Chefarzt Dr. med. Burcin Özüyaman

- Asklepios Klinik Weißenfels –

Update Kardiologie – ACS, Herzinsuffizienz und Antikoagulation

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Mögliche Interessenskonflikte:

- Boehringer-Ingelheim (z.B. Pradaxa)
- Bayer (z.B. Xarelto)
- Bristol-Myers Squibb (z.B. Eliquis)
- Daiichi-Sankyo (z.B. Lixiana, Efient)
- Chiesi (z.B. Foster)
- Novartis (z.B. Entresto)
- Astra Zeneca (z.B. Brilique)
- Berlin-Chemie (z.B. Ranexa, Nebilet, Tioblis)
- Servier (z.B. Procorolan)
- Falk Foundation (z.B. Salofalk)

Excel-Studie (NEJM 11/2019)

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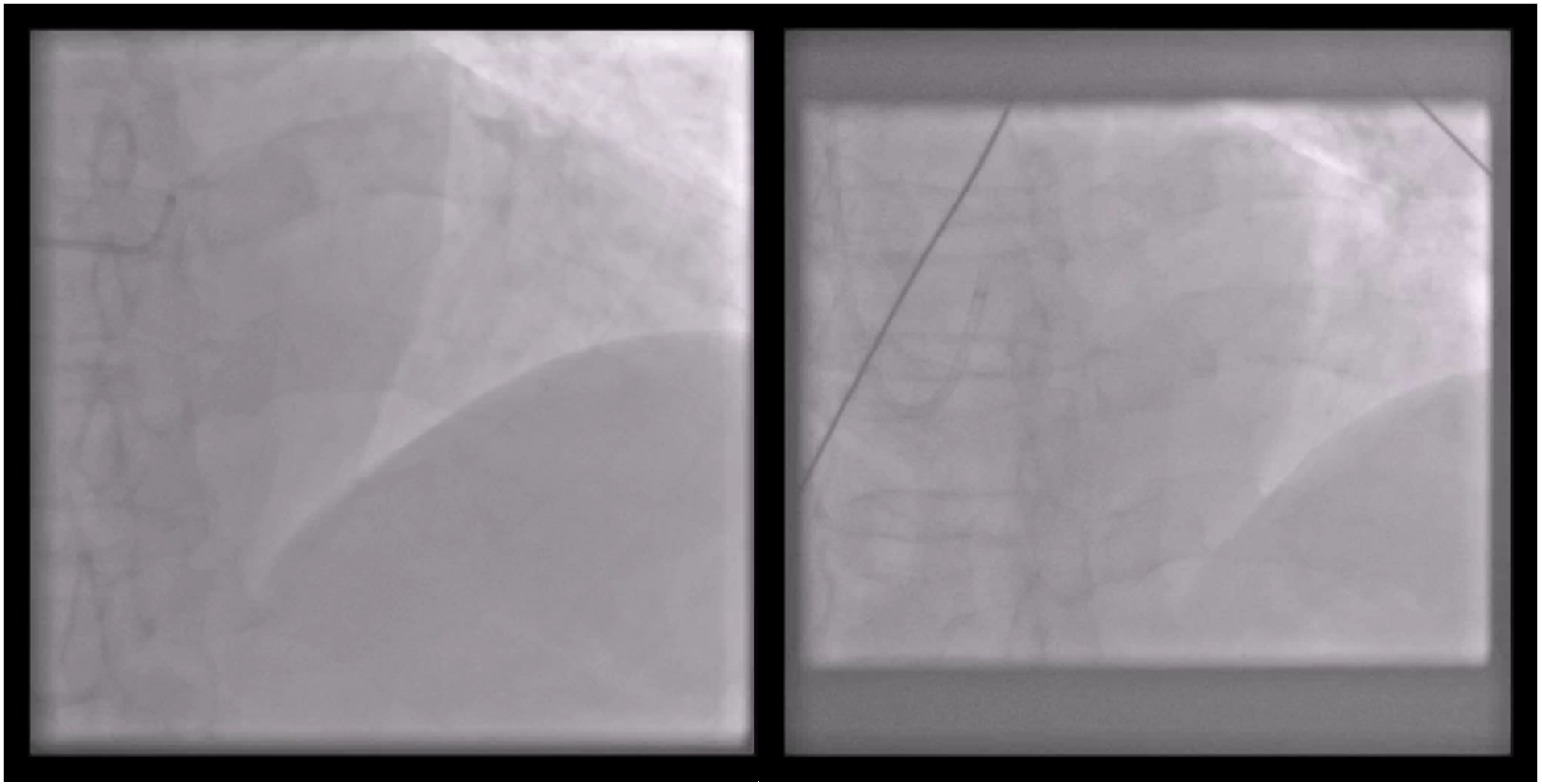

Are Higher Operator Volumes for Unprotected Left Main Stem Percutaneous Coronary Intervention Associated With Improved Patient Outcomes? A Survival Analysis of 6724 Procedures From the British Cardiovascular Intervention Society National Database

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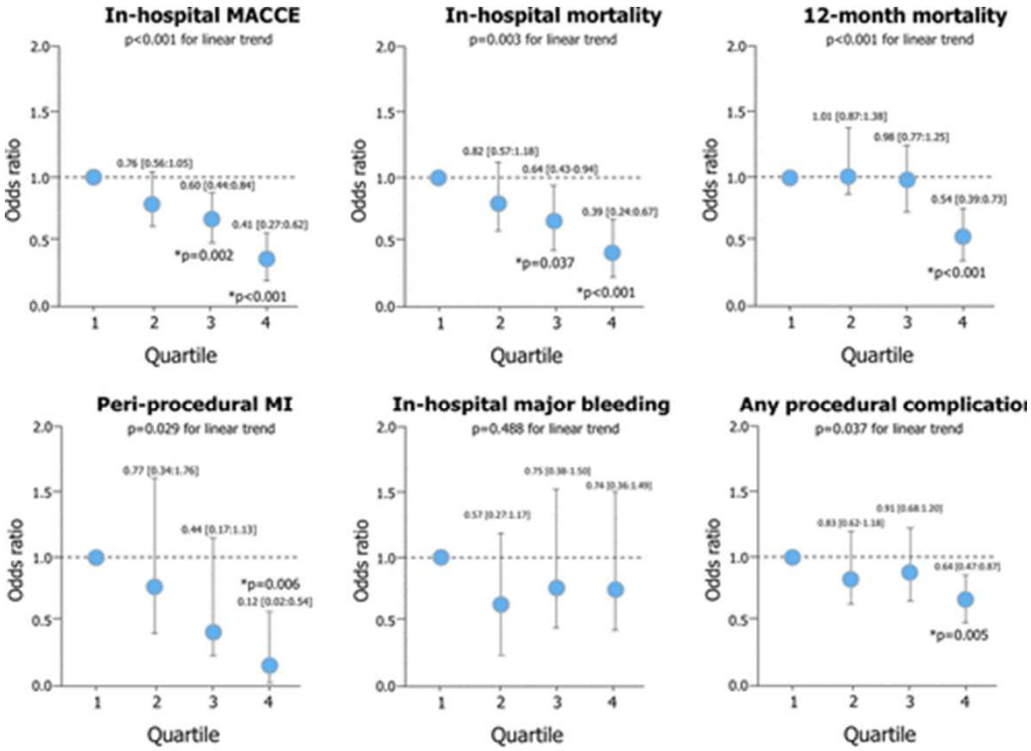
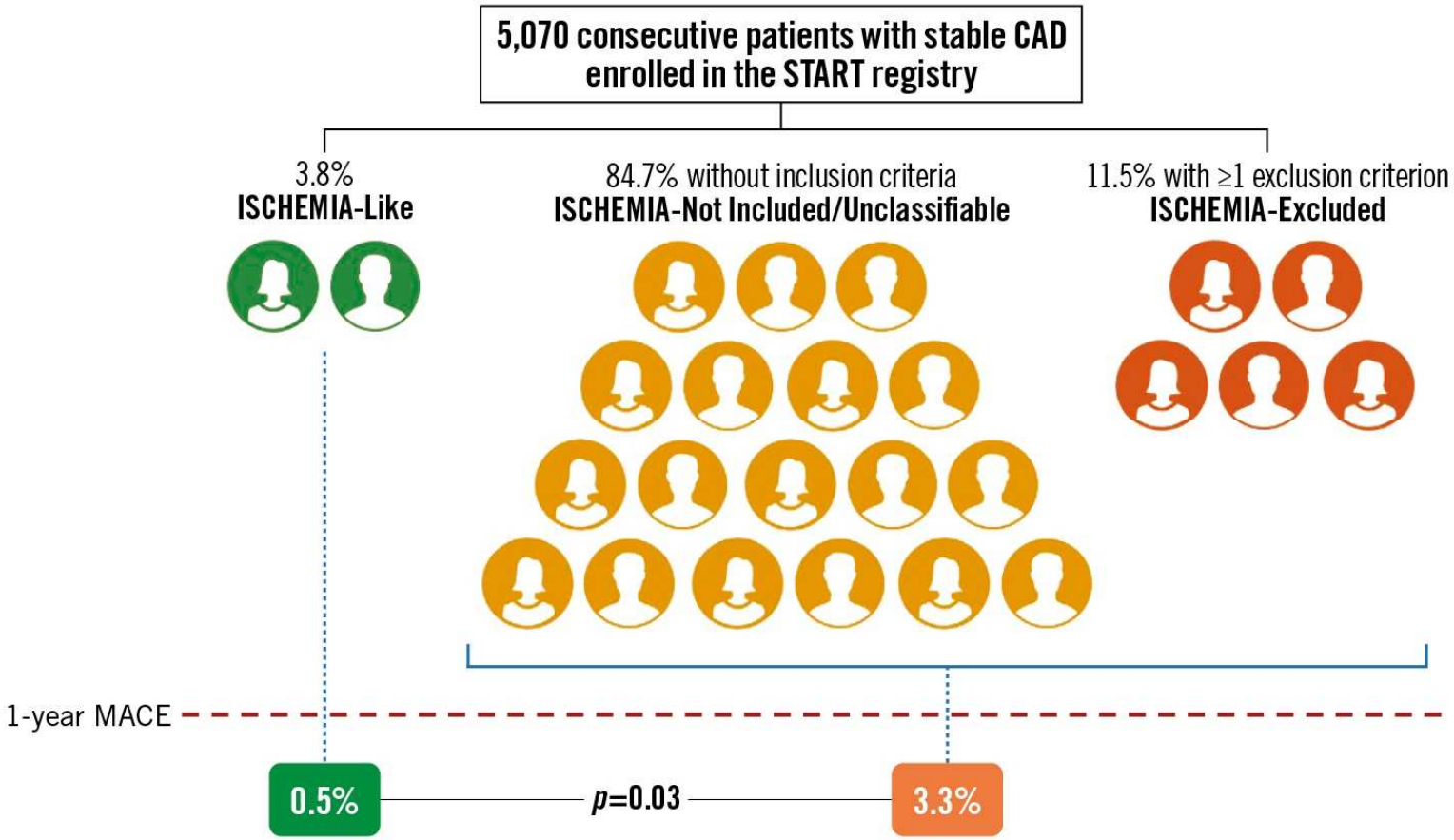
Table 2. Procedural Variables by Quartile of uLMS-PCI Operator Volume, 2012 to 2014 (Table view)

Variable	Q1	Q2	Q3	Q4	*P* Value
No. of operators	347	134	59	29	…
Annualized median operator uLMS-PCI/y	2 (1–3)	5 (4–6)	10 (8–12)	21 (17–29)	…
No. of vessels attempted ±SD	1.92±0.86	1.95±0.84	2.15±0.90	2.50±0.95	<0.001
Femoral access, n (%)	727 (44.4)	653 (38.8)	617 (36.1)	503 (29.9)	<0.001
Ad hoc PCI, n (%)	648 (42.1)	678 (41.6)	649 (39.1)	538 (34.1)	<0.001
Circulatory support, n (%)	82 (5.2)	73 (4.6)	59 (3.5)	33 (2.1)	<0.001
Restenosis indication, n (%)	89 (5.9)	92 (5.8)	104 (6.8)	121 (10.6)	<0.001
Intracoronary imaging, n (%)	639 (44.2)	717 (47.6)	742 (47.4)	809 (54.9)	0.001
Target vessels, n (%)					
Left main only	498 (30.4)	448 (26.7)	353 (20.7)	279 (16.4)	<0.001
Left main+/proximal LAD	784 (47.9)	868 (51.7)	957 (56.0)	1083 (63.7)	<0.001
Left main stem/proximal LAD/LCx	274 (16.7)	302 (18.0)	417 (24.4)	563 (33.2)	<0.001
Left main+1 vessel	786 (48.1)	833 (49.6)	819 (48.0)	717 (42.2)	<0.001
LMS+2 vessels	336 (20.5)	377 (22.5)	495 (29.0)	629 (37.0)	<0.001
LMS+3 vessels	17 (1.0)	21 (1.3)	40 (2.3)	75 (4.4)	<0.001
Microcatheter, n (%)	26 (2.1)	25 (2.0)	63 (4.8)	58 (4.4)	<0.001
Rotational atherectomy, n (%)	94 (7.4)	166 (13.3)	211 (16.2)	299 (22.7)	<0.001
Laser atherectomy, n (%)	2 (0.2)	2 (0.2)	8 (0.6)	9 (0.6)	0.011
Glycoprotein inhibitor, n (%)	331 (21.9)	272 (17.8)	273 (16.6)	250 (15.1)	<0.001
Largest stent, mm (±SD)	4.02±0.69	4.11±0.64	4.13±0.65	4.31±0.62	<0.001
Longest stent, mm (±SD)	23.4±11.1	24.8±11.7	25.4±11.4	30.6±13.8	<0.001
No. of stents used, ±SD	1.85±1.21	1.99±1.34	2.14±1.33	2.61±1.66	<0.001



ISCHEMIA Studie: Das Patientenkollektiv entspricht nicht der “wahren” Welt



Key exclusion criteria were an estimated glomerular filtration rate below 30 ml per minute per 1.73 m2 of body-surface area, a recent acute coronary syndrome, unprotected left main stenosis of at least 50%, a left ventricular ejection fraction of less than 35%, New York Heart Association class III or IV heart failure, and unacceptable angina despite the use of medical therapy at maximum acceptable doses (ISCHEMIA-Studie NEJM doi/full/10.1056/nejmoa1915922).

MASTER DAPT

Dual Antiplatelet Therapy after PCI in Patients at High Bleeding Risk

Valgimigli M et al. DOI: 10.1056/NEJMoa2108749

CLINICAL PROBLEM

In patients at high risk for bleeding after the implantation of a drug-eluting coronary stent, the appropriate duration of dual antiplatelet therapy to reduce the risk of ischemic complications, while minimizing bleeding risk, is unclear.

CLINICAL TRIAL

Design: A multicenter, randomized, open-label trial compared 1 month of dual antiplatelet therapy with longer treatment after the placement of a drug-eluting stent in patients at high risk for bleeding.

Intervention: 4579 patients at high bleeding risk who had received dual antiplatelet therapy for 1 month after undergoing implantation of a biodegradable-polymer sirolimus-eluting stent were randomly assigned to switch to single antiplatelet therapy (abbreviated therapy) or to continue dual antiplatelet therapy for at least 2 additional months (standard therapy). There were three primary outcomes: net adverse clinical events (death from any cause, myocardial infarction, stroke, or major bleeding), major adverse cardiac or cerebral events (death from any cause, myocardial infarction, or stroke), and major or clinically relevant nonmajor bleeding. Abbreviated therapy was tested for noninferiority to standard therapy with regard to the first two outcomes and for superiority with regard to the third outcome.

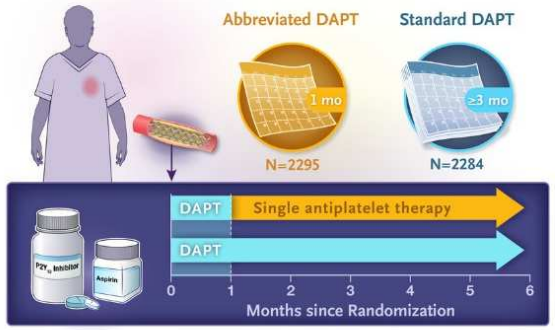
RESULTS

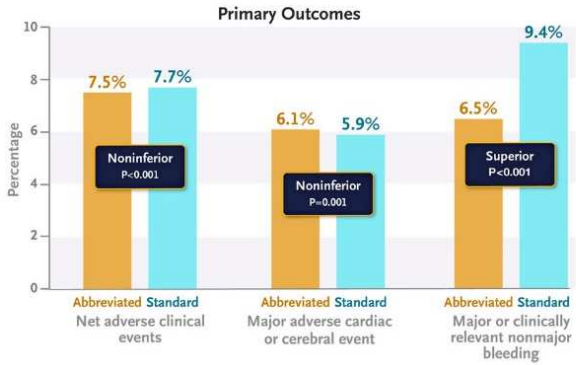
During the 335 days after randomization, abbreviated therapy was noninferior to standard therapy for preventing net adverse clinical events and major adverse cardiac or cerebral events. In addition, abbreviated therapy was superior to standard therapy for limiting major or clinically relevant nonmajor bleeding events.

LIMITATIONS

- Approximately 4% of the patients who underwent screening, and 22% of the patients who were eligible for the trial, were enrolled.
- The duration of dual antiplatelet therapy varied in the standard-therapy group, as did the type of single antiplatelet therapy used in the abbreviated-therapy group.
- The results may not apply to patients who are at lower risk for bleeding or those who receive other stent types.

Links: Full Article | NEJM Quick Take | Editorial





Secondary Outcomes

Outcome	Abbreviated	Standard	Hazard Ratio
Death	3.3%	3.6%	0.92; 95% CI, 0.67 to 1.26
Stroke	0.7%	1.4%	0.52; 95% CI, 0.28 to 0.95
Myocardial Infarction	2.7%	2.1%	1.30; 95% CI, 0.88 to 1.91
Bleeding	8.9%	13.5%	0.64; 95% CI, 0.54 to 0.76

CONCLUSIONS

In patients at high risk for bleeding after receiving a drug-eluting stent, 1 month of dual antiplatelet therapy was noninferior to at least 2 months of additional treatment for preventing adverse clinical events overall and was associated with a lower risk of bleeding events.

Standard-Antikoagulation Sachsen-Anhalt:

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- ASS-Gabe periprozedural

Duale Therapie mit (N)OAK + Clopidogrel 75mg/die + PPI

CAVE! Kein Einsatz von Prasugrel oder Ticagrelor

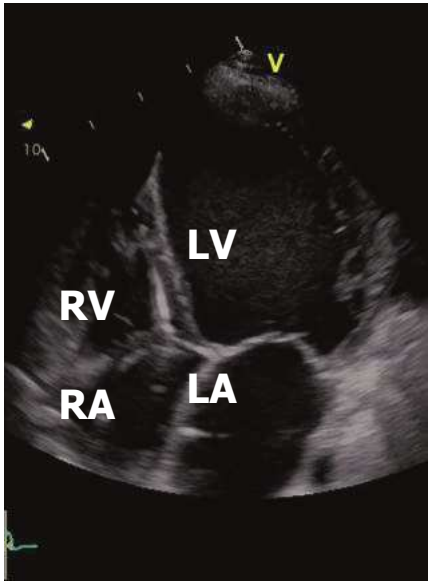
Dabigatran	2x150mg	2x110mg (Alter >80 Jahre oder Verapamil)
Rivaroxaban	1x15mg	1x10mg/die (GFR < 50ml/min)
Apixaban	2x5mg	2x2,5mg (Alter > 80 Jahre; Gewicht<60Kg;Krea >133 µmol/l – Cave: mind. 2 von 3 Kriterien)
Edoxaban	1x60mg	1x30mg (CrCl <50ml/min oder Gewicht <60 Kg oder Komed. mit Verapamil, Dronedaron)
VKA	Ziel INR 2-2,5	Cave! Ggf. abw. Ziel INR für mechanische Herzklappen beachten!

- Therapiedauer: 6 Monate bei elektiver PTCA und ACS

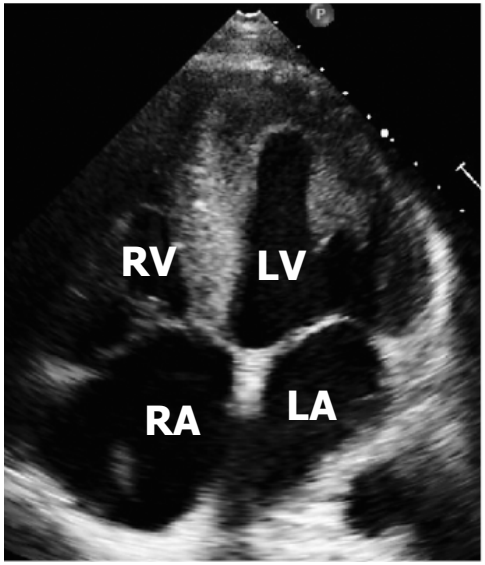
Definition der Herzinsuffizienz

Herzinsuffizienz mit reduzierter linksventrikulärer Ejektionsfraktion (Heart Failure with reduced Ejection Fraction, HFrEF)	Herzinsuffizienz mit geringgradig eingeschränkter linksventrikulärer Ejektionsfraktion (heart failure with mid-range Ejection fraction, HFmrEF)	Herzinsuffizienz mit erhaltener linksventrikulärer Ejektionsfraktion (Heart Failure with preserved Ejection Fraction, HFpEF)
Symptome +/- Zeichen*	Symptome +/- Zeichen*	Symptome +/- Zeichen*
LVEF < 40%	LVEF 40-49%	LVEF ≥ 50%
	• erhöhte natriuretische Peptide (BNP > 35 pg/ml und/oder NT-proBNP > 125 pg/mL) • echokardiografisch objektivierte strukturelle oder funktionelle Störungen des linken Ventrikels	

* nicht zwingend bei frühen Stadien und bei Patienten unter Diuretika-Therapie



HFrEF



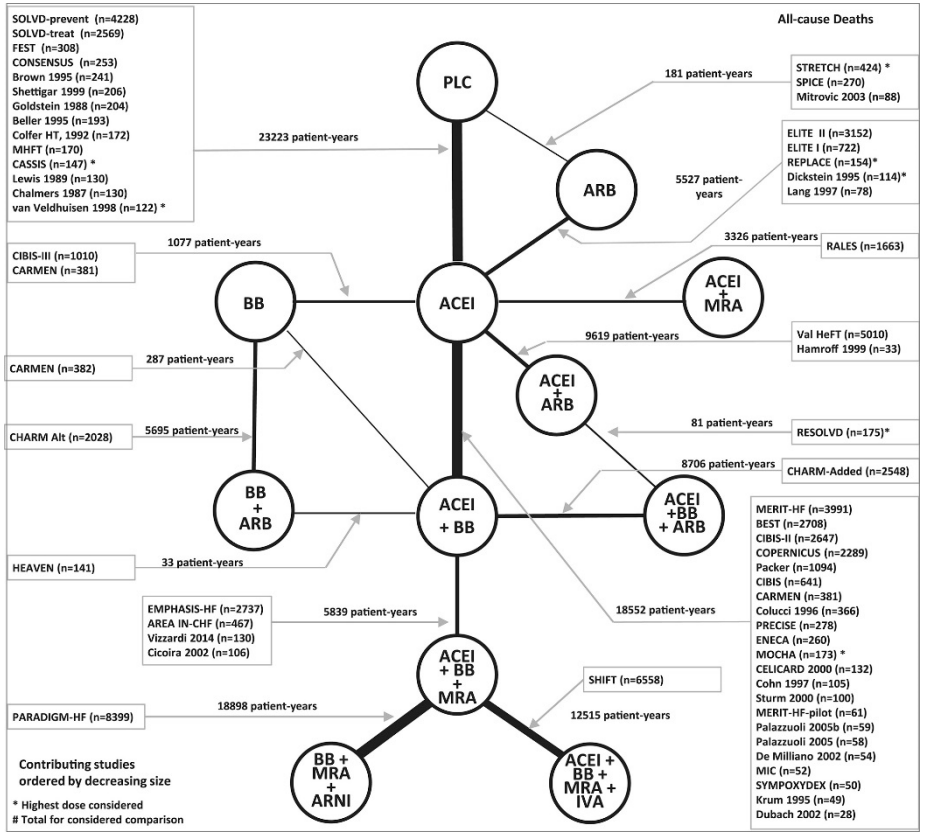
HFpEF

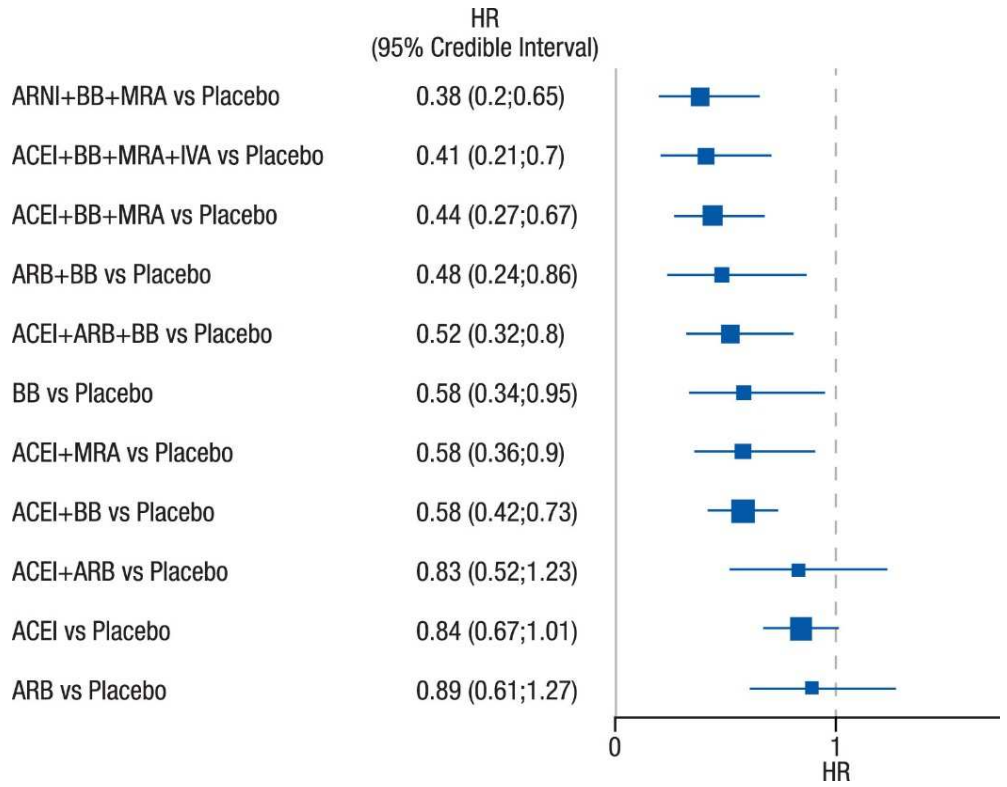
Medikamentöse Stufentherapie nach NYHA-Klassen bei Herzinsuffizienz mit reduzierter LVEF

		NYHA I (asymptomatische LV-Dysfunktion)	NYHA II	NYHA III	NYHA IV (nur in enger Kooperation mit Kardiologen)
prognoseverbessernd	**ACE-Hemmer**	indiziert	indiziert	indiziert	indiziert
	Angiotensinrezeptor-blocker	bei ACE-Hemmer Intoleranz	bei ACE-Hemmer Intoleranz	bei ACE-Hemmer Intoleranz	bei ACE-Hemmer Intoleranz
	Betarezeptorenblocker	nach Myokardinfarkt oder bei Hypertonie	indiziert	indiziert	indiziert
	Mineralokortikoid-rezeptorantagonisten		indiziert*	indiziert	indiziert
	Ivabradin		bei Betarezeptoren-blocker-Intoleranz oder additiv bei Patienten mit Herzfrequenz ≥ 75/min	bei Betarezeptoren-blocker-Intoleranz oder additiv bei Patienten mit Herzfrequenz ≥ 75/min	bei Betarezeptoren-blocker-Intoleranz oder additiv bei Patienten mit Herzfrequenz ≥ 75/min
	Sacubitril/Valsartan		als ACE-Hemmer/ARB-Ersatz bei persistierender Symptomatik**	als ACE-Hemmer/ARB-Ersatz bei persistierender Symptomatik**	als ACE-Hemmer/ARB-Ersatz bei persistierender Symptomatik**
symptomverbessernd	**Diuretika**		bei Flüssigkeitsretention	indiziert	indiziert
	Digitalisglykoside			bei Sinusrhythmus als Reservemittel (mit niedrigem Zielserumspiegel)	bei Sinusrhythmus als Reservemittel (mit niedrigem Zielserumspiegel)
		bei nicht beherrschbarem tachyarrhythmischem Vorhofflimmern			

Bei bestehender HI-Symptomatik Intensivierung der Therapie (bitte auftitrieren alle 2–4 Wochen bzw. rechtzeitiges Ergänzen einer Medikation)

Additiver Nutzen der medikamentösen Stufentherapie von HFrEF-Patienten (Abnahme d. Mortalität)





Zukunft der medikamentösen Stufentherapie

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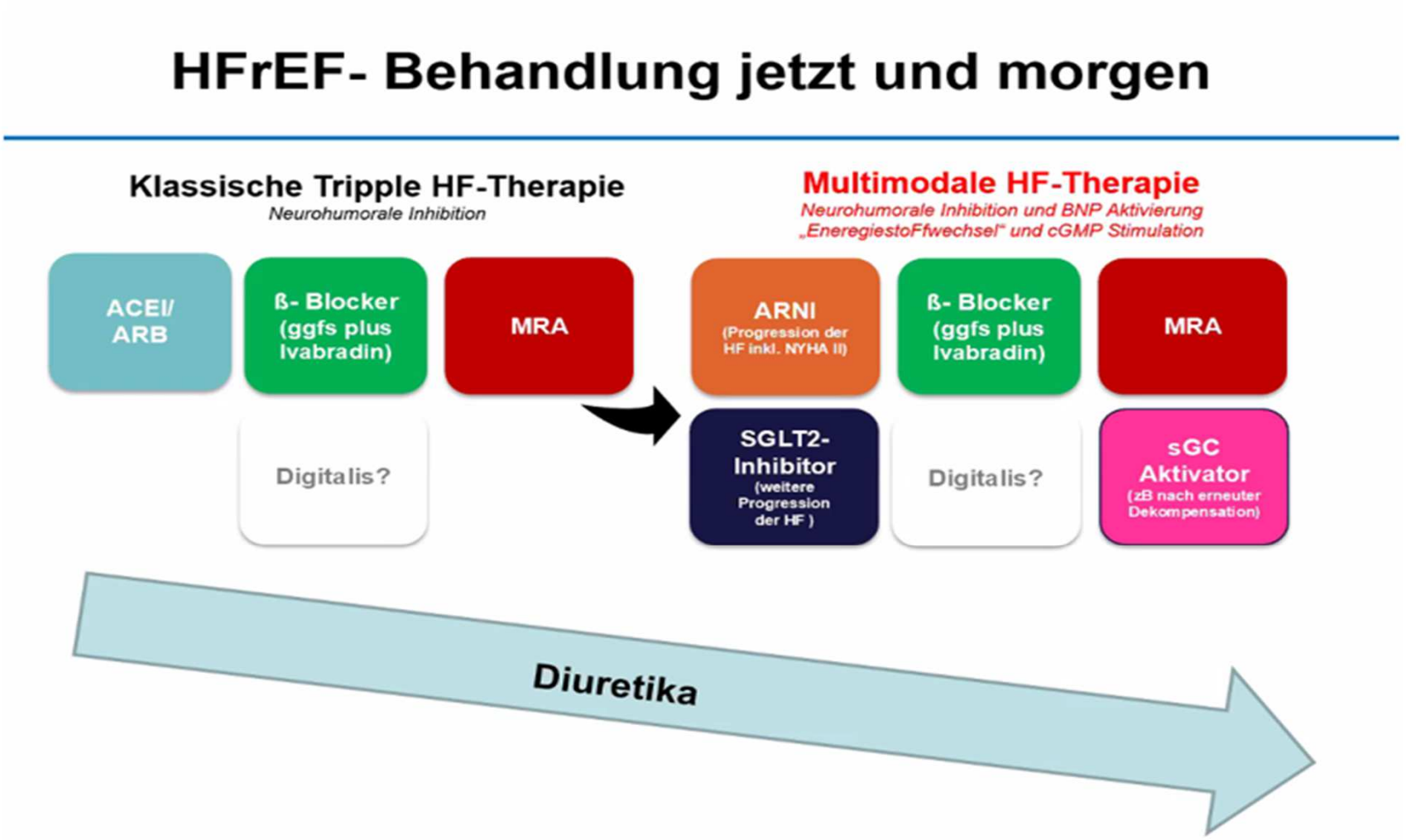

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SGLT2 inhibitors: the statins of the 21st century

Eugene Braunwald [1,2*]

[1]TIMI Study Group, Division of Cardiovascular Medicine, Brigham and Women's Hospital, Hale Building for Transformative Medicine, Suite 7022, 60 Fenwood Road, Boston, MA 02115, USA; and [2]Department of Medicine, Harvard Medical School, Boston, MA, USA

A relatively small number of drugs have been responsible for major advances in medical practice. The discovery, development, and elucidation of the mechanisms of action of aspirin, penicillin, and statins are remarkable success stories, each with some surprises and each crowned by a Nobel Prize. The sodium glucose co-transporter inhibitors have been proven effective in the treatment of type 2 diabetes mellitus, various forms of heart failure, and kidney failure and represent *the, or one of the*, major pharmacological advances in cardiovascular medicine in the 21st century.

A bit of history

The story begins in 1835, when C. Petersen, a French chemist, isolated phlorizin from the root bark of the apple tree, which was first used in the treatment of malaria. In 1886, von Mering, a German professor of medicine, discovered the glucosuric and consequent plasma glucose lowering effects of phlorizin.[1]

During the first half of the 20th century, it was learned that the glu-

SGLT2is, dapagliflozin, canagliflozin, and empagliflozin, for reducing plasma glucose in persons with T2DM. Early placebo-controlled trials with these agents showed that in appropriate doses they lowered HgbA1c by an absolute amount of around 0.6%, caused moderate reductions in body weight and blood pressure, and were generally well tolerated. They were considered to be reasonably effective second-tier anti-diabetic agents, and were usually added to metformin or a sulfonylurea.

EMPEROR-Reduced: Studiendesign

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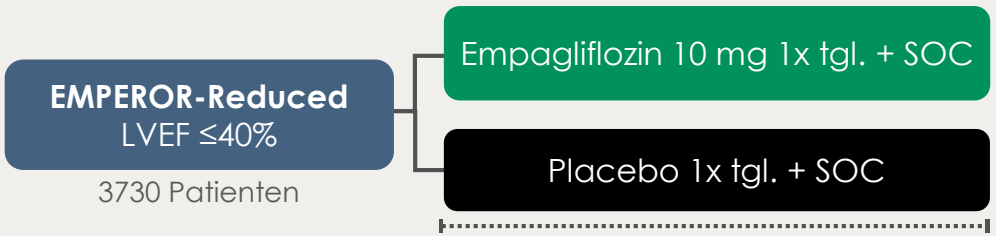
Randomisierte doppelblinde Placebo-kontrollierte Phase-III-Studie

Studienziel: Wirksamkeit und Verträglichkeit von Empagliflozin im Vergleich zu Placebo zusätzlich zu adäquater Standardtherapie (SOC) bei Patienten mit Herzinsuffizienz und reduzierter Ejektionsfraktion (HFrEF)

Population: mit/ohne T2D, Alter ≥18 Jahre, chronische Herzinsuffizienz (NYHA-Klasse II–IV)

Studiendesign



Endpunkte

PRIMÄRER KOMBINIERTER ENDPUNKT

Zeit bis zum ersten Ereignis (adjudizierte HHI oder adjudizierter CV-Tod)

KONFIRMATORISCHE SEKUNDÄRE ENDPUNKTE

- Rate der Abnahme der geschätzten glomerulären Filtrationsrate (CKD-EPI) gegenüber Baseline

CV, kardiovaskulär; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; LVEF, linksventrikuläre Ejektionsfraktion; NYHA, New York Heart Association; T2D, Typ-2-Diabetes; tgl., täglich Packer M et al. Eur J Heart Fail 2019;21:1270-1278; Packer M et al. N Engl J Med 2020;383:1413-1424

Primärer Endpunkt: Kombination aus kardiovaskulärem Tod oder Hospitalisierung aufgrund einer Herzinsuffizienz

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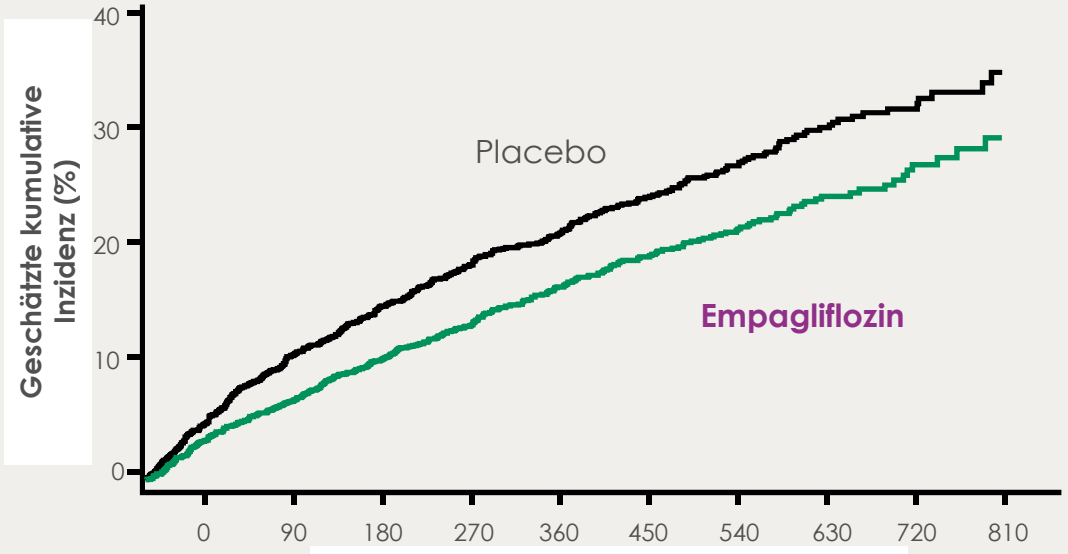


Patienten mit Risiko										
Placebo	1867	1715	1612	1345	1108	854	611	410	224	109
Empagliflozin	1863	1763	1677	1424	1172	909	645	423	231	101

RRR 25%

ARR 5.2%

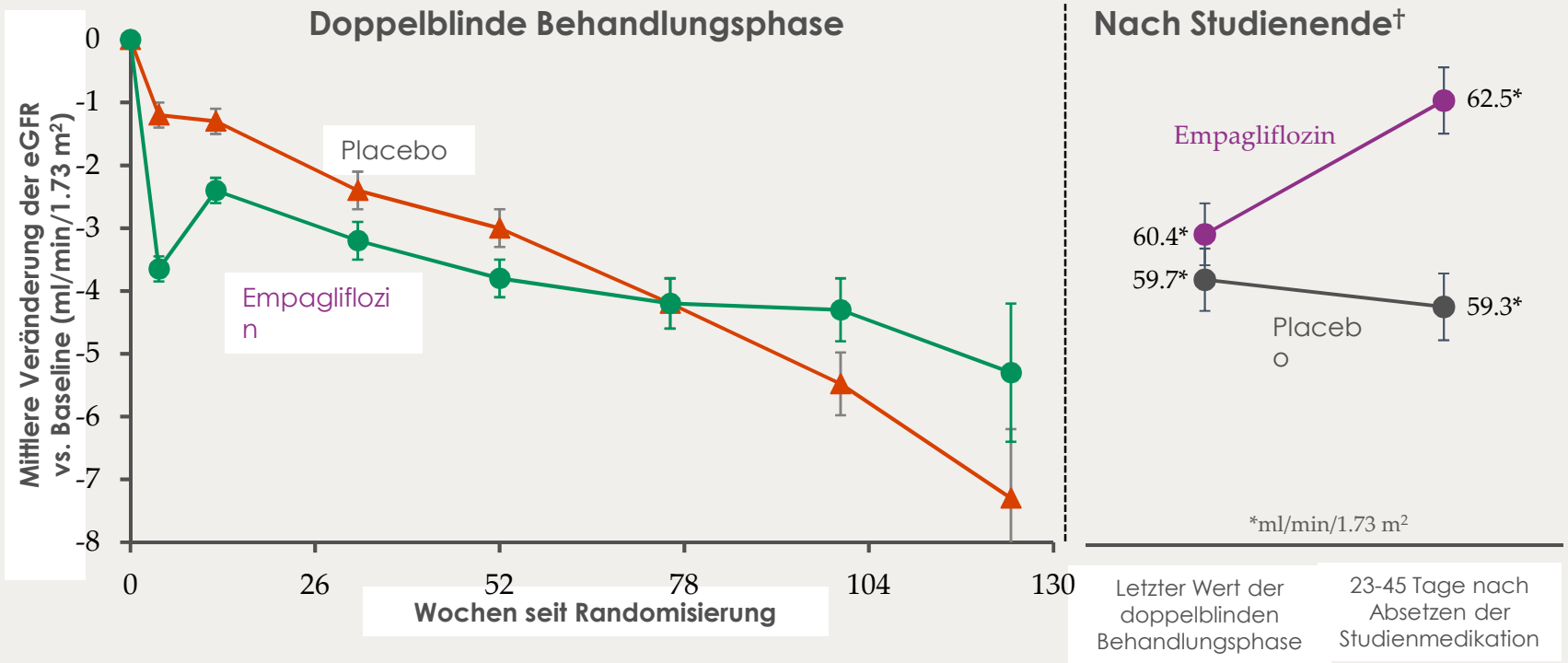
NNT = 19 (16 Monate)

HR 0.75
(95% KI 0.65-0.86)
p<0.001

Empagliflozin:
361 Patienten mit Ereignis
Rate: **16/100** Patientenjahre
Placebo:
462 Patienten mit Ereignis
Rate: **21/100** Patientenjahre

Cox Regressionsmodell einschließlich Kovariaten Alter, Geschlecht, Region, Behandlung, Baseline eGFR, Diabetes-Status und LVEF. CV, kardiovaskulär; eGFR, geschätzte glomeruläre Filtrationsrate; LVEF, linksventrikuläre Ejektionsfraktion; ARR, absolute Risikoreduktion; RRR, relative Risikoreduktion. NNT, Anzahl der notwendigen Behandlungen Packer M et al. N Engl J Med 2020;383:1413-1424

Empagliflozin verlangsamte den Abfall der GFR versus Placebo



Digitalis-Glykoside

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Presseinformation

16. Dezember 2019

MHH-Ärzte wollen Therapie von Herzinsuffizienz verbessern

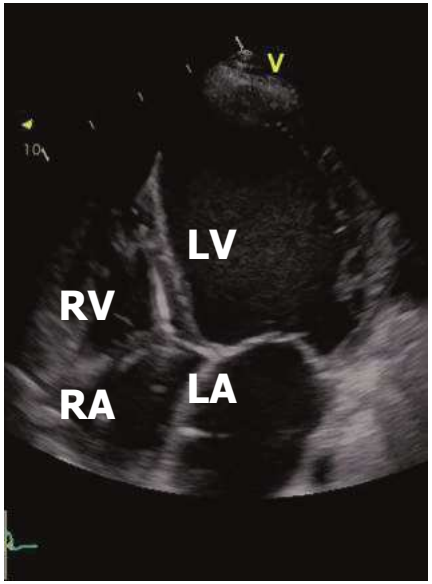
Bundesministerium für Bildung und Forschung fördert Digitoxin-Studie mit weiteren 3,8 Millionen Euro

In Deutschland leiden etwa drei Millionen Menschen an einer chronischen fortgeschrittenen Herzschwäche. Die Erkrankung ist eine der häufigsten Ursachen dafür, dass Patientinnen oder Patienten ins Krankenhaus eingewiesen werden müssen oder an den Folgen sterben. In einer großen, multizentrischen Untersuchung prüfen Wissenschaftlerinnen und Wissenschaftler der Klinik für Kardiologie und Angiologie der Medizinischen Hochschule Hannover (MHH) die Wirksamkeit des Medikamentes Digitoxin. Jetzt hat das Bundesministerium für Bildung und Forschung (BMBF) die Verlängerung der „DIGIT-HF-Studie" bis zum Jahr 2024 bewilligt. Es stellt für die zweite Förderperiode etwa 3,8 Millionen Euro zur Verfügung. Mit weiteren 700.000 Euro unterstützt die Brauckmann-Wittenberg-Herz-Stiftung das Projekt.

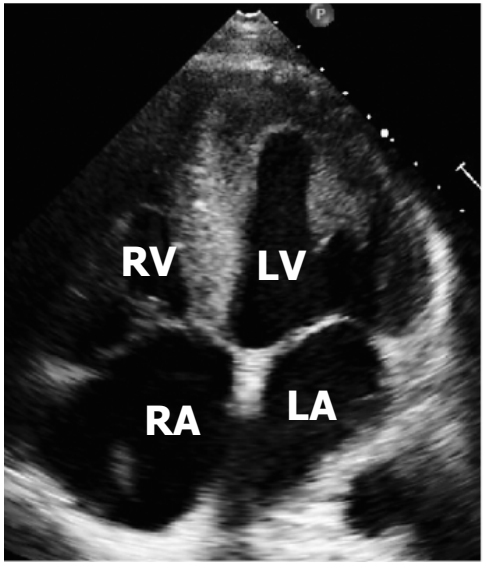
Definition der Herzinsuffizienz

Herzinsuffizienz mit reduzierter linksventrikulärer Ejektionsfraktion (Heart Failure with reduced Ejection Fraction, HFrEF)	Herzinsuffizienz mit geringgradig eingeschränkter linksventrikulärer Ejektionsfraktion (heart failure with mid-range Ejection fraction, HFmrEF)	Herzinsuffizienz mit erhaltener linksventrikulärer Ejektionsfraktion (Heart Failure with preserved Ejection Fraction, HFpEF)
Symptome +/- Zeichen*	Symptome +/- Zeichen*	Symptome +/- Zeichen*
LVEF < 40%	LVEF 40-49%	LVEF ≥ 50%
	• erhöhte natriuretische Peptide (BNP > 35 pg/ml und/oder NT-proBNP > 125 pg/mL) • echokardiografisch objektivierte strukturelle oder funktionelle Störungen des linken Ventrikels	

* nicht zwingend bei frühen Stadien und bei Patienten unter Diuretika-Therapie

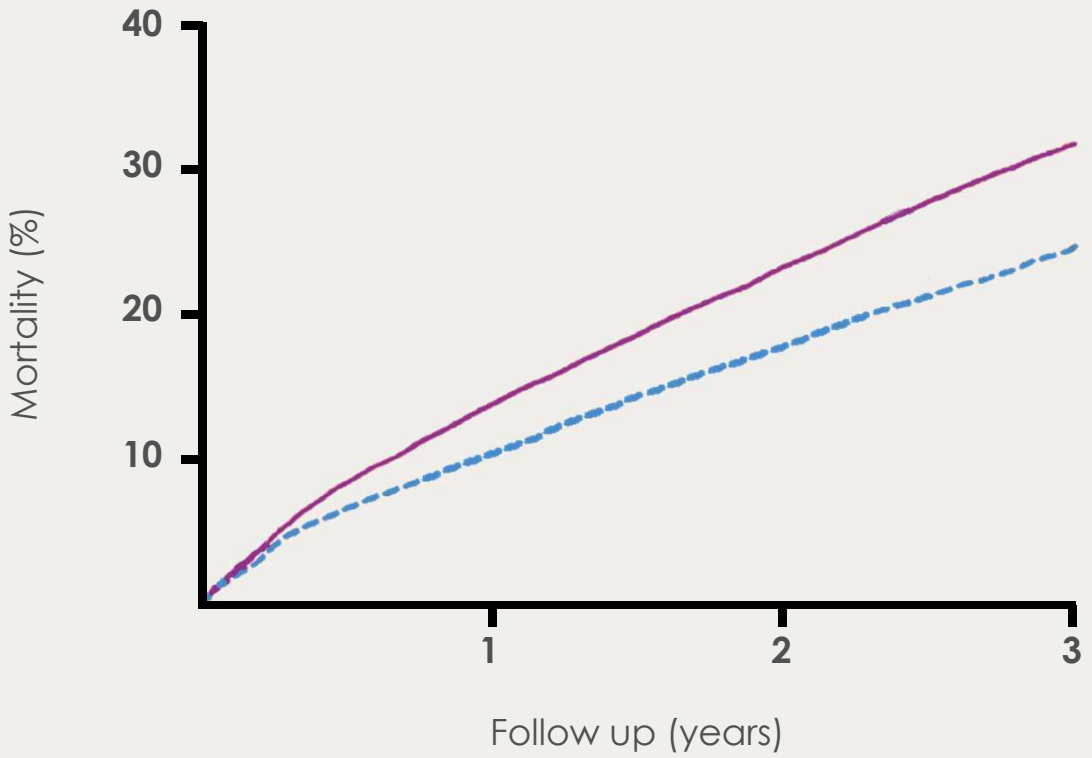


HFrEF



HFpEF

Both, HFpEF and HFrEF are associated with high mortality rates



Metanalysis (n=31 studies)*

n=41.972 patients

HFpEF: n=10.347

HFrEF: n=31.625

*Analysis based on individual patient data, adjusted for age, sex, etiology, hypertension, diabetes and atrial fibrillation; MAGGIC Group Eur Heart J 2012;33:1750.

EMPEROR-Preserved study design

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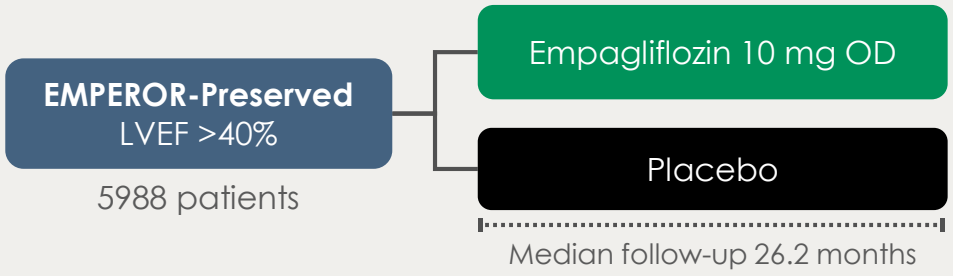
Phase III trial* in patients with HFpEF

Aim: To investigate the safety and efficacy of empagliflozin versus placebo in patients with HF with **preserved ejection fraction**

Population: T2D and non-T2D, aged ≥18 years, chronic HF (NYHA class II–IV)



COMPOSITE PRIMARY ENDPOINT

- **Time to first event of adjudicated CV death or adjudicated HHF**

CONFIRMATORY KEY SECONDARY ENDPOINTS

- **First and recurrent adjudicated HHF**
- **Slope of change in eGFR (CKD-EPI) from baseline**

*Randomized, double-blind, placebo-controlled trial.
CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; eGFR, estimated glomerular filtration rate; NYHA, New York Heart Association; OD, once daily. Anker SD et al. Eur J Heart Fail. 2019;21:1279; Anker S et al. N Engl J Med. 2021; 10.1056/NEJMoa2107038.

Empagliflozin demonstrated a clinically meaningful 21% RRR in the primary endpoint of CV death or HHF

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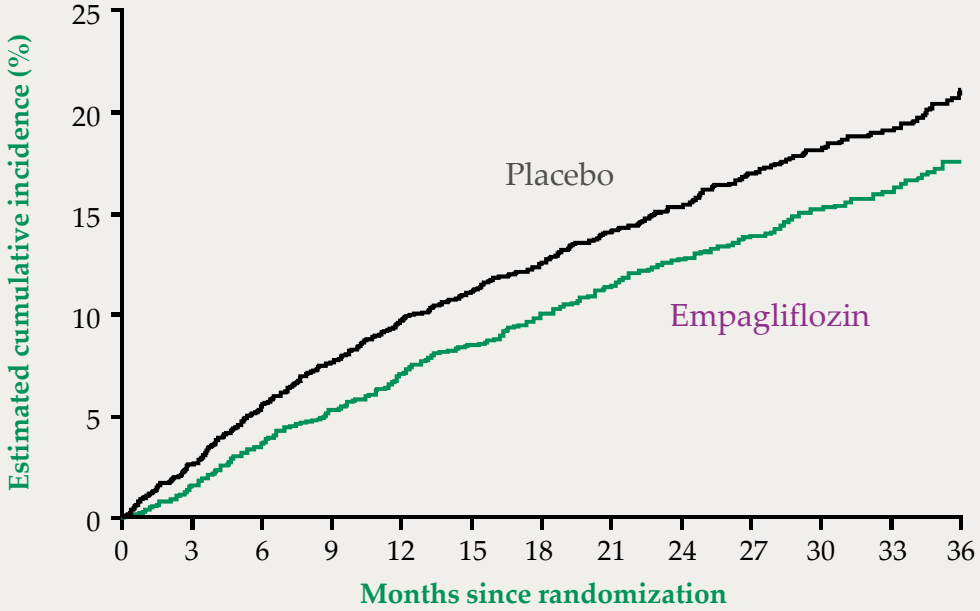


Patients at risk

Placebo	2991	2888	2786	2706	2627	2424	2066	1821	1534	1278	961	681	400
Empagliflozin	2997	2928	2843	2780	2708	2491	2134	1858	1578	1332	1005	709	402

RRR 21%

ARR 3.3%

NNT*=31

HR: 0.79
(95% CI: 0.69-0.90)
$p<0.001$

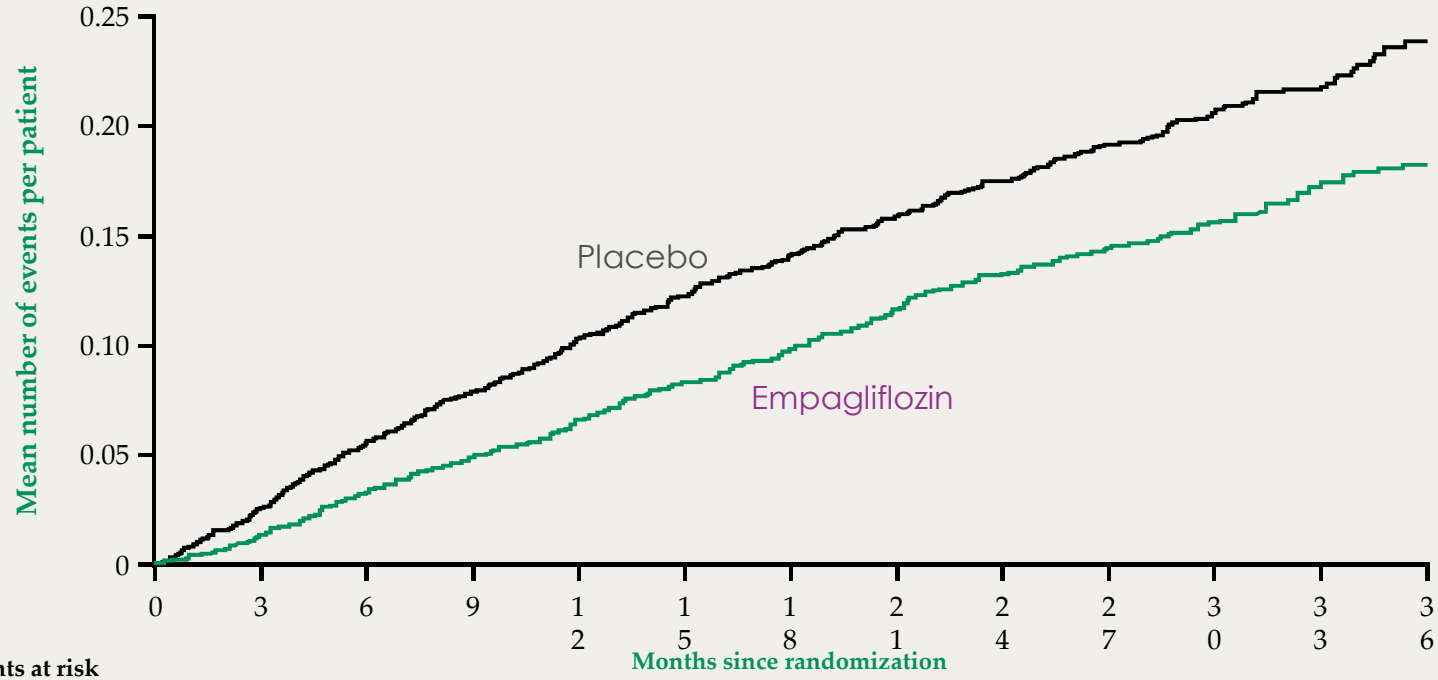
Empagliflozin:
415 (13.8%) patients with event
Rate: 6.9/100 patient-years
Placebo:
511 (17.1%) patients with event
Rate: 8.7/100 patient-years

*During a median trial period of 26 months. ARR, absolute risk reduction; CI, confidence interval; HR, hazard ratio; NNT, number needed to treat; RRR, relative risk reduction. Anker S et al. N Engl J Med. 2021; 10.1056/NEJMoa2107038.

Empagliflozin reduced first and recurrent HHF by 27% in a confirmatory secondary endpoint

ASKLEPIOS

SC-DE-02271



Patients at risk

Placebo	2991	2945	2901	2855	2816	2618	2258	1998	1695	1414	1061	747	448
Empagliflozin	2997	2962	2913	2869	2817	2604	2247	1977	1684	1429	1081	765	446

RRR 27%

HR: 0.73
(95% CI: 0.61-0.88)
p<0.001

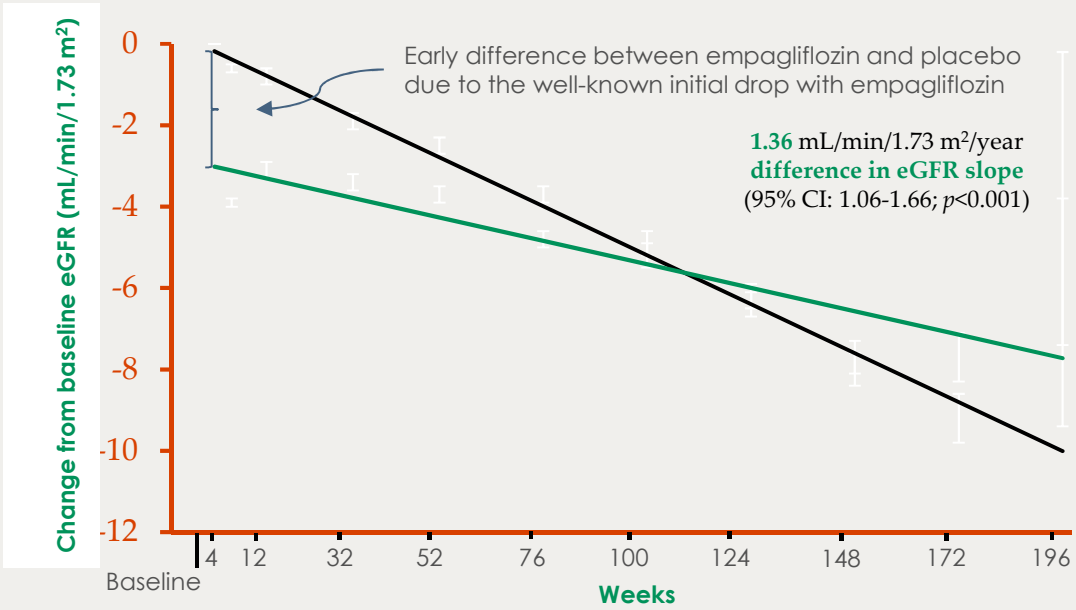
Empagliflozin: 407 patients with event
Placebo: 541 patients with event

Anker S et al. N Engl J Med. 2021; 10.1056/NEJMoa2107038.

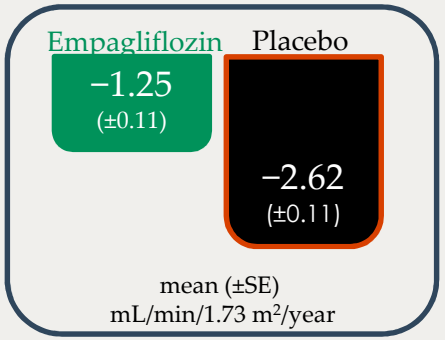
Empagliflozin protected the kidney by significantly slowing the decline in kidney function

ASKLEPIOS

SC-DE-02271



The rate of eGFR decline in patients treated with empagliflozin was half that of patients treated with placebo



eGFR slope = rate of decline (and is a measure for long-term renal function). eGFR slope is analysed based on on-treatment data using a random coefficient model including age, baseline eGFR and baseline LVEF as linear covariates and sex, region, baseline diabetes status, and baseline by time and treatment by time interactions as fixed effects; the model allows for randomly varying slope and intercept between patients.
eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; SE, standard error.
Developed from data reported in Anker S et al. N Engl J Med. 2021; 10.1056/NEJMoa2107038.

Zukunft der medikamentösen Stufentherapie

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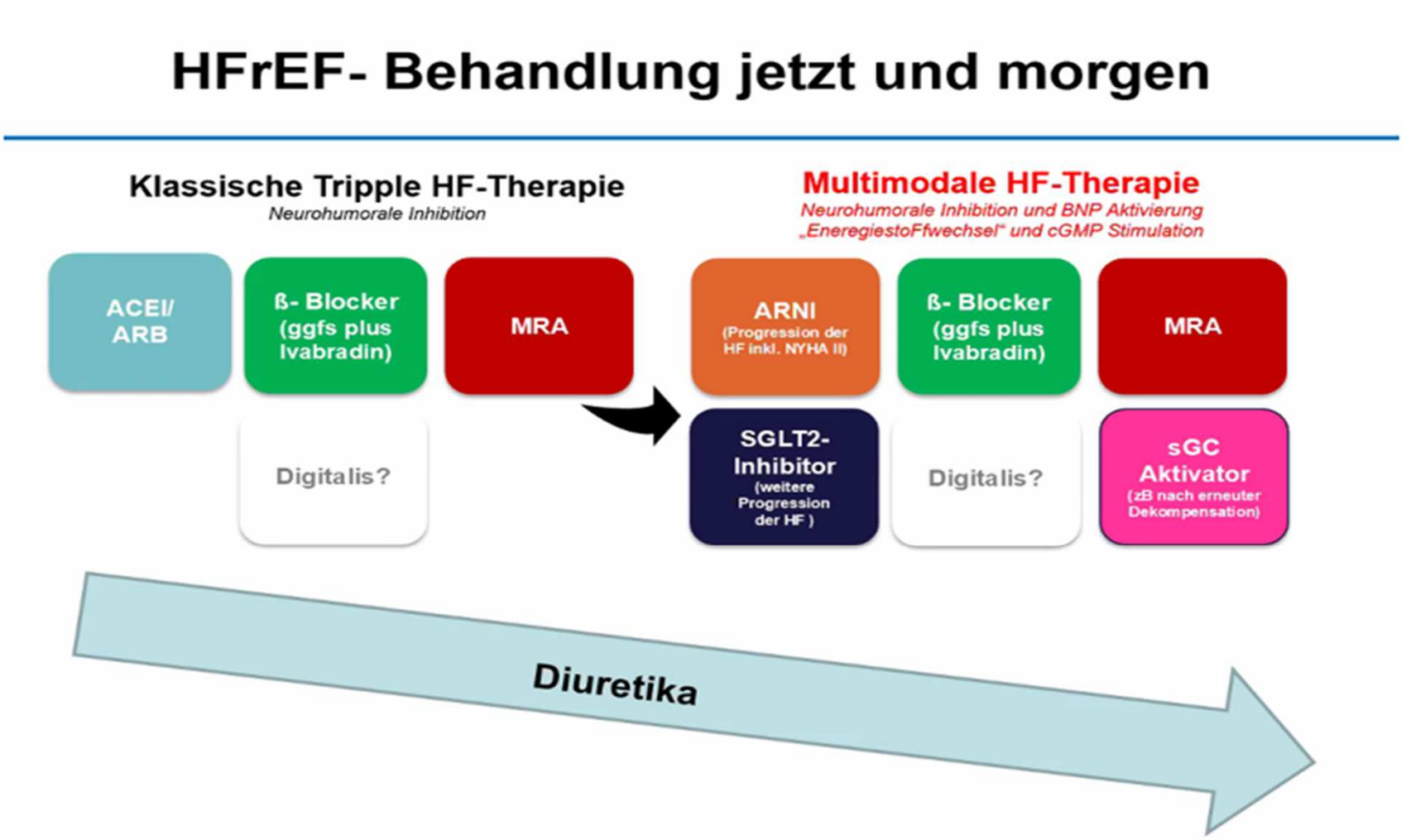
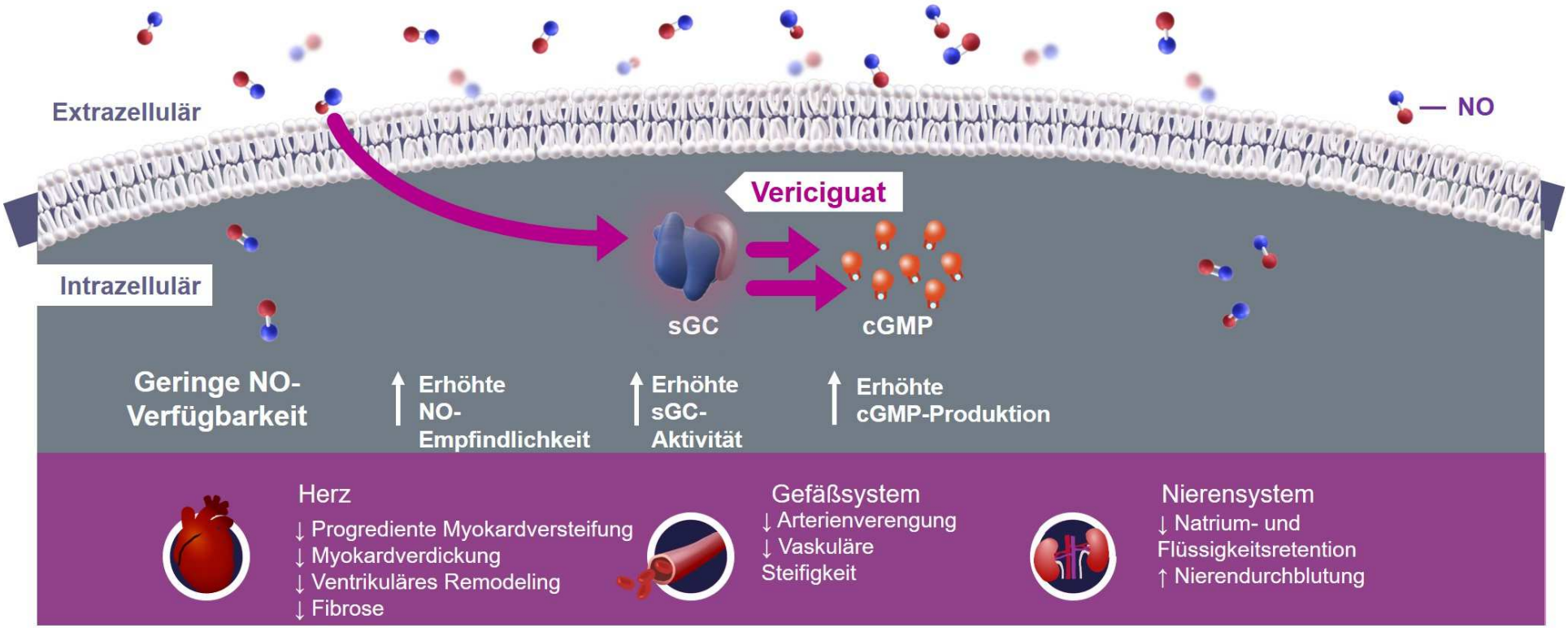


Der NO-sGC-cGMP Signalweg wird erstmals in der Herzinsuffizienz adressiert



Ergebnisse der VICTORIA Studie im primären Endpunkt

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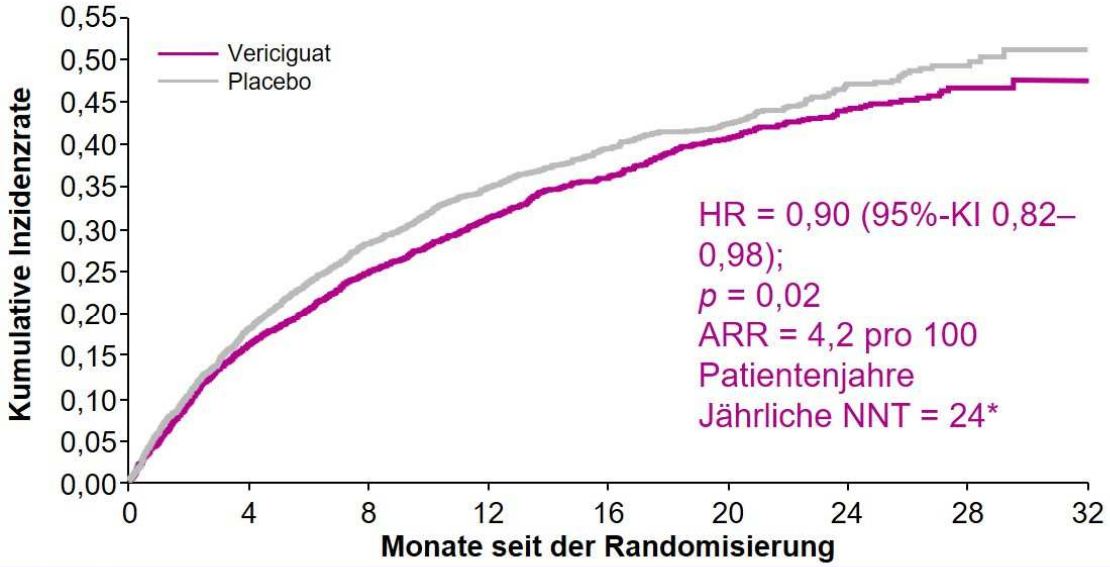
Zeit bis zum CV-Tod oder zur ersten HFH



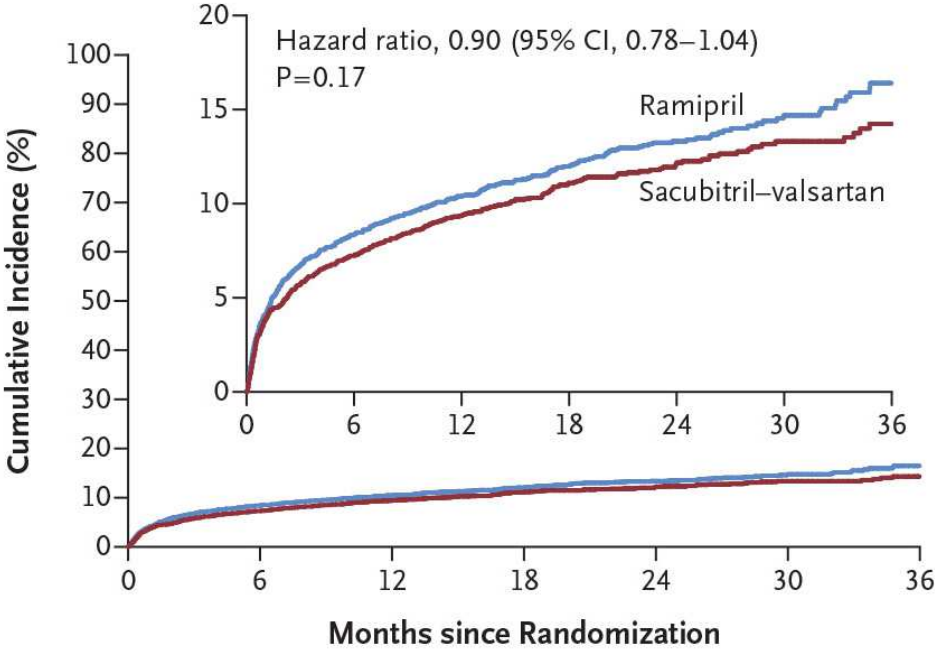
Anzahl Risikopatienten									
Vericiguat	2526	2099	1621	1154	826	577	348	125	1
Placebo	2524	2053	1555	1097	772	559	324	110	0

- Mediane Behandlungsdauer für Beurteilung des primären Endpunkts: 10,8 Monate
- Die jährlichen Ereignisraten für Vericiguat und Placebo pro 100 Patientenjahre betrugen 33,6 bzw. 37,8.

*Berechnungen: jährliche NNT = 100/4,2 = 24.
ARR: absolute Ratenreduktion; CV: kardiovaskulär; HFH: HF-bedingte Hospitalisierung; HR: Hazard Ratio; KI: Konfidenzintervall; NNT: Anzahl der notwendigen Behandlungen (Number Needed to Treat).
1. Armstrong PW et al. *N Engl J Med.* 2020;382:1883–1893.

Angiotensin Receptor–Neprilysin Inhibition in Acute Myocardial

ASKLEPIOS
PARADISE-MI



RESEARCH SUMMARY

Angiotensin Receptor–Neprilysin Inhibition in Acute Myocardial Infarction

Pfeffer MA et al. DOI: 10.1056/NEJMoa2104508

CLINICAL PROBLEM

The angiotensin receptor–neprilysin inhibitor sacubitril–valsartan appears to improve outcomes more effectively than angiotensin-converting–enzyme (ACE) inhibitor therapy in patients with symptomatic heart failure. Whether sacubitril–valsartan may improve outcomes in patients with acute myocardial infarction is unknown.

CLINICAL TRIAL

Design: An international, multicenter, randomized, double-blind, active-comparator trial examined whether sacubitril–valsartan was superior to the ACE inhibitor ramipril in reducing the risk of death from cardiovascular causes or incident heart failure in patients with acute myocardial infarction.

Intervention: 5661 adults without a history of heart failure who had had a myocardial infarction in the previous week — complicated by a reduced left ventricular ejection fraction, pulmonary congestion, or both — were randomly assigned to receive sacubitril–valsartan or ramipril twice daily. The primary outcome was a composite of death from cardiovascular causes or incident heart failure (hospitalization for heart failure or symptomatic outpatient heart failure).

RESULTS

Efficacy: During a median follow-up of 22 months, the incidence of the primary outcome did not differ significantly between the sacubitril–valsartan and ramipril groups.

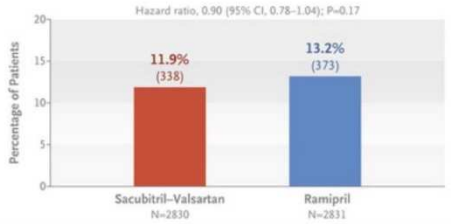
Safety: A similar percentage of patients in each group discontinued the trial drug because of adverse events. Hypotension was more common with sacubitril–valsartan, and cough was more common with ramipril.

LIMITATIONS AND REMAINING QUESTIONS

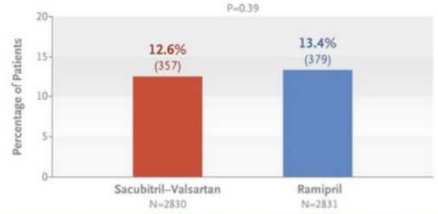
- The effects of sacubitril–valsartan on other outcomes, including death from cardiovascular causes alone or death from any cause, were not studied in the present trial except in exploratory analyses.

Links: Full Article | NEJM Quick Take

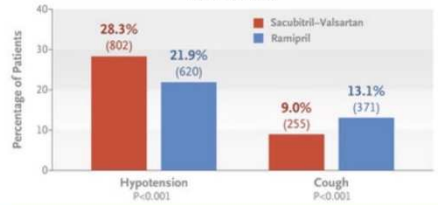
Death from Cardiovascular Causes or Incident Heart Failure (Primary Composite Outcome)



Treatment Discontinuation because of Adverse Events



Adverse Events

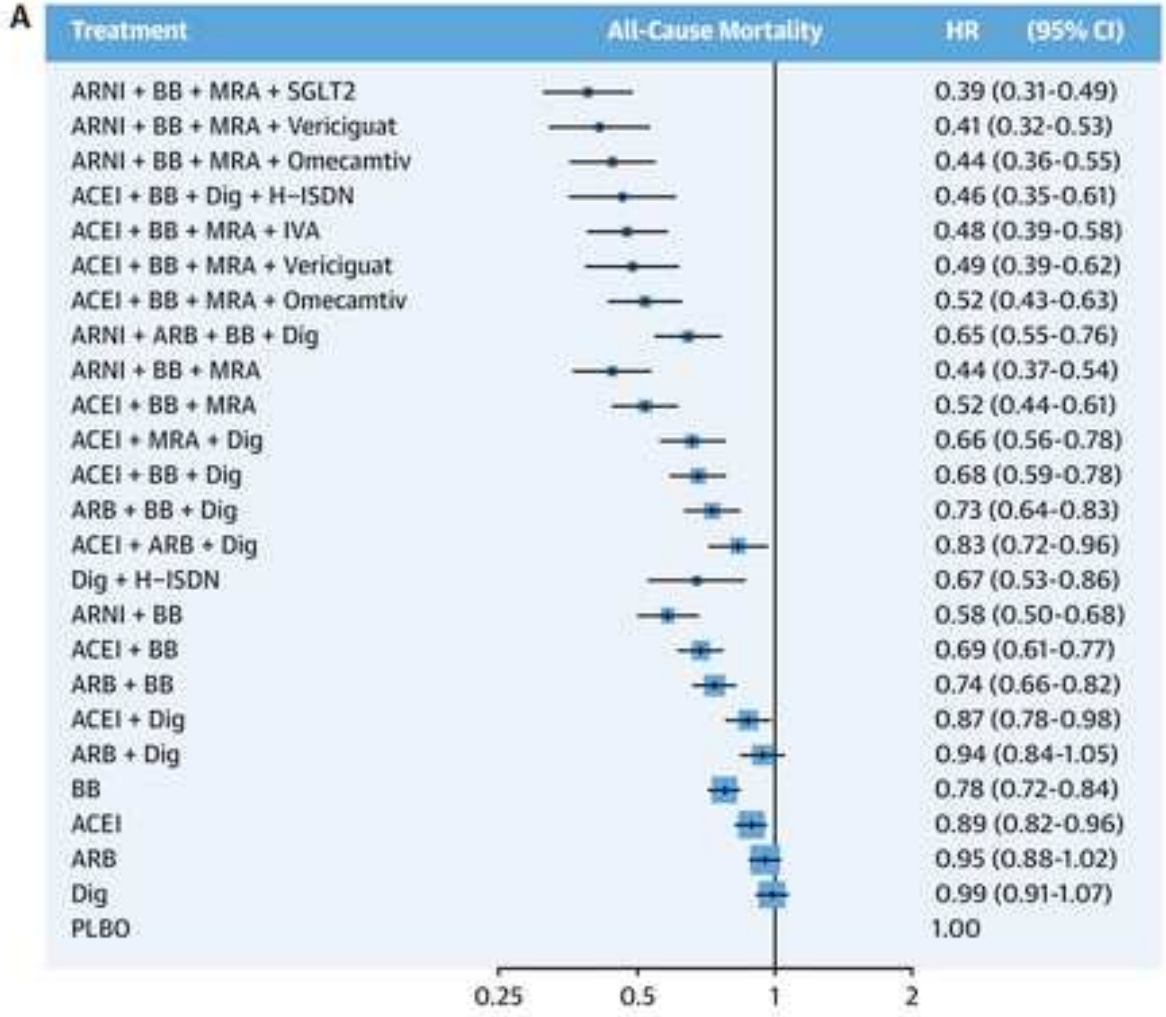


CONCLUSIONS

In patients with acute myocardial infarction plus a reduced left ventricular ejection fraction, pulmonary congestion, or both, sacubitril–valsartan was not associated with a lower combined risk of death from cardiovascular causes or incident heart failure than ramipril.

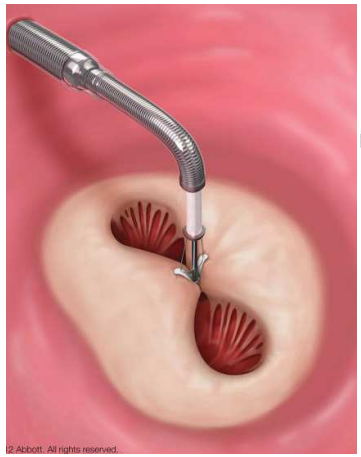
Additiver Nutzen der medikamentösen Stufentherapie von HFrEF-Patienten (Abnahme d. Mortalität)

ASKLEPIOS

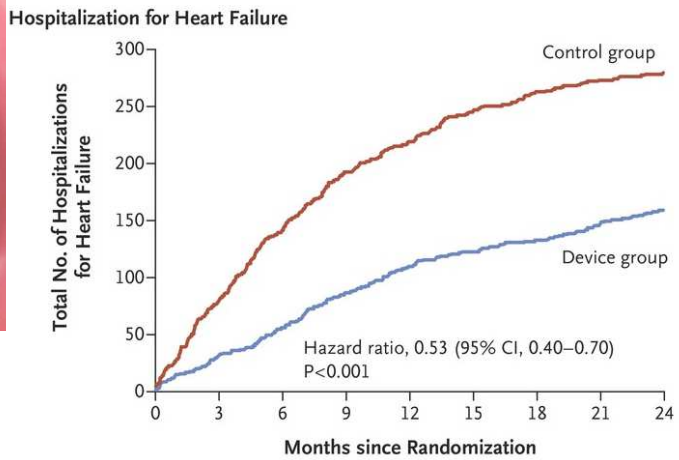


Tromp, J. et al. J Am Coll Cardiol HF. 2022;10(2):73-84.

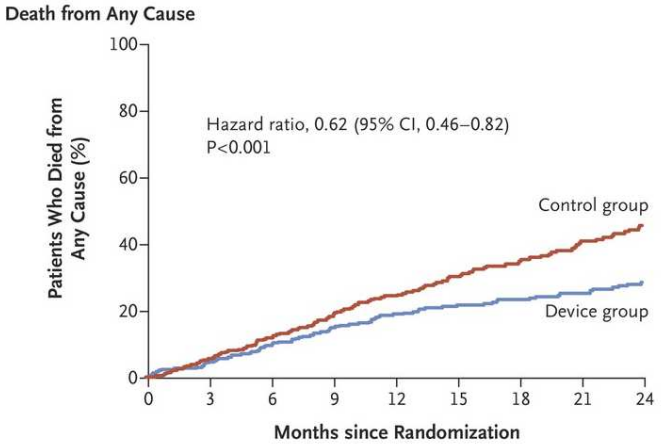
Mitra-Clip



COAPT-Studie

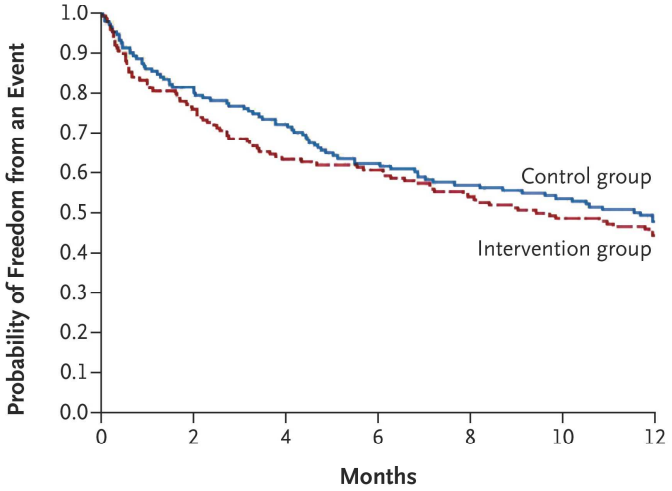


No. at Risk									
Control group	312	294	271	245	219	176	145	121	88
Device group	302	286	269	253	236	191	178	161	124



No. at Risk									
Control group	312	294	271	245	219	176	145	121	88
Device group	302	286	269	253	236	191	178	161	124

Mitra-FR Studie



No. at Risk							
Control group	152	123	109	94	86	80	73
Intervention group	151	114	95	91	81	73	67

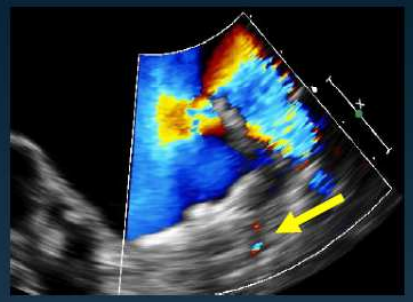
Amulet und Watchman System zum LAA-Verschluß

Amulet™
Left Atrial Appendage Occluders

WATCHMAN™
LAA Closure Device

LAA patency at 45-day TEE

AMULET
13.7%
(n=13/95)



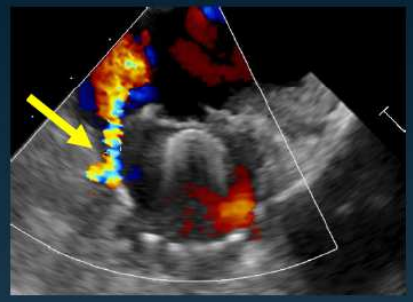
NO PDL >5mm

NO MULTIPLE PDLs

VS.

0.50 (0.27-0.91);
P= 0.020

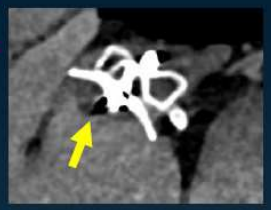
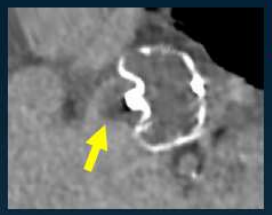
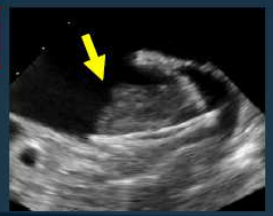
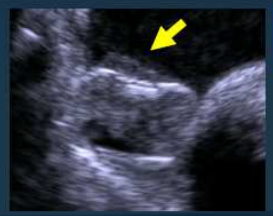
WATCHMAN/FLX
27.5%
(n=25/91)



NO PDL >5mm

2.2% MULTIPLE PDLs
(all in Watchman 2.5)

Device Related Thrombus at 45 days

	AMULET		WATCHMAN/FLX	
CCTA				
Definite DRT	0.9% (n=1/107)	 VS.	 3.0% (n=3/101)	0.31 (0.03-2.98); P= 0.285
Definite or possible DRT	3.7% (n=4/107)	VS.	9.9% (n=10/101)	0.38 (0.12-1.17); P= 0.076
TEE				
	2.1% (n=2/95)	 VS.	 5.5% (n=5/91)	0.38 (0.08-1.93); P= 0.225
«as treated population»	1.1% (n=1/92)	VS.	6.4% (n=6/94)	0.17 (0.02-1.39); P= 0.058

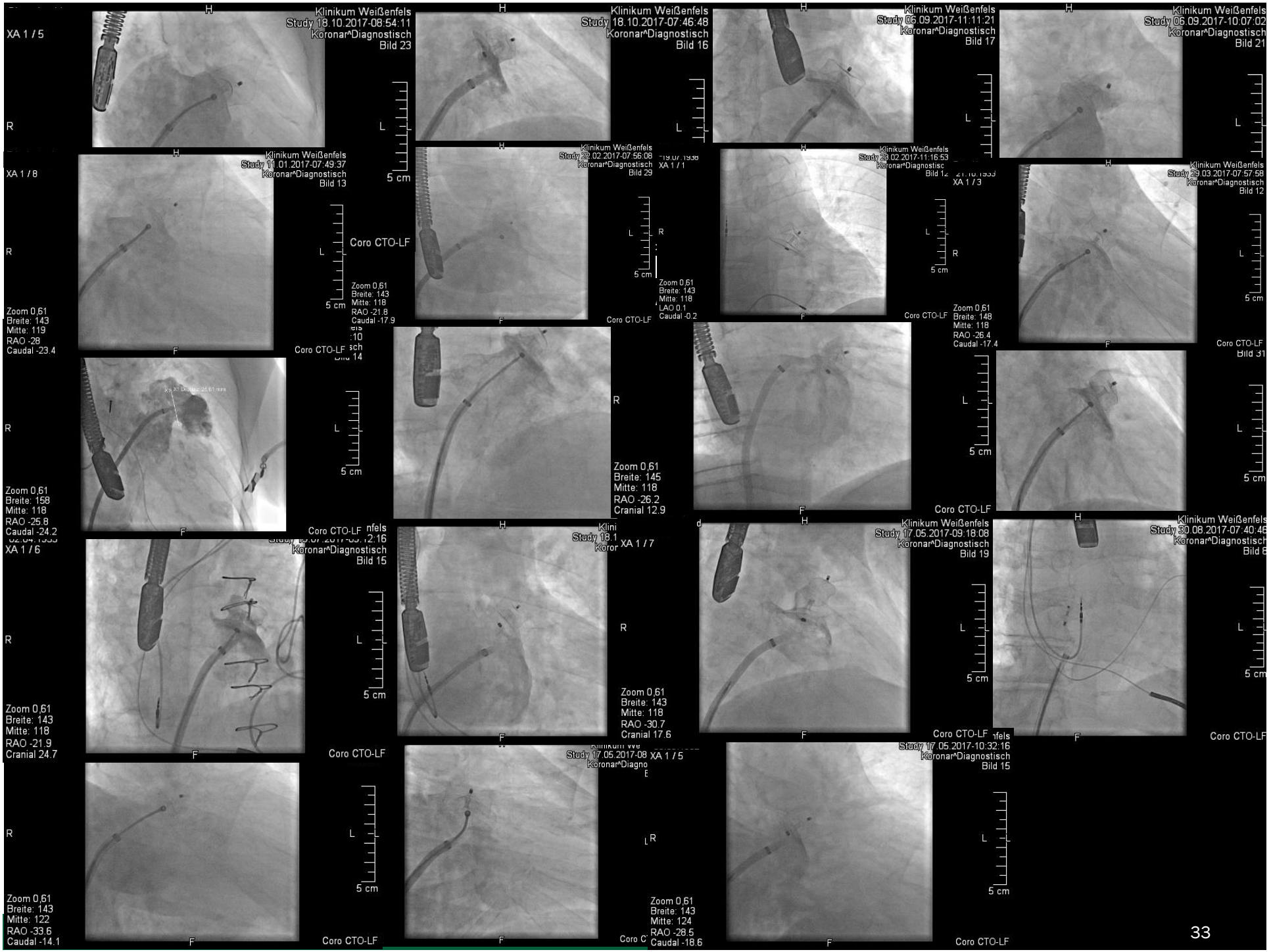
CRF TCT

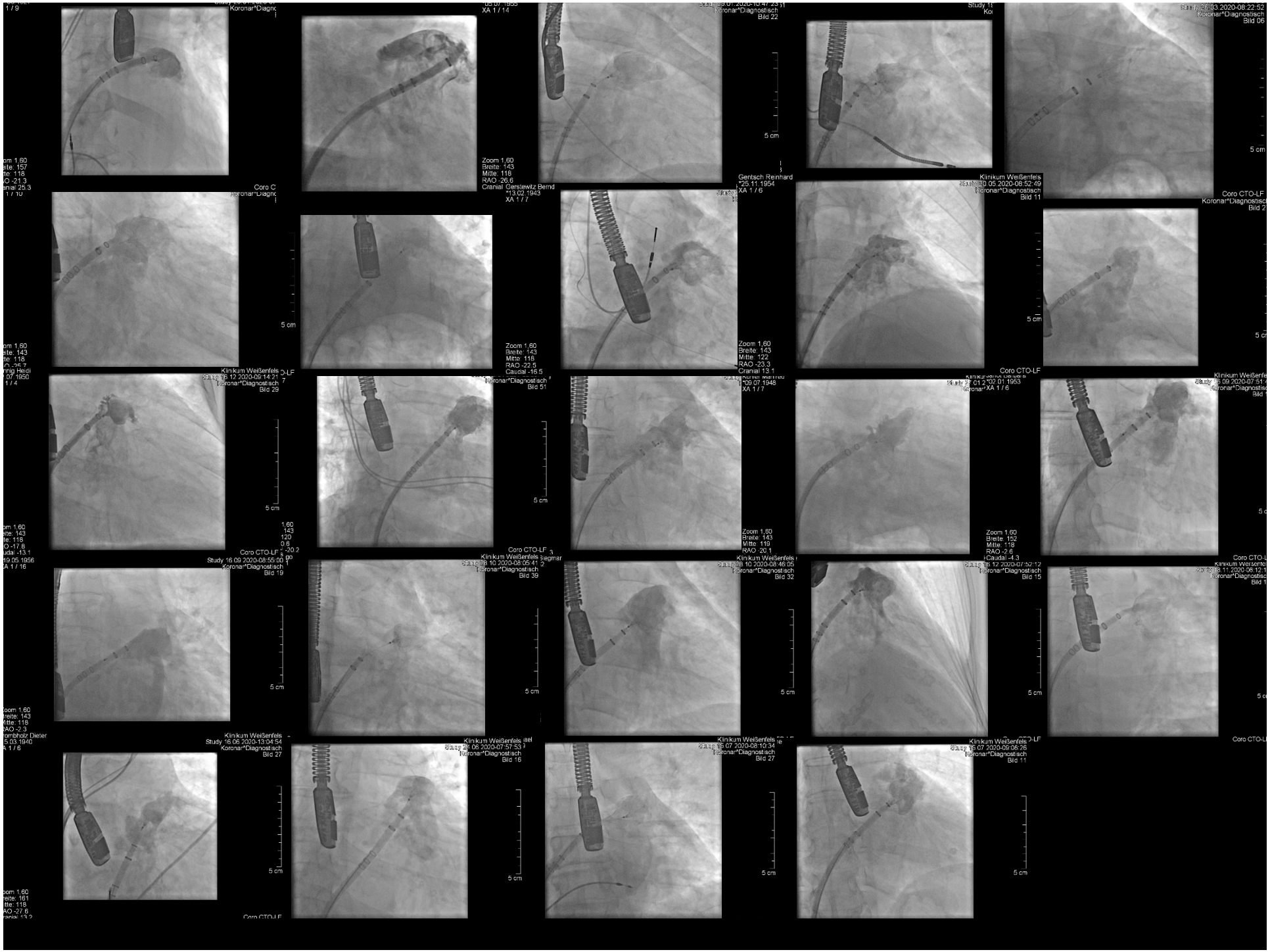
Procedure related complications

	Amulet (N=111)	Watchman/FLX (N=110)	Amulet vs Watchman Risk ratio (95% CI)	P value
Major procedure related complication, no. (%) *	**10 (9.0%)**	**3 (2.7%)**	**3.30 (0.93 - 11.68)**	**0.047**
Death, no. (%)	2 (1.8%)	0 (0.0%)		0.498
Cerebrovascular event, no. (%)	2 (1.8%)	0 (0.0%)		0.498
Systemic embolism, no. (%)	0 (0.0%)	0 (0.0%)		1
Major bleeding (BARC 3-5), no. (%) ¶	8 (7.2%)	2 (1.8%)	3.96 (0.86 - 18.25)	0.054
Clinically relevant pericardial effusion, no. (%)	4 (3.6%)	0 (0.0%)		0.122
Device embolization, no. (%)	1 (0.9%)	1 (0.9%)	0.99 (0.06 - 16.04)	0.995
Acute kidney injury, no. (%)	0 (0.0%)	0 (0.0%)		

*** Composite of death, CVE, systemic embolism, major bleeding, cardiac tamponade, device embolization, or acute kidney injury occurring within 7 days or thereafter if deemed procedure-related.**

¶ All 4 cardiac tamponades observed within 45 days after LAAC occurred in the Amulet group


Klinikum Weißenfels
Study 18.10.2017-08:54:11
Koronar^Diagnostisch
Bild 23
XA 1 / 5
Klinikum Weißenfels
Study 18.10.2017-07:46:48
Koronar^Diagnostisch
Bild 16
Klinikum Weißenfels
Study 06.09.2017-11:11:21
Koronar^Diagnostisch
Bild 17
Klinikum Weißenfels
Study 06.09.2017-10:07:02
Koronar^Diagnostisch
Bild 21
Klinikum Weißenfels
Study 11.01.2017-07:49:37
Koronar^Diagnostisch
Bild 13
XA 1 / 8
Coro CTO-LF
Zoom 0,61
Breite: 143
Mitte: 119
RAO -28
Caudal -23.4
Klinikum Weißenfels
Study 22.02.2017-07:56:08
Koronar^Diagnostisch
Bild 29
XA 1 / 1
Zoom 0,61
Breite: 143
Mitte: 118
RAO -21.8
Caudal -17.9
Zoom 0,61
Breite: 143
Mitte: 118
LAO 0.1
Caudal -0.2
Klinikum Weißenfels
Study 23.02.2017-11:16:53
Koronar^Diagnostisc
Bild 12
XA 1 / 3
Zoom 0,61
Breite: 148
Mitte: 118
RAO -26.4
Caudal -17.4
Klinikum Weißenfels
Study 29.03.2017-07:57:58
Koronar^Diagnostisch
Bild 12
Coro CTO-LF
Bild 14
Zoom 0,61
Breite: 158
Mitte: 118
RAO -25.8
Caudal -24.2
Zoom 0,61
Breite: 145
Mitte: 118
RAO -26.2
Cranial 12.9
Coro CTO-LF
Bild 31
Klinikum Weißenfels
Study 17.05.2017-09:18:08
Koronar^Diagnostisch
Bild 19
Klinikum Weißenfels
Study 30.08.2017-07:40:46
Koronar^Diagnostisch
Bild 8
XA 1 / 6
Coro CTO-LF
Bild 15
Zoom 0,61
Breite: 143
Mitte: 118
RAO -21.9
Cranial 24.7
Klini
Study 18.1
Koror
XA 1 / 7
Zoom 0,61
Breite: 143
Mitte: 118
RAO -30.7
Cranial 17.6
Coro CTO-LF
Study 17.05.2017-10:32:16
Koronar^Diagnostisch
Bild 15
Zoom 0,61
Breite: 143
Mitte: 122
RAO -33.6
Caudal -14.1
Coro CTO-LF
Study 17.05.2017-08
Koronar^Diagno
XA 1 / 5
Zoom 0,61
Breite: 143
Mitte: 124
RAO -28.5
Caudal -18.6
Coro CTO-LF
5 cm



STOP AF

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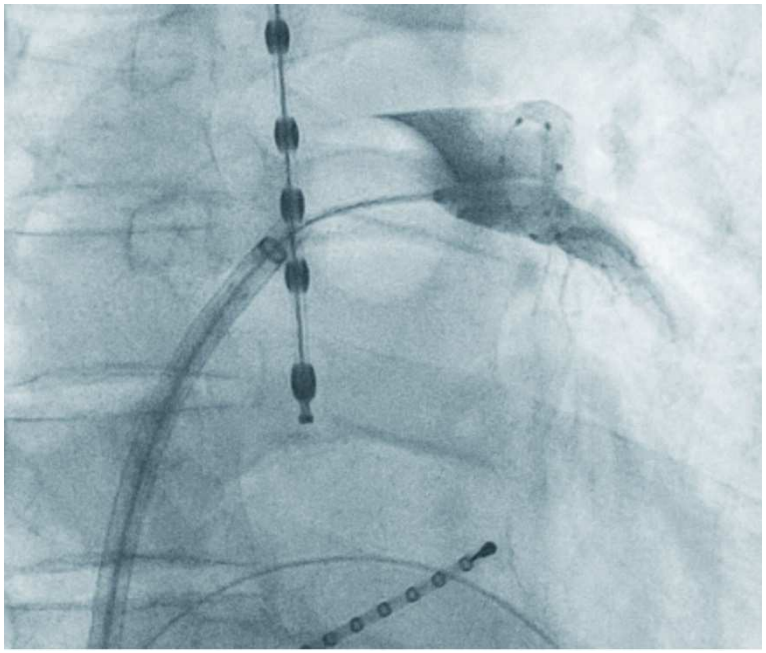
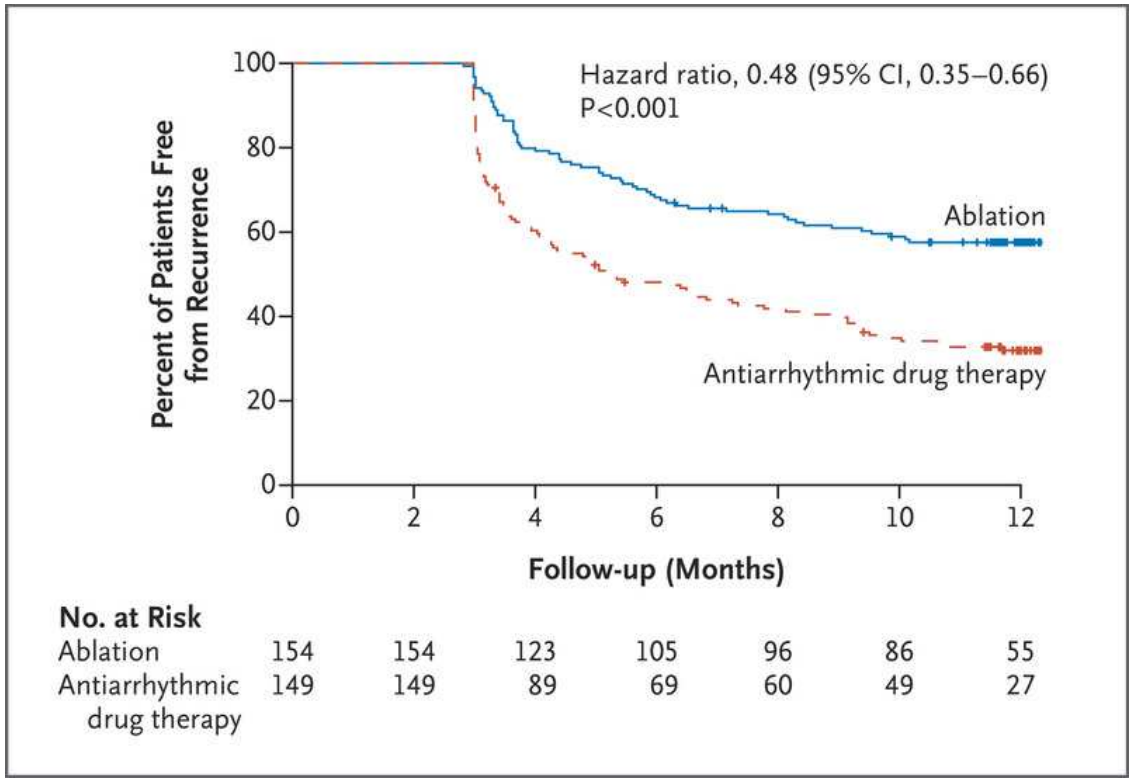
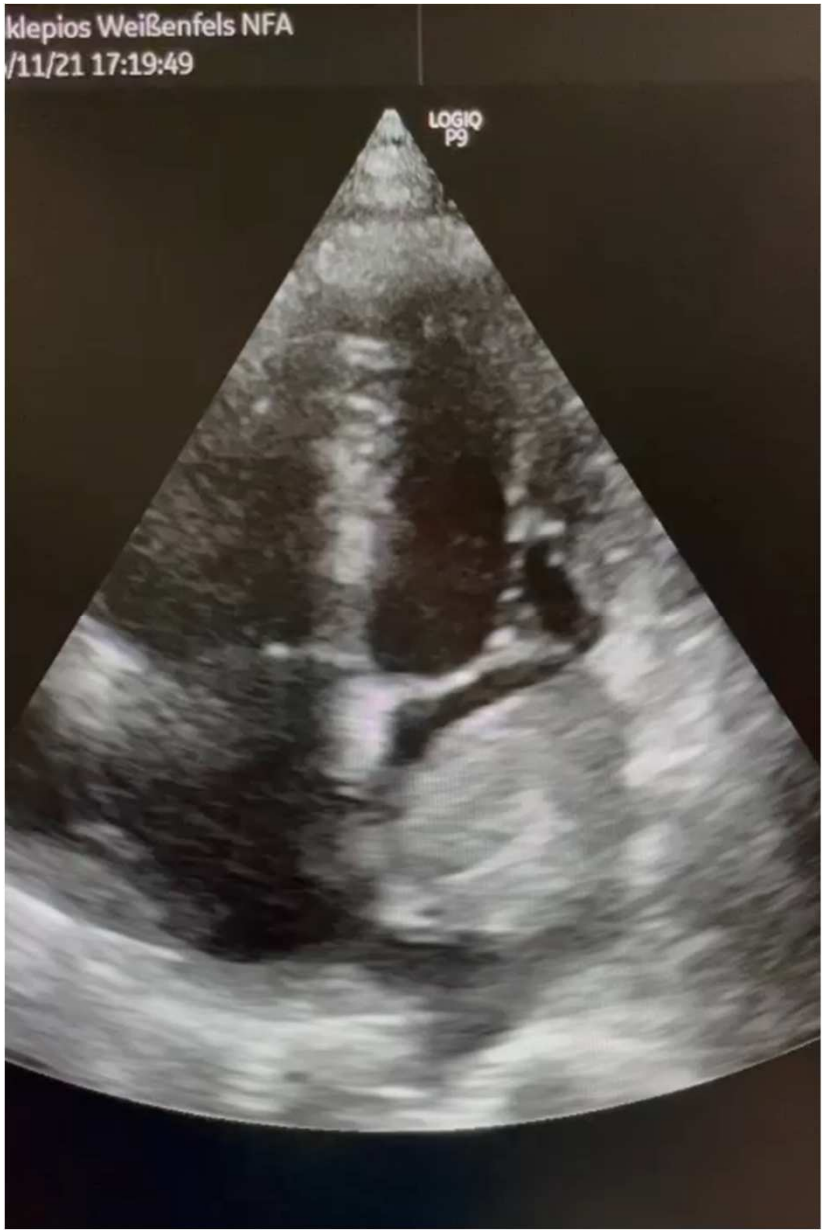




Was ist das ☺

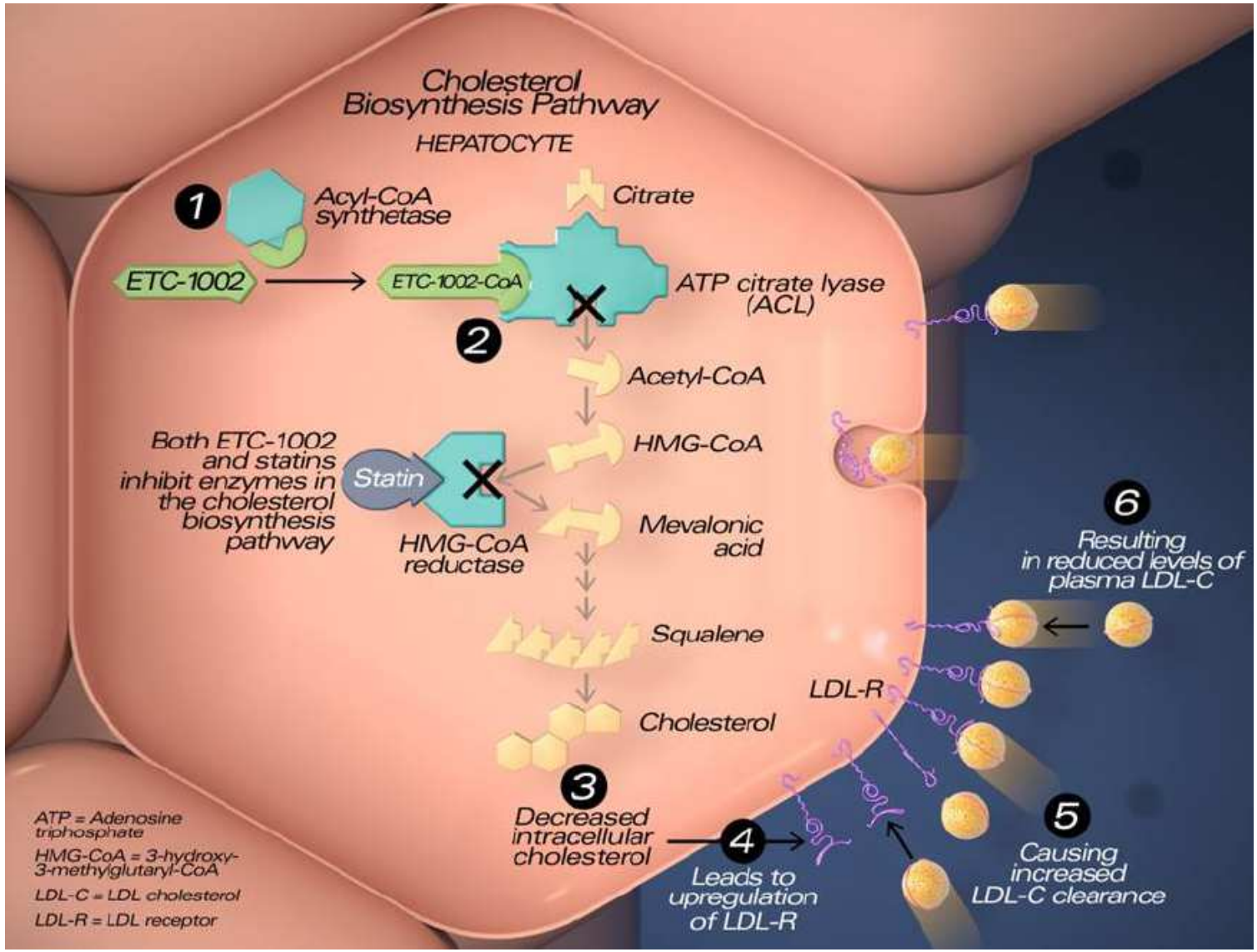


Was ist das ☺

Vielen Dank für Ihre Aufmerksamkeit!

Effect of Bempedoic Acid vs Placebo Added to Maximally Tolerated Statins on Low-Density Lipoprotein Cholesterol in Patients at High Risk for Cardiovascular Disease - The CLEAR Clinical Trial

ASKLEPIOS



TOMAHAWK trial #ESCCongress

Immediate angiography after out-of-hospital cardiac arrest

Conclusion

Early coronary angiography in out-of-hospital cardiac arrest (OHCA) patients without ST-segment elevation is not superior to a delayed/selective approach.

Impact on clinical practice

The usefulness and timing of coronary angiography in OHCA survivors without ST-segment elevation are uncertain. In up to one-third of these patients, acute MI is the cause of cardiac arrest, suggesting that diagnostic coronary angiography and potential percutaneous coronary intervention could be beneficial.

Study objectives

The TOMAHAWK trial examined whether immediate coronary angiography for treating or ruling out acute coronary events in OHCA survivors without ST-segment elevation is beneficial for all-cause mortality at 30 days compared with initial intensive care unit (ICU) assessment and delayed/selective angiography.

Who and what?

- Age ≥ 30 years
- Successful resuscitation after OHCA
- Possible cardiac cause of arrest
- No ST-segment elevation on post-resuscitation ECG
- Shockable or non-shockable rhythms were included

554 patients

randomised 1:1 at hospital admission

Immediate coronary angiography

Initial ICU assessment

Delayed/selective angiography

Primary endpoint

All-cause mortality at 30 days

Early angiography was not superior to a delayed/selective approach

54.0%

46.0%

HR: 1.28 (95% CI: 1.00-1.63); log-rank *p=0.058*

No differences in the primary endpoint were observed in pre-specified subgroups, including those with shockable versus non-shockable rhythm.

Composite secondary endpoint

All-cause death or severe neurological deficit at 30 days

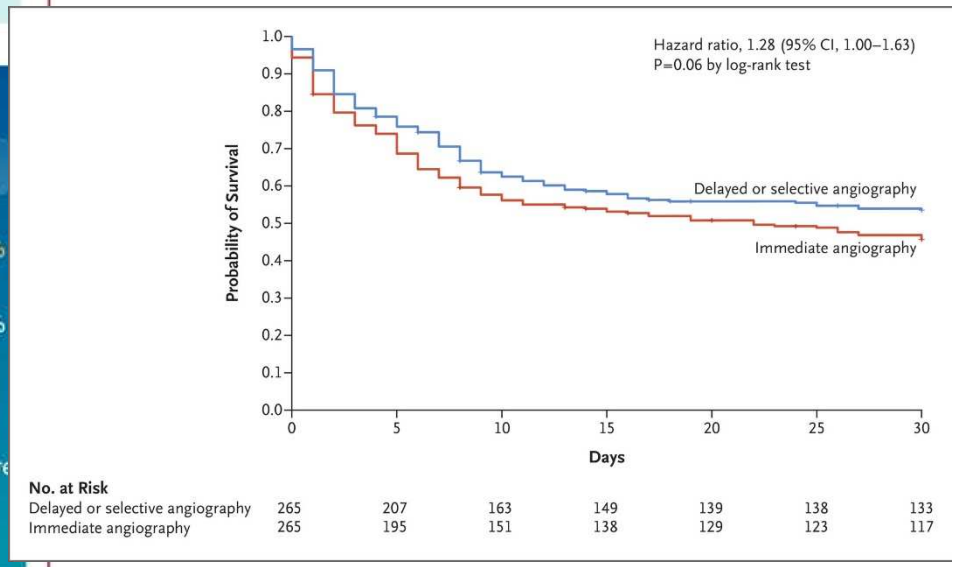
More frequent in the immediate angiography group

Relative risk 1.16; 95% CI 1.002-1.34

ESC

ASKLEPIOS

TOMAHAWK



Effect of Bempedoic Acid vs Placebo Added to Maximally Tolerated Statins on Low-Density Lipoprotein Cholesterol in Patients at High Risk for Cardiovascular Disease The CLEAR Wisdom Randomized Clinical Trial

ASKLEPIOS

JAMA Network™

QUESTION To what extent does bempedoic acid lower low-density lipoprotein cholesterol (LDL-C) levels in patients at high cardiovascular risk who have ongoing hypercholesterolemia, despite the use of maximally tolerated lipid-lowering therapy?

CONCLUSION In this randomized clinical trial, bempedoic acid provided additional LDL-C lowering in patients who did not achieve an adequate response to lipid-lowering therapy when compared with placebo.

POPULATION

496 Men
283 Women

Adults with atherosclerotic CVD and/or familial hypercholesterolemia with LDL-C of ≥70 mg/dL despite statin therapy

Mean age: 64 years

LOCATIONS

86 Clinical sites in North America and Europe

INTERVENTION

779 Patients randomized and analyzed

522
Bempedoic acid
Bempedoic acid tablets, 180 mg/d for 52 weeks

257
Placebo
Placebo tablets, once daily for 52 weeks

PRIMARY OUTCOME

Percent change in LDL-C levels from baseline to week 12

FINDINGS

Mean change in LDL-C levels at week 12

Bempedoic acid Mean change: **−15.1%**

Mean LDL-C at baseline 120.4 mg/dL → Mean LDL-C at week 12 97.6 mg/dL

Placebo Mean change: **2.4%**

Mean LDL-C at baseline 120.4 mg/dL → Mean LDL-C at week 12 122.8 mg/dL

The between-group difference was significant:
-17.4% (95% CI, −21.0% to -13.9%); $P < .001$

Goldberg AC, Leiter LA, Stroes ESG, et al. Effect of bempedoic acid vs placebo added to maximally tolerated statins on low-density lipoprotein cholesterol in patients at high risk for cardiovascular disease: the CLEAR Wisdom randomized clinical trial [published November 12, 2019]. *JAMA*. doi:10.1001/jama.2019.16585

Effect of Bempedoic Acid vs Placebo Added to Maximally Tolerated Statins on Low-Density Lipoprotein Cholesterol in Patients at High Risk for Cardiovascular Disease The CLEAR Wisdom Randomized Clinical Trial

Table 3. Treatment-Emergent Adverse Events and Key Safety Laboratory Parameters

Parameter	Bempedoic Acid (n = 522)	Placebo (n = 257)
Overview of AEs, No. (%)		
Any AE	366 (70.1)	182 (70.8)
Serious AE	106 (20.3)	48 (18.7)
Study drug-related AEs	91 (17.4)	32 (12.5)
Discontinuation because of AE	57 (10.9)	22 (8.6)
Fatal treatment-emergent AE	6 (1.1)	2 (0.8)
Most common AEs, No. (%)[a]		
Nasopharyngitis	27 (5.2)	13 (5.1)
Urinary tract infection	26 (5.0)	5 (1.9)
Hyperuricemia	22 (4.2)	5 (1.9)
Upper respiratory tract infection	19 (3.6)	9 (3.5)
Arthralgia	18 (3.4)	8 (3.1)
Diarrhea	16 (3.1)	7 (2.7)
Angina pectoris	16 (3.1)	5 (1.9)
Osteoarthritis	16 (3.1)	5 (1.9)
Dizziness	8 (1.5)	9 (3.5)
Lower respiratory tract infection	8 (1.5)	8 (3.1)
Fatigue	6 (1.1)	9 (3.5)
AEs of special interest, No. (%)		
Myalgia	15 (2.9)	8 (3.1)
Muscle spasms	11 (2.1)	3 (1.2)
Pain in extremity	11 (2.1)	1 (0.4)
Muscular weakness	2 (0.4)	1 (0.4)
New-onset or worsening diabetes	36 (6.9)	19 (7.4)
Blood uric acid increased	14 (2.7)	1 (0.4)
Gout	11 (2.1)	2 (0.8)
Blood creatinine increased	4 (0.8)	1 (0.4)
Glomerular filtration rate decreased	4 (0.8)	1 (0.4)
Neurocognitive disorders	3 (0.6)	1 (0.4)
Laboratory results		
ALT or AST >3× ULN, No. (%)[b]	6 (1.1)	2 (0.8)
Creatine kinase >5× ULN, No. (%)[b]	0	1 (0.4)
Mean (SD) change, baseline to wk 52		
Uric acid, mg/dL[c]	0.6 (1.2)	0.1 (1.1)
Creatinine, mg/dL	0.05 (0.16)	0.01 (0.12)
eGFR, mL/min/1.73 m^2	-3.8 (10.2)	-1.1 (10.8)

Neues pathophysiologisches Ziel für eine Population mit erheblichem medizinischem Bedarf

ASKLEPIOS

ARR: absolute Ratenreduktion; CV: kardiovaskulär; HF: Herzinsuffizienz; LVEF: linksventrikuläre Ejektionsfraktion; NNT: Anzahl der notwendigen Behandlungen (Number Needed to Treat); sGC: lösliche Guanylatcyclase.

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4. Greene SJ et al. *JAMA Cardiol*. 2018;3:252–259.