IX Congresso
Novas Fronteiras em Medicina Cardiovascular
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The Village Praia D'El Rey - Óbidos

# Antithrombotic strategies in the acute setting

Daniel Caldeira MD PhD

New frontiers in intensive cardiovascular care

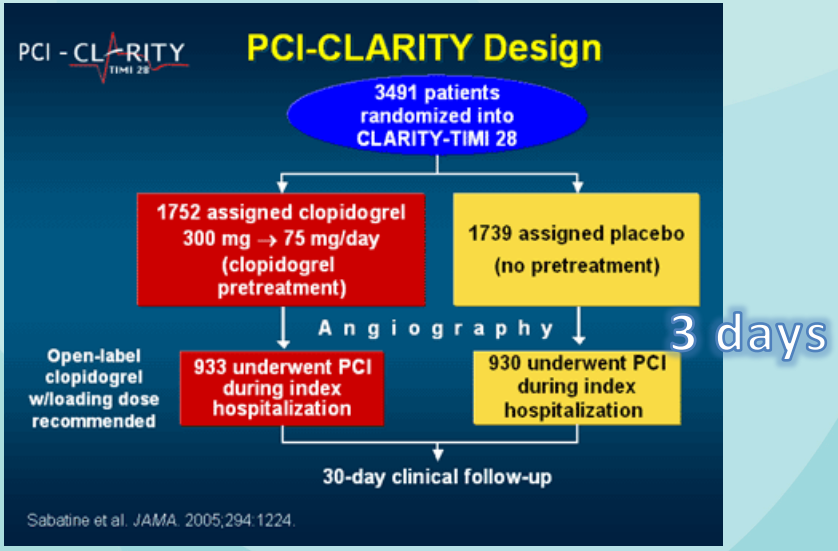
# Contents

1. Loading dose / Pretreatment timing with P2Y12 inhibitors
2. The clinical impact of morphine
3. Managing oral antiplatelet and oral anticoagulants in patients with AF and ACS w/ PCI

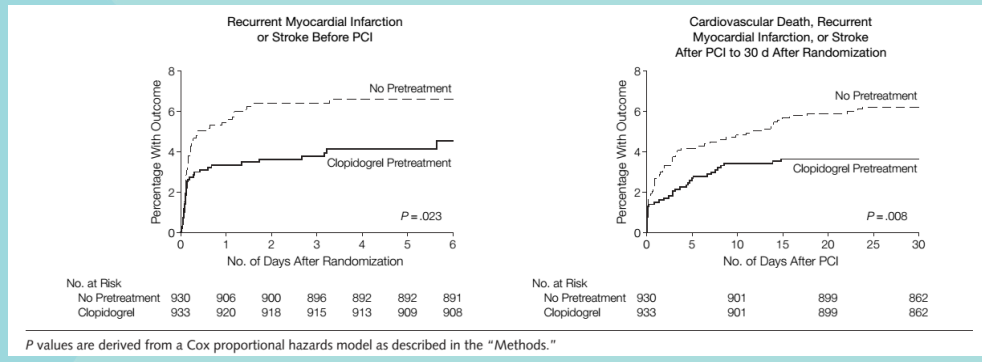
# Pretreatment with P2Y12 inhibitors in ACS

## STEMI

To provide an early antithrombotic millieu in patients ACS
Reducing the myonecrosis




**Effect of Clopidogrel Pretreatment Before Percutaneous Coronary Intervention in Patients With ST-Elevation Myocardial Infarction Treated With Fibrinolytics**
The PCI-CLARITY Study




JAMA. 2005 Sep 14;294(10):1224-32.

# Pretreatment with P2Y12 inhibitors in ACS

## STEMI

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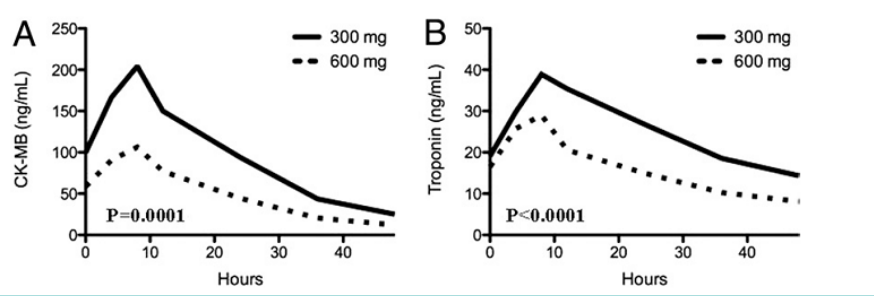



**Outcome Comparison of 600- and 300-mg Loading Doses of Clopidogrel in Patients Undergoing Primary Percutaneous Coronary Intervention for ST-Segment Elevation Myocardial Infarction**

Results From the ARMYDA-6 MI
(Antiplatelet therapy for Reduction of MYocardial Damage during Angioplasty-Myocardial Infarction) Randomized Study

| | 600-mg Clopidogrel (n = 103) | 300-mg Clopidogrel (n = 98) | p Value |
|---|---|---|---|
| 30-day MACE | 6 (5.8) | 15 (15.0) | 0.049 |
| Individual components | | | |
| Death | 4 (3.9) | 7 (7.1) | 0.48 |
| Reinfarction | 1 (0.98) | 5 (5.1) | 0.19 |
| TVR | 1 (0.98) | 7 (7.1) | 0.06 |
| Stroke | 0 | 1 (1.0) | 0.98 |
| Death + reinfarction | 5 (4.9) | 12 (12.2) | 0.10 |
| Death + reinfarction + stroke | 5 (4.9) | 13 (13.2) | 0.07 |
| Death + reinfarction + TVR | 6 (5.8) | 14 (14.2) | 0.08 |
| Definite or probable stent thrombosis | 1 (0.98) | 4 (4.1) | 0.34 |

Patti et al. JACC Vol. 58, No. 15, 2011

# Pretreatment with P2Y12 inhibitors in ACS

## STEMI

1862 STEMI patients <6 hours
180 mg ticagrelor
Time difference 31 minutes

No bleeding risk differences

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

### Prehospital Ticagrelor in ST-Segment Elevation Myocardial Infarction

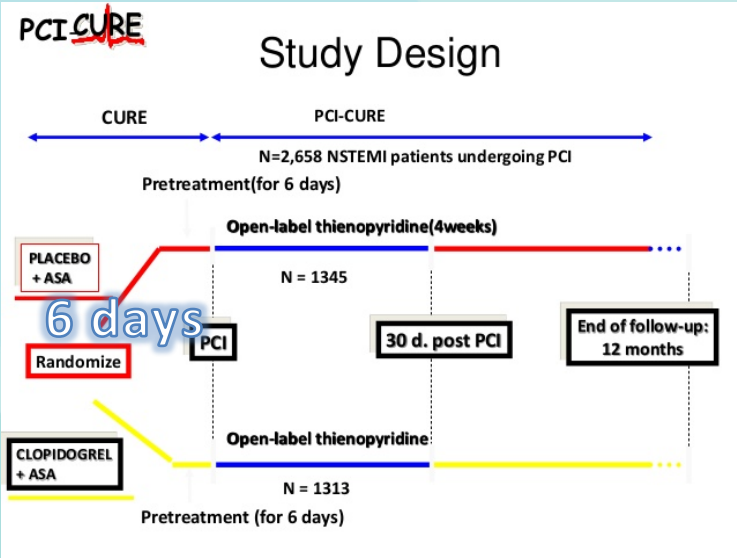
| End Point | Prehospital Ticagrelor (N=906) | In-Hospital Ticagrelor (N=952) | Odds Ratio (95% CI)† | P Value† | Difference (95% CI)‡ |
|---|---|---|---|---|---|
| | *no./no. of patients who could be evaluated (%)* | | | | |
| Coprimary end points | | | | | |
| Absence of ST-segment elevation resolution ≥70% before PCI | 672/774 (86.8) | 722/824 (87.6) | 0.93 (0.69 to 1.25) | 0.63 | −0.008 (−0.041 to 0.025) |
| Absence of TIMI flow grade 3 in infarct-related artery at initial angiography | 681/824 (82.6) | 711/856 (83.1) | 0.97 (0.75 to 1.25) | 0.82 | −0.004 (−0.040 to 0.032) |

| Variable | Prehospital Ticagrelor | In-Hospital Ticagrelor | Odds Ratio (95% CI) | P Value |
|---|---|---|---|---|
| Ischemic end point | | | | |
| No. of patients who could be evaluated | 906 | 952 | | |
| Composite of death, myocardial infarction, stroke, urgent revascularization, or definite stent thrombosis — no. (%) | 41 (4.5) | 42 (4.4) | 1.03 (0.66 to 1.60) | 0.91 |
| Composite of death, myocardial infarction, or urgent revascularization — no. (%) | 39 (4.3) | 34 (3.6) | 1.22 (0.76 to 1.94) | 0.42 |
| Stent thrombosis — no. (%) | | | | |
| Definite at ≤24 hr after index PCI | 0 | 8 (0.8) | — | 0.008‡ |
| Definite at 30 days | 2 (0.2) | 11 (1.2) | 0.19 (0.04 to 0.86) | 0.02‡ |
| Definite or probable at 30 days¶ | 21 (2.3) | 20 (2.1) | 1.11 (0.60 to 2.05) | 0.75 |

# Pretreatment with P2Y12 inhibitors in ACS

## NSTE-ACS

To provide an early antithrombotic millieu in patients ACS
Reducing the myonecrosis

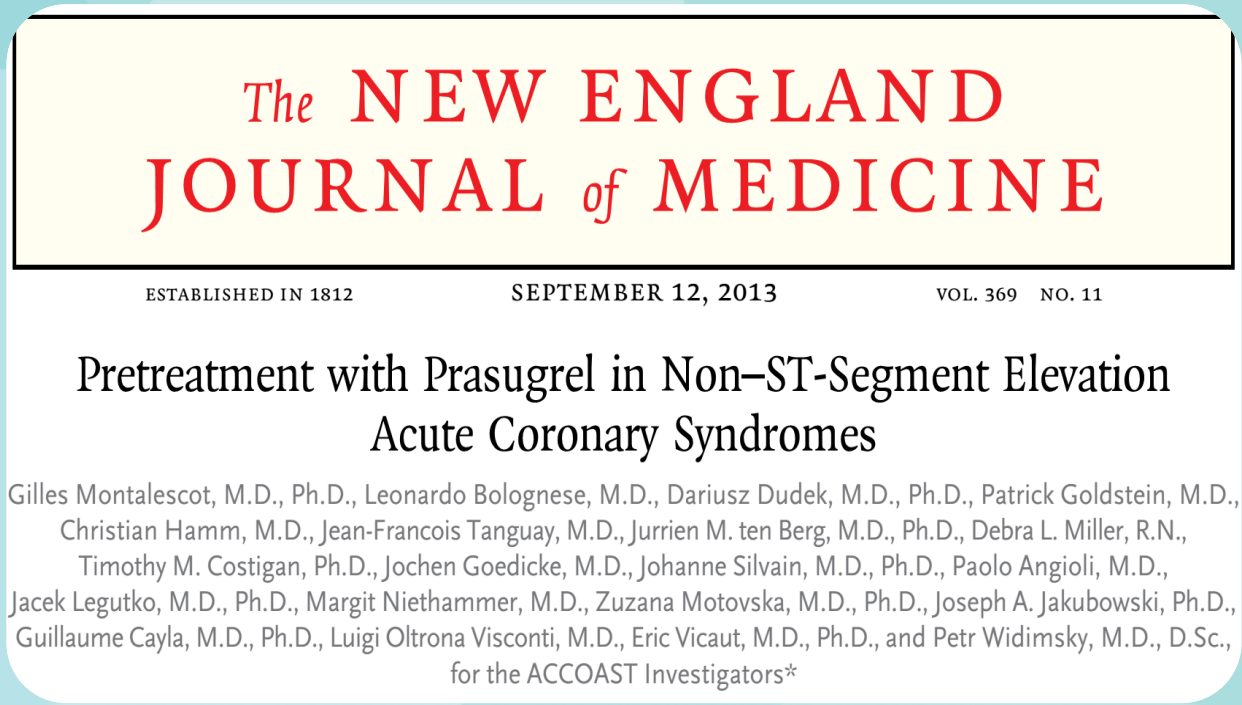



**Effects of pretreatment with clopidogrel and aspirin followed by long-term therapy in patients undergoing percutaneous coronary intervention: the PCI-CURE study** *Lancet* 2001; **358:** 527–33

| | Placebo (n=1345) | Clopidogrel (n=1313) | Relative risk (95% CI) | p |
|---|---|---|---|---|
| **Events before PCI** | | | | |
| Myocardial infarction or refractory ischaemia | 206 (15·3%) | 159 (12·1%) | 0·76 (0·62–0·93) | 0·008 |
| Myocardial infarction | 68 (5·1%) | 47 (3·6%) | 0·68 (0·47–0·99) | 0·04 |
| **Events from PCI to 30 days** | | | | |
| CV death, myocardial infarction, urgent revascularisation | 86 (6·4%) | 59 (4·5%) | 0·70 (0·50–0·97) | 0·03 |
| CV death, myocardial infarction | 59 (4·4%) | 38 (2·9%) | 0·66 (0·44–0·99) | 0·04 |
| CV death | 13 (1·0%) | 14 (1·1%) | 1·10 (0·52–2·35) | |
| Myocardial infarction | 51 (3·8%) | 28 (2·1%) | 0·56 (0·35–0·89) | |
| Q-wave myocardial infarction | 32 (2·4%) | 11 (0·8%) | 0·35 (0·18–0·70) | |
| Urgent revascularisation | 38 (2·8%) | 25 (1·9%) | 0·67 (0·41–1·11) | |

# Pretreatment with P2Y12 inhibitors in ACS

## NSTE-ACS



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 12, 2013 VOL. 369 NO. 11

Pretreatment with Prasugrel in Non–ST-Segment Elevation Acute Coronary Syndromes

Gilles Montalescot, M.D., Ph.D., Leonardo Bolognese, M.D., Dariusz Dudek, M.D., Ph.D., Patrick Goldstein, M.D., Christian Hamm, M.D., Jean-Francois Tanguay, M.D., Jurrien M. ten Berg, M.D., Ph.D., Debra L. Miller, R.N., Timothy M. Costigan, Ph.D., Jochen Goedicke, M.D., Johanne Silvain, M.D., Ph.D., Paolo Angioli, M.D., Jacek Legutko, M.D., Ph.D., Margit Niethammer, M.D., Zuzana Motovska, M.D., Ph.D., Joseph A. Jakubowski, Ph.D., Guillaume Cayla, M.D., Ph.D., Luigi Oltrona Visconti, M.D., Eric Vicaut, M.D., Ph.D., and Petr Widimsky, M.D., D.Sc., for the ACCOAST Investigators*

# Pretreatment with P2Y12 inhibitors in ACS

## NSTE-ACS - Prasugrel

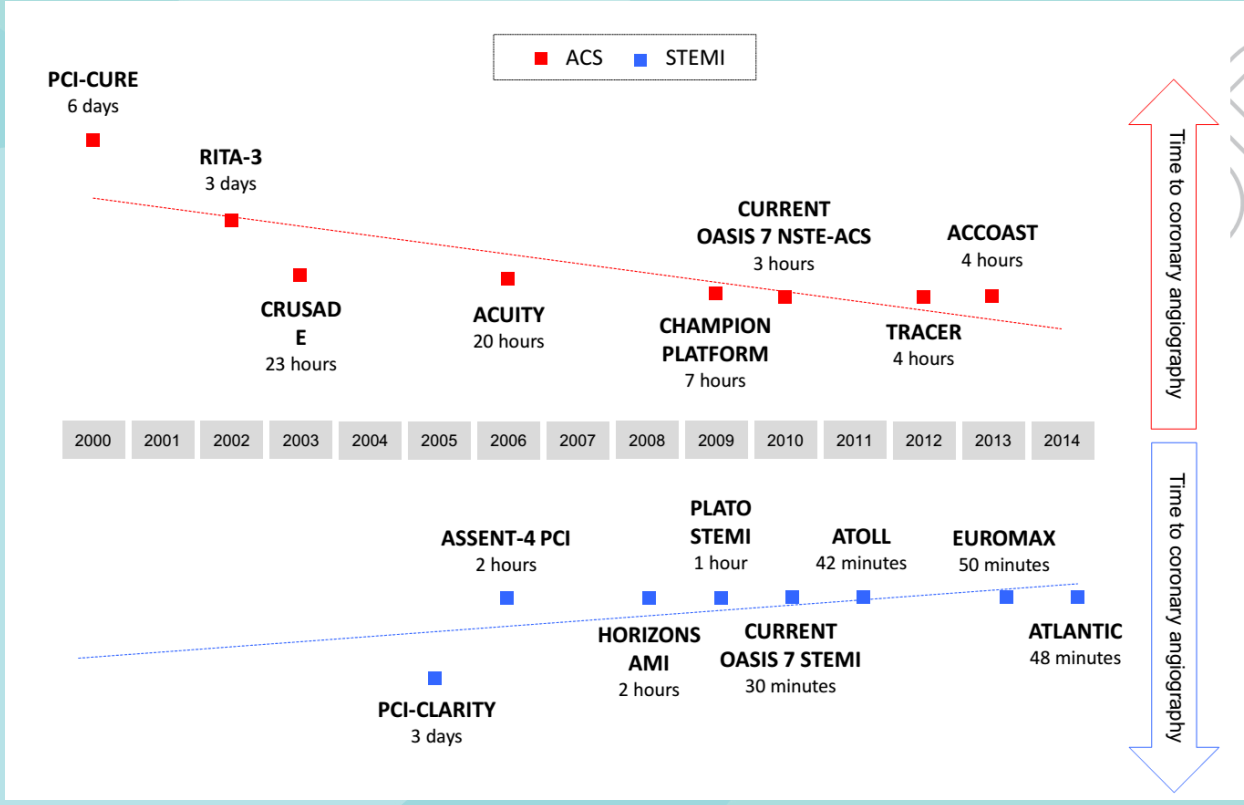
| End Point | Pretreatment (N = 2037) | No Pretreatment (N = 1996) | Hazard Ratio (95% CI) | P Value |
|---|---|---|---|---|
| | *no. of patients (%)* | | | |
| **7 Days** | | | | |
| Death from cardiovascular causes, myocardial infarction, stroke, urgent revascularization, or glycoprotein IIb/IIIa bailout: primary end point | 203 (10.0) | 195 (9.8) | 1.02 (0.84–1.25) | 0.81 |
| Death | | | | |
| From any cause | 8 (0.4) | 10 (0.5) | 0.78 (0.31–1.98) | 0.61 |
| From cardiovascular cause | 7 (0.3) | 10 (0.5) | 0.69 (0.26–1.80) | 0.44 |
| Myocardial infarction | 119 (5.8) | 109 (5.5) | 1.07 (0.83–1.39) | 0.60 |
| Stroke | 8 (0.4) | 10 (0.5) | 0.78 (0.31–1.98) | 0.60 |
| Urgent revascularization | 22 (1.1) | 26 (1.3) | 0.83 (0.47–1.46) | 0.52 |
| Glycoprotein IIb/IIIa bailout | 76 (3.7) | 78 (3.9) | 0.96 (0.70–1.31) | 0.79 |

# Pretreatment with P2Y12 inhibitors in ACS

## NSTE-ACS - Prasugrel

| End Point | Pretreatment (N = 2037) | No Pretreatment (N = 1996) | Hazard Ratio (95% CI) | P Value |
|---|---|---|---|---|
| | *no. of patients (%)* | | | |
| **7 Days** | | | | |
| All CABG-related or non–CABG-related TIMI major bleeding: key safety end point | 52 (2.6) | 27 (1.4) | 1.90 (1.19–3.02) | 0.006 |
| Non–CABG-related TIMI major bleeding | 27 (1.3) | 9 (0.5) | 2.95 (1.39–6.28) | 0.003 |
| Fatal bleeding | 1 (<0.1) | 0 | NE | NE |
| Life-threatening bleeding | 17 (0.8) | 3 (0.2) | 5.56 (1.63–19.0) | 0.002 |

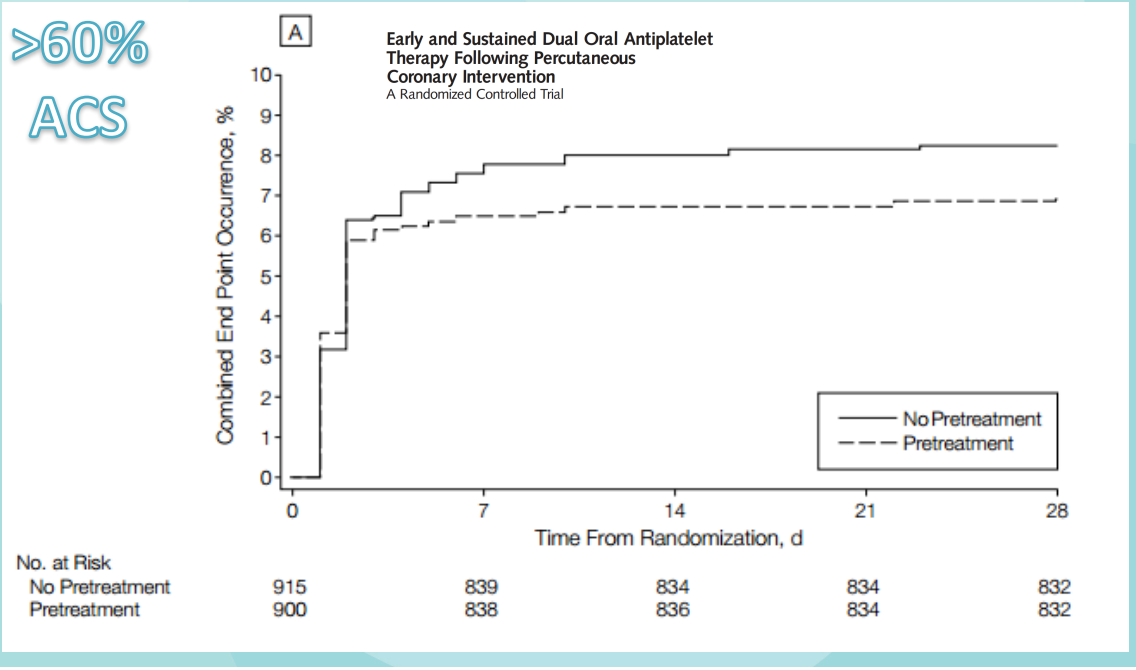
# Pretreatment with P2Y12 inhibitors in ACS

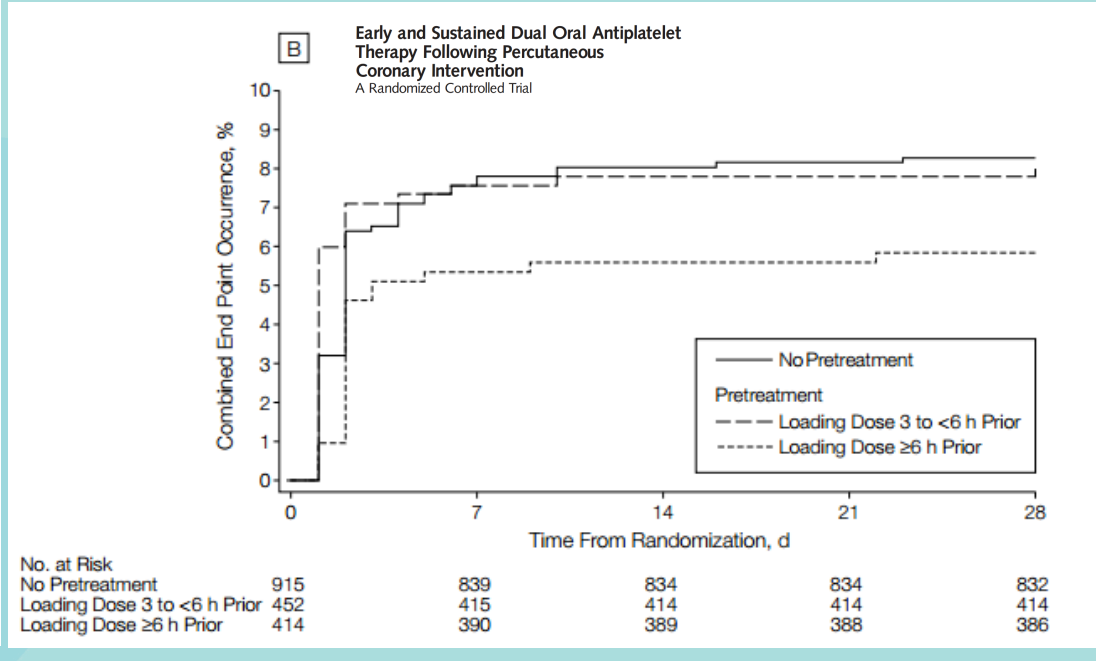



Davide Capodanno MD, PhD & Dominick J. Angiolillo MD, PhD (2016): Reviewing the controversy surrounding pre-treatment with $P2Y_{12}$ inhibitors in acute coronary syndrome patients, Expert Review of Cardiovascular Therapy, DOI: 10.1586/14779072.2016.1164035

# Pretreatment with P2Y12 inhibitors in ACS

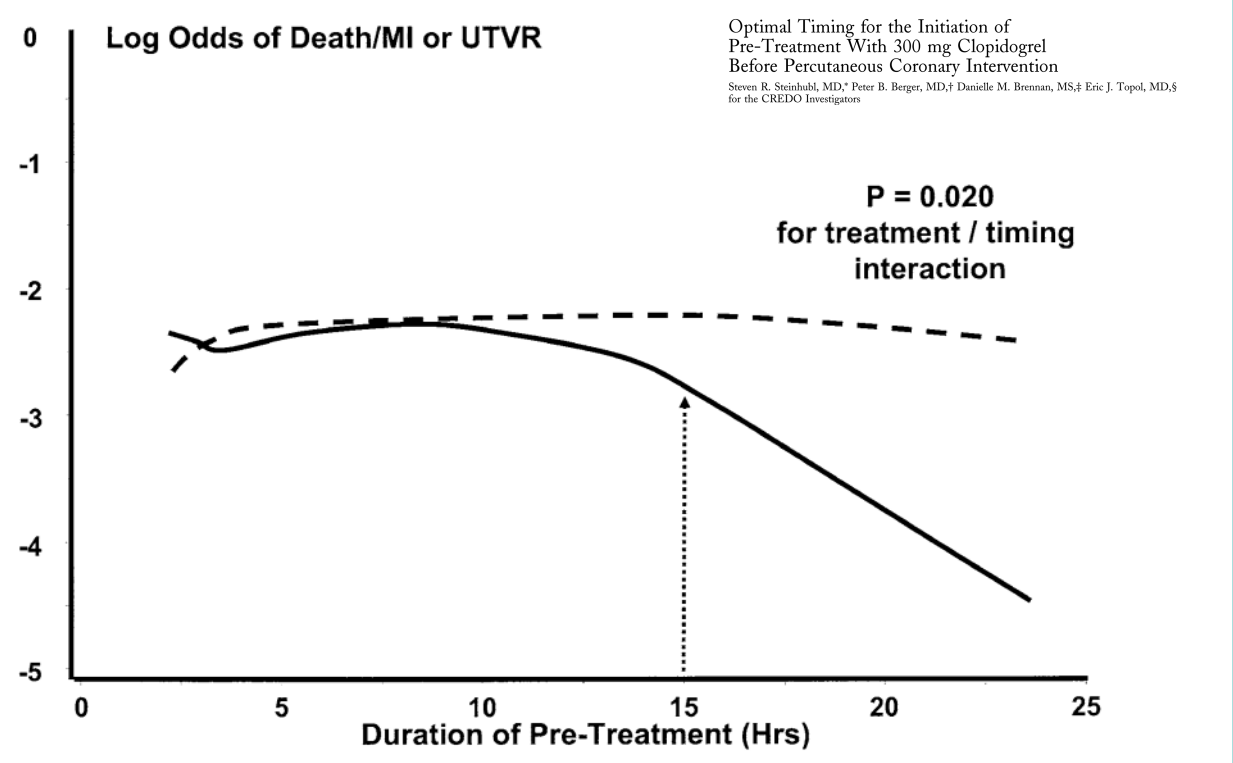
>60%
ACS




Antithrombotic strategies in the acute setting

# Pretreatment with P2Y12 inhibitors in ACS




Optimal Timing for the Initiation of
Pre-Treatment With 300 mg Clopidogrel
Before Percutaneous Coronary Intervention

Steven R. Steinhubl, MD,* Peter B. Berger, MD,† Danielle M. Brennan, MS,‡ Eric J. Topol, MD,§
for the CREDO Investigators

# What the guidelines say…

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

| | | |
|---|---|---|
| Pre-treatment with a $P2Y_{12}$ inhibitor is generally recommended in patients in whom coronary anatomy is known and the decision to proceed to PCI is made as well as in patients with STEMI.[20,23,38] | I | A |
| In patients with NSTE-ACS undergoing invasive management, ticagrelor administration (180 mg loading dose, 90 mg twice daily), or clopidogrel (600 mg loading dose, 75 mg daily dose) if ticagrelor is not an option, should be considered as soon as the diagnosis is established. | IIa | C |

# What the guidelines say…

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

| | | |
|---|---|---|
| In NSTE-ACS patients in whom coronary anatomy is not known, it is not recommended to administer prasugrel.[25] | III | B |

## 2018 ESC/EACTS Guidelines on myocardial revascularization

**Recommendations for antithrombotic treatment in patients with non-ST-elevation acute coronary syndromes undergoing percutaneous coronary intervention**

| | | |
|---|---|---|
| Administration of prasugrel in patients in whom coronary anatomy is not known is not recommended.[165] | III | B |

# Pretreatment with P2Y12 inhibitors

## Problems in NSTE-ACS – particularly with prasugrel

1. Some patients are kept in medical therapy
2. Other patients may have complex CAD

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 12, 2013 VOL. 369 NO. 11

Pretreatment with Prasugrel in Non–ST-Segment Elevation Acute Coronary Syndromes

| End Point | Pretreatment (N=2037) | No Pretreatment (N=1996) | Hazard Ratio (95% CI) | P Value |
|---|---|---|---|---|
| | *no. of patients (%)* | | | |
| **7 Days** | | | | |
| All CABG-related or non–CABG-related TIMI major bleeding: key safety end point | 52 (2.6) | 27 (1.4) | 1.90 (1.19–3.02) | 0.006 |
| Non–CABG-related TIMI major bleeding | 27 (1.3) | 9 (0.5) | 2.95 (1.39–6.28) | 0.003 |
| Fatal bleeding | 1 (<0.1) | 0 | NE | NE |
| Life-threatening bleeding | 17 (0.8) | 3 (0.2) | 5.56 (1.63–19.0) | 0.002 |

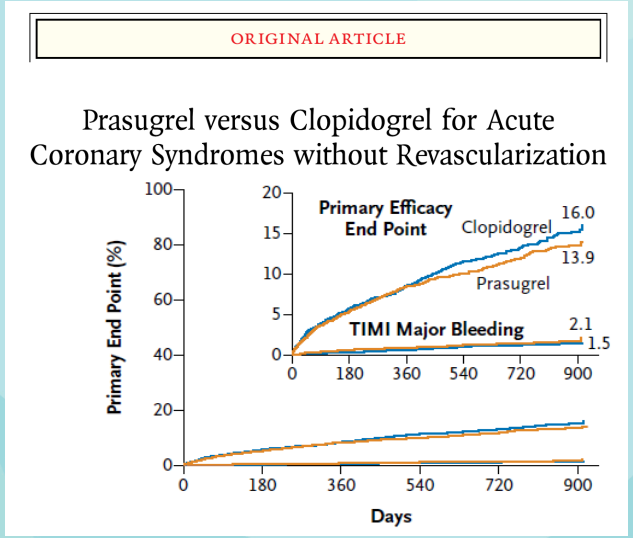
Medical therapy - 25%
CABG - 6%

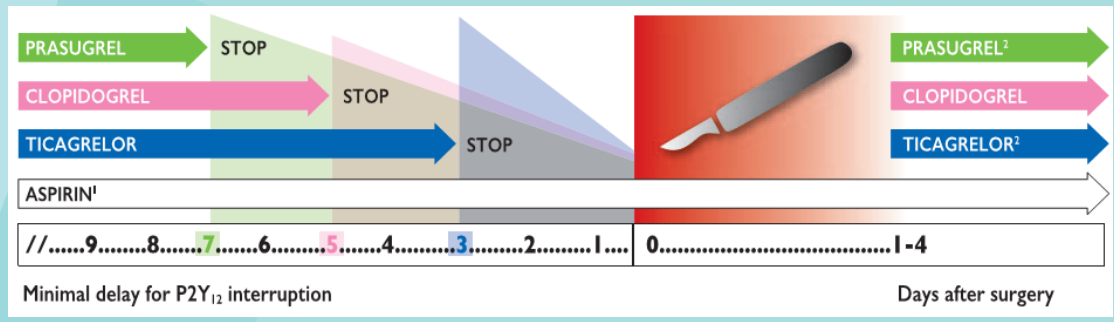
N Engl J Med 2013;369:999-1010.

# Pretreatment with P2Y12 inhibitors

## Problems in NSTE-ACS - particularly with prasugrel

1. Some patients are kept in medical therapy
2. Other patients may have complex CAD



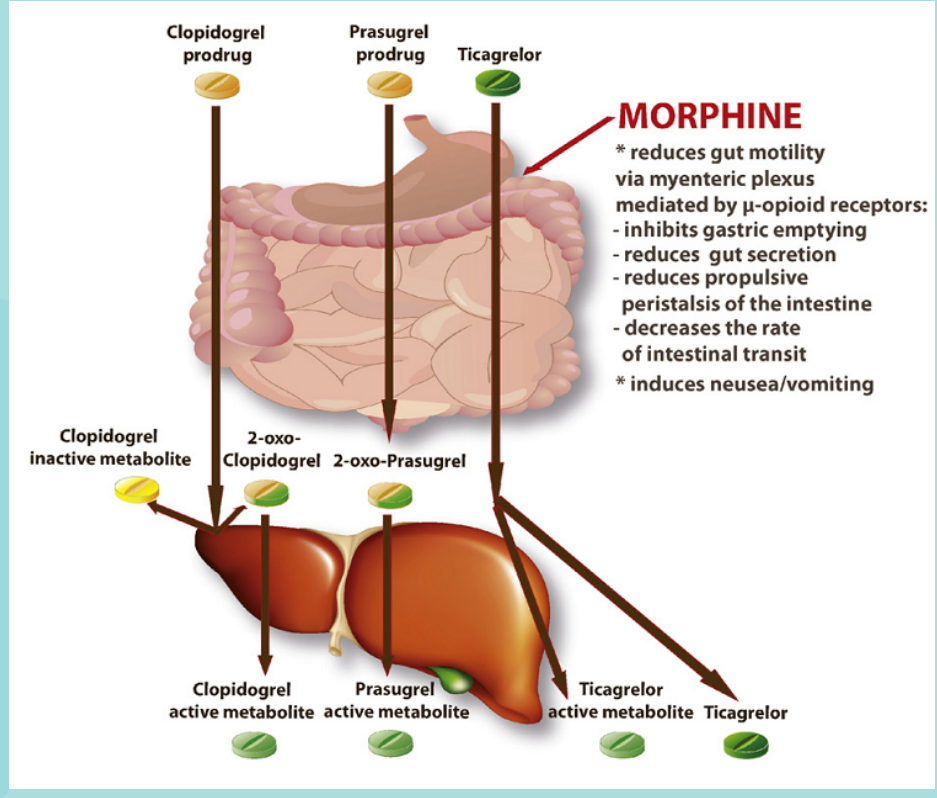




N Engl J Med 2012;367:1297-309
European Heart Journal (2018)39, 213–254

# Recent evidence has shown that some drugs cecrease the time to full action of antiplatelet drugs and that may have a prognostic impact in ACS

A clue that pretreatment and its early timing might be relevant

# Time for ‘adequate’ pharmacodynamic seems to be relevant - Morphine



# Morphine and ACS

Open access Research

BMJ Open

## Morphine in acute coronary syndrome: systematic review and meta-analysis

Gonçalo Silva Duarte,[1,2] Afonso Nunes-Ferreira,[3] Filipe Brogueira Rodrigues,[1,2] Fausto J Pinto,[3] Joaquim J Ferreira,[4,5] Joao Costa,[5,6] Daniel Caldeira[1,2,3]

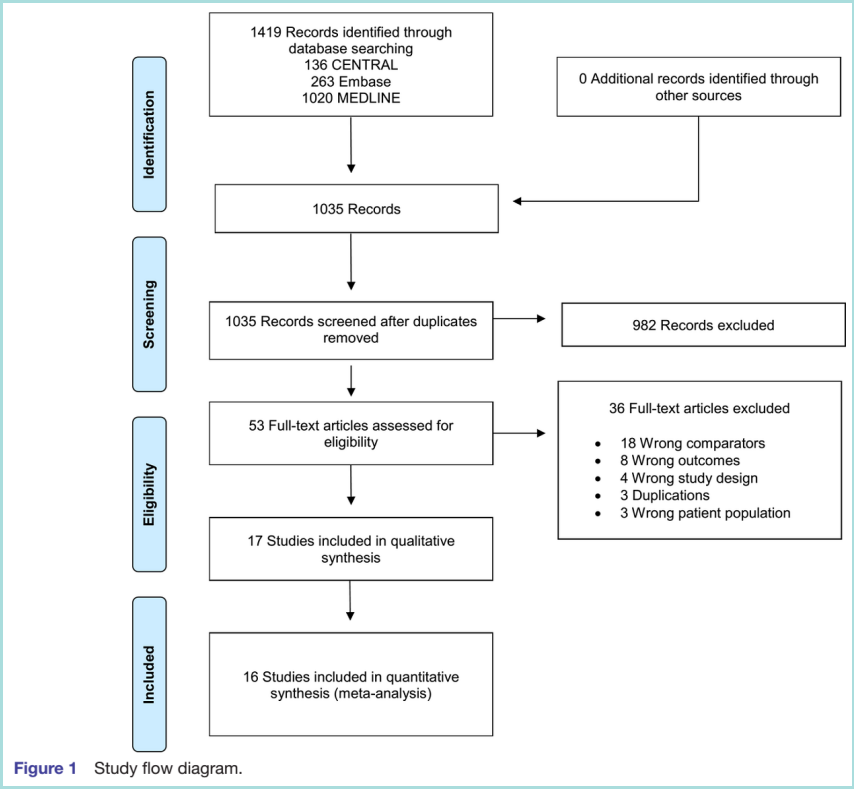



**Figure 1** Study flow diagram.

# Morphine and ACS

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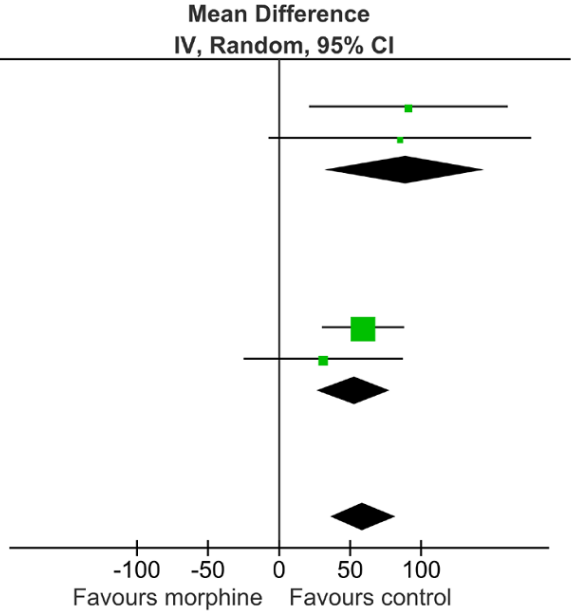
| Study or Subgroup | Morphine Mean | SD | Total | Control Mean | SD | Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| **RCTs** | | | | | | | | |
| Kubica 2015 | 209.3 | 130.4 | 35 | 118.3 | 165.9 | 35 | 11.1% | 91.00 [21.09, 160.91] |
| Thomas 2016 | 190 | 71 | 6 | 105 | 91 | 6 | 6.4% | 85.00 [-7.35, 177.35] |
| **Subtotal (95% CI)** | | | **41** | | | **41** | **17.5%** | **88.81 [33.07, 144.55]** |
| Heterogeneity: Tau² = 0.00; Chi² = 0.01, df = 1 (P = 0.92); I² = 0% | | | | | | | | |
| Test for overall effect: Z = 3.12 (P = 0.002) | | | | | | | | |
| **Observational studies** | | | | | | | | |
| Bellandi 2016 | 235 | 79 | 74 | 176 | 120 | 108 | 65.1% | 59.00 [30.08, 87.92] |
| Franchi 2015 | 202 | 92 | 16 | 171 | 93.1 | 30 | 17.3% | 31.00 [-25.05, 87.05] |
| **Subtotal (95% CI)** | | | **90** | | | **138** | **82.5%** | **53.11 [27.42, 78.81]** |
| Heterogeneity: Tau² = 0.00; Chi² = 0.76, df = 1 (P = 0.38); I² = 0% | | | | | | | | |
| Test for overall effect: Z = 4.05 (P < 0.0001) | | | | | | | | |
| **Total (95% CI)** | | | **131** | | | **179** | **100.0%** | **59.37 [36.04, 82.71]** |
| Heterogeneity: Tau² = 0.00; Chi² = 2.07, df = 3 (P = 0.56); I² = 0% | | | | | | | | |
| Test for overall effect: Z = 4.99 (P < 0.00001) | | | | | | | | |
| Test for subgroup differences: Chi² = 1.30, df = 1 (P = 0.25), I² = 23.1% | | | | | | | | |



# Morphine and ACS

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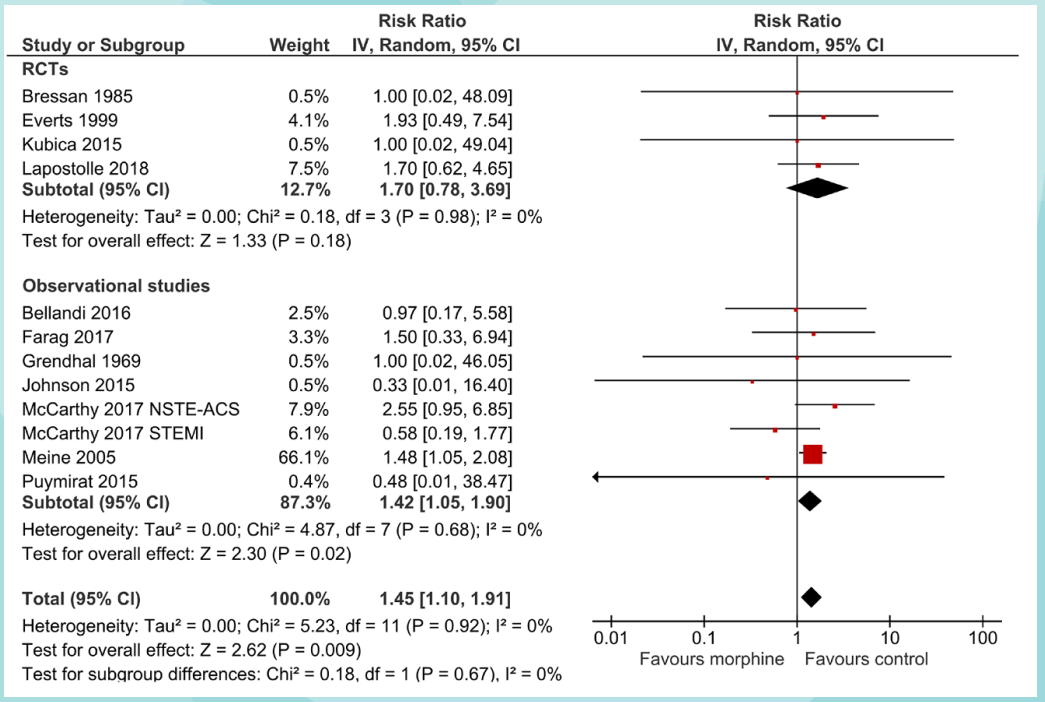
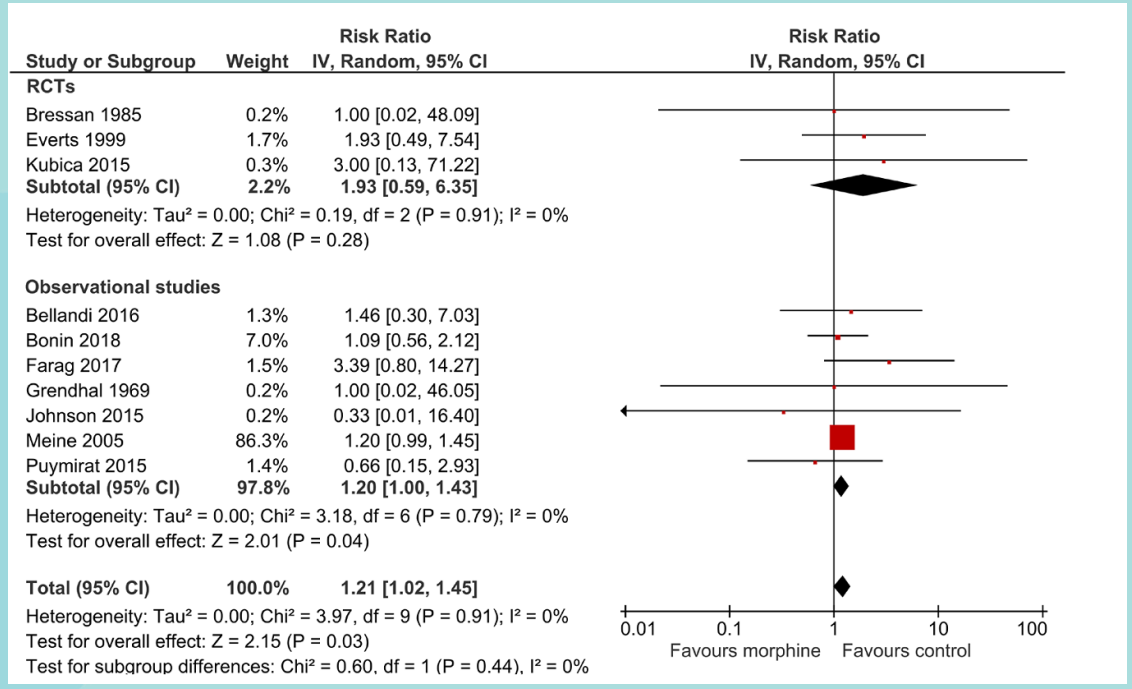
## In-hospital mortality




## MACE



# In ACS about 10% of patients with ACS develop AF during the early stages

This requires a careful thought about the antithrombotic strategies



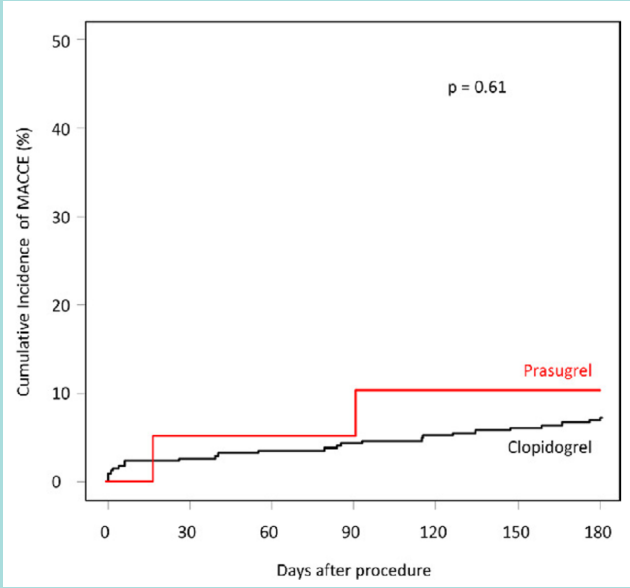
Caldeira D, FMUL, CCUL, CHULM, CAML.

# ACS and AF undergoing PCI

## The harms of triple therapy with new P2Y12 inhibitors

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

| Adverse Event | Prasugrel (n = 21) | Clopidogrel (n = 356) | Unadjusted HR (95% CI) | p Value |
|---|---|---|---|---|
| TIMI bleeding | | | | |
| Major and minor | 6 (28.6) | 24 (6.7) | 4.6 (1.9–11.4) | <0.001 |
| Major | 3 (14.3) | 10 (2.8) | 6.1 (1.6–22.1) | 0.006 |
| Minor | 3 (14.3) | 14 (3.9) | 3.8 (1.1–13.1) | 0.04 |
| MACCE | 2 (9.5) | 25 (7.0) | 1.4 (0.3–6.1) | 0.61 |
| Death | 2 (9.5) | 14 (3.9) | 2.6 (0.6–11.5) | 0.20 |
| Myocardial infarction | 0 | 7 (2.0) | — | 0.99 |
| Stent thrombosis | 0 | 2 (0.6) | — | 0.99 |
| Stroke | 1 (4.8) | 6 (1.7) | 3.1 (0.4–25.4) | 0.30 |
| Ischemic | 0 | 5 (1.4) | | 0.99 |
| Hemorrhagic | 1 (4.8) | 1 (0.3) | 18 (1.1–292) | 0.04 |




J Am Coll Cardiol. 2013 May 21;61(20):2060-6.

# ACS and AF undergoing PCI

## The harms of triple therapy with new P2Y12 inhibitors

**Ticagrelor Versus Clopidogrel as Part of Dual or Triple Antithrombotic Therapy: a Systematic Review and Meta-Analysis**

Cardiovascular Drugs and Therapy

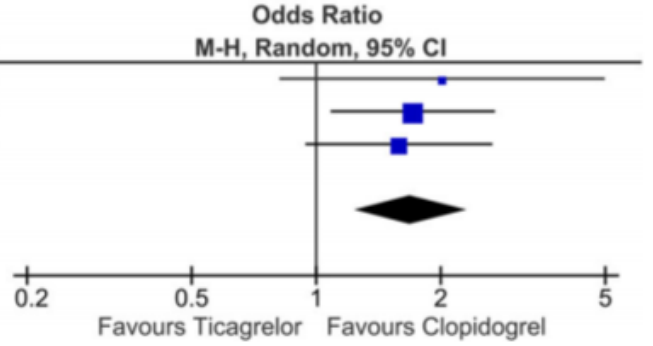
https://doi.org/10.1007/s10557-018-6795-9

**Triple antithrombotic therapy**

| Study or Subgroup | Ticagrelor Events | Ticagrelor Total | Clopidogrel Events | Clopidogrel Total | Weight | Odds Ratio M-H, Random, 95% CI | Year |
|---|---|---|---|---|---|---|---|
| PIONEER AF-PCI | 8 | 21 | 157 | 671 | 12.4% | 2.01 [0.82, 4.95] | 2016 |
| RE-DUAL (D:110 mg) | 34 | 91 | 230 | 890 | 49.5% | 1.71 [1.09, 2.69] | 2017 |
| RE-DUAL (D:150 mg) | 25 | 73 | 171 | 691 | 38.1% | 1.58 [0.95, 2.65] | 2017 |
| **Total (95% CI)** | | **185** | | **2252** | **100.0%** | **1.70 [1.24, 2.33]** | |
| Total events | 67 | | 558 | | | | |

Heterogeneity: Tau² = 0.00; Chi² = 0.21, df = 2 (P = 0.90); I² = 0%

Test for overall effect: Z = 3.27 (P = 0.001)




Cardiovasc Drugs Ther. 2018 May 15. doi: 10.1007/s10557-018-6795-9.

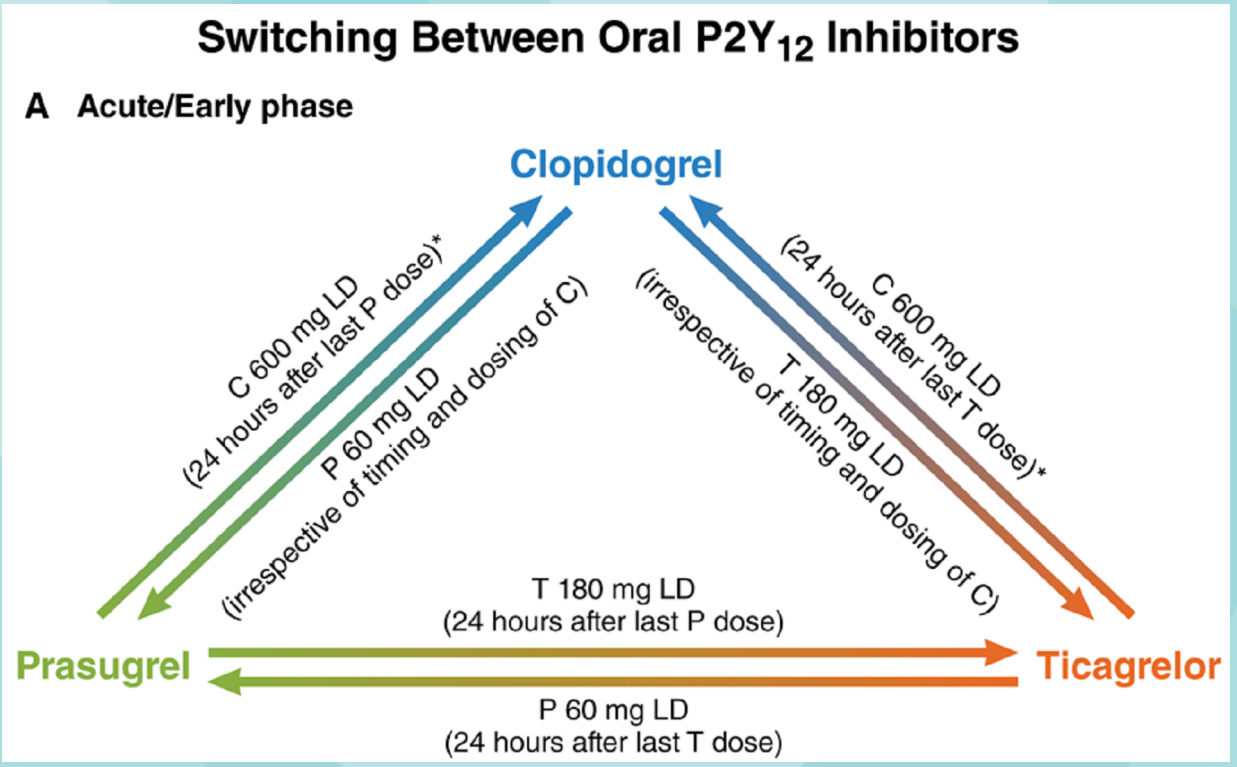
# Switch P2Y12 inhibitors

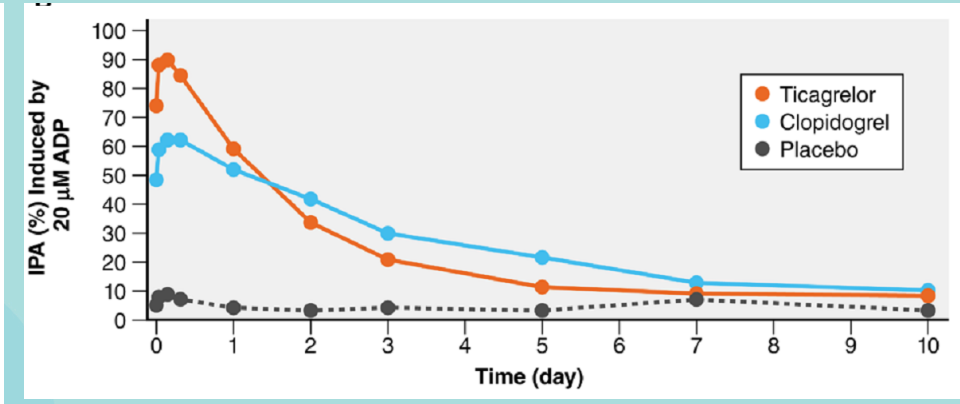
WHITE PAPER

## International Expert Consensus on Switching Platelet $P2Y_{12}$ Receptor–Inhibiting Therapies

*Circulation.* 2017;136:1955–1975. DOI: 10.1161/CIRCULATIONAHA.117.031164

# Switch P2Y12 inhibitors




Circulation.2017;136:1955–1975

# Strategies with antiplatelets and NOACs

## PIONEER AF-PCI

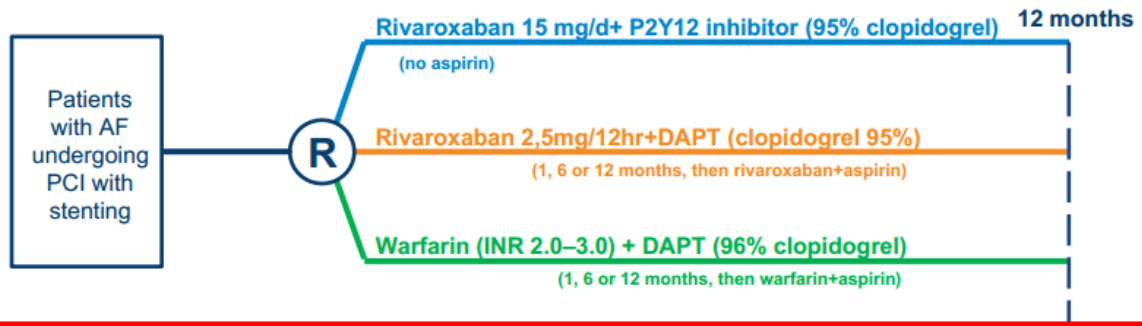
ORIGINAL ARTICLE

Prevention of Bleeding in Patients with Atrial Fibrillation Undergoing PCI

*N Engl J Med. 2016*;375:2423-2434

PIONEER AF-PCI

N=2124
30% ACS

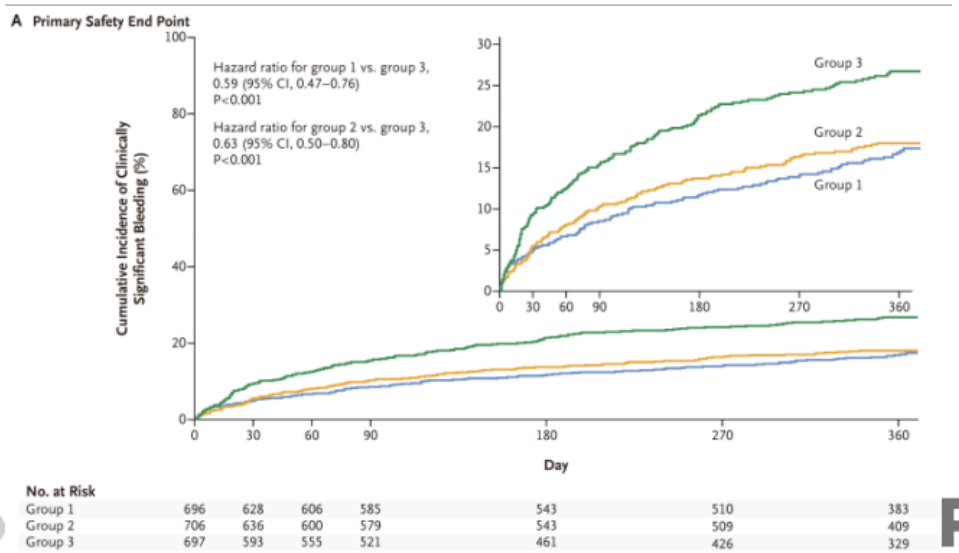



**Primary endpoint: TIMI clinically significant bleeding (major or minor requiring medical attention)**

# Strategies with antiplatelets and NOACs

## PIONEER AF-PCI

**major or clinically relevant non-major bleeding events**




Triple therapy (Warfarin +aspirin+clopidogrel)

Rivaroxaban 2,5mg/12hr + aspirin+clopidogrel

Rivaroxaban 15 mg/d + clopidogrel

PIONEER AF-PCI

# Strategies with antiplatelets and NOACs

## PIONEER AF-PCI

**major or clinically relevant non-major bleeding events**

Riva 15 + clopi | Riva 2,5 +aas+clopi | Warf+aas +clopi

Table 2. Cumulative Incidence of the Primary Safety End Point and Its Components, with Stratification According to Intended Duration of DAPT.*

| Cohort and End Point | Group 1 | Group 2 | Groups 1 and 2 | Group 3 | Group 1 vs. Group 3 | | Group 2 vs. Group 3 | | Groups 1 and 2 vs. Group 3 | |
|---|---|---|---|---|---|---|---|---|---|---|
| | No. of Participants with Events (Kaplan–Meier Event Rate) | | | | Hazard Ratio (95% CI) | P Value | Hazard Ratio (95% CI) | P Value | Hazard Ratio (95% CI) | P Value |
| All participants — no. | 696 | 706 | 1402 | 697 | | | | | | |
| Clinically significant bleeding | 109 (16.8) | 117 (18.0) | 226 (17.4) | 167 (26.7) | 0.59 (0.47–0.76) | <0.001 | 0.63 (0.50–0.80) | <0.001 | 0.61 (0.50–0.75) | <0.001 |
| Major bleeding | 14 (2.1) | 12 (1.9) | 26 (2.0) | 20 (3.3) | 0.66 (0.33–1.31) | 0.23 | 0.57 (0.28–1.16) | 0.11 | 0.61 (0.34–1.09) | 0.09 |
| Minor bleeding | 7 (1.1) | 7 (1.1) | 14 (1.1) | 13 (2.2) | 0.51 (0.20–1.28) | 0.14 | 0.50 (0.20–1.26) | 0.13 | 0.51 (0.24–1.08) | 0.07 |
| Bleeding requiring medical attention | 93 (14.6) | 102 (15.8) | 195 (15.2) | 139 (22.6) | 0.61 (0.47–0.80) | <0.001 | 0.67 (0.52–0.86) | 0.002 | 0.64 (0.51–0.80) | <0.001 |

PIONEER AF-PCI

# Strategies with antiplatelets and NOACs

## PIONEER AF-PCI

**Ischemic events**

Riva 15 + clopi | Riva 2,5 +aas+clopi | Warf+aas +clopi

Table 3. Cumulative Incidence of Secondary Efficacy End Points, with Stratification According to Intended Duration of DAPT.*

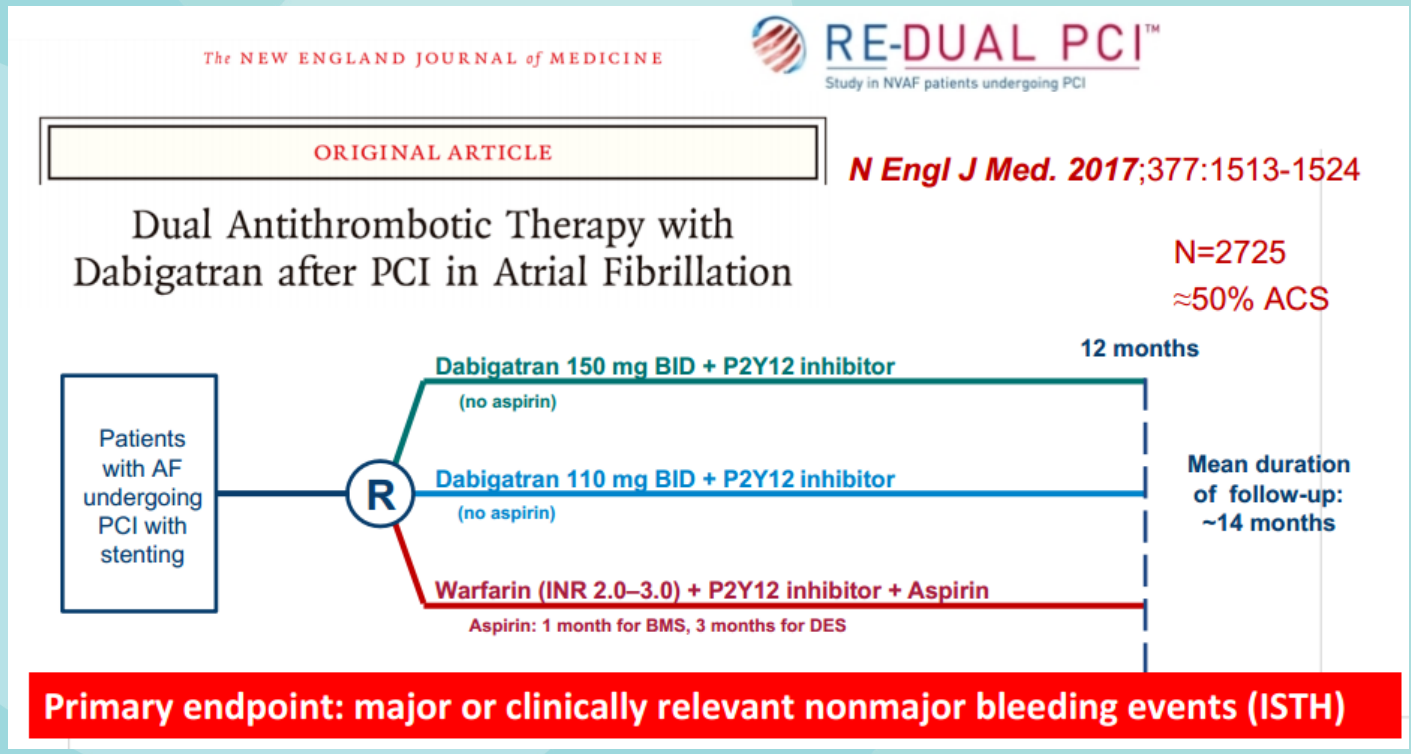
| Cohort and End Point | Group 1 | Group 2 | Group 3 | Group 1 vs. Group 3 | | Group 2 vs. Group 3 | |
|---|---|---|---|---|---|---|---|
| | No. of Participants with Events (Kaplan–Meier Event Rate) | | | Hazard Ratio (95% CI) | P Value | Hazard Ratio (95% CI) | P Value |
| **All participants — no.** | 694 | 704 | 695 | | | | |
| Major adverse cardiovascular event | 41 (6.5) | 36 (5.6) | 36 (6.0) | 1.08 (0.69–1.68) | 0.75 | 0.93 (0.59–1.48) | 0.76 |
| Death from cardiovascular causes | 15 (2.4) | 14 (2.2) | 11 (1.9) | 1.29 (0.59–2.80) | 0.52 | 1.19 (0.54–2.62) | 0.66 |
| Myocardial infarction | 19 (3.0) | 17 (2.7) | 21 (3.5) | 0.86 (0.46–1.59) | 0.62 | 0.75 (0.40–1.42) | 0.37 |
| Stroke | 8 (1.3) | 10 (1.5) | 7 (1.2) | 1.07 (0.39–2.96) | 0.89 | 1.36 (0.52–3.58) | 0.53 |
| Stent thrombosis | 5 (0.8) | 6 (0.9) | 4 (0.7) | 1.20 (0.32–4.45) | 0.79 | 1.44 (0.40–5.09) | 0.57 |
| Major adverse cardiovascular event or stent thrombosis | 41 (6.5) | 36 (5.6) | 36 (6.0) | 1.08 (0.69–1.68) | 0.75 | 0.93 (0.59–1.48) | 0.76 |

**Underpowered!**

PIONEER AF-PCI

# Strategies with antiplatelets and NOACs

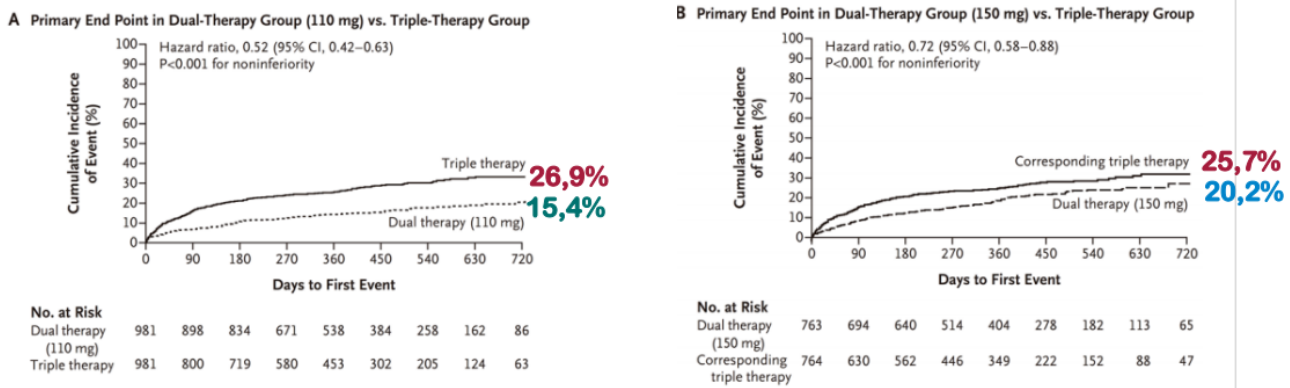
## RE-DUAL PCI



# Strategies with antiplatelets and NOACs

## RE-DUAL PCI

**major or clinically relevant non-major bleeding events**




RE-DUAL PCI™
Study in NVAF patients undergoing PCI

# Strategies with antiplatelets and NOACs

## RE-DUAL PCI

**major or clinically relevant non-major bleeding events**

Table 2. Safety End Points.*

| End Point | Dual Therapy with Dabigatran, 110 mg (N=981) | Triple Therapy with Warfarin (N=981) | Hazard Ratio (95% CI) | P Value† | Dual Therapy with Dabigatran, 150 mg (N=763) | Corresponding Triple Therapy with Warfarin (N=764) | Hazard Ratio (95% CI) | P Value† |
|---|---|---|---|---|---|---|---|---|
| | no. (%) | | | | no. (%) | | | |
| Primary end point: ISTH major or clinically relevant nonmajor bleeding | 151 (15.4) | 264 (26.9) | 0.52 (0.42–0.63) | <0.001 (<0.001 for noninferiority) | 154 (20.2) | 196 (25.7) | 0.72 (0.58–0.88) | 0.002 (<0.001 for noninferiority) |
| ISTH major bleeding | 49 (5.0) | 90 (9.2) | 0.52 (0.37–0.74) | <0.001 | 43 (5.6) | 64 (8.4) | 0.64 (0.43–0.94) | 0.02 |
| Total bleeding | 266 (27.1) | 421 (42.9) | 0.54 (0.46–0.63) | <0.001 | 254 (33.3) | 316 (41.4) | 0.72 (0.61–0.84) | <0.001 |
| Intracranial hemorrhage | 3 (0.3) | 10 (1.0) | 0.30 (0.08–1.07) | 0.06 | 1 (0.1) | 8 (1.0) | 0.12 (0.02–0.98) | 0.047 |
| TIMI major bleeding | 14 (1.4) | 37 (3.8) | 0.37 (0.20–0.68) | 0.002 | 16 (2.1) | 30 (3.9) | 0.51 (0.28–0.93) | 0.03 |
| TIMI major or minor bleeding | 29 (3.0) | 69 (7.0) | 0.41 (0.26–0.63) | <0.001 | 27 (3.5) | 48 (6.3) | 0.53 (0.33–0.85) | 0.009 |

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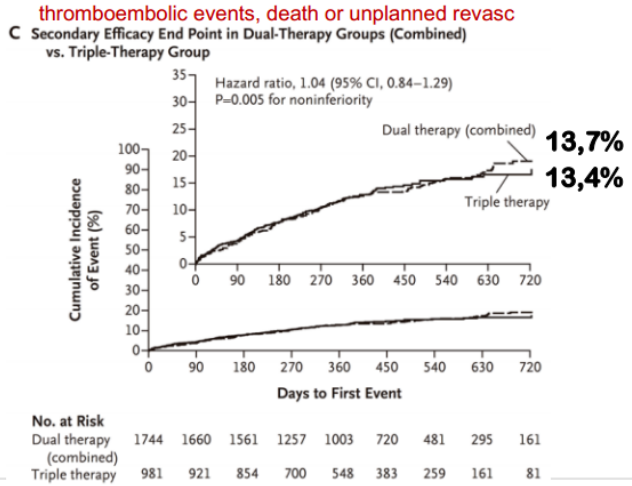
# Strategies with antiplatelets and NOACs

## RE-DUAL PCI

**Ischemic events**




**thromboembolic events or death**

| | | |
|---|---|---|
| Dabigatran 110mg+Clopi | 11,0% | P=0,07 |
| Triple ther (WAR) | 8,5% | |
| Dabigatran 150mg+Clopi | 7,9% | P=0,88 |
| Triple ther (WAR) | 7,9% | |

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Study in NVAF patients undergoing PCI

# Strategies with antiplatelets and NOACs

## RE-DUAL PCI

**Ischemic events**

Table 3. Efficacy End Points.*

| End Point | Dual Therapy with Dabigatran (Combined) vs. Triple Therapy with Warfarin | | | | Dual Therapy with Dabigatran (110 mg) vs. Triple Therapy with Warfarin | | | |
|---|---|---|---|---|---|---|---|---|
| | Combined Dual-Therapy Groups (N=1744) | Triple-Therapy Group (N=981) | Hazard Ratio (95% CI) | P Value† | 110-mg Dual-Therapy Group (N=981) | Triple-Therapy Group (N=981) | Hazard Ratio (95% CI) | P Value† |
| | *no. (%)* | | | | *no. (%)* | | | |
| Composite efficacy end point: thromboembolic events, death, or unplanned revascularization | 239 (13.7) | 131 (13.4) | 1.04 (0.84–1.29) | 0.74 (0.005 for noninferiority) | 149 (15.2) | 131 (13.4) | 1.13 (0.90–1.43) | 0.30 |
| Thromboembolic events or death | 168 (9.6) | 83 (8.5) | 1.17 (0.90–1.53) | 0.25 (0.11 for noninferiority) | 108 (11.0) | 83 (8.5) | 1.30 (0.98–1.73) | 0.07 |
| Death | | | | | 55 (5.6) | 48 (4.9) | 1.12 (0.76–1.65) | 0.56 |
| Myocardial infarction | | | | | 44 (4.5) | 29 (3.0) | 1.51 (0.94–2.41) | 0.09 |
| Stroke | | | | | 17 (1.7) | 13 (1.3) | 1.30 (0.63–2.67) | 0.48 |
| Definite stent thrombosis | | | | | 15 (1.5) | 8 (0.8) | 1.86 (0.79–4.40) | 0.15 |

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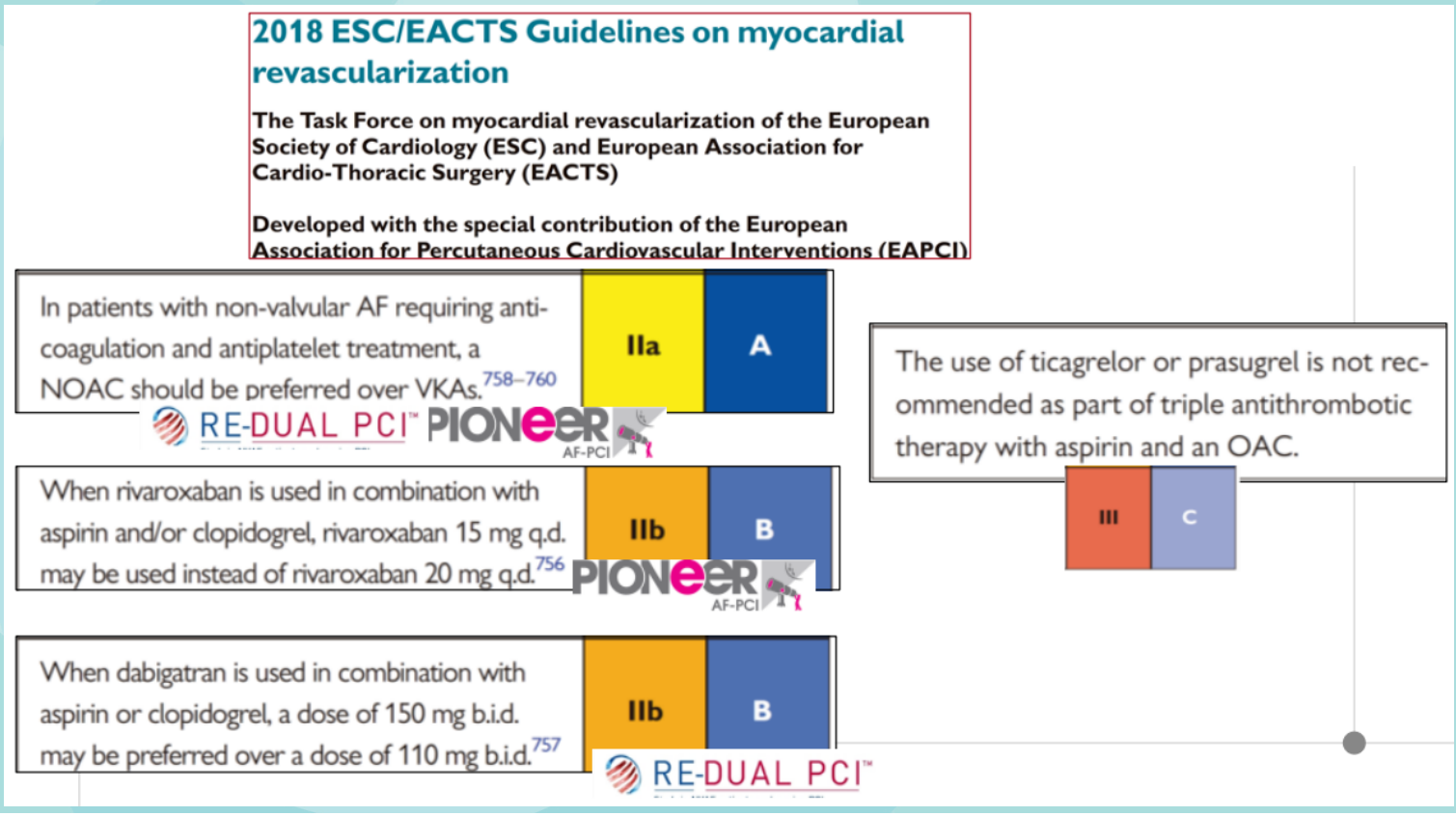
RE-DUAL PCI™
Study in NVAF patients undergoing PCI

# Guidelines

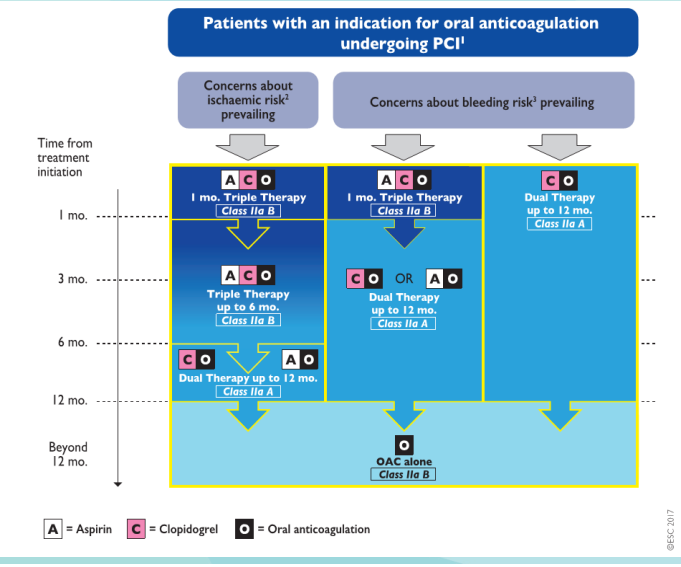

2018 ESC/EACTS Guidelines on myocardial revascularization
The Task Force on myocardial revascularization of the European Society of Cardiology (ESC) and European Association for Cardio-Thoracic Surgery (EACTS)
Developed with the special contribution of the European Association for Percutaneous Cardiovascular Interventions (EAPCI)
In patients with non-valvular AF requiring anti-coagulation and antiplatelet treatment, a NOAC should be preferred over VKAs.[758–760]
IIa
A
RE-DUAL PCI
PIONEER AF-PCI
When rivaroxaban is used in combination with aspirin and/or clopidogrel, rivaroxaban 15 mg q.d. may be used instead of rivaroxaban 20 mg q.d.[756]
IIb
B
PIONEER AF-PCI
When dabigatran is used in combination with aspirin or clopidogrel, a dose of 150 mg b.i.d. may be preferred over a dose of 110 mg b.i.d.[757]
IIb
B
RE-DUAL PCI
The use of ticagrelor or prasugrel is not rec-ommended as part of triple antithrombotic therapy with aspirin and an OAC.
III
C

# Guidelines

## Consistency

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

**The Task Force for dual antiplatelet therapy in coronary artery disease of the European Society of Cardiology (ESC) and of the European Association for Cardio-Thoracic Surgery (EACTS)**




### 2018 ESC/EACTS Guidelines on myocardial revascularization

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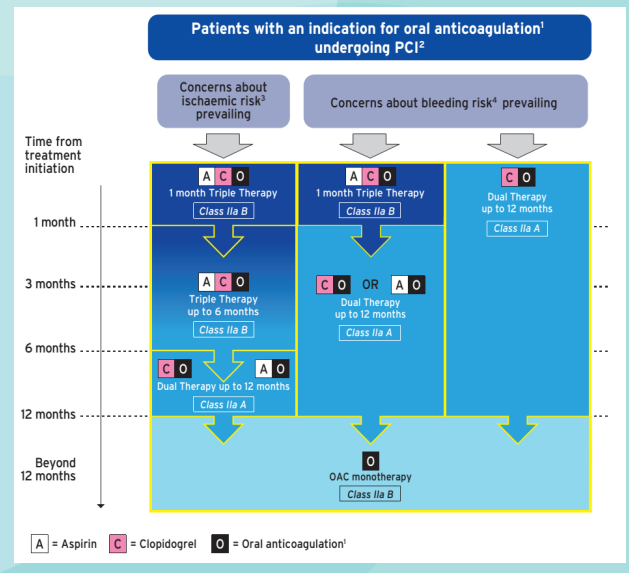
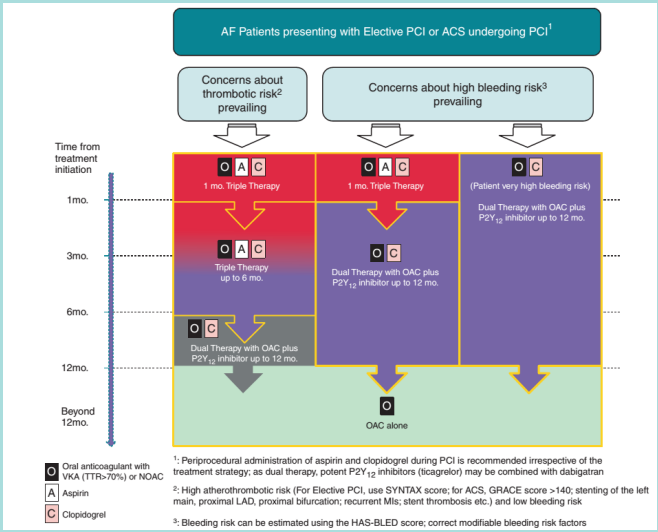
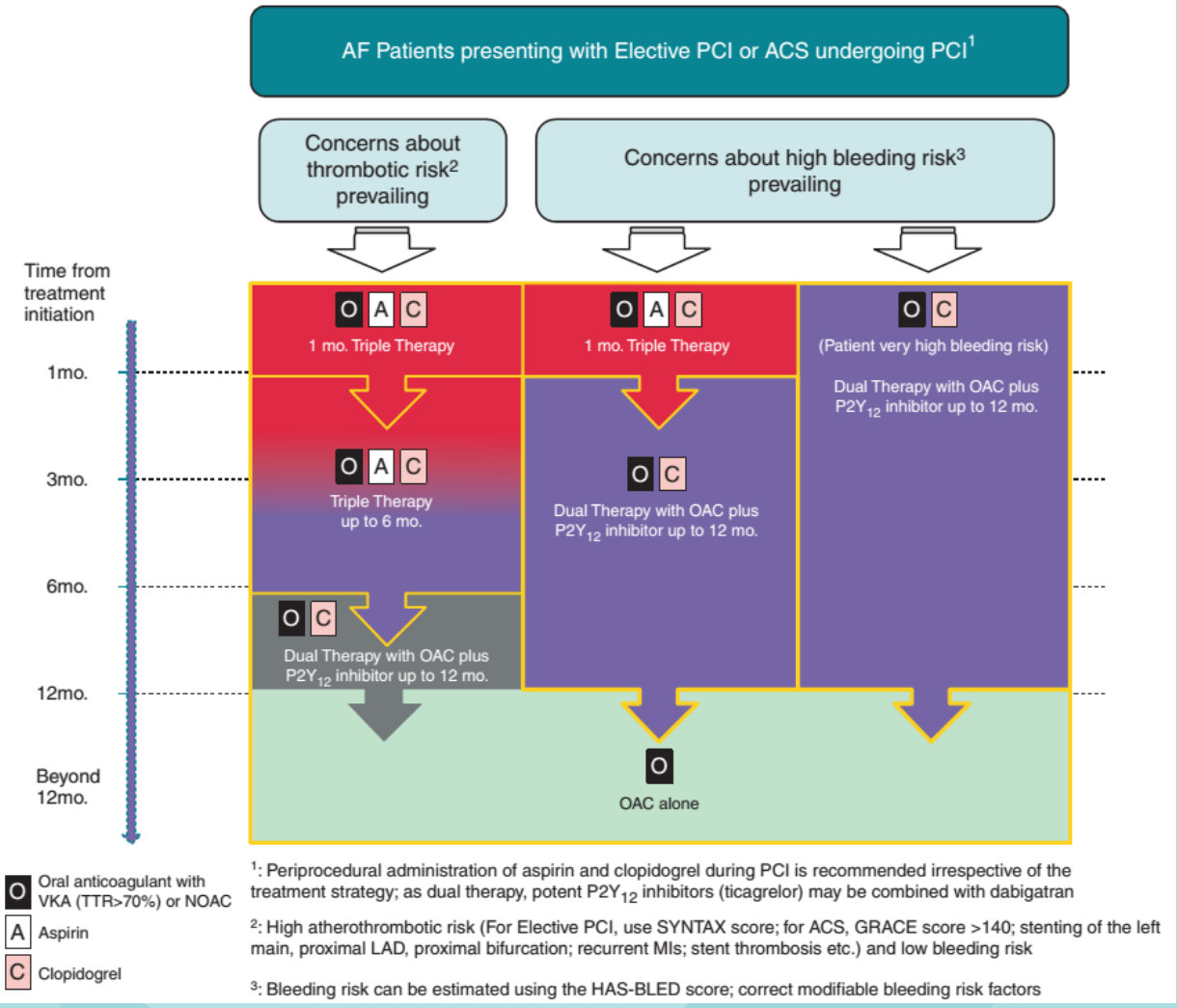



### 2018 Joint European consensus document on the management of antithrombotic therapy in atrial fibrillation patients presenting with acute coronary syndrome and/or undergoing percutaneous cardiovascular interventions: a




Antithrombotic strategies in the acute setting




**2018 Joint European consensus document on the management of antithrombotic therapy in atrial fibrillation patients presenting with acute coronary syndrome and/or undergoing percutaneous cardiovascular interventions: a**

# Conclusions

Pretreatment with P2Y12 inhibitors has a prognostic impact.
The timing for pretreatment is relevant:
- Post-angiography has advantages;
- Benefits seem to fade if angiography takes longer.

Morphine delays the effect of antiplatelet drugs.
- Is associated to increased risk of inhospital mortality;

For patients with AF and ACS with PCI:
- Triple therapy: prefer clopidogrel; prefer NOACs over VKA;
- Dual therapy:

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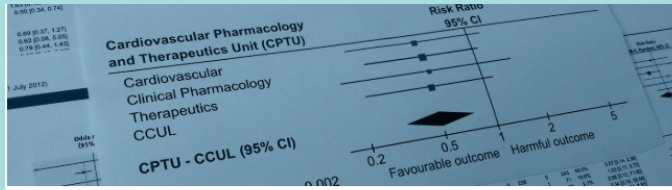


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# LOREM ISPUM DOLOR SIT AMET

## LOREM ISPUM DOLOR SIT AMET SED DIAM

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