ESC Kongress 2019

Koronare Herzkrankheit

Herzinsuffizienz

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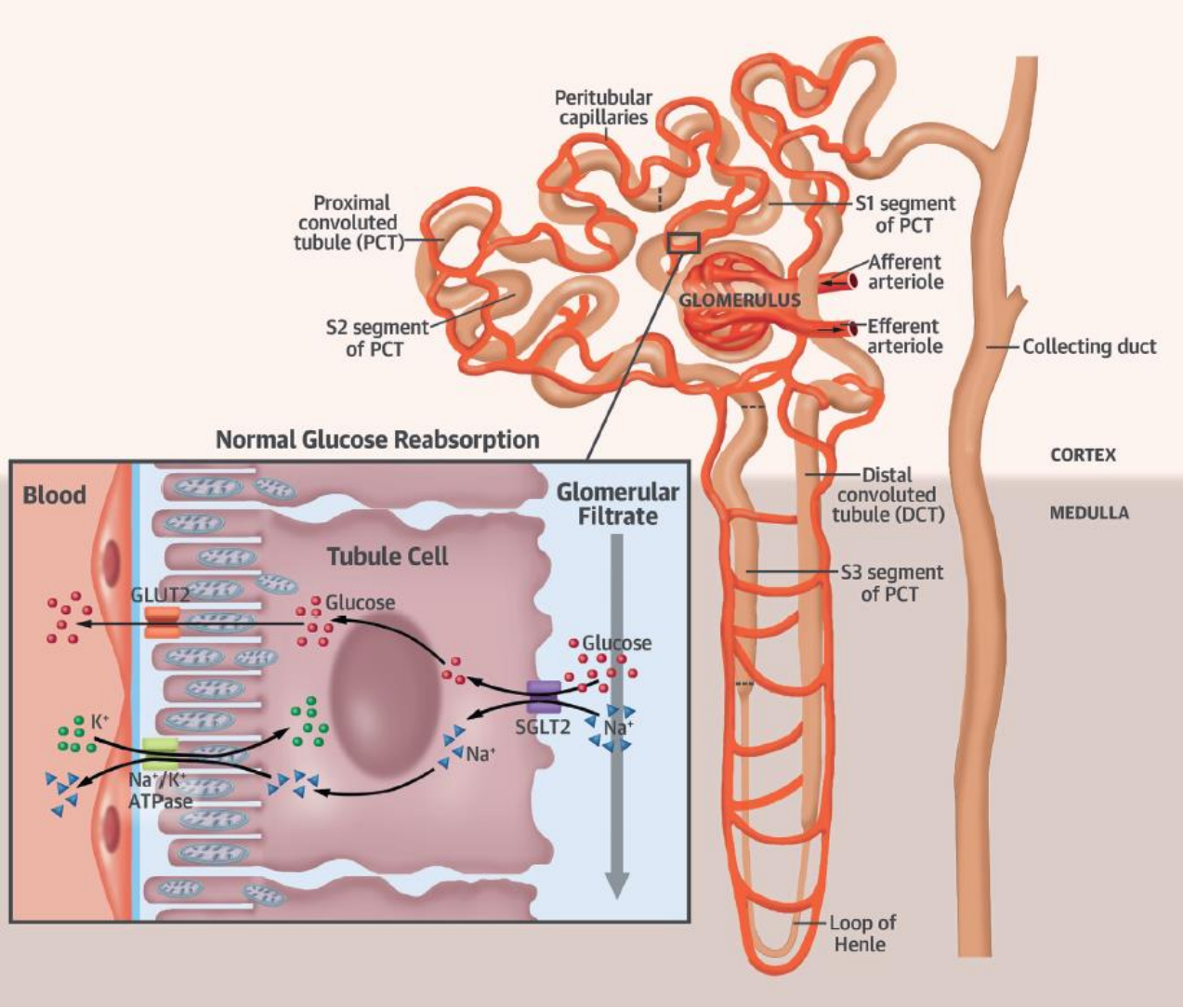
SGLT-2-Inhibitoren



Zelniker&Braunwald. J Am Coll Cardiol 2018;72:1845-55

DAPA-HF

- **Was wir schon wussten**
  - SGLT-2-Hemmer reduzieren bei Patienten mit Diabetes die Inzidenz von Hospitalisation wegen HF (Details aber nicht bekannt)
- **Was wir noch nicht wussten**
  - Sind SGLT-2-Hemmer effektiv bei Patienten mit etablierter HFrEF?
  - Wenn ja, nur bei Diabetes?

DAPA-HF

- 4744 Patienten mit HFrEF (LVEF ≤40%) mit guter Baseline-Therapie mit/ohne DM (je ca. 50%)
- Dapagliflozin 1x10 mg/d versus Placebo
- FU 18 Monate

DAPA-HF

- Paper noch nicht publiziert, aber:
- 26% Risikoreduktion CV Tod oder Verschlechterung HI ($p<0.001$)
- 18% Risikoreduktion CV Tod ($p=0.03$)
- 17% Risikoreduktion all-cause Tod ($p=0.02$)
- Verbesserung QoL
- UND: Effekte gleich bei DM oder ohne DM
- Keine Probleme mit Hypos

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Angiotensin–Neprilysin Inhibition in Heart Failure with Preserved Ejection Fraction

S.D. Solomon, J.J.V. McMurray, I.S. Anand, J. Ge, C.S.P. Lam, A.P. Maggioni, F. Martinez, M. Packer, M.A. Pfeffer, B. Pieske, M.M. Redfield, J.L. Rouleau, D.J. van Veldhuisen, F. Zannad, M.R. Zile, A.S. Desai, B. Claggett, P.S. Jhund, S.A. Boytsov, J. Comin-Colet, J. Cleland, H.-D. Düngen, E. Goncalvesova, T. Katova, J.F. Kerr Saraiva, M. Lelonek, B. Merkely, M. Senni, S.J. Shah, J. Zhou, A.R. Rizkala, J. Gong, V.C. Shi, and M.P. Lefkowitz, for the PARAGON-HF Investigators and Committees

PARAGON

- **Was wir schon wussten**
  - Sac/Val effektiv bei HFrEF (LVEF <40%)
  - Keine Therapie für HFpEF
- **Was wir noch nicht wussten**
  - Ist Sac/Val effektiv bei HFpEF (LVEF ≥50%)?
  - Oder bei HFmrEF (LVEF 40-49%)?

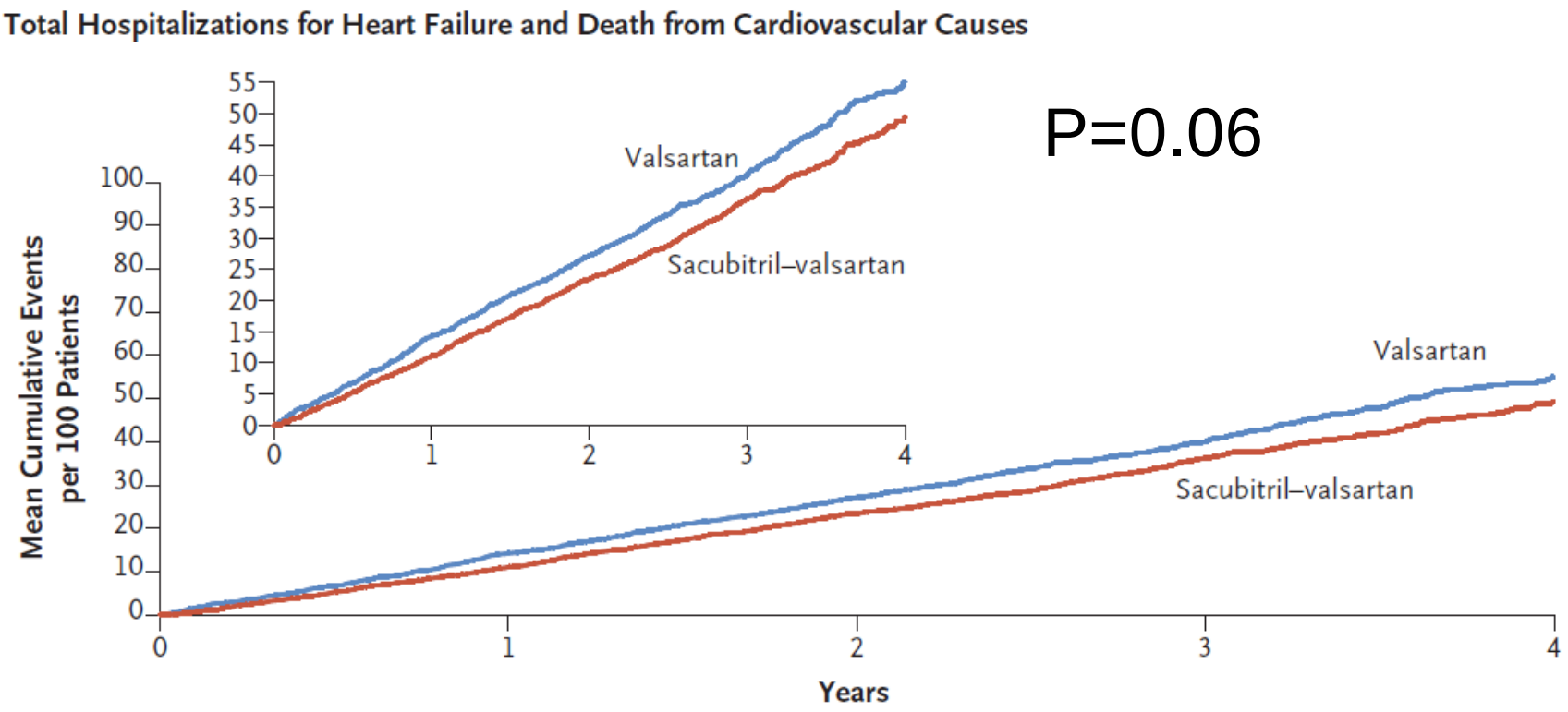
N=4822

LVEF ≥45%

NT-proBNP oder BNP↑

Sac/Val versus Val

HF Hosp oder CV Tod



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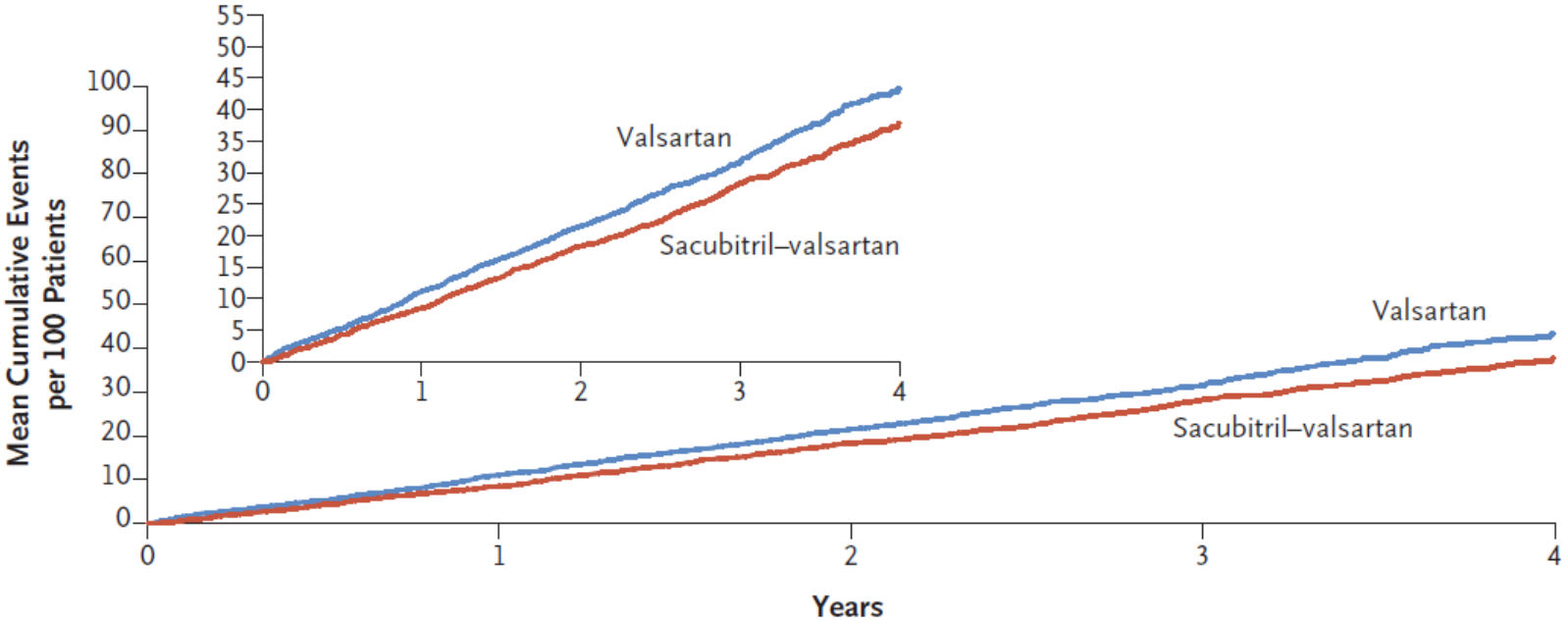
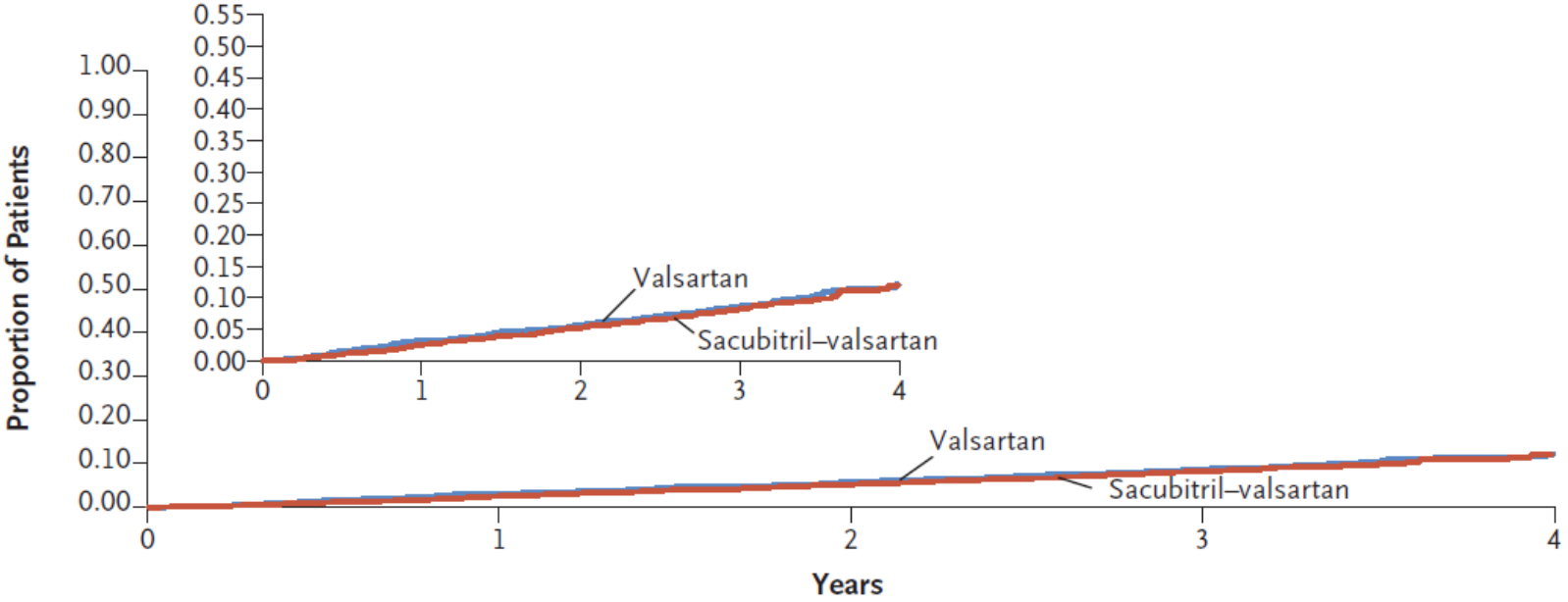
B Total Hospitalizations for Heart Failure



C Death from Cardiovascular Causes



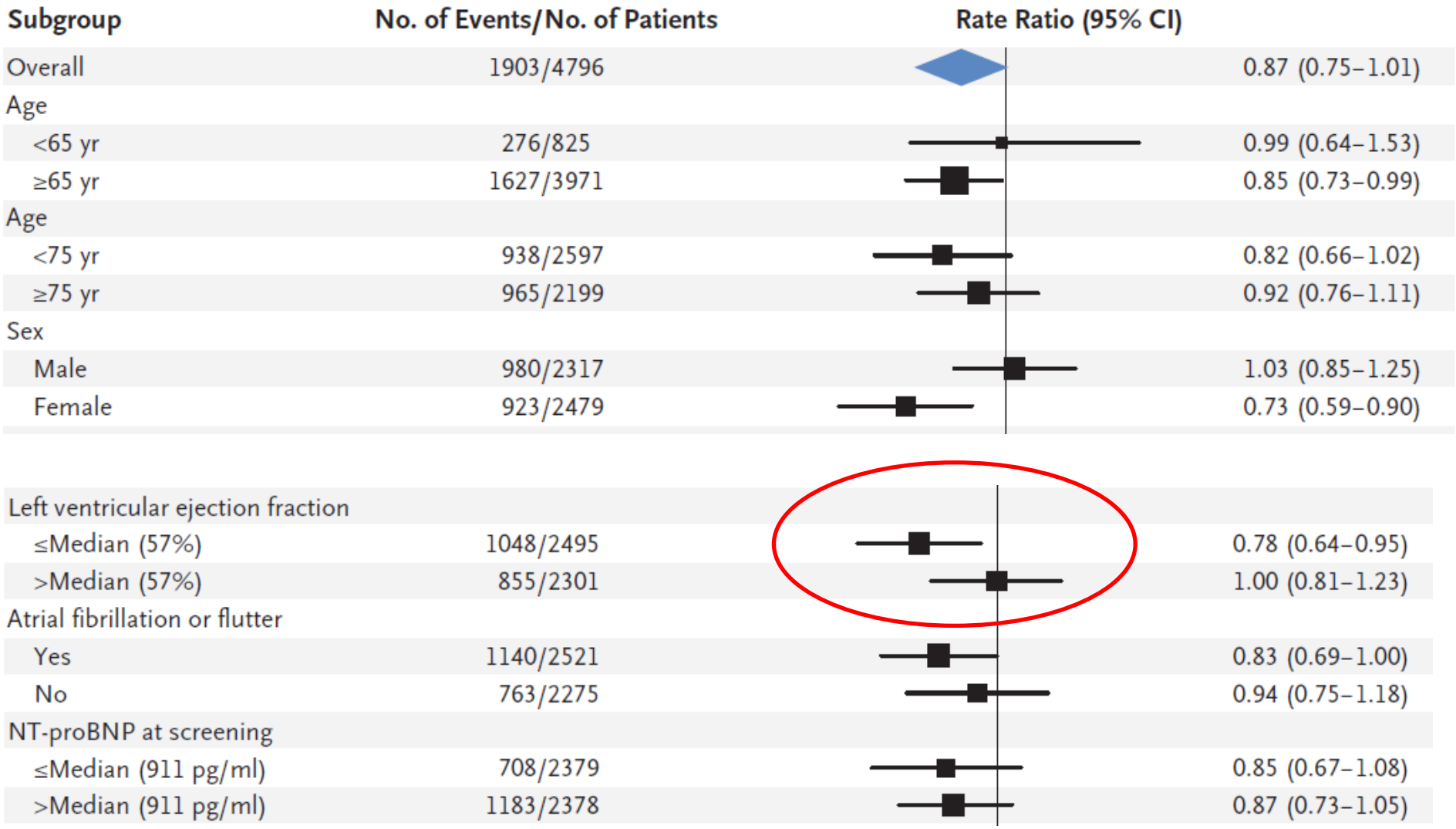

Subgroup
No. of Events/No. of Patients
Rate Ratio (95% CI)
Overall 1903/4796 0.87 (0.75–1.01)
Age
<65 yr 276/825 0.99 (0.64–1.53)
≥65 yr 1627/3971 0.85 (0.73–0.99)
Age
<75 yr 938/2597 0.82 (0.66–1.02)
≥75 yr 965/2199 0.92 (0.76–1.11)
Sex
Male 980/2317 1.03 (0.85–1.25)
Female 923/2479 0.73 (0.59–0.90)
Left ventricular ejection fraction
≤Median (57%) 1048/2495 0.78 (0.64–0.95)
>Median (57%) 855/2301 1.00 (0.81–1.23)
Atrial fibrillation or flutter
Yes 1140/2521 0.83 (0.69–1.00)
No 763/2275 0.94 (0.75–1.18)
NT-proBNP at screening
≤Median (911 pg/ml) 708/2379 0.85 (0.67–1.08)
>Median (911 pg/ml) 1183/2378 0.87 (0.73–1.05)

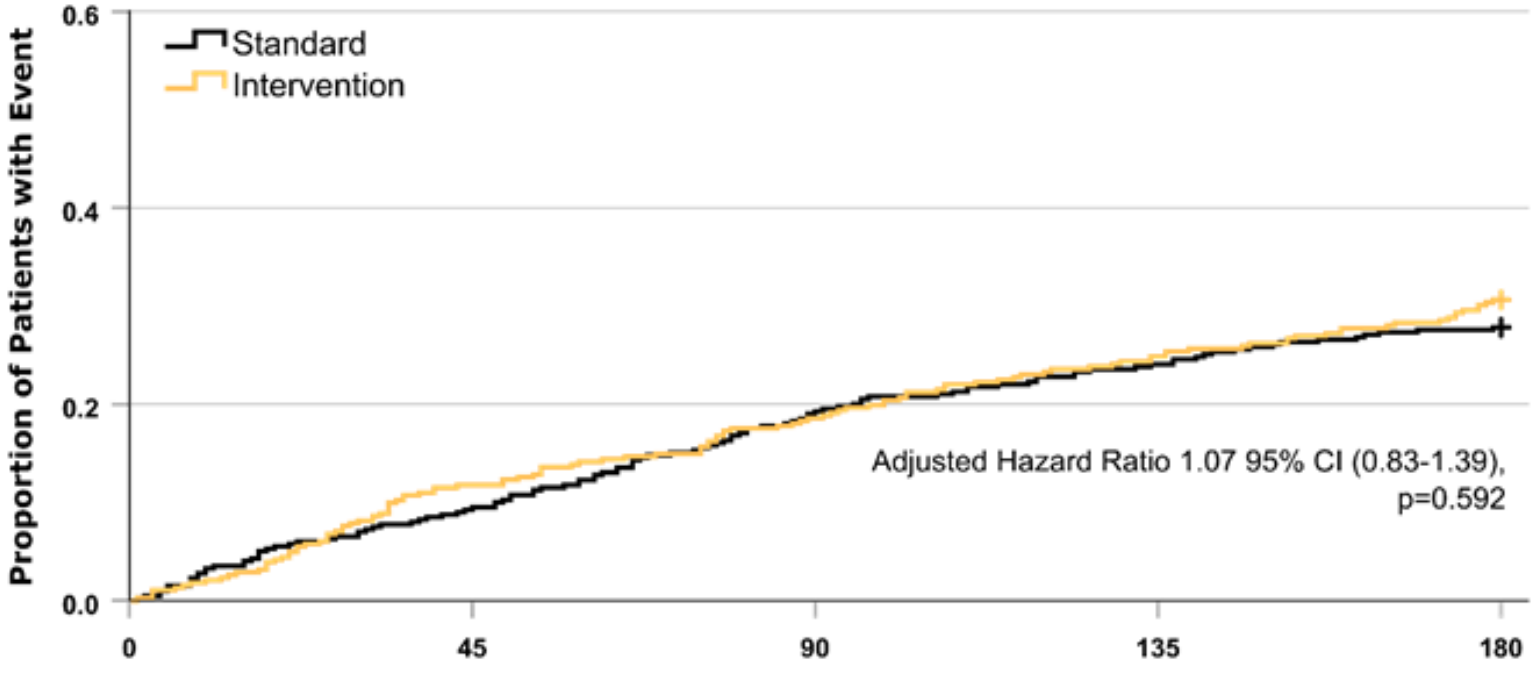
Table 3. Adverse Events during Randomized Treatment.

Event	Sacubitril–Valsartan (N = 2407)	Valsartan (N = 2389)	P Value
Hypotension with systolic blood pressure <100 mm Hg — no. (%)	380 (15.8)	257 (10.8)	<0.001
Elevated serum creatinine — no. (%)			
≥2.0 mg/dl	261 (10.8)	328 (13.7)	0.002
≥2.5 mg/dl	97 (4.0)	109 (4.6)	0.36
≥3.0 mg/dl	38 (1.6)	40 (1.7)	0.79
Elevated serum potassium — no./total no. (%)			
>5.5 mmol/liter	316/2386 (13.2)	361/2367 (15.3)	0.048
>6.0 mmol/liter	75/2386 (3.1)	101/2367 (4.3)	0.04
Angioedema — no. (%)	14 (0.6)	4 (0.2)	0.02
Liver-related adverse event — no. (%)	151 (6.3)	178 (7.5)	0.11

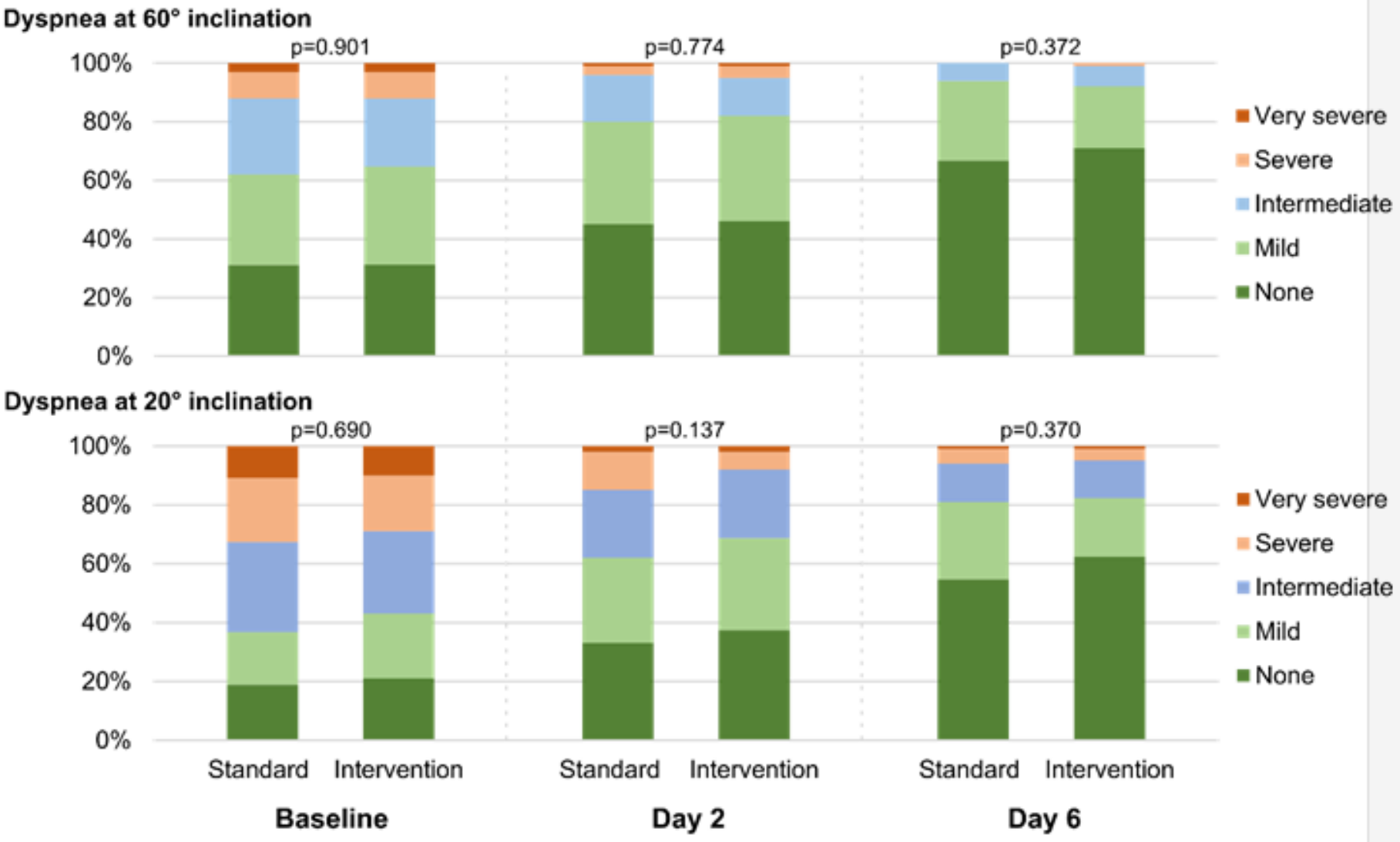
GALACTIC

- **Was wir schon wussten**
  - Diverse kurzzeitig verabreichte IV-Medikamente ohne mittelfristigen Effekt
- **Was wir noch nicht wussten**
  - Ist eine akute, aggressive, kombinierte Vasodilatator-Therapie (po, transdermal, Diuretika-sparend) effektiv?

788 Patienten mit AHF randomisiert zu «early goal-directed afterload reduction» (hochdosiert Nitroderm, Hydralazin, frühzeitig und schnell aufdosiert ACE-Hemmer/ARB) versus Standard-Therapie (Randomisierung 5 h nach Eintritt)



No at risk					
Standard	399	361	322	303	288
Intervention	382	337	311	287	265


Dyspnea at 60° inclination
p=0.901
p=0.774
p=0.372
100%
80%
60%
40%
20%
0%
Very severe
Severe
Intermediate
Mild
None
Dyspnea at 20° inclination
p=0.690
p=0.137
p=0.370
100%
80%
60%
40%
20%
0%
Very severe
Severe
Intermediate
Mild
None
Standard
Intervention
Standard
Intervention
Standard
Intervention
Baseline
Day 2
Day 6

ESC European Society of Cardiology

European Heart Journal (2019) **00**, 1–21
doi:10.1093/eurheartj/ehz641

FASTTRACK CLINICAL RESEARCH
Heart failure/cardiomyopathy

How to diagnose heart failure with preserved ejection fraction: the HFA–PEFF diagnostic algorithm: a consensus recommendation from the Heart Failure Association (HFA) of the European Society of Cardiology (ESC)

Burkert Pieske[1,2,3,4]*, Carsten Tschöpe[1,2,5], Rudolf A. de Boer [6], Alan G. Fraser[7], Stefan D. Anker[1,2,5,8], Erwan Donal[9], Frank Edelmann[1,2], Michael Fu[10], Marco Guazzi[11,12], Carolyn S.P. Lam[13,14], Patrizio Lancellotti[15], Vojtech Melenovsky[16], Daniel A. Morris[1], Eike Nagel [17,18], Elisabeth Pieske-Kraigher[1], Piotr Ponikowski[19], Scott D. Solomon[20], Ramachandran S. Vasan[21], Frans H. Rutten [22], Adriaan A. Voors[6], Frank Ruschitzka[23], Walter J. Paulus[24], Petar Seferovic[25] and Gerasimos Filippatos[26,27]

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Complete Revascularization with Multivessel PCI for Myocardial Infarction

Shamir R. Mehta, M.D., David A. Wood, M.D., Robert F. Storey, M.D., Roxana Mehran, M.D., Kevin R. Bainey, M.D., Helen Nguyen, B.Sc., Brandi Meeks, M.Sc., Giuseppe Di Pasquale, M.D., Jose López-Sendón, M.D., David P. Faxon, M.D., Laura Mauri, M.D., Sunil V. Rao, M.D., Laurent Feldman, M.D., P. Gabriel Steg, M.D., Álvaro Avezum, M.D., Tej Sheth, M.D., Natalia Pinilla-Echeverri, M.D., Raul Moreno, M.D., Gianluca Campo, M.D., Benjamin Wrigley, M.D., Sasko Kedev, M.D., Andrew Sutton, M.D., Richard Oliver, M.D., Josep Rodés-Cabau, M.D., Goran Stanković, M.D., Robert Welsh, M.D., Shahar Lavi, M.D., Warren J. Cantor, M.D., Jia Wang, M.Sc., Juliet Nakamya, Ph.D., Shrikant I. Bangdiwala, Ph.D., and John A. Cairns, M.D., for the COMPLETE Trial Steering Committee and Investigators*

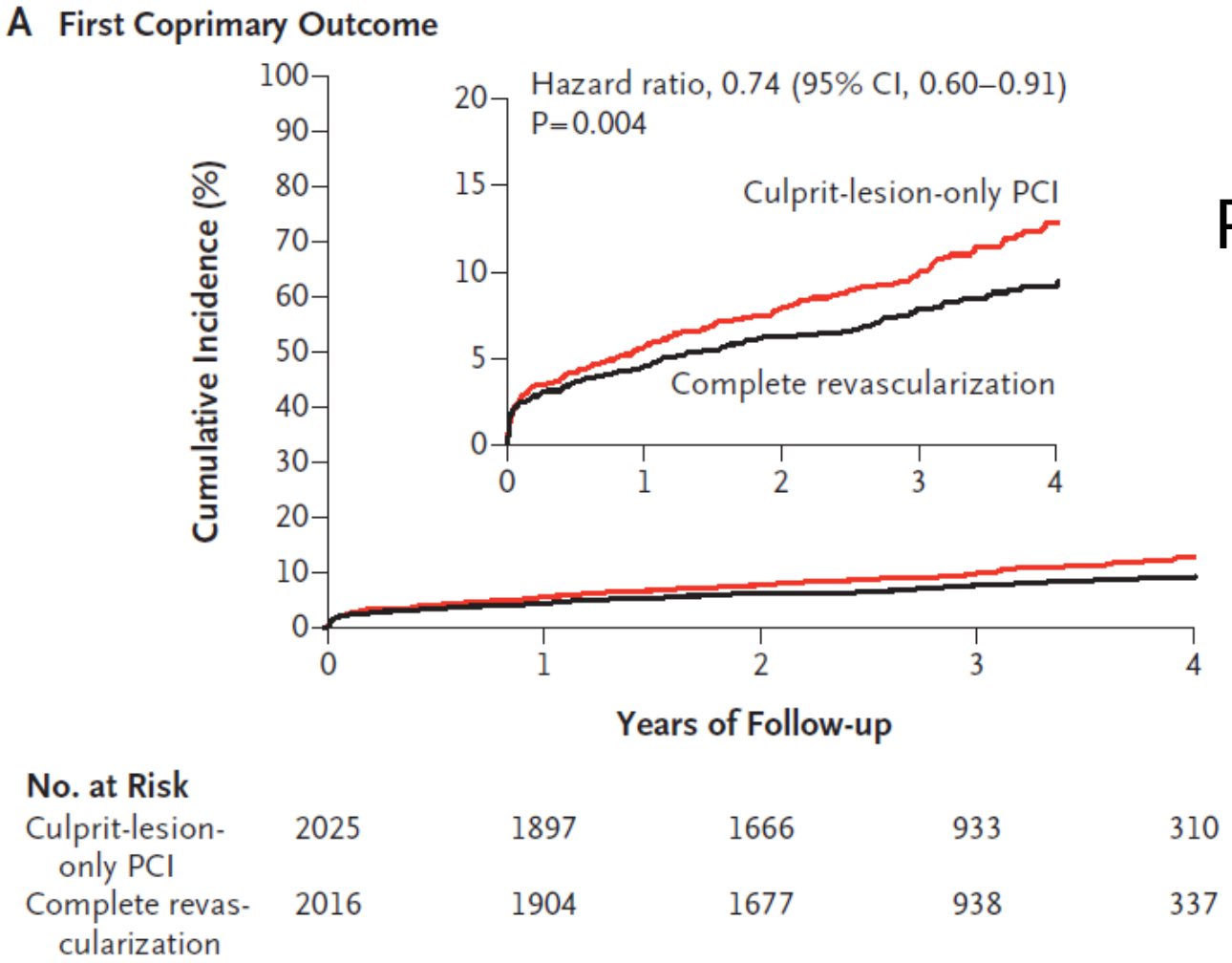
COMPLETE

- **Was wir schon wussten**
  - Primäre PCI besser als Lyse bei STEMI
  - PCI von non-culprit lesions ws. auch wichtig (aber relativ kleine Studien)
- **Was wir noch nicht wussten**
  - Effekt der non-culprit lesion PCI
  - Timing der non-culprit lesion PCI

COMPLETE

- 4041 Patienten mit STEMI und erfolgreicher PCI der culprit lesion vor maximal 72 Stunden
- Randomisierung PCI aller anderen Läsionen ≥2.5 mm und ≥70% (oder 50-69%+FFR ≤0.80) inklusive CTOs* versus keine weitere PCI
- Timing: spätestens 45 Tage nach primärer PCI

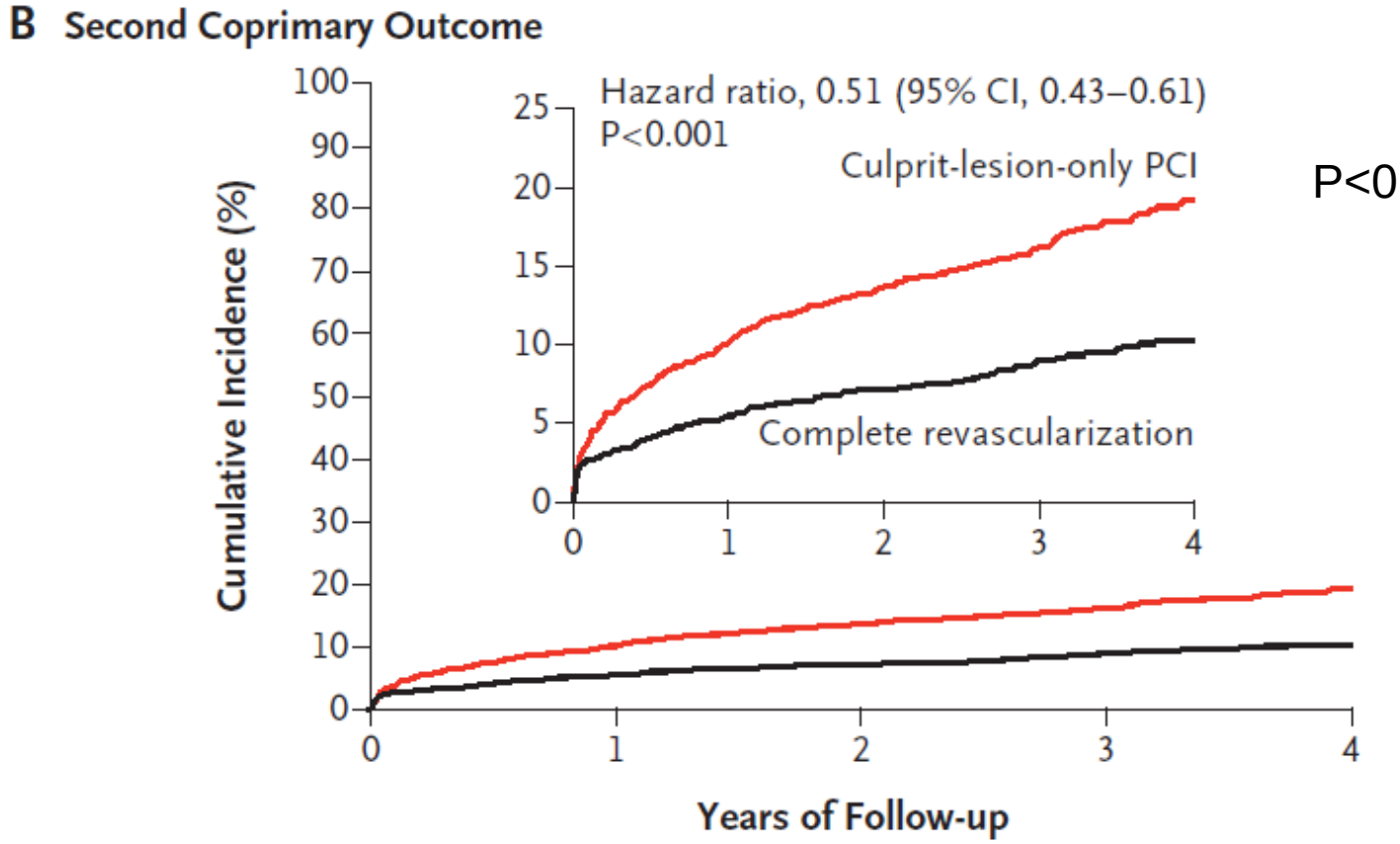
Co-primärer EP 1: CV Tod oder Myokardinfarkt



P=0.004

Sicherheit: Blutungen und Kontrastnephropathie: kein Unterschied

Co-primärer EP 2: CV Tod oder Myokardinfarkt oder Ischämie-getriebene Revaskularisation



P<0.001

No. at Risk					
Culprit-lesion-only PCI	2025	1808	1559	865	294
Complete revascularization	2016	1886	1659	925	329

Subgroup	First Coprimary Outcome			
	Complete revascularization	Culprit-lesion-only PCI	Hazard ratio (95% CI)	P value for interaction
	no. of events/ total no. of patients (% per person-yr)			
Overall	158/2016 (2.7)	213/2025 (3.7)	0.74 (0.60–0.91)	
Intended timing of nonculprit-lesion PCI				0.62
During index hospitalization	101/1353 (2.7)	130/1349 (3.5)	0.77 (0.59–1.00)	
After hospital discharge	57/663 (2.7)	83/676 (3.9)	0.69 (0.49–0.97)	

	Second Coprimary Outcome			
	Complete revascularization	Culprit-lesion-only PCI	Hazard ratio (95% CI)	P value for interaction
	no. of events/ total no. of patients (% per person-yr)			
	179/2016 (3.1)	339/2025 (6.2)	0.51 (0.43–0.61)	
				0.27
	113/1353 (3.0)	227/1349 (6.6)	0.47 (0.38–0.59)	
	66/663 (3.1)	112/676 (5.4)	0.59 (0.43–0.79)	

Timing der non-culprit lesion-PCI spielte keine Rolle

Variable	PRAMI	CvLPRIT	DANAMI-3–PRIMULTI	Compare-Acute	COMPLETE
No. of patients	465	296	627	885	4041
Mean age — yr	62	65	63	61	62
Male sex — %	78	81	81	77	80
Median follow-up — mo	23	12	27	12	36
Median time from randomization to second procedure — days	0 (same time as index procedure)	<2	2	0 (same time as index procedure)	1 (during admission); 23 (after discharge)†
FFR measurement of nonculprit lesions obtained	No	No	Yes	Yes	Yes (in <1% of patients)
Events with treatment of culprit lesion only — no./total no. of patients					
Death	16/231	10/146	11/313	10/590	106/2025
Cardiovascular death	10/231	7/146	9/313	6/590	64/2025
Myocardial infarction	20/231	4/146	16/313	28/590	160/2025
Revascularization	46/231	16/146	52/313	103/590	160/2025
Events with complete revascularization vs. treatment of culprit lesion only — hazard ratio (95% CI)					
Cardiovascular death or myocardial infarction	0.36 (0.18–0.73)	NA	0.80 (0.45–1.45)	NA	0.74 (0.60–0.91)
Death	NA	0.38 (0.12–1.20)	1.40 (0.63–3.00)	0.80 (0.25–2.56)	0.91 (0.69–1.20)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

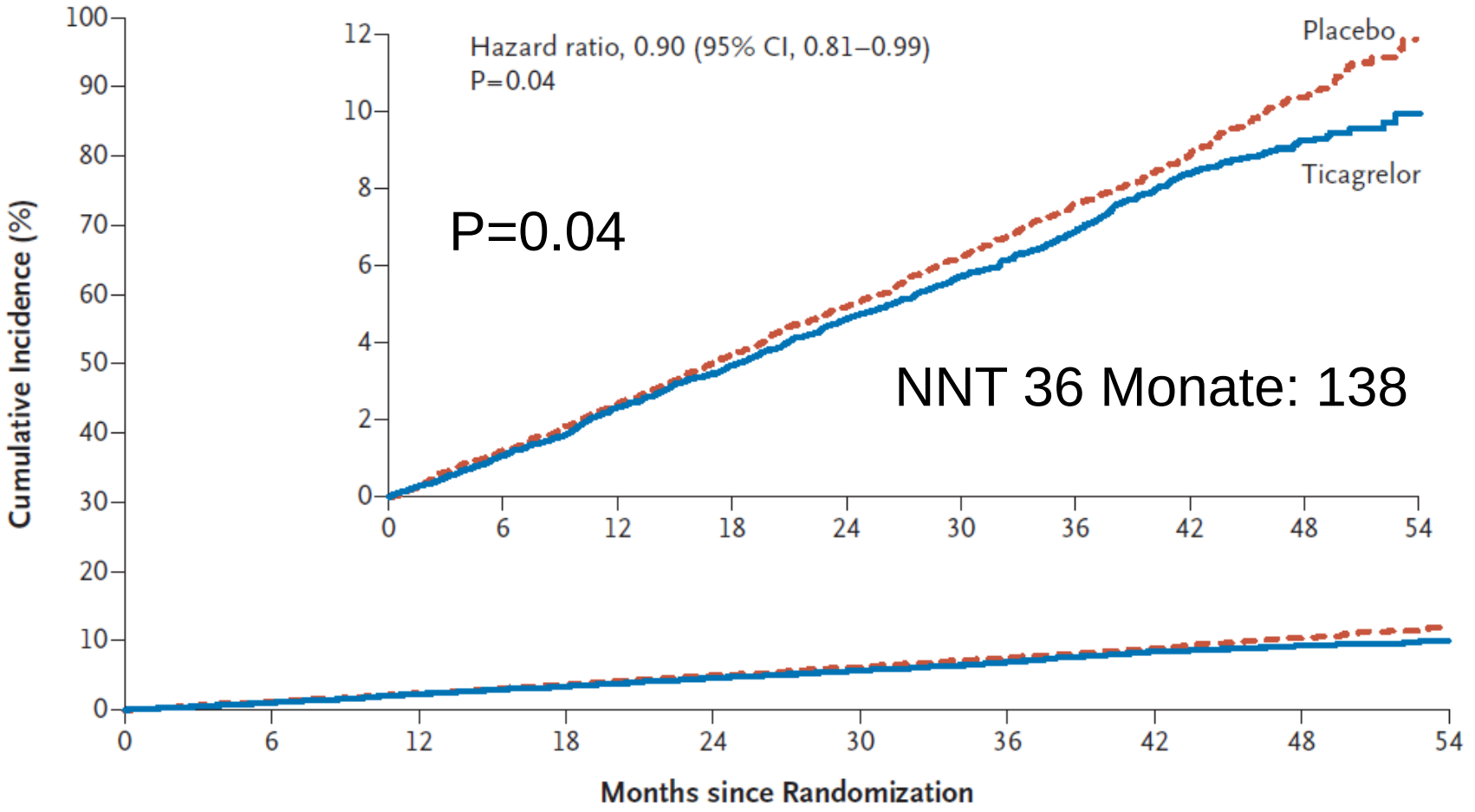
Ticagrelor in Patients with Stable Coronary Disease and Diabetes

P.G. Steg, D.L. Bhatt, T. Simon, K. Fox, S.R. Mehta, R.A. Harrington, C. Held, M. Andersson, A. Himmelmann, W. Ridderstråle, M. Leonsson-Zachrisson, Y. Liu, G. Opolski, D. Zateyshchikov, J. Ge, J.C. Nicolau, R. Corbalán, J.H. Cornel, P. Widimský, and L.A. Leiter, for the THEMIS Steering Committee and Investigators*

THEMIS

- **Was wir schon wussten**
  - Duale Tc-Hemmung essentiell nach PCI/Infarkt, bis 12 Mt
  - Ticagrelor ist Clopidogrel beim ACS überlegen
- **Was wir noch nicht wussten**
  - Duale Tc-Hemmung effektiv >12 Monate nach PCI/Infarkt effektiv?

Primärer EP: Tod, MI, Stroke



No. at Risk										
Ticagrelor	9619	9416	9237	9074	8909	8692	5974	3664	1684	170
Placebo	9601	9414	9246	9076	8909	8692	5934	3682	1685	174

(viele Therapieabbrüche)

Outcome	Ticagrelor (N=9562)		Placebo (N=9531)		Hazard Ratio (95% CI)	P Value
	Patients with Event	Event Rate	Patients with Event	Event Rate		
	no. (%)	*no./100 patient-yr*	*no. %*	*no./100 patient-yr*		
Adjudicated adverse events†						
TIMI major bleeding	206 (2.2)	0.89	100 (1.0)	0.38	2.32 (1.82–2.94)	<0.001
TIMI major or minor bleeding	285 (3.0)	1.23	129 (1.4)	0.49	2.49 (2.02–3.07)	<0.001
TIMI major or minor bleeding or medical attention for bleeding	1072 (11.2)	4.61	485 (5.1)	1.85	2.51 (2.26–2.80)	<0.001
PLATO major bleeding	310 (3.2)	1.33	145 (1.5)	0.55	2.41 (1.98–2.93)	<0.001
BARC bleeding score‡						
3, 4, or 5	341 (3.6)	1.47	163 (1.7)	0.62	2.36 (1.96–2.84)	<0.001
4 or 5	17 (0.2)	0.07	11 (0.1)	0.04	1.73 (0.81–3.69)	0.16
5	17 (0.2)	0.07	10 (0.1)	0.04	1.90 (0.87–4.15)	0.11
Intracranial hemorrhage	70 (0.7)	0.30	46 (0.5)	0.18	1.71 (1.18–2.48)	0.005

Number needed to harm bei 36 Monaten: 93

Composite of irreversible harm (Tod, MI, Stroke, tödliche Blutung, intrazerebrale Blutung): kein Unterschied

ORIGINAL ARTICLE

Ticagrelor or Prasugrel in Patients with Acute Coronary Syndromes

S. Schüpke, F.-J. Neumann, M. Menichelli, K. Mayer, I. Bernlochner, J. Wöhrle, G. Richardt, C. Liebetrau, B. Witzenbichler, D. Antoniucci, I. Akin, L. Bott-Flügel, M. Fischer, U. Landmesser, H.A. Katus, D. Sibbing, M. Seyfarth, M. Janisch, D. Boncompagni, R. Hilz, W. Rottbauer, R. Okrojek, H. Möllmann, W. Hochholzer, A. Migliorini, S. Cassese, P. Mollo, E. Xhepa, S. Kufner, A. Strehle, S. Leggewie, A. Allali, G. Ndrepepa, H. Schühlen, D.J. Angiolillo, C.W. Hamm, A. Hapfelmeier, R. Tölg, D. Trenk, H. Schunkert, K.-L. Laugwitz, and A. Kastrati, for the ISAR-REACT 5 Trial Investigators*

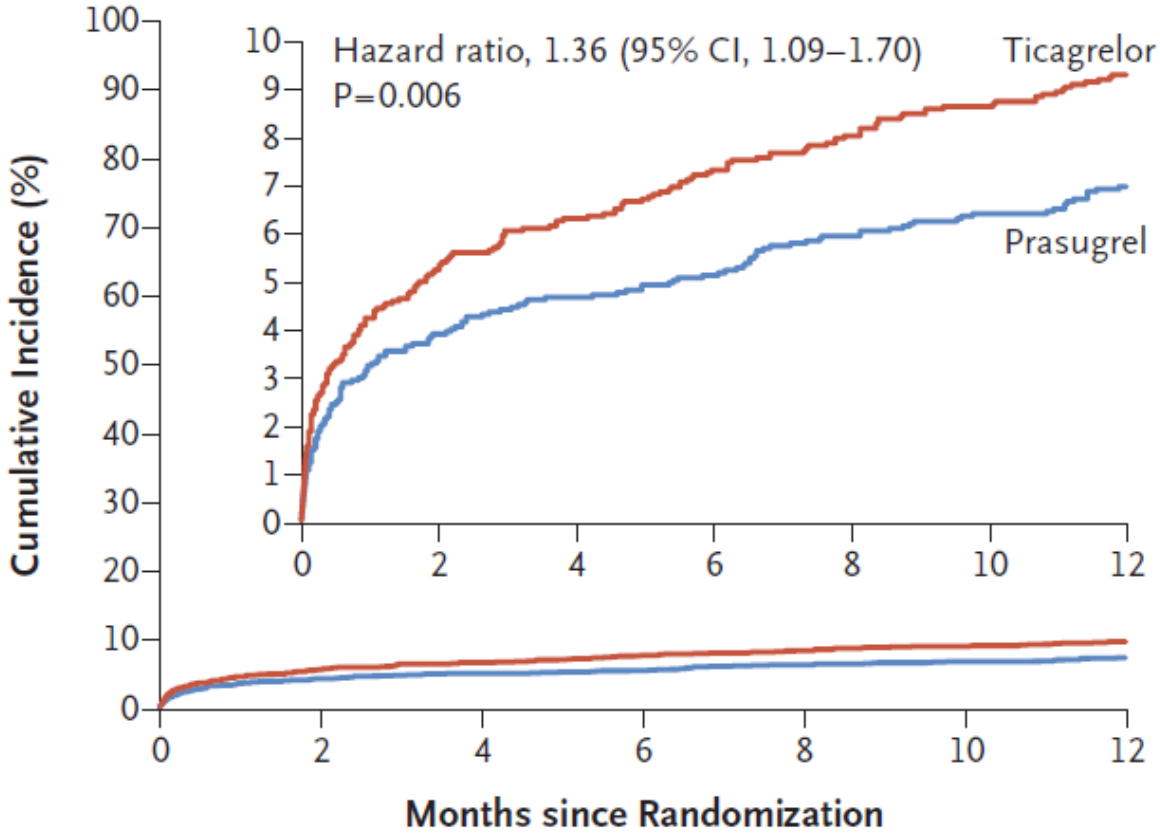
ISAR-REACT 5

- **Was wir schon wussten**
  - Prasugrel ist Clopidogrel beim ACS überlegen
  - Ticagrelor ist Clopidogrel beim ACS überlegen
- **Was wir noch nicht wussten**
  - Prasugrel oder Ticagrelor besser (bisher keine Direktvergleich)?

ISAR-REACT 5

- 4018 Patienten mit ACS (STEMI, NSTEMI, UA) und invasiver Strategie
- Randomisierung **Ticagrelor** 2x90 mg (Ladedosis 180 mg ASAP nach Randomisierung) **versus Prasugrel** 1x10 mg (Ladedosis 60 m ASAP nach Randomisierung beim STEMI, sonst erst nach diagnostischer Angiografie; Erhaltungsdosis 5 mg für Alter >75 Jahre und Gewicht <60 kg)

Primärer EP: Tod, MI, Stroke nach einem Jahr



No. at Risk

Ticagrelor	2012	1877	1857	1835	1815	1801	1722
Prasugrel	2006	1892	1877	1862	1839	1829	1803

Major bleeding: kein Unterschied

ORIGINAL ARTICLE

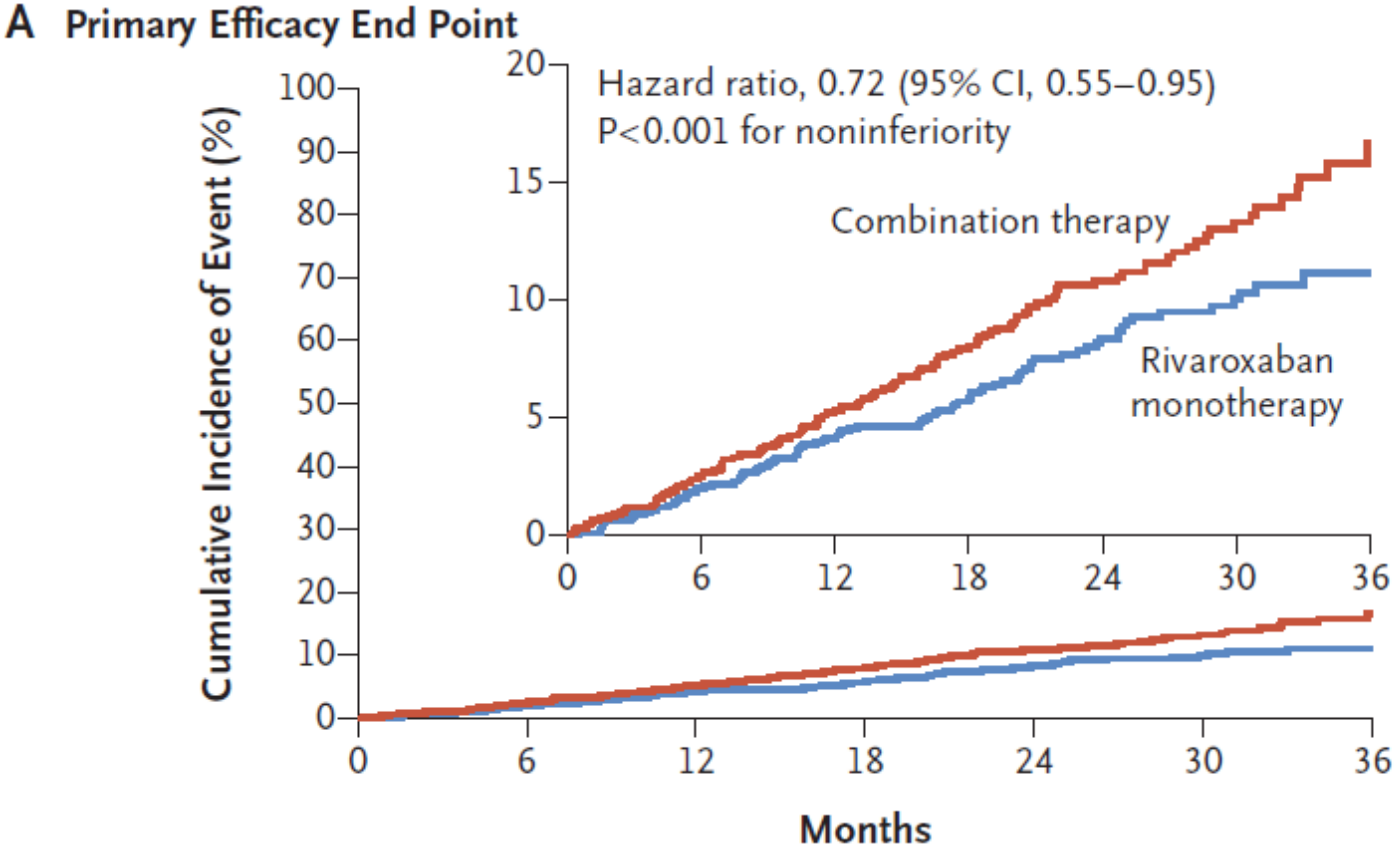
Antithrombotic Therapy for Atrial Fibrillation with Stable Coronary Disease

Satoshi Yasuda, M.D., Ph.D., Koichi Kaikita, M.D., Ph.D.,
Masaharu Akao, M.D., Ph.D., Junya Ako, M.D., Ph.D., Tetsuya Matoba, M.D., Ph.D.,
Masato Nakamura, M.D., Ph.D., Katsumi Miyauchi, M.D., Ph.D.,
Nobuhisa Hagiwara, M.D., Ph.D., Kazuo Kimura, M.D., Ph.D.,
Atsushi Hirayama, M.D., Ph.D., Kunihiko Matsui, M.D., M.P.H.,
and Hisao Ogawa, M.D., Ph.D., for the AFIRE Investigators*

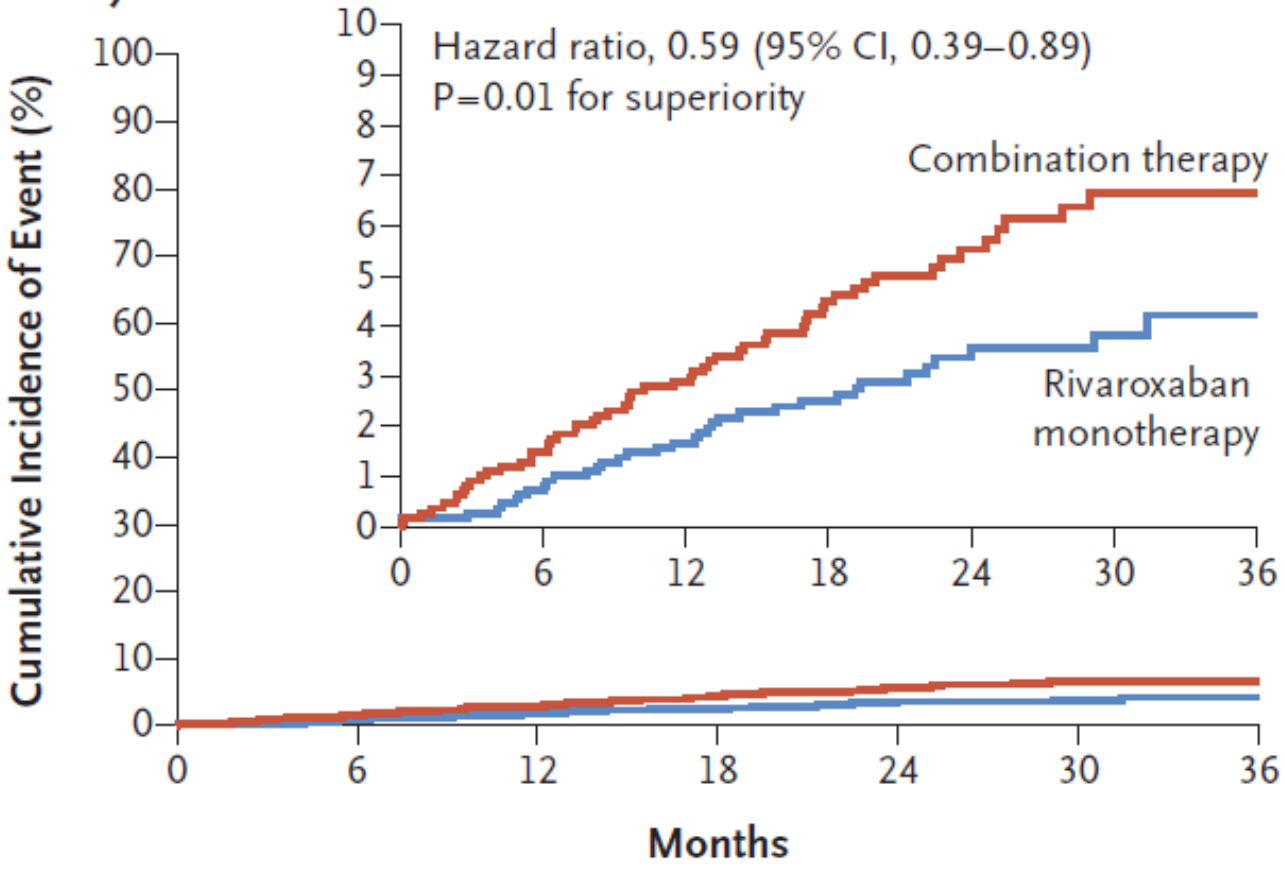
AFIRE

- **Was wir schon wussten**
  - OAK mit VAK (z.b. be VHF) bei chronischer KHK ausreichen, d.h. kein zusätzliches Aspirin notwendig
  - ASA-Wirkung quasi durch VKA vermittelt
- **Was wir noch nicht wussten**
  - Gilt dies auch für NOACs, oder brauche wir da zusätzlich Aspirin?

Riva 15 mg + ASA 100 mg versus RIVA 15 mg Mono bei AF und chronischer KHK mit St. n. PCI oder CABP vor mehr als einem Jahr



B **Primary Safety End Point**



No. at Risk							
Combination therapy	1099	1055	962	750	506	294	80
Rivaroxaban monotherapy	1099	1074	994	786	526	312	89

ESC
European Society of Cardiology
European Heart Journal (2019) **00**, 1–71
doi:10.1093/eurheartj/ehz425

ESC GUIDELINES

2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes

The Task Force for the diagnosis and management of chronic coronary syndromes of the European Society of Cardiology (ESC)

Authors/Task Force Members: Juhani Knuuti* (Finland) (Chairperson), William Wijns* (Ireland) (Chairperson), Antti Saraste (Finland), Davide Capodanno (Italy), Emanuele Barbato (Italy), Christian Funck-Brentano (France), Eva Prescott (Denmark), Robert F. Storey (United Kingdom), Christi Deaton (United Kingdom), Thomas Cuisset (France), Stefan Agewall (Norway), Kenneth Dickstein (Norway), Thor Edvardsen (Norway), Javier Escaned (Spain), Bernard J. Gersh (United States of America), Pavel Svitil (Czech Republic), Martine Gilard (France), David Hasdai (Israel), Robert Hatala (Slovak Republic), Felix Mahfoud (Germany), Josep Masip (Spain), Claudio Muneretto (Italy), Marco Valgimigli (Switzerland), Stephan Achenbach (Germany), Jeroen J. Bax (Netherlands)

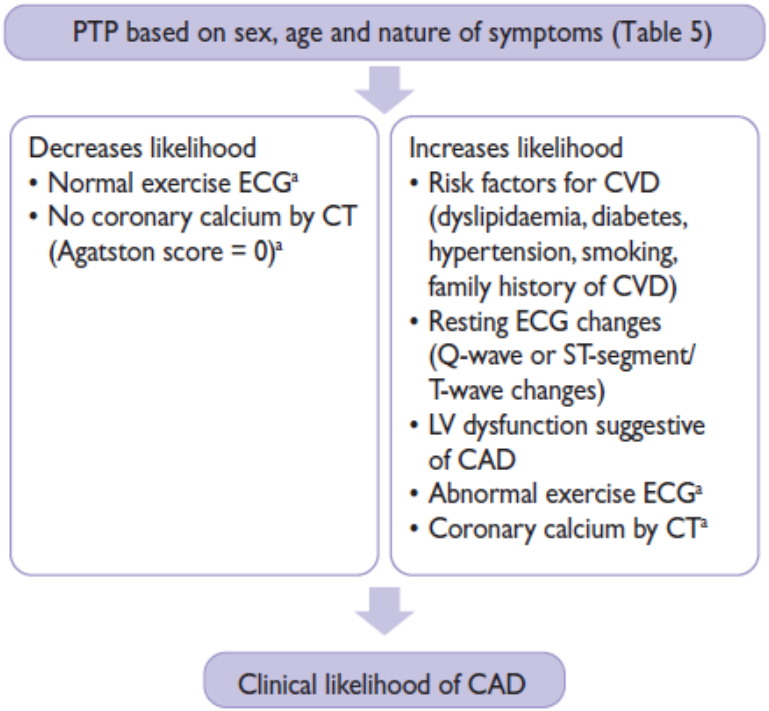
Bei **symptomatischen** Patienten mit typischer oder atypischer Angina pectoris ist das Risiko für das Vorliegen einer KHK erhöht (Tab. 2). Hier empfiehlt sich ein nicht-invasiver Test. Die Belastung soll, wenn immer möglich physiologisch, am besten mittels Ergometrie, durchgeführt werden. Alternativ dazu können auch bildgebende Untersuchungen mit physiologischer oder pharmakologischer (Adenosin, Dobutamin) Belastung erfolgen (Echo, MPS, cMRI).

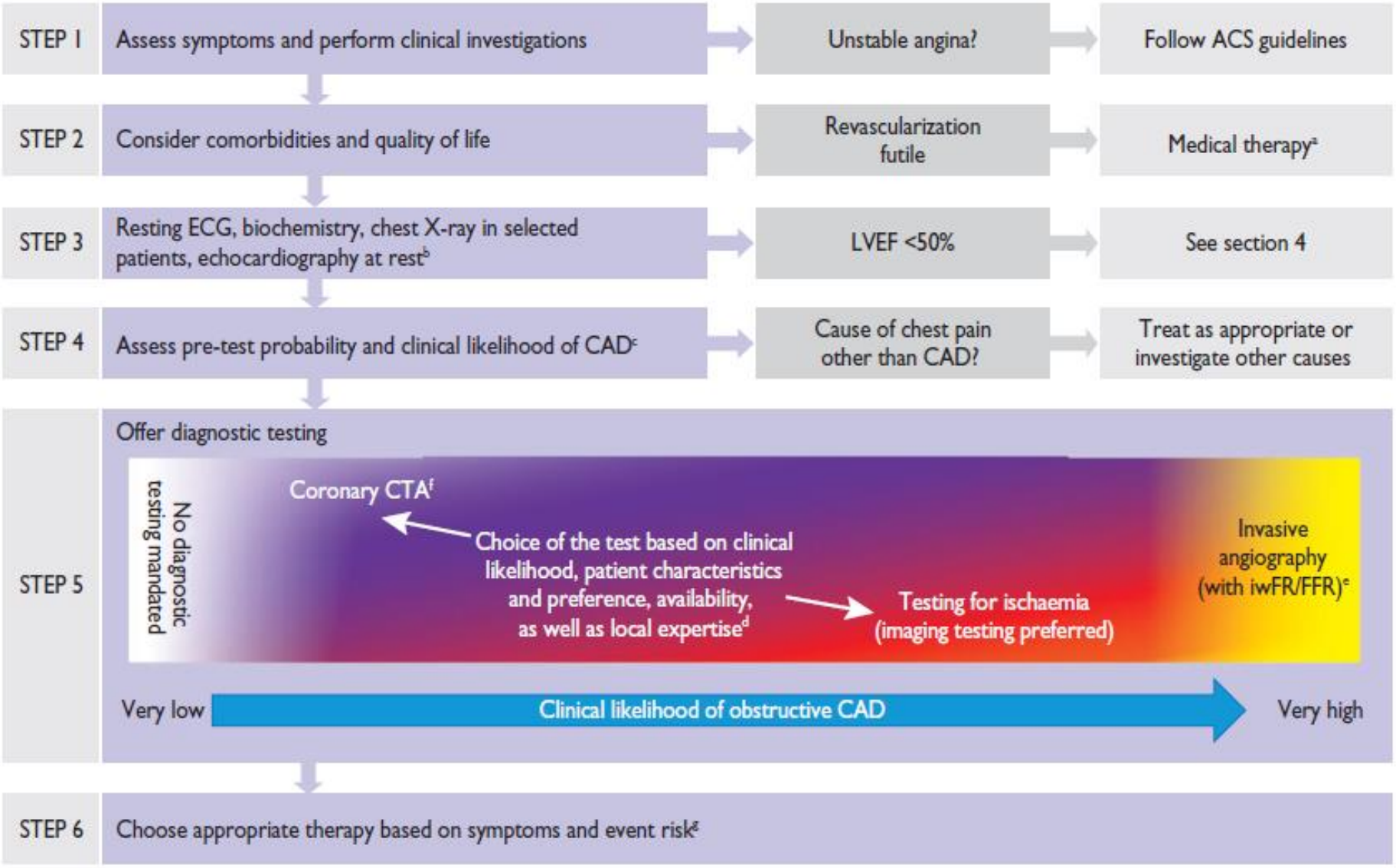
	Typische Angina	Typische Angina	Atypische Angina	Atypische Angina	Extrakardiale Thoraxschmerzen	Extrakardiale Thoraxschmerzen
Alter	Mann	Frau	Mann	Frau	Mann	Frau
30–39	59	28	29	10	18	5
40–49	69	37	38	14	25	8
50–59	77	47	49	20	34	12
60–69	84	58	59	28	44	17
70–79	89	68	69	37	54	24
> 80	93	76	78	47	65	32

CV Manual KSSG 2019

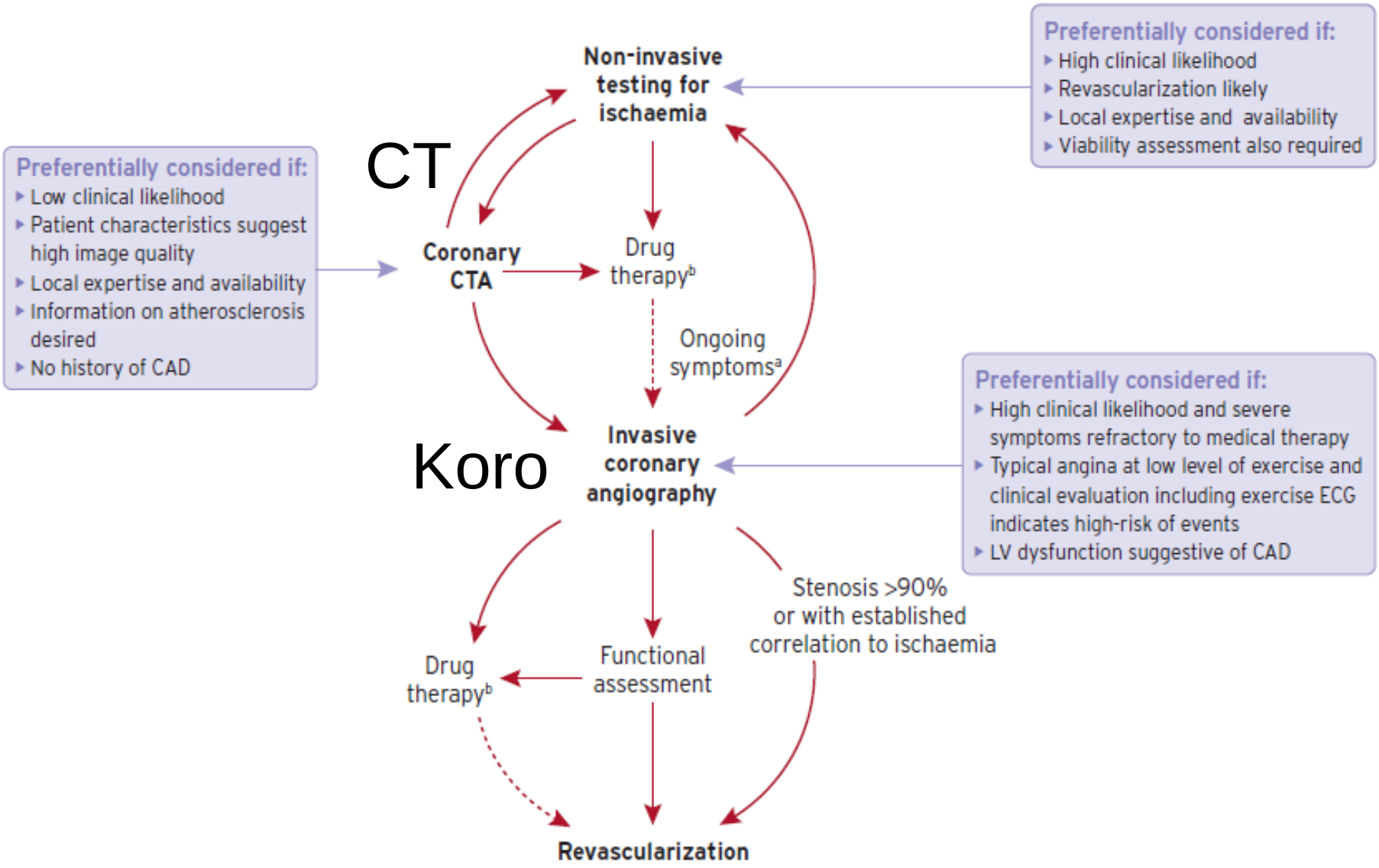
Table 5 Pre-test probabilities of obstructive coronary artery disease in 15 815 symptomatic patients according to age, sex, and the nature of symptoms in a pooled analysis[64] of contemporary data[7,8,62]

	Typical		Atypical		Non-anginal		Dyspnoea[a]	
Age	Men	Women	Men	Women	Men	Women	Men	Women
30–39	3%	5%	4%	3%	1%	1%	0%	3%
40–49	22%	10%	10%	6%	3%	2%	12%	3%
50–59	32%	13%	17%	6%	11%	3%	20%	9%
60–69	44%	16%	26%	11%	22%	6%	27%	14%
70+	52%	27%	34%	19%	24%	10%	32%	12%




STEP 1
Assess symptoms and perform clinical investigations
Unstable angina?
Follow ACS guidelines
STEP 2
Consider comorbidities and quality of life
Revascularization futile
Medical therapy[a]
STEP 3
Resting ECG, biochemistry, chest X-ray in selected patients, echocardiography at rest[b]
LVEF <50%
See section 4
STEP 4
Assess pre-test probability and clinical likelihood of CAD[c]
Cause of chest pain other than CAD?
Treat as appropriate or investigate other causes
STEP 5
Offer diagnostic testing
No diagnostic testing mandated
Coronary CTA[f]
Choice of the test based on clinical likelihood, patient characteristics and preference, availability, as well as local expertise[d]
Testing for ischaemia (imaging testing preferred)
Invasive angiography (with iwFR/FFR)[e]
Very low
Clinical likelihood of obstructive CAD
Very high
STEP 6
Choose appropriate therapy based on symptoms and event risk[g]

Nicht-invasiver Test



Changes in major recommendations			
2013	**Class[a]**	**2019**	**Class[a]**
Exercise ECG is recommendedas the initial test to establish a diagnosis of stable CAD in patients withsymptoms of angina and intermediate PTP of CAD (15–65%), free of anti-ischaemic drugs, unless they cannot exercise or display ECG changes that make the ECG non-evaluable.	I	Exercise ECG is recommended for the assessment of exercise tolerance, symptoms, arrhythmias, BP response, and event risk in selected patients.	I
		Exercise ECG may be considered as an alternative test to rule-in or rule-out CAD when other non-invasive or invasive imaging methods are not available.	IIb
Exercise ECG should be considered in patients on treatment to evaluate control of symptoms and ischaemia.	IIa	Exercise ECG may be considered in patients on treatment to evaluate control of symptoms and ischaemia.	IIb
For second-line treatment it is recommended that long-acting nitrates, ivabradine, nicorandil, or ranolazine are added according to heart rate, BP, and tolerance.	IIa	Long-acting nitrates should be considered as a second-line treatment option when initial therapy with a beta-blocker and/or a non-DHP-CCB is contraindicated, poorly tolerated, or inadequate in controlling angina symptoms.	IIa
For second-line treatment, trimetazidine may be considered,	IIb	Nicorandil, ranolazine, ivabradine, or trimetazidine should be considered as a second-line treatment to reduce angina frequency and improve exercise tolerance in subjects who cannot tolerate, have contraindications to, or whose symptoms are not adequately controlled by beta-blockers, CCBs, and long-acting nitrates.	IIa
		In selected patients, the combination of a beta-blocker or a CCB with second-line drugs (ranolazine, nicorandil, ivabradine, and trimetazidine) may be considered for first-line treatment according to heart rate, BP, and tolerance.	IIb