management of antithrombotic therapy in atrial fibrillation patients presenting with acute coronary syndrome and/or undergoing percutaneous coronary or valve interventions: a joint consensus document of the European Society of Cardiology Working Group on Thrombosis, European Heart Rhythm Association (EHRA), European Association of Percutaneous Cardiovascular Interventions (EAPCI) and European Association of Acute Cardiac Care (ACCA) endorsed by the Heart Rhythm Society (HRS) and Asia-Pacific Heart Rhythm Society (APHRS)

Task Force Members: Gregory Y.H. Lip* (UK, Chairman), Stephan Windecker (Switzerland)†, Kurt Huber (Austria)‡, Paulus Kirchhof (UK)‡, Francisco Marin (Spain), Jurriën M. Ten Berg (Netherlands), Karl Georg Haeusler (Germany), Giuseppe Boriani (Italy), Davide Capodanno (Italy), Martine Gilard (France), Uwe Zeymer (Germany), Deirdre Lane (UK, Patient Representative).
Document Reviewers: Robert F. Storey (Review Co-ordinator), Hector Bueno, Jean-Philippe Collet, Laurent Fauchier, Sigrun Halvorsen, Maddalena Lettino, Joao Morais, Christian Mueller, Tatjana S. Potpara, Lars Hvilsted Rasmussen, Andrea Rubboli, Juan Tamargo, Marco Valgimigli, and Jose L. Zamorano

Strategia AntiTrombotica dopo STENT

Rischio Emorragico
Basso o Moderato (HAS-BLED 0-2)

	SCAD		ACS
Stroke risk moderato CHA_2DS_2-VASC 0 - 1	**OAC + ASA + CLO** *per 1 mese (max 6 mesi)* **OAC + CLO (ASA)** *per 12 mesi* **OAC** *> 12 mesi*	***alternativa*** **ASA + CLO** *per 12 mesi*	**OAC + ASA + CLO** *per 6 mesi* **OAC + CLO (ASA)** *per 12 mesi* **OAC** *> 12 mesi*
Stroke risk alto CHA2DS2-VASC ≥ 2	**OAC + ASA + CLO** *per 1 mese (max 6 mesi)* **OAC + CLO (ASA)** *per 12 mesi* **OAC** *> 12 mesi*	***alternativa*** **OAC + CLO** *per 1 mese*	**OAC + ASA + CLO** *per 6 mesi* **OAC + CLO (ASA)** *per 12 mesi* **OAC** *> 12 mesi*

Modificato da: Management of antithrombotic therapy in atrial fibrillation patients presenting with acute coronary syndrome and/or undergoing percutaneous coronary or valve intervention. European Heart Journal 2014;eurheartj.ehu298

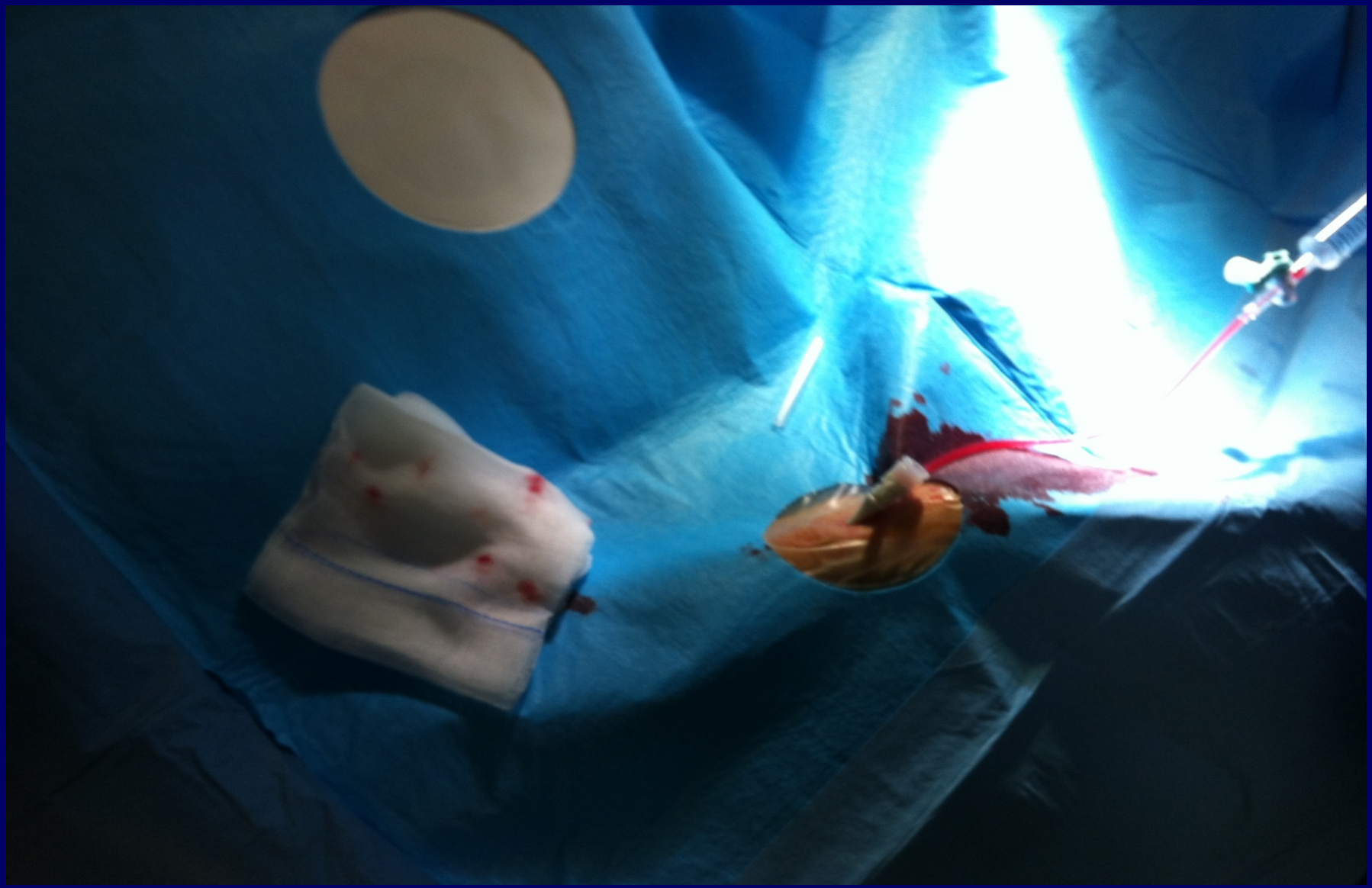
Strategia AntiTrombotica dopo STENT

Rischio Emorragico Alto (HAS-BLED ≥ 3)

	SCAD		ACS	
Stroke risk moderato CHA_2DS_2-VASC 0 - 1	**OAC + CLO** *per 12 mesi* **OAC** *> 12 mesi*	***alternativa ASA + CLO per 12 mesi***	**OAC + ASA + CLO** *per 1 mese* **OAC + CLO (ASA)** *per 12 mesi* **OAC** *> 12 mesi*	***alternativa*** **OAC + CLO** *per 1 mese*
Stroke risk alto CHA2DS2-VASC ≥ 2	**OAC + ASA + CLO** *per 1 mese* **OAC + CLO (ASA)** *per 12 mesi* **OAC** *> 12 mesi*		**OAC + ASA + CLO** *per 1 mese* **OAC + CLO (ASA)** *per 12 mesi* **OAC** *> 12 mesi*	***alternativa*** **OAC + CLO** *per 1 mese*

Modificato da: Management of antithrombotic therapy in atrial fibrillation patients presenting with acute coronary syndrome and/or undergoing percutaneous coronary or valve intervention. European Heart Journal 2014;eurheartj.ehu298

Action # 2: radial approach in cath lab

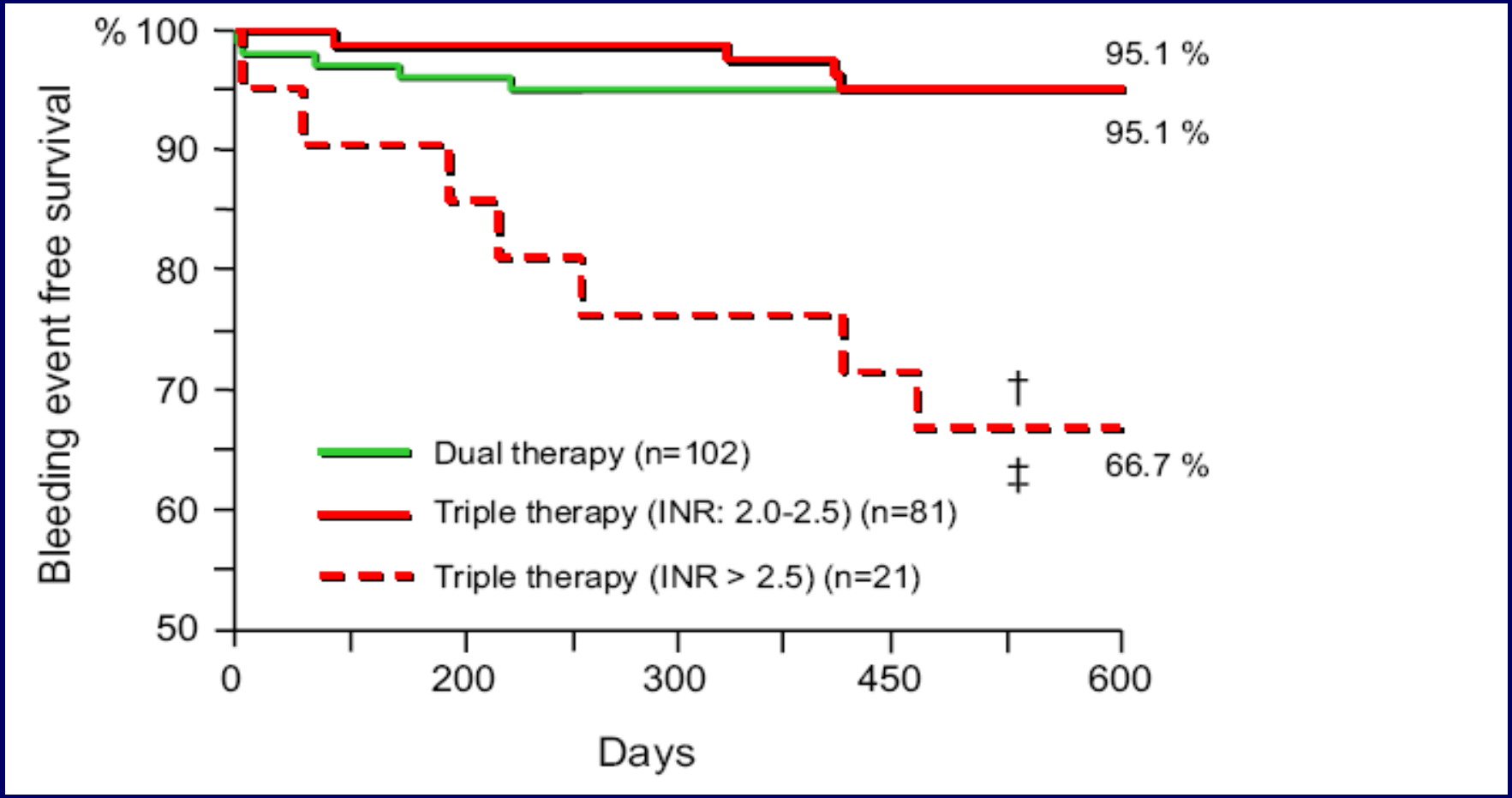


Action # 3: Short Duration of Triple Therapy

	Class	LOE
❑ DES to be avoided, or strictly limited to those clinical and/or anatomical situations (long lesions, small vessels, diabetes, etc.) where significant benefit over BMS is expected	IIa	C

Lip GYH et al. Thromb & Haemost 2010;103:13-28

Action # 4: Lower Target INR



† Log Rank, p<0.0001 vs dual therapy

‡ Log Rank, p<0.0001 vs triple therapy (INR: 2.0-2.5)

Rossini R et al. Am J Cardiol 2008;102:1618-23

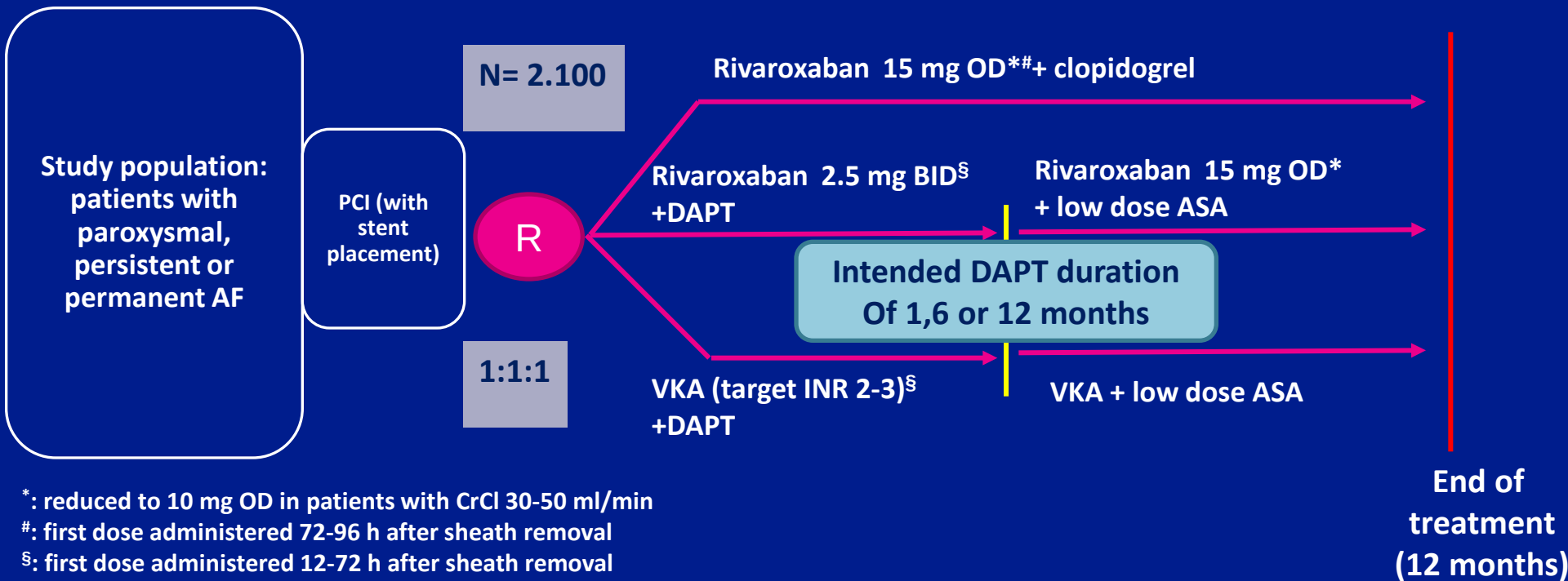
Action # 5: Gastric Protection

	Class	LOE
❑ throughout TT, gastric protection with either PPIs, H_2-receptor antagonists or antacids, is recommended	IIa	C

Lip GYH et al. Thromb & Haemost 2010;103:13-28

PIONEER AF - PCI: Study Design

Open label, randomized, controlled, multi-center study exploring two treatment strategies of rivaroxaban and a dose adjusted oral VKA treatment strategy in patients with AF who undergo PCI



*: reduced to 10 mg OD in patients with CrCl 30-50 ml/min
#: first dose administered 72-96 h after sheath removal
§: first dose administered 12-72 h after sheath removal

Clinicaltrials.gov: NCT01830543

PIONEER AF - PCI: Endpoints

Primary endpoints:

- **Composite of TIMI major bleeding, minor bleeding and bleeding requiring medical attention (known collectively as clinically significant bleeding at 12 months**

Secondary endpoints:

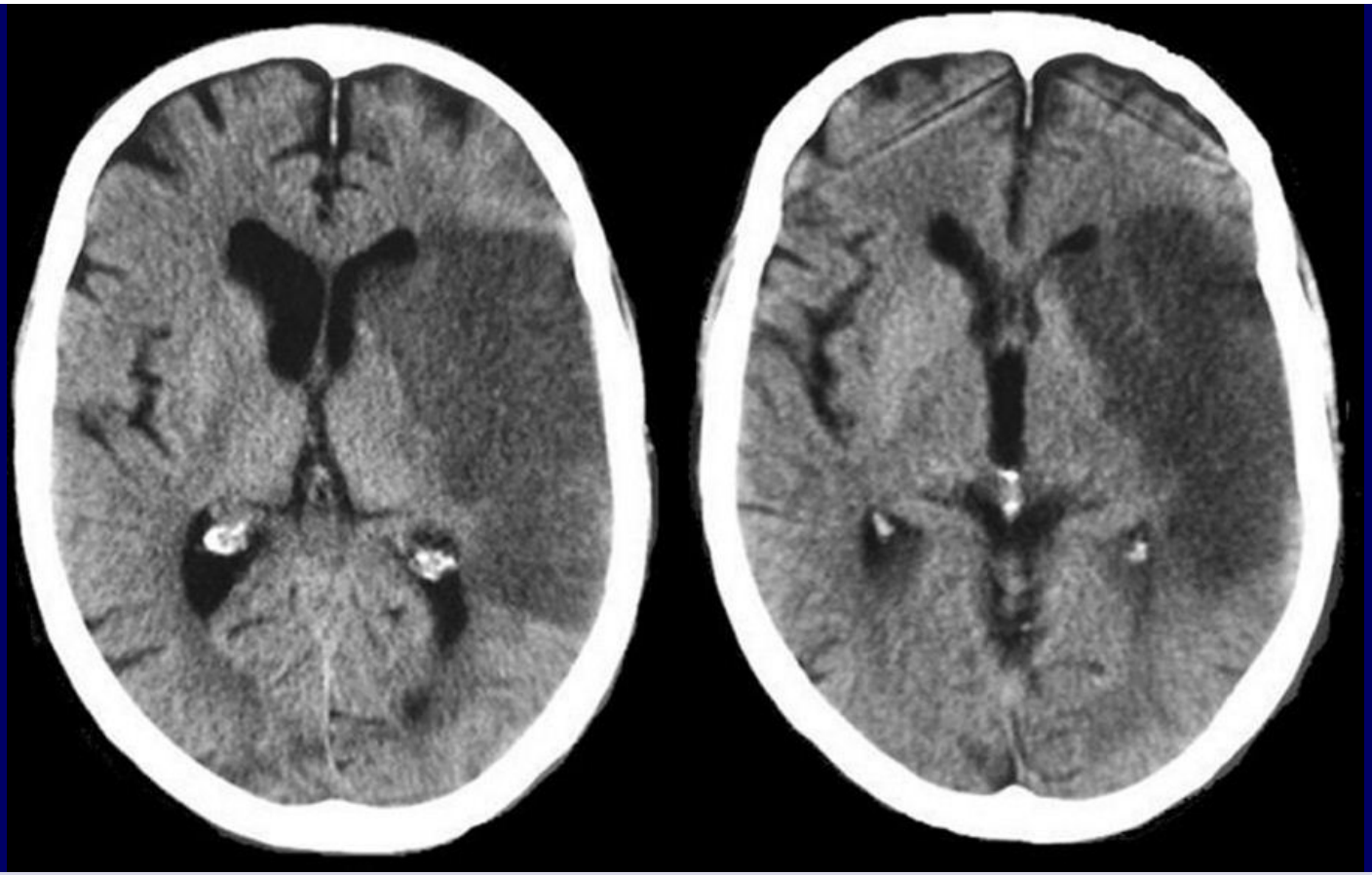
- **Separate components of the primary endpoint**
- **Composite of adverse CV events (cardiovascular death, MI, stroke) at the end of the prespecified duration of DAPT and at month 12**
- **Stent thrombosis**

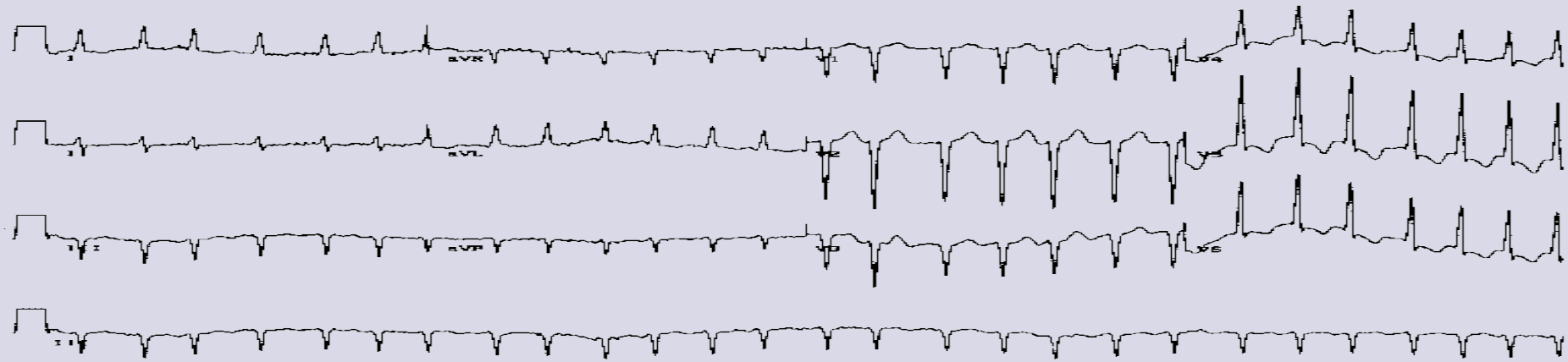
Anticipated timelines: first patient visit: Apr 2014

last patient visit: Q2 2015

Clinicaltrials.gov: NCT01830543

MARIA, 76 a : STROKE, BPCO, IRC





Dopo quanto tempo si può iniziare la terapia OAC in paziente con FA e STROKE recente ?

1. Dopo una settimana
2. Dopo 15 giorni
3. Dopo 1 mese
4. Chiedo al Primario !

Stroke in Italia

Incidenza

200.000 NUOVI CASI PER ANNO

- **80 % NUOVI EPISODI**
- **20 % RECIDIVE**

Terza causa di morte

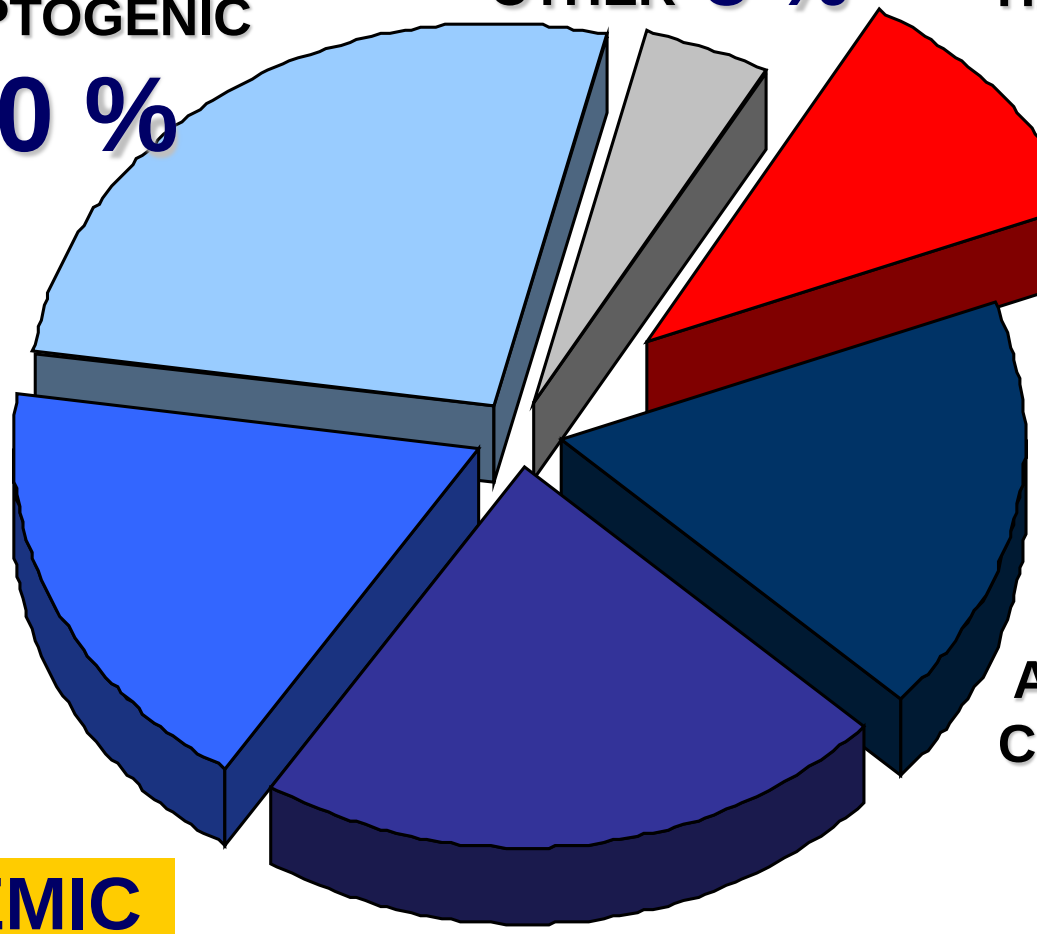
Prevalenza

6,5 % fascia d'eta 65-84 anni

- **7,4 % uomini**
- **5,9 % donne**

Istituto Superiore di Sanità : Progetto Cuore

Classification of Stroke



CRYPTOGENIC
30 %

OTHER 5 %

HAEMORRHAGIC
12 %

CARDIAC EMBOLISM
20 %

ATHEROSCLEROTIC CEREBROVASCULAR DISEASE
20 %

SMALL WESSEL DISEASE
" LACUNES "
25 %

ISCAHEMIC STROKE = 88 %

Kolominsky P.L. – Stroke 2001 32:27 35-2740

European Heart Rhythm association guidelines of the use of NAO in patient of non-valvular AF

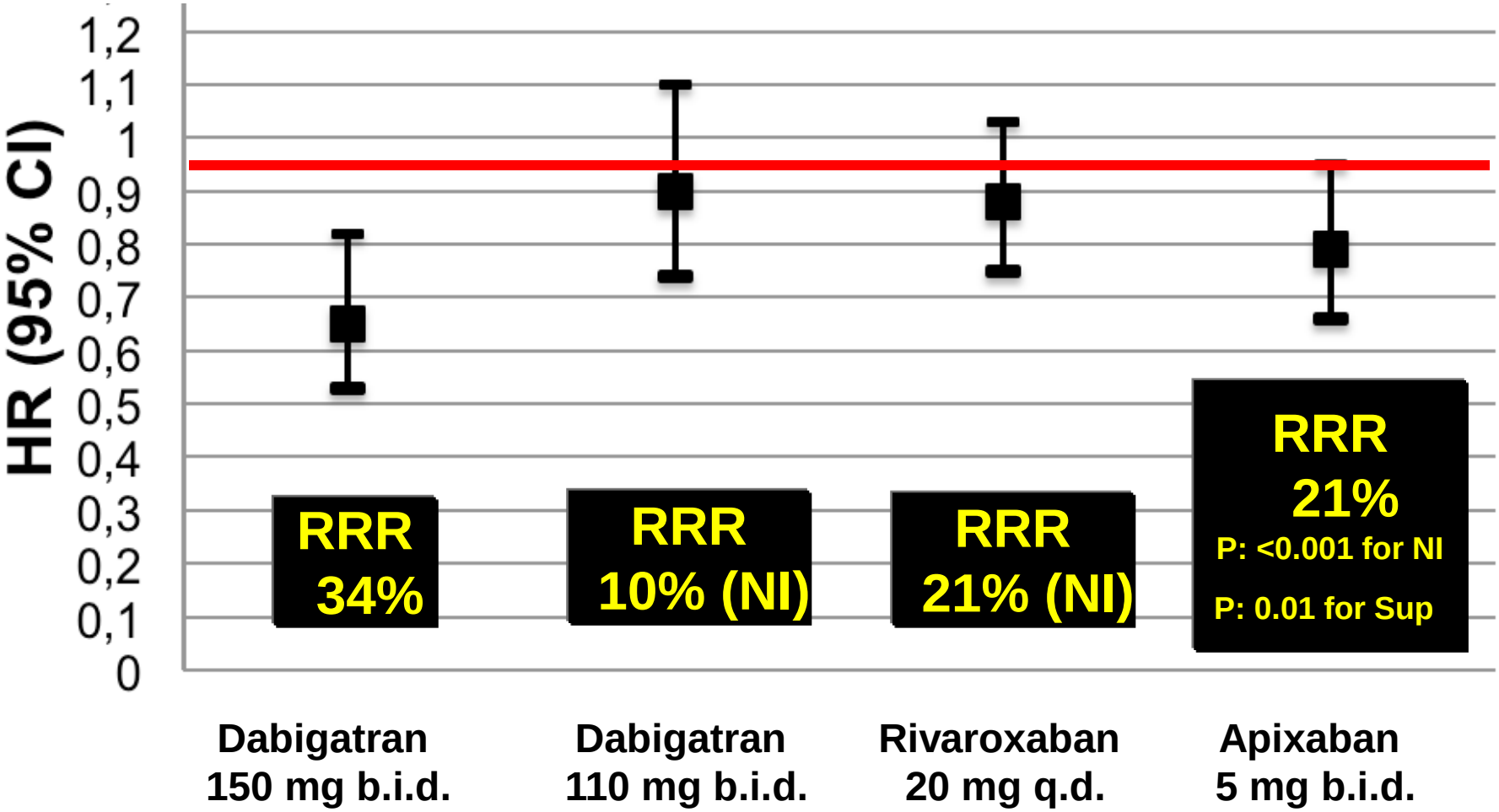
Non ci sono studi clinici riguardo la ripresa dell'anticoagulazione dopo STROKE

Regola del 1 – 3 – 6 – 12 giorni	
TIA →	1 giorno
Piccolo e non disabilitante stroke →	3 giorni
Moderato stroke →	6 giorni
Esteso stroke coinvolgente gran parte del territorio dell'arteria →	12 – 20 giorni

Eur Heart J 2013;34(27):2094-106

Quale OAC nel Paziente con FA e STROKE recente ?

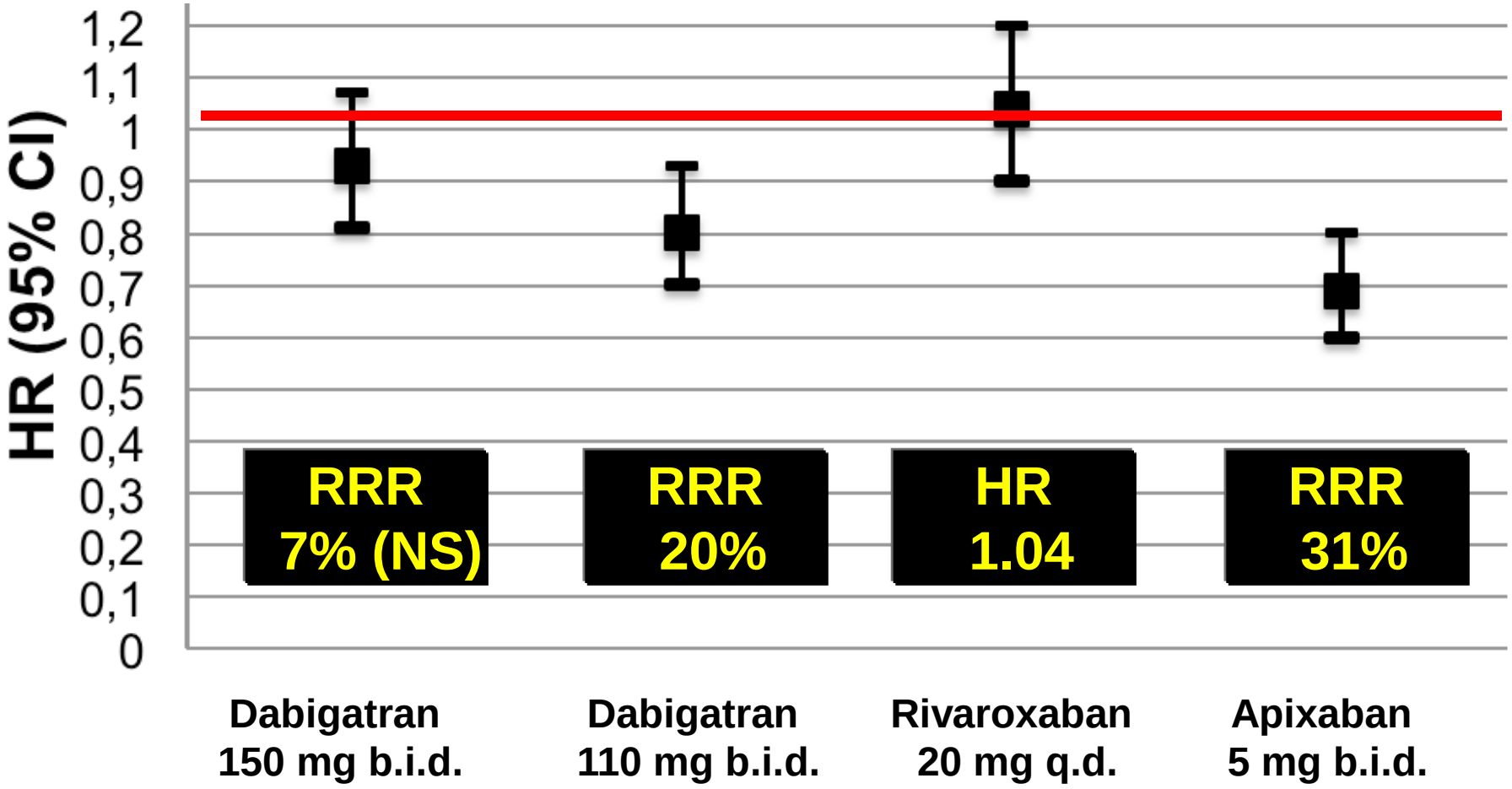
Stroke or Systemic Embolism
NOACs Vs VKA in AF



De Caterina R, Husted S, Wallentin L et al.

JACC Vol. 59, No. 16, 2012
April 17, 2012:1413–25

Major Bleedings
NOACs Vs VKA in AF



De Caterina R, Husted S, Wallentin L et al.

JACC Vol. 59, No. 16, 2012
April 17, 2012:1413–25

APIXABAN : l'unico NAO con la Triplice Superiorità

SUPERIORE
nella prevenzione dell'ictus/embolia sistemica

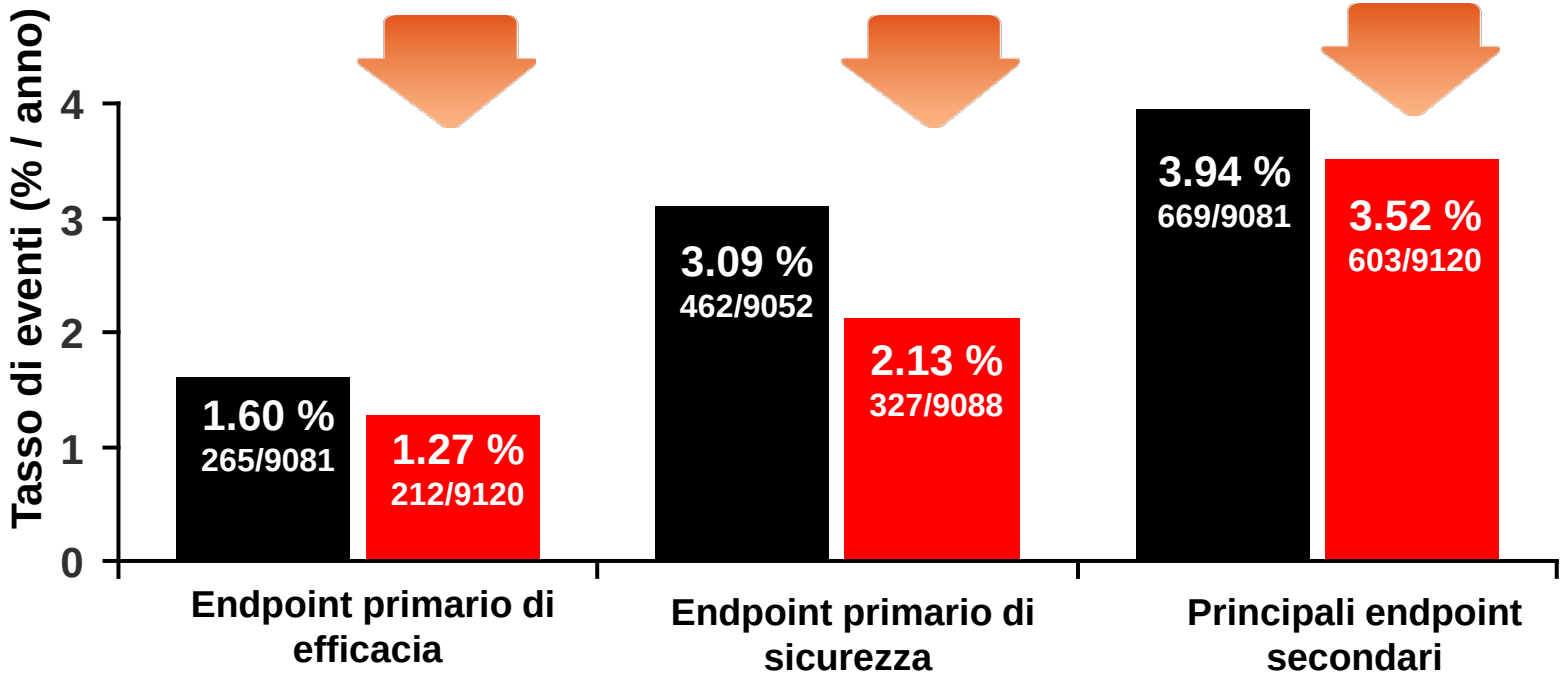
- 21 % RRR
p=0.01

SUPERIORE
nella riduzione dei sanguinamenti maggiori

- 31 % RRR
p<0.001

SUPERIORE
nella riduzione della mortalità per tutte le cause

- 11 % RRR
p=0.047



- 18.201 Pazienti
- Apixaban 5 bid Vs. Warfarin
- Durata mediana del follow-up 1.8 anni

Apixaban
Warfarin (target INR 2.0-3.0)

Granger et al. N Engl J Med 2011;365:981-92.

Linee guida STROKE

Stroke
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association | American Stroke Association

Guidelines for the Prevention of Stroke in Patients With Stroke and Transient Ischemic Attack: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

Walter N. Kernan, Bruce Ovbiagele, Henry R. Black, Dawn M. Bravata, Marc I. Chimowitz, Michael D. Ezekowitz, Margaret C. Fang, Marc Fisher, Karen L. Furie, Donald V. Heck, S. Claiborne (Clay) Johnston, Scott E. Kasner, Steven J. Kittner, Pamela H. Mitchell, Michael W. Rich, DeJuran Richardson, Lee H. Schwamm and John A. Wilson

Linee guida per la prevenzione di stroke in pazienti che hanno avuto già uno stroke o un attacco ischemico transitorio (TIA) (PREVENZIONE SECONDARIA)

Kernan WN et al Stroke 2014

Raccomandazioni FA e STROKE

	Classe	Livello di evidenza	Indicazione
VKA	**I**	**A**	**Prevenzione dello stroke ricorrente in pazienti con NVAF sia parossistica, sia permanente.**
APIXABAN	**I**	**A**	**Prevenzione dello stroke ricorrente in pazienti con NVAF sia parossistica, sia permanente**
DABIGATRAN	**I**	**B**	**Prevenzione dello stroke ricorrente in pazienti con NVAF sia parossistica, sia permanente**

La scelta dell' agente antitrombotico deve essere individualizzata sulla base dei fattori di rischio, costi, tollerabilità, preferenza del paziente, potenziali interazioni farmacologiche e altre caratteristiche cliniche incluse la funzione renale e il TTR se il paziente era già in terapia con AVK

Kernan WN et al Stroke 2014

Raccomandazioni FA e STROKE

	Classe	Livello di evidenza	Indicazione
RIVAROXABAN	**IIA**	**B**	L'uso di **Rivaroxaban** è ragionevole per la prevenzione degli stroke ricorrenti in pazienti con FANV

Kernan WN et al Stroke 2014