Antithrombozytäre De-Eskalationsstrategien in der Langzeitphase nach ACS

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DEUTSCHES ZENTRUM FÜR
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3. Februar 2018

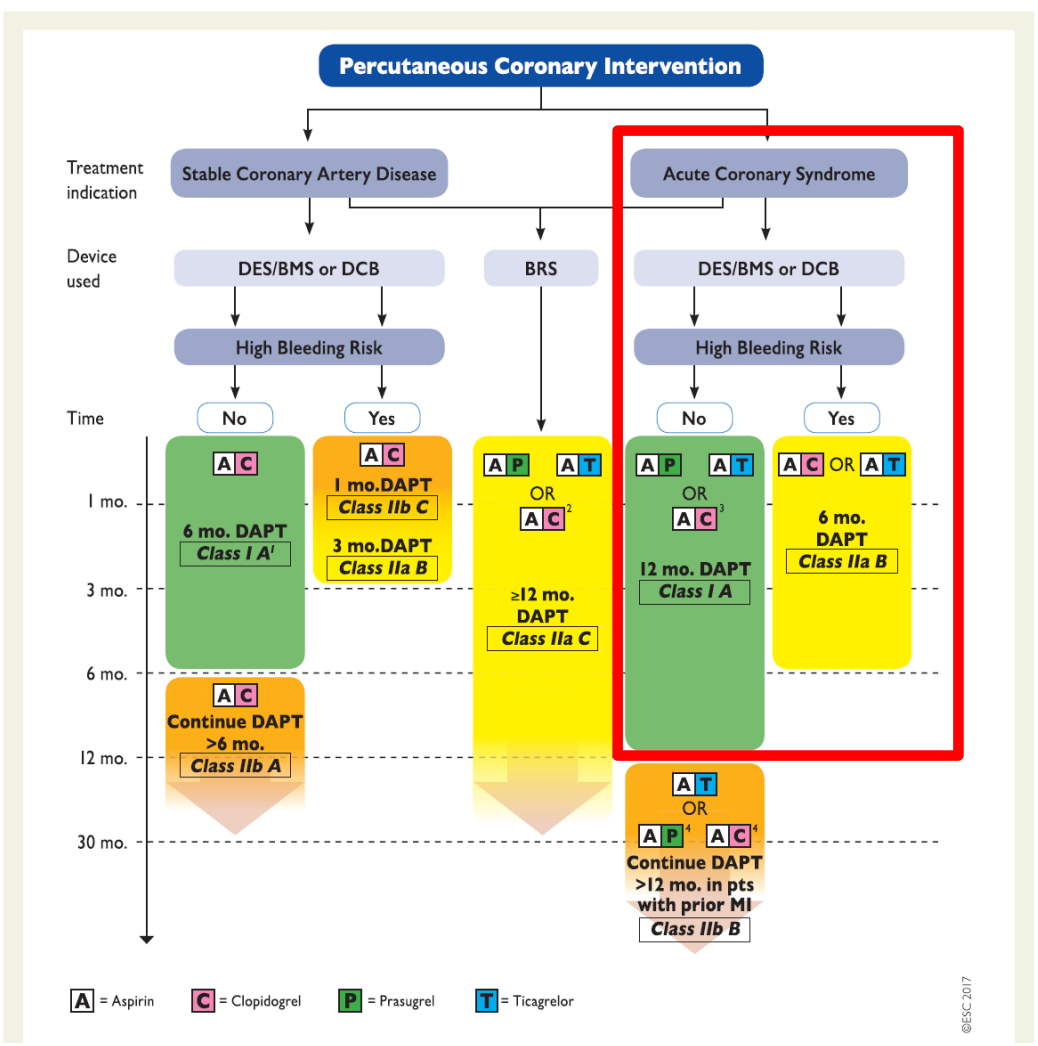
DAPT Empfehlungen in 2018

Recommendations on $P2Y_{12}$ inhibitor selection and timing

	Recommendations	Class[a]	Level[b]
ACS	In patients with ACS, ticagrelor (180 mg loading dose, 90 mg twice daily) on top of aspirin[c] is recommended, regardless of initial treatment strategy, including patients pre-treated with clopidogrel (which should be discontinued when ticagrelor is commenced) unless there are contraindications.[20]	I	B
ACS	In patients with ACS undergoing PCI, prasugrel (60 mg loading dose, 10 mg daily dose) on top of aspirin is recommended for $P2Y_{12}$ inhibitor-naïve patients with NSTE-ACS or initially conservatively managed STEMI if indication for PCI is established, or in STEMI patients undergoing immediate coronary catheterization[c] unless there is a high risk of life-threatening bleeding or other contraindications.[23]	I	B
ACS	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
ACS	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
SCAD	In patients with stable CAD, pre-treatment with clopidogrel may be considered if the probability of PCI is high.	IIb	C
SCAD	Clopidogrel (600 mg loading dose, 75 mg daily dose) on top of aspirin is recommended in stable CAD patients undergoing coronary stent implantation and in ACS patients who cannot receive ticagrelor or prasugrel, including those with prior intracranial bleeding or indication for OAC.[20,23,39,40]	I	A

ESC DAPT Guidelines, Valgimigli et al., EHJ 2017

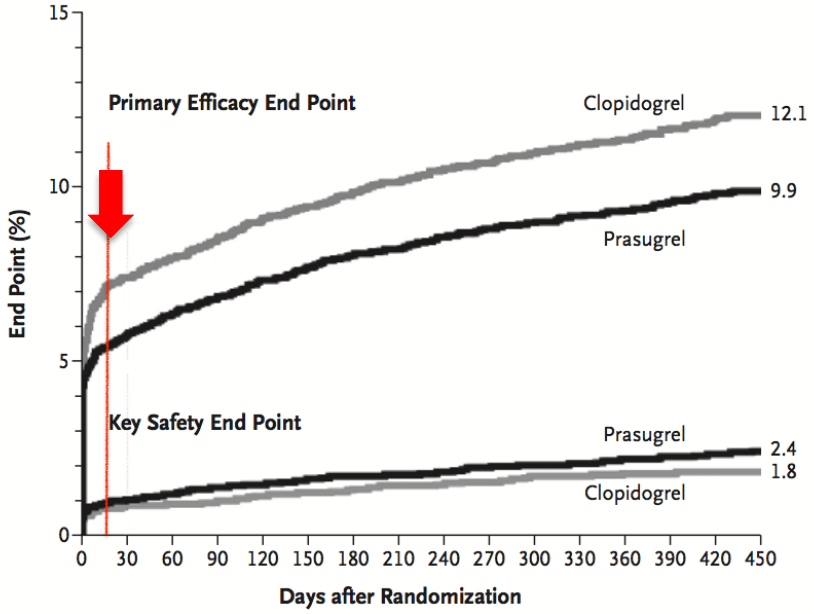
DAPT Dauer in 2018

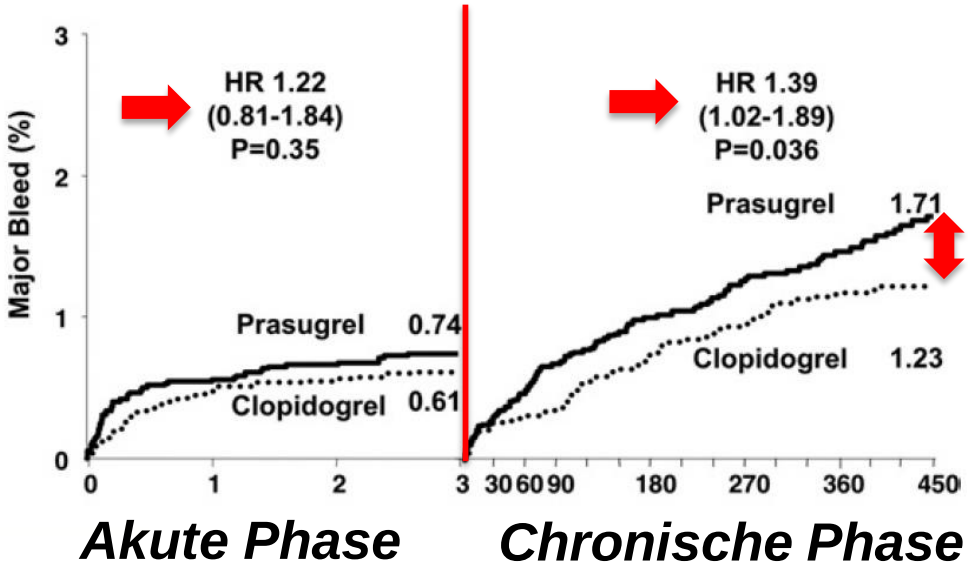


ESC DAPT Guidelines, Valgimigli et al., EHJ 2017

Prasugrel: Ischämien vs. Blutungen post PCI

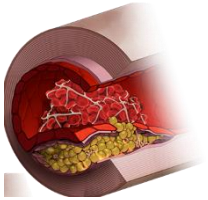
TRITON TIMI-38





Wiviott et al., NEJM 2007

Ticagrelor: Ischämien vs. Blutungen post PCI



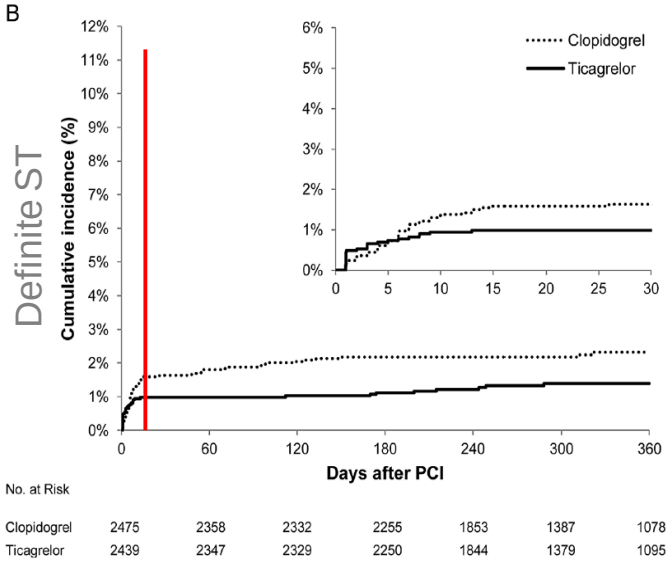


Table 5 Landmark analyses: first 30 days on study drug vs. after 30 days on study drug

	Ticagrelor (*n* = 9235), *n* (%)	Clopidogrel (*n* = 9186), *n* (%)	Hazard ratio (95% CI)	*P*-value
Non-CABG-related major bleeding				
First 30 days on study drug	224 (2.47)	199 (2.21)	1.123 (0.928–1.360)	0.23
After 30 days on study drug	149 (2.17)	113 (1.65)	1.338 (1.048–1.708)	0.02
+ Adjusting by bleeding events in first 30 days			1.329 (1.041–1.698)	0.02
+ Adjusting by PCI in first 30 days			1.332 (1.043–1.701)	0.02
Non-procedure-related major bleeding				
First 30 days on study drug	112 (1.25)	93 (1.05)	1.201 (0.912–1.581)	0.19
After 30 days on study drug	129 (1.90)	89 (1.30)	1.471 (1.123–1.927)	0.01
+ Adjusting by bleeding events in first 30 days			1.466 (1.119–1.920)	0.01
+ Adjusting by PCI in first 30 days			1.469 (1.121–1.925)	0.01

CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention.

Becker et al., EHJ 2011; Velders et al., Heart *2016*

Real-World Daten zu DAPT De-Eskalation (Switching)

Switching of adenosine diphosphate receptor inhibitor after hospital discharge among myocardial infarction patients: Insights from the Treatment with Adenosine Diphosphate Receptor Inhibitors: Longitudinal Assessment of Treatment Patterns and Events after Acute Coronary Syndrome (TRANSLATE-ACS) observational study

Marjorie E. Zettler, PhD, MPH,[a] Eric D. Peterson, MD, MPH,[b] Lisa A. McCoy, MS,[b] Mark B. Effron, MD,[a] Kevin J. Anstrom, PhD,[b] Timothy D. Henry, MD,[c] Brian A. Baker, PharmD,[d] John C. Messenger, MD,[e] David J. Cohen, MD,[f] and Tracy Y. Wang, MD, MHS, MSc[b], on behalf of the TRANSLATE-ACS Investigators *Indianapolis, IN; Durham, NC; Los Angeles, CA; Parsippany, NJ; Aurora, CO; and Kansas City, MO*

Table II. Factors independently associated with postdischarge switch from prasugrel or ticagrelor to clopidogrel

Parameter	OR	95% CI	P
High school graduate (or beyond)	0.629	0.451-0.877	<.01
Insurance for medications: Medicare/ Medicaid (vs private)	2.383	1.863-3.049	<.01
Insurance for medications: no/non-US (vs private)	1.543	1.067-2.231	.02
Prior MI	1.371	1.047-1.794	.02
Moderate/extreme financial hardship of current monthly medications	1.401	1.042-1.884	.03
Creatinine clearance (per 10-unit decrease)	1.059	1.109-1.012	.01
In-hospital bleeding event	2.236	1.408-3.553	<.01
Any home ADPri	0.593	0.393-0.896	.01

Abbreviation: OR, odds ratio.

Table I. Patient characteristics

	Discharged on clopidogrel			Discharged on prasugrel			Discharged on ticagrelor		
	Switch (n = 216)	No switch (n = 5741)	P	Switch (n = 383)	No switch (n = 2106)	P	Switch (n = 64)	No switch (n = 162)	P
Age (y), (median, IQR)	59 (51-67.5)	62 (54-70)	<.01	58 (50-64)	57 (50-63)	.19	62.5 (53-70)	60.5 (53-67)	.17

DAPT De-Eskalation **15 %** **28 %**

Zettler et al., AHJ 2017

TOPIC Studie

PRO

European Heart Journal (2017) 0, 1–9
doi:10.1093/eurheartj/ehx175

CLINICAL RESEARCH
Acute coronary syndromes

Benefit of switching dual antiplatelet therapy after acute coronary syndrome: the TOPIC (timing of platelet inhibition after acute coronary syndrome) randomized study

Thomas Cuisset[1,2,3]*, Pierre Deharo[1,3,4], Jacques Quilici[5], Thomas W. Johnson[4], Stéphanie Deffarges[1,3], Clémence Bassez[1,3], Guillaume Bonnet[1,3], Laurent Fourcade[6], Jean Philippe Mouret[1,3], Marc Lambert[1,3], Valentine Verdier Pierre Emmanuel Morange[2,3,8], Marie Christine Alessi[2,3,8], and Jean Louis Bonnet[1,2,3]

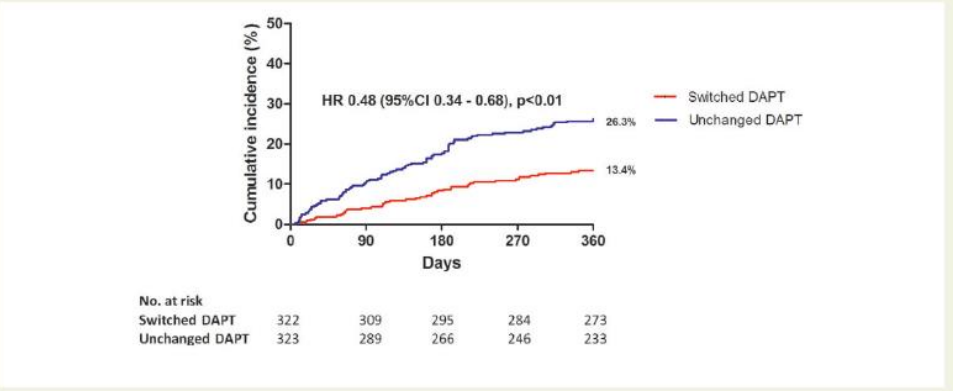


Figure 2 Incidence of the primary endpoint (net clinical benefit) at 1 year. HR, Hazard ratio.

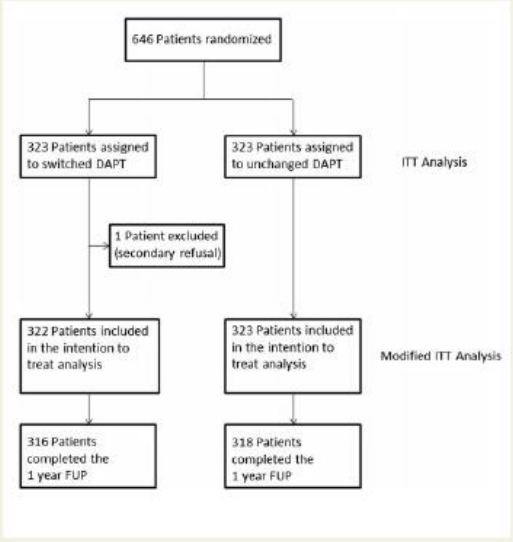


Figure 1 Flow chart. FUP, follow-up; ITT, intention to treat.

Table 3 Endpoints at 1 year

	Switched DAPT	Unchanged DAPT	HR (95%IC)	*P*-value
Net clinical benefit	43 (13.4%)	85 (26.3%)	0.48 (0.34–0.68)	<0.01
Any ischaemic event	30 (9.3%)	37 (11.5%)	0.48 (0.34–0.68)	0.36
Cardiovascular death	1 (0.3%)	4 (1.2%)	0.30 (0.05–1.73)	0.18
Unplanned revascularization	28 (8.7%)	30 (9.3%)	0.93 (0.56–1.55)	0.78
Stroke	1 (0.3%)	3 (0.9%)	0.37 (0.05–2.60)	0.32
All bleedings	30 (9.3%)	76 (23.5%)	0.39 (0.27–0.57)	<0.01
Bleeding BARC ≥ 2	13 (4.0%)	48 (14.9%)	0.30 (0.18–0.50)	<0.01
TIMI major	1 (0.3%)	4 (1.2%)	0.30 (0.05–1.73)	0.18
TIMI minor	9 (2.8%)	26 (8.0%)	0.37 (0.19–0.71)	<0.01
TIMI minimal	20 (6.2%)	46 (14.2%)	0.44 (0.27–0.71)	<0.01

Percentages are calculated from the Kaplan–Meier curve.
BARC, Bleeding Academic Research Consortium criteria; TIMI, thrombosis in myocardial infarction; DAPT, dual antiplatelet therapy.

Cuisset et al., EHJ 2017

SCOPE Register

CONTRA

Incidence and outcome of switching of oral platelet P2Y$_{12}$ receptor inhibitors in patients with acute coronary syndromes undergoing percutaneous coronary intervention: the SCOPE registry

Table 1. Baseline features of the overall population.

	N=1,363
Age (years)	73±5
Female gender, n (%)	382 (28.0)
Hypertension, n (%)	993 (72.8)
Hyperlipidaemia, n (%)	713 (52.3)
Previous smoker, n (%)	356 (26.1)
Diabetes mellitus, n (%)	458 (33.6)
Previous stroke/TIA, n (%)	114 (8.4)
Previous carotid surgery, n (%)	114 (8.4)
PAD, n (%)	203 (14.9)
Previous bleeding, n (%)	64 (4.7)
Renal dysfunction, n (%)	203 (14.9)
Dialysis, n (%)	41 (3.0)
Malignancy, n (%)	38 (2.9)
Severe COPD, n (%)	64 (4.8)
Previous ACS, n (%)	433 (31.8)
Previous PCI, n (%)	407 (29.9)
Previous CABG, n (%)	68 (5.0)
STEMI, n (%)	331 (24.3)
Killip class III-IV, n (%)	83 (6.1)
SBP, mmHg (mean±SD)	136±25
HR, bpm (mean±SD)	75±18
Ejection fraction, % (mean±SD)	49±9
Atrial fibrillation, n (%)	123 (12.3)
Hb, gr/dl (mean±SD)	12±1
Glycaemia, mg/dl (mean±SD)	143±87
Platelet count, x1,000 (mean±SD)	265±67

ACS: acute coronary syndrome; CABG: coronary artery bypass grafting; COPD: chronic obstructive pulmonary disease; Hb: haemoglobin; HR: heart rate; PAD: peripheral artery disease; PCI: percutaneous coronary intervention; SBP: systolic blood pressure; STEMI: ST-elevation myocardial infarction; TIA: transient ischaemic attack

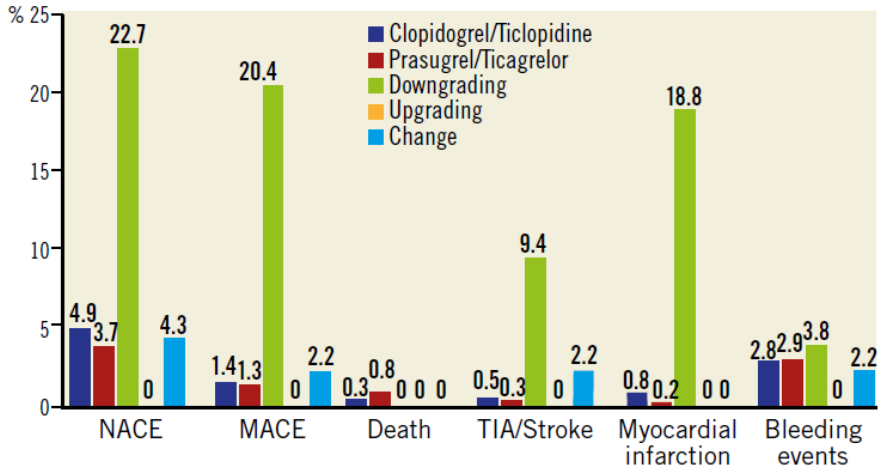
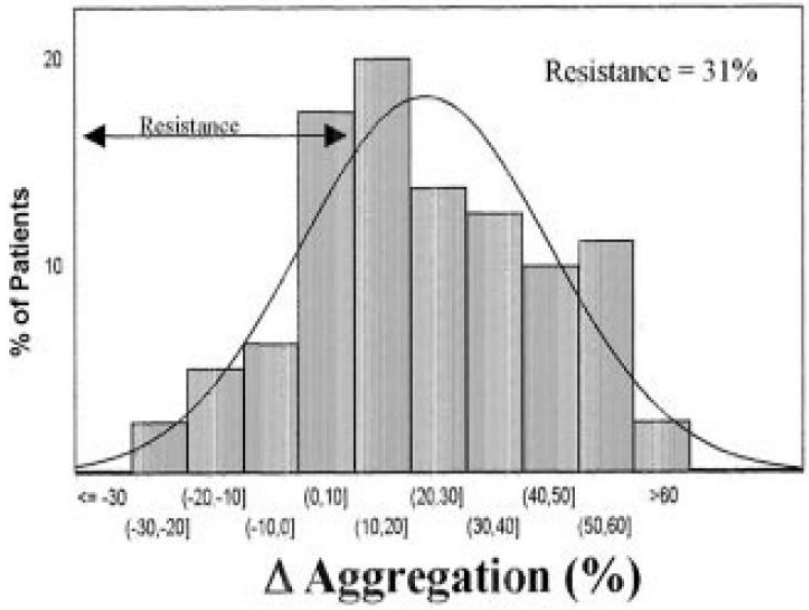
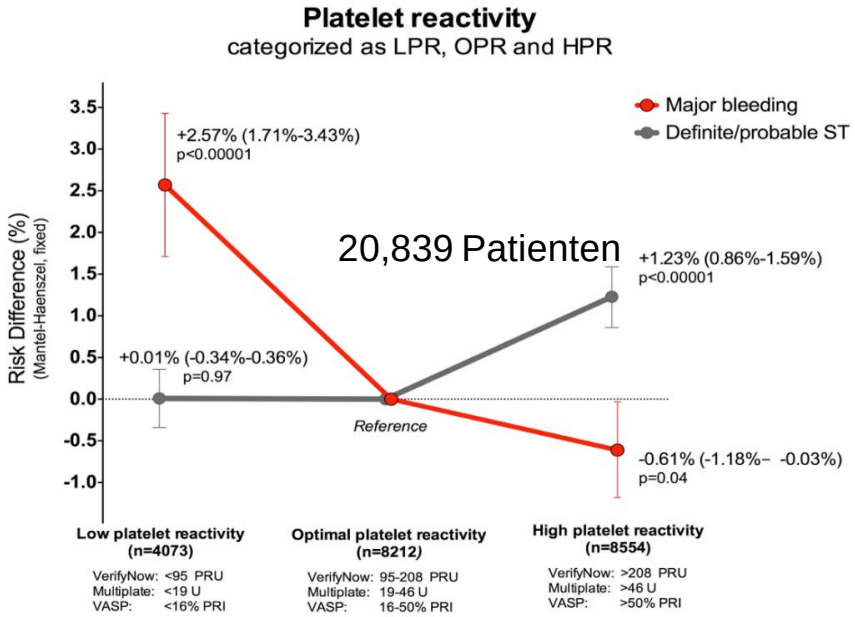


Figure 4. *Cumulative relative incidence at one-month follow-up of MACE, NACE, and single adverse events in patients treated with old or novel P2Y$_{12}$ receptor inhibitors (without switching) and in patients who received a switch (downgrade, upgrade or change) of oral antiplatelet therapies during the whole study period.*

De Luca et al., Eurointervention 2017

Clopidogrel: Wirkung & Outcome





- **Plattchenfunktionstestung (PFT)** als “Tool” um eine DAPT D**e-Eskalation sicherer** zu machen

Gurbel et al., Circulation 2003

Aradi, …, Sibbing, EHJ 2015

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TROPICAL ACS

Guided de-escalation of antiplatelet treatment in patients with acute coronary syndrome undergoing percutaneous coronary intervention (TROPICAL-ACS): a randomised, open-label, multicentre trial

Dirk Sibbing, Dániel Aradi*, Claudius Jacobshagen, Lisa Gross, Dietmar Trenk, Tobias Geisler, Martin Orban, Martin Hadamitzky, Béla Merkely, Róbert Gábor Kiss, András Komócsi, Csaba A Dézsi, Lesca Holdt, Stephan B Felix, Radoslaw Parma, Mariusz Klopotowski, Robert H G Schwinger, Johannes Rieber, Kurt Huber, Franz-Josef Neumann, Lukasz Koltowski, Julinda Mehilli, Zenon Huczek, Steffen Massberg, on behalf of the TROPICAL-ACS Investigators†*

Summary

Background Current guidelines recommend potent platelet inhibition with prasugrel or ticagrelor for 12 months after an acute coronary syndrome managed with percutaneous coronary intervention (PCI). However, the greatest anti-ischaemic benefit of potent antiplatelet drugs over the less potent clopidogrel occurs early, while most excess bleeding events arise during chronic treatment. Hence, a stage-adapted treatment with potent platelet inhibition in the acute phase and de-escalation to clopidogrel in the maintenance phase could be an alternative approach. We aimed to investigate the safety and efficacy of early de-escalation of antiplatelet treatment from prasugrel to clopidogrel guided by platelet function testing (PFT).

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See Online/Comment
http://dx.doi.org/10.1016/S0140-6736(17)32279-1

*Contributed equally

Sibbing, Aradi et al., Lancet 2017

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TROPICAL ACS

Ziel der **TROPICAL-ACS*** Studie war es, die Sicherheit und die Effektivität einer frühen und mittels Plättchenfunktionstestung gesteuerten De-Eskalation (Wechsel von Prasugrel zu Clopidogrel) der Plättchenhemmung zu untersuchen

** TROPICAL-ACS: **T**esting **R**esponsiveness T**o** **P**latelet **I**nhibition On **C**hronic **A**ntiplate**l**et Treatment For **A**cute **C**oronary **S**yndromes*

Überblick zur Studie: 33 Zentren in Europa

GERMANY

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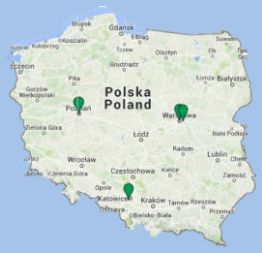

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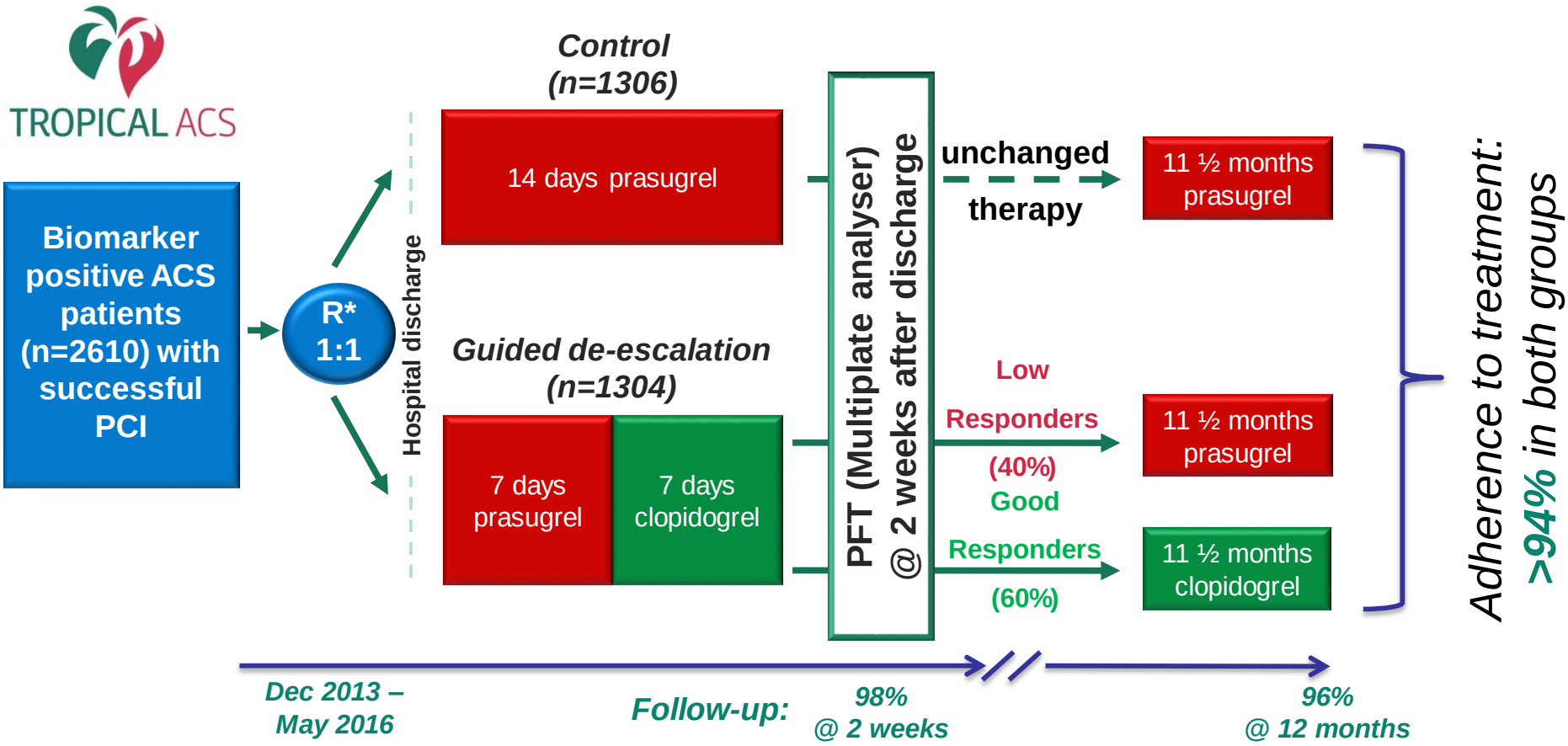
Patienten & Studienarme



TROPICAL ACS

Basischarakteristika

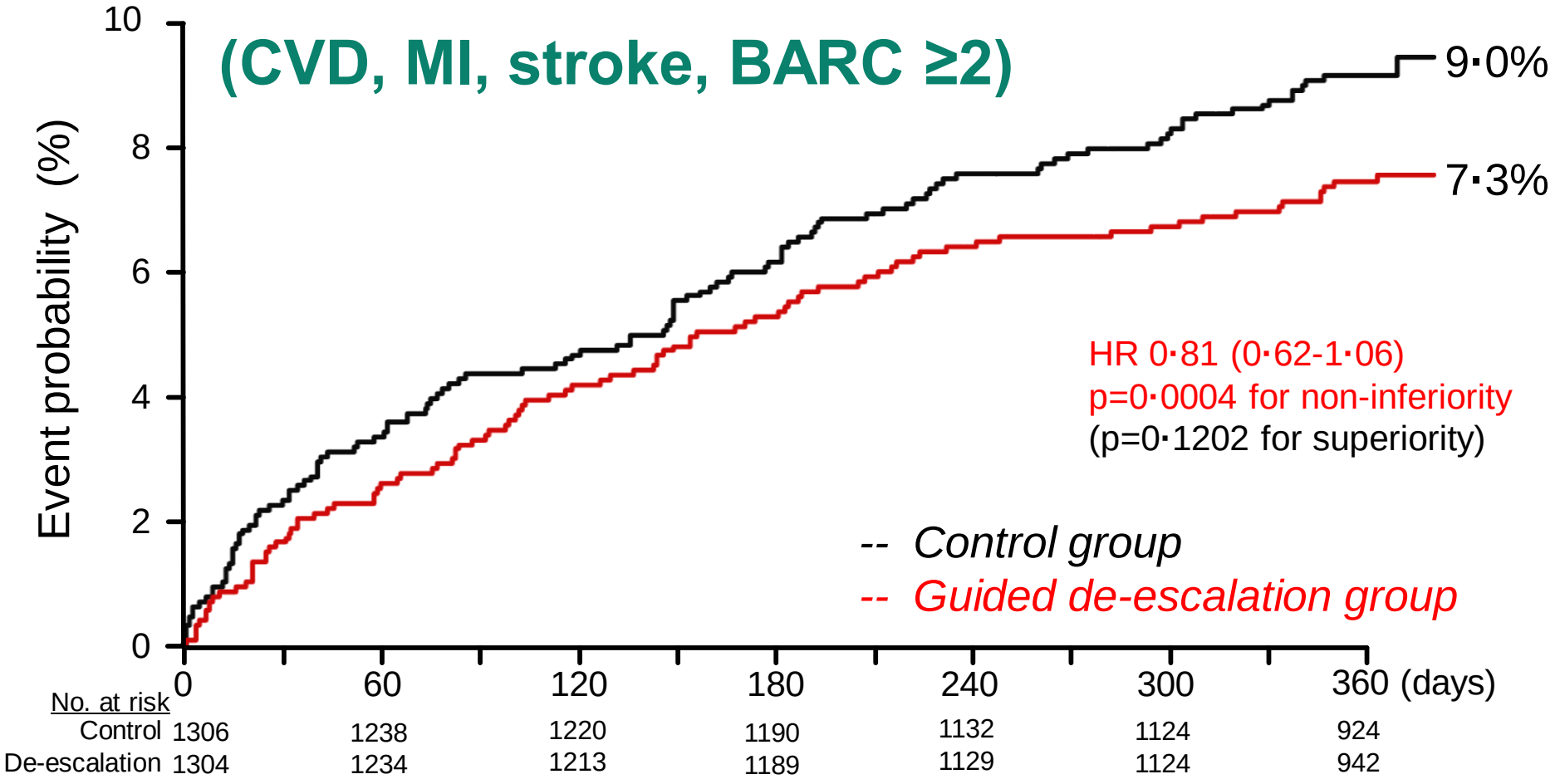
	Control group (n = 1306)	Guided de-escalation group (n = 1304)
Age, years	59 (SD 10)	59 (SD 10)
Female sex	283 (22%)	275 (21%)
Previous PCI	186 (14%)	173 (13%)
Previous CABG	46 (4%)	39 (3%)
Previous MI	153 (12%)	140 (11%)
Diabetes mellitus	287 (22%)	240 (18%)
Current smoker	591 (45%)	591 (45%)
Arterial hypertension	806 (62%)	793 (61%)
Hyperlipidaemia	529 (41%)	546 (42%)

TROPICAL ACS

Prozedurale Characteristica

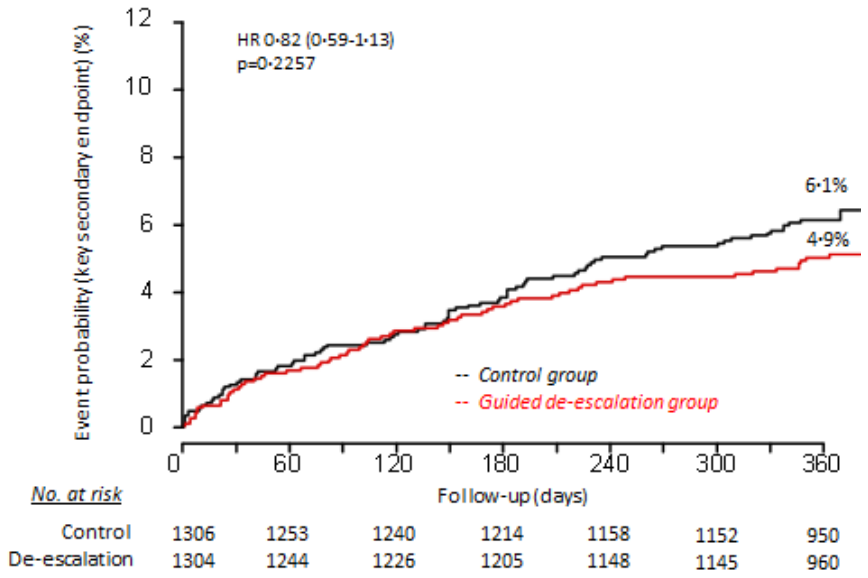
	Control group (n = 1306)	Guided de-escalation group (n = 1304)
STEMI **NSTEMI**	722 (55%) 584 (45%)	731 (56%) 573 (44%)
Access site: **Brachial** **Femoral** **Radial**	 3 (<1%) 541 (41%) 762 (58%)	 -- 523 (40%) 781 (60%)
Diseased vessels: **1** **2** **3**	 682 (52%) 345 (26%) 279 (21%)	 659 (51%) 359 (28%) 286 (22%)
Anticoagulant for PCI: **Bivalirudin** **LMWH** **UFH**	 55 (4%) 70 (5%) 1181 (90%)	 54 (4%) 72 (6%) 1178 (90%)
Stent type: **DES** **BMS** **BVS** **None (POBA)**	 1002 (77%) 208 (16%) 83 (6%) 13 (1%)	 1003 (77%) 224 (17%) 68 (5%) 9 (1%)

Primärer Studienendpunkt

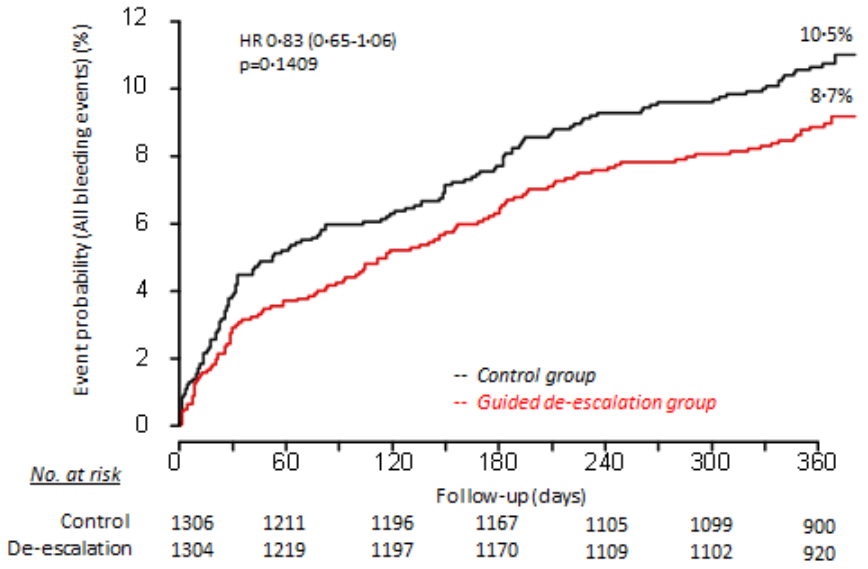


Blutungen

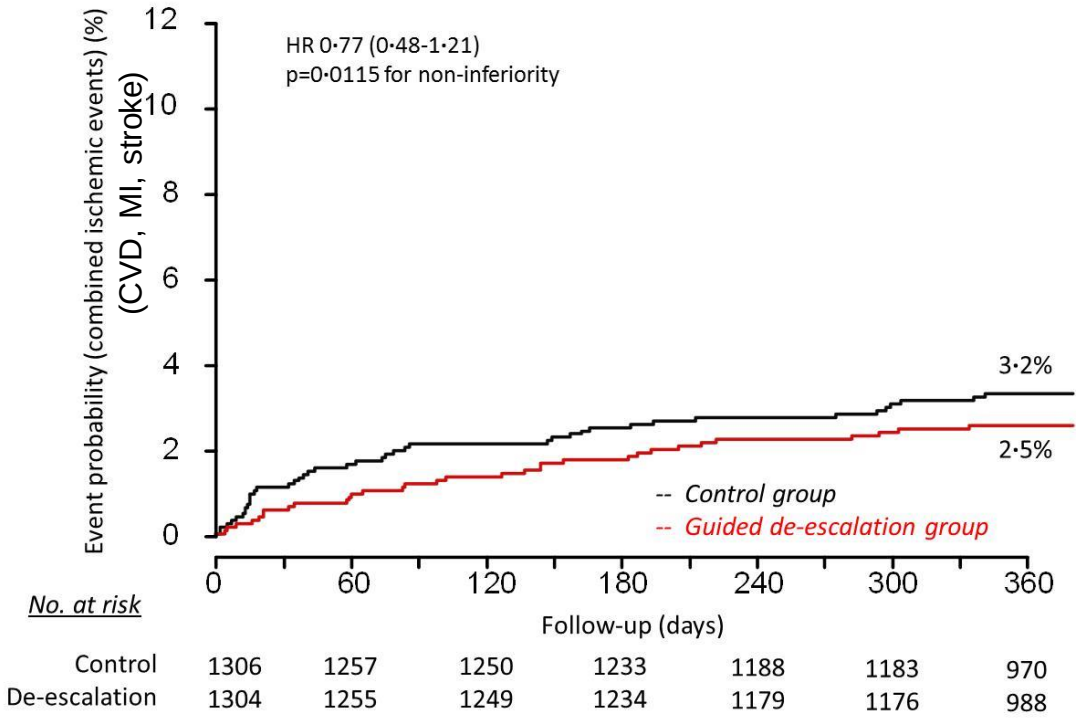
Key Secondary endpoint Bleeding BARC ≥2



All bleeding events (BARC 1 to 5)



Ischämien



- All-cause mortality:
  12 events (1%) in control vs. 11 (1%) in guided de-escalation group, p=0.85
- Definite ST:
  3 events (0.2%) in control vs. 2 (0.2%) in guided de-escalation group, p=0.66

Zusammenfassung

- Klinische (z.B. Blutungen oder hohes Blutungsrisiko) und ökonomische Faktoren sind Trigger für das Konzept der DAPT De-Eskalation nach ACS-PCI.
- Die aktuelle Datenlage zur uniformen De-Eskalation ist widersprüchlich
- TROPICAL-ACS etabliert eine “Guided DAPT De-escalation” als ein alternatives, praktikables, effektives und sicheres Therapiekonzept für ACS Patienten.

„Das war ´ s noch nicht!“

LMU LUDWIG-MAXIMILIANS-UNIVERSITÄT MÜNCHEN

Vielen Dank für die Aufmerksamkeit!