Changing antithrombotic strategy in Acute Coronary Syndrome

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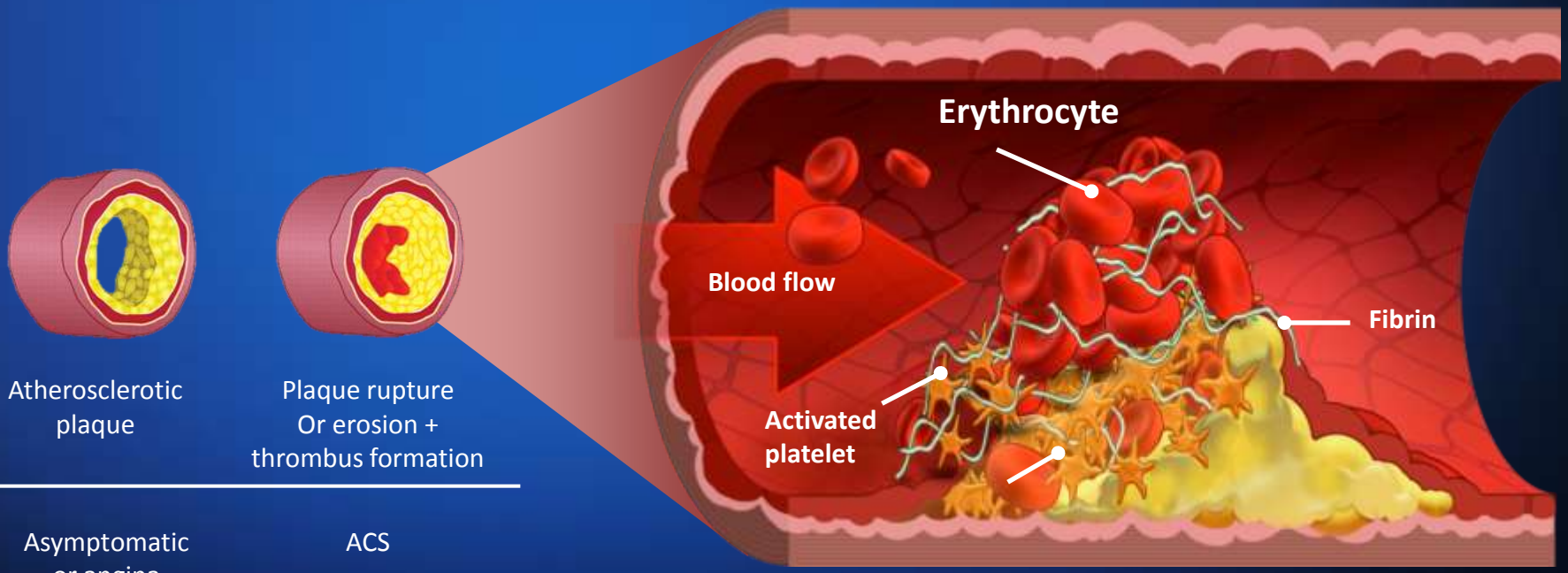
Pathophysiology of ACS

- ACS is associated with rupture of vulnerable plaque and a consequence of atherothrombosis.
- Both platelet activation and blood coagulation are directly involved in coronary thrombus formation
- Coronary artery thrombi are composed of platelets, fibrin and trapped erythrocytes.



ACS, acute coronary syndrome

1.Klingenberg R et al. Eur Heart J 2009;30:2838-2844. 2. Kolodgie *et al. Heart* 2004;90:1385–91. 3. Alsheikh-Ali *et al. Ann Intern Med* 2010;153:387–95. 4. *Insull. Am J Med.* 2009;122(1 Suppl):S3–S14.

Anti platelet therapy in ACS

- *CURE trial*
- *TRITON TIMI 38 trial*
- *PLATO trial*

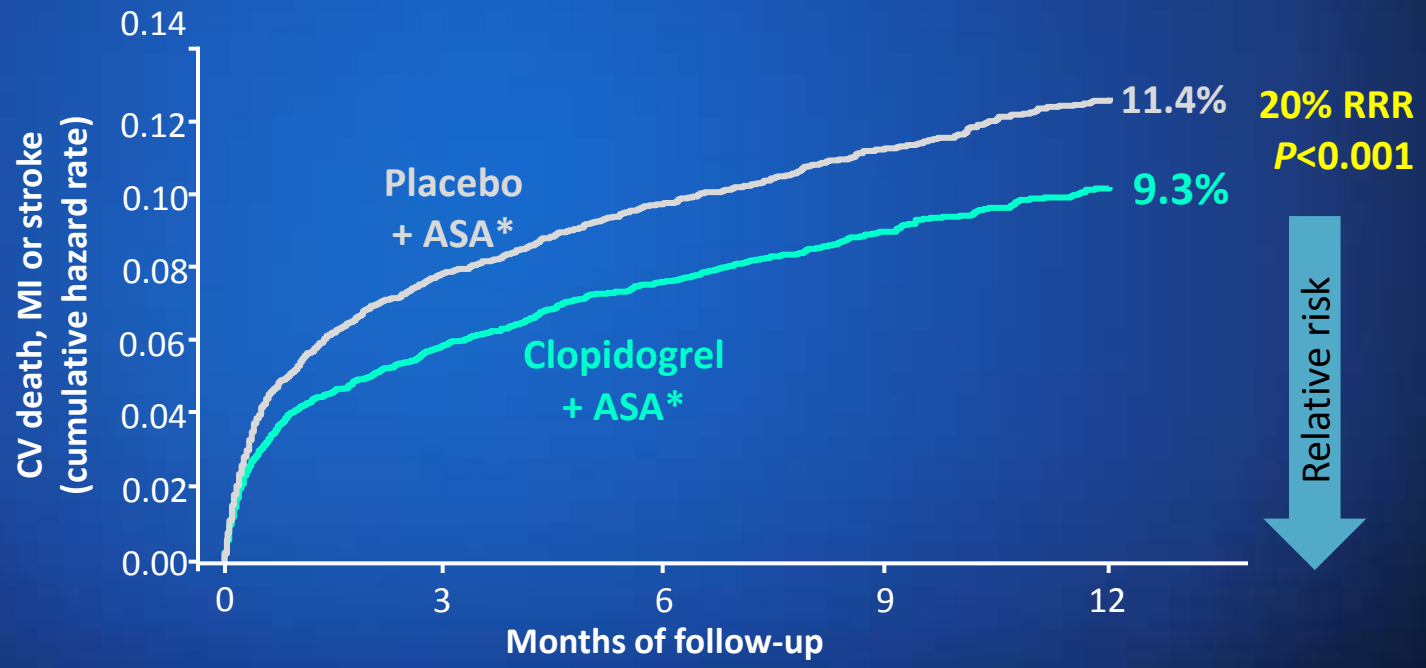
ACS, acute coronary syndrome; CURE, Clopidogrel in Unstable angina to prevent Recurrent Events

CURE:

- A randomized, double-blind, placebo-controlled trial.
- In 12,562 patients, comparing clopidogrel with placebo who presented with ACS without ST-segment elevation.

The first Primary Outcome

- **CV death, MI, stroke**
  - **20% reduction** of CV death, nonfatal MI & stroke (9.3% vs. 11.4%, *P*<0.001)



	Placebo + ASA* (n=6,303)	Clopidogrel + ASA* (n=6,259)
Major bleeding	2.7%	3.7%**

*In combination with standard therapy; **P=0.001

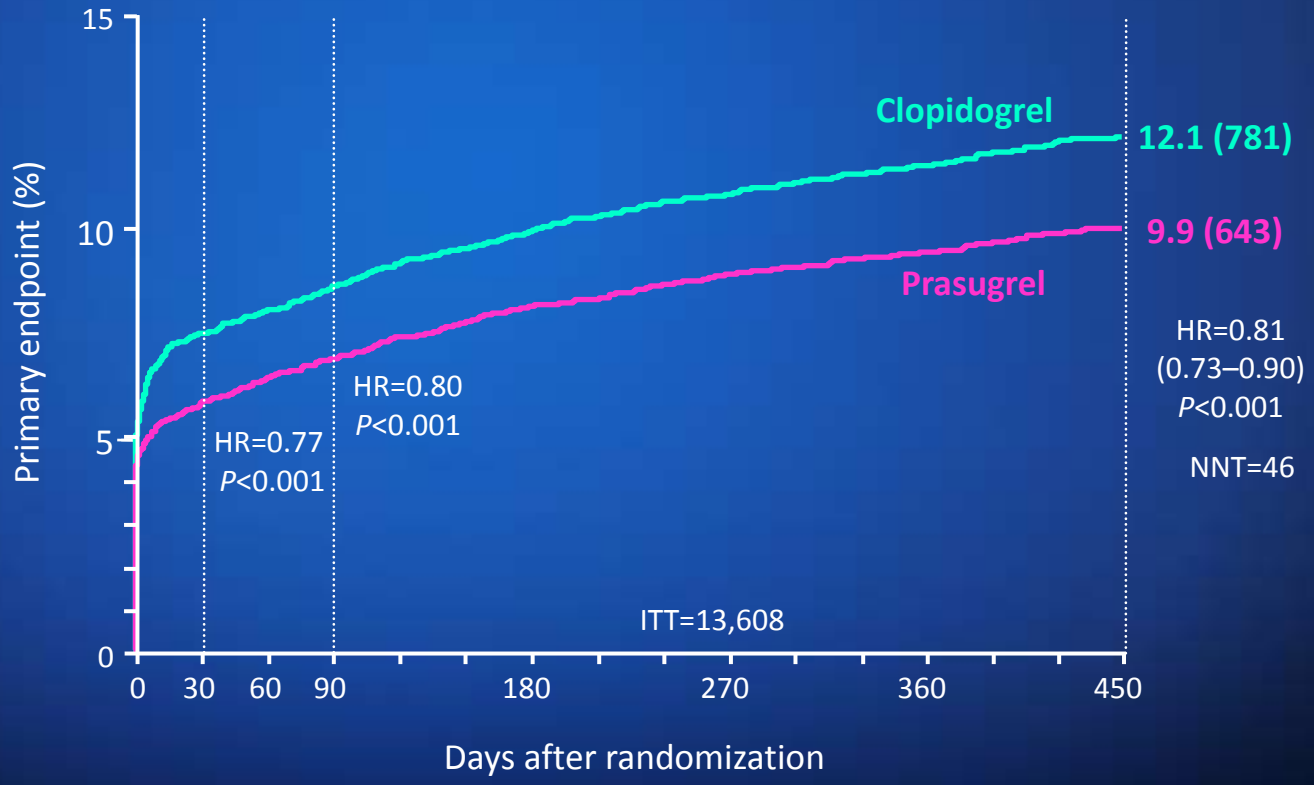
ASA, acetylsalicylic acid; CV, cardiovascular; MI, myocardial infarction; RRR, relative risk reduction.

N Engl J Med 2001;345: 494-502

TRITON TIMI 38: Primary endpoint

- Double blind, randomized trial.
- 13,608 patients with ACS awaiting PCI to usual care + prasugrel or clopidogrel.

- **CV death, MI, stroke**
  - Hazard ratio was **19% decreased** in prasugrel group. (*P*<0.001)

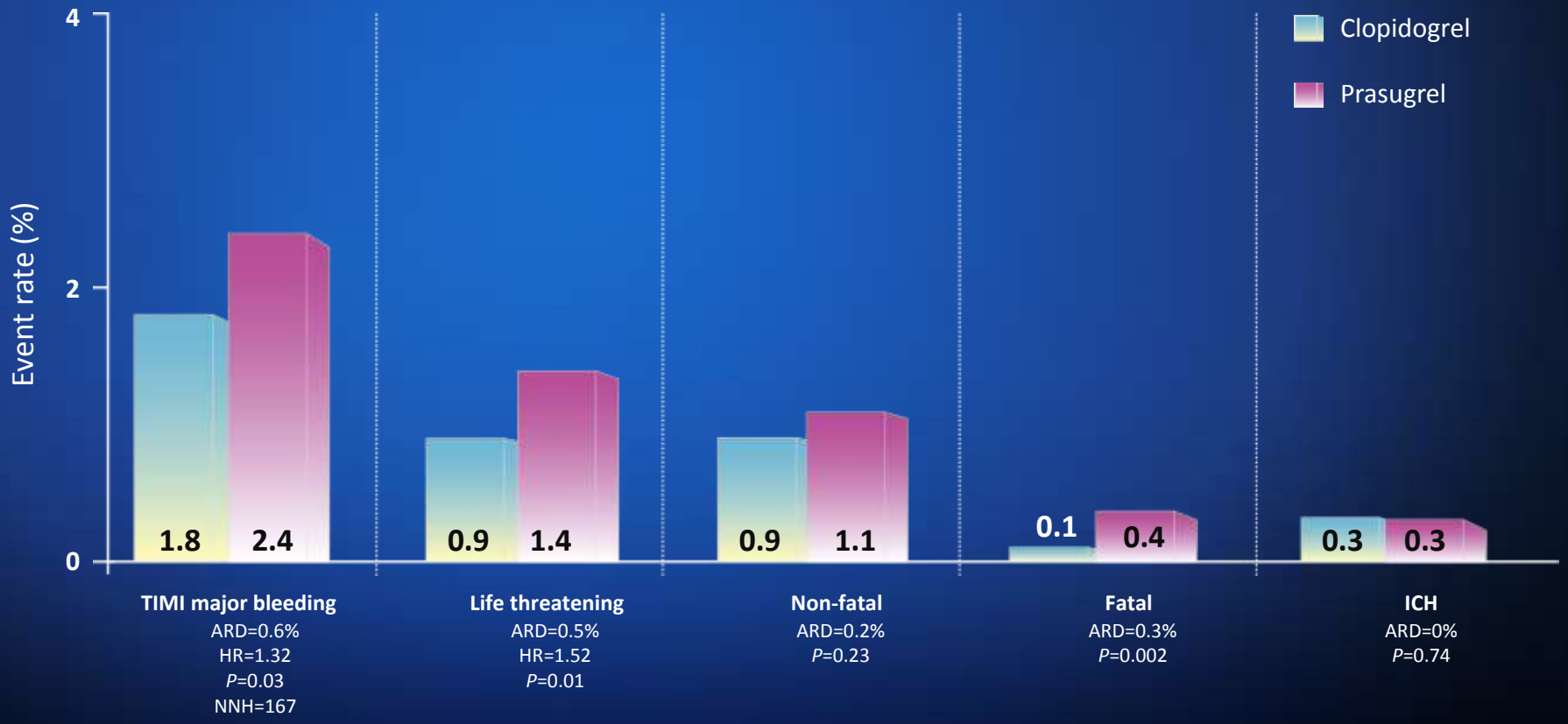


CV, cardiovascular; MI, myocardial infarction.

N Engl J Med 2007;357:2001-15.

TRITON TIMI 38:
Bleeding events

- **Fatal TIMI major bleeding** (safety cohort, N=13,457)
  - **Prasugrel 0.4% vs. clopidogrel 0.1% (*P*=0.002).**



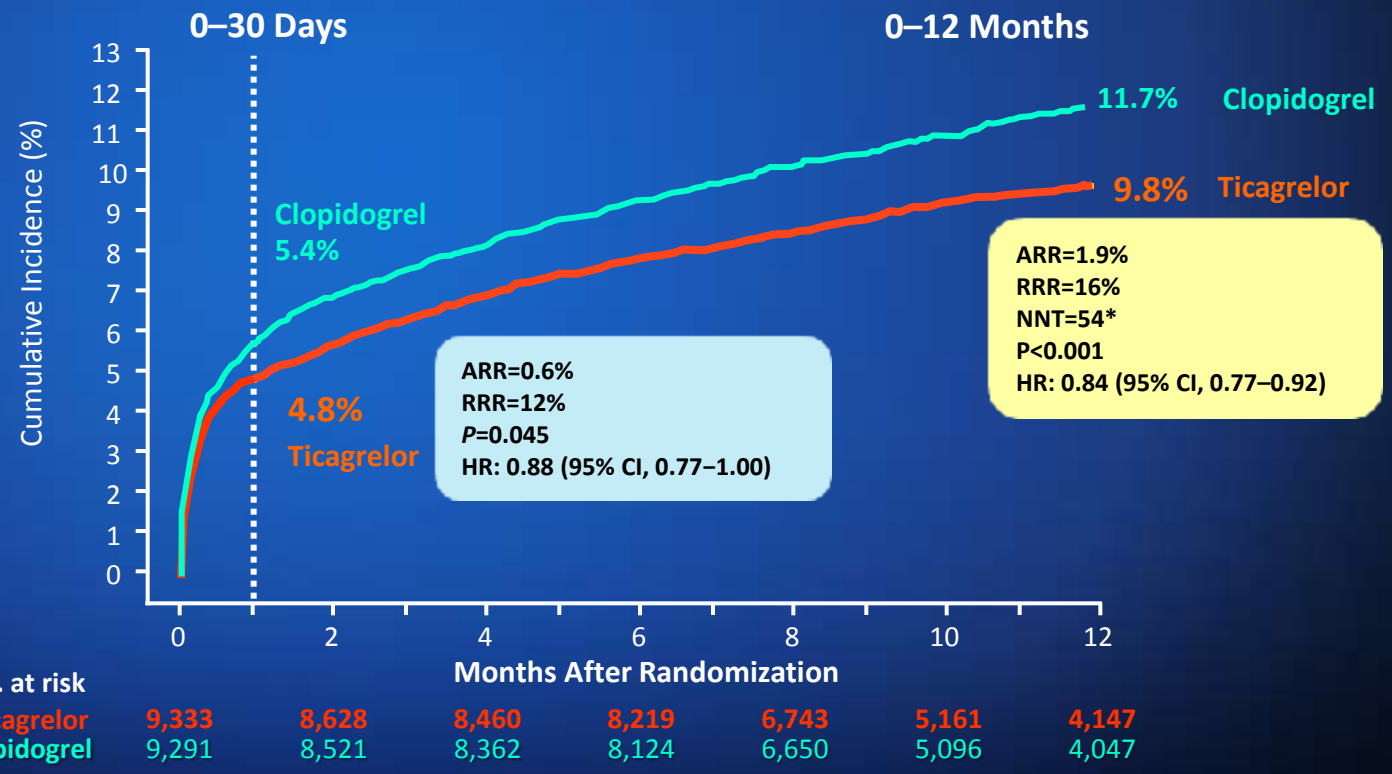
TIMI, Thrombolysis in Myocardial Infarction; CABG, coronaryartery bypass grafting; ICH, Intracranial hemorrhage.

N Engl J Med 2007;357:2001-15.

PLATO: Primary endpoint

- Multicenter, double-blind, randomized trial.
- Total 18,624 patients with ACS awaiting PCI to usual care + prasugrel or clopidogrel.

- **CV Death, MI, or Stroke**
  - Ticagrelor 9.8% vs. clopidogrel 11.7% (*P*<0.001).



Both groups included aspirin.
*NNT at one year.

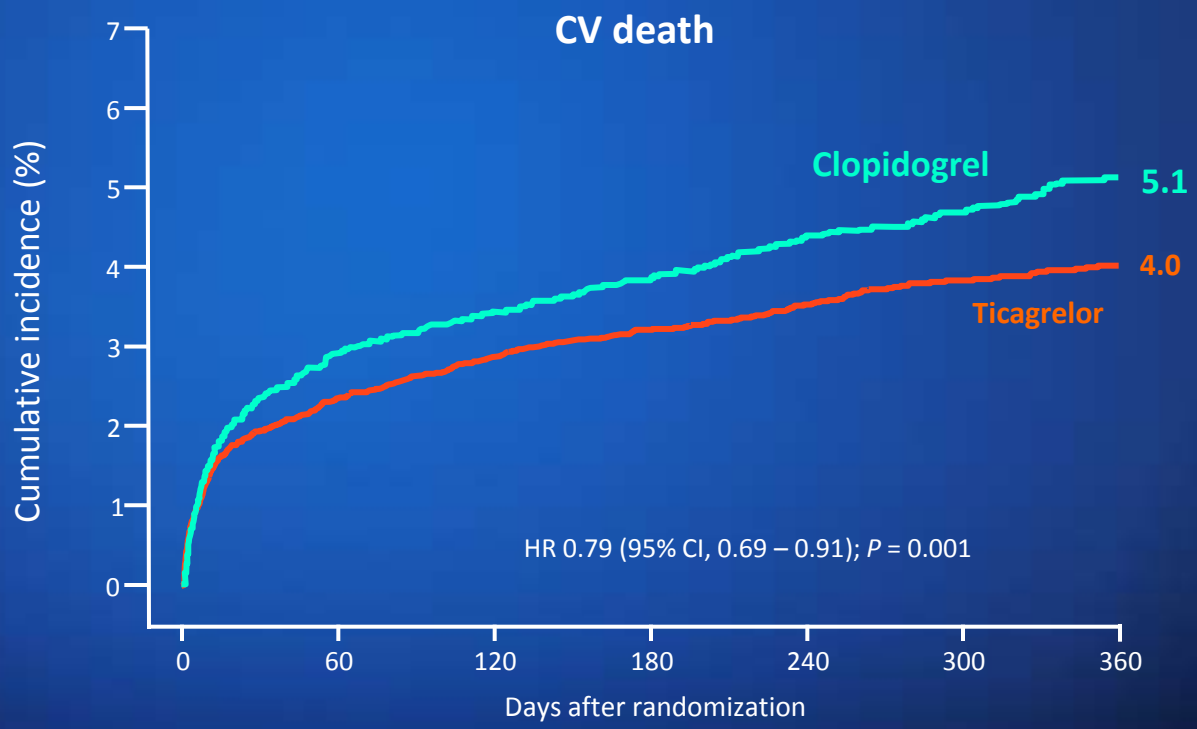
CV, cardiovascular; MI, myocardial infarction.

Wallentin L, et al. N Engl J Med. 2009;361:1045–1057.

PLATO:
Secondary efficacy endpoints

CV death

- Ticagrelor **4.0%** vs. clopidogrel **5.1%** (*P*=0.001)

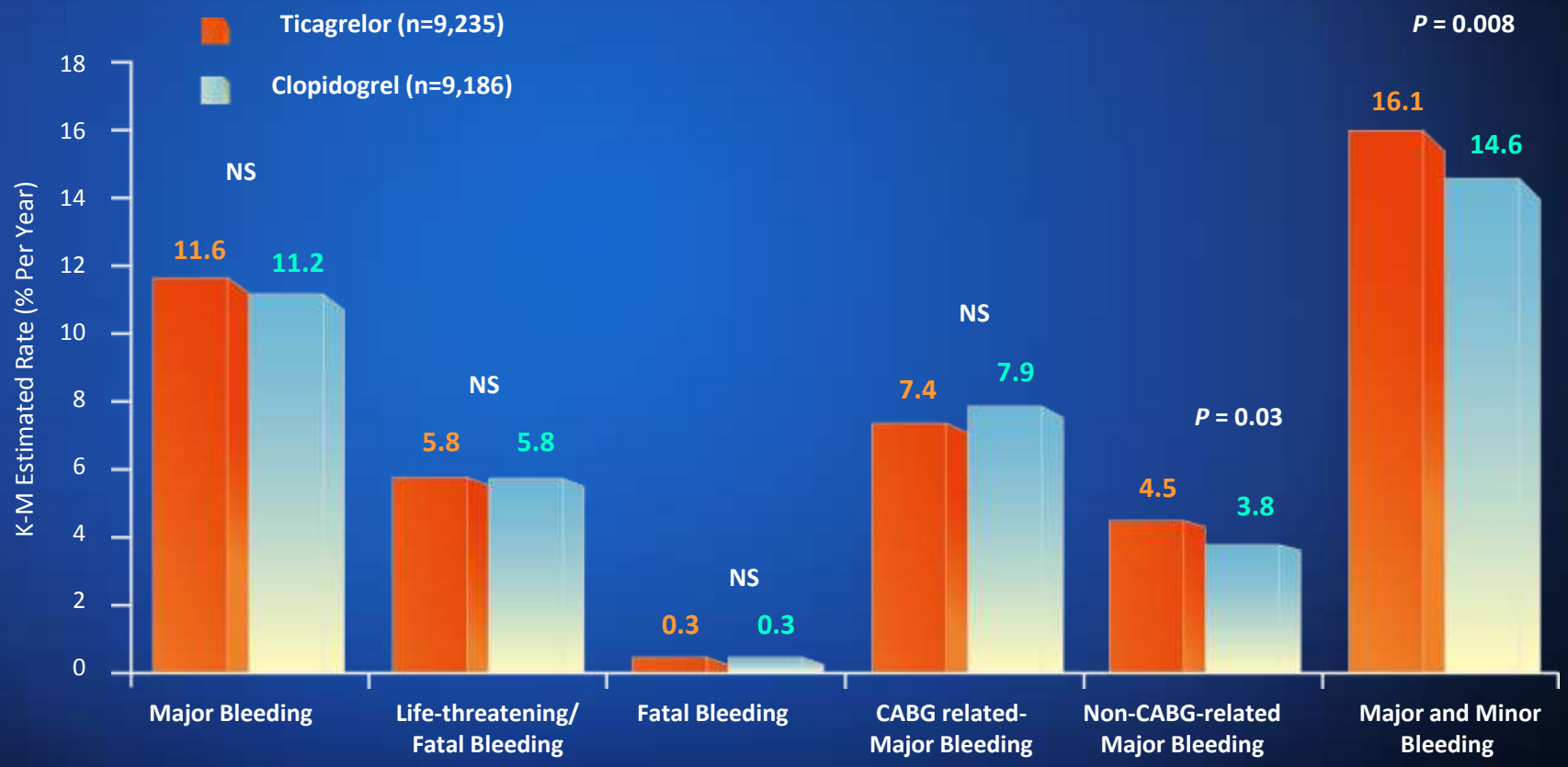


No. at risk							
Ticagrelor	9,333	8,294	8,822	8,626	7,119	5,482	4,419
Clopidogrel	9,291	8,865	8,780	8,589	7,079	5,441	4,364

CV, cardiovascular.

N Engl J Med 2009;361:1045-57

PLATO:
Safety end-point



All values presented by PLATO criteria.
Both groups included aspirin.

CABG, coronary artery bypass graft surgery; NS, not significant.

Wallentin L, et al. N Engl J Med. 2009;361:1045–1057.

2015 ESC guidelines

Platelet inhibition NSTE-ACS

Oral antiplatelet therapy

5.2.1. Aspirin & 5.2.2. $P2Y_{12}$ inhibitor

- ***Aspirin*** *is recommended for all patients without contraindications at an initial oral loading dosed of 150-300 mg (in aspirin-naive patients) and a maintenance dose of 75-100 mg/day long-term regardless of treatment strategy. (IA)*
- ***$P2Y_{12}$ inhibitor*** *is recommended, in addition to aspirin, for 12 months unless there are contraindications such as excessive risk of bleeds. (IA)*
  - ***Ticagrelor*** *(180 mg loading dose, 90 mg bid) is recommended, in the absence of contraindications, for all patients at moderate-to-high risk of ischemic 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). (IB)*
  - ***Prasugrel*** *(60 mg loading dose, 10 mg daily dose) is recommended in patients who are proceeding to PCI if no contraindication. (IB)*
  - ***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. (IB)*

ACS, acute coronary syndrome; VKA, vitamin K antagonist ; OAC, oral anticoagulation; NSTEMI, non-ST-elevation myocardial infarction; NSTE-ACS, non-ST-elevation ACS ; PCI, percutaneous coronary intervention

European Heart Journal 2016;37:267–315.

2014 AHA/ACC Guideline

Initial antiplatelet therapy in definite or likely NSTE –ACS

Oral antiplatelet therapy

4.3.1. Initial antiplatelet therapy in patients with definite or likely NSTE-ACS

- ***Aspirin***
  - *Non–enteric-coated aspirin to all patients promptly after presentation. (IA)*
  - *Aspirin maintenance dose continued indefinitely. (IA)*
- ***$P2Y_{12}$ inhibitors***
  - *Clopidogrel loading dose followed by daily maintenance dose in patients unable to take aspirin. (IB)*
  - *$P2Y_{12}$ inhibitor, in addition to aspirin, for up to 12 months for patients treated initially with either an early invasive or initial ischemia guided strategy (IB) :*
    - ✓ *Clopidogrel*
    - ✓ *Ticagrelor**
  - *Ticagrelor in preference to clopidogrel for patients treated with an early invasive or ischemia-guided strategy (IIa B)*

*The recommended maintenance dose of aspirin to be used with ticagrelor is 81 mg daily.

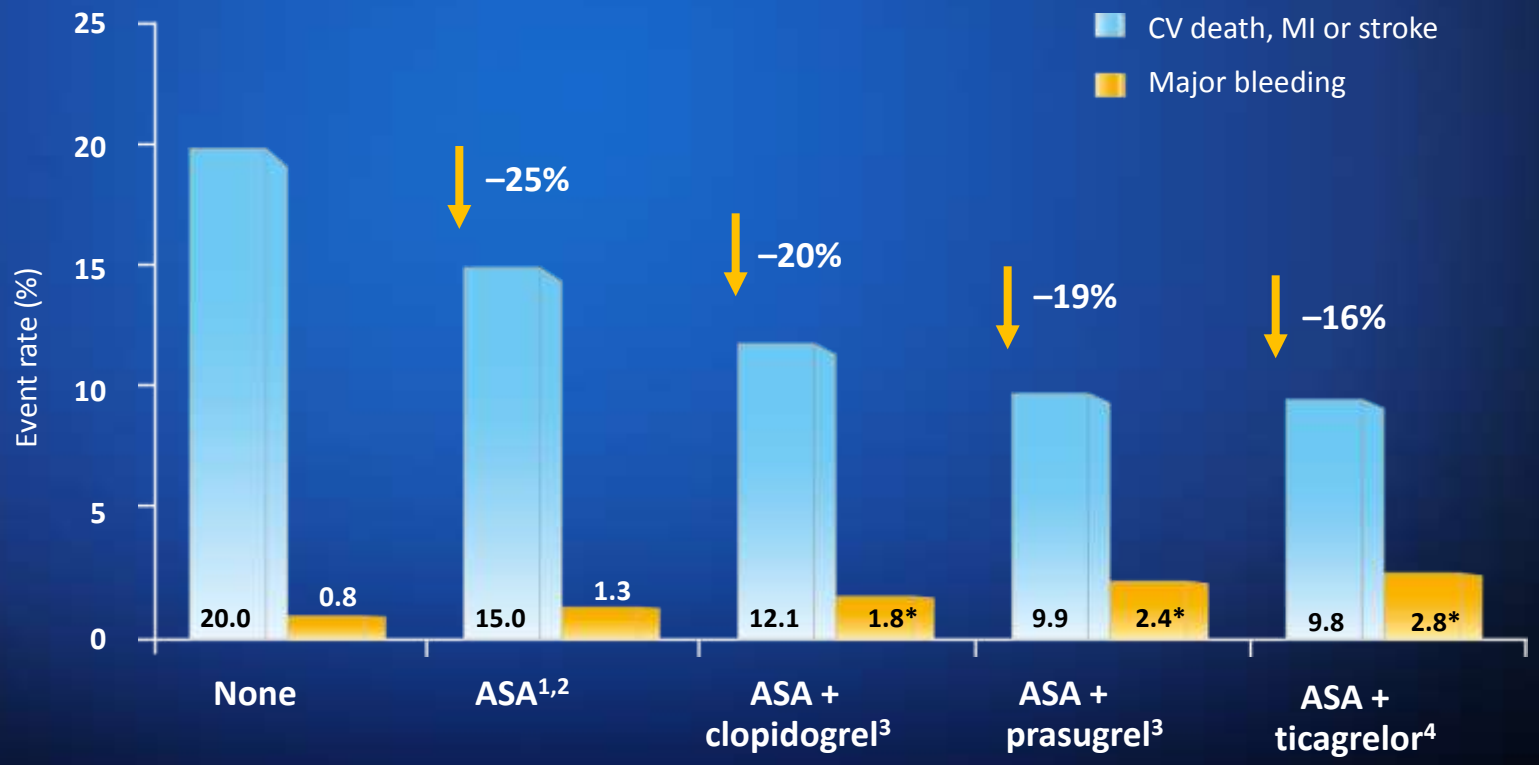
NSTE-ACS, non-ST-elevation acute coronary syndrome; ACS, acute coronary syndrome.

Circulation. 2014;130:e344-e426.

Unmet needs in 2nd prevention of ACS

DAPT is not enough

- Risk of major adverse CV events after ACS remains as high as 10%
- Attributable to a persistent hypercoagulable state after the index event .



*Major bleeding: non-CABG-related TIMI major bleeding

ASA, acetylsalicylic acid; CV, cardiovascular; MI, myocardial infacrtion.; CABG, coronary artery bypass graft surgery.

1. Antiplatelet Trialists' Collaboration, 1994; 2. Antithrombotic Trialists' Collaboration, 2002; 3. Wiviott et al, 2007; 4. Wallentin et al, 2009

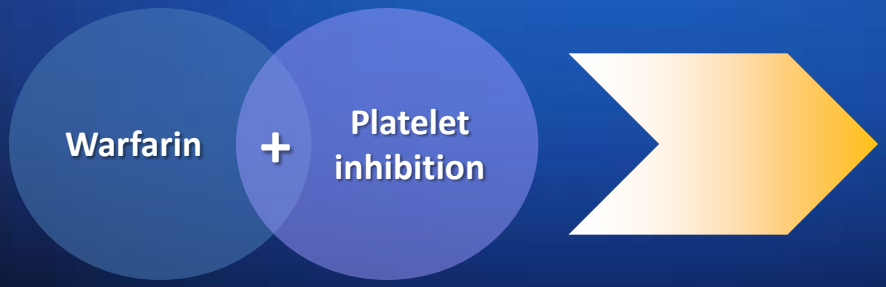
Rivaroxaban in patients with ACS

- *Oral anticoagulation therapy in ACS*
- *ATLAS ACS 2 TIMI 46*
- *ATLAS ACS 2 TIMI 51 & Sub-analysis*

ACS, acute coronary syndrome; ATLAS ACS, Anti-Xa Therapy to Lower Cardiovascular Events in Addition to Standard Therapy in Subjects with Acute Coronary Syndrome

Role of Warfarin in 2nd prevention of ACS

• **Warfarin**	- for many decades the only oral anticoagulant available in patients with **ACS**
• **Most commonly prescribed for VTE**	- Deep vein thrombosis (blood clots in the veins of the legs) - Pulmonary embolism (a blood clot in the lungs)
• **Also prescribed for**	- AF - A prosthetic (replacement or mechanical) heart valve - Acute myocardial infarction (heart attack) - Secondary prevention of stroke in AF



Preventing *thrombus formation* & *cardiovascular events*

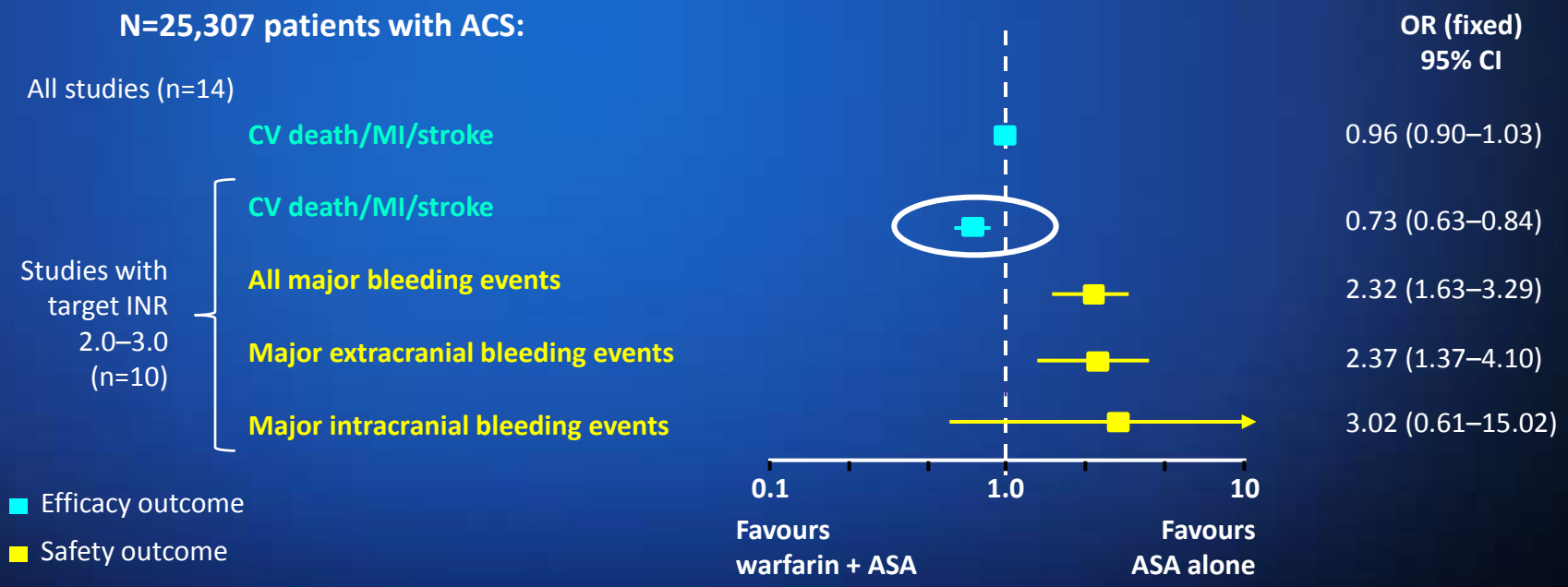
ACS, acute coronary syndrome; VTE, Venous Thromboembolism; AF,atrial fibrillation.

Cardiology 2014 129 224 - 232. http://www.nhs.uk/conditions/Anticoagulants-warfarin-/Pages/Introduction.aspx

Meta-analysis:
Warfarin therapy in ACS

Warfarin+ASA vs. ASA alone:

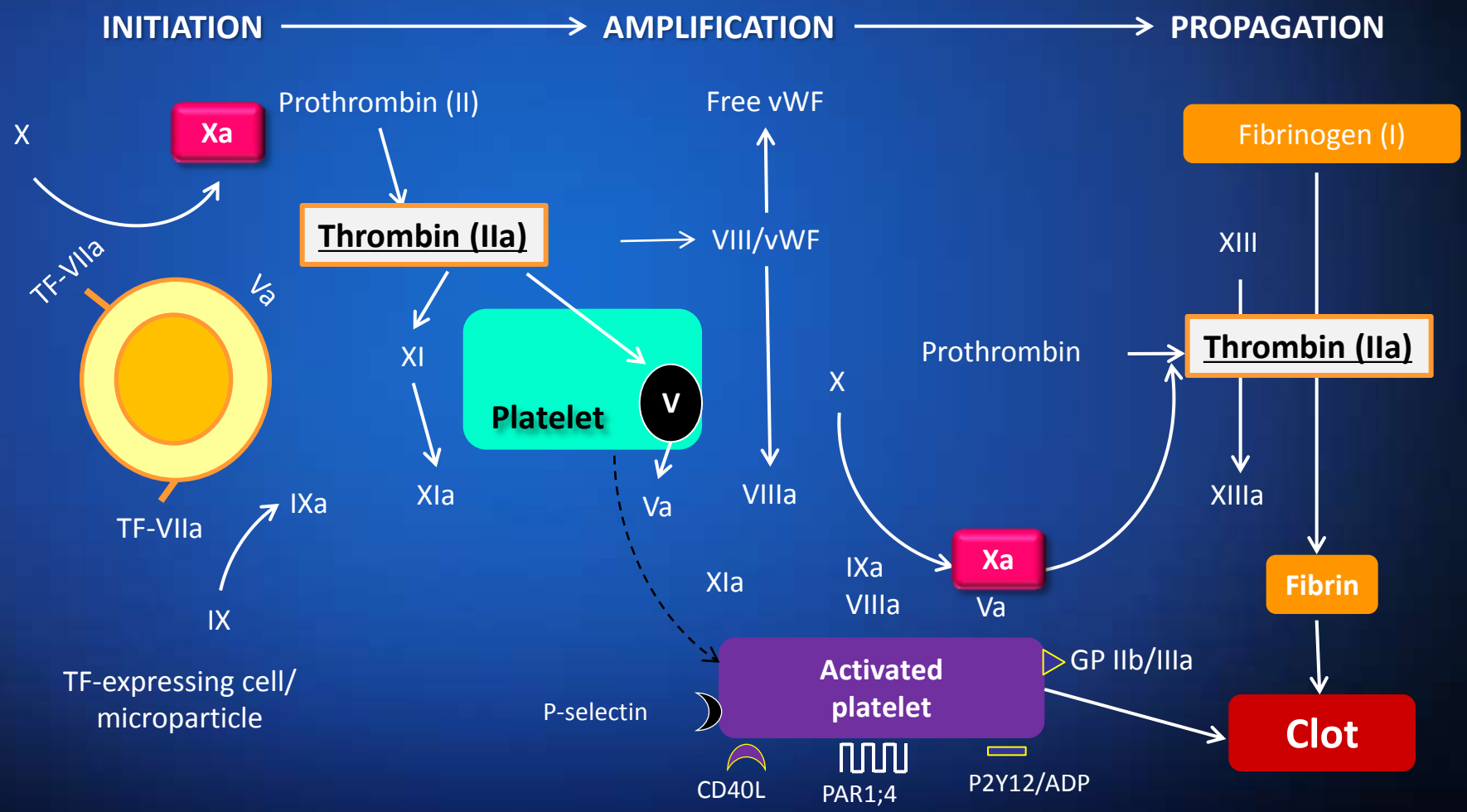
- Reduces CV death/MI/stroke in patients adjusted between INR 2–3.
- Increases the risk of major bleeding events.



ACS, acute coronary syndrome; ASA, acetylsalicylic acid; CI, confidence interval; CV, cardiovascular; INR, international normalized ratio; MI, myocardial infarction; OR, odds ratio.

Andreotti et al. Eur Heart J 2006;27:519–26.

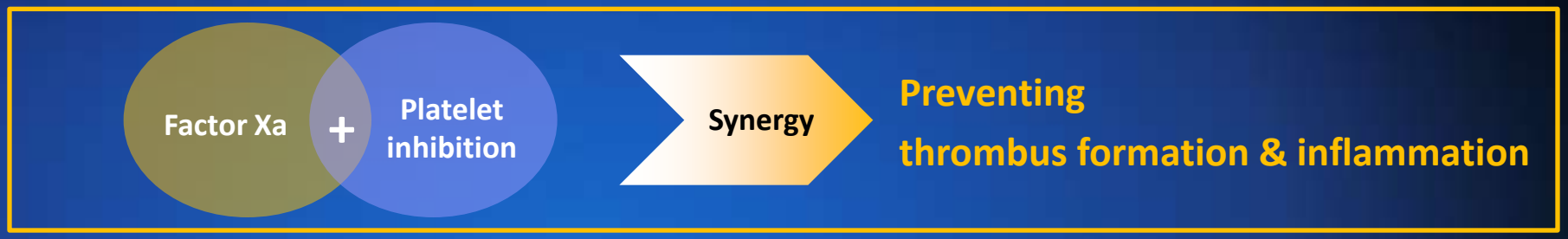
Thrombus formation



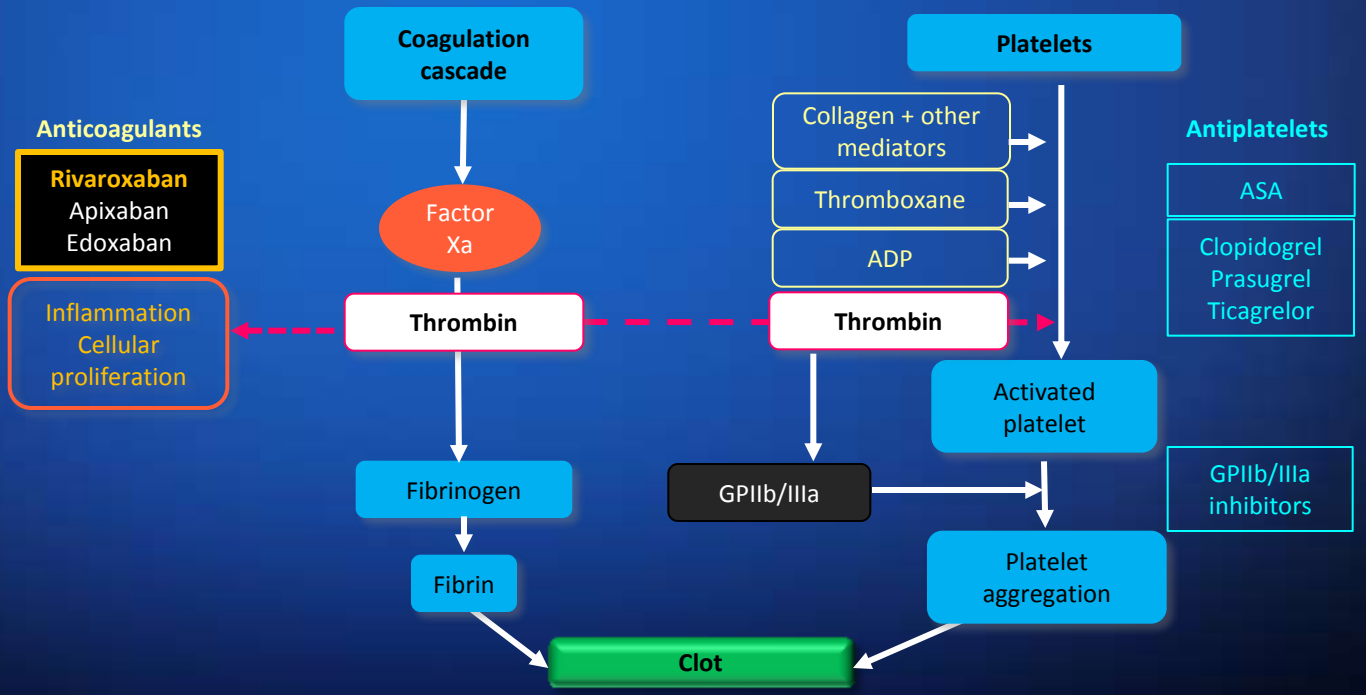
ADP, adenosine diphosphate; GP, glycoprotein; PAR, protease-activated receptor; TF, tissue factor; vWF, von Willebrand factor.

De Caterina et al. Thromb Haemost 2013;109:569–79.

NOAC in clot formation & stabilization in ACS



- **NOACs,** like factor Xa inhibitors (**rivaroxaban**) have been evaluated as treatment options for **ACS**.



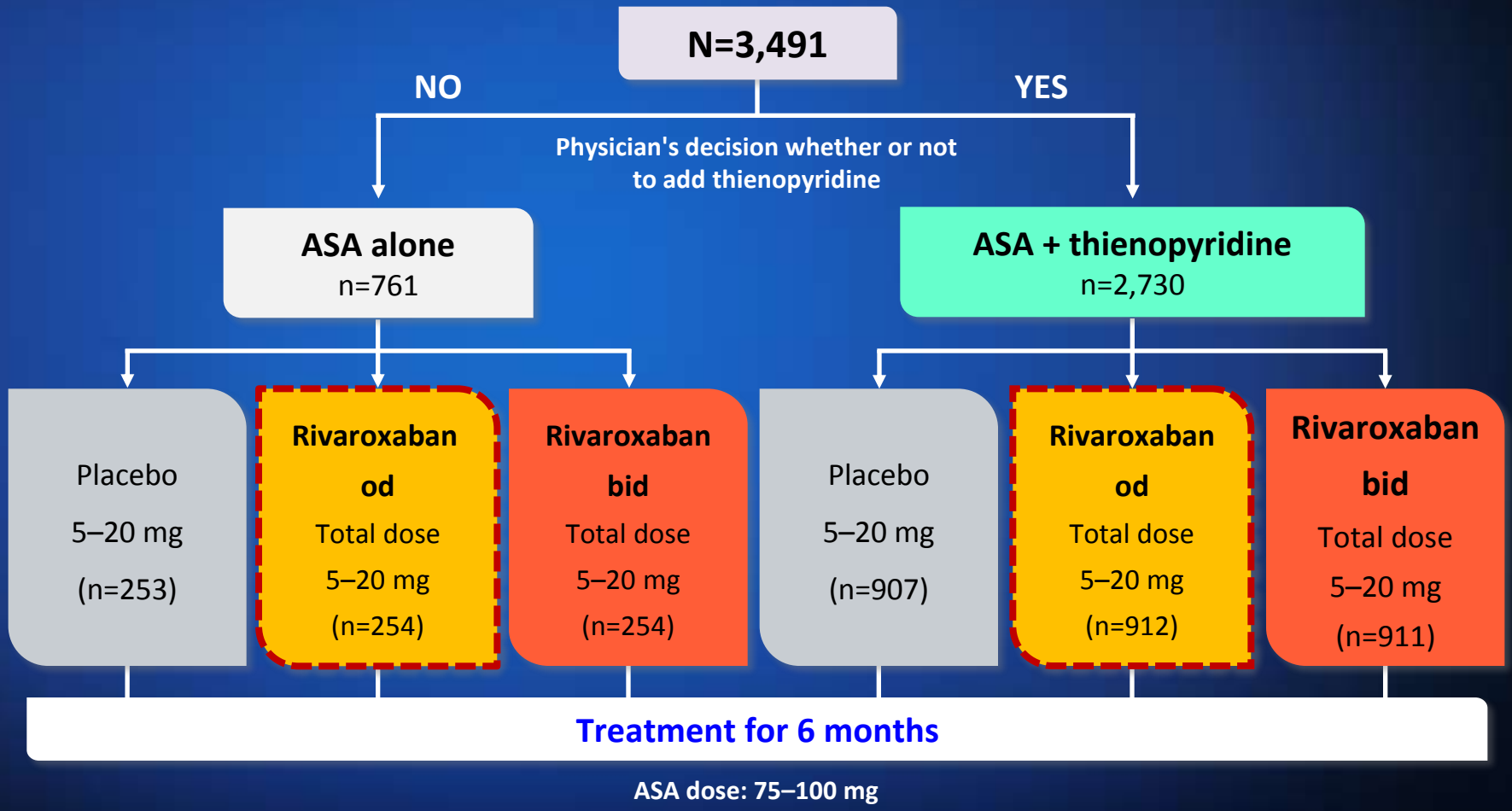
ACS, Acute coronary syndrome; NOACs, new oral anticoagulants; ASA, acetyl salicylic acid.

1. Cardiology 2014 129 224 - 232 2. Mackman N. Nature 2008;451:914–918

ATLAS ACS-TIMI 46

ATLAS ACS, Anti-Xa Therapy to Lower Cardiovascular Events in Addition to Standard Therapy in Subjects with Acute Coronary Syndrome.

ATLAS ACS 2-TIMI 46:
Study design



ATLAS ACS, Anti-Xa Therapy to Lower Cardiovascular Events in Addition to Standard Therapy in Subjects with Acute Coronary Syndrome; ASA, acetylsalicylic acid; ATLAS ACS, Anti-Xa Therapy to Lower Cardiovascular Events in Addition to Standard Therapy in Subjects with Acute Coronary Syndrome; bid, twice daily; od, once daily; TIMI, Thrombolysis In Myocardial Infarction.

Lancet 2009;374:29–38.

ATLAS ACS 2-TIMI 46:
Study endpoints

• **Main safety endpoint**	**Clinically significant bleeding** (a composite of TIMI major bleeding, TIMI minor bleeding and bleeding requiring medical attention).*
• **Main efficacy endpoint**	Time to death or the first episode of MI, stroke, or severe ischaemia requiring revascularization, up to 6 months from enrolment.
• **Secondary efficacy endpoint**	Time to death or the first episode of MI or stroke up to 6 months from enrolment.

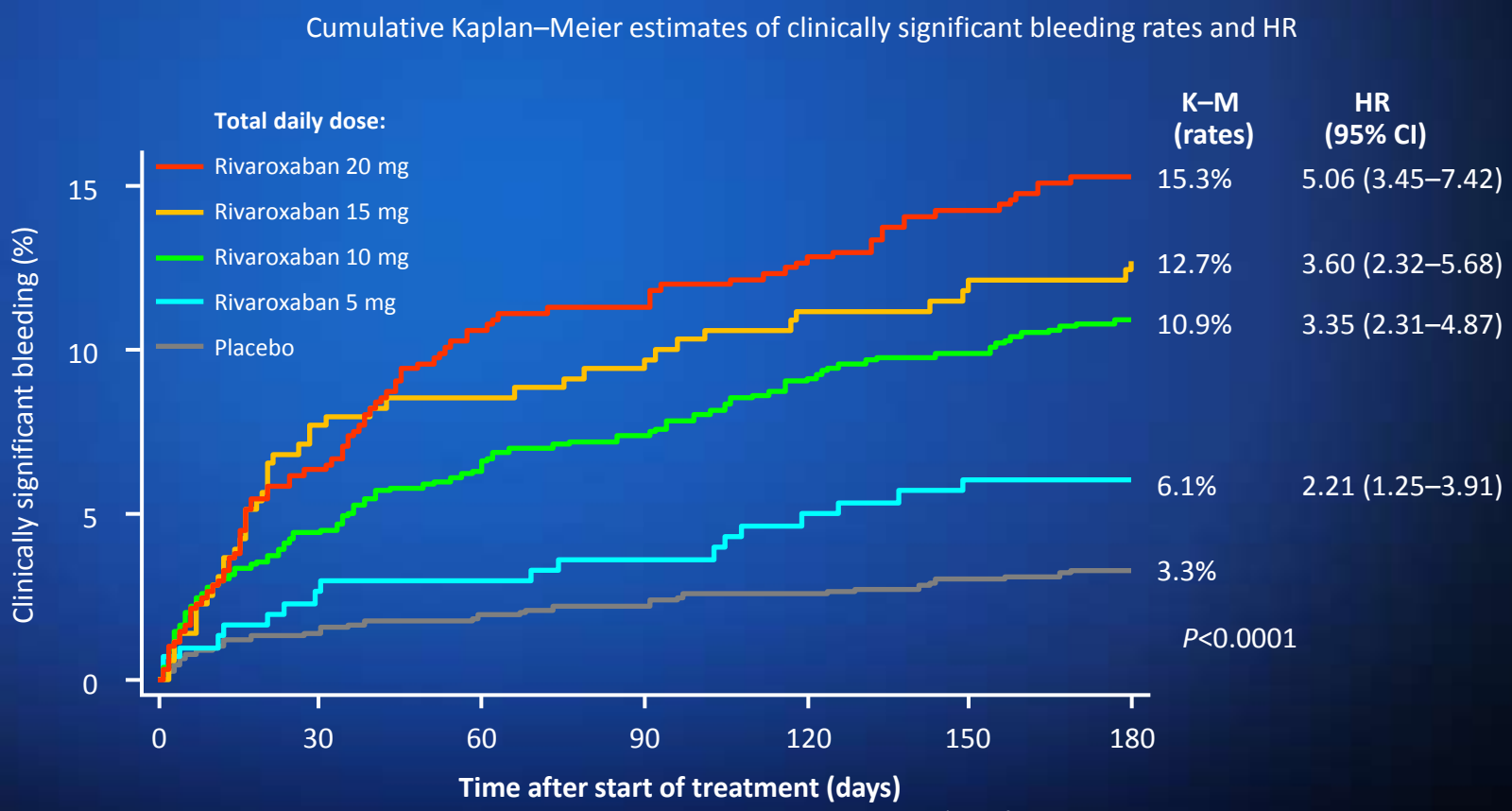
* The definition of 'clinically significant bleeding' was created to establish a sensitive tool for the ATLAS ACS TIMI 46 study. It was the first study where this composite safety endpoint was tested.

ATLAS ACS, Anti-Xa Therapy to Lower Cardiovascular Events in Addition to Standard Therapy in Subjects with Acute Coronary Syndrome; ACS, acute coronary syndrome; MI, myocardial infarction; TIMI, thrombolysis in myocardial infarction.

Lancet 2009;374:29–38.

ATLAS ACS 2-TIMI 46:
Bleeding rate

- **Bleeding increased with rivaroxaban in a dose-dependent manner.**



*One fatal intracranial haemorrhage in the ASA-only arm.

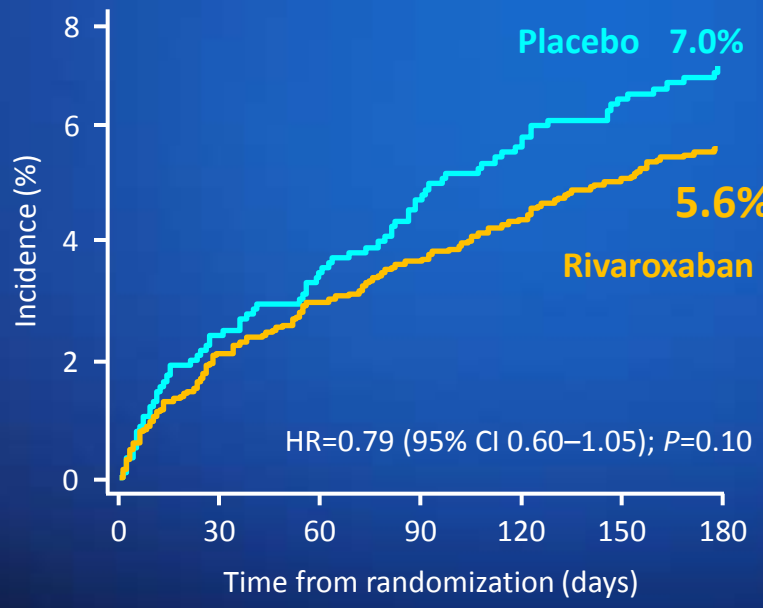
ATLAS ACS, Anti-Xa Therapy to Lower Cardiovascular Events in Addition to Standard Therapy in Subjects with Acute Coronary Syndrome; ASA, acetylsalicylic acid; CI, confidence interval; HR, hazard ratio; K–M, Kaplan–Meier.

Lancet 2009;374:29–38.

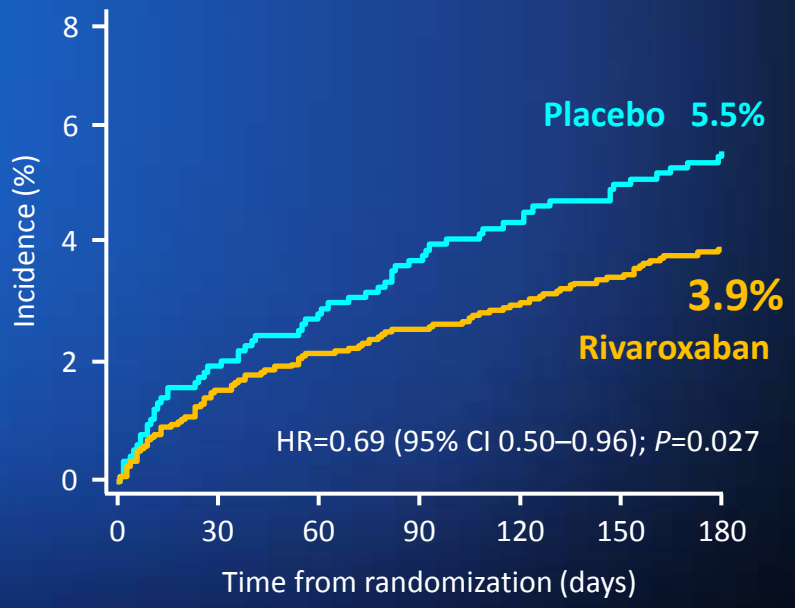
ATLAS ACS TIMI 46:
Major CV outcomes

- 21% reduction of primary efficacy endpoint (*P*=0.10)
- 31% reduction of secondary efficacy endpoint (*P*=0.027)

Composite of death*, MI, stroke, severe recurrent ischemia requiring revascularization (primary efficacy endpoint)



Composite of death*, MI, stroke (key secondary efficacy endpoint)



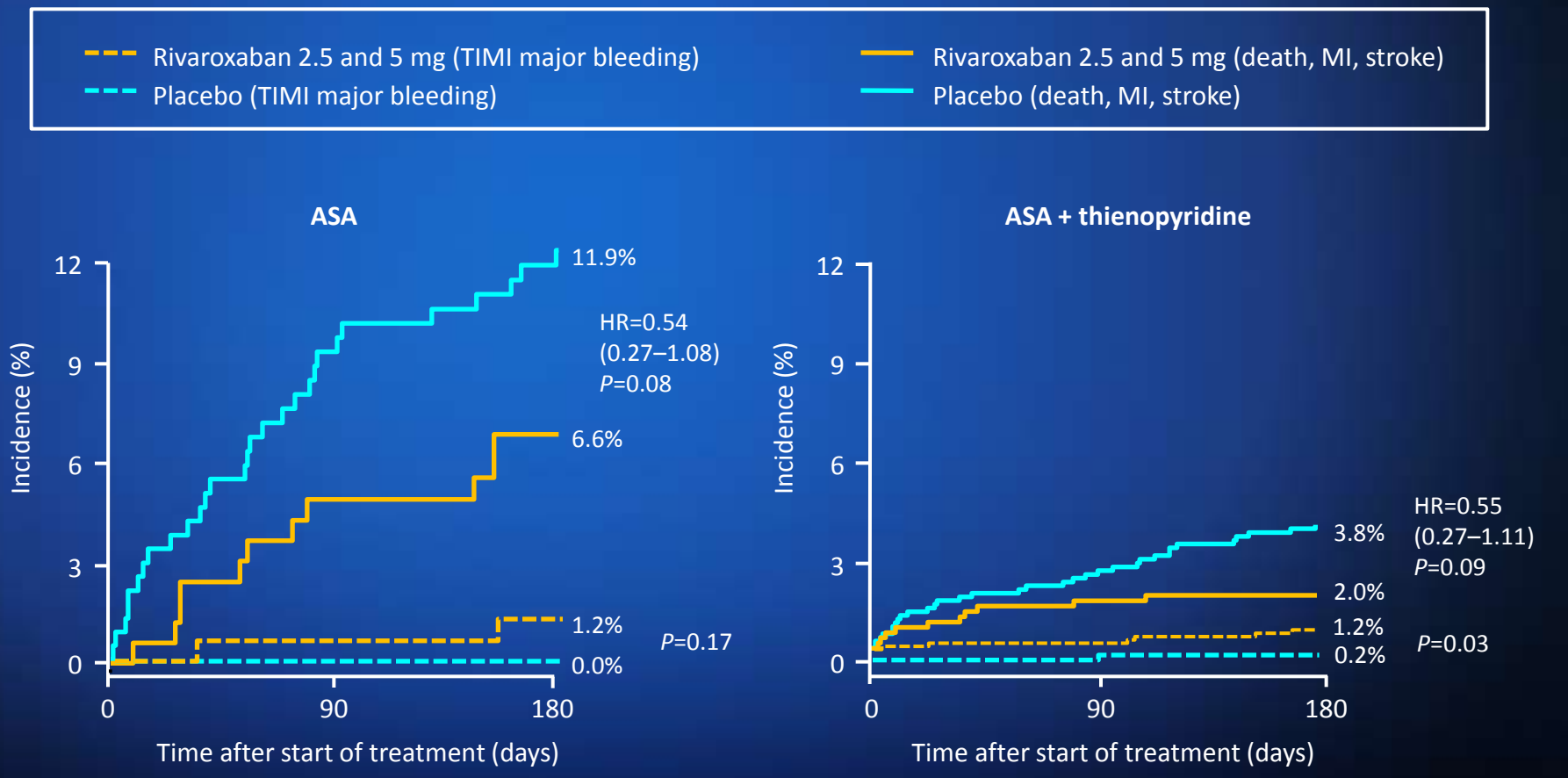
*All-cause death.

ATLAS ACS, Anti-Xa Therapy to Lower Cardiovascular Events in Addition to Standard Therapy in Subjects with Acute Coronary Syndrome; HR, hazard ratio; MI, myocardial infarction; CV, cardiovascular

Lancet 2009;374:29–38.

ATLAS ACS TIMI 46:
Efficacy - Safety profile

- **Both 2.5 mg and 5 mg bid doses of rivaroxaban showed a favorable efficacy-safety profile**



ATLAS ACS, Anti-Xa Therapy to Lower Cardiovascular Events in Addition to Standard Therapy in Subjects with Acute Coronary Syndrome; bid, twice daily; ASA, acetylsalicylic acid; MI, myocardial infarction; TIMI, thrombolysis In myocardial infarction; HR, hazard ratio; K–M, Kaplan–Meier.

1. Gibson *et al.* AHA 2008 (www.clinicaltrialresults.org); 2. Mega *et al. Lancet* 2009;374:29–38.

ATLAS ACS TIMI 46:
Summary & conclusion

- ***Safety***
  - Rivaroxaban increased bleeding in a dose-dependent manner versus placebo, with a significant dose trend ($p<0.0001$)
- ***Efficacy****
  - Primary efficacy endpoint: a trend towards reduction in the composite of death, MI, stroke and severe recurrent ischaemia versus placebo
  - Secondary efficacy endpoint: significant reduction in the rate of death, MI or stroke versus placebo
- ***Optimal dosage***
  - *Two lowest doses (2.5 and 5 mg bid)* offered the best balance between safety and efficacy and were selected for the Phase III trial.

Why choose the bid dosing regimen for the phase III study in patients with ACS?

- **Pharmacokinetic and pharmacodynamic profiles of rivaroxaban suggest lower peaks and higher troughs with bid versus od dosing and, therefore, more tightly-controlled anticoagulation.**

* Study was underpowered for efficacy.

ATLAS ACS, Anti-Xa Therapy to Lower Cardiovascular Events in Addition to Standard Therapy in Subjects with Acute Coronary Syndrome; bid, twice daily; MI, myocardial infarction; od, once daily.

Lancet 2009;374:29–38.

ATLAS ACS 2-TIMI 51

ATLAS ACS, Anti-Xa Therapy to Lower Cardiovascular Events in Addition to Standard Therapy in Subjects with Acute Coronary Syndrome.

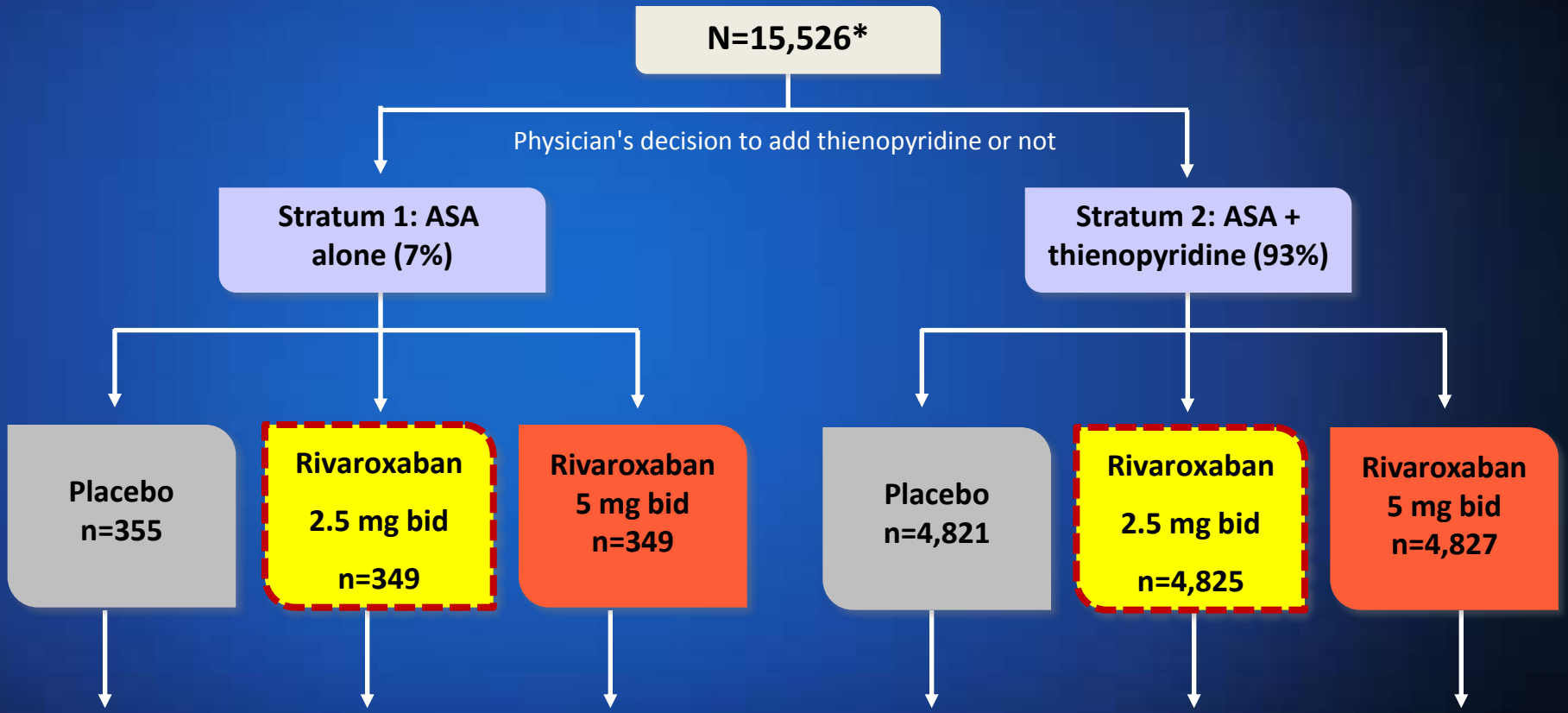
ATLAS ACS 2-TIMI 51:
Study design (1)

Objectives	To determine whether rivaroxaban, when added to antiplatelet therapy, was safe and reduced the risk of the composite of cardiovascular death, MI or stroke in patients with ACS compared with placebo
Primary efficacy endpoint	A composite of cardiovascular death, MI or stroke (ischaemic, haemorrhagic or uncertain).
Secondary efficacy endpoint	A composite of all-cause death, MI or stroke.
Main safety endpoint	Incidence of major bleeding not associated with CABG surgery (assessed according to the TIMI bleeding definition).
Other safety endpoint	- Other bleeding events classified according to the TIMI, GUSTO and rivaroxaban programme scales - Adverse events - Clinical laboratory tests - Liver safety assessments

ATLAS ACS, Anti-Xa Therapy to Lower Cardiovascular Events in Addition to Standard Therapy in Subjects with Acute Coronary Syndrome; ACS, acute coronary syndrome; STEMI, ST-Elevation Myocardial Infarction; NSTEMI, non- ST-Elevation Myocardial Infarction; CV, cardiovascular; MI, myocardial infarction; CABG, Coronary artery bypass graft surgery; TIMI, thrombolysis in myocardial infarction.

N Engl J Med 2012;366:9-19

ATLAS ACS 2-TIMI 51:
Study design (2)



ASA dose= 75–100 mg/day

*184 patients were excluded from the efficacy analyses prior to unblinding because of trial misconduct at three sites

ATLAS ACS, Anti-Xa Therapy to Lower Cardiovascular Events in Addition to Standard Therapy in Subjects with Acute Coronary Syndrome; bid, twice daily; ASA, acetylsalicylic acid.

Mega JL *et al. N Engl J Med* 2012;366:9-19

ATLAS ACS 2-TIMI 51:
Study population

- **Baseline Characteristics of the Patients**

  The study included patients (≥18 years of age) who had presented with symptoms suggestive of an ACS and in whom an STEMI, NSTEMI, or UA had been diagnosed.

	Rivaroxaban 2.5 mg bid (n=5174)	Rivaroxaban 5 mg bid (n=5176)	Placebo (n=5176)
Mean age, years (SD)	62 (9)	62 (9)	62 (9)
Male sex, %	75	74	75
Median weight, kg	78	78	78
Median CrCl, ml/min	85	85	86
Medical history, %			
Prior MI	26	27	27
Hypertension	67	68	68
Diabetes mellitus	32	32	32
Index diagnosis, %			
STEMI	50	50	51
NSTEMI	26	26	26
UA	24	24	24
PCI or CABG for index	61	60	60

ATLAS ACS, Anti-Xa Therapy to Lower Cardiovascular Events in Addition to Standard Therapy in Subjects with Acute Coronary Syndrome; STEMI, ST-Elevation Myocardial Infarction; NSTEMI, non- ST-Elevation Myocardial Infarction; ACS, acute coronary syndrome; MI, myocardial infacrtion; UA, unstable angina; PCI, percutaneous cardiovascular intervention; CABG, Coronary artery bypass graft surgery.

Mega JL *et al*. *N Engl J Med* 2012;366:9-19

ATLAS ACS 2 TIMI 51:
Baseline medications

- **Baseline medication**

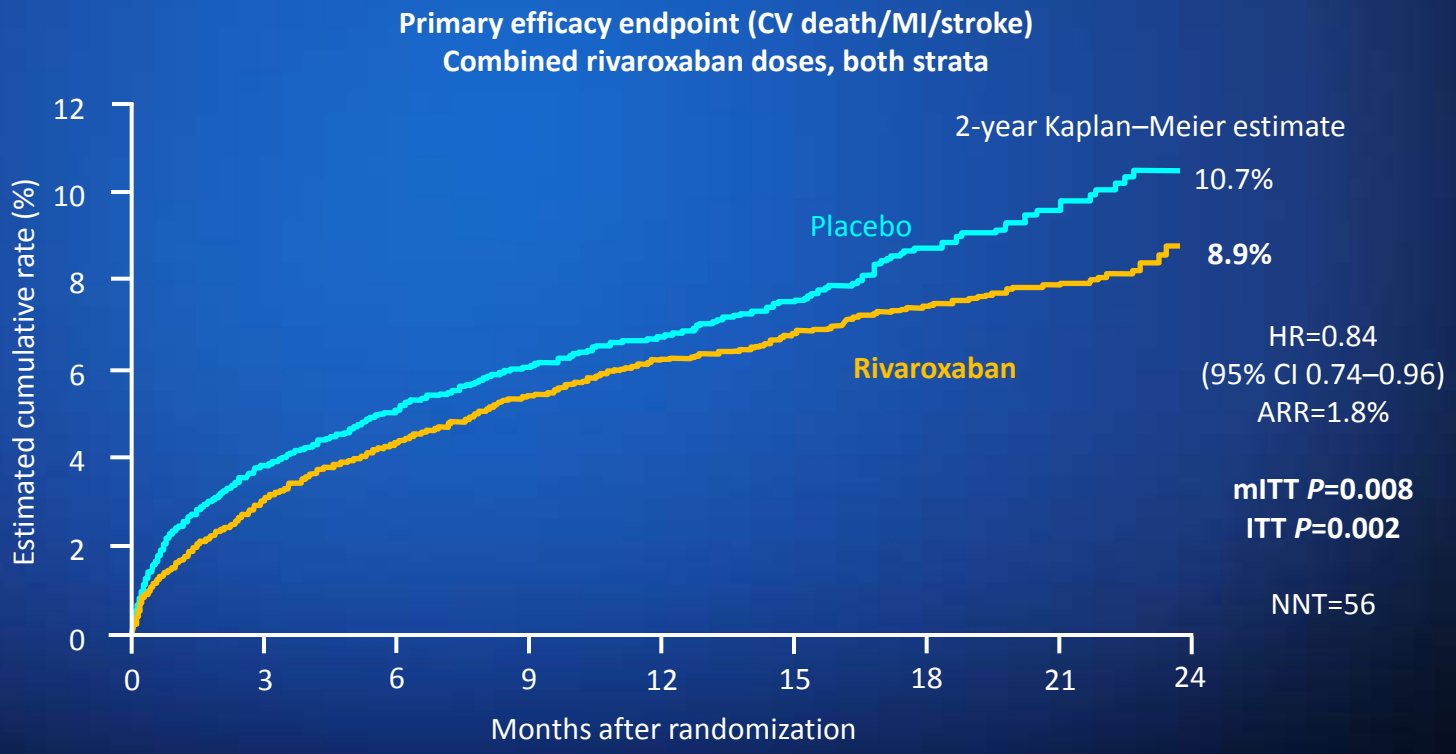
	Rivaroxaban 2.5 mg bid (n=5174)	Rivaroxaban 5 mg bid (n=5176)	Placebo (n=5176)
ASA, %	99	99	99
Thienopyridine, %	93	93	93
Beta-blocker, %	66	66	67
ACE inhibitor or ARB, %	39	38	40
Statin, %	83	84	84
Calcium channel blocker, %	16	14	15

ATLAS ACS, Anti-Xa Therapy to Lower Cardiovascular Events in Addition to Standard Therapy in Subjects with Acute Coronary Syndrome; ASA, acetylsalicylic acid; ACE, angiotensin-converting-enzyme ; ARB, angiotensin II receptor blocker; bid, twice daily

Mega JL *et al*. *N Engl J Med* 2012;366:9-19

ATLAS ACS 2-TIMI 51:
Primary efficacy endpoint (CV death/MI/stroke)

- **Primary efficacy endpoint**
  - ✓ **16% more reduction** in rivaroxaban vs. ASA alone

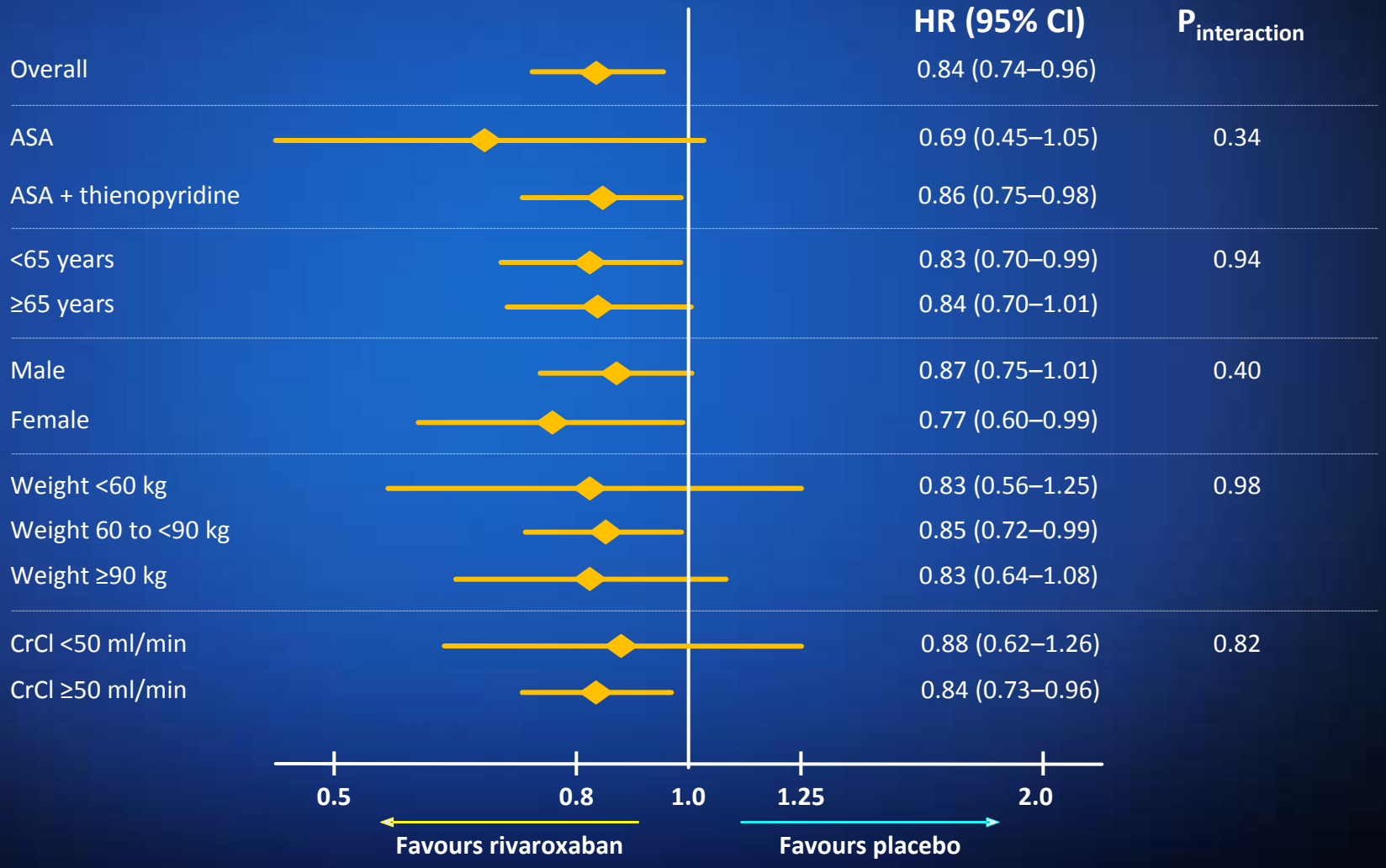


ATLAS ACS, Anti-Xa Therapy to Lower Cardiovascular Events in Addition to Standard Therapy in Subjects with Acute Coronary Syndrome; bid, twice daily; ITT, intention to treat; MI, myocardial infarction; mITT, modified intention to treat; TIMI, Thrombolysis In Myocardial Infarction.

Mega JL *et al*. *N Engl J Med* 2012;366:9-19

ATLAS ACS 2 TIMI 51:

Primary efficacy analysis patient subgroups (1)

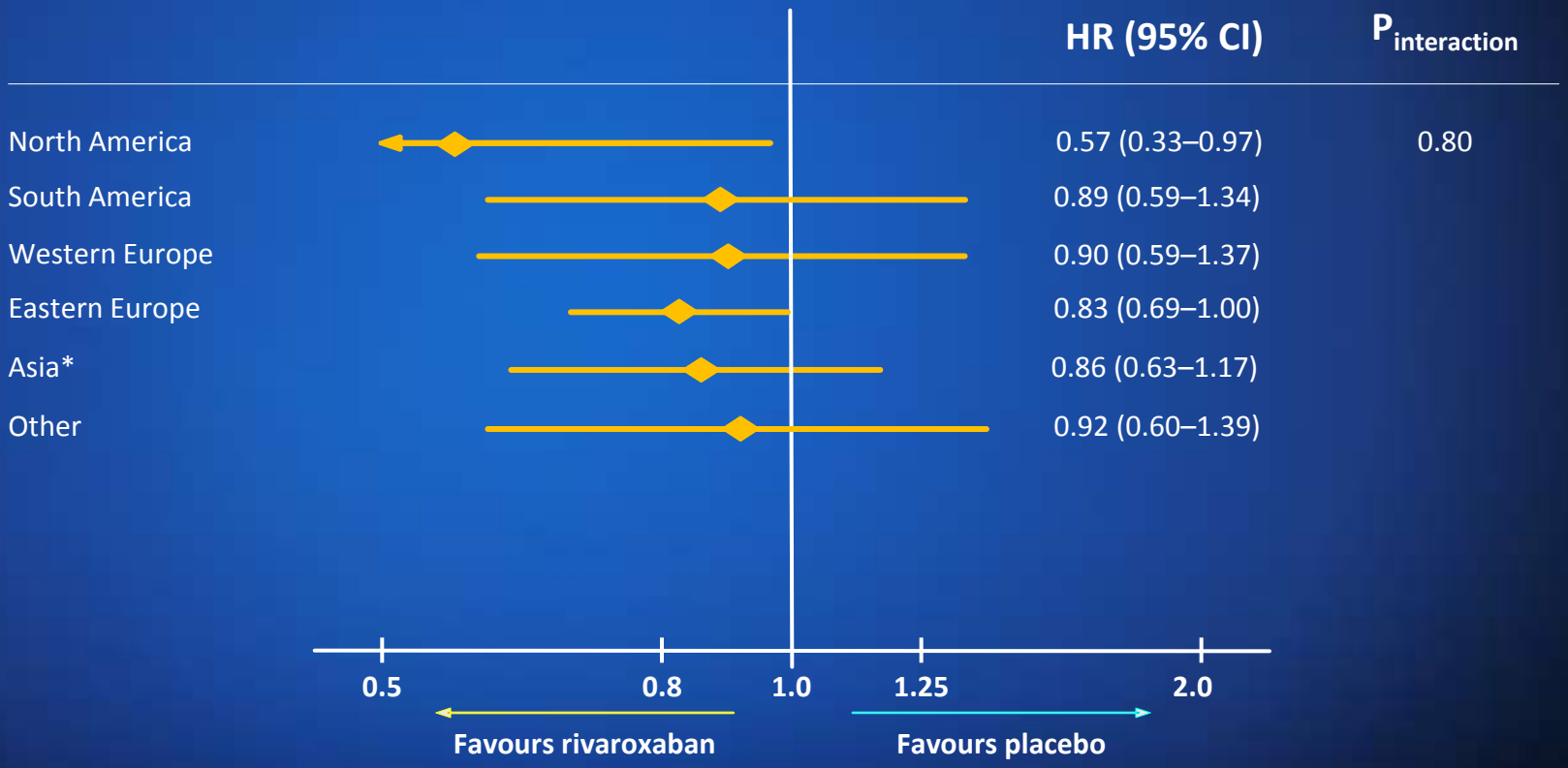


ATLAS ACS, Anti-Xa Therapy to Lower Cardiovascular Events in Addition to Standard Therapy in Subjects with Acute Coronary Syndrome; ASA, acetylsalicylic acid.

Mega JL *et al*. *N Engl J Med* 2012;366:9-19

ATLAS ACS 2 TIMI 51:

Primary efficacy analysis patient subgroups(3)



* ASIA, Republic of Korea, Thailand, China, Japan, Philippines, Malaysia

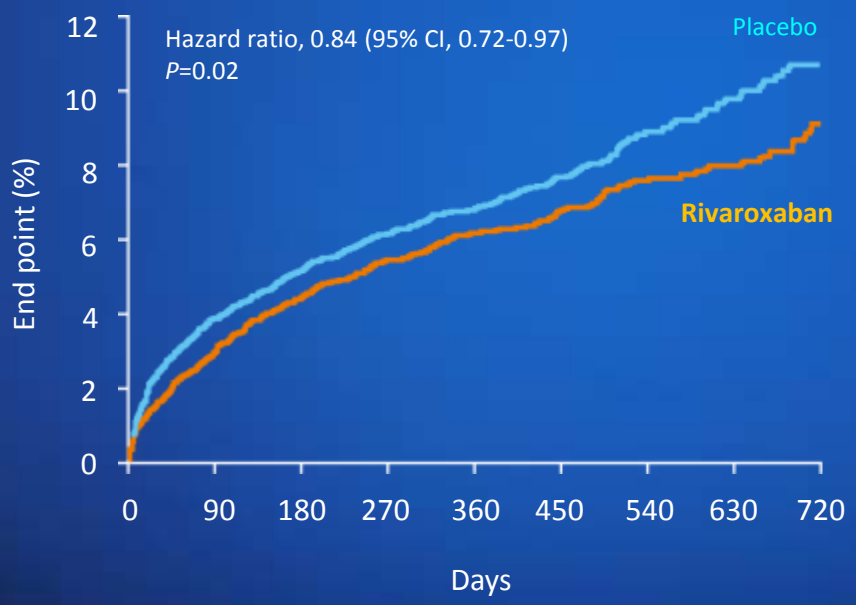
ATLAS ACS, Anti-Xa Therapy to Lower Cardiovascular Events in Addition to Standard Therapy in Subjects with Acute Coronary Syndrome; ASA, acetylsalicylic acid.

Mega JL et al. N Engl J Med 2012;366:9-19

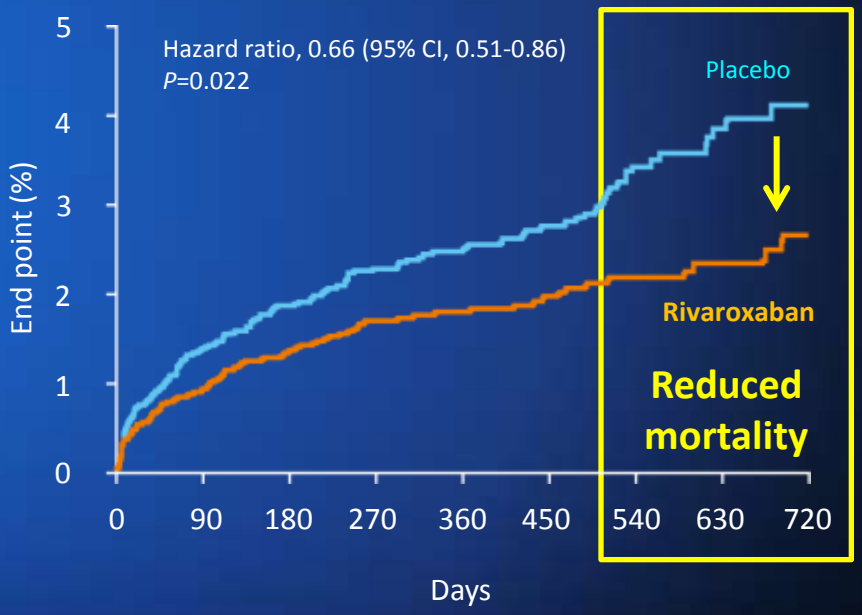
ATLAS ACS 2-TIMI 51:
Primary efficacy endpoint

- **in Rivaroxaban 2.5 mg bid**

Primary efficacy endpoint, 2.5mg BID



Death from cardiovascular causes, 2.5mg BID



ATLAS ACS, Anti-Xa Therapy to Lower Cardiovascular Events in Addition to Standard Therapy in Subjects with Acute Coronary Syndrome.

Mega JL et al. N Engl J Med 2012;366:9-19

ATLAS ACS 2 TIMI 51:
Rivaroxaban 2.5 mg bid

- Compared with placebo, **rivaroxaban 2.5 mg bid on top of ASA or ASA plus clopidogrel** showed:
  - ✓ A significant **16% RRR** in the risk of the composite of **CV death, MI or stroke** (*p*=0.02)
  - ✓ A significant **34% RRR** in the risk of **CV mortality**
  - ✓ A significant **32% RRR** in the risk of **all-cause mortality**
  - ✓ **A significant increase in non-CABG-related TIMI major bleeding (1.8% vs 0.6%; *p*<0.001)**
  - ✓ **Similar increase in fatal bleeding or fatal ICH**

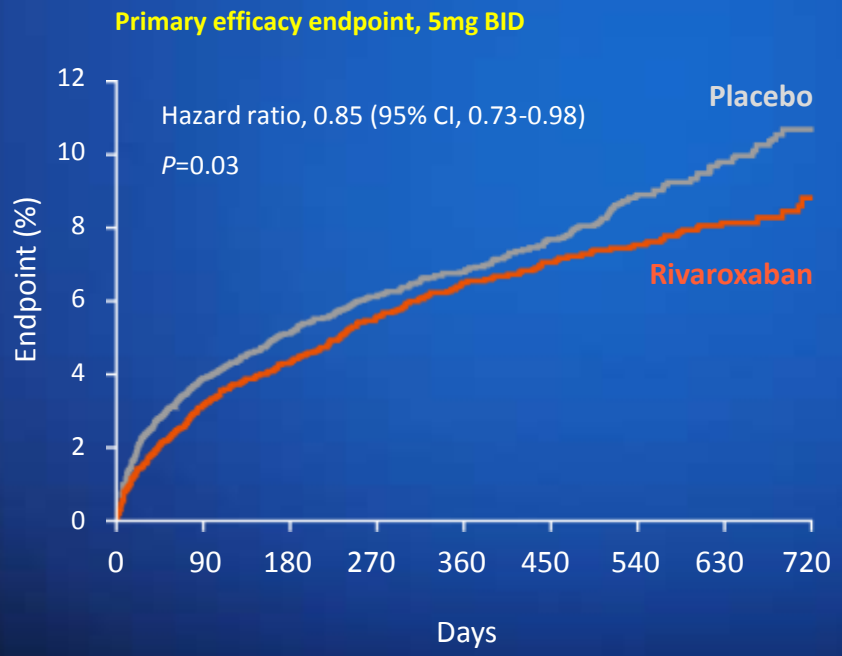
ATLAS ACS, Anti-Xa Therapy to Lower Cardiovascular Events in Addition to Standard Therapy in Subjects with Acute Coronary Syndrome; ASA, acetylsalicylic acid; CV, cardiovascular; MI, myocardial infarction; RRR, relative risk ratio; CABG, Coronary artery bypass graft surgery; TIMI, thrombolysis in myocardial infarction; ICH, intracranial hemorrhage; ACS, acute coronary syndrome.

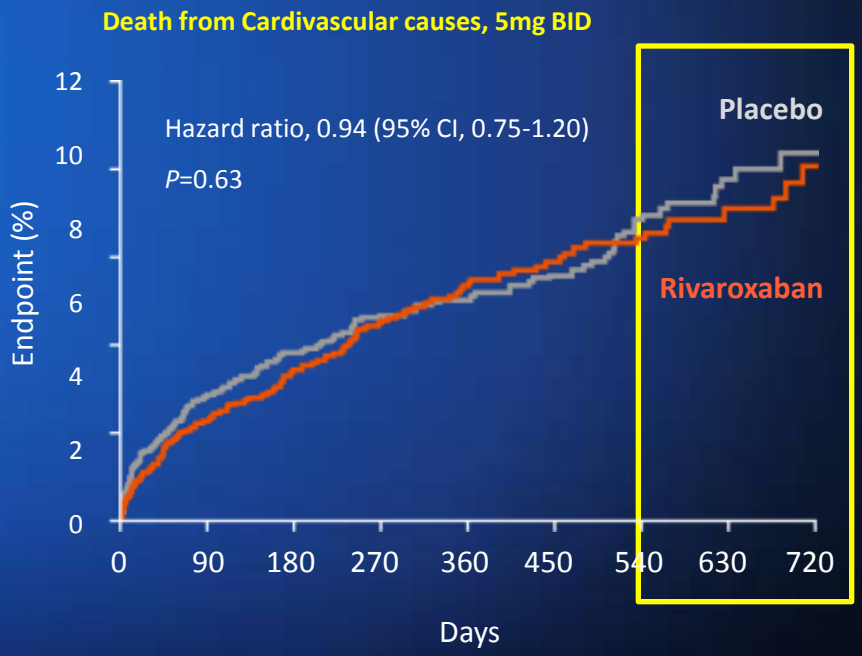
Mega JL et al. N Engl J Med 2012;366:9-19

ATLAS ACS 2-TIMI 51:
Primary efficacy endpoint

- **in Rivaroxaban 5 mg bid**

  in patients with a recent ACS, very low doses (2.5 mg) of an OAC appear to be most favorable.





ATLAS ACS, Anti-Xa Therapy to Lower Cardiovascular Events in Addition to Standard Therapy in Subjects with Acute Coronary Syndrome; ACS, acute coronary syndrome; OAC, oral anticoagulation.

Mega JL et al. N Engl J Med 2012;366:9-19

ATLAS ACS 2 TIMI 51:
Rivaroxaban 5 mg bid

- Compared with placebo, **rivaroxaban 5 mg bid on top of ASA or ASA and clopidogrel** showed:
  - A significant **15% RRR** in the risk of the composite of **CV death, MI or stroke** (p=0.03)
  - A significant **21% RRR** in the risk of **MI** (p=0.02)
  - No difference in CV and all-cause mortality
  - A significant increase in non-CABG-related TIMI major bleeding (2.4% vs 0.6%; p<0.001)

ATLAS ACS, Anti-Xa Therapy to Lower Cardiovascular Events in Addition to Standard Therapy in Subjects with Acute Coronary Syndrome; ASA, acetylsalicylic acid; CV, cardiovascular; MI, myocardial infarction; RRR, relative risk ratio; CABG, Coronary artery bypass graft surgery; TIMI, thrombolysis in myocardial infarction; ICH, intracranial hemorrhage; ACS, acute coronary syndrome.

Mega JL et al. N Engl J Med 2012;366:9-19

In ATLAS ACS 2 TIMI 51,

Rivaroxaban 2.5 mg bid significantly reduced

the risk of all-cause death, CV death, MI or stroke

in patients with ACS,

without increasing fatal bleeding

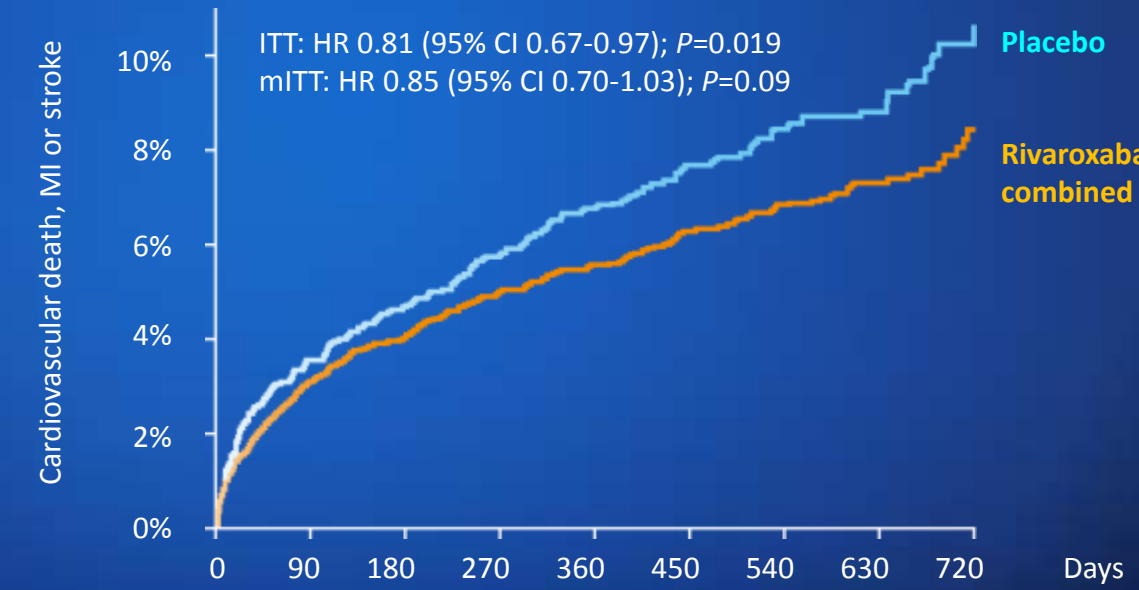
ATLAS ACS 2 TIMI 51:

Subanalysis of patients with recent STEMI

ATLAS ACS, Anti-Xa Therapy to Lower Cardiovascular Events in Addition to Standard Therapy in Subjects with Acute Coronary Syndrome; STEMI, ST-Elevation Myocardial Infarction.

ATLAS ACS 2-TIMI 51:
Substudy I . Stabilized patients after a STEMI

- **Objective:** The present analysis reports on the pre-specified subgroup of **STEMI** patients(n=7,817), in whom anticoagulant therapy has been of particular interest.
- In **STEMI** patients, rivaroxaban reduced **CV death, MI, or stroke** (ischemic, hemorrhagic, or stroke of uncertain cause)



Placebo	2599	2411	2236	1863	1535	1193	826	500	233
Rivaroxaban	5128	4766	4422	3666	3046	2362	1658	1039	464

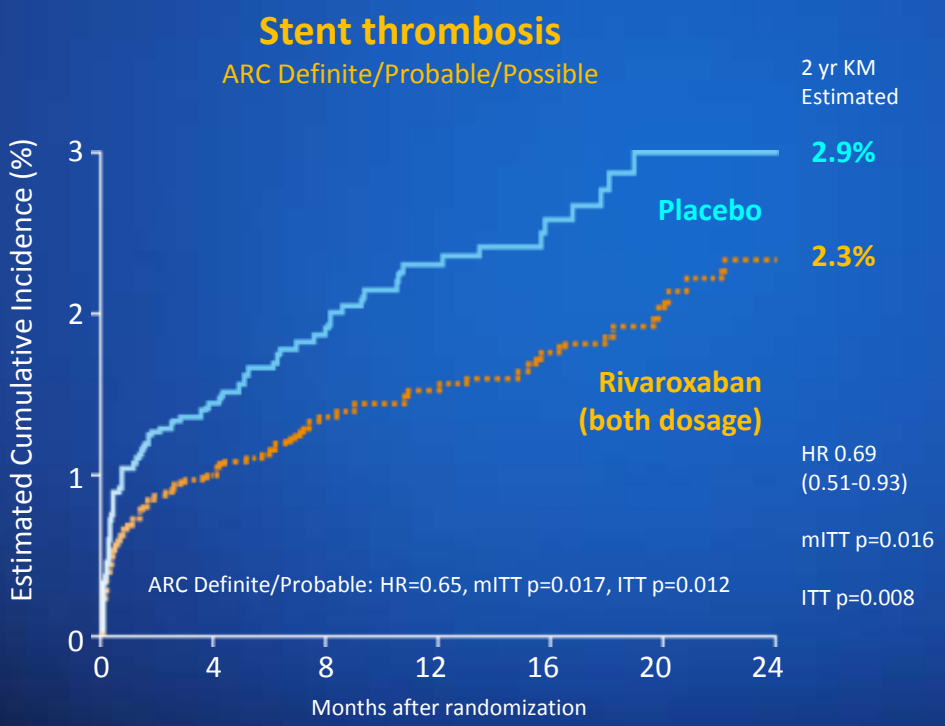
ATLAS ACS, Anti-Xa Therapy to Lower Cardiovascular Events in Addition to Standard Therapy in Subjects with Acute Coronary Syndrome; STEMI, ST-elevation myocardial infarction; mITT, modified intention-to-treat; ITT, intention-to-treat; HR, hazard ratio; CI, confidence interval; MI, myocardial infarction; CV, cardiovascular.

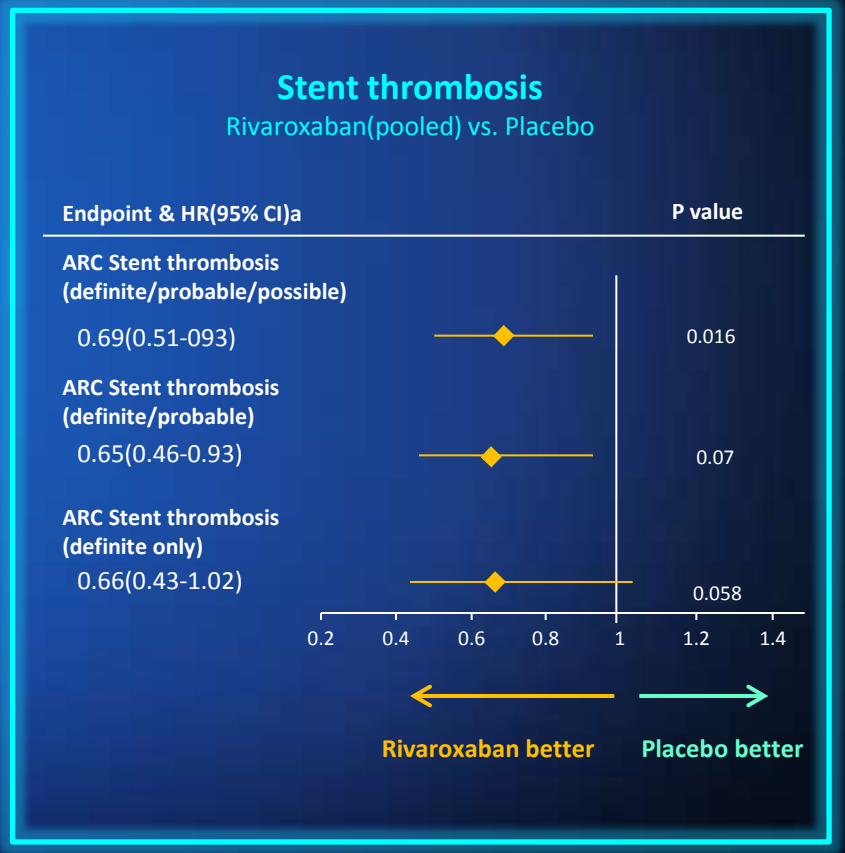
J Am Coll Cardiol. 2013;61:1853–9

Indication in STEMI, Stent thrombosis is not approved

ATLAS ACS 2-TIMI 51:
Substudy II . Reducing stent thrombosis

- **Rivaroxaban** significantly **reduced stent thrombosis in patients with ACS.**





ATLAS ACS, Anti-Xa Therapy to Lower Cardiovascular Events in Addition to Standard Therapy in Subjects with Acute Coronary Syndrome; ACS, acute coronary syndrome; ARC, Academic Research Consortium; CI, confidence interval.

J Am Coll Cardiol 2013;62:286–90

Indication in STEMI, Stent thrombosis is not approved

Summary

- **ATLAS ACS 2-TIMI 51** was specifically designed to test 2 low doses of **rivaroxaban in patients with a recent ACS**.
  - ✓ **Rivaroxaban significantly reduced** the primary efficacy end point of **death from CV causes, MI, or stroke,** as compared with placebo.
  - ✓ Rivaroxaban increased the risk of major bleeding and intracranial hemorrhage **but not the risk of fatal bleeding.**
- In ATLAS ACS 2-TIMI 51 substudy, **rivaroxaban reduced the primary efficacy endpoint of CV death, MI, or stroke** (ischemic, hemorrhagic, or stroke of uncertain cause) vs. placebo in **stabilized patients after STEMI.**
- Also, in another subgroup, **rivaroxaban significantly reduced definite, probable, or possible stent thrombosis in patients with ACS.**

ATLAS ACS, Anti-Xa Therapy to Lower Cardiovascular Events in Addition to Standard Therapy in Subjects with Acute Coronary Syndrome ; ACS, acute coronary syndrome; CV, cardiovascular; MI, myocardial infarction.

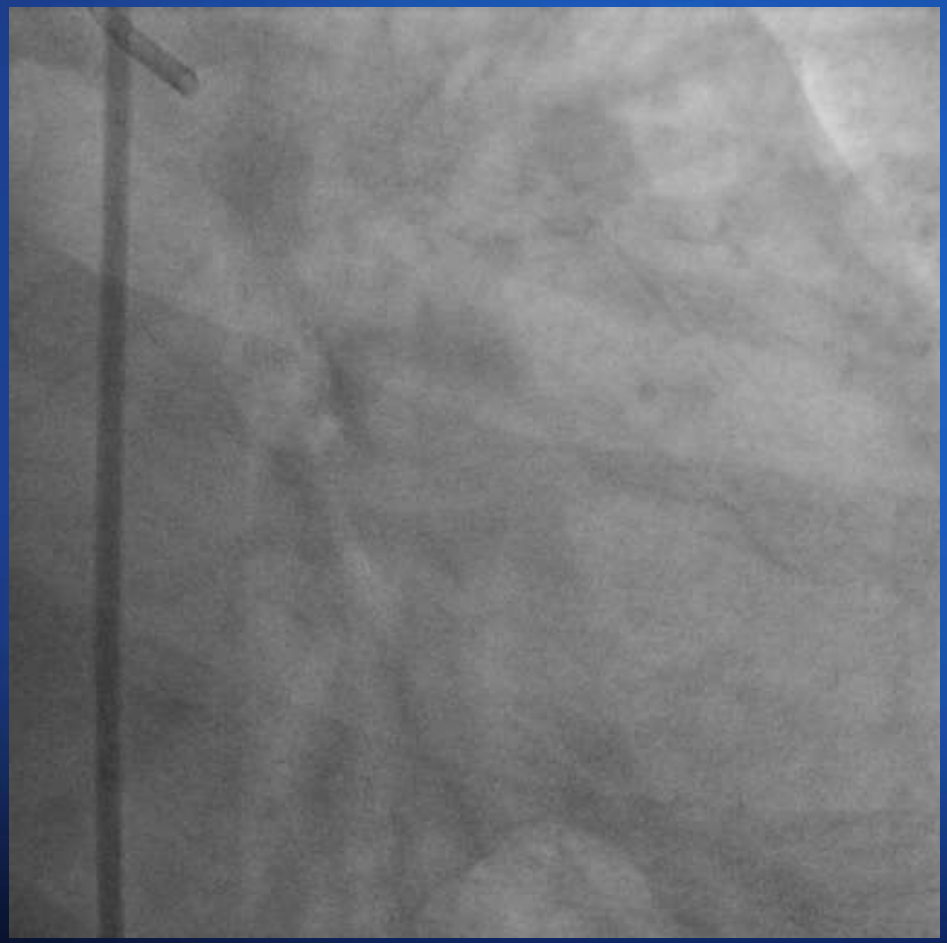
Indication in STEMI, Stent thrombosis is not approved

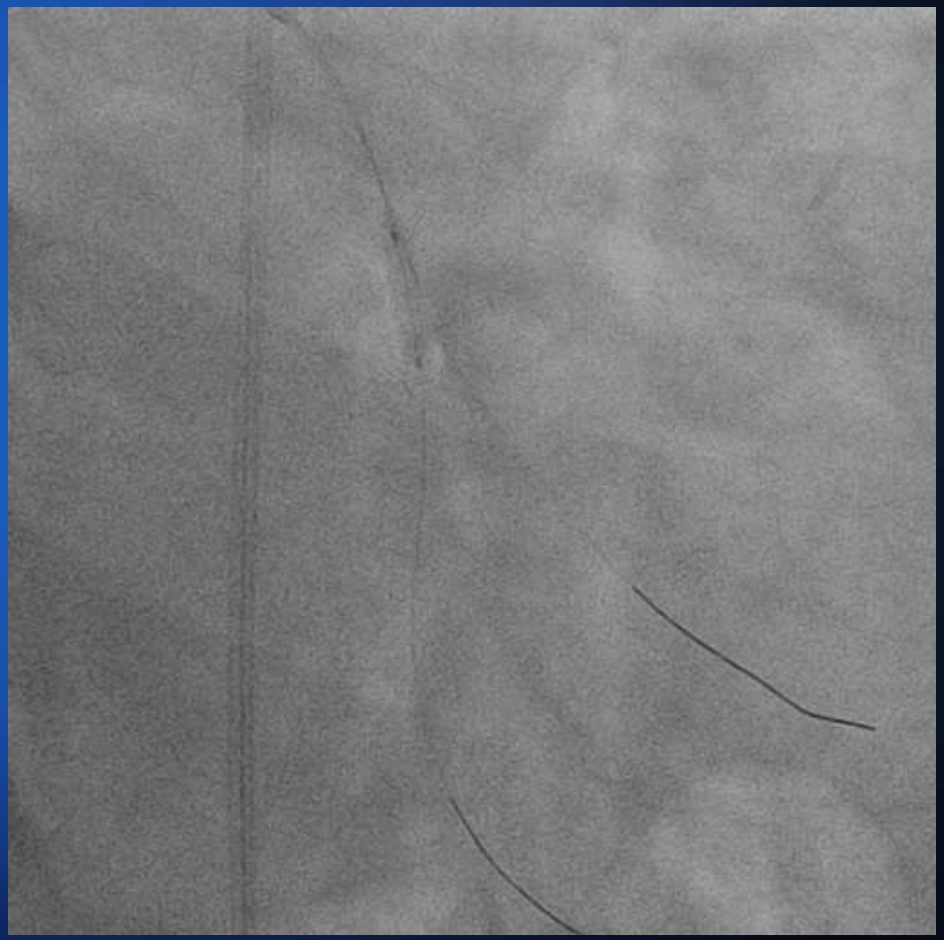
Brief History

- M / 51
- Severe Chest pain since 7 days

- Comorbidity
  - Hypertension

CAG (2016-12-22)





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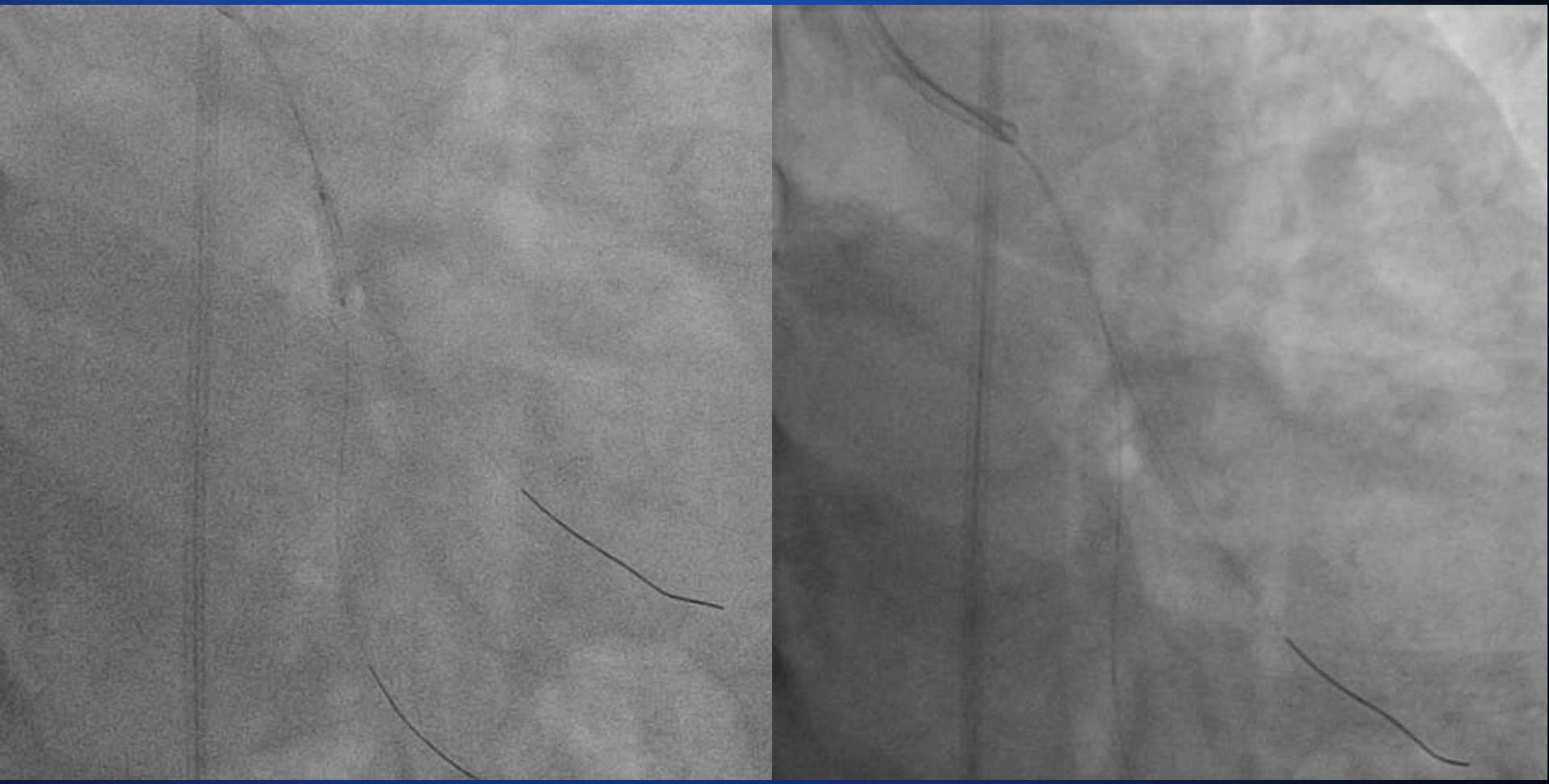
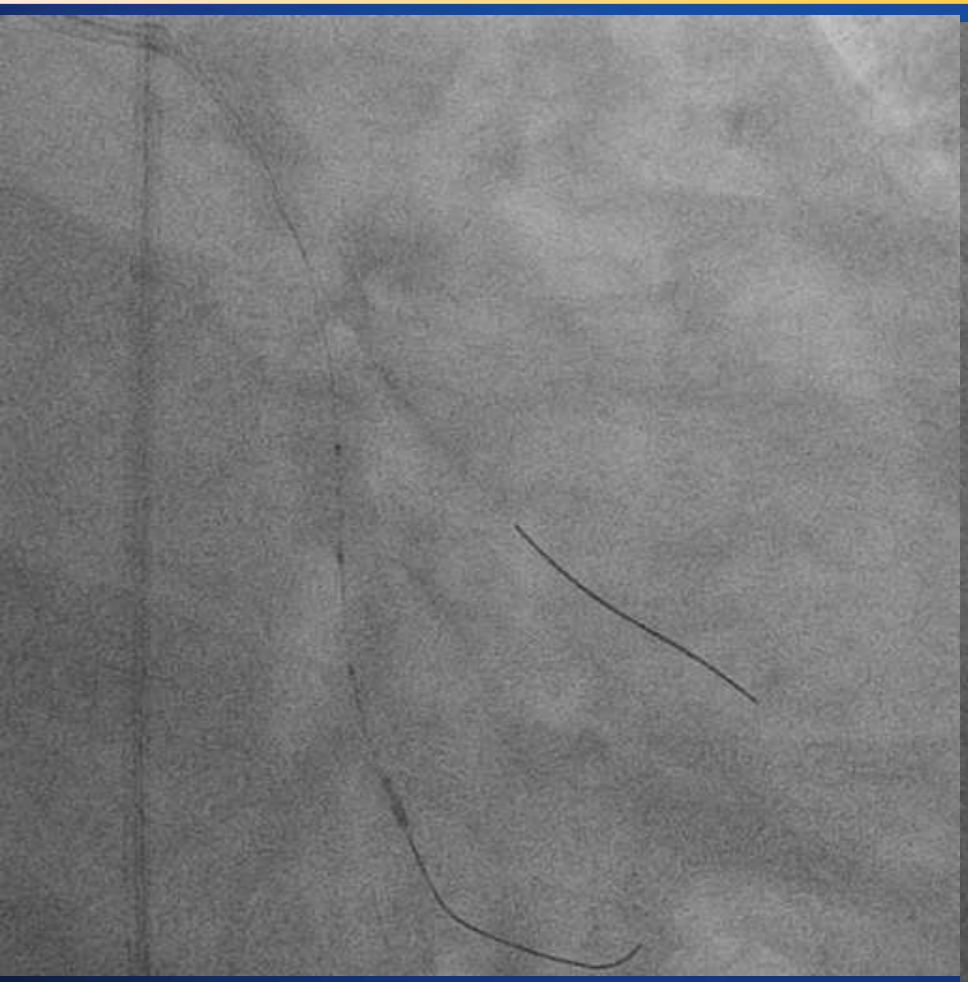
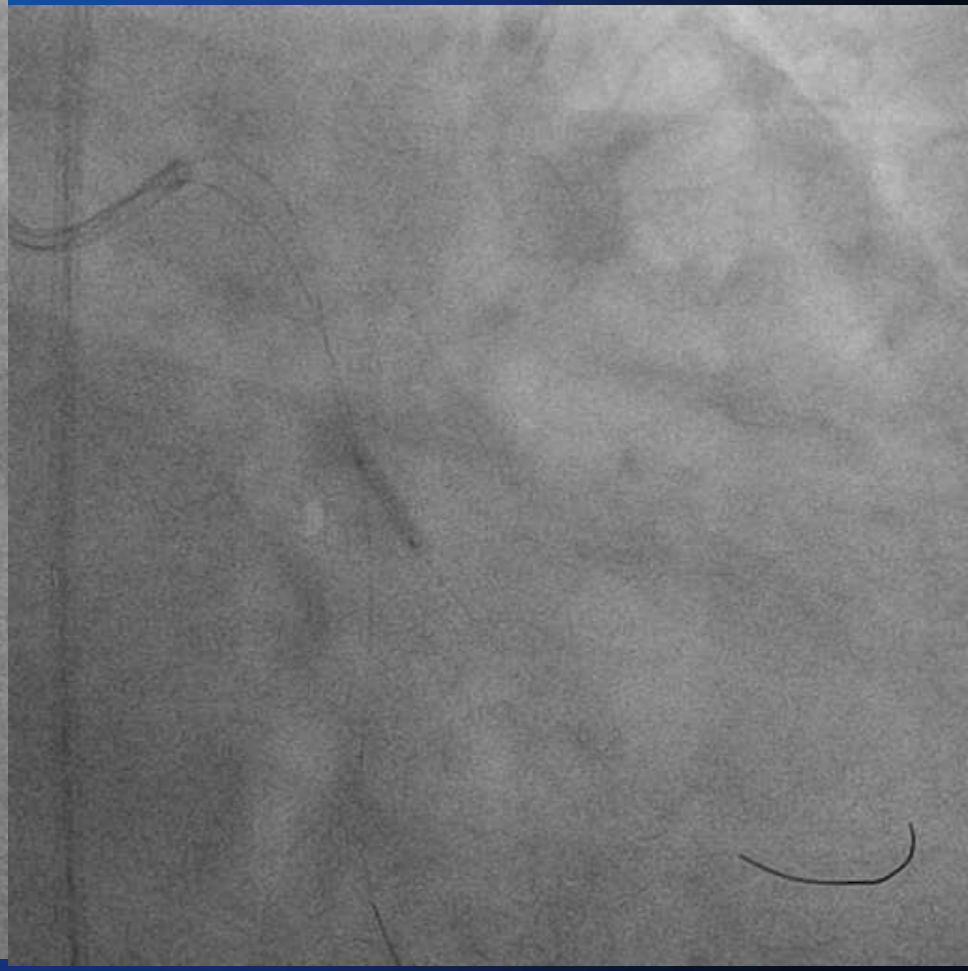


PCI balloon 2.5*12

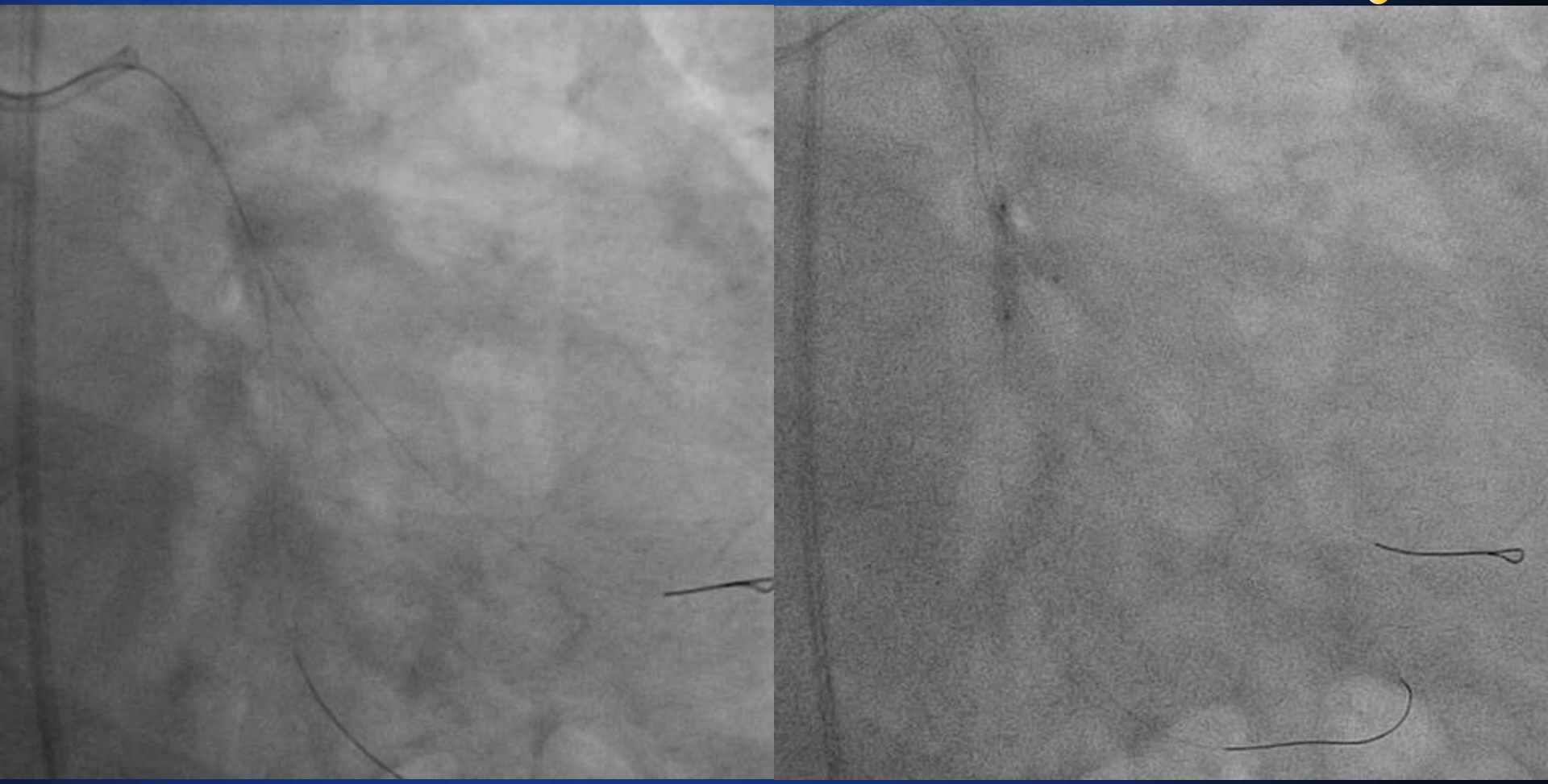
CAG (2016-12-22)





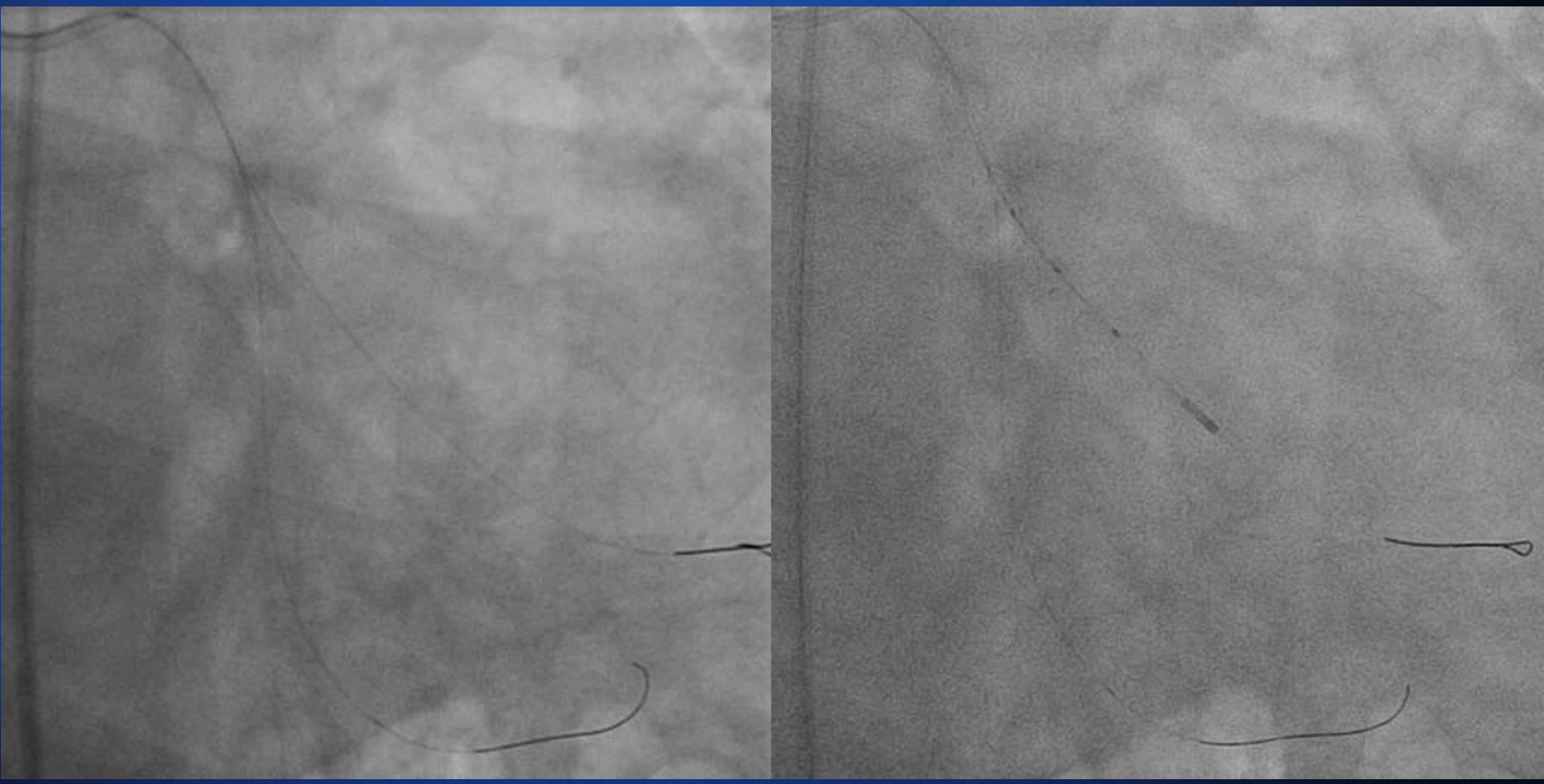
Thrombuster 7Fr
PCI balloon 2.5*12

CAG (2016-12-22)



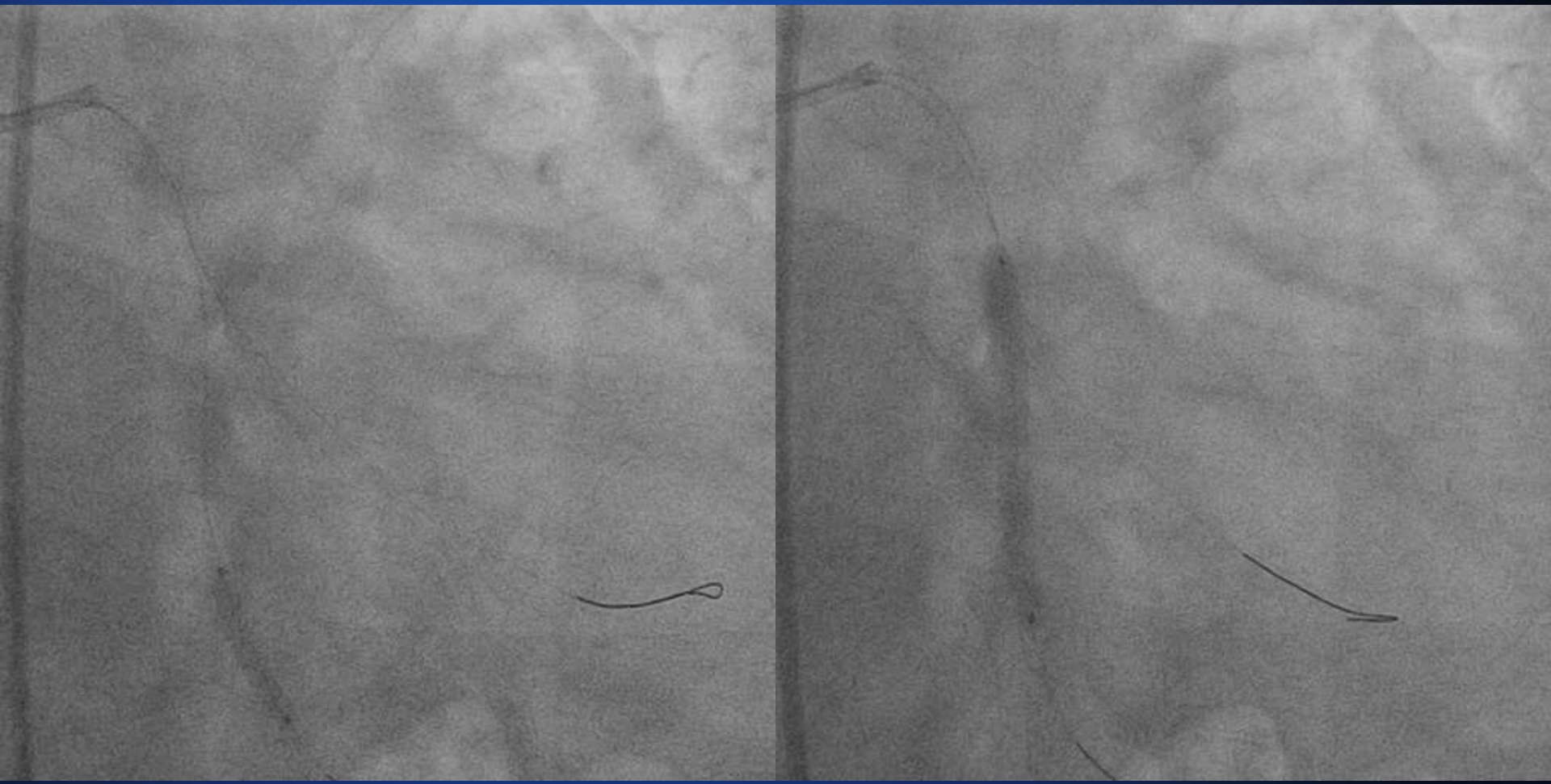
PCI balloon 2.5*12 at 1st OM
PCI balloon 3.0*14 at dLCx

CAG (2016-12-22)



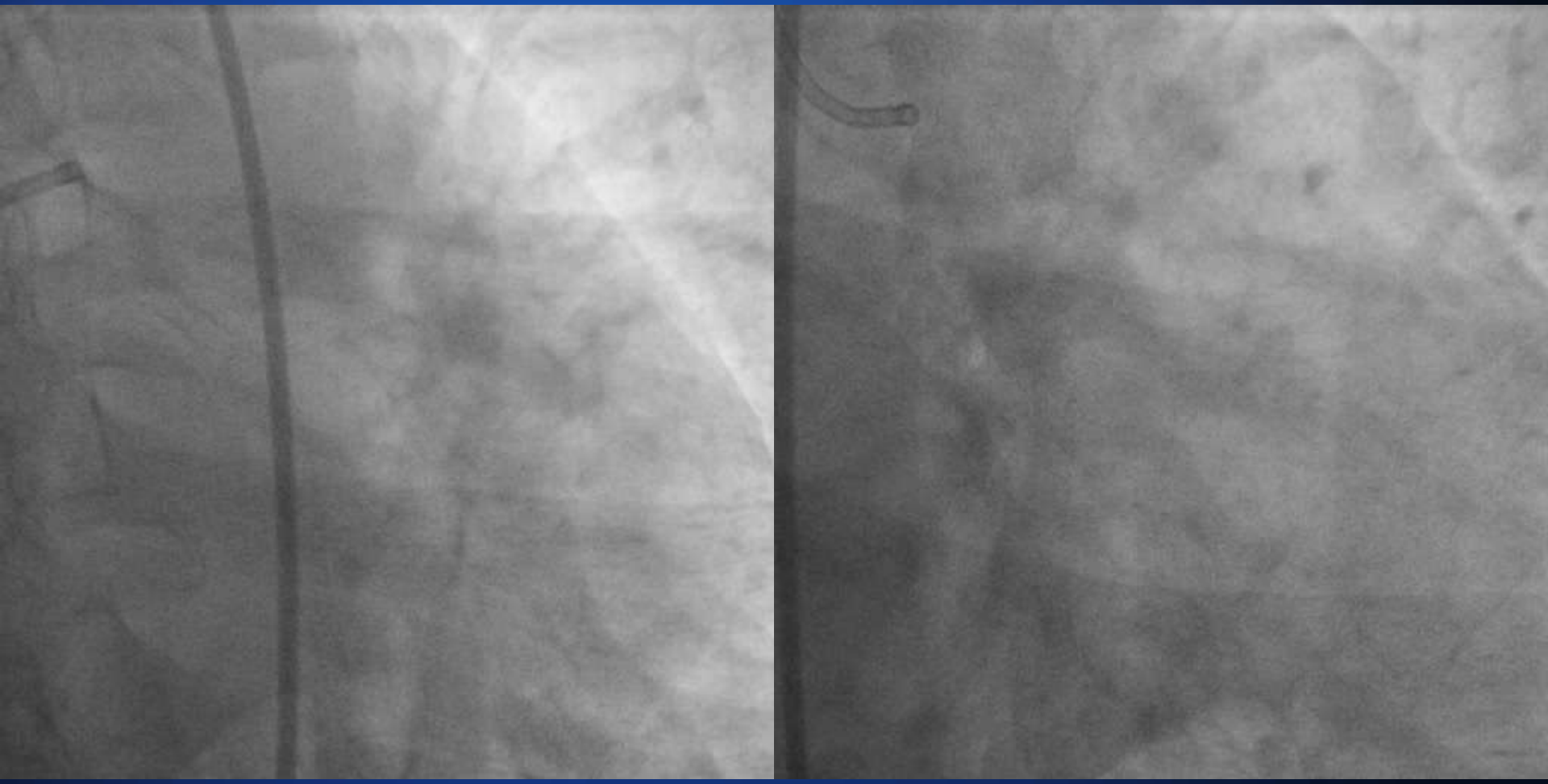
Thrombuster 7Fr

CAG (2016-12-22)



Orsiro 3.0*18 at far dLCx
Orsiro 4.0*40 at d~far dLCx

CAG (2016-12-22)



Medication

Astrix 100mg qD

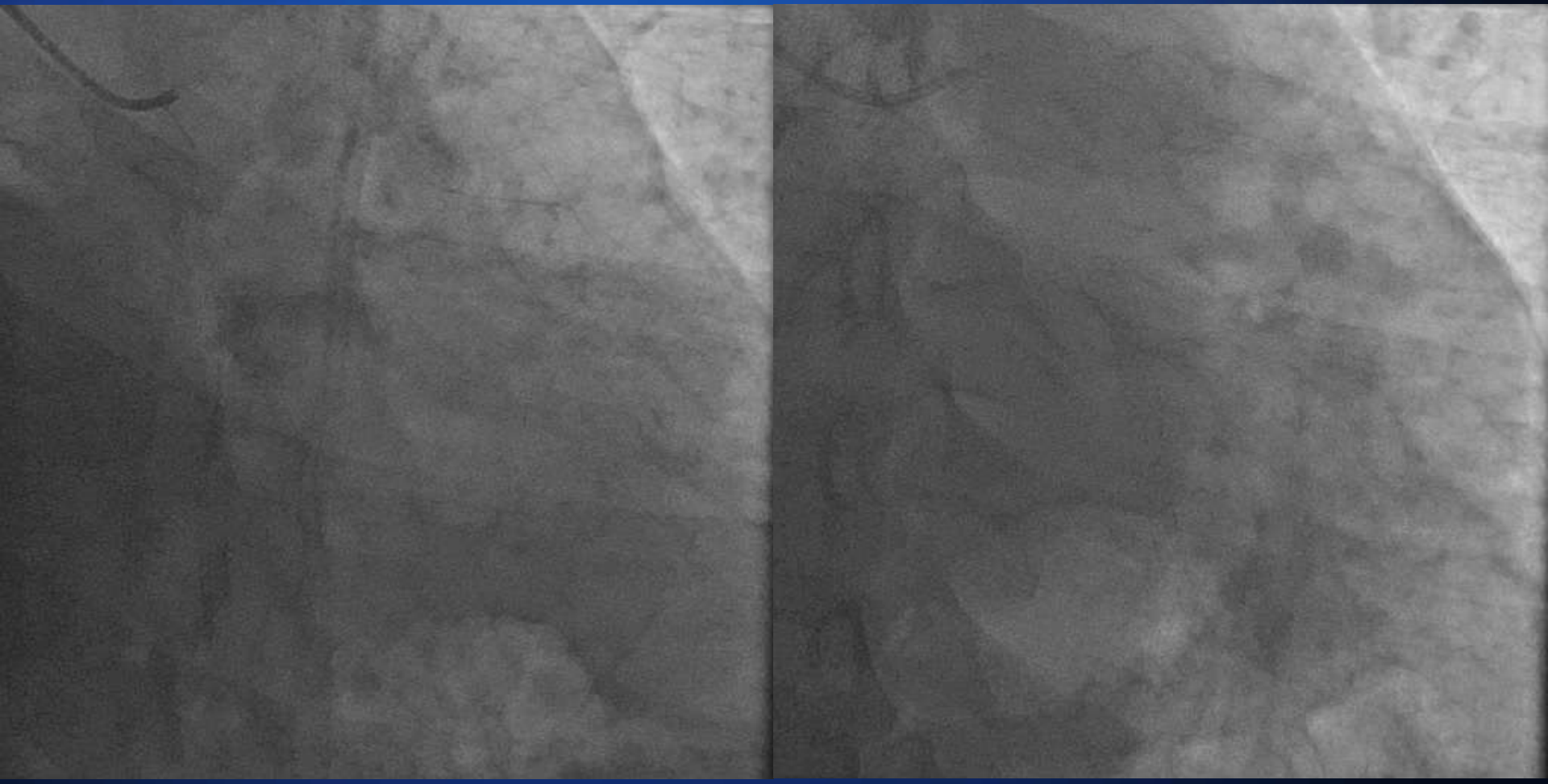
Brilinta 90mg BID

Vivacor 20mg qD

Concor 5mg qD

Xarelto 2.5mg BID

Follow-up CAG at 2-month later



Long-term therapy after an ACS,

the addition of rivaroxaban 2.5mg bid

appears to be an attractive option

Thanks for your Attention