



II CONGRESSO INTERREGIONALE SIMEU ABRUZZO MOLISE
“ITINERARI IN EMERGENZA URGENZA”

**SCA: doppia antiaggregazione
Rivisitazione delle L.G. ESC**

Marcello Caputo
UOC di Cardiologia e UTIC
Chieti

6-7 maggio 2016
Auditorium Rettorato
Università “G. D’Annunzio”
Chieti

PIETRE MILIARI NELLA GESTIONE DELLE SCA

ANTITROMBOTICI

UFH

EBPM

Bivalirudina

Fondaparinux

ANTIPIASTRINICI

Aspirina

ANTI
GP IIb/IIIa

Clopidogrel

Prasugrel

Ticagrelor

STRATEGIA TERAPEUTICA

Conservativa

Invasiva precoce

PRISM-PLUS

REPLACE 2

ICTUS

TRITON

PURSUIT

CURE

ISAR-REACT 2

PLATO

ESSENCE

TACTICS TIMI-18

OASIS-5

ACUITY

1994

1995

1996

1997

1998

1999

2000

2001

2002

2003

2004

2005

2006

2008

PCI

~ 5% stents



~85% stents



Drug-eluting stents



Rischio Ischemico

Rischio emorragico

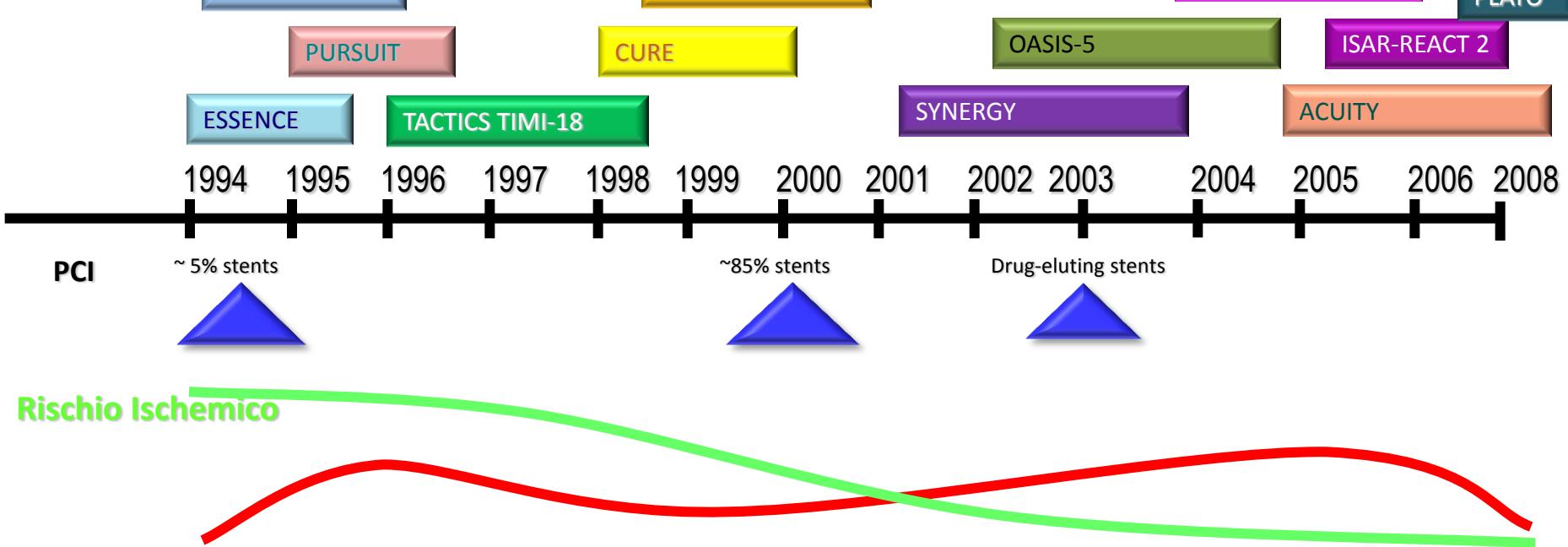


Table 8 P2Y₁₂ inhibitors

| | Clopidogrel | Prasugrel | Ticagrelor | Cangrelor |
|--|---|---|---|--|
| Chemical class | Thienopyridine | Thienopyridine | Cyclopentyl-triazolopyrimidine | Stabilized ATP analogue |
| Administration | Oral | Oral | Oral | Intravenous |
| Dose | 300–600 mg orally then 75 mg a day | 60 mg orally then 10 mg a day | 180 mg orally then 90 mg twice a day | 30 µg/kg bolus and 4 µg/kg/min infusion |
| Dosing in CKD | | | | |
| • Stage 3 (eGFR 30–59 mL/min/1.73m ²) | No dose adjustment | No dose adjustment | No dose adjustment | No dose adjustment |
| • Stage 4 (eGFR 15–29 mL/min/1.73m ²) | No dose adjustment | No dose adjustment | No dose adjustment | No dose adjustment |
| • Stage 5 (eGFR <15 mL/min/1.73m ²) | Use only for selected indications (e.g. stent thrombosis prevention) | Not recommended | Not recommended | No dose adjustment |
| Binding reversibility | Irreversible | Irreversible | Reversible | Reversible |
| Activation | Prodrug, with variable liver metabolism | Prodrug, with predictable liver metabolism | Active drug, with additional active metabolite | Active drug |
| Onset of loading dose effect^a | 2–6 hours ^b | 30 min ^b | 30 min ^b | 2 min |
| Duration of effect | 3–10 days | 7–10 days | 3–5 days | 1–2 hours |
| Withdrawal before surgery | 5 days ^c | 7 days ^c | 5 days ^c | 1 hour |
| Plasma half-life of active P2Y₁₂ inhibitor^d | 30–60 min | 30–60 min ^e | 6–12 hours | 5–10 min |
| Inhibition of adenosine reuptake | No | No | Yes | Yes ('inactive' metabolite only) |



European Heart Journal (2016) 37, 267–315
doi:10.1093/eurheartj/ehv320

ESC GUIDELINES



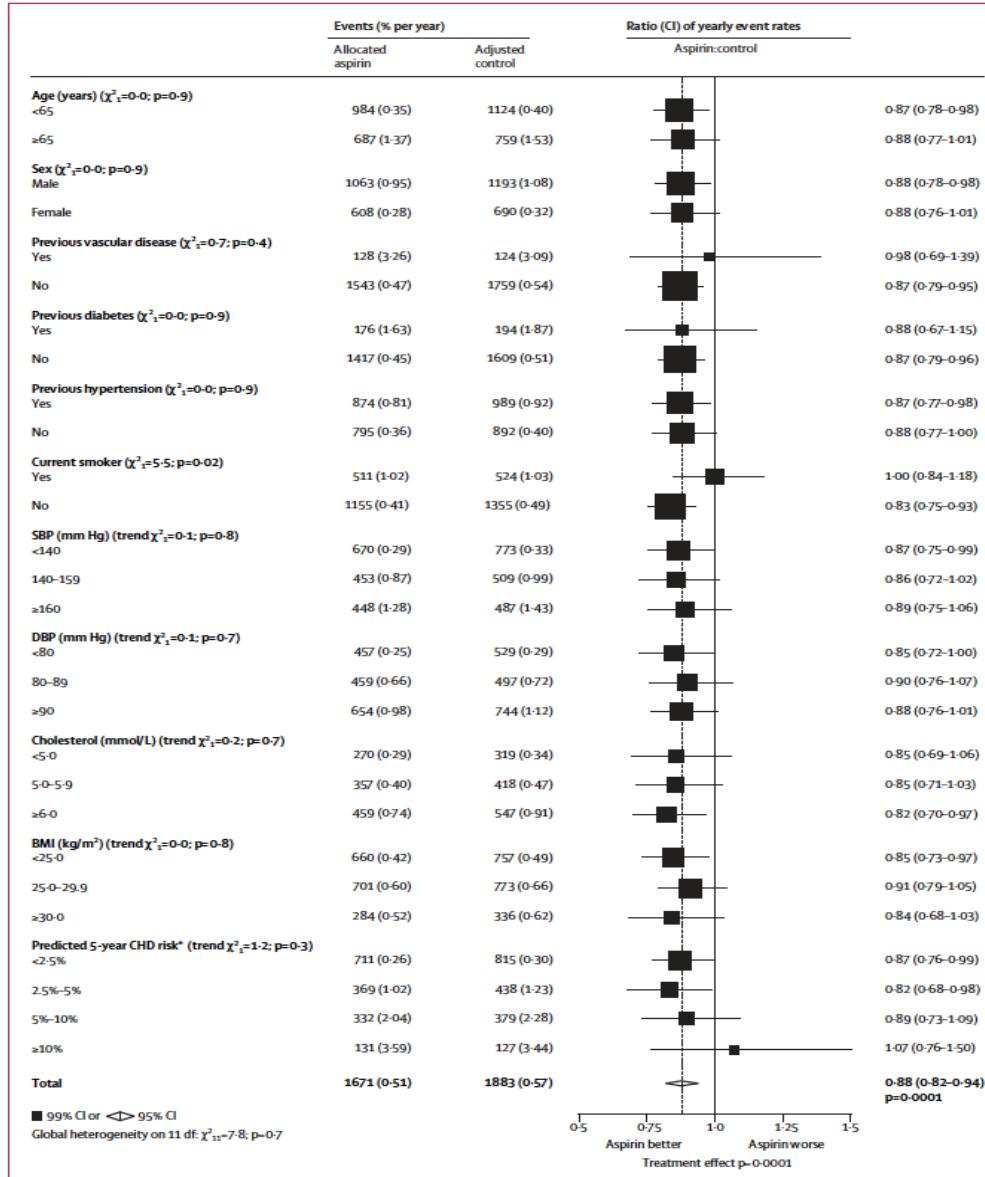
2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation

**Task Force for the Management of Acute Coronary Syndromes
in Patients Presenting without Persistent ST-Segment Elevation
of the European Society of Cardiology (ESC)**

| Recommendations | Class | Level | Ref. |
|---|-------|-------|---------|
| Oral antiplatelet therapy | | | |
| Aspirin is recommended for all patients without contraindications at an initial oral loading dose of 150–300 mg (in aspirin-naïve patients) and a maintenance dose of 75–100 mg/day long-term regardless of treatment strategy. | I | A | 129–132 |

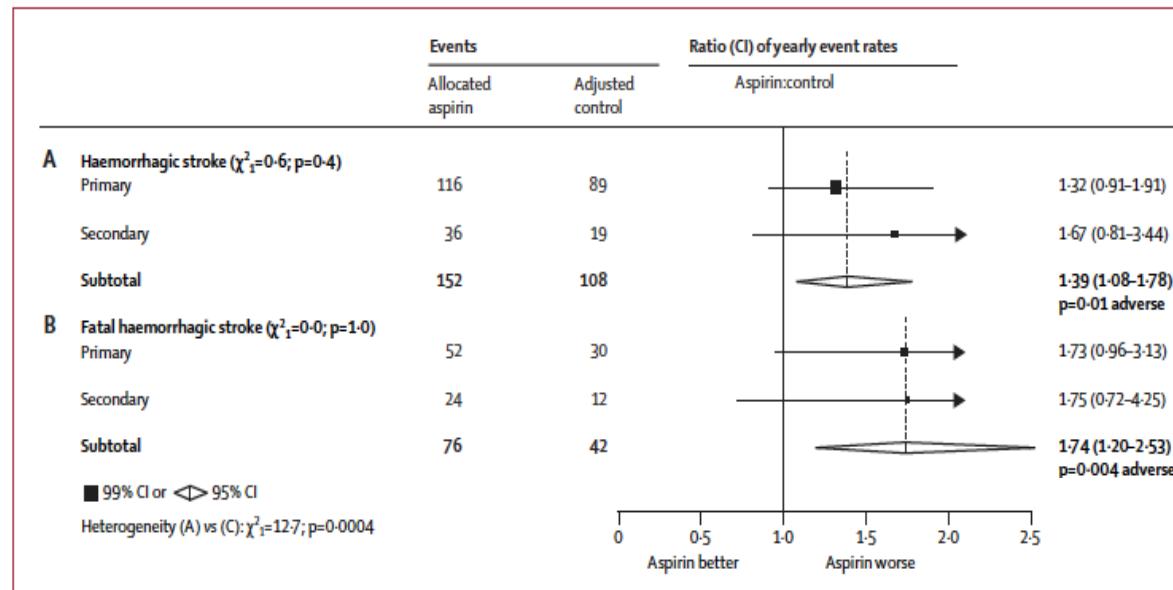
Aspirin in the primary and secondary prevention of vascular disease

Antithrombotic Trialists' (ATT) Collaboration



Aspirin in the primary and secondary prevention of vascular disease

Antithrombotic Trialists' (ATT) Collaboration

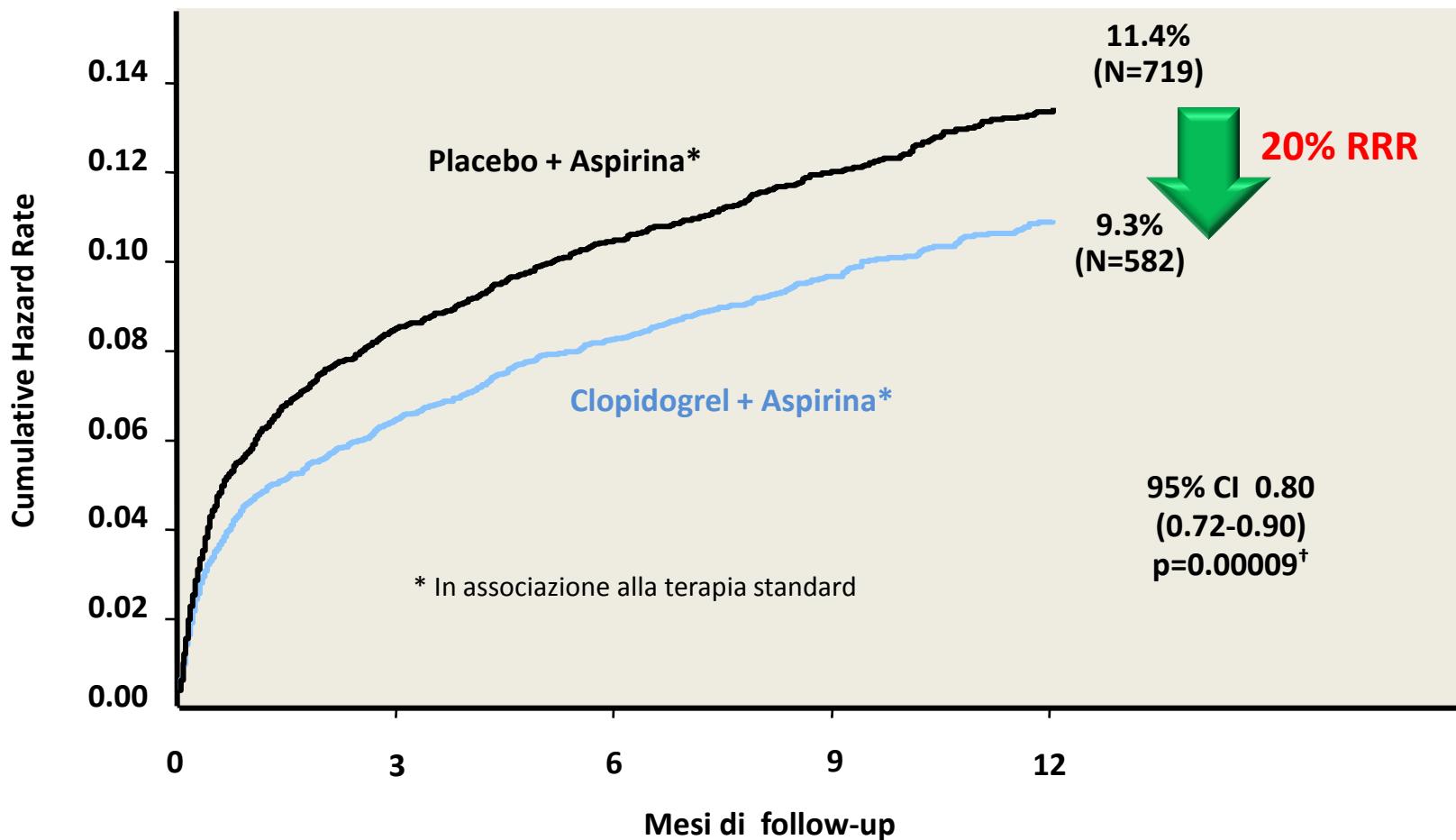


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| Aspirin is recommended for all patients without contraindications at an initial oral loading dose of 150–300 mg (in aspirin-naïve patients) and a maintenance dose of 75–100 mg/day long-term regardless of treatment strategy. | I | A | 129–132 |
| A P2Y12 inhibitor is recommended, in addition to aspirin, for 12 months unless there are contraindications such as excessive risk of bleeds. | I | A | Analysis from CURE PLATO TRITON-TIMI 38 |
| <ul style="list-style-type: none"> <input type="checkbox"/> Ticagrelor (180 mg loading dose, 90 mg twice daily) is recommended, in the absence of contraindications, for all patients at moderate-to-high risk of ischaemic events (e.g. elevated cardiac troponins), regardless of initial treatment strategy and including those pretreated with clopidogrel (which should be discontinued when ticagrelor is started). | I | B | PLATO |
| <ul style="list-style-type: none"> <input type="checkbox"/> Prasugrel (60 mg loading dose, 10 mg daily dose) is recommended in patients who are proceeding to PCI if no contraindication. | I | B | TRITON-TIMI 38, ACCOAST |
| <ul style="list-style-type: none"> <input type="checkbox"/> Clopidogrel (300–600 mg loading dose, 75 mg daily dose) is recommended for patients who cannot receive ticagrelor or prasugrel or who require oral anticoagulation. | I | B | Analysis from CURE |

NEWS!

ANTIAGGREGANTI PIASTRINICI INIBITORI INDIRETTI DI P2Y12: CLOPIDOGREL

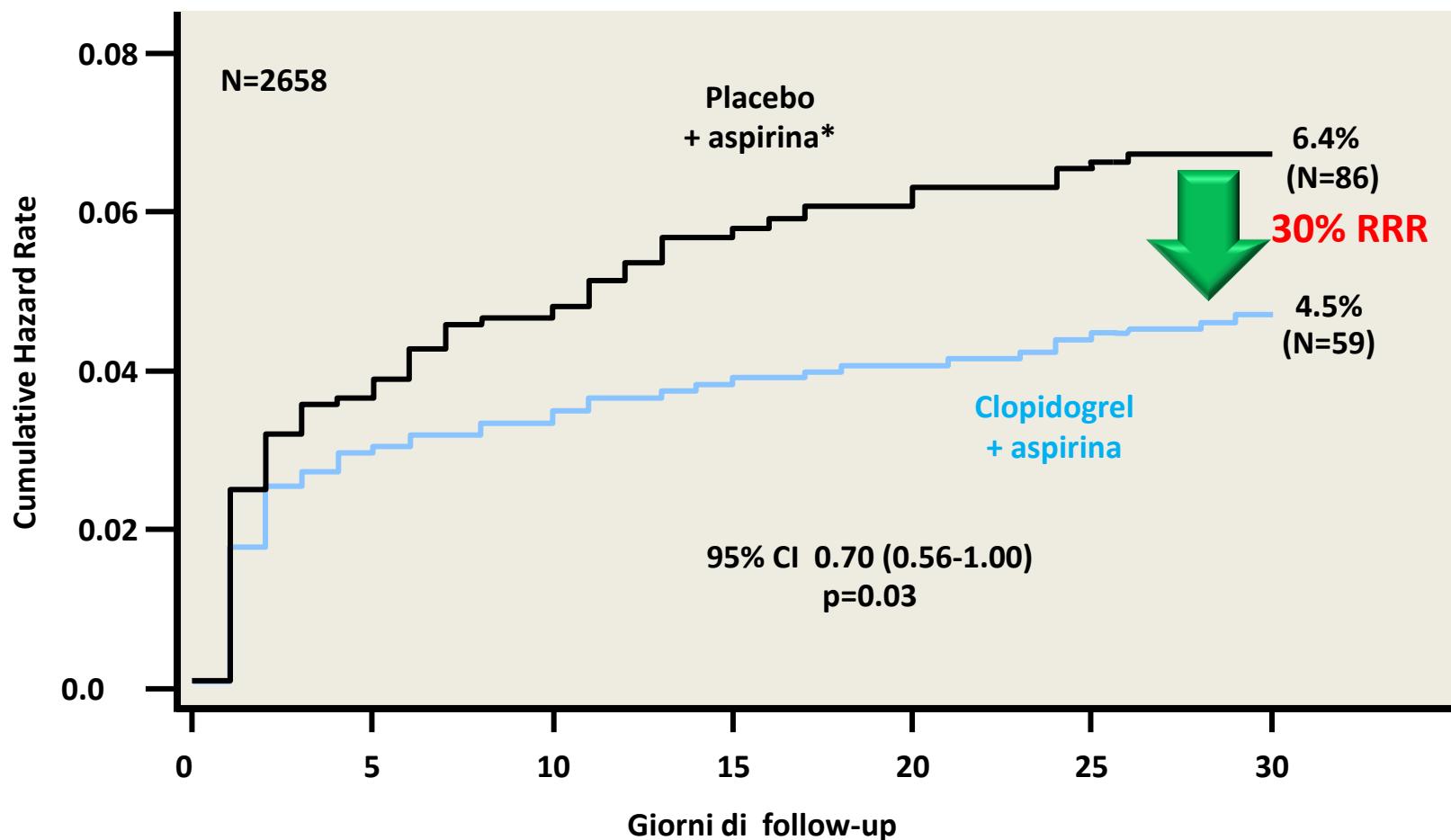
CURE End Point Primario a 12 mesi



[CURE Investigators](#). N Engl J Med 2001;345:494-502

ANTIAGGREGANTI PIASTRINICI INIBITORI INDIRETTI DI P2Y12: CLOPIDOGREL

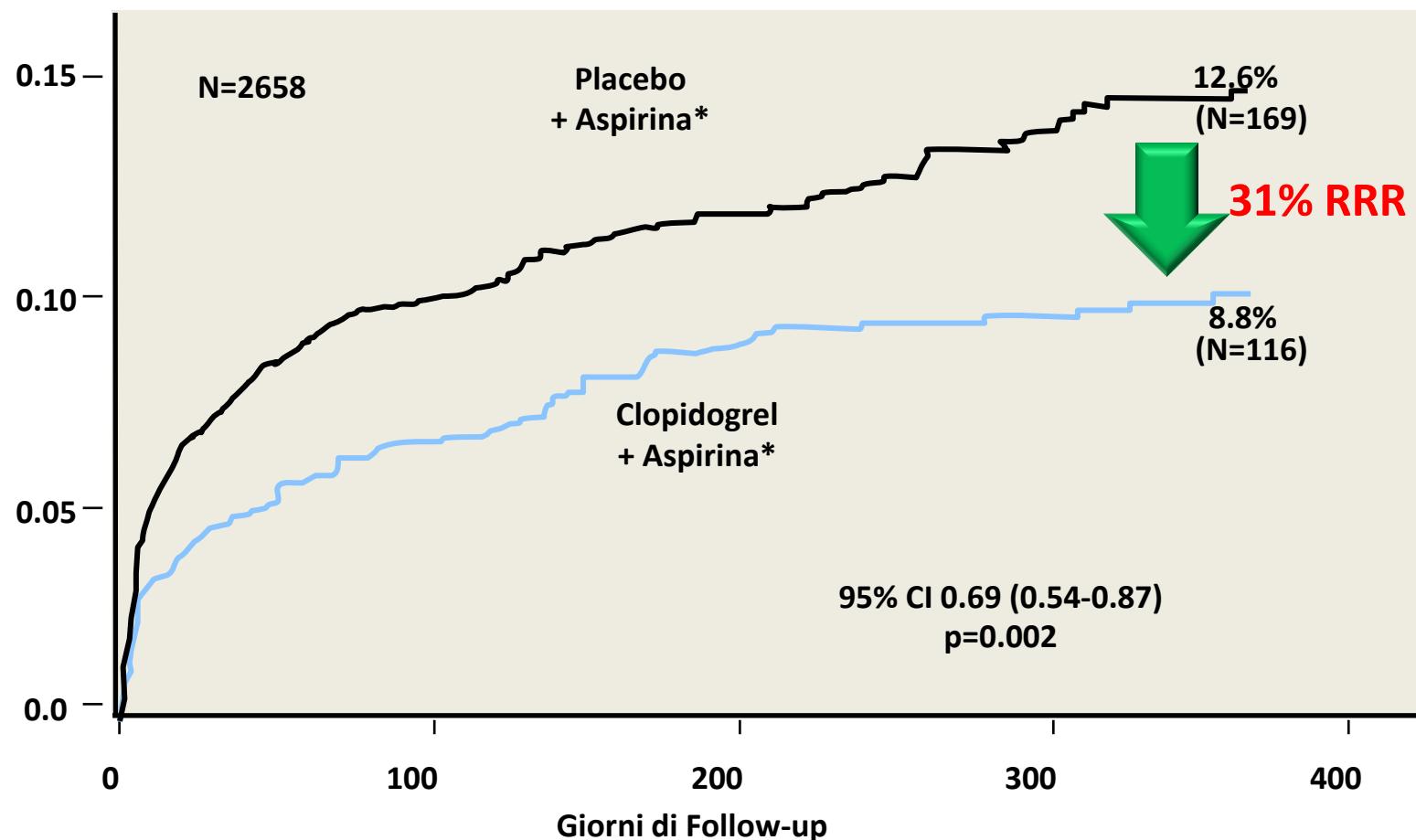
CURE End Point Primario: a 30 giorni dalla PCI



[Mehta SR](#) Lancet 2001;358:527-533

ANTIAGGREGANTI PIASTRINICI INIBITORI INDIRETTI DI P2Y12: CLOPIDOGREL

PCI-CURE End point composito alla fine del follow up

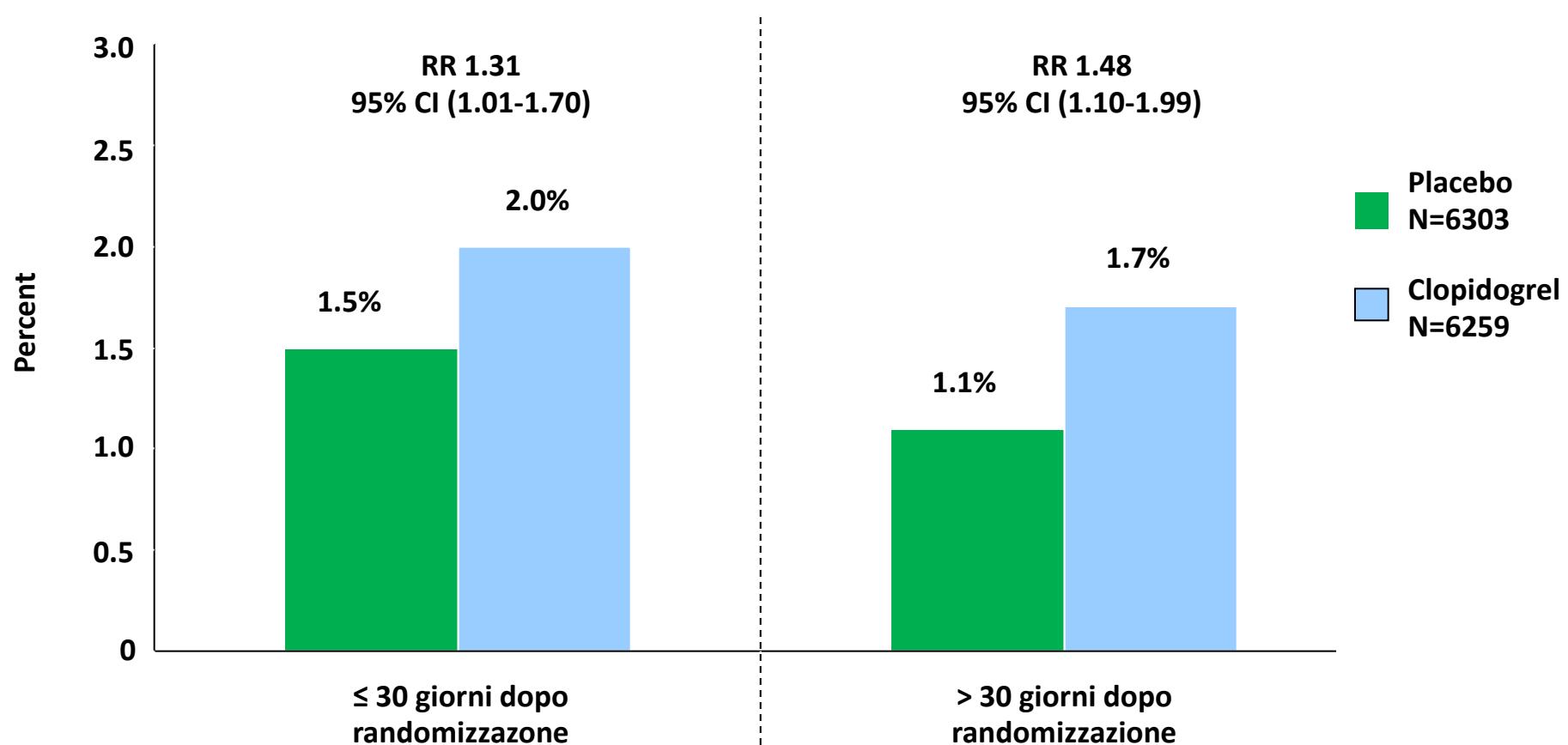


[CURE Investigators](#). *N Engl J Med* 2001;345:494-502

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ANTIAGGREGANTI PIASTRINICI INIBITORI INDIRETTI DI P2Y12: CLOPIDOGREL

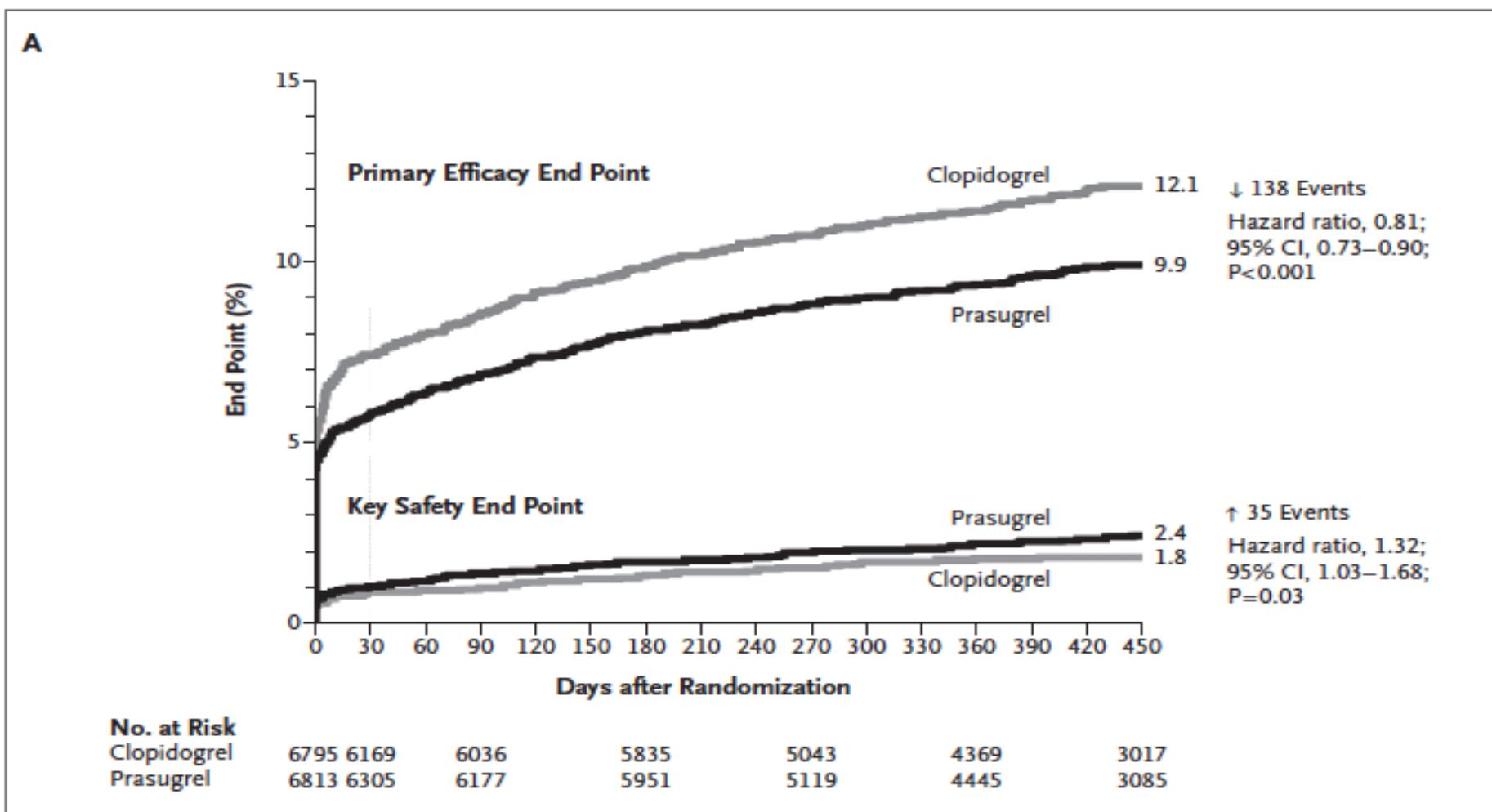
CURE Sanguinamenti Maggiori – precoci e tardivi



[CURE Investigators](#). *N Engl J Med* 2001;345:494-502

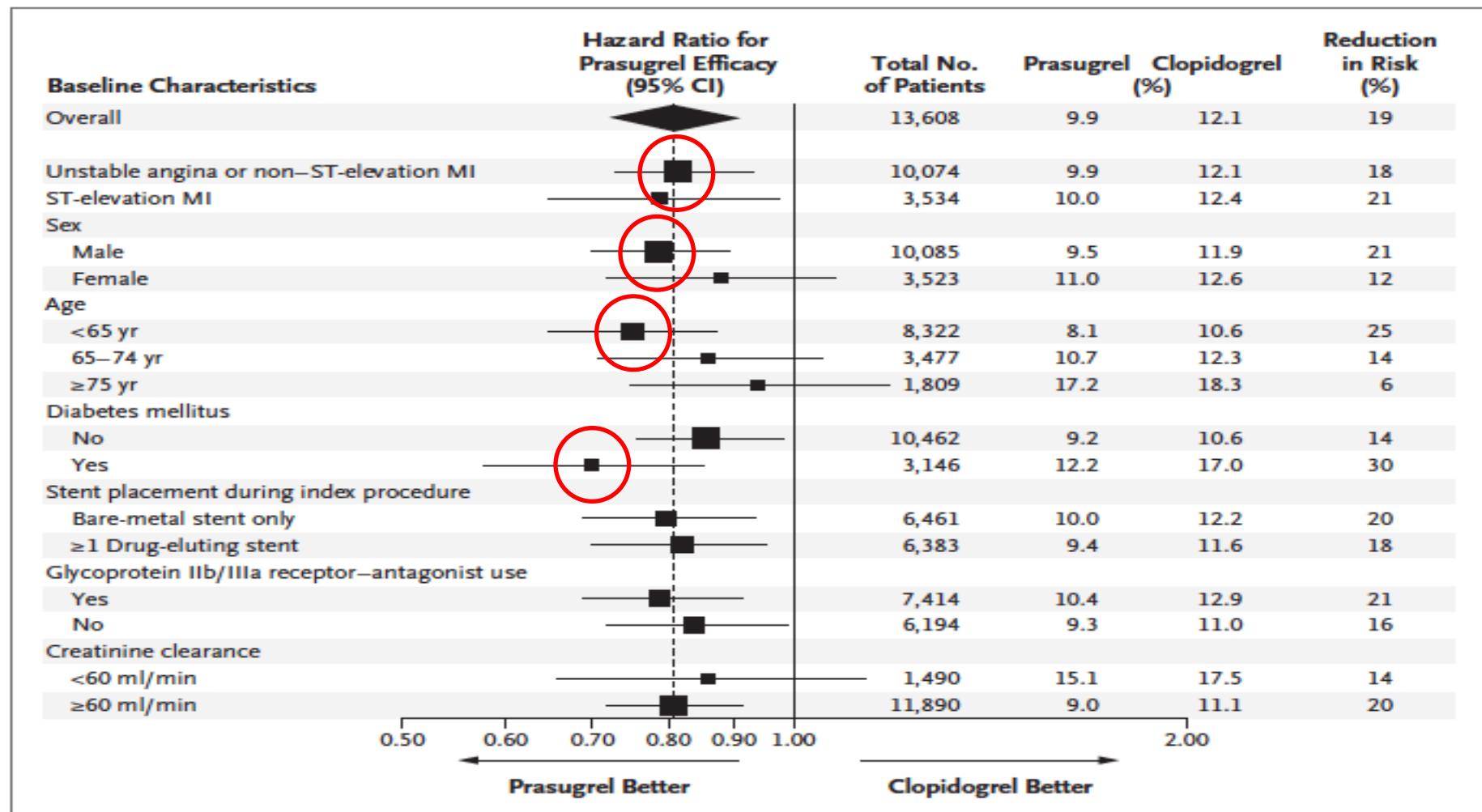
ANTIAGGREGANTI PIASTRINICI INIBITORI INDIRETTI DI P2Y12: PRASUGREL

TRITON-TIMI 38 End point primari di efficacia e sicurezza



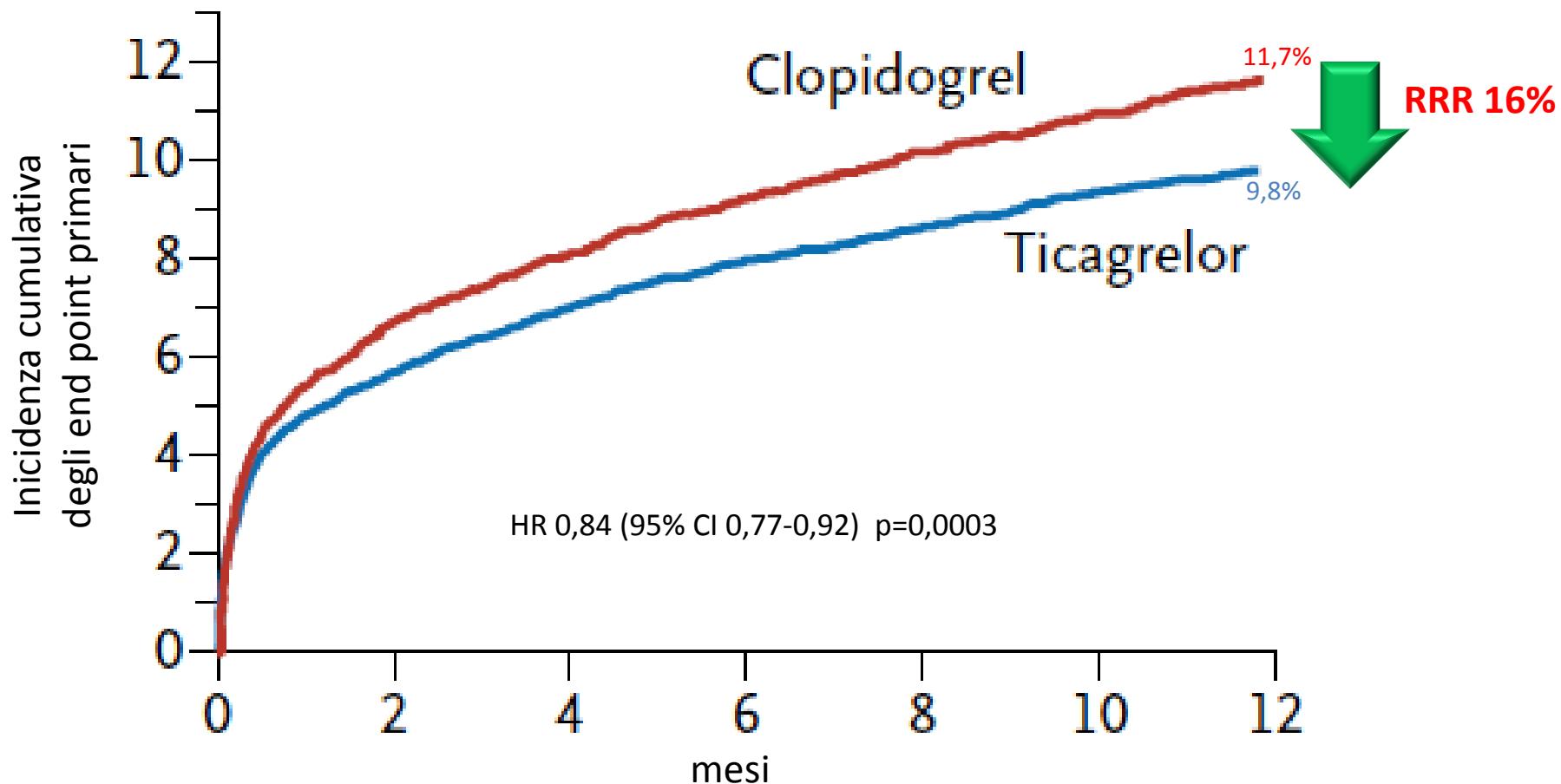
ANTIAGGREGANTI PIASTRINICI INIBITORI INDIRETTI DI P2Y12: PRASUGREL

TRITON-TIMI 38



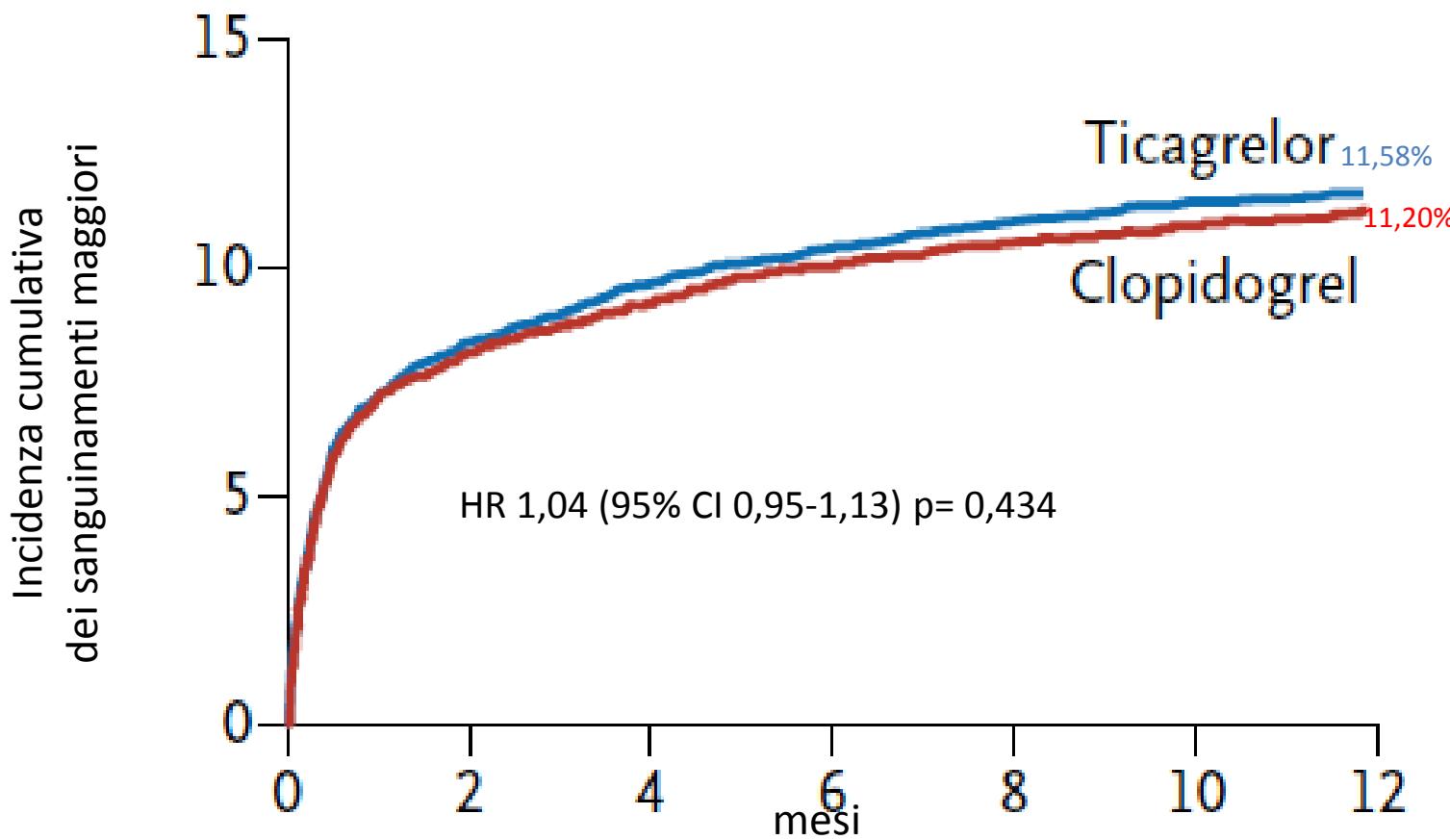
ANTIAGGREGANTI PIASTRINICI INIBITORI INDIRETTI DI P2Y12: TICAGRELOR

PLATO End point primario: morte cardiovascolare, IM e Stroke



ANTIAGGREGANTI PIASTRINICI INIBITORI INDIRETTI DI P2Y12: TICAGRELOR

PLATO End point: sanguinamenti maggiori

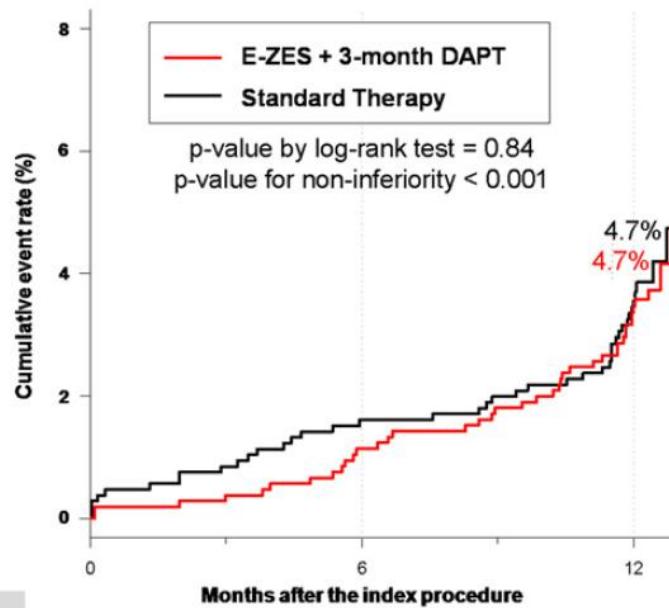
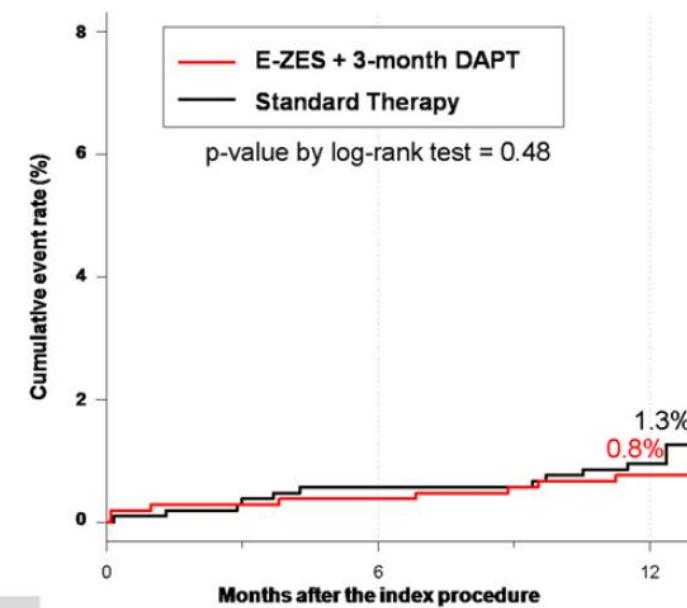


| Recommendations | Class | Level | Ref. |
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| <ul style="list-style-type: none"> <input type="checkbox"/> Prasugrel (60 mg loading dose, 10 mg daily dose) is recommended in patients who are proceeding to PCI if no contraindication. | I | B | TRITON-TIMI 38, ACCOAST |
| <ul style="list-style-type: none"> <input type="checkbox"/> Clopidogrel (300–600 mg loading dose, 75 mg daily dose) is recommended for patients who cannot receive ticagrelor or prasugrel or who require oral anticoagulation. | I | B | Analysis from CURE |
| P2Y12 inhibitor administration for a shorter duration of 3–6 months after DES implantation may be considered in patients deemed at high bleeding risk. | IIb | A | RESET (2012) OPTIMIZE (2013) EXCELLENT (2012) ISAR-SAFE (2015) |

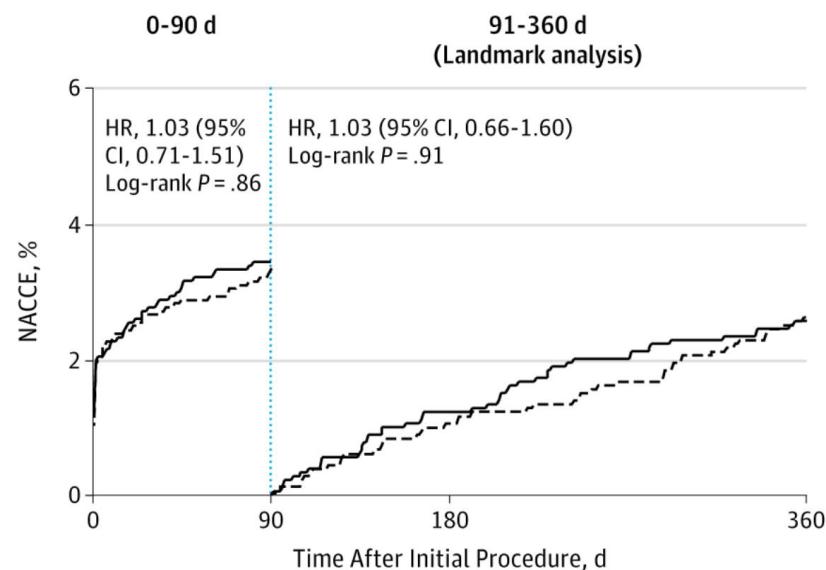
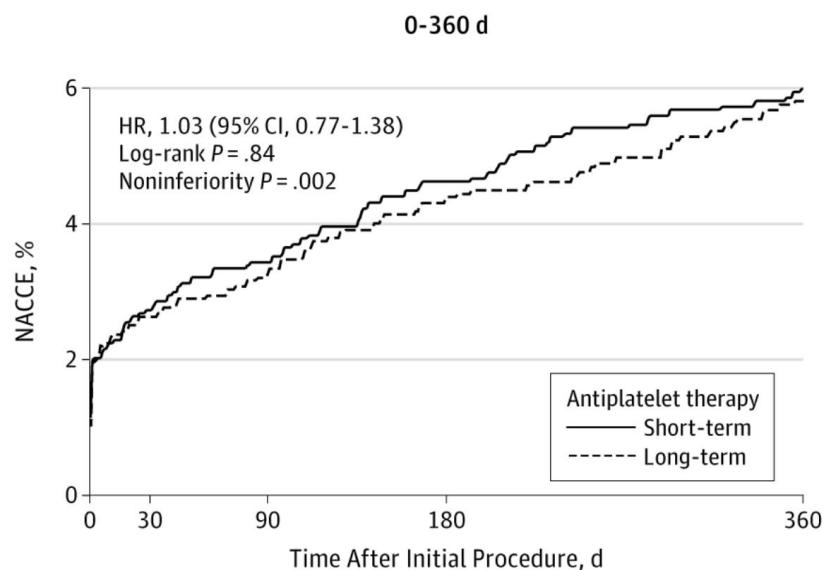
NEWS!

A New Strategy for Discontinuation of Dual Antiplatelet Therapy

The RESET Trial (REal Safety and Efficacy of 3-month dual antiplatelet Therapy following Endeavor zotarolimus-eluting stent implantation)

A**B**

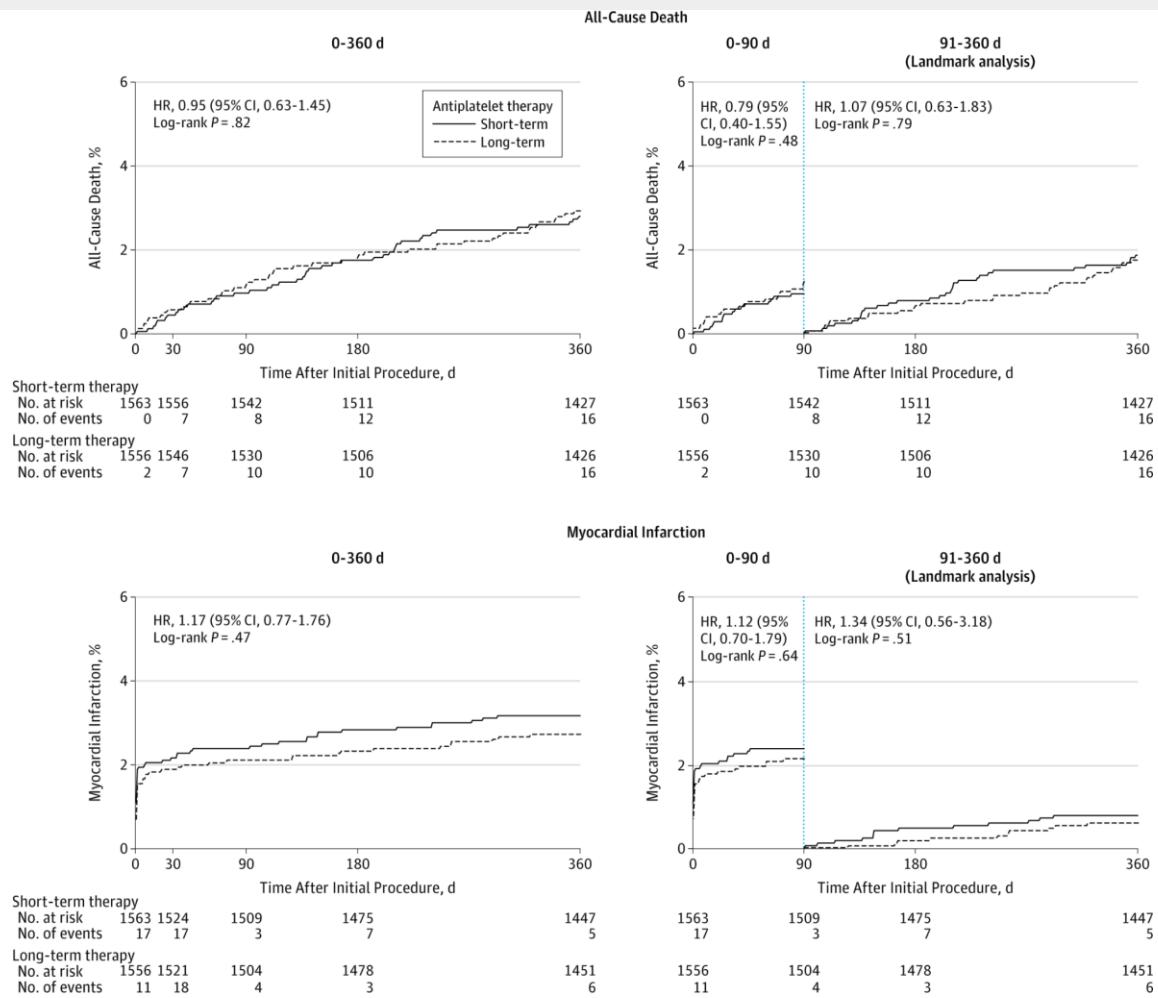
The OPTIMIZE Randomized Trial



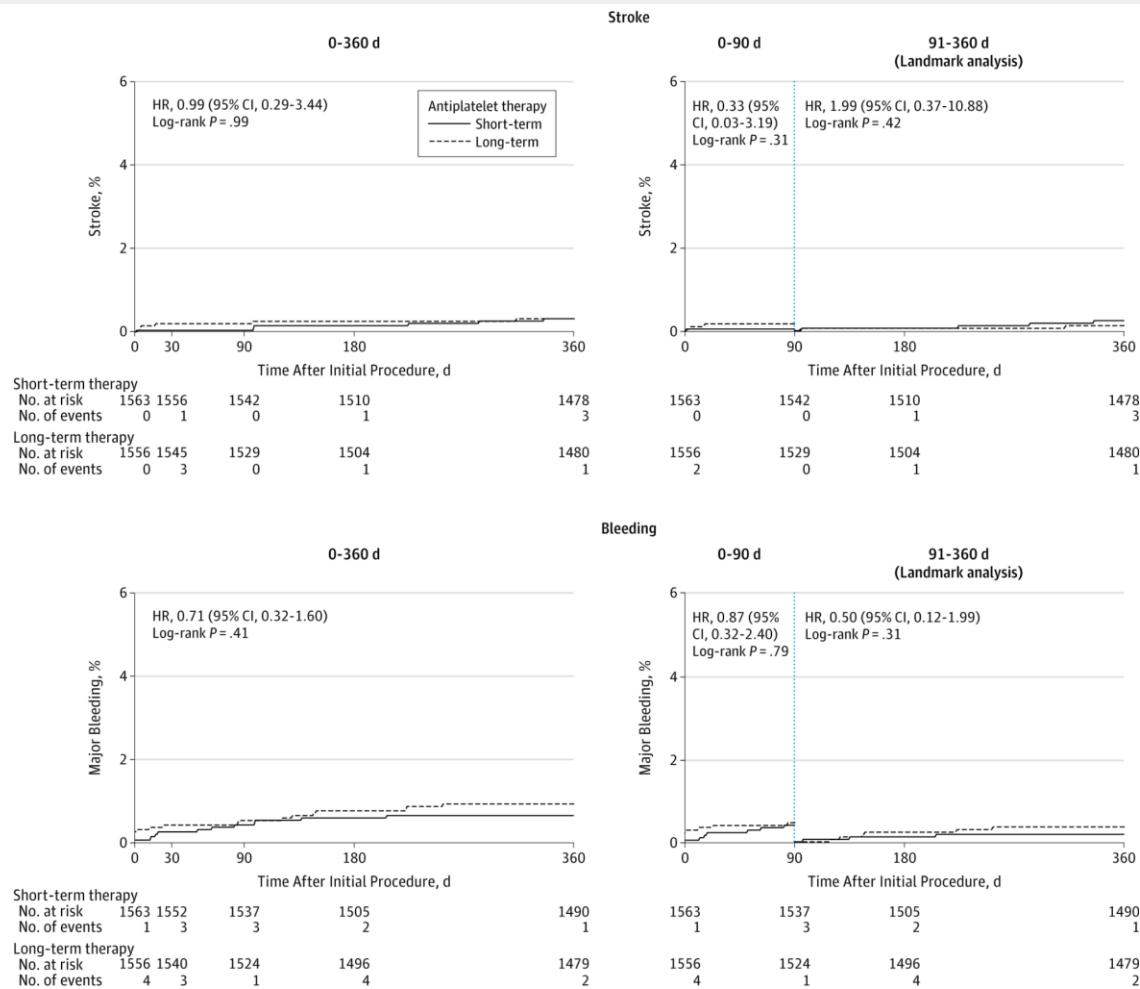
| Short-term therapy | | | | |
|--------------------|------|------|------|------|
| No. at risk | 1563 | 1520 | 1504 | 1468 |
| No. of events | 18 | 25 | 11 | 18 |
| Long-term therapy | | | | |
| No. at risk | 1556 | 1514 | 1497 | 1466 |
| No. of events | 16 | 25 | 11 | 16 |

| | | | | | | | |
|------|----|------|----|------|----|------|----|
| 1563 | 18 | 1504 | 11 | 1468 | 18 | 1384 | 21 |
| 1556 | 16 | 1497 | 11 | 1466 | 16 | 1381 | 22 |

The OPTIMIZE Randomized Trial

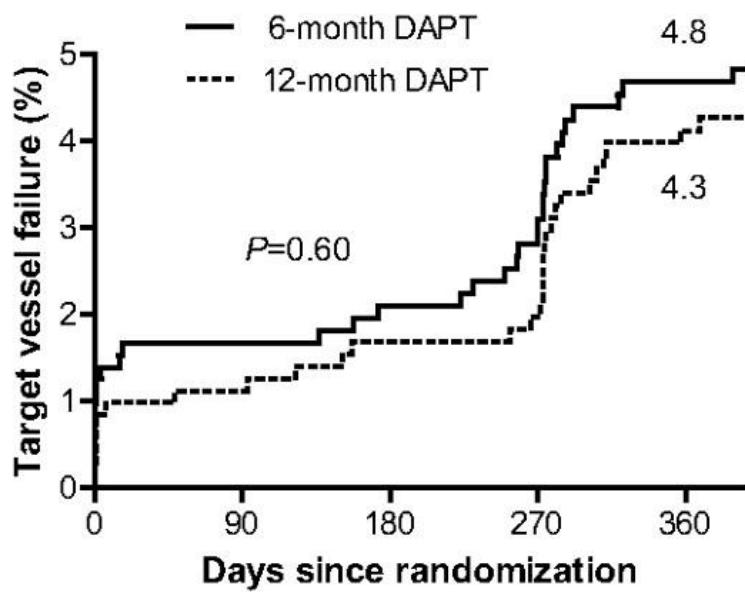


The OPTIMIZE Randomized Trial

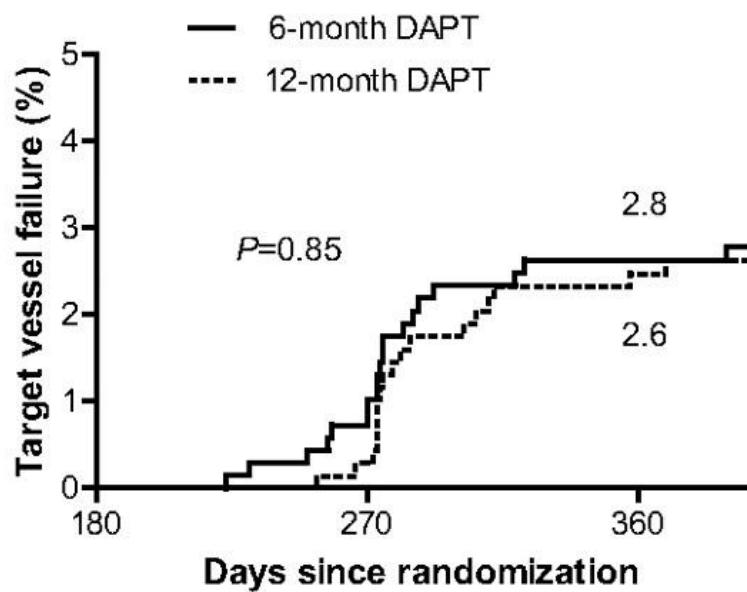


EXCELLENT Study

A



B



| | | | | | |
|---------------|-----|-----|-----|-----|-----|
| 6-month DAPT | 722 | 692 | 686 | 680 | 663 |
| 12-month DAPT | 721 | 697 | 692 | 687 | 668 |

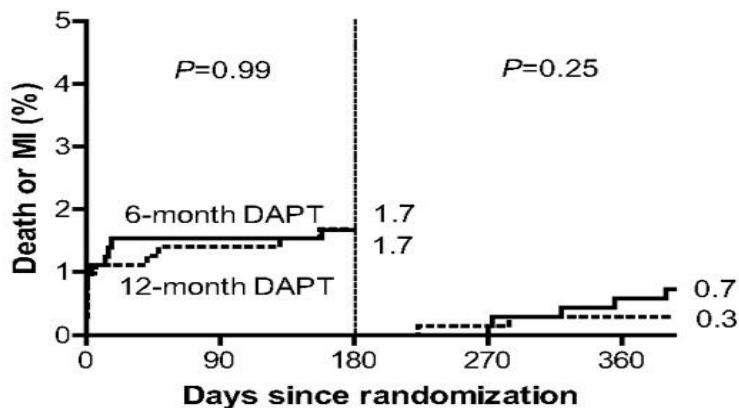
| | | | |
|---------------|-----|-----|-----|
| 6-month DAPT | 686 | 680 | 663 |
| 12-month DAPT | 692 | 687 | 668 |



American
Heart
Association®

EXCELLENT Study

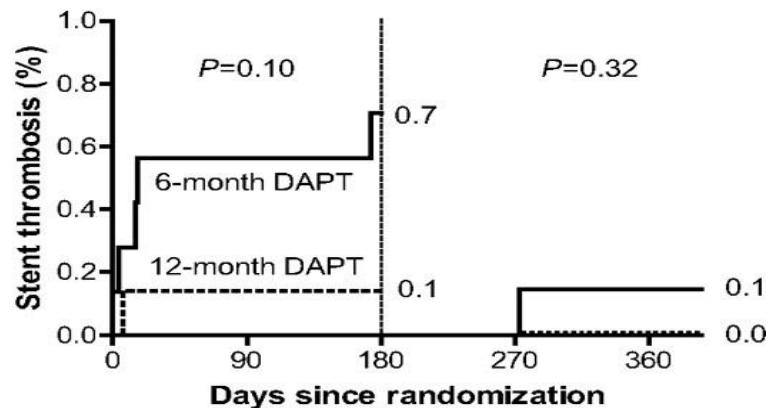
A



| | 722 | 693 | 689 | 688 | 681 |
|--------------|-----|-----|-----|-----|-----|
| 6-month DAPT | 722 | 693 | 689 | 688 | 681 |

| | 721 | 696 | 694 | 691 | 686 |
|---------------|-----|-----|-----|-----|-----|
| 12-month DAPT | 721 | 696 | 694 | 691 | 686 |

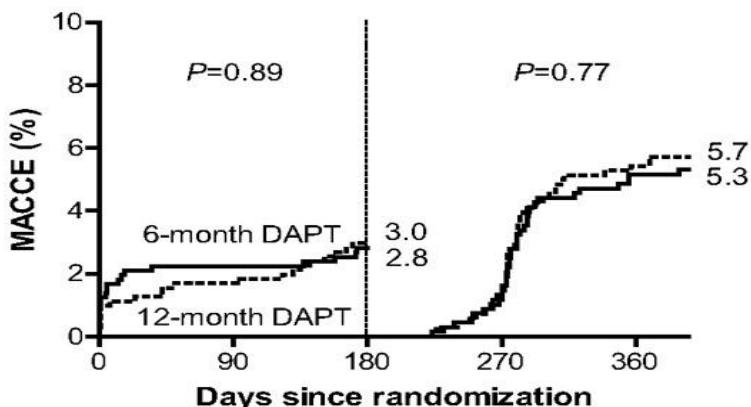
B



| | 722 | 699 | 695 | 694 | 688 |
|--------------|-----|-----|-----|-----|-----|
| 6-month DAPT | 722 | 699 | 695 | 694 | 688 |

| | 721 | 703 | 701 | 698 | 694 |
|---------------|-----|-----|-----|-----|-----|
| 12-month DAPT | 721 | 703 | 701 | 698 | 694 |

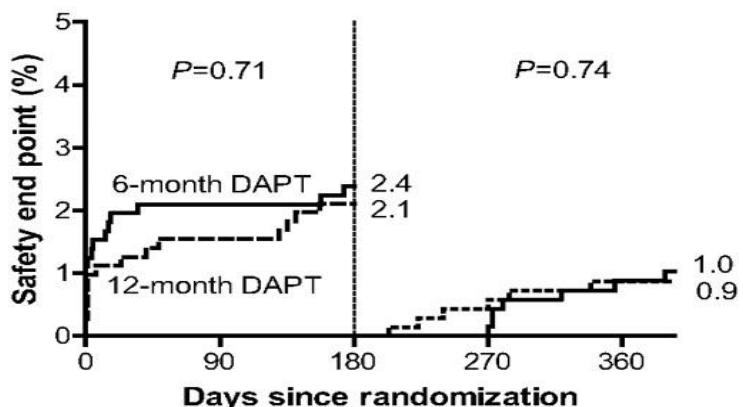
C



| | 722 | 689 | 682 | 672 | 643 |
|--------------|-----|-----|-----|-----|-----|
| 6-month DAPT | 722 | 689 | 682 | 672 | 643 |

| | 721 | 695 | 686 | 676 | 643 |
|---------------|-----|-----|-----|-----|-----|
| 12-month DAPT | 721 | 695 | 686 | 676 | 643 |

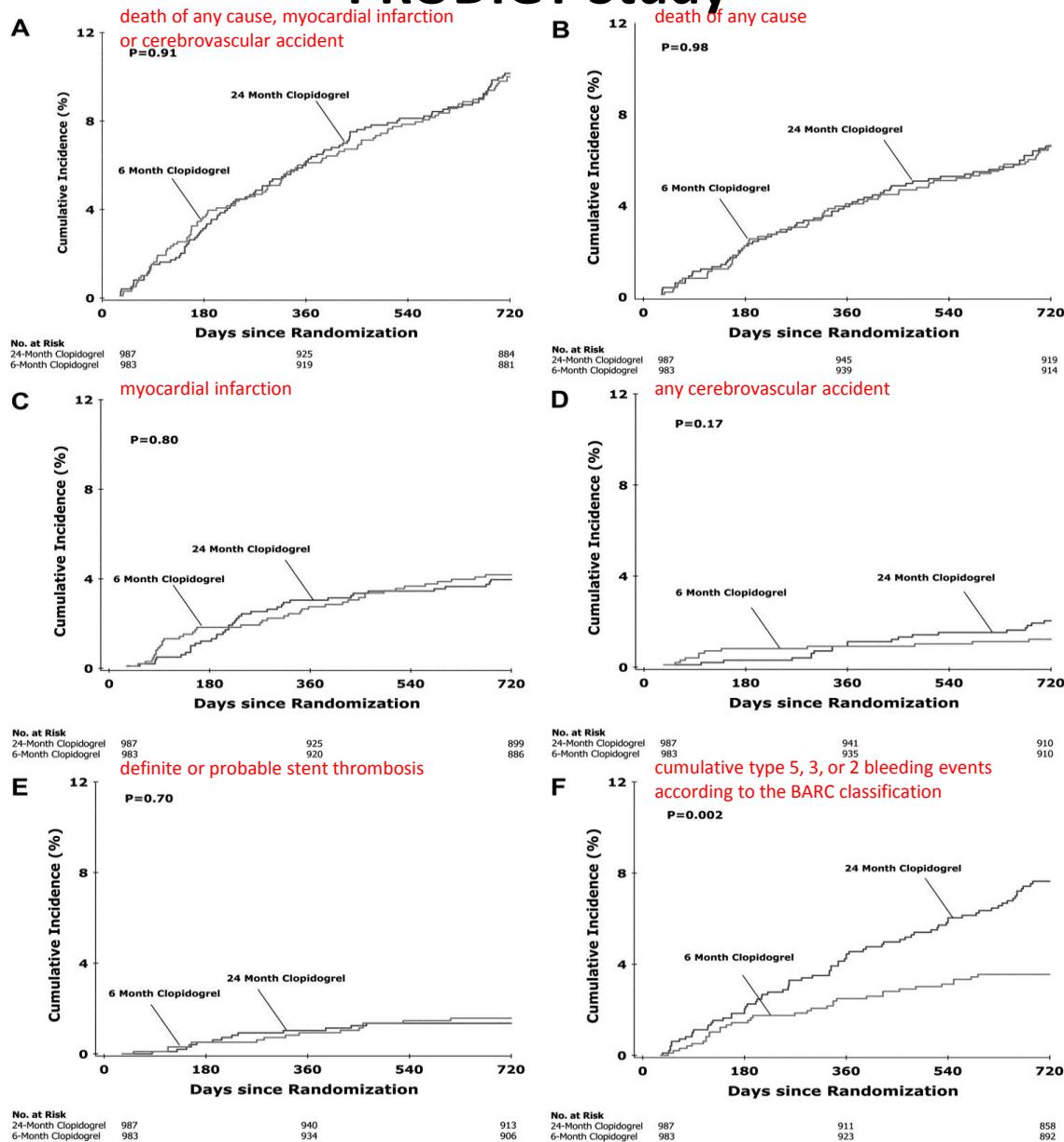
D



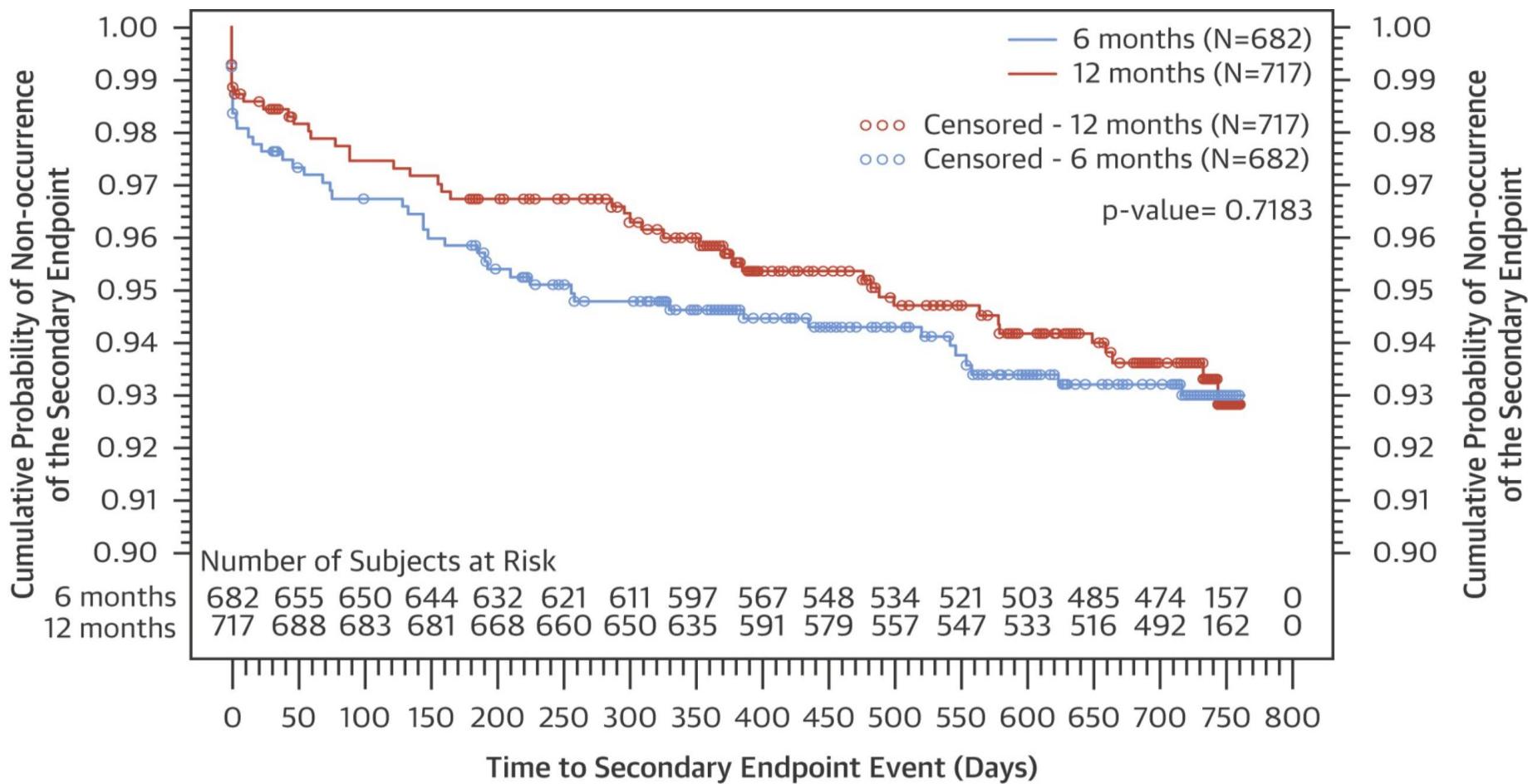
| | 722 | 690 | 685 | 684 | 675 |
|--------------|-----|-----|-----|-----|-----|
| 6-month DAPT | 722 | 690 | 685 | 684 | 675 |

| | 721 | 696 | 692 | 687 | 680 |
|---------------|-----|-----|-----|-----|-----|
| 12-month DAPT | 721 | 696 | 692 | 687 | 680 |

PRODIGY Study



The SECURITY Randomized Clinical Trial



| Recommendations | Class | Level | Ref. |
|--|-------|-------|---|
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| <input type="checkbox"/> Prasugrel (60 mg loading dose, 10 mg daily dose) is recommended in patients who are proceeding to PCI if no contraindication. | I | B | TRITON-TIMI 38, ACCOAST |
| <input type="checkbox"/> Clopidogrel (300–600 mg loading dose, 75 mg daily dose) is recommended for patients who cannot receive ticagrelor or prasugrel or who require oral anticoagulation. | I | B | Analysis from CURE |
| P2Y12 inhibitor administration for a shorter duration of 3–6 months after DES implantation may be considered in patients deemed at high bleeding risk. | IIb | A | RESET (2012) OPTIMIZE (2013) EXCELLENT (2012) ISAR-SAFE (2015) |
| It is not recommended to administer prasugrel in patients in whom coronary anatomy is not known. | III | B | ACCOAST |



Background

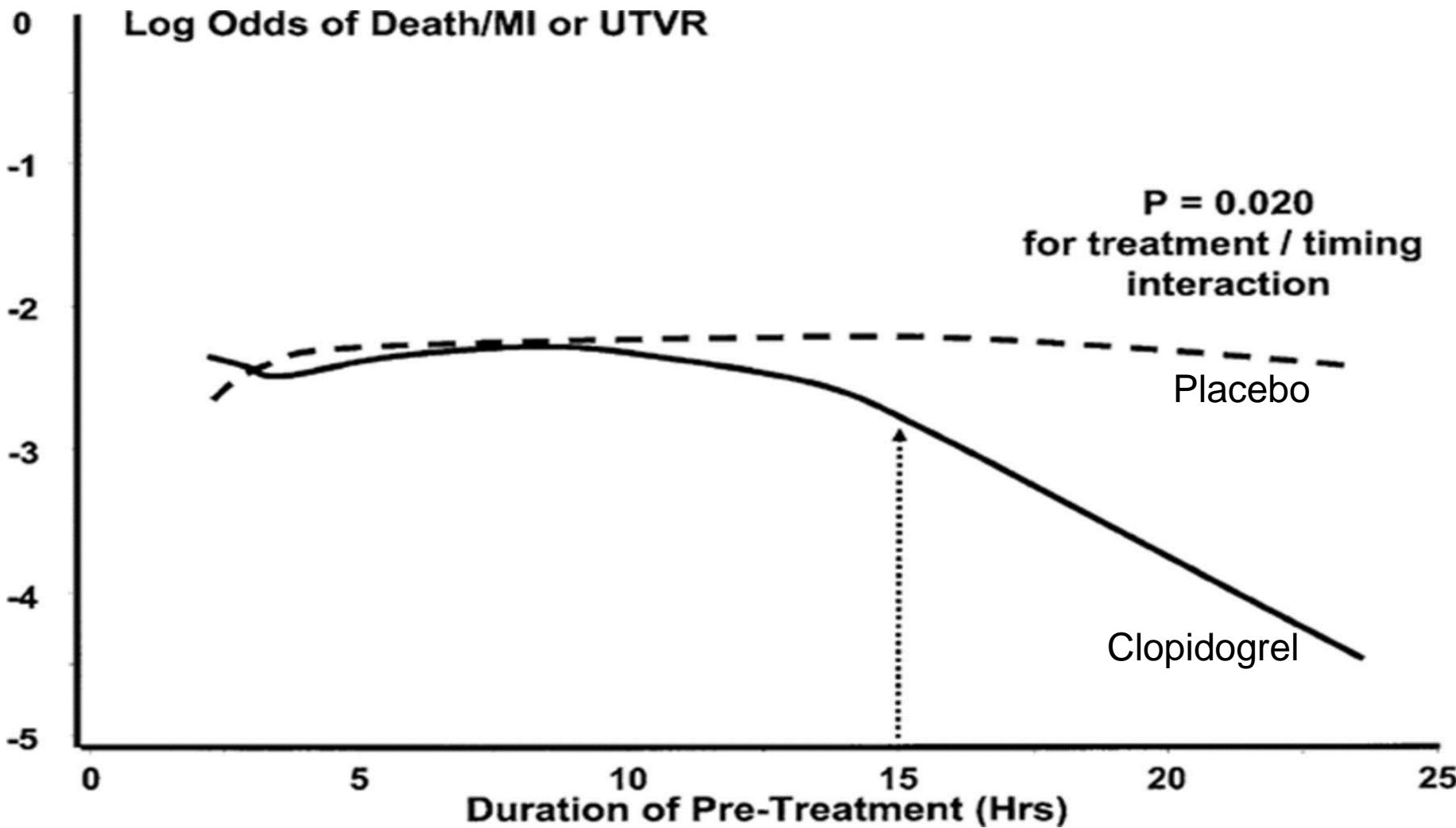
| Title | Citation | | Class | LOE |
|---|---|--|-------------|-------------|
| 2011 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation | European Heart Journal 2011;32:2999–3054 | “A P2Y ₁₂ inhibitor as soon as possible ” Clopidogrel 600mg Ticagrelor | I I I | A B B |
| 2010 ESC/EACTS guidelines on myocardial revascularization | European Heart Journal 2010;31:20:2501–2555 | “Clopidogrel 600mg as soon as possible ” | I | C |



Background

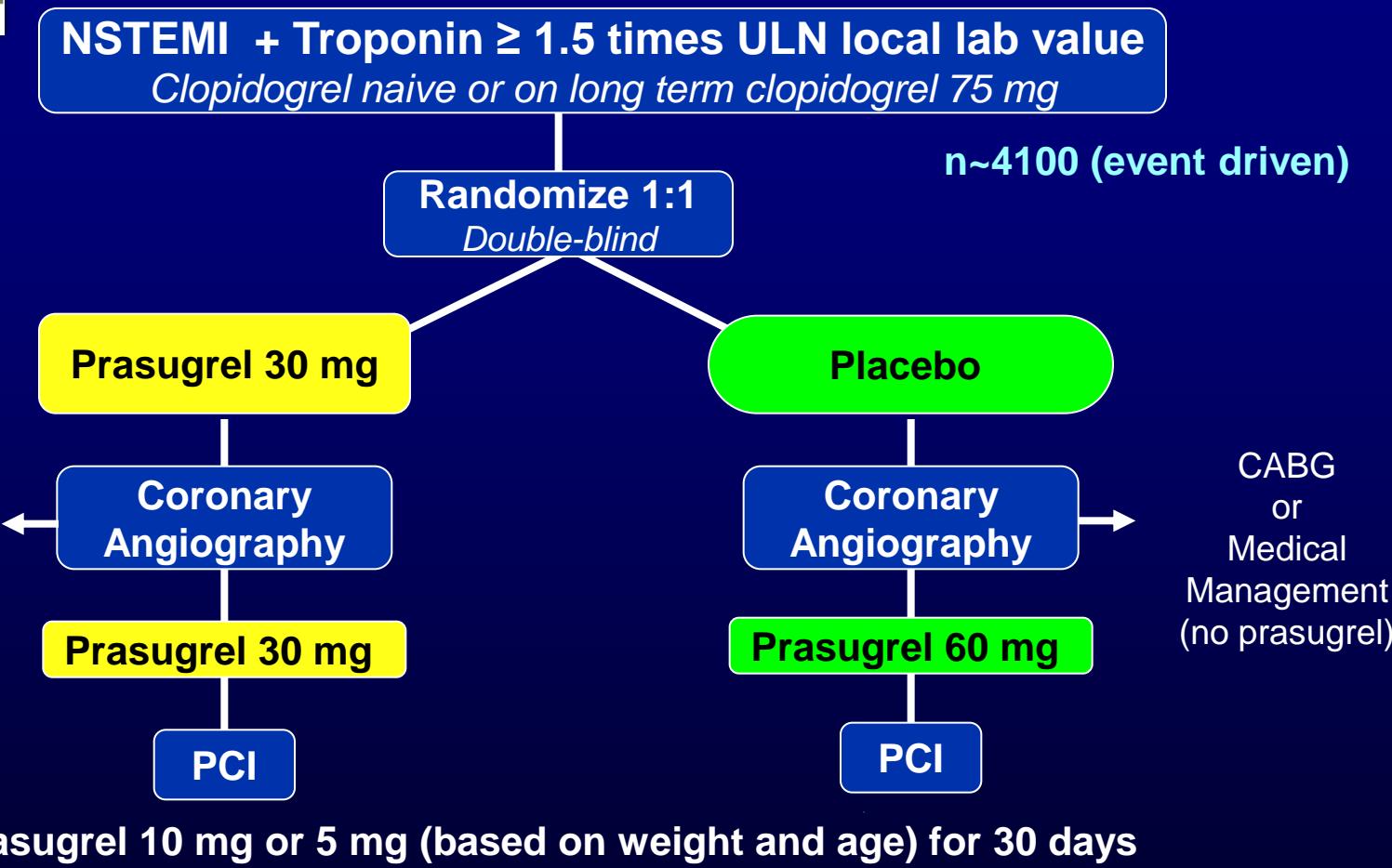
- Pre-treatment with aspirin and a P2Y₁₂ antagonist has been a class I recommendation and common practice for the treatment of NSTE-ACS
- However, no trial has ever randomized patients presenting with NSTE-ACS, invasively managed, to pre-treatment with clopidogrel, prasugrel or ticagrelor vs. no pre-treatment.

Relationship between the duration of clopidogrel treatment before percutaneous coronary intervention and log odds of the primary end point in the Clopidogrel for the Reduction of Events During Observation (CREDO) Trial.



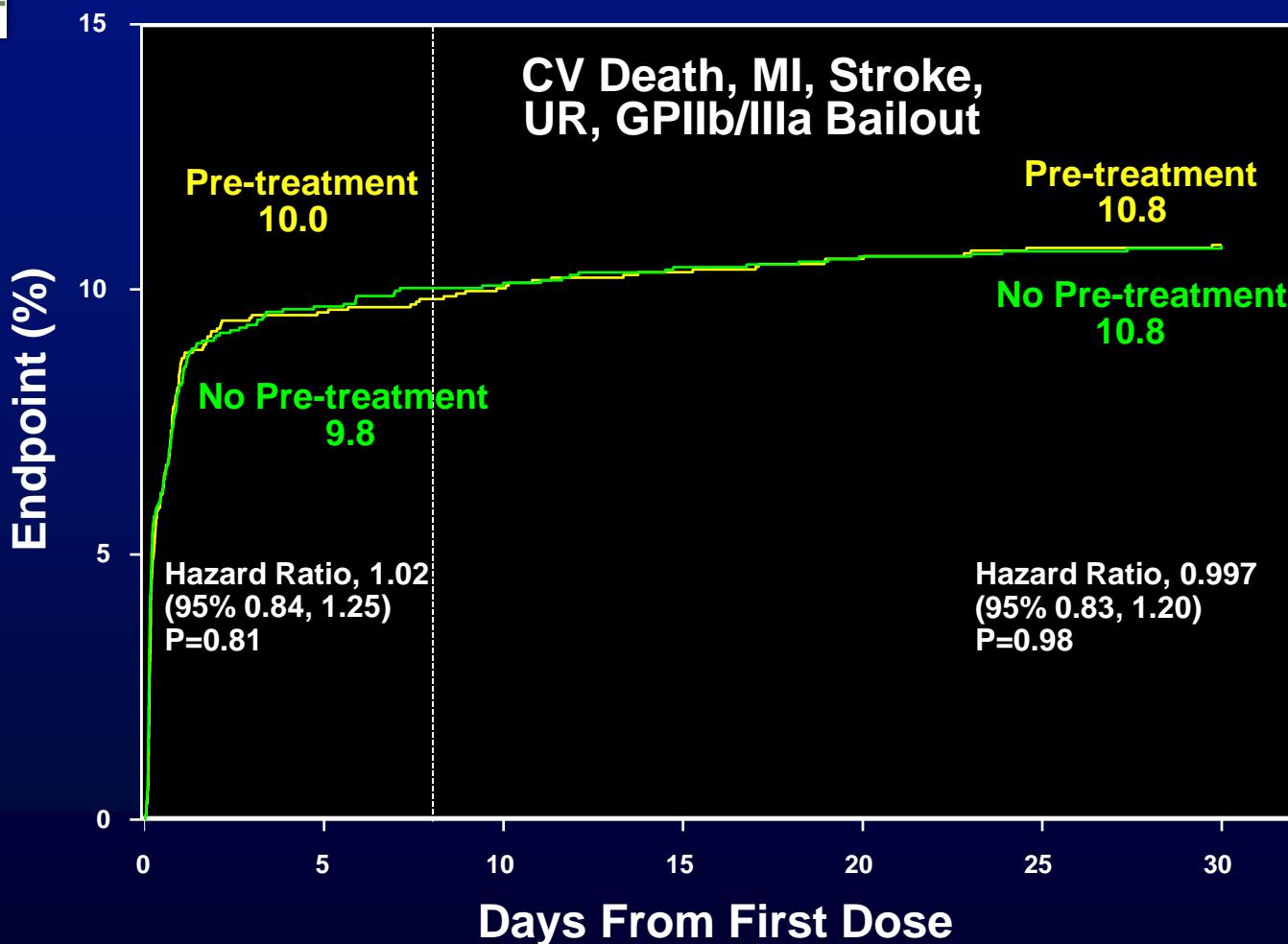


ACCOAST design



1° Endpoint: CV Death, MI, Stroke, Urg Revasc, GP IIb/IIIa bailout, at 7 days

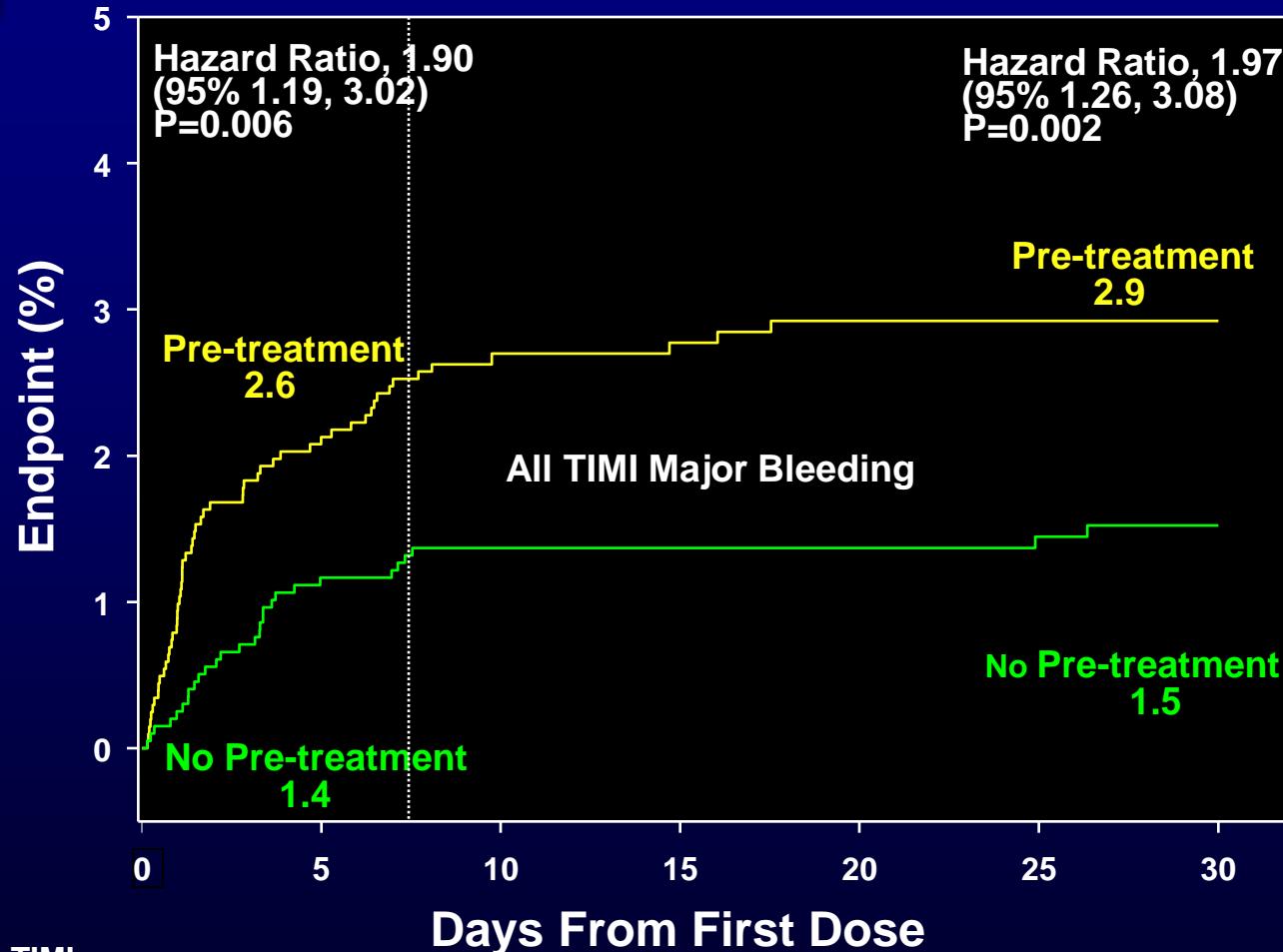
1° Efficacy End Point @ 7 + 30 days (All Patients)



No. at Risk, Primary
Efficacy End Point:

| | | | | | | | |
|------------------|------|------|------|------|------|------|------|
| No pre-treatment | 1996 | 1788 | 1775 | 1769 | 1762 | 1752 | 1621 |
| Pre-treatment | 2037 | 1821 | 1809 | 1802 | 1797 | 1791 | 1616 |

All TIMI (CABG or non-CABG) Major Bleeding (All Treated patients)



No. at Risk, All TIMI

Major Bleeding:

No pre-treatment

1996

1947

1328

1297

1288

1284

1263

Pre-treatment

2037

1972

1339

1310

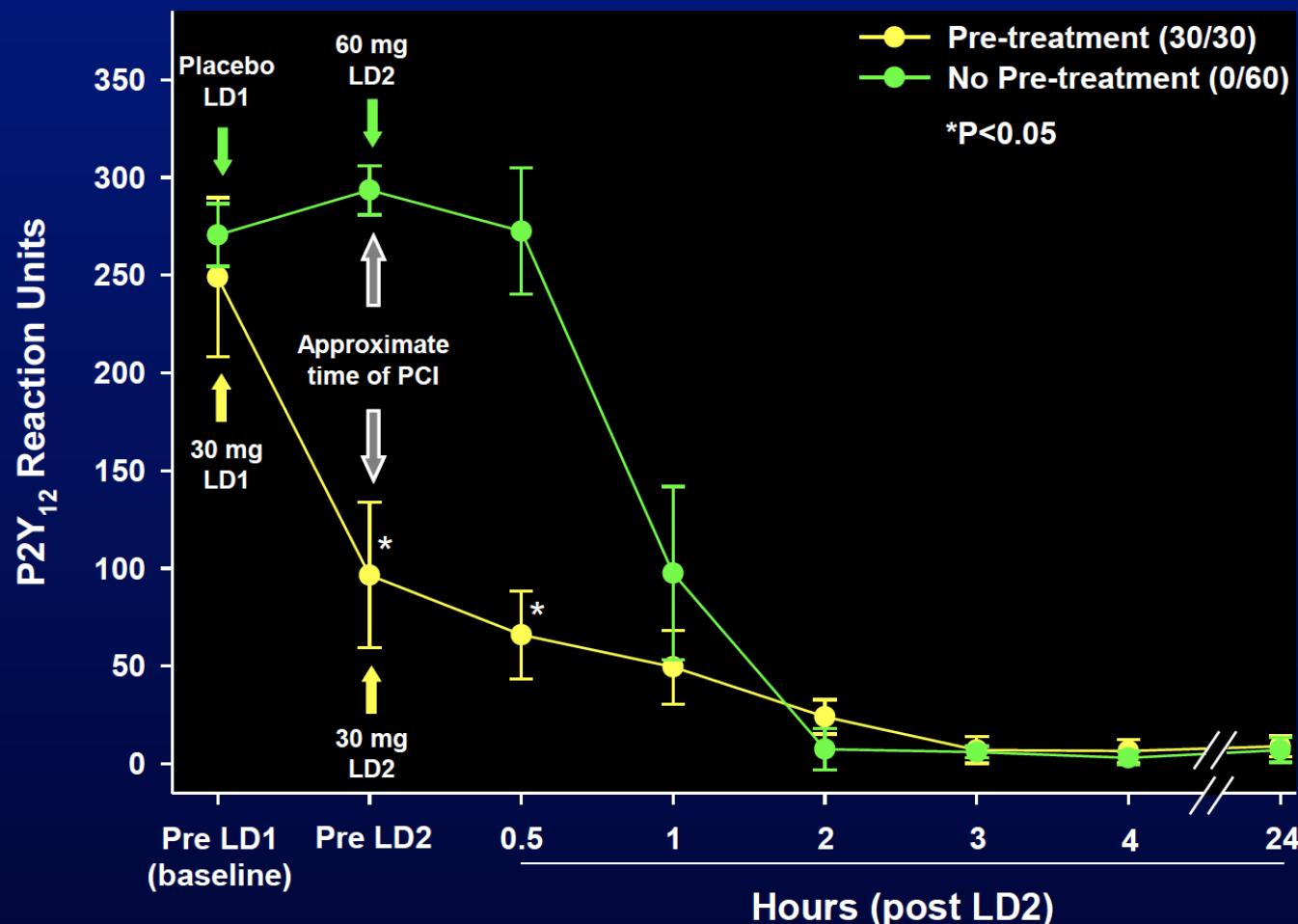
1299

1297

1280



Pharmacodynamic Sub-Study



Data presented as median \pm SEM. * p<0.05 relative to the No pre-treatment group. LD = loading dose.
Pretreatment=Prasugrel 30 mg/Prasugrel 30 mg; No Pre-treatment=Placebo/Prasugrel 60 mg

A realistic and pragmatic approach would be to make the decision to initiate P2Y12 receptor inhibitor prior to defining the revascularization strategy according to the intended agent and expected delay to obtaining angiography. In patients with a short delay (< 24–48 hours) from admission to angiography, pretreatment should be avoided; in patients with a delay from admission to angiography of > 48 hours, pretreatment with either clopidogrel (on the basis of old data) or ticagrelor (without data) may be considered.

Prof. Jean-Philippe Collet (FR)

The new insights provided by the ACCOAST trials have important every-day practical implications: in patients with an intermediate risk and a short delay (< 24) from admission to angiography, pretreatment should be avoided; in high-risk patients with a delay from admission to angiography of > 24 hours, pretreatment with either clopidogrel (on the basis of old data) or ticagrelor (without data) may be considered.

Dr Leonardo Bolognese, MD, FESC (IT)

| Recommendations | Class | Level | Ref. |
|--|-------|-------|------------------------------------|
| Intravenous antiplatelet therapy | | | |
| GPIIb/IIIa inhibitors during PCI should be considered for bailout situations or thrombotic complications. | IIa | C | |
| Cangrelor may be considered in P2Y12 inhibitor-naive patients undergoing PCI. | IIb | A | CHAMPION-PCI CHAMPION PLATFORM |
| It is not recommended to administer GPIIb/IIIa inhibitors in patients in whom coronary anatomy is not known. | III | A | ACUITY (2007), EARLY ACS (2009) |

NEWS!

| Recommendations | Class | Level | Ref. |
|--|-------|-------|---|
| Long-term P2Y12 inhibition | | | |
| P2Y12 inhibitor administration in addition to aspirin beyond 1 year may be considered after careful assessment of the ischaemic and bleeding risks of the patient. | IIb | A | DAPT (2014), PEGASUS-TIMI 54 (2015) |

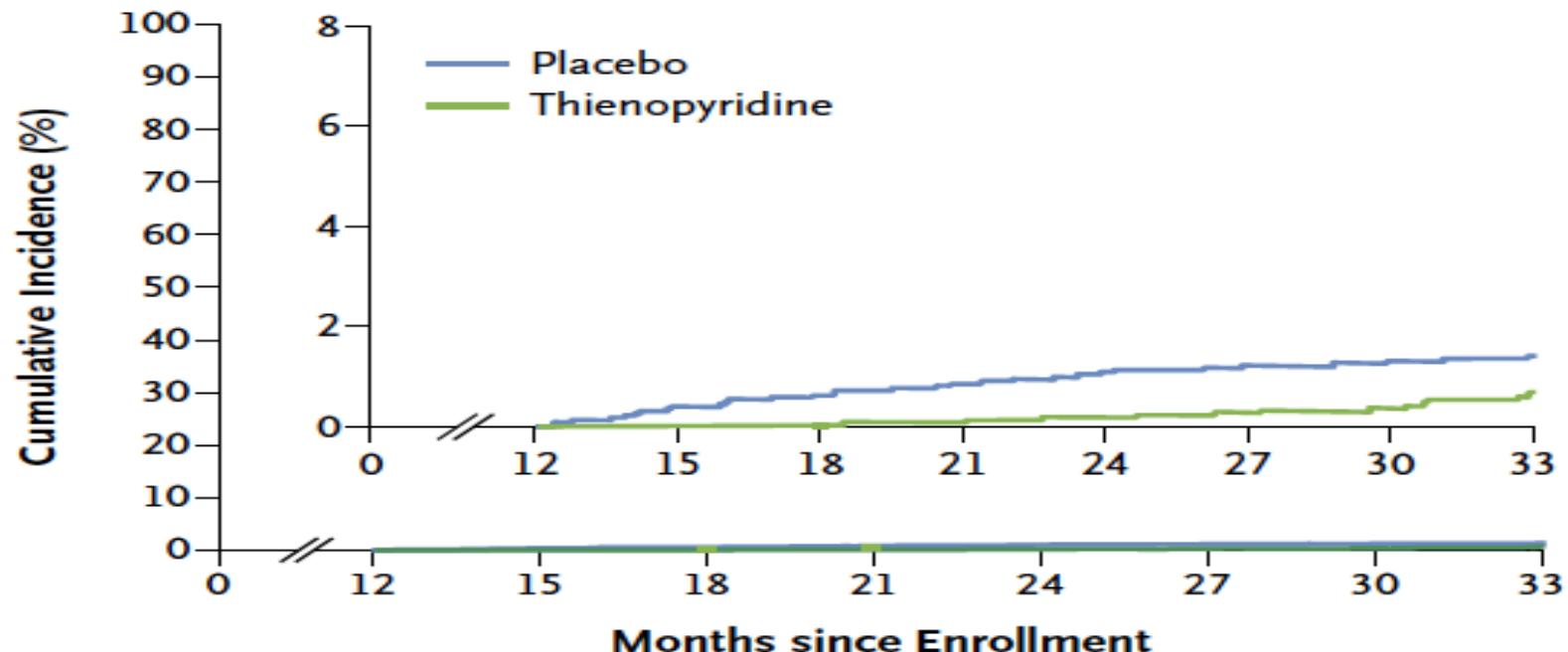
NEWS!

Twelve or 30 Months of Dual Antiplatelet Therapy after Drug-Eluting Stents DAPT Study

Stent Thrombosis

12–30 mo Thienopyridine vs. placebo, 0.4% vs. 1.4%;
hazard ratio, 0.29; $P<0.001$

12–33 mo Thienopyridine vs. placebo, 0.7% vs. 1.4%;
hazard ratio, 0.45; $P<0.001$



No. at Risk

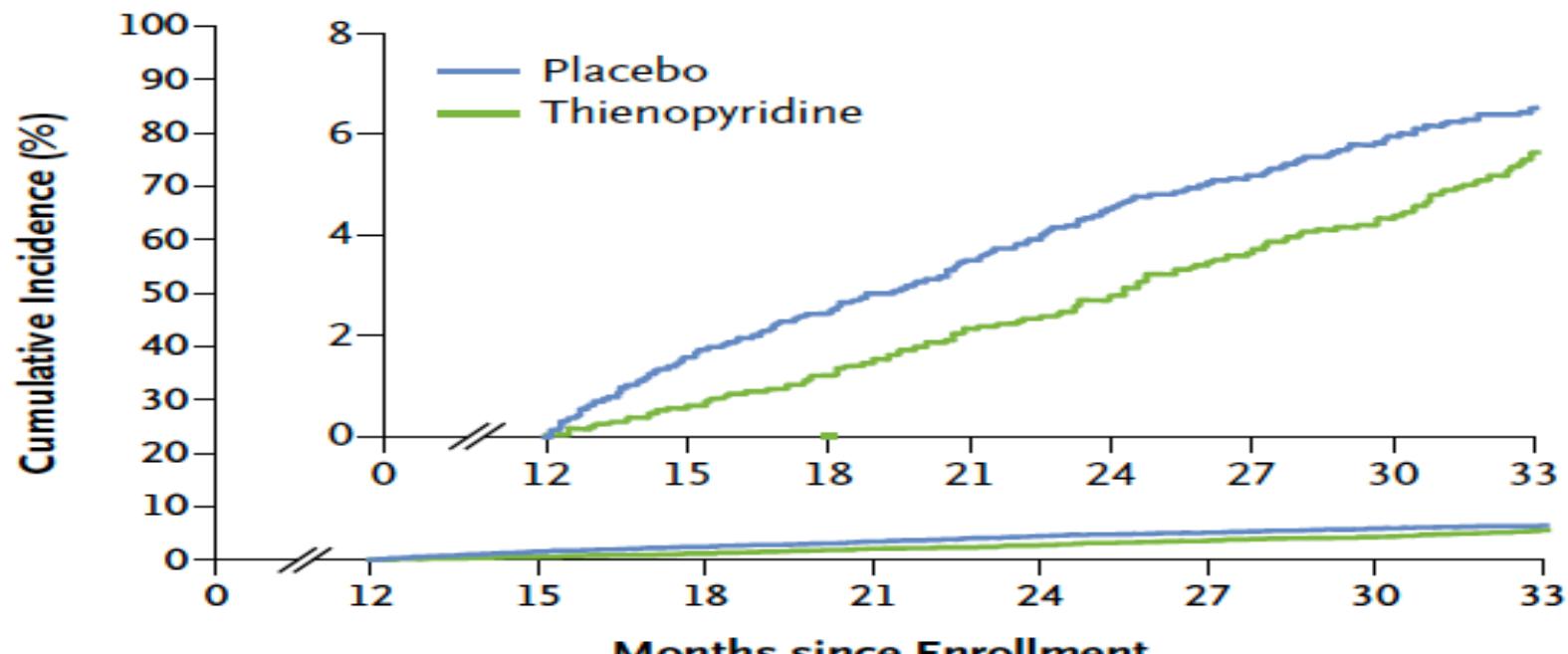
| | 12 | 15 | 18 | 21 | 24 | 27 | 30 | 33 |
|----------------|------|------|------|------|------|------|------|------|
| Thienopyridine | 5020 | 4934 | 4870 | 4828 | 4765 | 4686 | 4642 | 3110 |
| Placebo | 4941 | 4845 | 4775 | 4721 | 4651 | 4603 | 4556 | 3105 |

Twelve or 30 Months of Dual Antiplatelet Therapy after Drug-Eluting Stents DAPT Study

Major Adverse Cardiovascular and Cerebrovascular Events

12–30 mo Thienopyridine vs. placebo, 4.3% vs. 5.9%;
hazard ratio, 0.71; $P<0.001$

12–33 mo Thienopyridine vs. placebo, 5.6% vs. 6.5%;
hazard ratio, 0.82; $P=0.02$



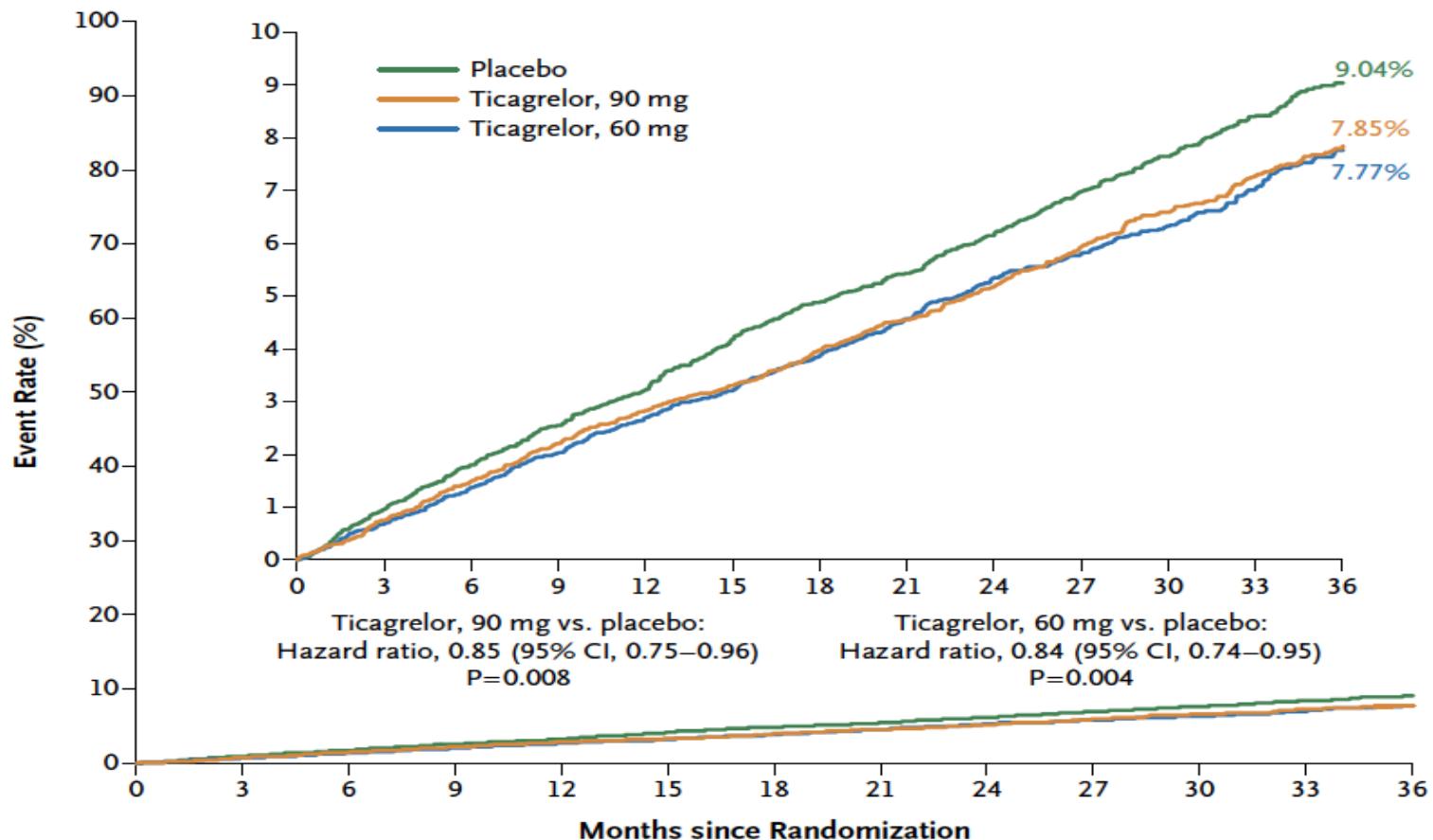
No. at Risk

| | | | | | | | | |
|----------------|------|------|------|------|------|------|------|------|
| Thienopyridine | 5020 | 4917 | 4840 | 4778 | 4702 | 4611 | 4554 | 3029 |
| Placebo | 4941 | 4799 | 4715 | 4635 | 4542 | 4476 | 4412 | 2997 |

Twelve or 30 Months of Dual Antiplatelet Therapy after Drug-Eluting Stents DAPT Study

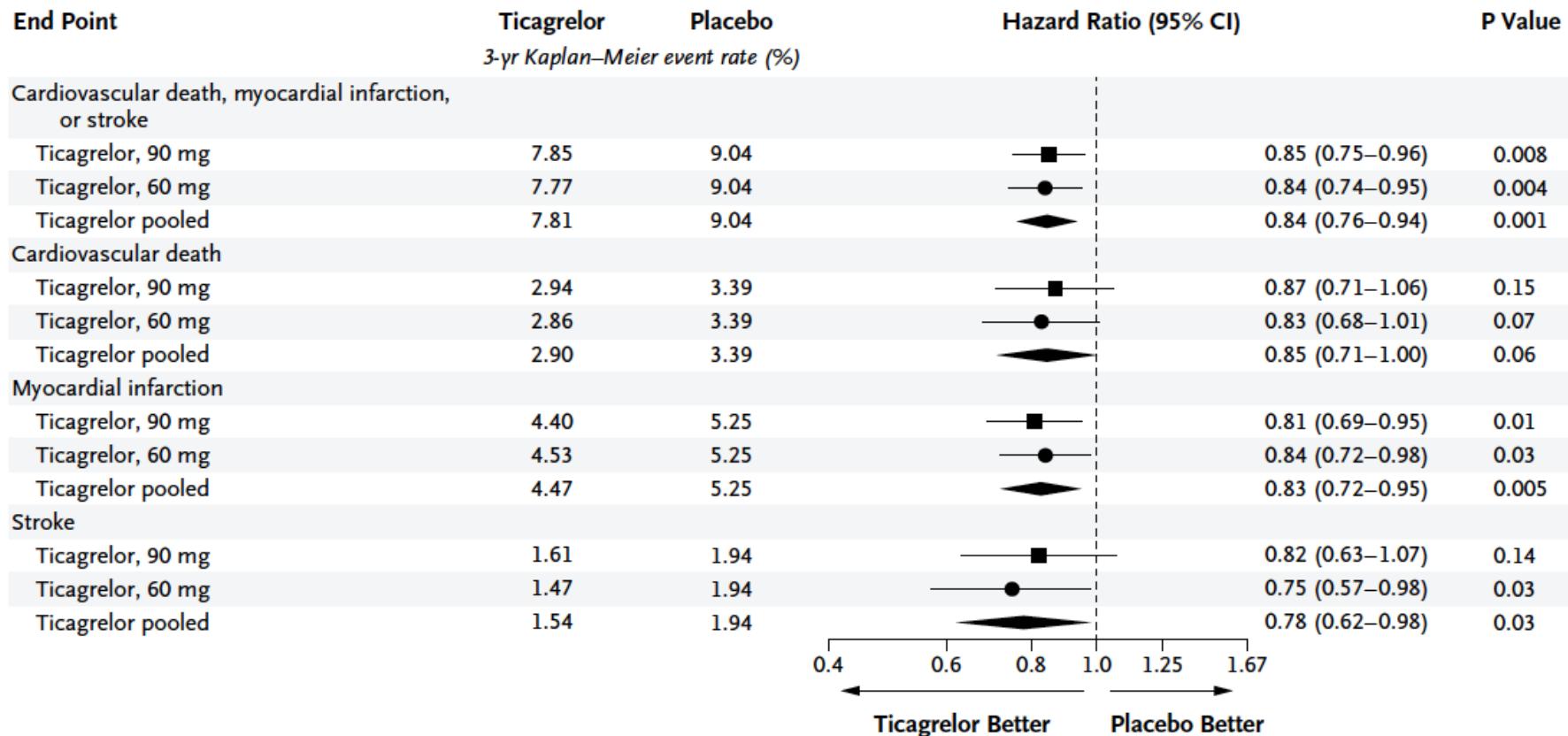
| Bleeding Complications | Continued Thienopyridine (N = 4710) | Placebo (N = 4649) | Difference | Two-Sided P Value for Difference |
|---------------------------|--|-----------------------|-------------------------------|--|
| | no. of patients (%) | | percentage points (95% CI) | |
| GUSTO severe or moderate† | 119 (2.5) | 73 (1.6) | 1.0 (0.4 to 1.5) | 0.001 |
| Severe | 38 (0.8) | 26 (0.6) | 0.2 (-0.1 to 0.6) | 0.15 |
| Moderate | 81 (1.7) | 48 (1.0) | 0.7 (0.2 to 1.2) | 0.004 |
| BARC type 2, 3, or 5 | 263 (5.6) | 137 (2.9) | 2.6 (1.8 to 3.5) | <0.001 |
| Type 2 | 145 (3.1) | 72 (1.5) | 1.5 (0.9 to 2.1) | <0.001 |
| Type 3 | 122 (2.6) | 68 (1.5) | 1.1 (0.6 to 1.7) | <0.001 |
| Type 5 | 7 (0.1) | 4 (0.1) | 0.1 (-0.1 to 0.2) | 0.38 |

Long-Term Use of Ticagrelor in Patients with Prior Myocardial Infarction PEGASUS-TIMI 54 Study



| No. at Risk | | | | | | | | | | | | | | |
|-------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|--|
| Placebo | 7067 | 6979 | 6892 | 6823 | 6761 | 6681 | 6508 | 6236 | 5876 | 5157 | 4343 | 3360 | 2028 | |
| Ticagrelor, 90 mg | 7050 | 6973 | 6899 | 6827 | 6769 | 6719 | 6550 | 6272 | 5921 | 5243 | 4401 | 3368 | 2038 | |
| Ticagrelor, 60 mg | 7045 | 6969 | 6905 | 6842 | 6784 | 6733 | 6557 | 6270 | 5904 | 5222 | 4424 | 3392 | 2055 | |

Long-Term Use of Ticagrelor in Patients with Prior Myocardial Infarction PEGASUS-TIMI 54 Study



Long-Term Use of Ticagrelor in Patients with Prior Myocardial Infarction PEGASUS-TIMI 54 Study

| End Point | Ticagrelor, 90 mg (N=6988) | Ticagrelor, 60 mg (N=6958) | Placebo (N=6996) | Ticagrelor, 90 mg vs. Placebo | Hazard Ratio (95% CI) | P Value | Ticagrelor, 60 mg vs. Placebo | Hazard Ratio (95% CI) | P Value |
|--|----------------------------------|----------------------------------|---------------------|----------------------------------|--------------------------|------------------|----------------------------------|--------------------------|---------|
| | number (percent) | | | | | | | | |
| Bleeding | | | | | | | | | |
| TIMI major bleeding | 127 (2.60) | 115 (2.30) | 54 (1.06) | 2.69 (1.96–3.70) | <0.001 | 2.32 (1.68–3.21) | <0.001 | | |
| TIMI minor bleeding | 66 (1.31) | 55 (1.18) | 18 (0.36) | 4.15 (2.47–7.00) | <0.001 | 3.31 (1.94–5.63) | <0.001 | | |
| Bleeding requiring transfusion | 122 (2.43) | 105 (2.09) | 37 (0.72) | 3.75 (2.59–5.42) | <0.001 | 3.08 (2.12–4.48) | <0.001 | | |
| Bleeding leading to study-drug discontinuation | 453 (7.81) | 354 (6.15) | 86 (1.50) | 5.79 (4.60–7.29) | <0.001 | 4.40 (3.48–5.57) | <0.001 | | |
| Fatal bleeding or nonfatal intracranial hemorrhage | 32 (0.63) | 33 (0.71) | 30 (0.60) | 1.22 (0.74–2.01) | 0.43 | 1.20 (0.73–1.97) | 0.47 | | |
| Intracranial hemorrhage | 29 (0.56) | 28 (0.61) | 23 (0.47) | 1.44 (0.83–2.49) | 0.19 | 1.33 (0.77–2.31) | 0.31 | | |
| Hemorrhagic stroke | 4 (0.07) | 8 (0.19) | 9 (0.19) | 0.51 (0.16–1.64) | 0.26 | 0.97 (0.37–2.51) | 0.94 | | |
| Fatal bleeding | 6 (0.11) | 11 (0.25) | 12 (0.26) | 0.58 (0.22–1.54) | 0.27 | 1.00 (0.44–2.27) | 1.00 | | |
| Other adverse event | | | | | | | | | |
| Dyspnea | 1205 (18.93) | 987 (15.84) | 383 (6.38) | 3.55 (3.16–3.98) | <0.001 | 2.81 (2.50–3.17) | <0.001 | | |
| Event leading to study-drug discontinuation | 430 (6.50) | 297 (4.55) | 51 (0.79) | 8.89 (6.65–11.88) | <0.001 | 6.06 (4.50–8.15) | <0.001 | | |
| Serious adverse event | 22 (0.41) | 23 (0.45) | 9 (0.15) | 2.68 (1.24–5.83) | 0.01 | 2.70 (1.25–5.84) | 0.01 | | |
| Renal event | 166 (3.30) | 173 (3.43) | 161 (2.89) | 1.17 (0.94–1.46) | 0.15 | 1.17 (0.94–1.45) | 0.15 | | |
| Bradyarrhythmia | 107 (2.04) | 121 (2.32) | 106 (1.98) | 1.15 (0.88–1.50) | 0.31 | 1.24 (0.96–1.61) | 0.10 | | |
| Gout | 115 (2.28) | 101 (1.97) | 74 (1.51) | 1.77 (1.32–2.37) | <0.001 | 1.48 (1.10–2.00) | 0.01 | | |

| Recommendations | Class | Level | Ref. |
|--|-------|-------|---------------|
| General recommendations | | | |
| A proton pump inhibitor in combination with DAPT is recommended in patients at higher than average risk of gastrointestinal bleeds (i.e. history of gastrointestinal ulcer/haemorrhage, anticoagulant therapy, chronic NSAID/corticosteroid use or two or more of the following: age ≥ 65 years, dyspepsia, gastro-oesophageal reflux disease, Helicobacter pylori infection, chronic alcohol use). | I | B | COGENT (2010) |
| In patients on P2Y12 inhibitors who need to undergo non-emergency major non-cardiac surgery, postponing surgery for at least 5 days after cessation of ticagrelor or clopidogrel, and for 7 days for prasugrel, should be considered if clinically feasible and unless the patient is at high risk of ischaemic events. | IIa | C | |
| In case of a non-cardiac surgical procedure that cannot be postponed or of a bleeding complication, discontinuation of the P2Y12 inhibitor may be considered after a minimum of 1 and 3 months from PCI with BMS and new-generation DES, respectively. | IIb | C | |

Conclusioni

La duplice terapia antiaggregante (DAPT), basata sull'associazione di aspirina ed un inibitore di P2Y12, è raccomandata in tutti i pazienti affetti da SCA.

I nuovi inibitori di P2Y12 (ticagrelor, prasugrel) sono da preferirsi al clopidogrel

Le precedenti LG del 2011 consigliavano l'assunzione degli antiaggreganti appena posta la diagnosi, indipendentemente da quando il paziente sarebbe entrato nella sala di emodinamica (il cosiddetto pretrattamento). A seguito dei risultati del **trial ACCOAST**, il pretrattamento con prasugrel nei pazienti in SCA-NSTE non è raccomandato (COR III, LOE B).

Riguardo il pretrattamento con ticagrelor e clopidogrel, nessun trial ha individuato il giusto timing di somministrazione in caso di strategia invasiva programmata: pertanto, resta un “gap in evidences” non colmato e che richiede ulteriori approfondimenti.

Entrano a far parte dell'armamentario terapeutico antiaggregante nel NSTEMI il **cangrelor** (nuovo inibitore di P2Y12) per uso endovenoso e, per via orale, il **vorapaxar** (inibitore selettivo del recettore PAR-1 della trombina).

Conclusioni

Escono definitivamente di scena **gli inibitori delle glicoproteine IIb/IIIa** in pretrattamento (COR III, LOE A) nei pazienti nei quali non è nota l'anatomia coronarica, il cui ruolo resta confinato all'utilizzo in sala di emodinamica durante PCI.

La giusta **durata della DAPT** resta argomento di discussione e dovrebbe esser basata sulla valutazione individuale del rischio ischemico versus quello emorragico (cosiddetta tailored duration).

L'estensione della DAPT oltre i convenzionali 12 mesi dovrebbe essere considerata nei pazienti a basso rischio di sanguinamento con alto rischio ischemico fino a 30 mesi (con prasugrel o clopidogrel) o fino a 48 mesi (con ticagrelor, preferibilmente riducendo dopo un anno la posologia a 60 mg bid) in base ai risultati dei **trial DAPT e PEGASUS** (COR IIb, LOE A).

La durata della DAPT può essere ridotta nei pazienti ad alto rischio di sanguinamento a 3-6 mesi (COR IIb, LOE A), alla luce dei miglioramenti tecnologici degli stent medicati e della drastica riduzione dei casi di trombosi intrastent.

Conclusioni

L'approccio radiale rispetto a quello femorale è incentivato in considerazione dei risultati derivanti dagli studi **RIVAL** (The Radial Vs femorAL access for coronary intervention) e **MATRIX** (Minimizing Adverse Haemorrhagic Events by TRansradial Access Site and Systemic Implementation of angioX) che dimostrano una superiorità del primo nella riduzione delle complicanze vascolari, degli eventi di sanguinamento maggiori e di tutte le cause di mortalità.