Management of MI Pharmacological vs Mechanical Therapy

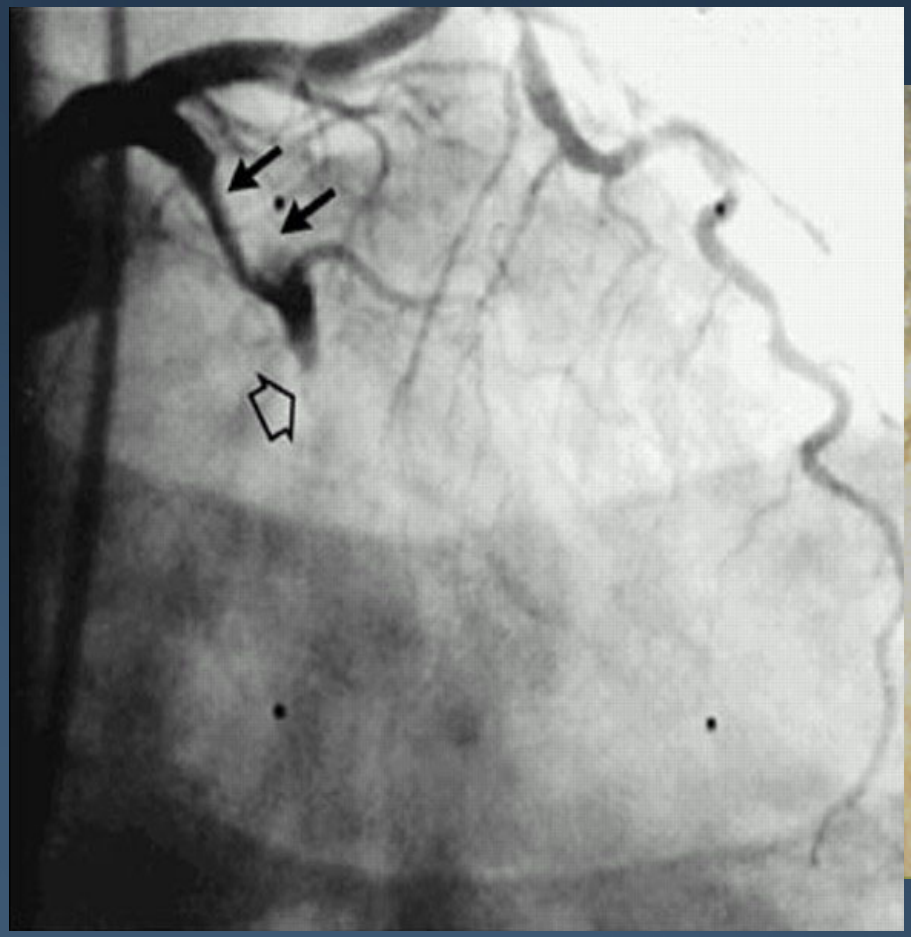
Dr Victor Elliott, Bsc, MBBS,DM,FSCI

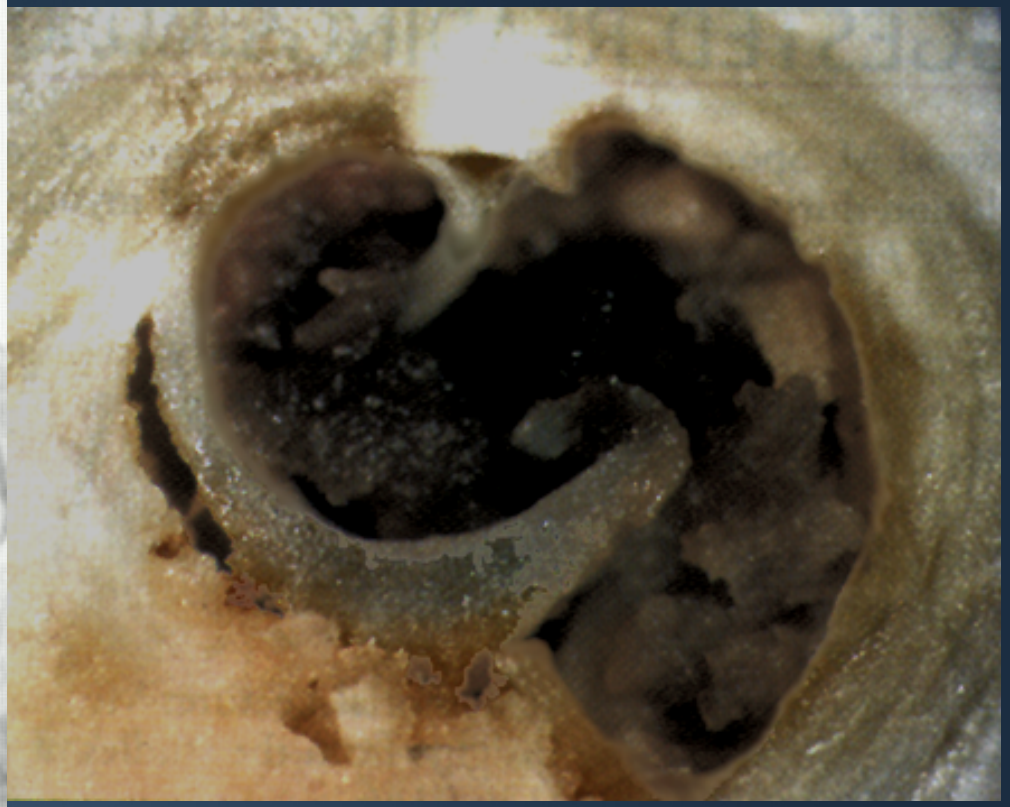
Consultant Cardiologist

Summer School

2013

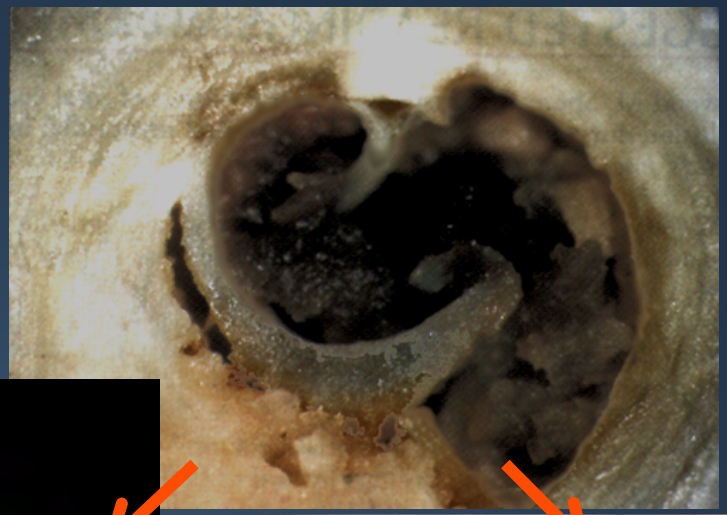
AMI: Pathophysiology

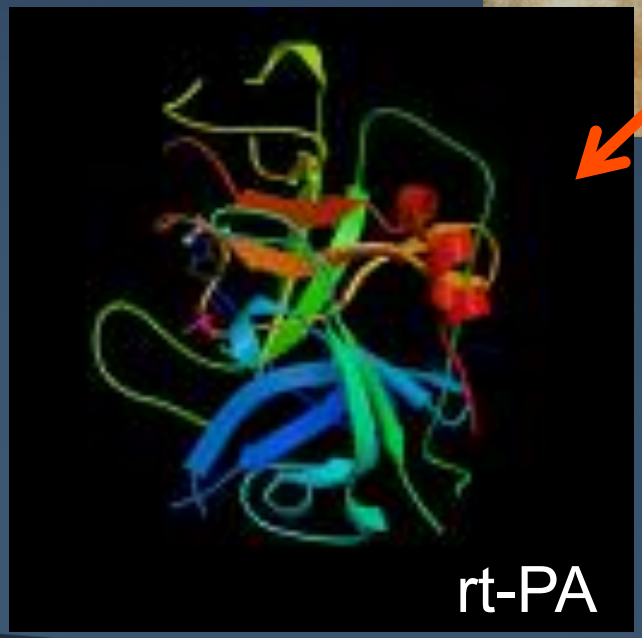


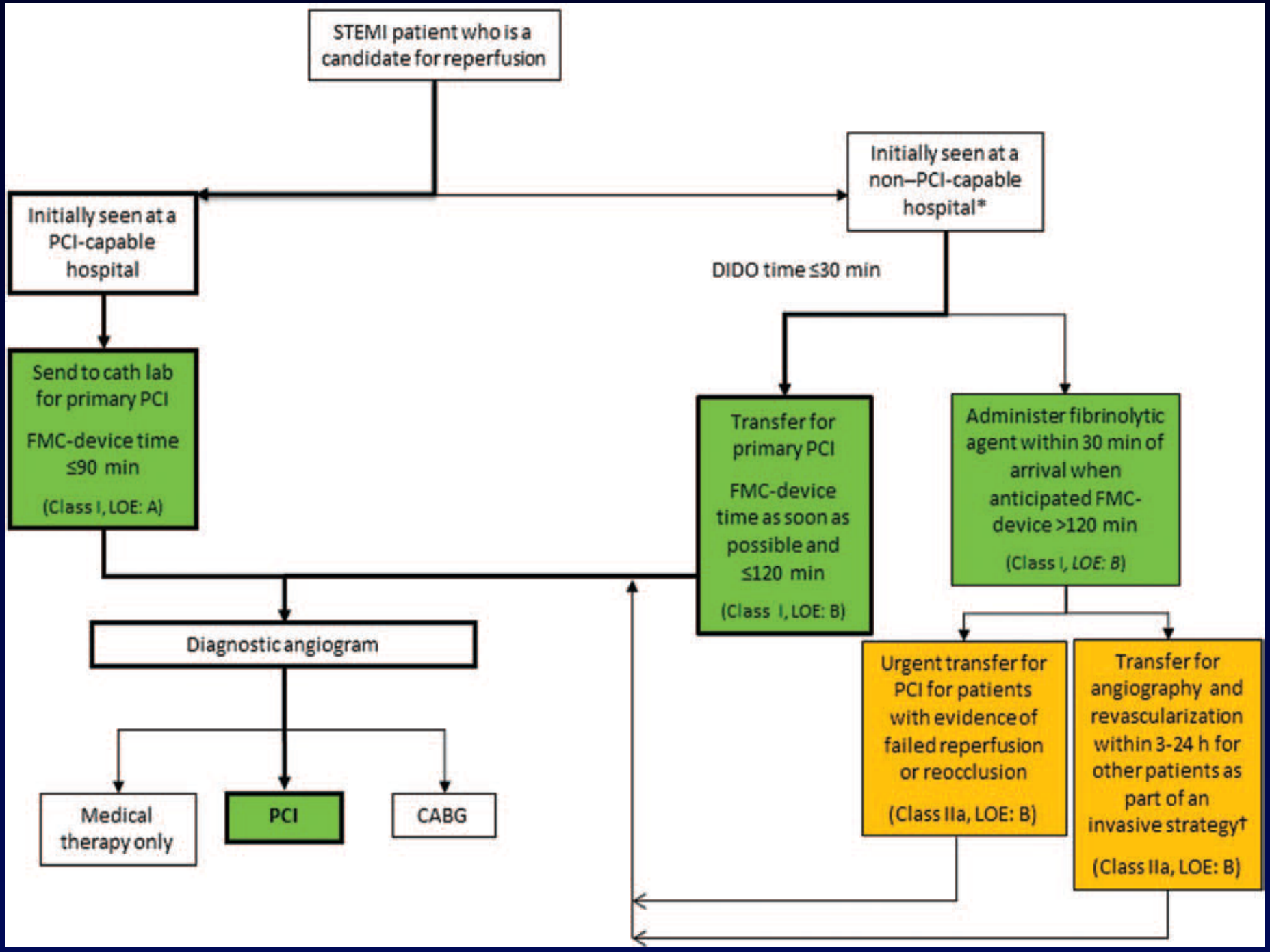


Ruptured plaque with occlusive thrombus

Treatment of Acute Coronary Thrombosis





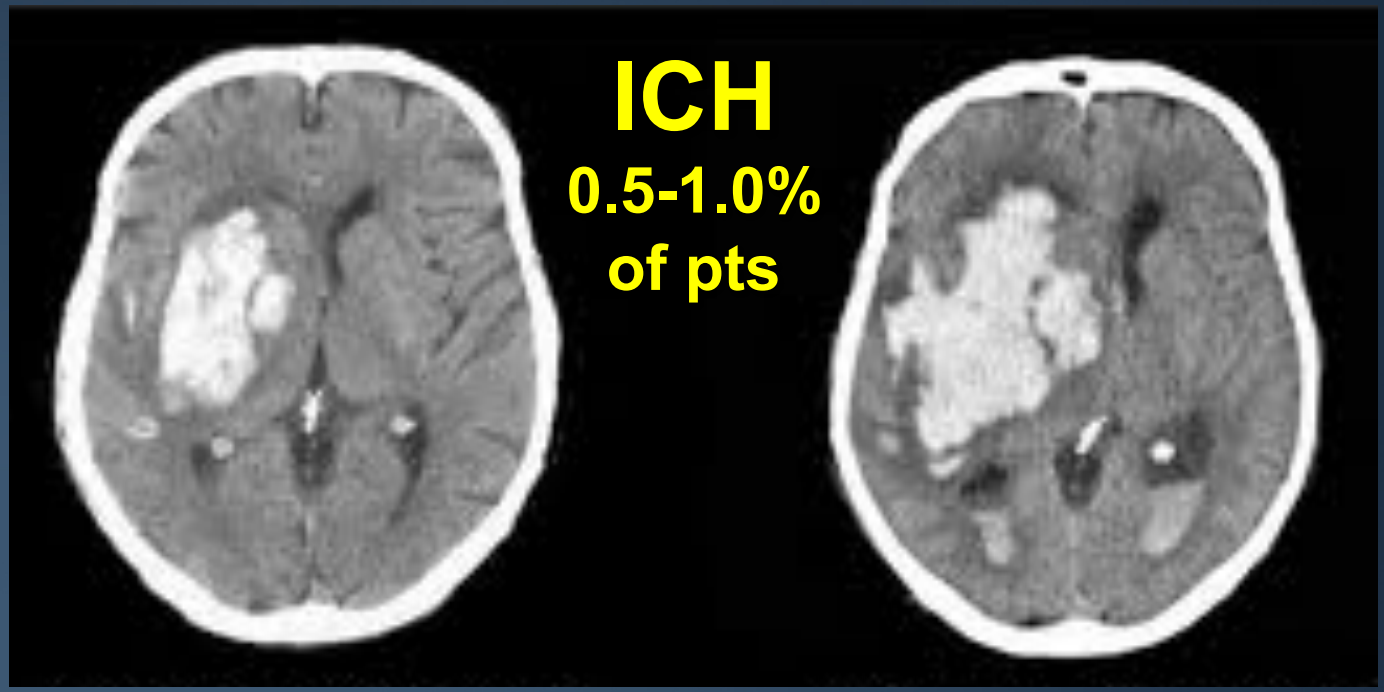

STEMI patient who is a candidate for reperfusion
Initially seen at a PCI-capable hospital
Initially seen at a non–PCI-capable hospital*
DIDO time ≤30 min
Send to cath lab for primary PCI
FMC-device time ≤90 min
(Class I, LOE: A)
Transfer for primary PCI
FMC-device time as soon as possible and ≤120 min
(Class I, LOE: B)
Administer fibrinolytic agent within 30 min of arrival when anticipated FMC-device >120 min
(Class I, LOE: B)
Diagnostic angiogram
Medical therapy only
PCI
CABG
Urgent transfer for PCI for patients with evidence of failed reperfusion or reocclusion
(Class IIa, LOE: B)
Transfer for angiography and revascularization within 3-24 h for other patients as part of an invasive strategy†
(Class IIa, LOE: B)

Fibrinolytic therapy

Did save lives compared to placebo, BUT

- At best, restored TIMI 3 flow in 55% (rt-PA), +
- ↑ Incidence of recurrent ischemia and reinfarction

+



2 hours after t-PA

6 hours after t-PA

Reperfusion; 2013 guidelines

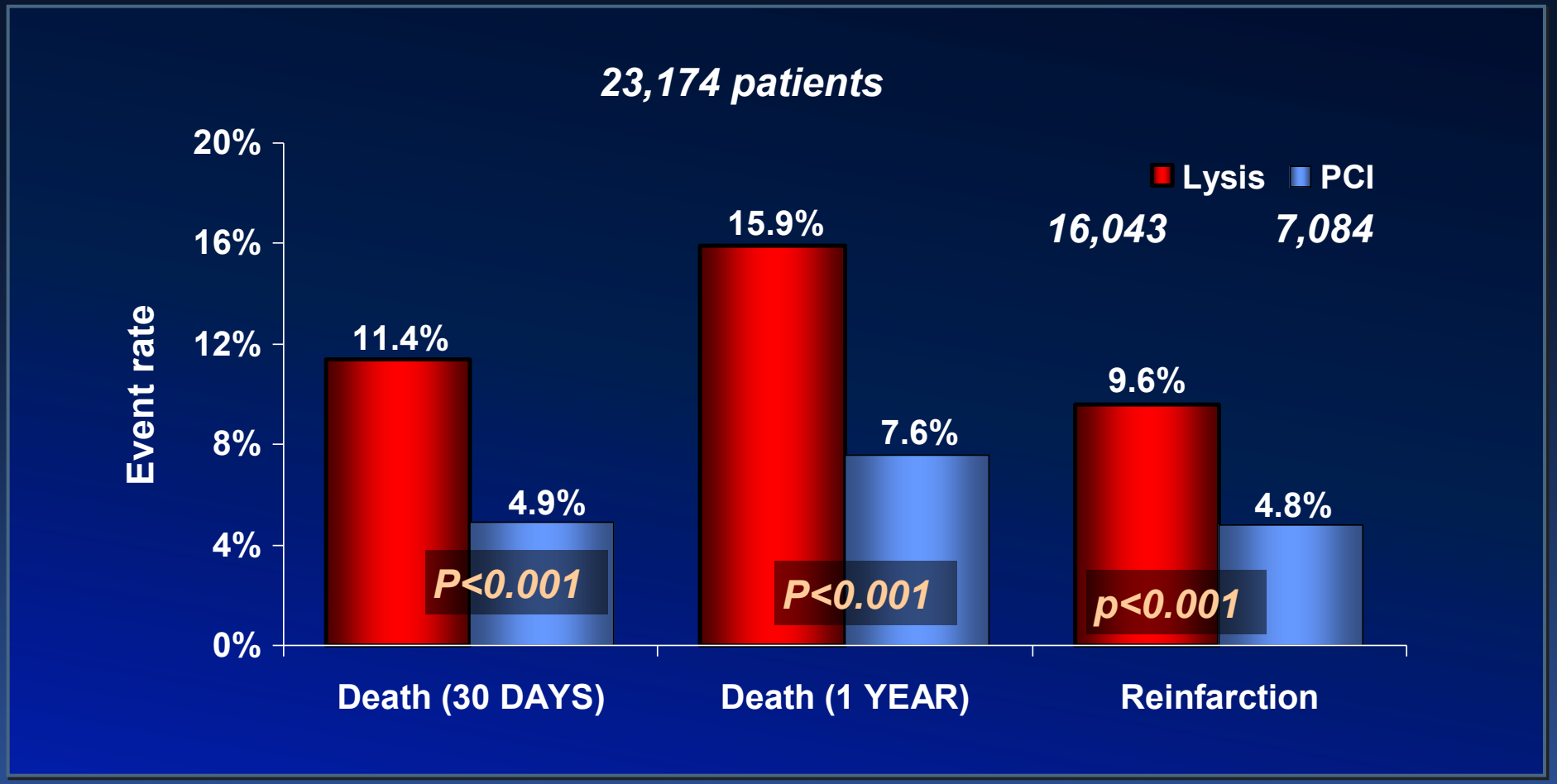
- Primary PCI is the recommended method of reperfusion when it can be performed in a timely fashion by experienced operators. *(Level of Evidence: A)*

- Emergency medical services transport directly to a PCI-capable hospital for primary PCI is the recommended triage strategy for patients with STEMI, with an ideal FMC-to-device time system goal of 90 minutes or less. *(Level of Evidence: B)*

Reperfusion

- Immediate transfer to a PCI-capable hospital for primary PCI is the recommended triage strategy for patients with STEMI who initially arrive at or are transported to a non–PCI-capable hospital, with an FMC-to-device time system goal of 120 minutes or less. (Level of Evidence: B)

Primary PCI versus Thrombolytics Swedish Heart Intensive Care Admissions Registry (RIKS-HIA)



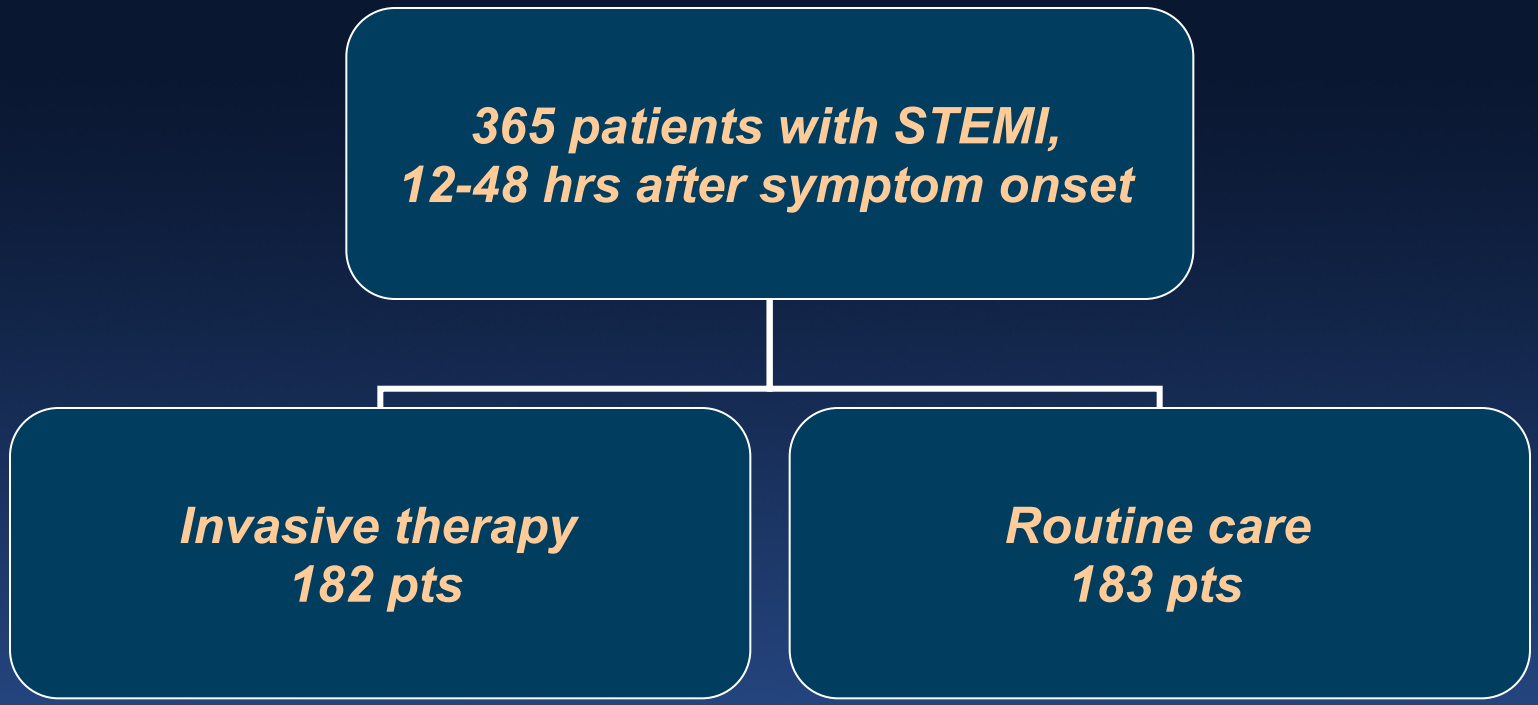
Stenestrand, U. et al. JAMA 2006;296:1749-1756.

Conclusions
Primary PCI and Reperfusion Times

- Primary PCI when immediately available it offers superior and safer reperfusion
- Effectiveness is time dependent and best results seen with the lowest door-to-balloon times
- Elderly and complicated patients show a greater magnitude of benefit with primary PCI
- Skilled centers and operators that minimize PCI related delays enhance benefits
- Rapidly transferred patients also benefit from primary PCI

Mechanical Reperfusion in Patients With Acute Myocardial Infarction Presenting More Than 12 Hours From Symptom Onset: A Randomized Controlled Trial

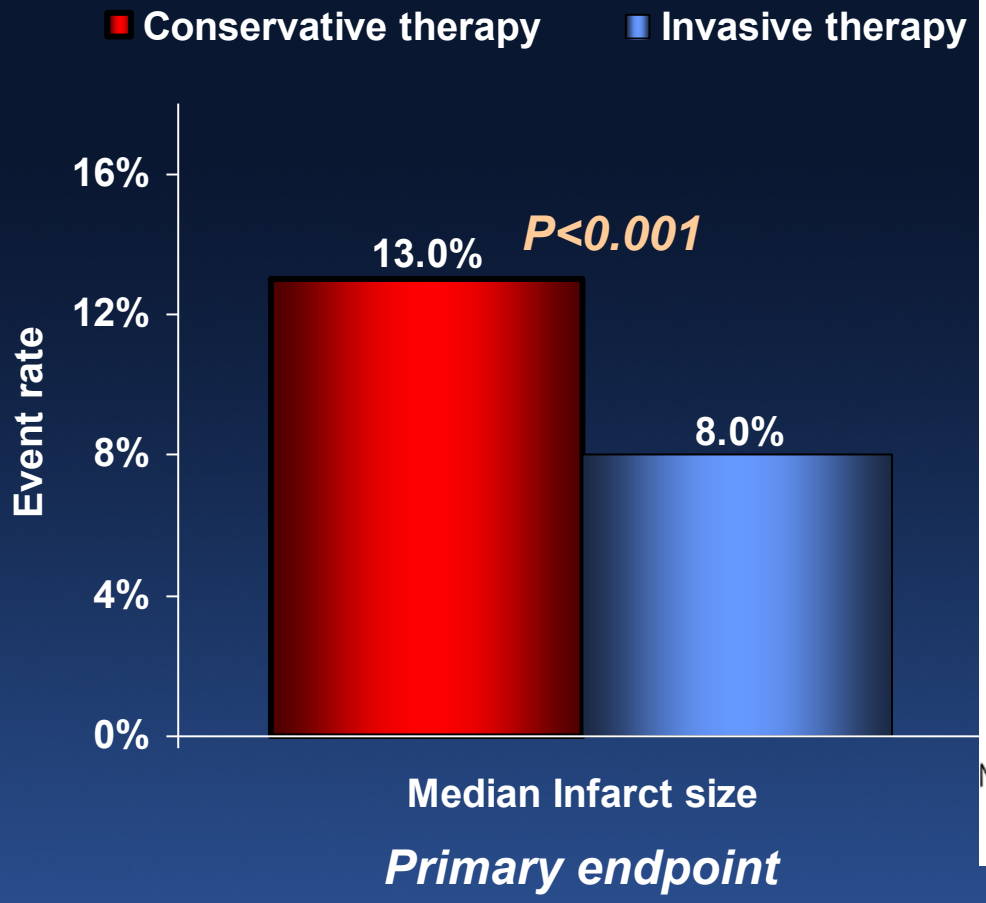
The BRAVE-2 Trial



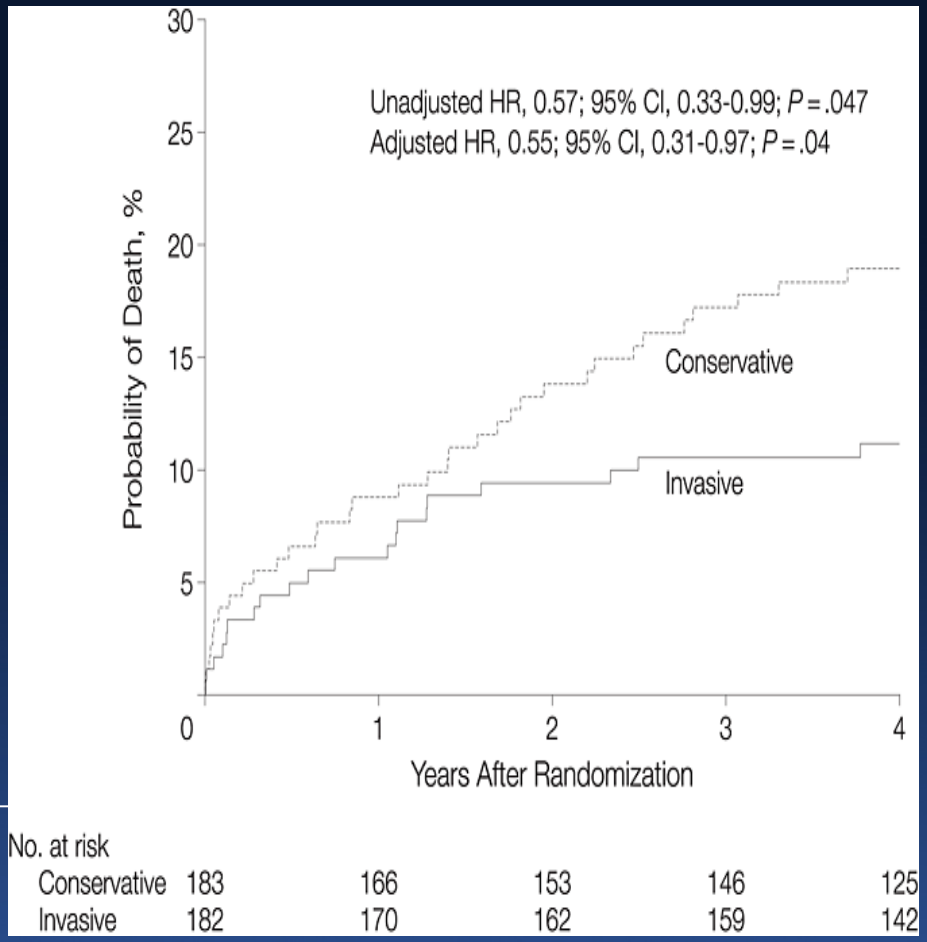
Primary endpoint was final infarct size
Tc99m sestamibi SPECT

Schomig, A. et al. JAMA 2005; 293:2865-2872.

The BRAVE-2 Trial



Primary endpoint



Conclusions Late Presentations and Completed Infarcts

- Patients presenting late after STEMI may benefit from primary PCI
- Benefits are seen in those with residual symptoms, inducible ischemia, large myocardium at risk, and complications
- No advantage is seen in those with no residual ischemia and persistently occluded arteries

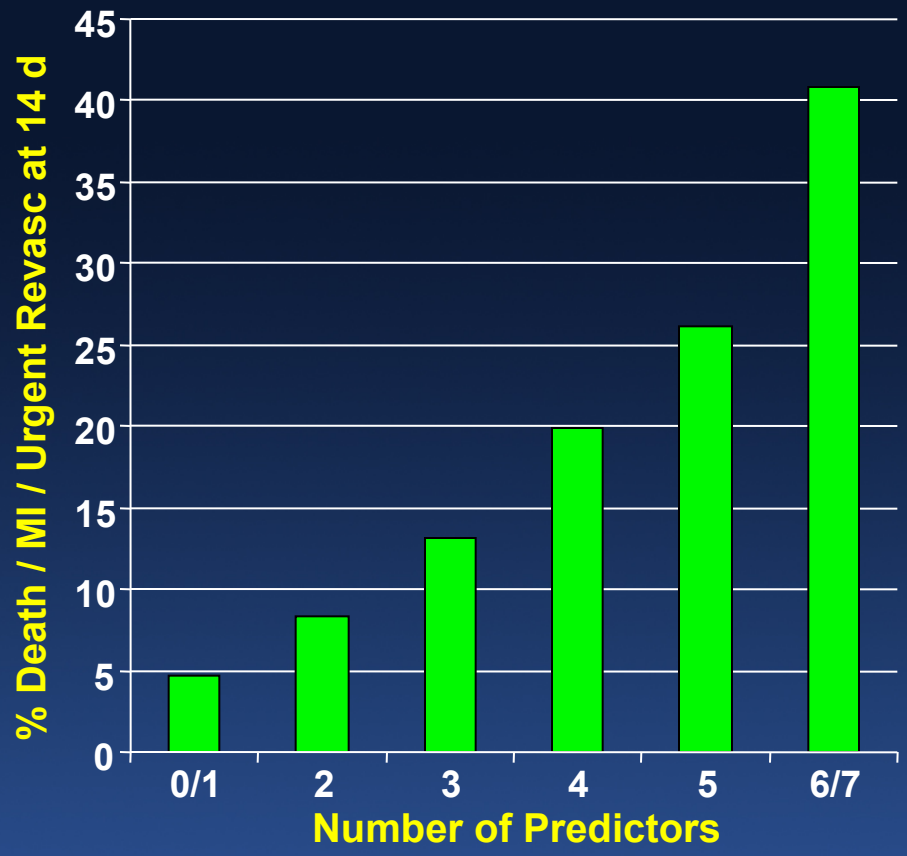
LATE, DANAMI I, SWISSI II, OAT

Reperfusion Therapy Lessons Learned

- The earlier the presentation the greater the myocardial salvage
- Infarct duration and time to reperfusion is highly correlated with survival
- Effective reperfusion is primary goal in STEMI
- Complete reperfusion is correlated with survival
- ST resolution and symptom resolution are best clinical measures of reperfusion
- TIMI 3 flow and myocardial blush are best angiographic measures of reperfusion

TIMI Risk Score for UA/NSTEMI: 7 Independent Predictors

1. Age ≥65 y
2. ≥3 CAD risk factors (high cholesterol, family history, hypertension, diabetes, smoking)
3. Prior coronary stenosis ≥50%
4. Aspirin in last 7 days
5. ≥2 anginal events ≤24 h
6. ST-segment deviation
7. Elevated cardiac markers (CK-MB or troponin)



Antman EM, et al. *JAMA*. 2000;284(7):835-842.

Timing of Arteriography in UA/NSTEMI

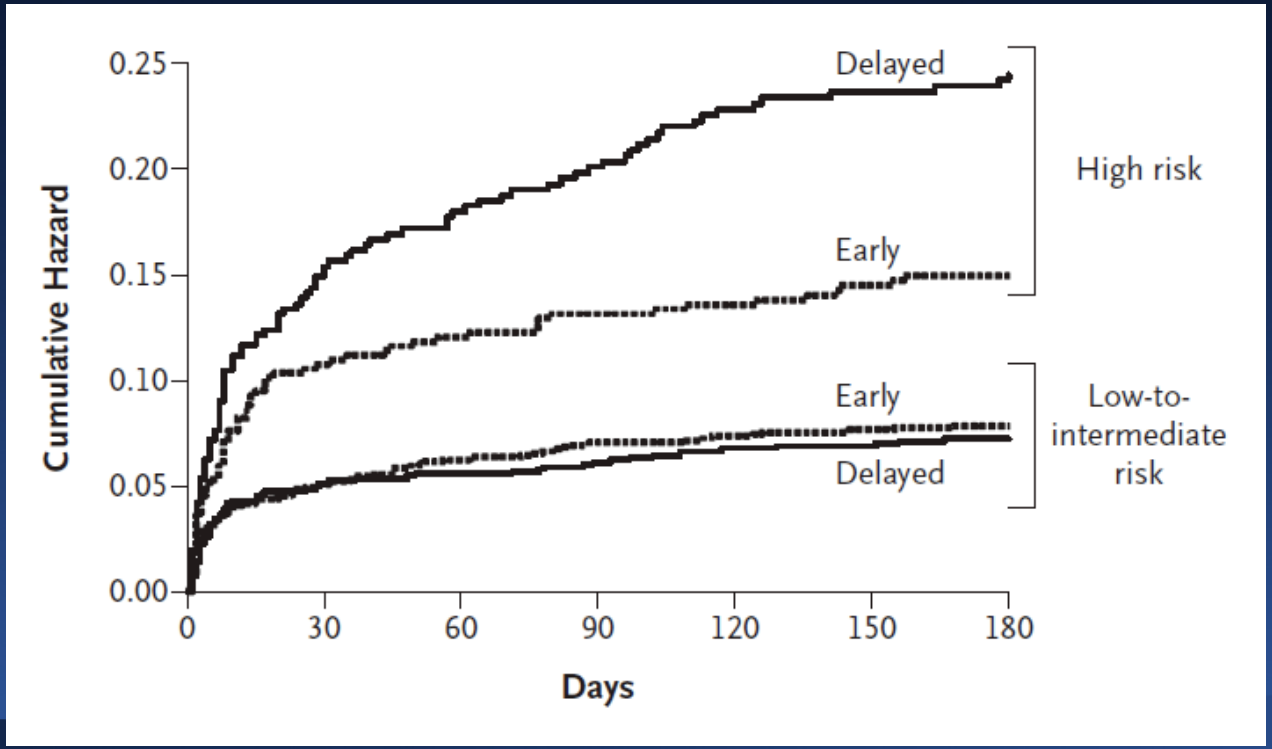
Early prevents adverse events in highest risk patients

Patients with a GRACE score > 140 had higher overall event rates.

The benefit of early intervention occurs in high risk patients.

The benefit continues to accumulate late after the procedure.

Death, MI, Stroke



Mehta et al. NEJM 2009; 360:2165-75

CARDIOVASCULAR RESEARCH FOUNDATION
A Passion for Innovation

Mount Sinai HEART

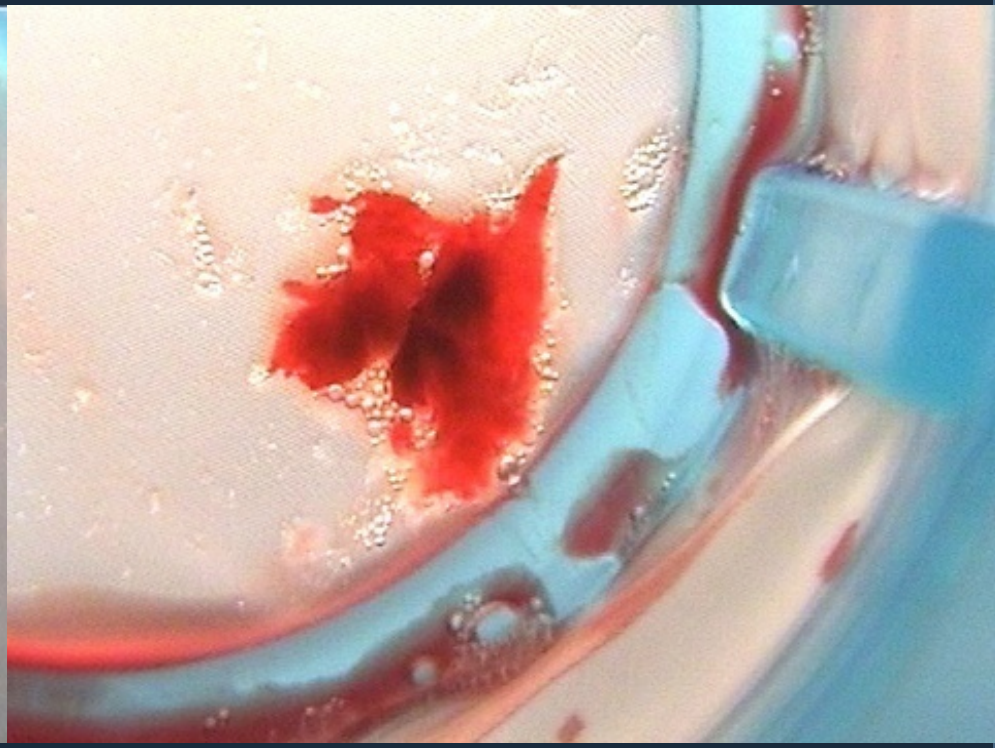
2011 ACS / NSTEMI Guideline Recommendations for Invasive Rx

- Class I
  - An early invasive strategy with intent to perform revascularization (if appropriate) is indicated in UA / NSTEMI
    - High risk clinical characteristics
      - Positive enzymes, ST segment changes, Strongly positive noninvasive testing. Refractory angina, electical instability, haemodynamically unstable.
    - High risk anatomy
- Class IIa
  - It is reasonable for initially stabilized high-risk patients with UA/NSTEMI (GRACE risk score greater than 140) to undergo an early invasive strategy within 12 to 24 hours of admission. For patients not at high risk, an early invasive approach is also reasonable. (Level of Evidence: B)

et al. *J Am Coll Cardiol.* 2011;57:e215-367

Distal Protection and Thrombectomy in AMI

Macroscopic embolic debris can be retrieved from >75% of cases

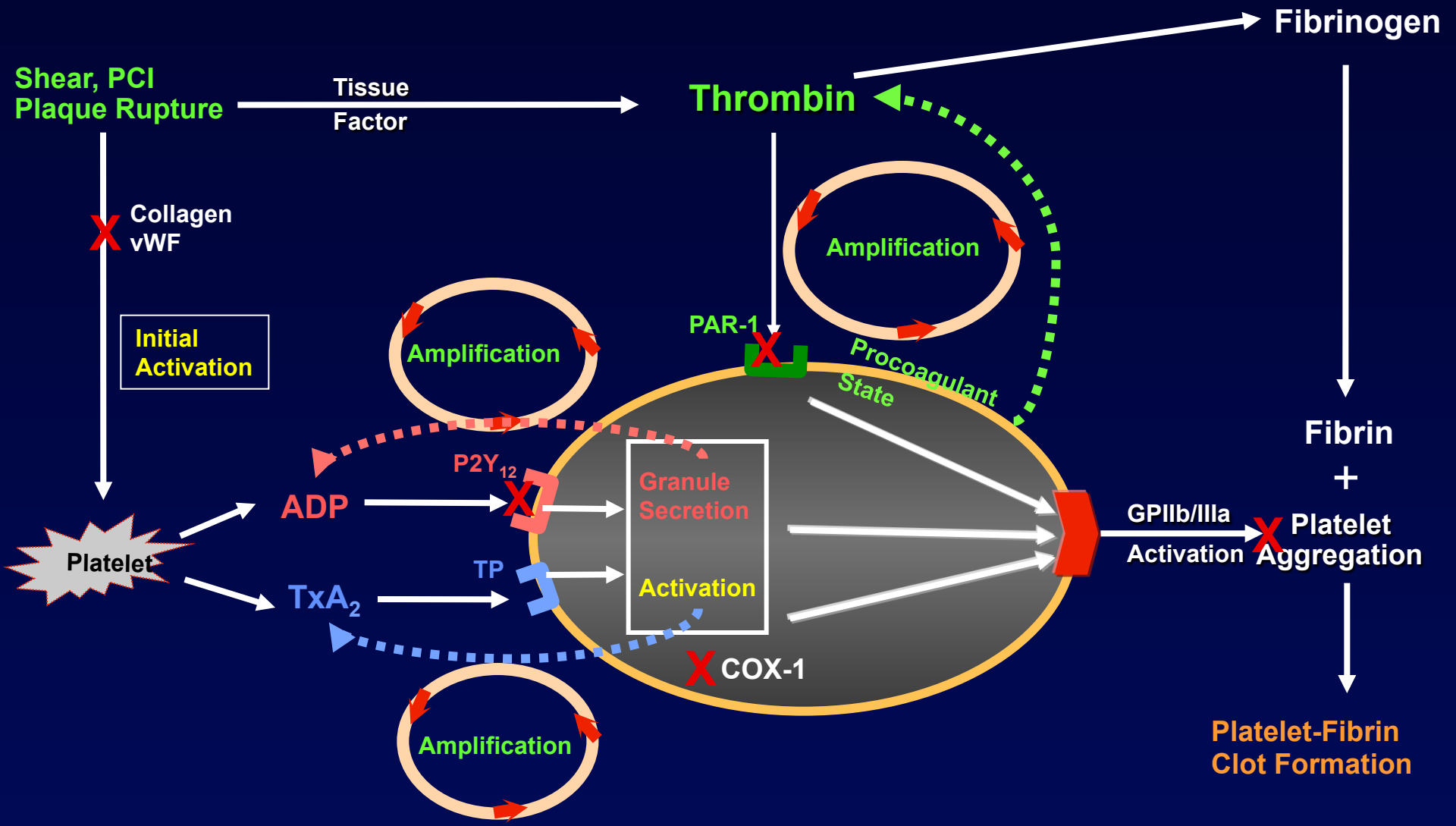


Aspiration Thrombectomy, 2013 Guidelines

Class IIa

- 1. Manual aspiration thrombectomy is reasonable for patients undergoing primary PCI. (Level of Evidence: B)

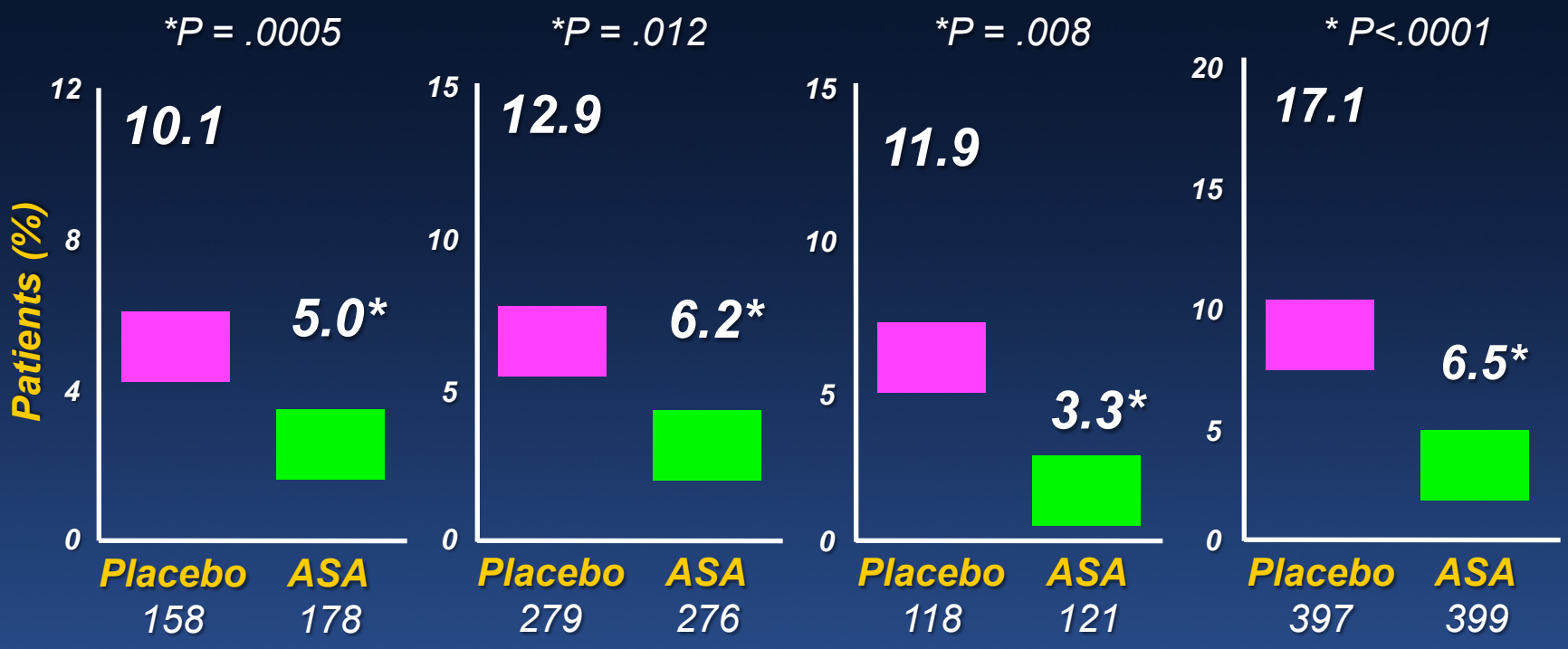
Central Role of Platelets and Interaction with Coagulation in the Genesis of Thrombosis



Adapted from Gurbel PA et al. *J Am Coll Cardiol.* 2007;50:1822-34.

Aspirin in UA/Non-ST-Elevation MI

Death or MI



Lewis HD Jr, et al. N Engl J Med. 1983;309:396-403.

Cairns JA, et al. N Engl J Med. 1985;313:1369-1375.

Theroux P, et al. N Engl J Med. 1988;319:1105-1111.

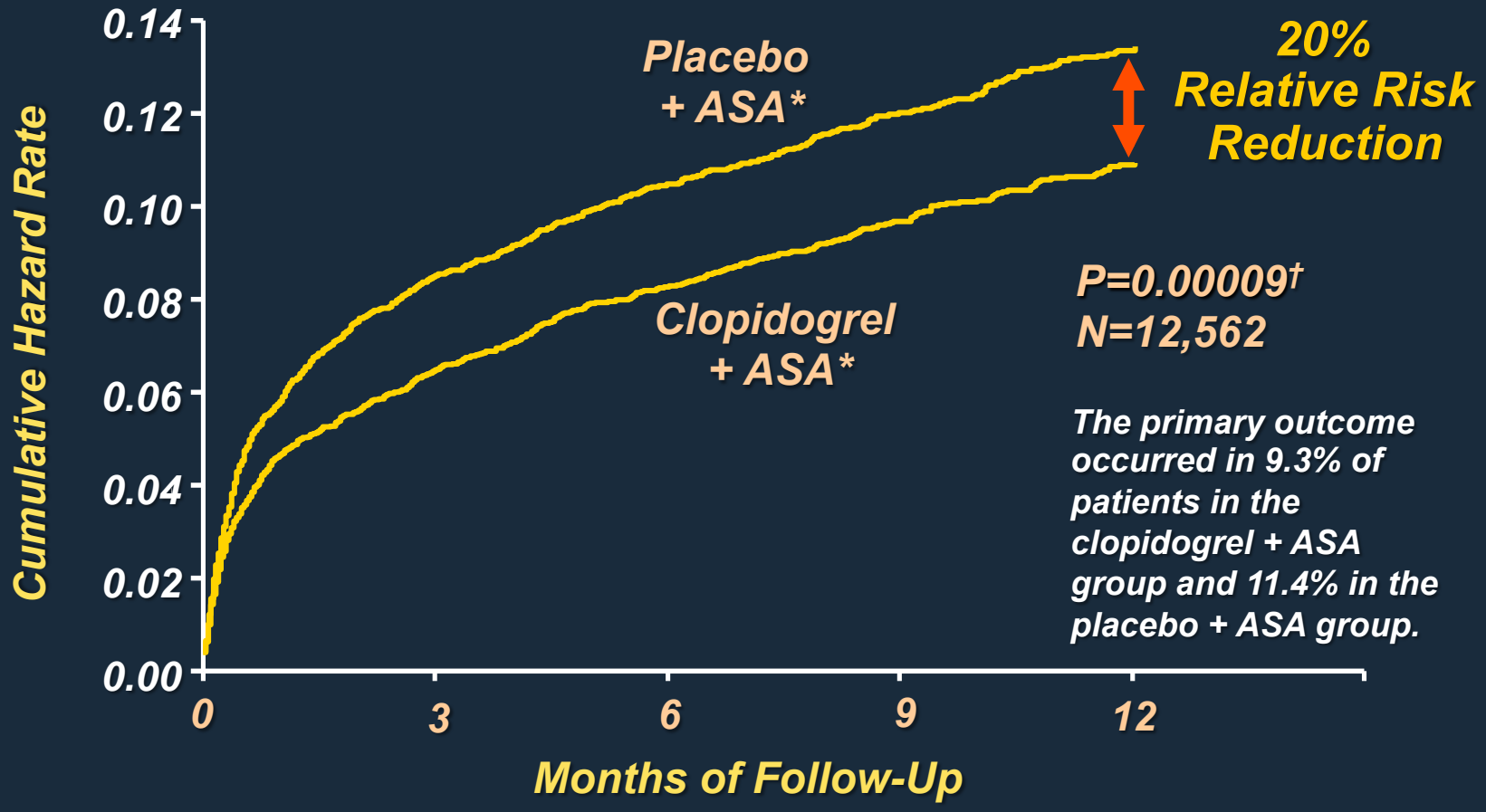
The RISC Group. Lancet. 1990;336:827-830.

CARDIOVASCULAR RESEARCH FOUNDATION
A Passion for Innovation

Mount Sinai HEART

CURE

Primary End Point: MI/Stroke/CV Death

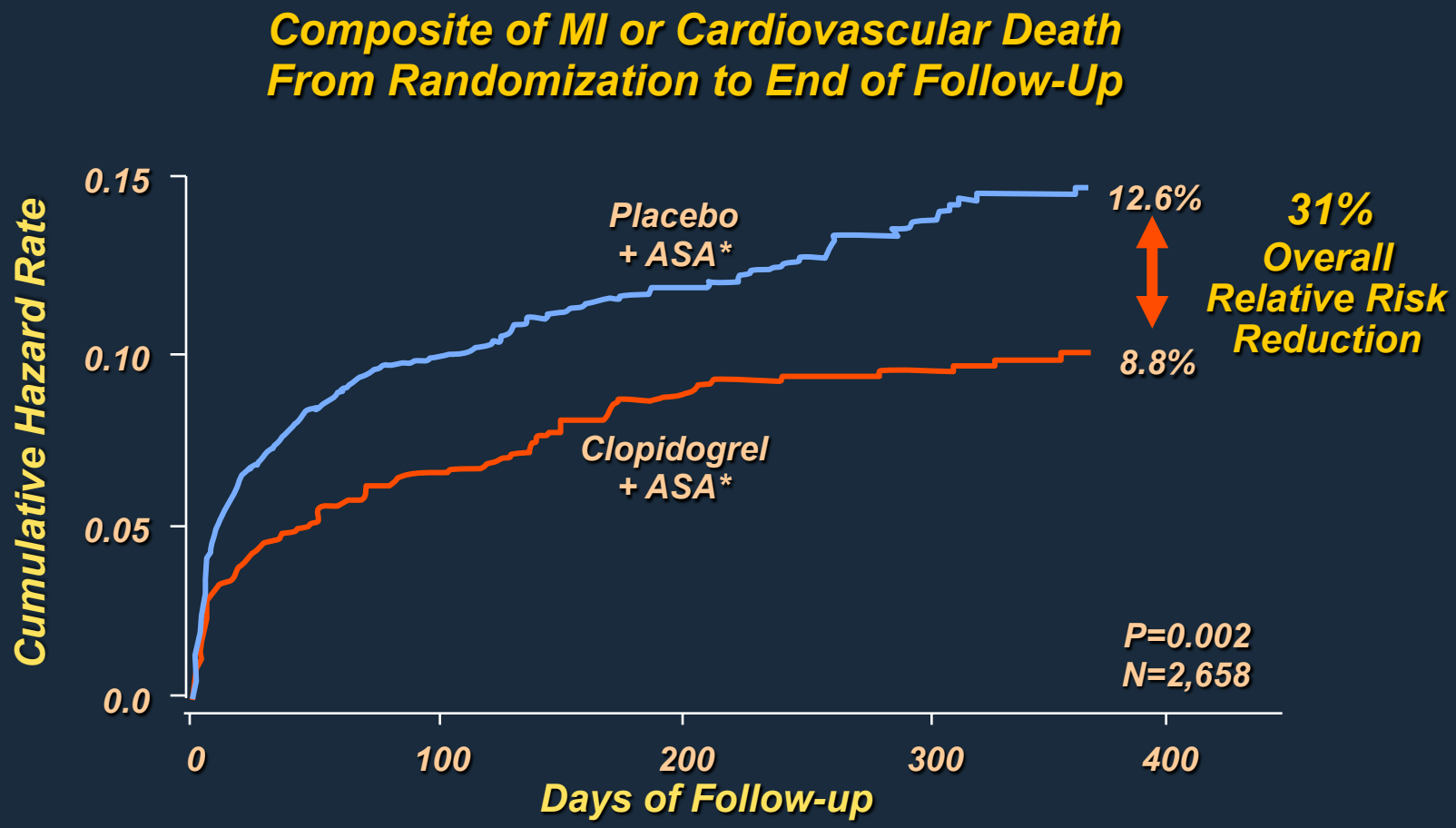


* Other standard therapies used as appropriate.

† PLAVIX Prescribing Information.

Adapted with permission (2002) from the Massachusetts Medical Society. The CURE Trial Investigators. N Engl J Med. 2001;345:494-502.

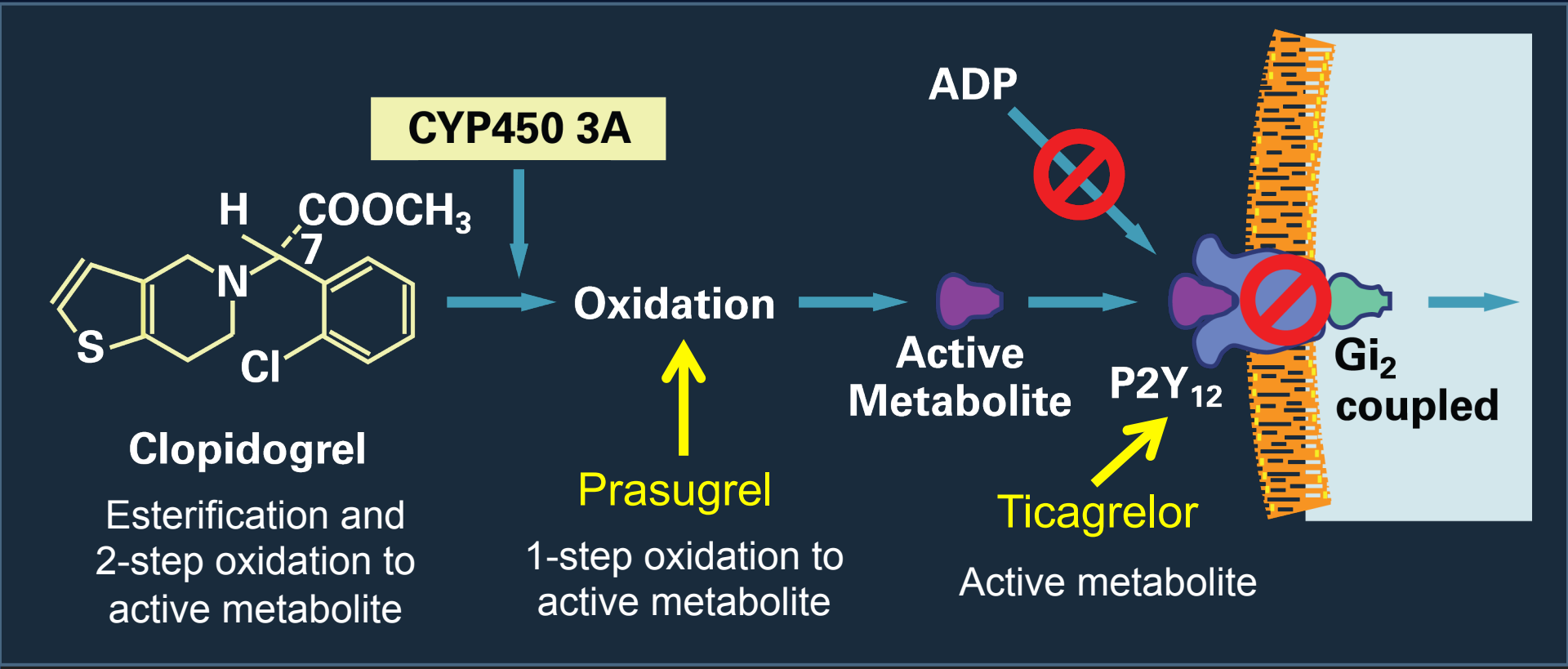
Overall Long-Term Results



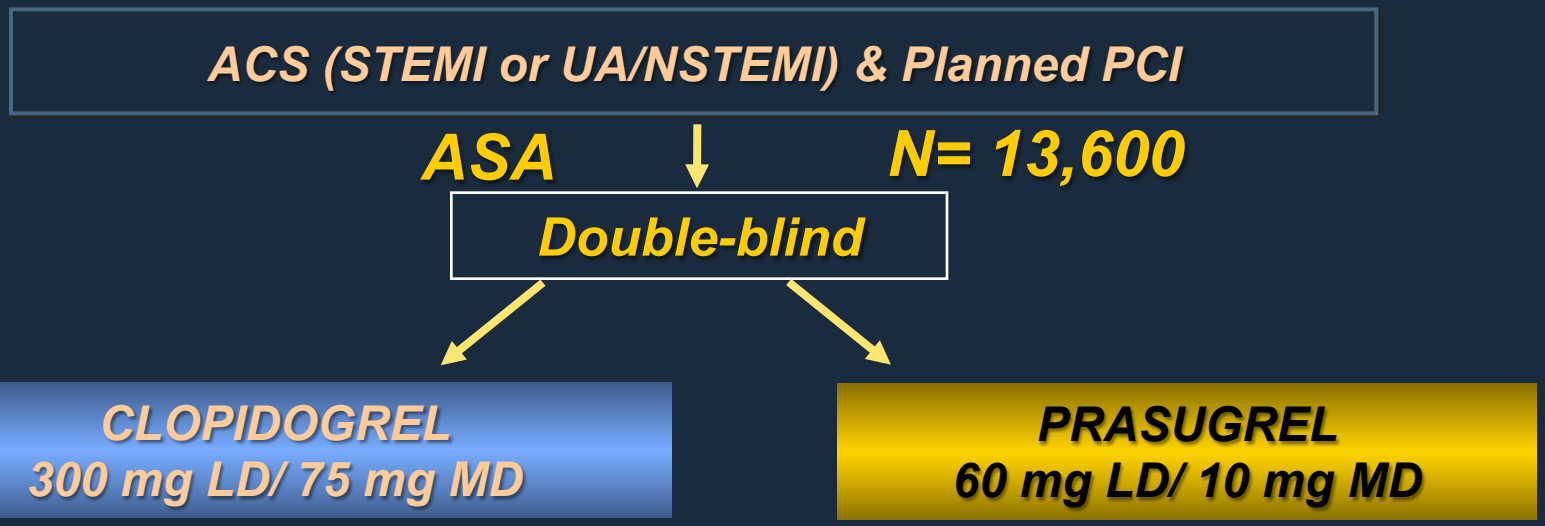
* In addition to other standard therapies.

Mehta SR, et al, for the CURE Investigators. Lancet. 2001;358:527-533.

The therapeutic target for thienopyridines and CPTPs is the platelet $P2Y_{12}$ receptor



TRITON-Study Design

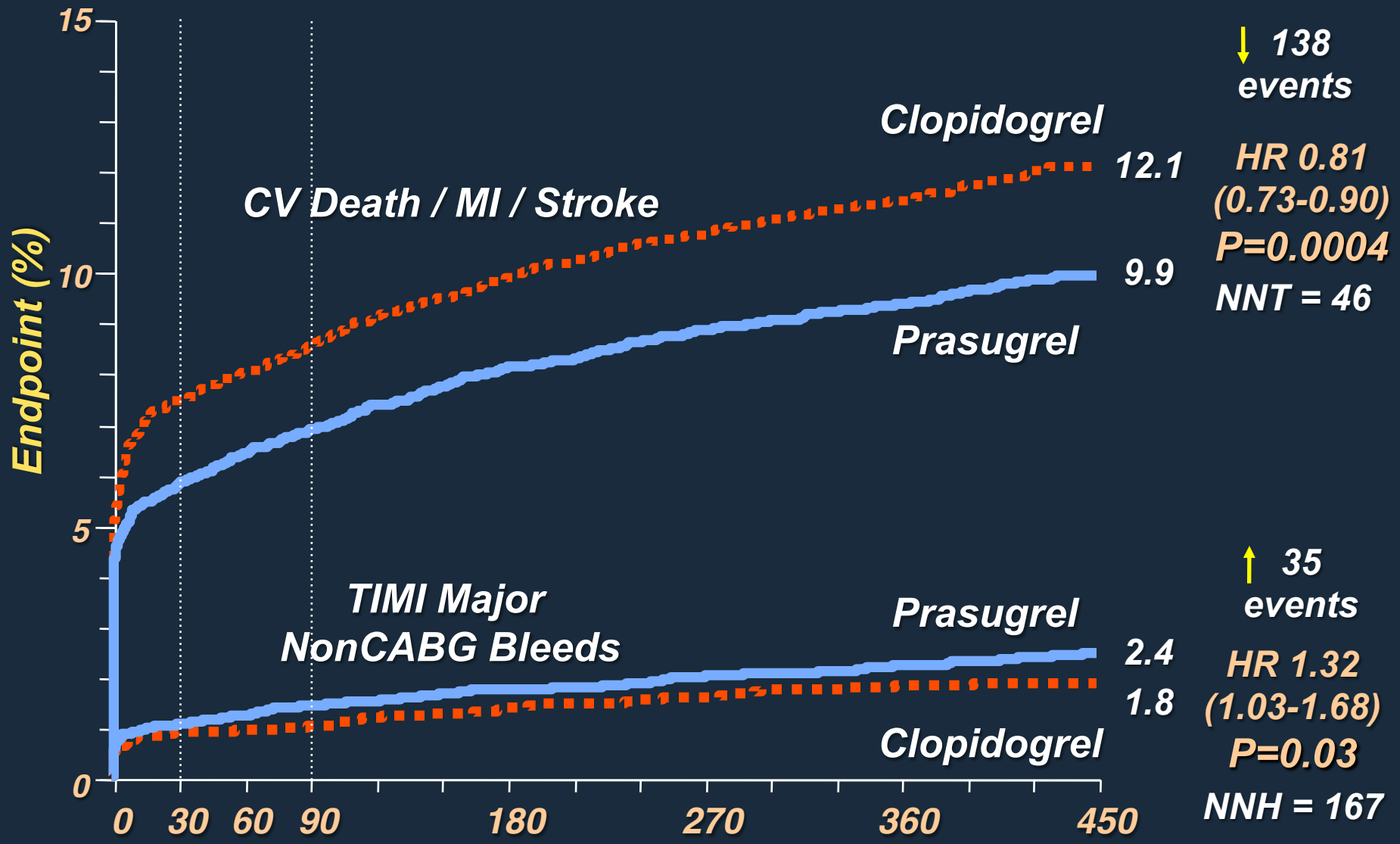


Median duration of therapy – 12 months

1º endpoint: CV death, MI, Stroke
2º endpoints: CV death, MI, Stroke, Rehosp-Rec Isch, CV death, MI, UTVR
Stent Thrombosis (ARC definite/prob.)

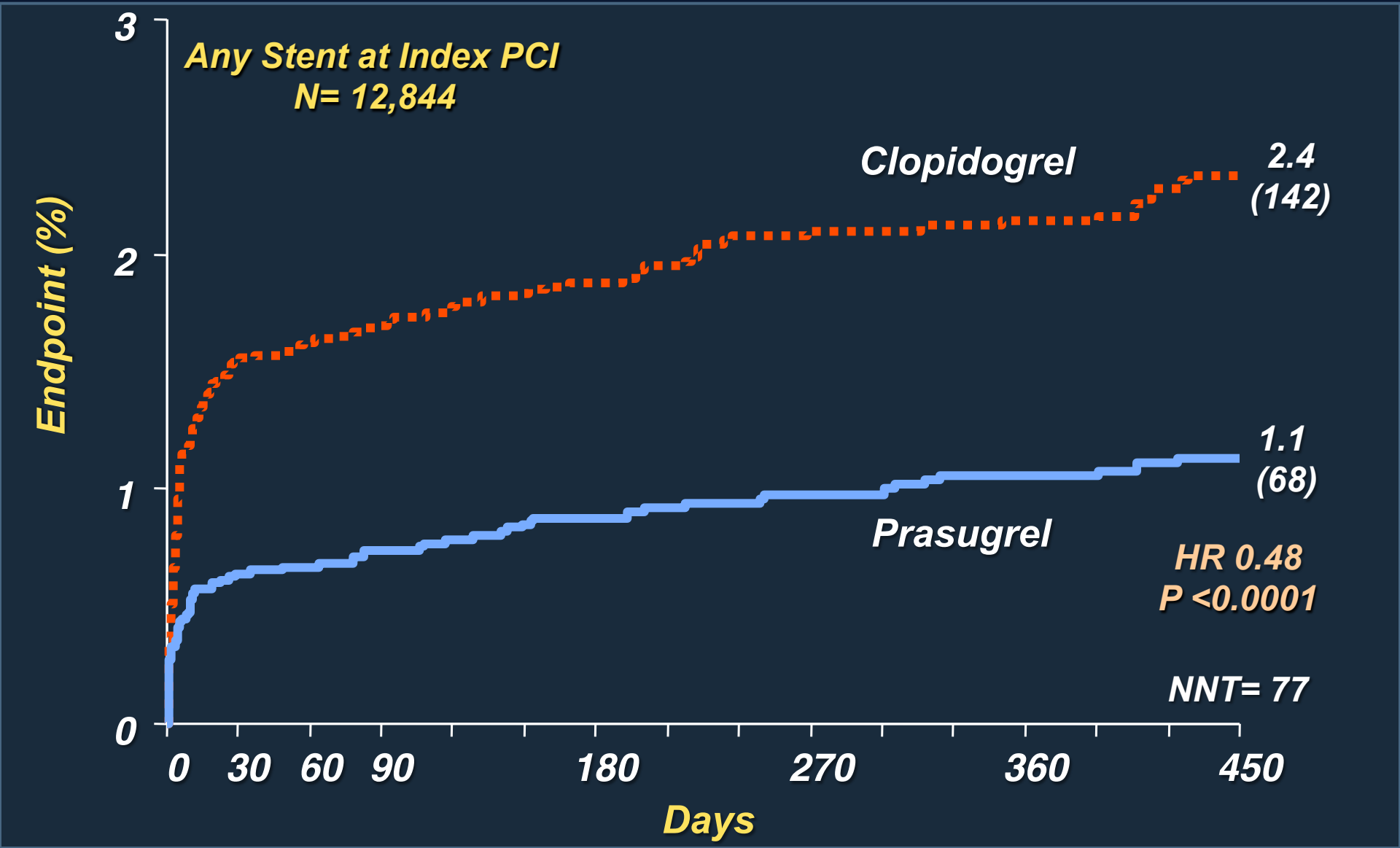
Safety endpoints: TIMI major bleeds, Life-threatening bleeds
Key Substudies: Pharmacokinetic, Genomic

Balance of Efficacy and Safety

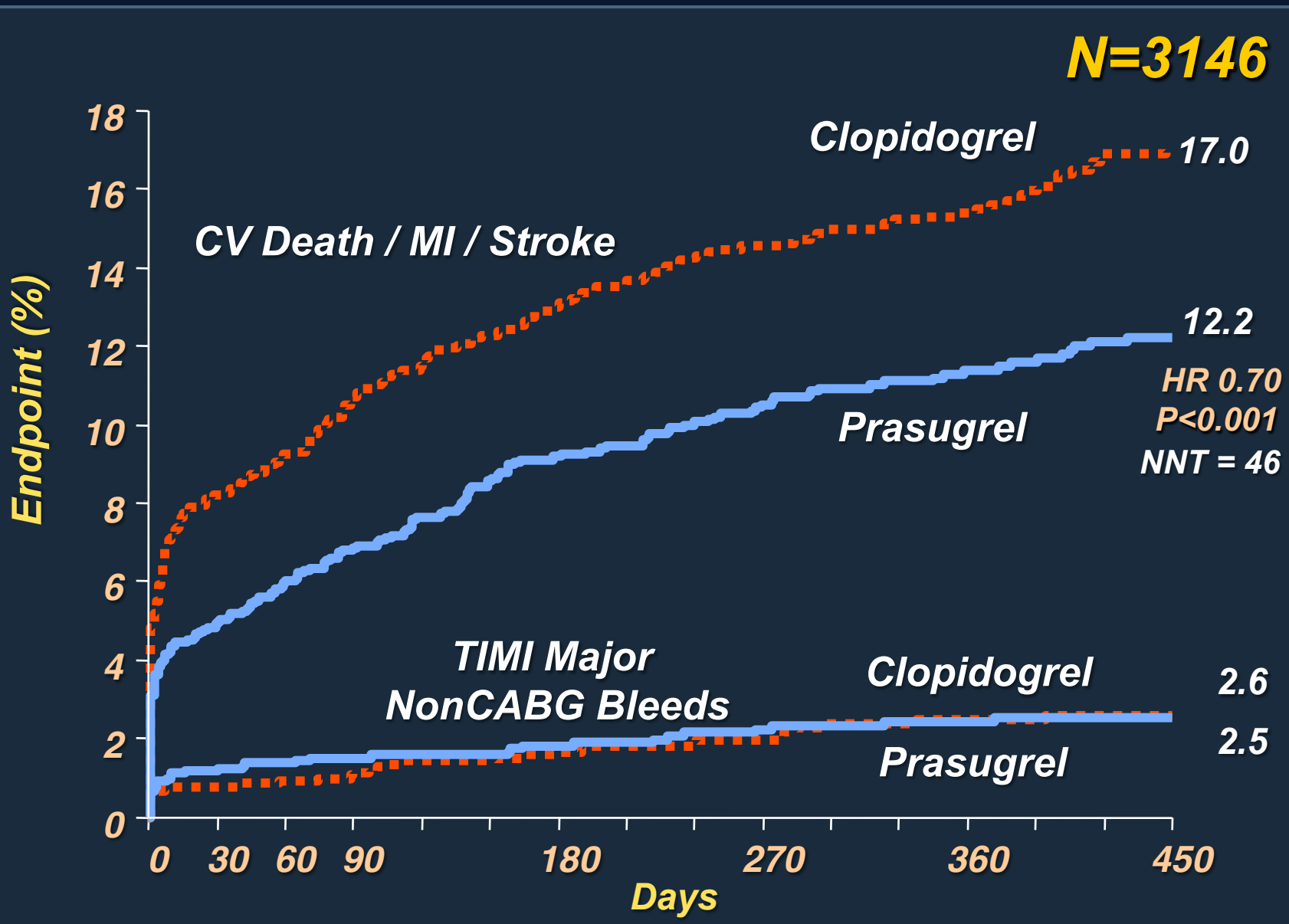


Wiviott SD, et al. N Engl J Med. 2007;357:2001-2015.

Stent Thrombosis (ARC Definite + Probable)



Diabetic Subgroup



Black Box Warning with Prasugrel

1. Contraindicated in patients with pathologic bleeding (such as peptic ulcer or ICH) and in those with a history of TIA or stroke.
2. In patients age 75 and older, prasugrel is generally not recommended because of the increased risk of intracranial and fatal bleeding and uncertain benefit, except in high-risk situations (patients with diabetes or a history of prior MI). In these situations, the drug's effect appears to be greater, and its use may be considered.
3. Use cautiously in patients who weigh less than 60 kg because of the increased risk of bleeding.
4. Use cautiously in patients at risk for increased bleeding from trauma, surgery, or other pathologic conditions and in those with severe hepatic impairment.

PLATO

August 30, 2009 at 08.00 CET

The NEW ENGLAND JOURNAL of MEDICINE

Ticagrelor versus Clopidogrel in Patients with Acute Coronary Syndromes

Lars Wallentin, M.D., Ph.D., Richard C. Becker, M.D., Andrzej Budaj, M.D., Ph.D., Christopher P. Cannon, M.D., Håkan Emanuelsson, M.D., Ph.D., Claes Held, M.D., Ph.D., Jay Horrow, M.D., Steen Husted, M.D., D.Sc., Stefan James, M.D., Ph.D., Hugo Katus, M.D., Kenneth W. Mahaffey, M.D., Benjamin M. Scirica, M.D., M.P.H., Allan Skene, Ph.D., Philippe Gabriel Steg, M.D., Robert F. Storey, M.D., D.M., and Robert A. Harrington, M.D., for the PLATO Investigators*

PLATO study design

NSTE-ACS (moderate-to-high risk) STEMI (if primary PCI)
Clopidogrel-treated or -naive;
randomised within 24 hours of index event
(N=18,624)

Clopidogrel
If pre-treated, no additional loading dose;
if naive, standard 300 mg loading dose,
then 75 mg qd maintenance;
(additional 300 mg allowed pre PCI)

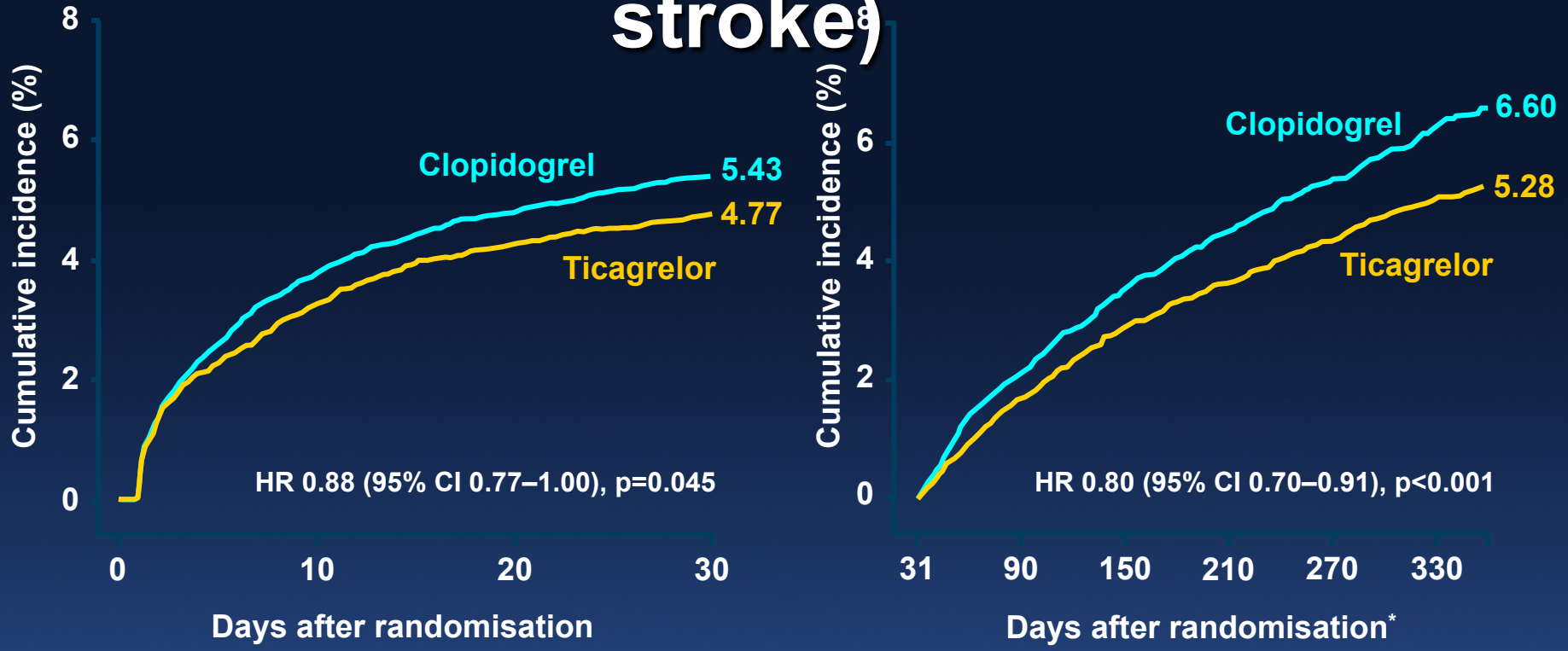
Ticagrelor
180 mg loading dose, then
90 mg bid maintenance;
(additional 90 mg pre-PCI)

6–12-month exposure

Primary endpoint: CV death + MI + Stroke
Primary safety endpint: Total major bleeding

PCI = percutaneous coronary intervention; ASA = acetylsalicylic acid;
CV = cardiova[illegible]A = transient ischaemic attack

Primary efficacy endpoint over time (composite of CV death, MI or stroke)



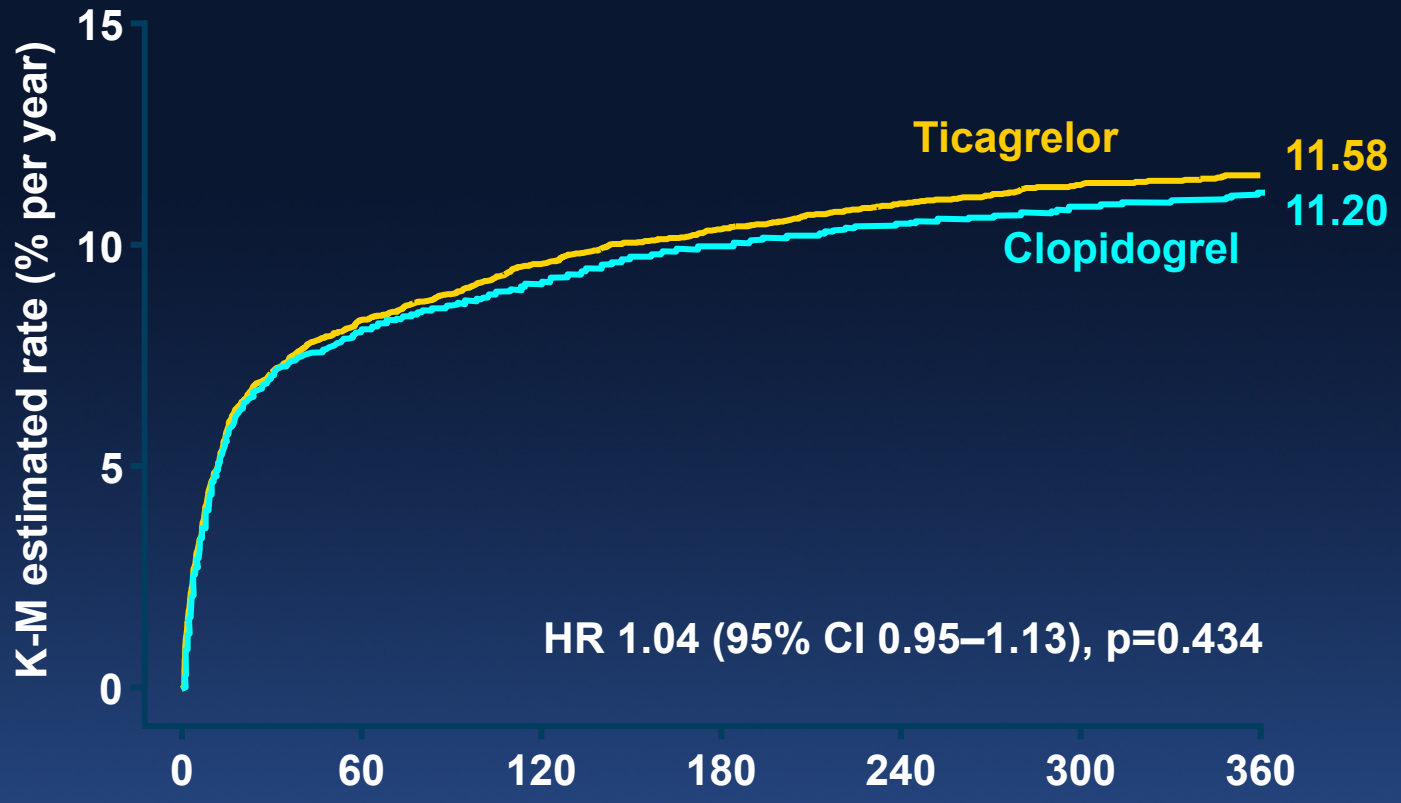
No. at risk										
Ticagrelor	9,333	8,942	8,827	8,763	8,673	8,543	8,397	7,028	6,480	4,822
Clopidogrel	9,291	8,875	8,763	8,688	8,688	8,437	8,286	6,945	6,379	4,751

*Excludes patients with any primary event during the first 30 days

CARDIOVASCULAR RESEARCH FOUNDATION
A Passion for Innovation

Mount Sinai HEART

Time to major bleeding – primary safety event



No. at risk							
Ticagrelor	9,235	7,246	6,826	6,545	5,129	3,783	3,433
Clopidogrel	9,186	7,305	6,930	6,670	5,209	3,841	3,479

CARDIOVASCULAR RESEARCH FOUNDATION
A Passion for Innovation

Mount Sinai HEART

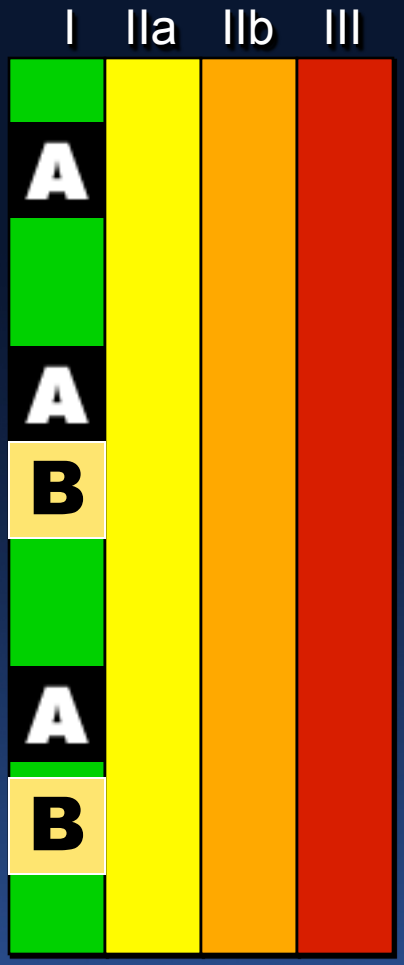
Antiplatelets

- Aspirin 162 to 325 mg should be given before primary PCI. (Level of Evidence: B)
- After PCI, aspirin should be continued indefinitely. (Level of Evidence: A)
- A loading dose of a P2Y12 receptor inhibitor should be given as early as possible or at time of primary PCI to patients with STEMI. Options include
- a. Clopidogrel 600 mg (Level of Evidence: B); or
- b. Prasugrel 60 mg (Level of Evidence: B); or
- c. Ticagrelor 180 mg. (Level of Evidence: B)

Antiplatelets

- P2Y12 inhibitor therapy should be given for 1 year to patients with STEMI who receive a stent (bare-metal or drug-eluting) during primary PCI using the following maintenance doses:
- a. Clopidogrel 75 mg daily (Level of Evidence: B); or
- b. Prasugrel 10 mg daily (Level of Evidence: B); or
- c. Ticagrelor 90 mg twice a day. (Level of Evidence: B)

ACC/AHA Guidelines 2007+2011 Anti-Coagulant Therapy



Anticoagulant therapy added ASAP

For an invasive strategy-

Enoxaparin or UFH

Bivalirudin

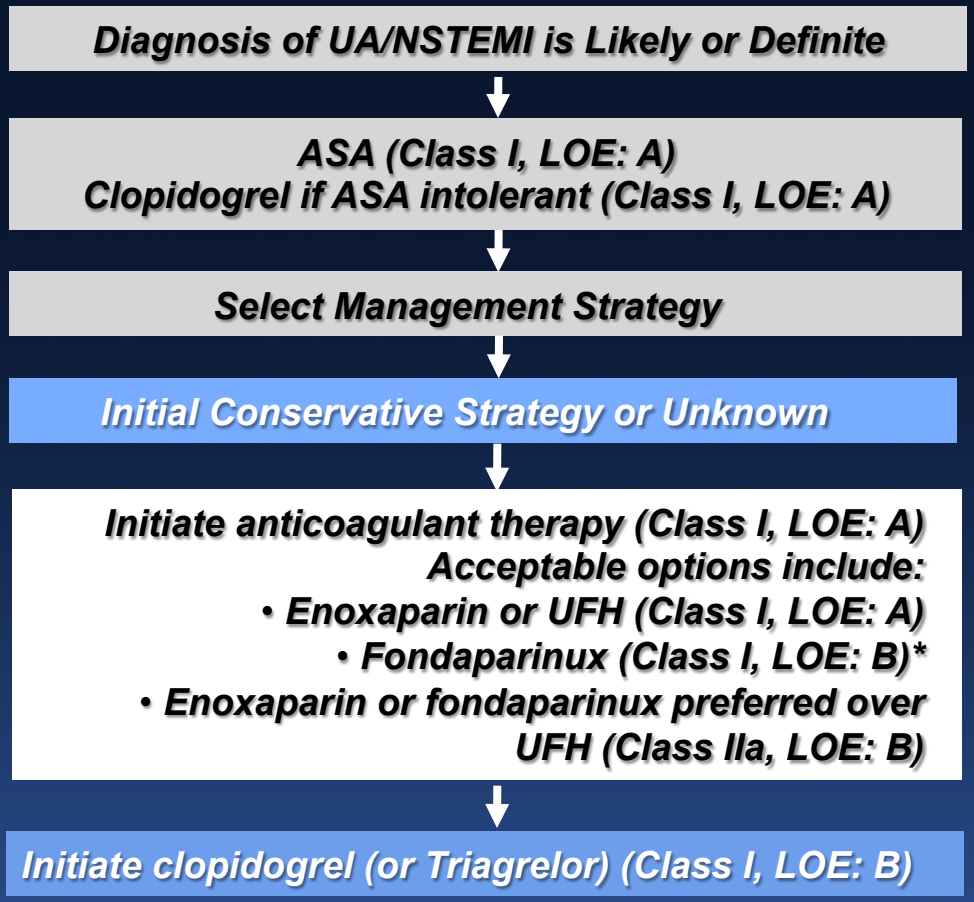
For a conservative strategy-

Enoxaparin, or UFH*

Fondaparinux, esp. if increased risk of bleeding

* Class IIA: Enoxaparin or fondaparinum preferred over UFH

ACC/AHA Guideline Recommendations for Initial Management of UA/NSTEMI – Conservative Strategy



Wright RS, et al. J Am Coll Cardiol. 2011;57:1920-1959

Statins

Class I

- High-intensity statin therapy should be initiated or continued in all patients with STEMI and no contraindications to its use. (Level of Evidence: B)

2010+: Do whatever it takes to reduce time from symptom onset to ER arrival and time from ER arrival to PCI!