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KERCKHOFF KLINIK

Akutes Koronarsyndrom

Update

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Conflict of Interest – Disclosure

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Christian W. Hamm

Affiliation/Financial Relationship	**Company**
Honoraria for lectures:	Abbott, AstraZeneca ,Bayer, Boehringer Ingelheim, CVRx, BRAHMS, Daiichi Sankyo, Medtronic, Lilly, MSD, SanofiAventis, Pfizer, Roche, Servier, The Med. Comp., Boston Scientific, Gilead
Honoraria for advisory board activities:	Aspen, AstraZeneca, Bayer, BRAHMS, CVRx, Boehringer Ingelheim, Medtronic, SHS, Zoll
Participation in clinical trials:	AstraZeneca, Boston Scientific,
Financial shares and options:	no

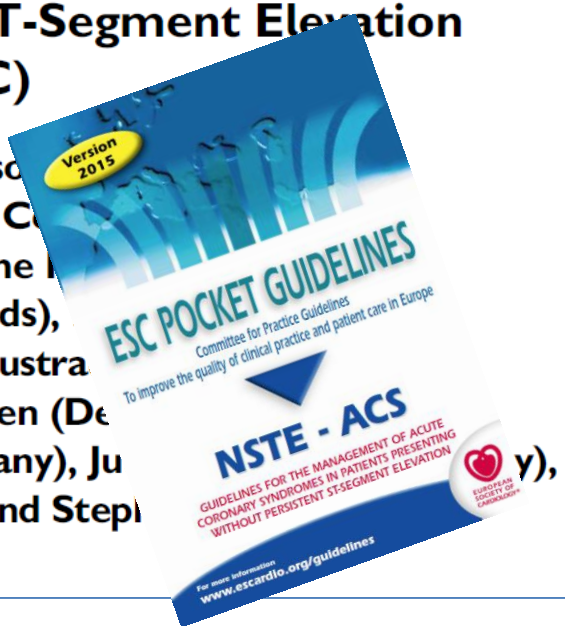
ACS - -Update

- Diagnose
- Therapie

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)

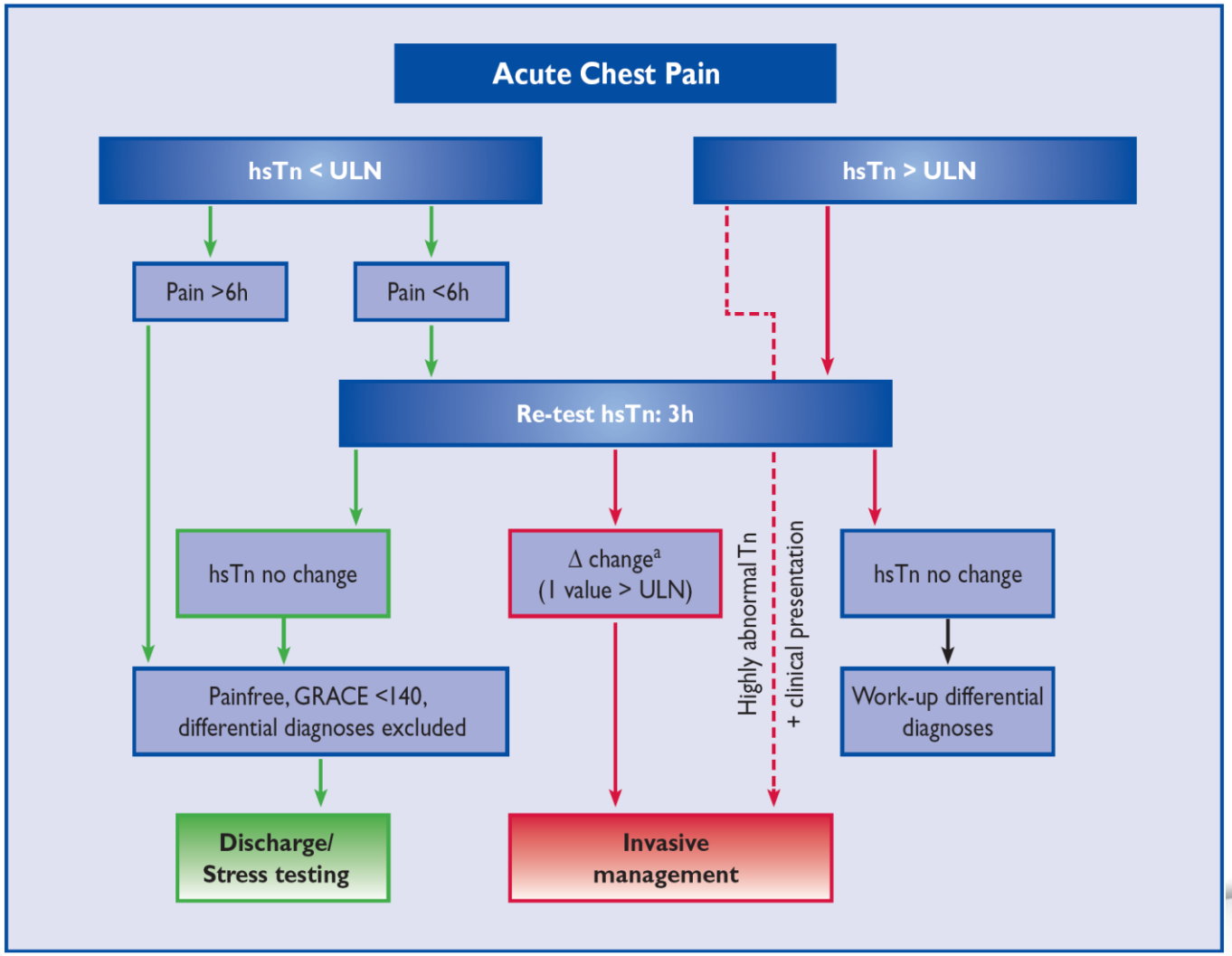
**Authors/Task Force Members: Marco Roffi* (Chairperso
Carlo Patrono* (Co-Chairperson) (Italy), Jean-Philippe C
Christian Mueller† (Switzerland), Marco Valgimigli† (The
Felicita Andreotti (Italy), Jeroen J. Bax (The Netherlands),
(Germany), Carlos Brotons (Spain), Derek P. Chew (Austra
(Switzerland), Gerd Hasenfuss (Germany), Keld Kjeldsen (De
Patrizio Lancellotti (Belgium), Ulf Landmesser (Germany), Ju y),
Debabrata Mukherjee (USA), Robert F. Storey (UK), and Step
(Switzerland)**



**ESC Committee for Practice Guidelines,
Review Coordinators, Reviewers, ESC staff, EHJ**

ACS Algorithm in ESC Guideline 2011

"Rule-out"



"Rule-in"

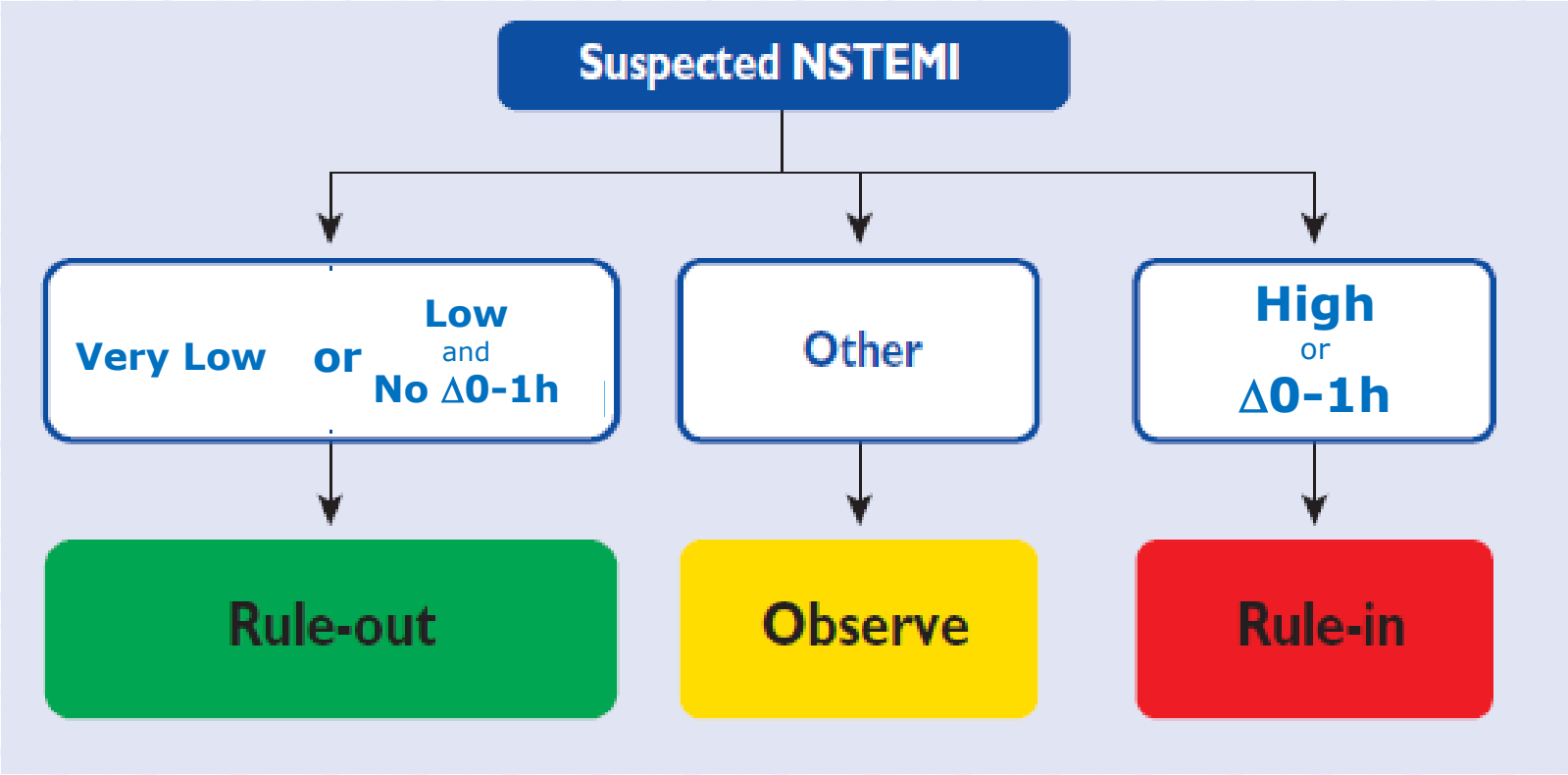
Recommendations for diagnosis & risk stratification

	It is recommended to measure cardiac troponins with sensitive or high-sensitivity assays and obtain the results within 60 minutes.	I	A
	A rapid rule-out protocol at 0h and 3h is recommended if high-sensitivity cardiac troponin tests are available.	I	B
Neues Protokoll	A rapid rule-out and rule-in protocol at 0h and 1h is recommended if a high-sensitivity cardiac troponin test with a validated 0h/1h algorithm is available. Additional testing after 3–6h is indicated if the first two troponin measurements are not conclusive and the clinical condition is still suggestive of ACS.	I	B

Roffi M, Patrono C, et al.: 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. *EHJ* doi:10.1093/eurheartj/ehv320

EUROPEAN SOCIETY OF CARDIOLOGY®

0 h/1 h Rule-in and rule-out algorithms using high-sensitivity cardiac troponins (hs-cTn) assays in patients presenting with suspected NSTEMI



- Negative predictive value >98% for acute MI
- Positive predictive value 75-80% for acute MI
- Cut-offs for « rule-in » and « rule-out » assay specific

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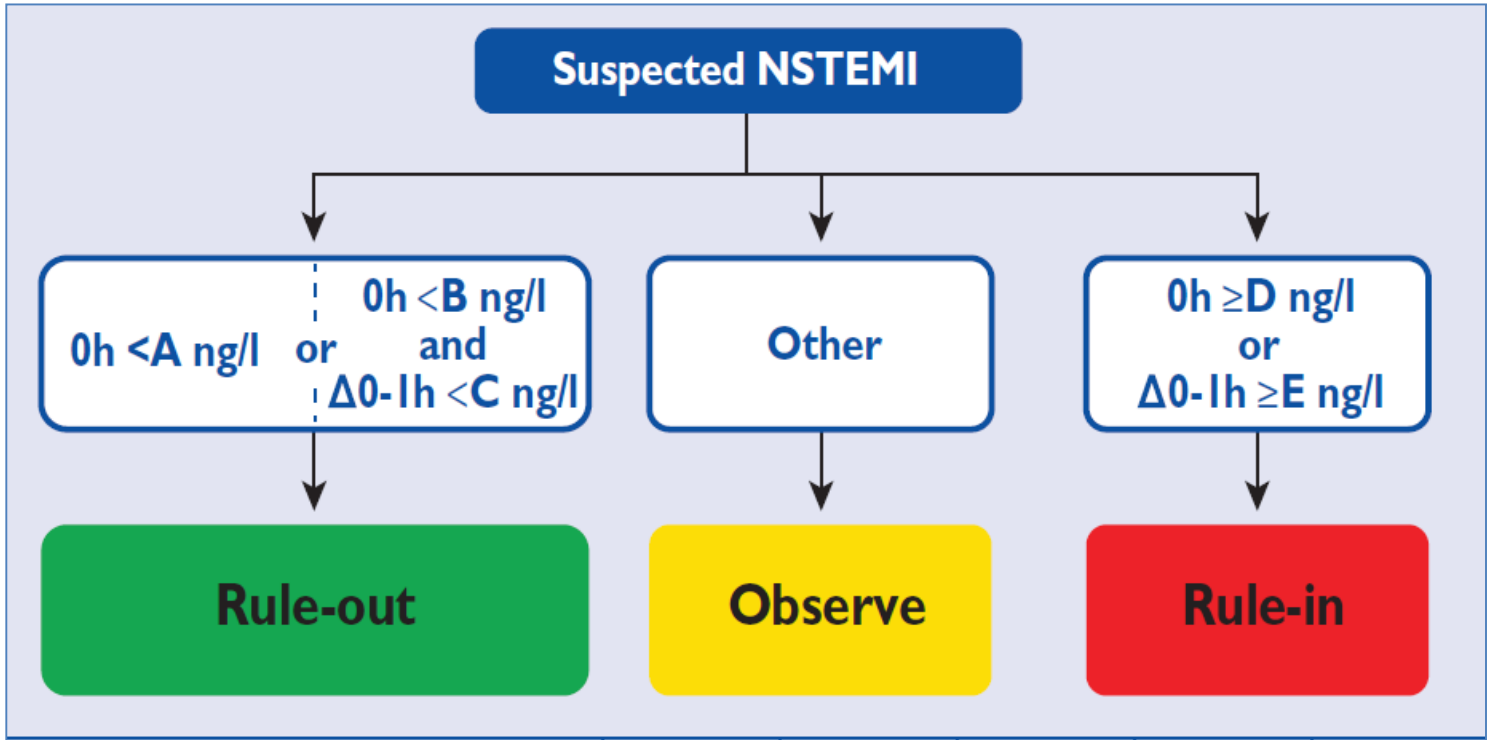
0 h/1 h Rule-in and rule-out algorithms using high-sensitivity cardiac troponins (hs-cTn) assays



	A	B	C	D	E
hs-cTnT (Elecsys)	5	12	3	52	5
hs-cTnI (Architect)	2	5	2	52	6

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APACE Studie: 1 Std. Algorithmus

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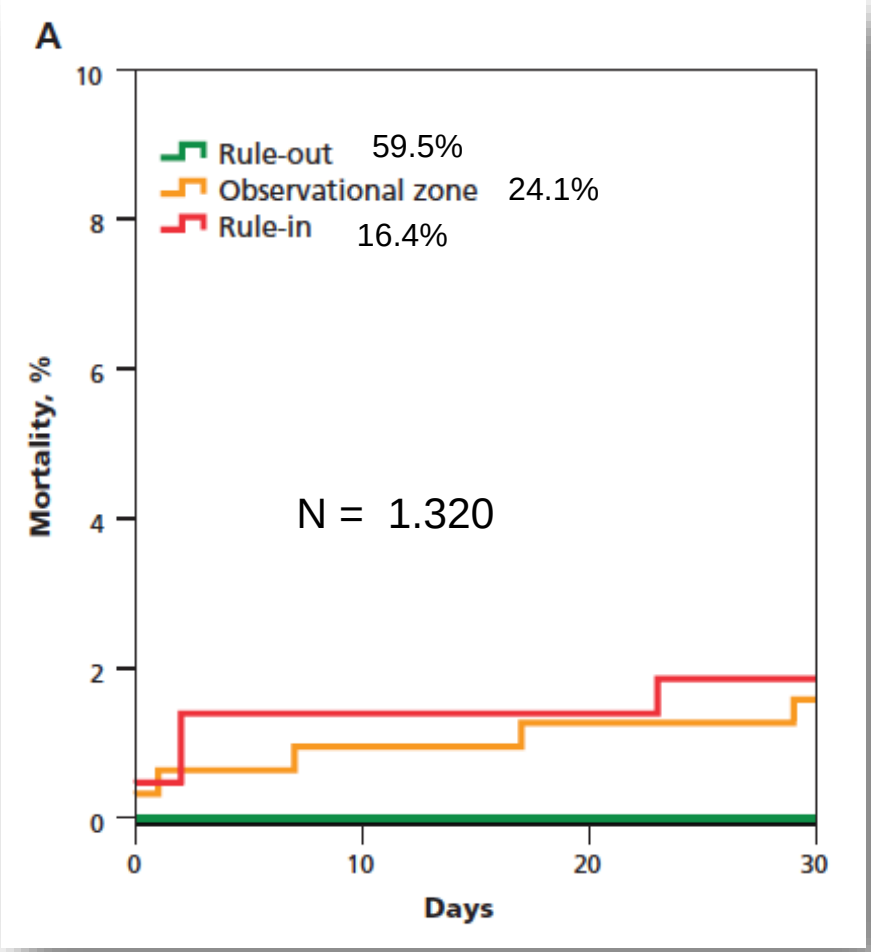
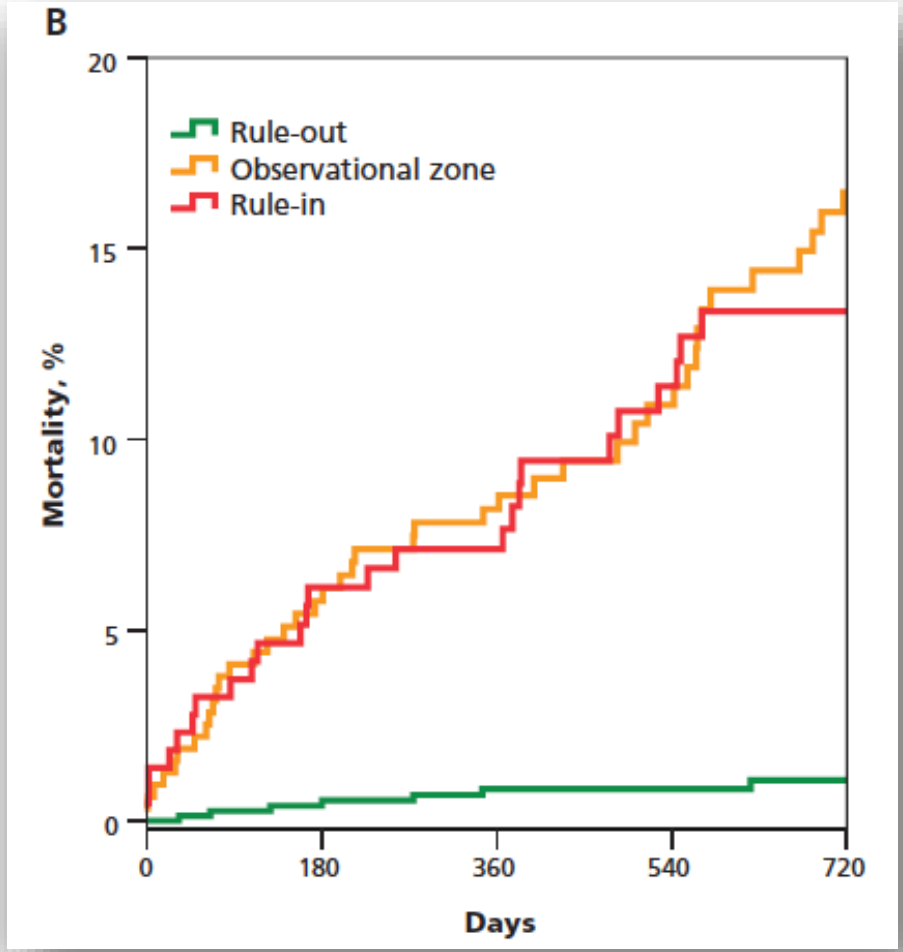
hs Troponin T

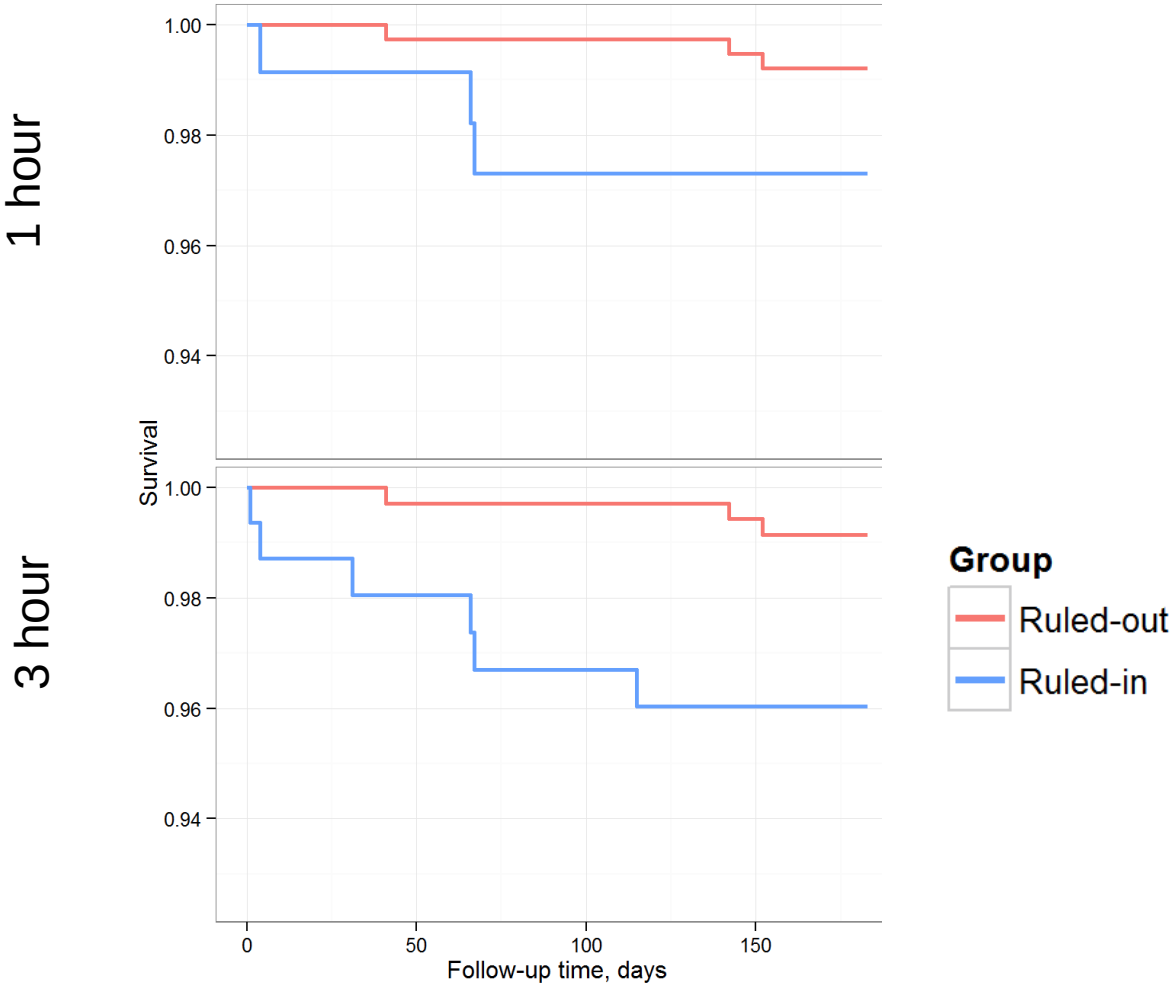




Reichlin et al., CMAJ 2015,187:E243-252

BACC - Studie

Troponin I: Cut-off 6 ng/L



99.7% of all patients at median follow up of 183 days

6 months mortality rate

Rule-out	6 ng/L
1h	3 deaths
3h	3 deaths

N = 1045

Neumann JT, JAMA Cardiol. 2016;1:397

hsTroponin I nur bei Aufnahme

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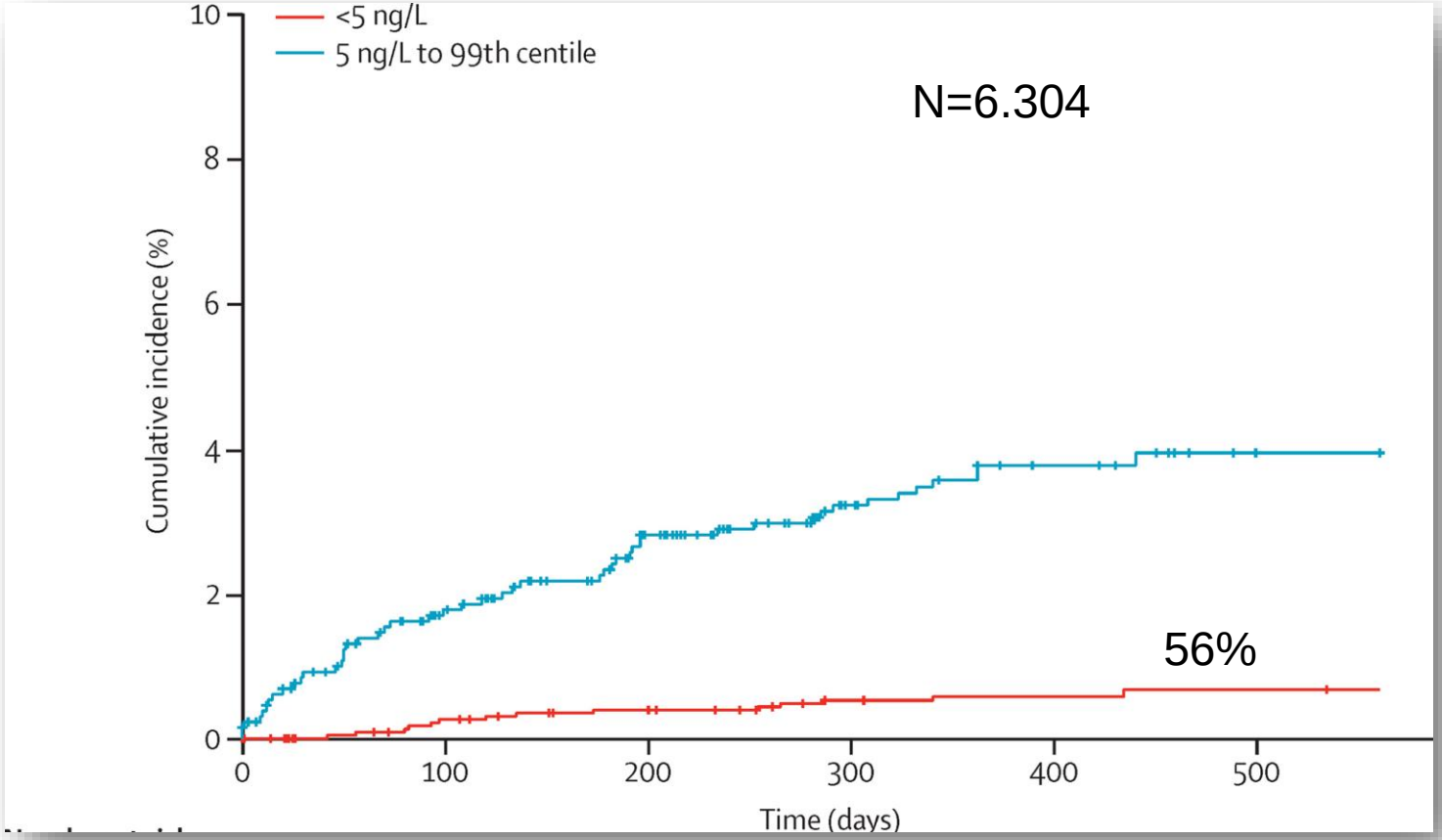

Shah; et al. The Lancet 2015 386, 2481-2488

hs Troponin und CT

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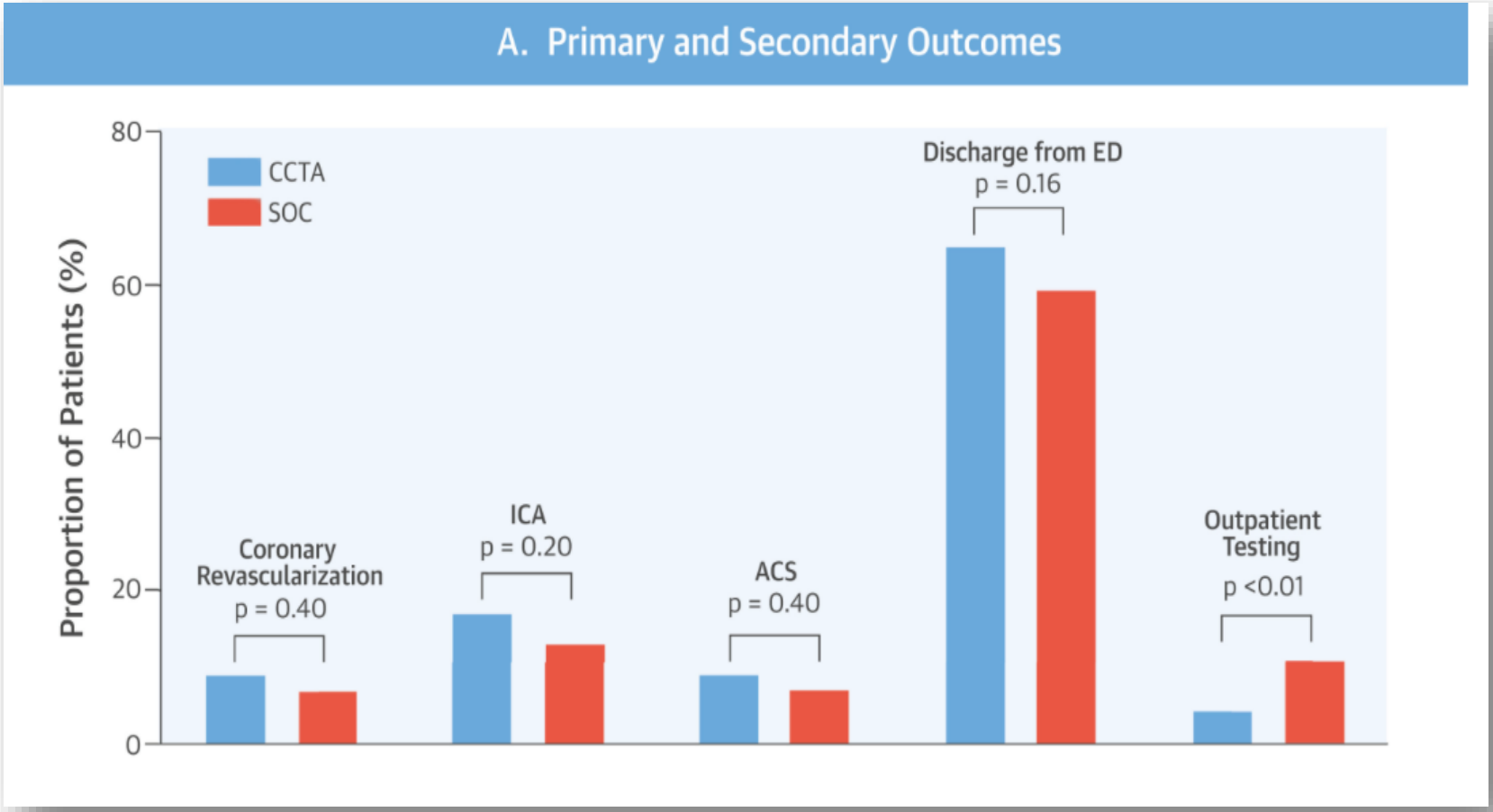

Dedic A, et al. J Am Coll Cardiol. 2016;67:16

Fazit: hsTroponin in ACS

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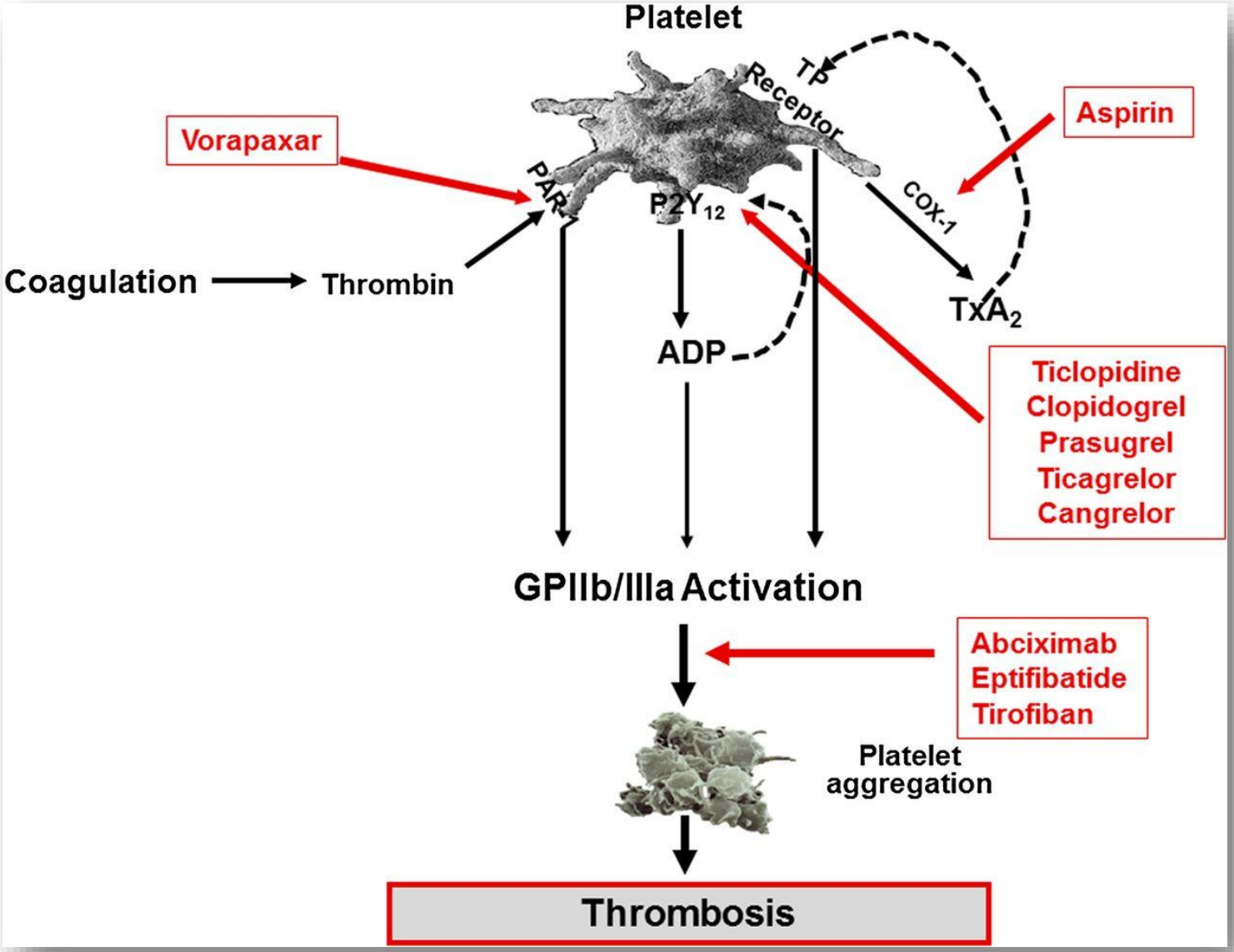
- “Rule out”
  - Einfacher und schneller (1 Std.)
  - Betrifft ca. 60% Chest Pain Patienten
- “Rule in”
  - Komplexer:
    - ca. 20% eindeutig
    - ca. 20% “observational”

ACS - -Update

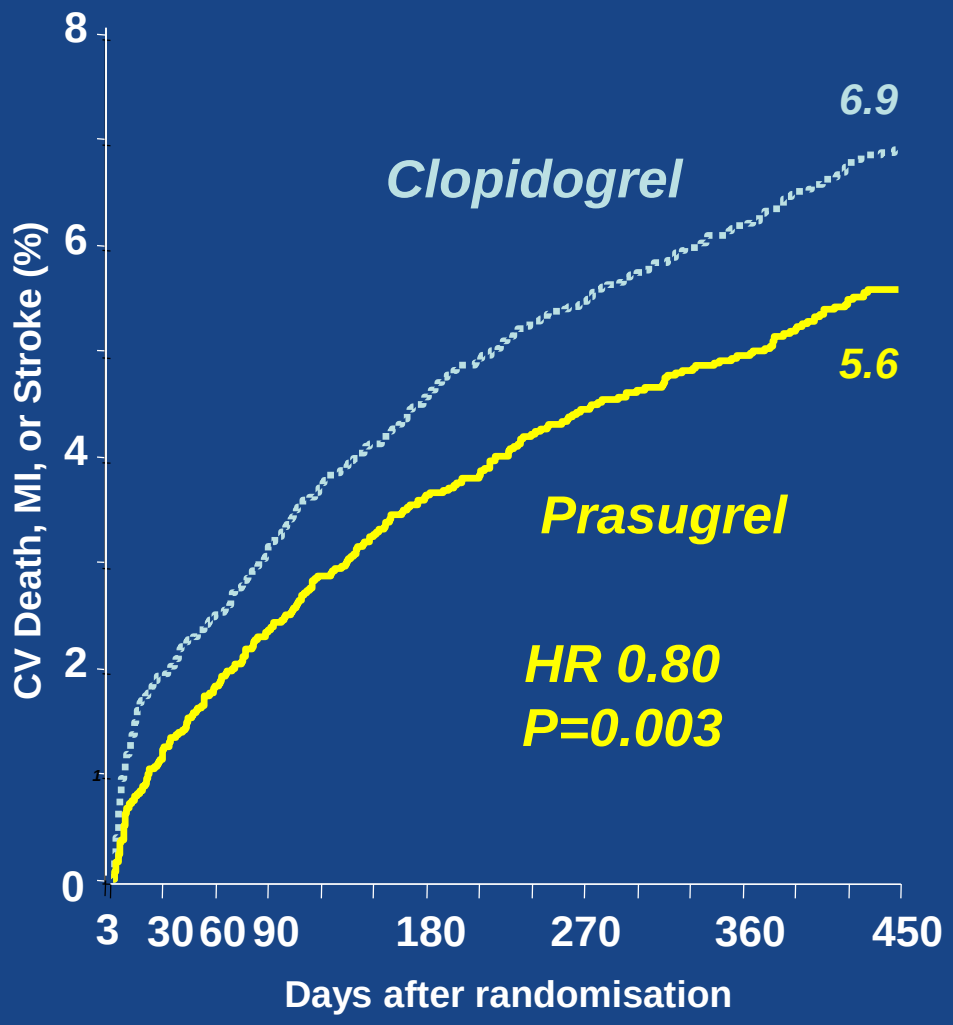
- Diagnose

- Therapie

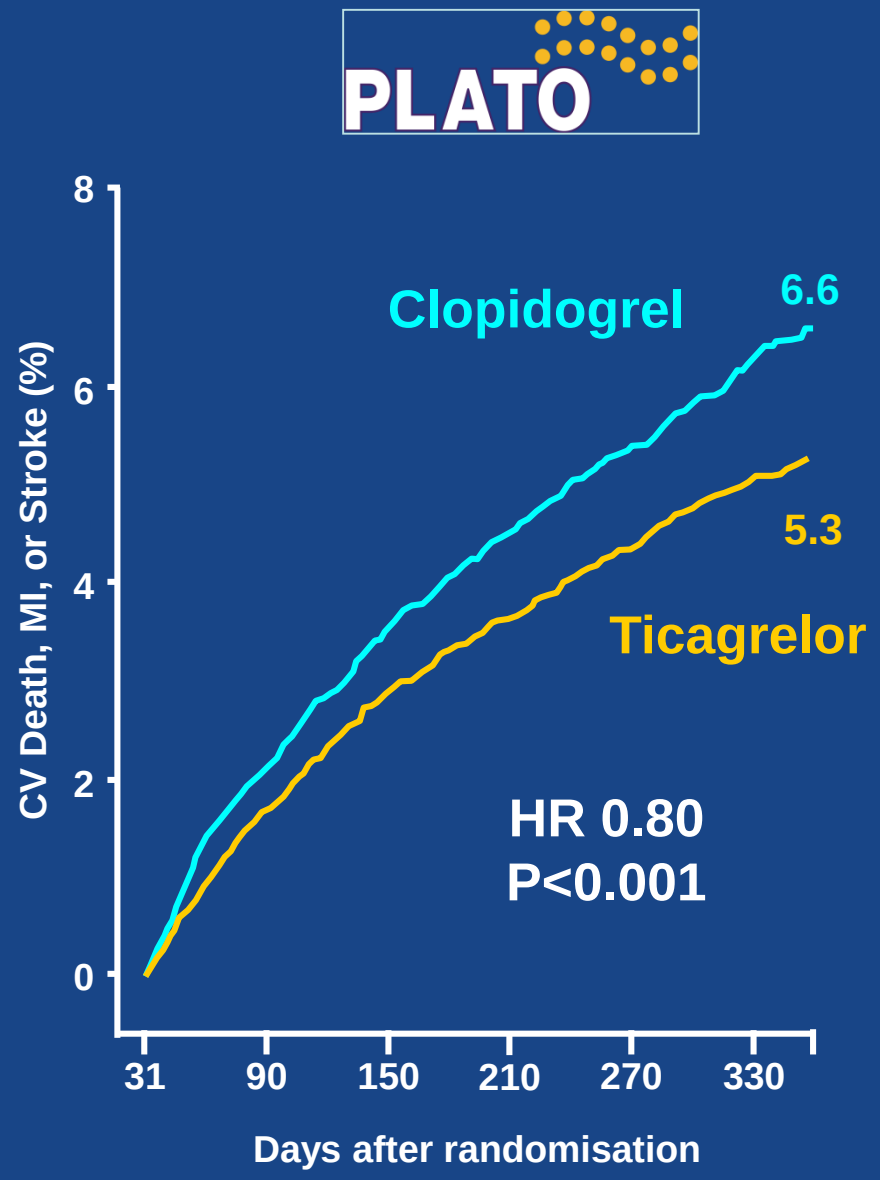
ACS: Plättchenhemmer



Event Rate Curves With $P2Y_{12}$ Inhibition



Wiviott SD et al. *NEJM* 2007;357:2001-15



Wallentin L, et al. *NEJM* 2009;361:1045-57

Plättchenhemmer bei ACS in Leitlinien

	NSTEMI	STEMI
ASA	+++	+++
Ticagrelor/ Prasugrel	+++	+++
Clopidogrel	+	+
Cangrelor	+	(+)
GP IIb/IIIa	+	++

PRAGUE 18

Randomized patients:

n = 1230

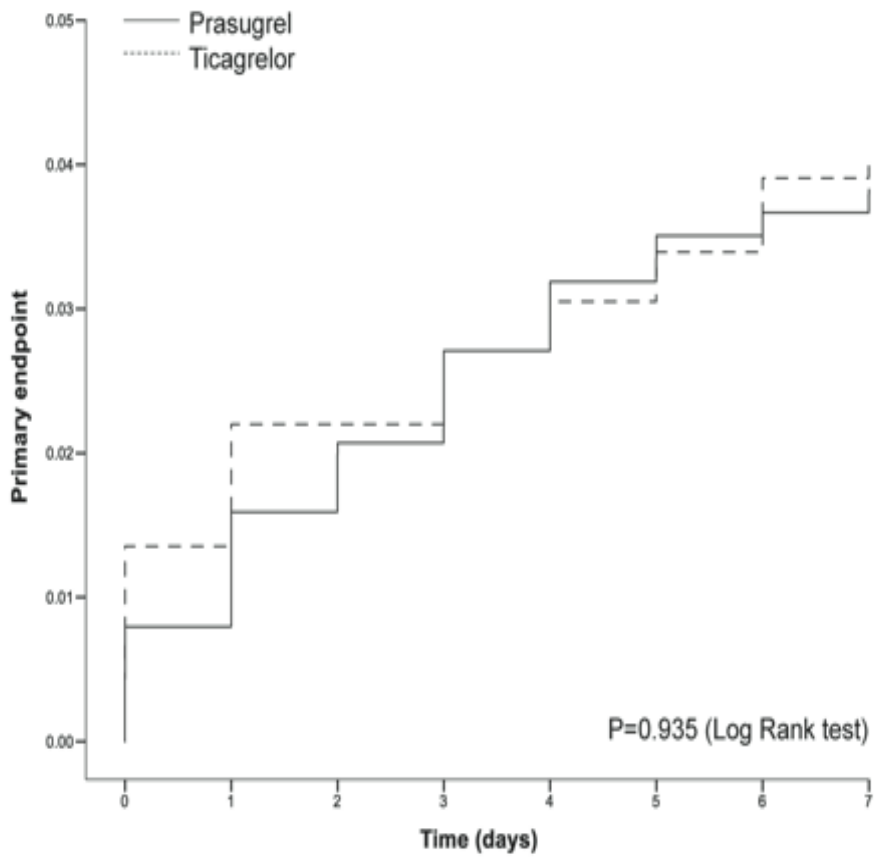
Prasugrel: n = 634

First dose given to all 634.

Ticagrelor: n = 596

First dose given to all 596.

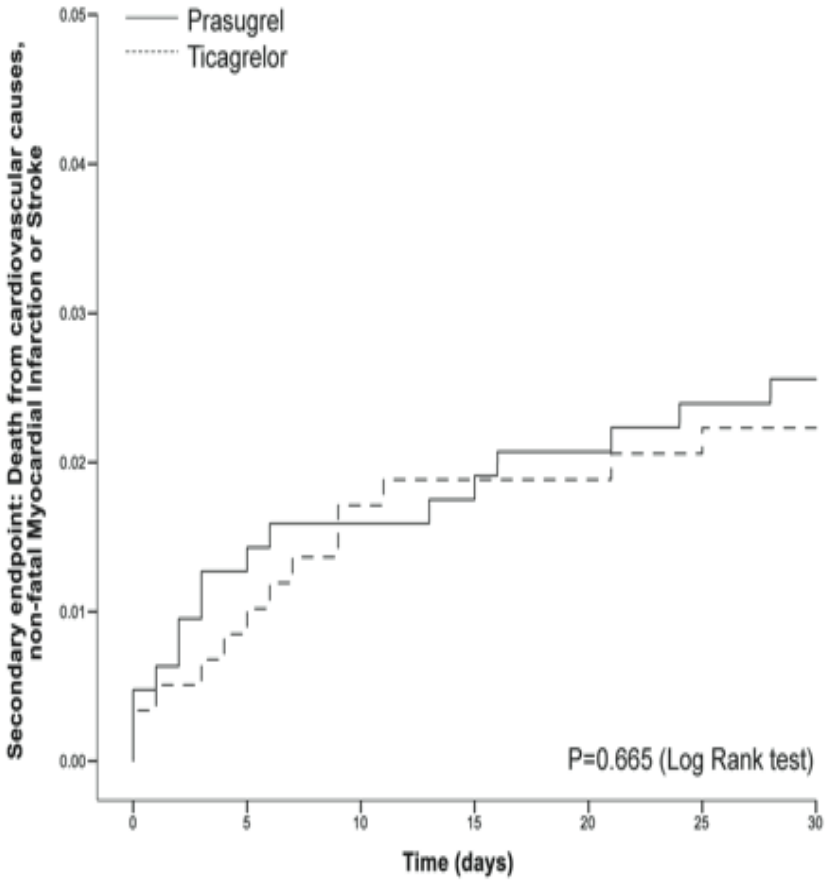
Primary end-point (7 days)



No at risk

Time (day)	1	2	3	4	5	6	7
Prasugrel (N=634)	629	624	621	617	614	612	611
Ticarelor (N=596)	588	583	583	580	578	576	573

Key secondary end point (30 days)



No at risk

Time (day)	5	10	15	20	25	30
Prasugrel (N=634)	626	623	622	619	617	616
Ticarelor (N=596)	591	585	583	583	582	580

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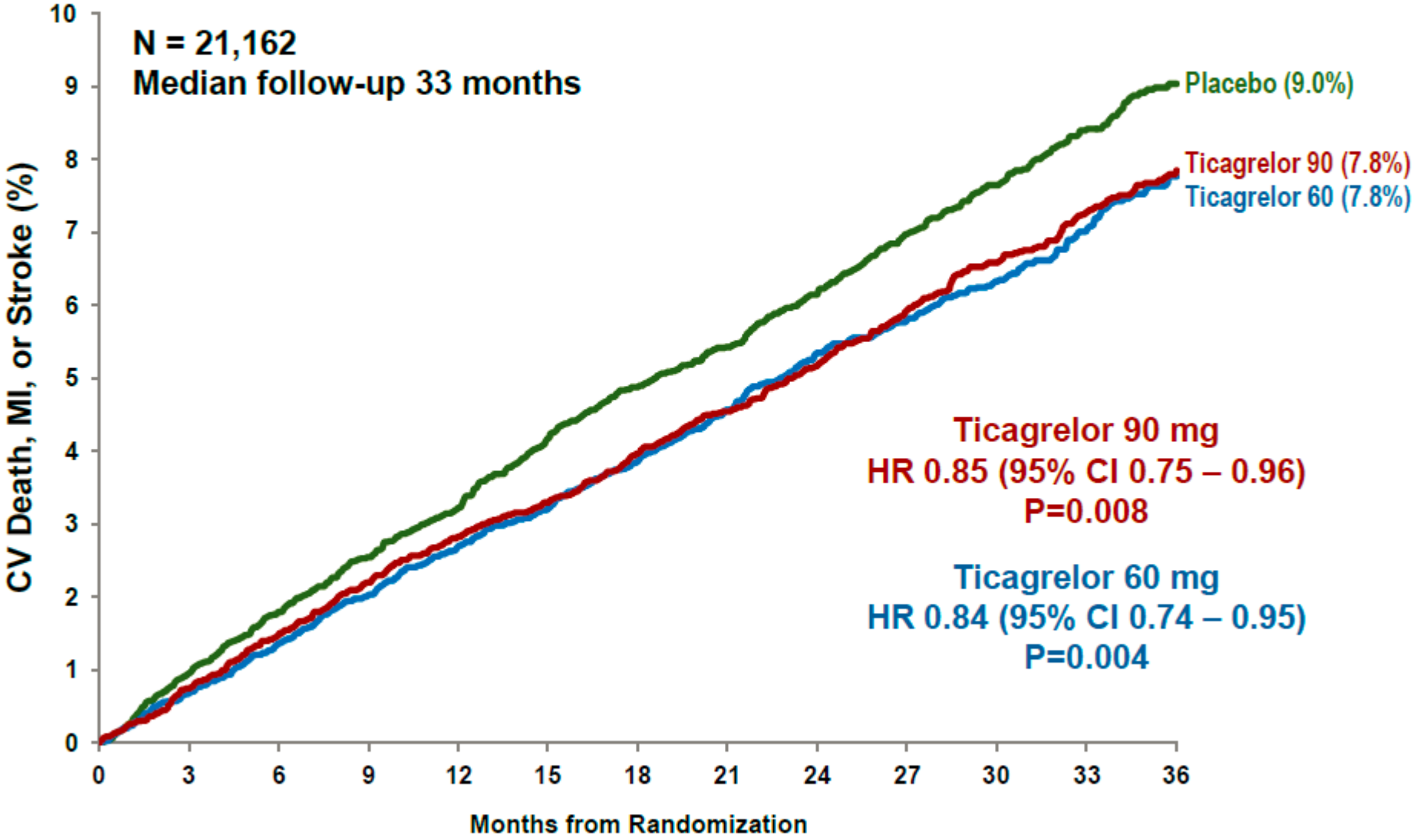
Recommendations for platelet inhibition in NSTE-ACS 2015

	Class	Level
Oral antiplatelet therapy		
Aspirin is recommended for all patients without contra-indications at an initial oral loading dose of 150–300 mg (in aspirin-naïve patients) and a maintenance dose of 75–100 mg daily long-term regardless of treatment strategy.	I	A
A $P2Y_{12}$ inhibitor is recommended, in addition to aspirin, **for 12 months** unless there are contraindications such as excessive risk of bleeds.	I	A
• **Ticagrelor** (180 mg loading dose, 90 mg twice daily) is recommended, in the absence of contraindications[d], 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
• **Prasugrel** (60 mg loading dose, 10 mg daily dose) is recommended in patients who are proceeding to PCI if no contraindication.	I	B
• 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
$P2Y_{12}$ 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
It is not recommended to administer prasugrel in patients in whom coronary anatomy is not known.	III	B

Duale Anti-Plättchen Therapie

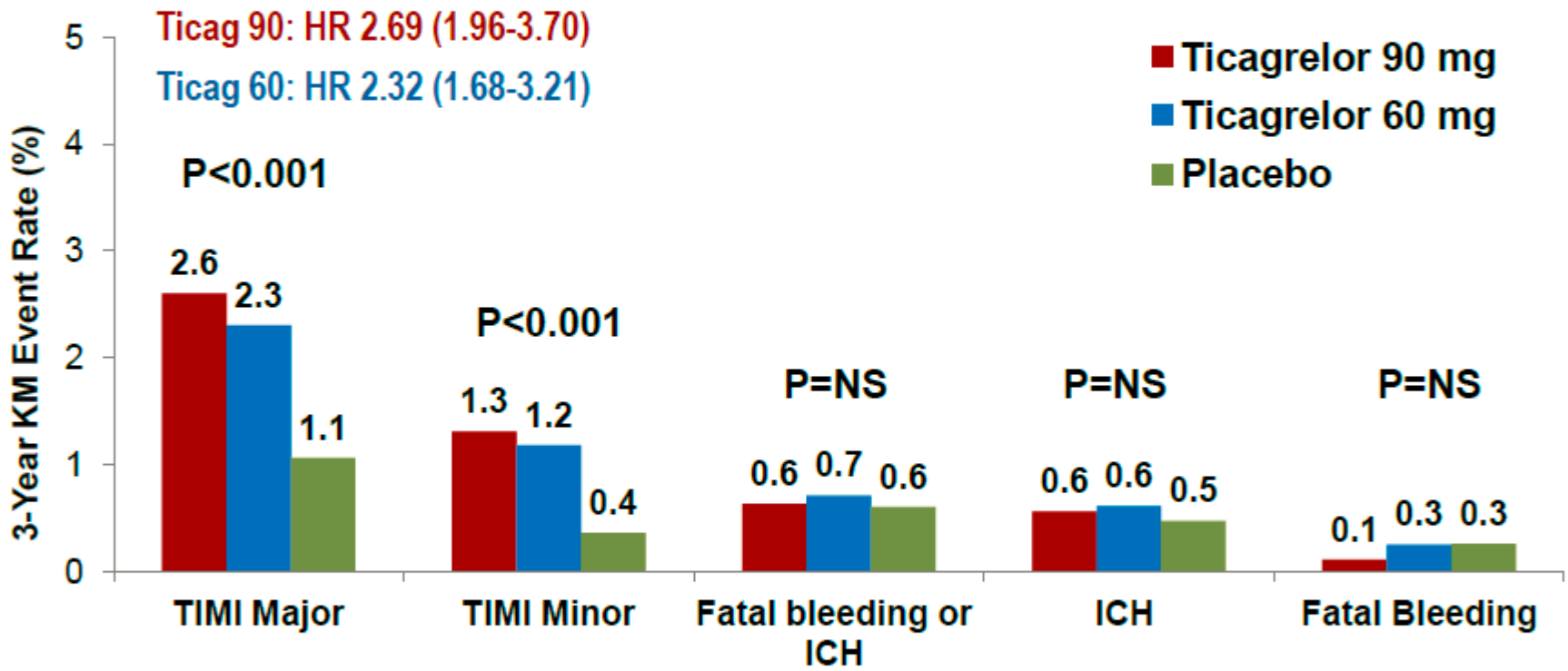
- **12 Monate lang genug?**
  - » **Wer länger?**

Primary Endpoint



Bonaca et al., *The New England Journal of Medicine* 2015

Bleeding



Bonaca et al., *The New England Journal of Medicine* 2015

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Zulassung zur verlängerten DAPT mit Ticagrelor 60 mg

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Studienpopulation

N = 21.162 Patienten
(Ticagrelor: **90 mg** 7050, **60 mg** 7045

Patienten mit 1-3 Jahre zurückliegendem MI
und
≥ 1 zusätzlichem Risikofaktor für Atherothrombose

Einschlusskriterien:
- Alter ≥ 50 Jahre
- MI in der Anamnese (1 bis 3 Jahre vor Randomisierung) **und**
- mind. einer der folgenden Risikofaktoren:
  - ≥ 65 Jahre
  - Medikamentös behandelter Diabetes mellitus
  - ≥ 1 MI in der Vorgeschichte
  - Koronare Mehrgefäßerkrankung
  - Chronische nicht-terminale Niereninsuffizienz (eGFR < 60 ml/min)

Zulassungspopulation

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

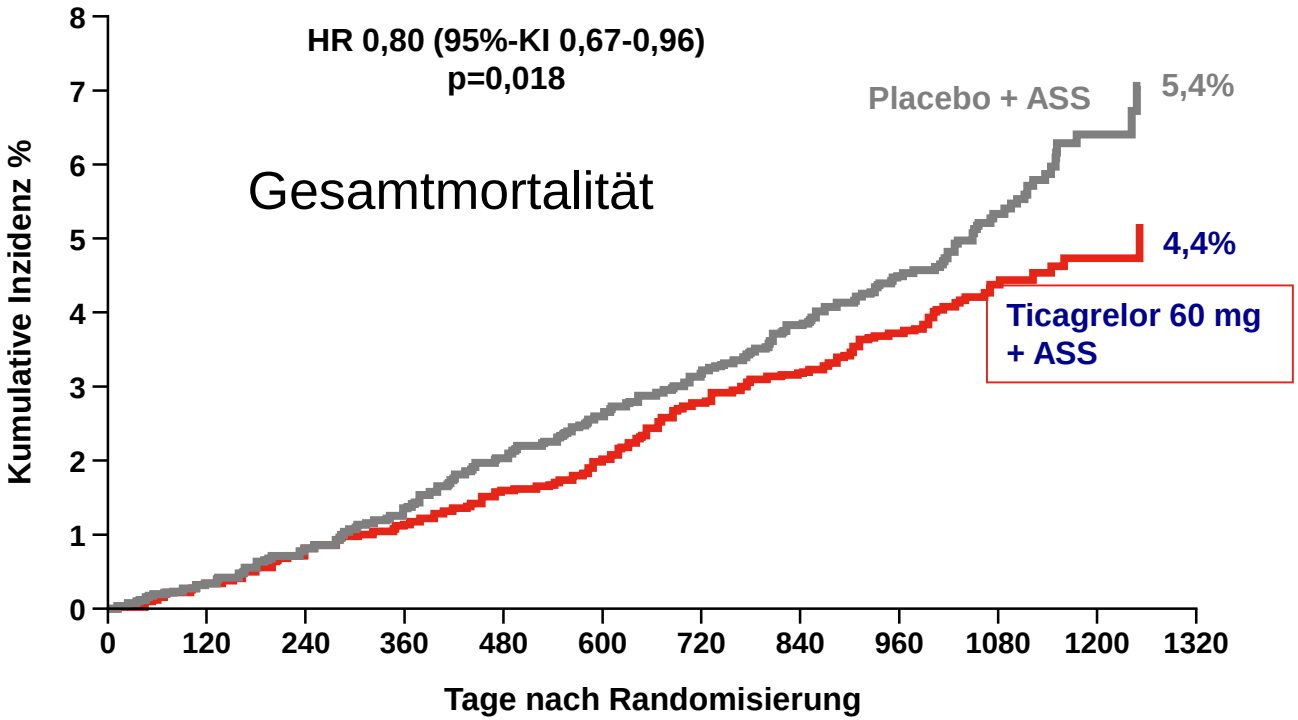
N = 10.779 Patienten
(Ticagrelor **60 mg** 5388, Placebo 5391)

Patienten mit mind. 1 Jahr bis zu 2 Jahre zurückliegendem MI
und
hohem Risiko für die Entwicklung eines atherothrombotischen Ereignisses

Beginn der Behandlung innerhalb eines Jahres nach Beendigung einer vorherigen Behandlung mit einem ADP-Rezeptorblocker

Etwa drei Viertel der Studienteilnehmer aus PEGASUS unter Ticagrelor 60 mg entsprechen der Zulassung

PEGASUS-Zulassungspopulation



Patienten unter Risiko:

Ticagrelor + ASS	5388	5367	5343	5323	5296	5021	4642	3853	2854	1606	553
Placebo	5391	5373	5346	5314	5275	4984	4619	3854	2797	1596	586

IQWiG Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen

»Bei der Gesamtmortalität zeigt sich ein Hinweis auf einen Zusatznutzen der Kombination gegenüber der ASS-Monotherapie«

Entscheidung: DAPT Langzeittherapie?

Wer ?

- **Evaluation nach 12 Monaten:**
  - **Thromb. Risiko?**
  - **Kürzlich geblutet?**
  - **Nebenwirkungen?**
  - **Adhärenz?**
  - **Relat. Kontraindikationen (Afib.)**

Thrombotisches Risiko

- **Diabetes mellitus**
- **Mehrere frühere STEMI**
- **Niereninsuffizienz**
- **MVD / CABG**
- **PAD**
- **Raucher**
- **Herzinsuffizienz / niedr. EF**

Blutungsrisiko

- **Früher/ Risiko ICH**
- **Größere Blutungen**
- **Blutungsdiathese**
- **Orale Antikoagulation**
- **Niedrig. BMI, Anämie**

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Danke !

Risikoreduktion in Studien mit Ticagrelor