

Grazer Fortbildungstage 2024

Die Niere-eine Herzensangelegenheit?

Georg Parsché

Disclosures

Bezahlte Fortbildungen:

Böhringer Ingelheim, Cardiac Dimensions, Daiichi Sankyo

Vortragstätigkeit:

Novartis, Kwizda, Bayer, Novo Nordisc



Formen der Herzinsuffizienz

HF with reduced EF (HFrEF):

- HF with LVEF $\leq 40\%$

HF with mildly reduced EF (HFmrEF):

- HF with LVEF 41–49%

HF with preserved EF (HFpEF):

- HF with LVEF $\geq 50\%$

HF with improved EF (HFimpEF):

- HF with a baseline LVEF $\leq 40\%$, a ≥ 10 point increase from baseline LVEF, and a second measurement of LVEF $> 40\%$

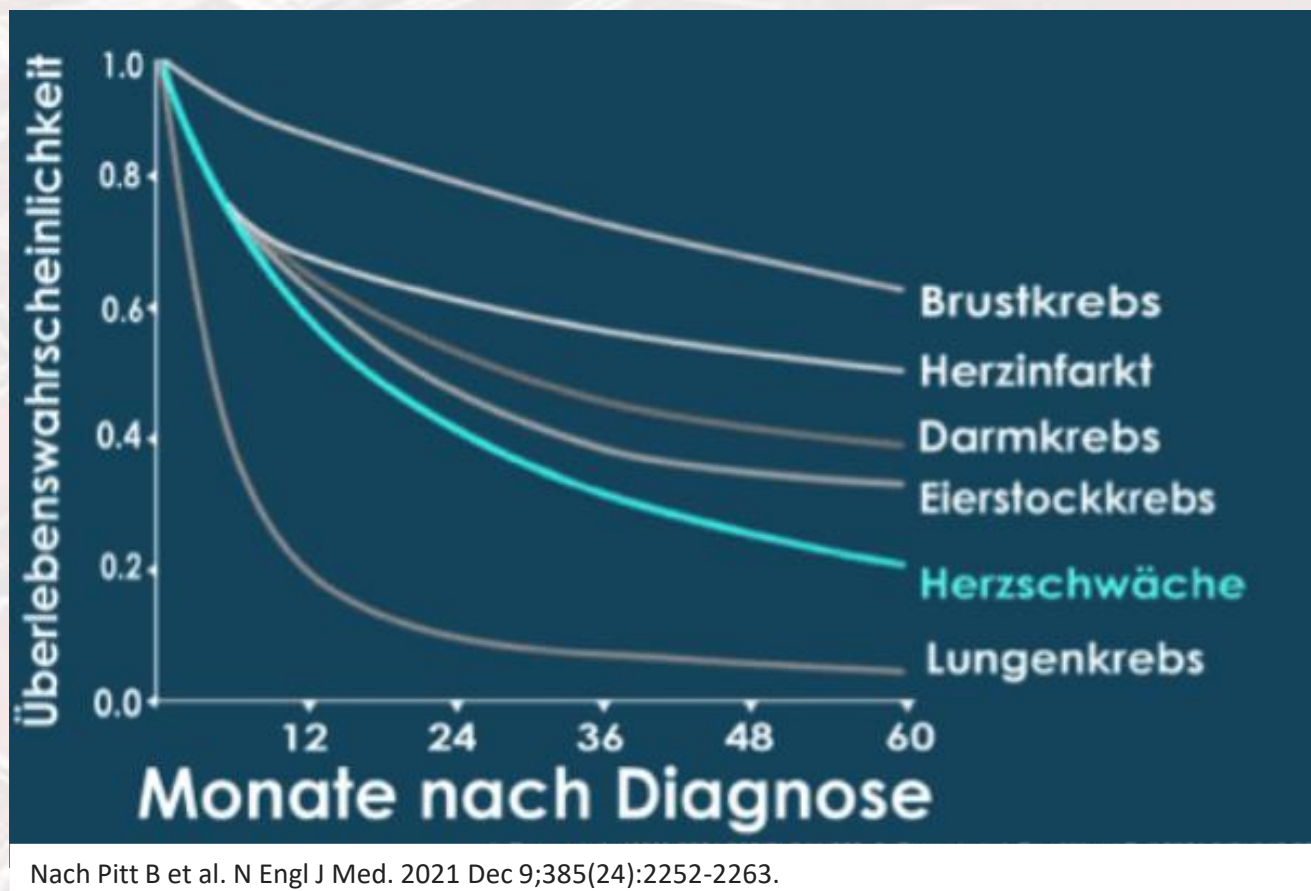
Bozkurt B et al. J Card Fail. 2021 Feb 7:S1071-9164(21)00050-6.

HI-Therapie: von der HFrEF zur HFimpEF



Quelle: Georg Parsché

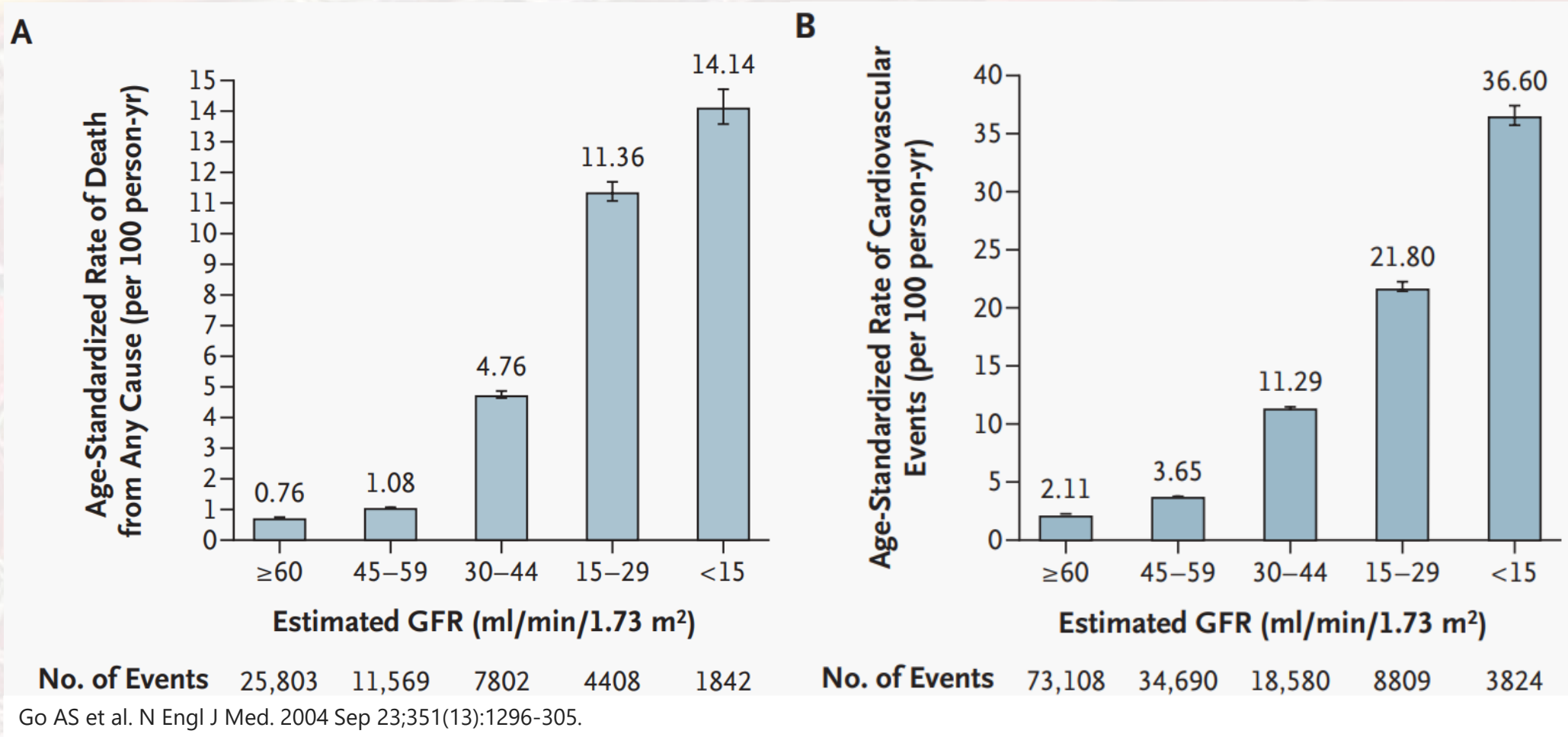
Prognose der Herzinsuffizienz



Gliederung

- Kardiovaskulärer Risikofaktor CKD/Proteinurie
- Therapie der HI
- Verhinderung der HI durch Nephroprotektion

Niereninsuffizienz: ein unabhängiger CV-Risikofaktor



UACR als früher Marker für CKD



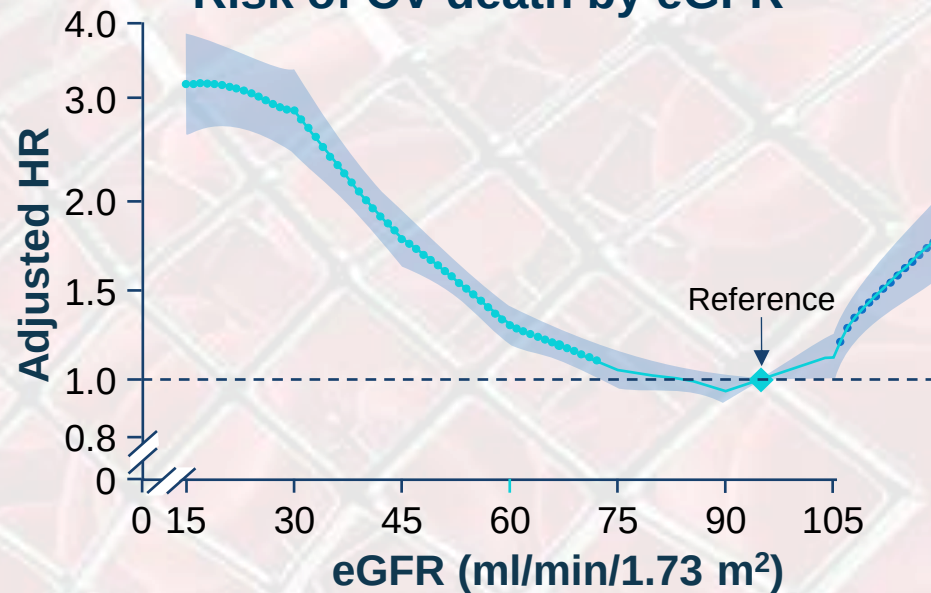
CKD = eGFR <60 ml/min/1.73 m² for >3 months¹

**and
OR**

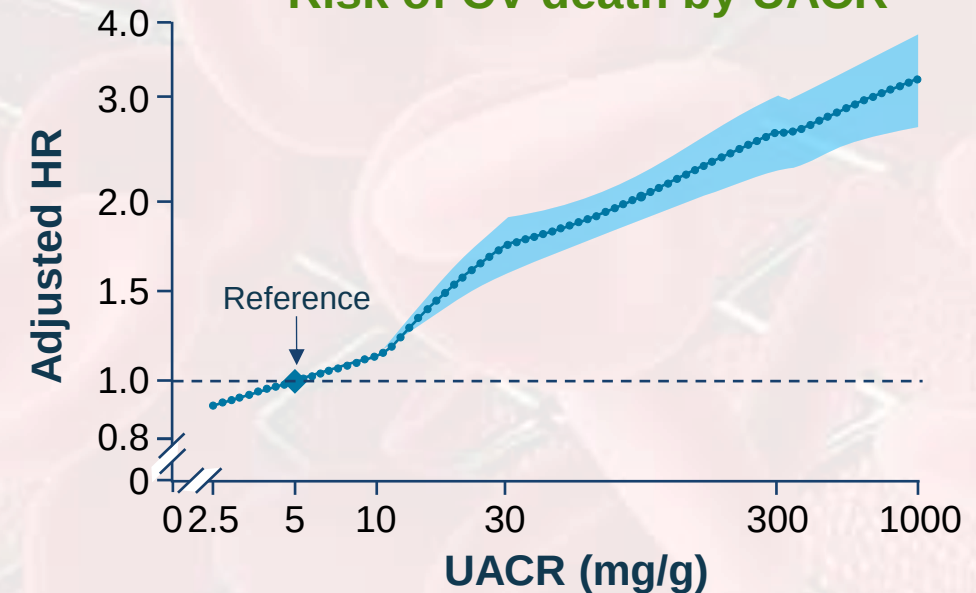


**CKD = albuminuria
UACR >30 mg/g for >3 months¹**

Risk of CV death by eGFR*²



Risk of CV death by UACR*²



Adapted from Matsushita K, *et al.* 2015

*Adjusted for age, sex, race or ethnic origin, smoking, SBP, antihypertensive drugs, diabetes, total and HDL cholesterol concentrations, and albuminuria (UACR or dipstick) or eGFR, as appropriate; dots represent statistical significance ($p < 0.05$); all axes are log scales except for the eGFR axis

CKD=Chronic kidney disease; CV=Cardiovascular; eGFR=estimated glomerular filtration rate; HR=hazard ratio; SBP=systolic blood pressure; T2D=type-2-diabetes; UACR =Urine albumin-to-creatinine ratio

Urin-Albumin-Kreatinin-Ratio (UACR)

- **Erklärung AKR (Albumin-Kreatinin-Ratio):** Ist gleichzusetzen mit der Menge an ausgeschiedenem Albumin im 24-Stunden-Sammelharn. Die Albuminkonzentration wird nicht auf das Urinvolumen, sondern auf die Kreatininkonzentration im Harn bezogen.
- Die **Proteinurie** ist der **wichtigste Risikofaktor**, die Prognose der chronischen Niereninsuffizienz bzw. das **kardioresnale Risiko** betreffend. Die Höhe der UACR steht stellvertretend für das Ausmaß der Proteinurie.

Einteilung nach AKR:

- Normal: <30 mg/g Krea (A1)
- Mikroalbuminurie: 30-300 mg/gKrea (A2)
- Makroalbuminurie 300-3000 mg/g Krea (A3)

KDIGO-Klassifikation

Grams ME et al. JAMA. 2023 Oct 3;330(13):1266-1277.

CKD is classified based on: • Cause (C) • GFR (G) • Albuminuria (A)				Albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–299 mg/g 3–29 mg/mmol	≥300 mg/g ≥30 mg/mmol
GFR categories (ml/min/1.73 m²) Description and range	G1	Normal or high	≥90	Screen 1	Treat 1	Treat 3
	G2	Mildly decreased	60–89	Screen 1	Treat 1	Treat 3
	G3a	Mildly to moderately decreased	45–59	Treat 1	Treat 2	Treat 3
	G3b	Moderately to severely decreased	30–44	Treat 2	Treat 3	Treat 3
	G4	Severely decreased	15–29	Treat* 3	Treat* 3	Treat 4+
	G5	Kidney failure	<15	Treat 4+	Treat 4+	Treat 4+

Low risk (if no other markers of kidney disease, no CKD)
High risk

Moderately increased risk
Very high risk

CKD - Risiko in Abh. Von GFR und UACR

Grams ME et al. JAMA. 2023 Oct 3;330(13):1266-1277.

	Urine albumin to creatinine ratio, mg/g					Urine albumin to creatinine ratio, mg/g				
Overall	<10	10-29	30-299	300-999	≥1000	<10	10-29	30-299	300-999	≥1000
eGFR, mL/min/1.73 m ² using creatinine alone	All-cause mortality: 82 cohorts 26 444 384 participants; 2 604 028 events					Myocardial infarction: 64 cohorts 22 838 356 participants; 451 063 events				
≥105	1.6	2.2	2.9	4.3	5.8	1.1	1.4	2.0	2.7	3.8
90-104	Reference	1.3	1.8	2.6	3.1	Reference	1.3	1.6	2.2	3.2
60-89	1.0	1.3	1.7	2.2	2.8	1.1	1.3	1.6	2.2	3.1
45-59	1.3	1.6	2.0	2.4	3.1	1.4	1.7	2.0	2.8	3.7
30-44	1.8	2.0	2.5	3.2	3.9	1.9	2.0	2.4	3.2	4.3
15-29	2.8	2.8	3.3	4.1	5.6	2.7	3.1	3.1	4.2	5.1
<15	4.6	5.0	5.3	6.0	7.0	4.6	5.6	4.8	6.0	6.0
eGFR, mL/min/1.73 m ² using creatinine alone	Kidney failure with replacement therapy: 57 cohorts 25 466 956 participants; 158 846 events					Heart failure: 61 cohorts 24 603 016 participants; 1 132 443 events				
≥105	0.5	1.2	2.9	7.7	25	1.2	1.7	2.7	4.2	6.9
90-104	Reference	1.8	4.3	12	43	Reference	1.3	2.0	2.8	4.2
60-89	2.3	4.9	10	27	85	1.1	1.4	1.9	2.7	4.2
45-59	13	19	37	89	236	1.6	1.8	2.4	3.4	5.0
30-44	50	58	115	240	463	2.2	2.5	3.1	4.2	6.5
15-29	283	301	443	796	1253	3.6	3.5	4.1	5.8	8.1
<15	770	1040	1618	2297	2547	5.1	5.7	5.8	7.9	9.9

Albuminuria as a Risk Marker for Heart Failure

CENTRAL ILLUSTRATION Albuminuria as a Risk Marker for Heart Failure

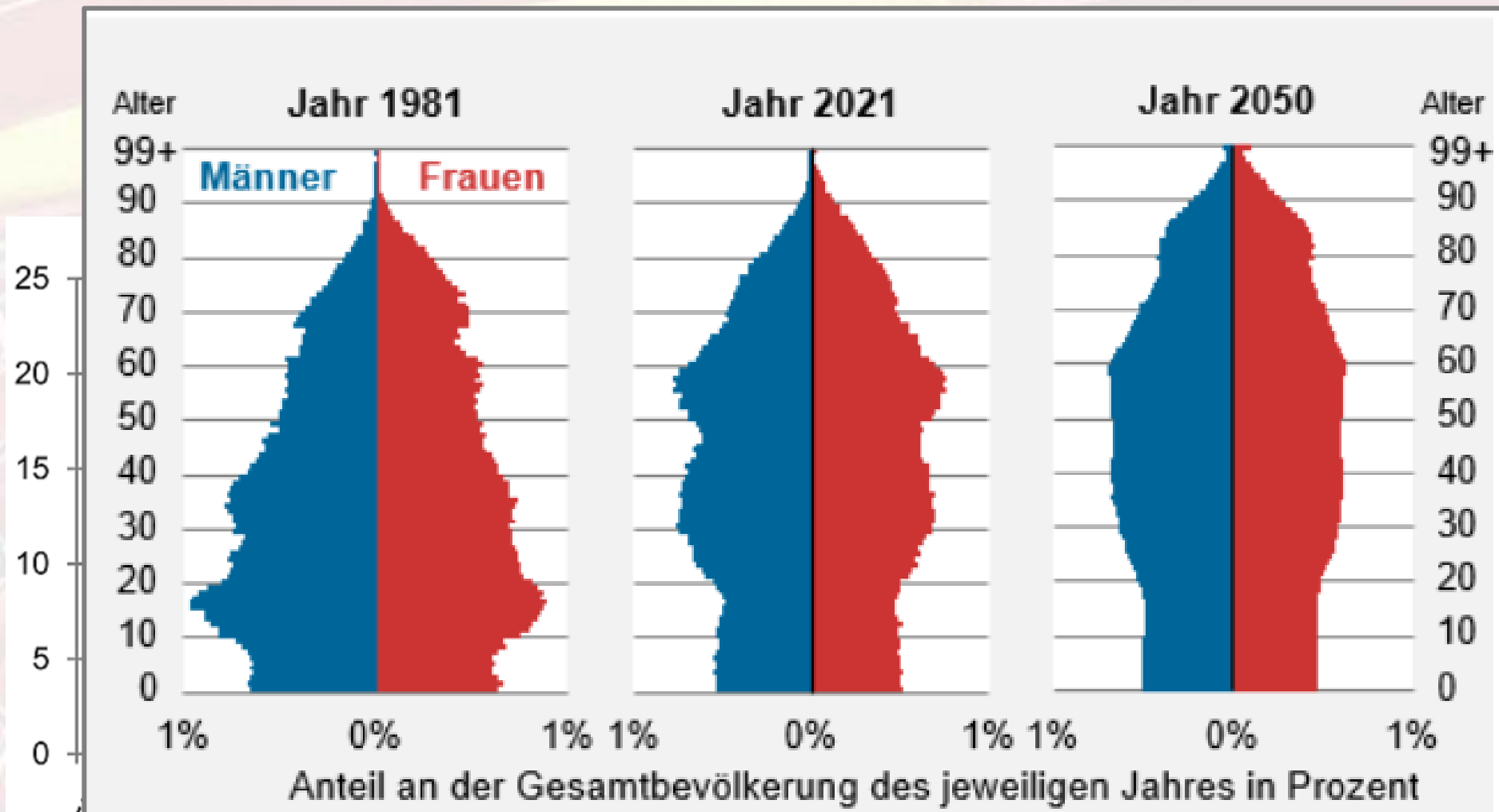


Finerenon und SGLT 2-Inhibitoren reduzieren Albuminurie

- SOLVD Trial
↑Albuminuria → ↑1.8 x risk of HHF
- CHARM Trial
↑Albuminuria → ↑30-70% risk of HHF
- GISSI-HF and CHARM Trials
Strong independent predictor of adverse prognosis in HF irrespective of HTN or T2DM



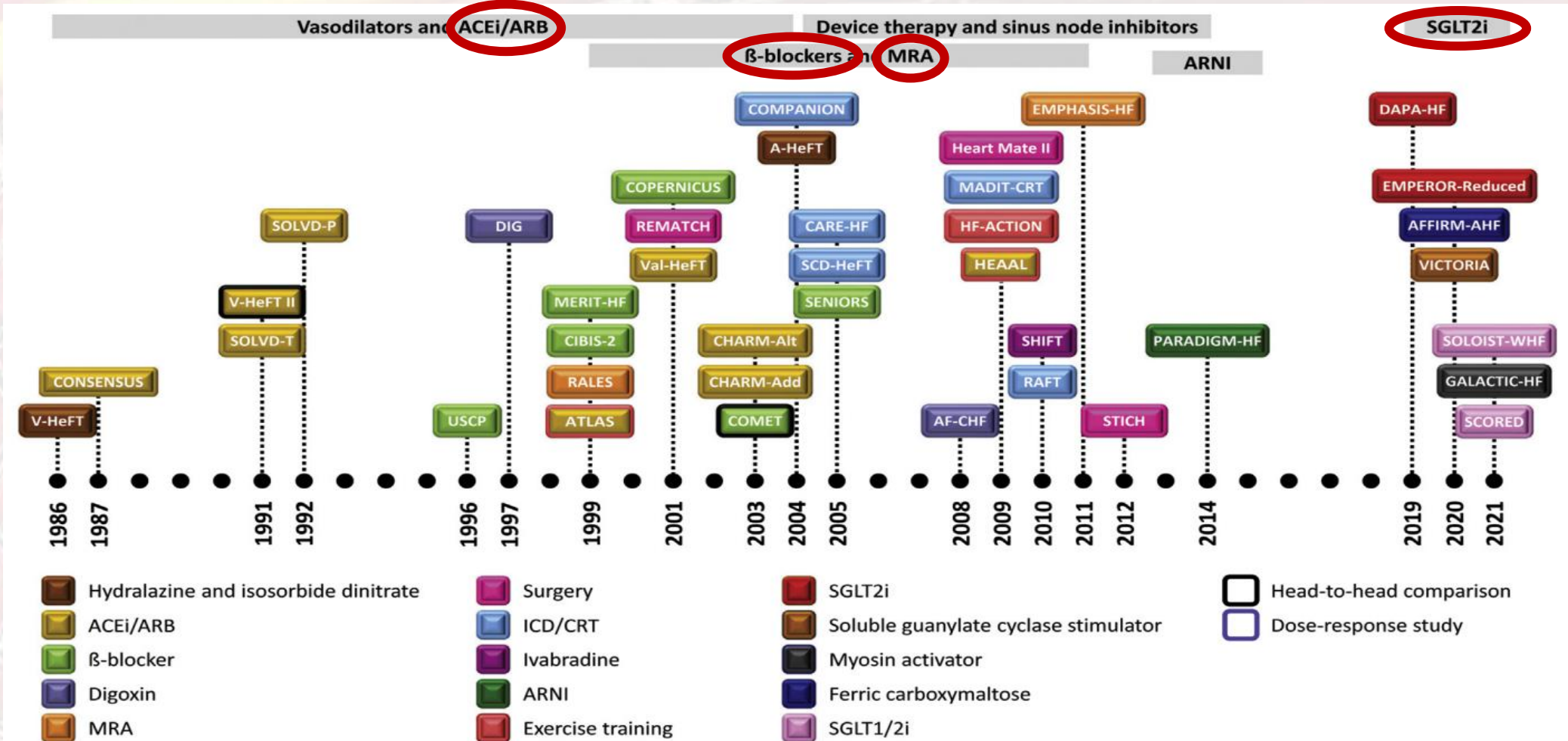
- FHS Study
↑Albuminuria → ↑2.7 x risk of incident HF
- MESA Study
↑Albuminuria → ↑2.7 x risk of incident HF
- ARIC Study
↑Albuminuria → ↑2.5 x risk of incident HF



Quelle: Bundesamt für Statistik: ESPOP (bis 2009), STATPOP
(ab 2010); Szenario AR-00-2020; Fachstelle für Statistik
Kanton St.Gallen: BevSzen-SG-12-a-2022-2050

© FfS-SG / P28

Geschichte der Herzinsuffizienztherapie



Sharma A et al. JACC Basic Transl Sci. 2022 Mar 2;7(5):504-517

Empfehlungen ESC-Leitlinie 2021/23

ACE-I is recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.

I

A

Beta-blocker is recommended for patients with stable HFrEF to reduce the risk of HF hospitalization and death.

I

A

MRA is recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.

I

A

Dapagliflozin or empagliflozin are recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.

I

A

Sacubitril/valsartan is recommended as a replacement for an ACE-I in patients with HFrEF to reduce the risk of HF hospitalization and death.

I

B

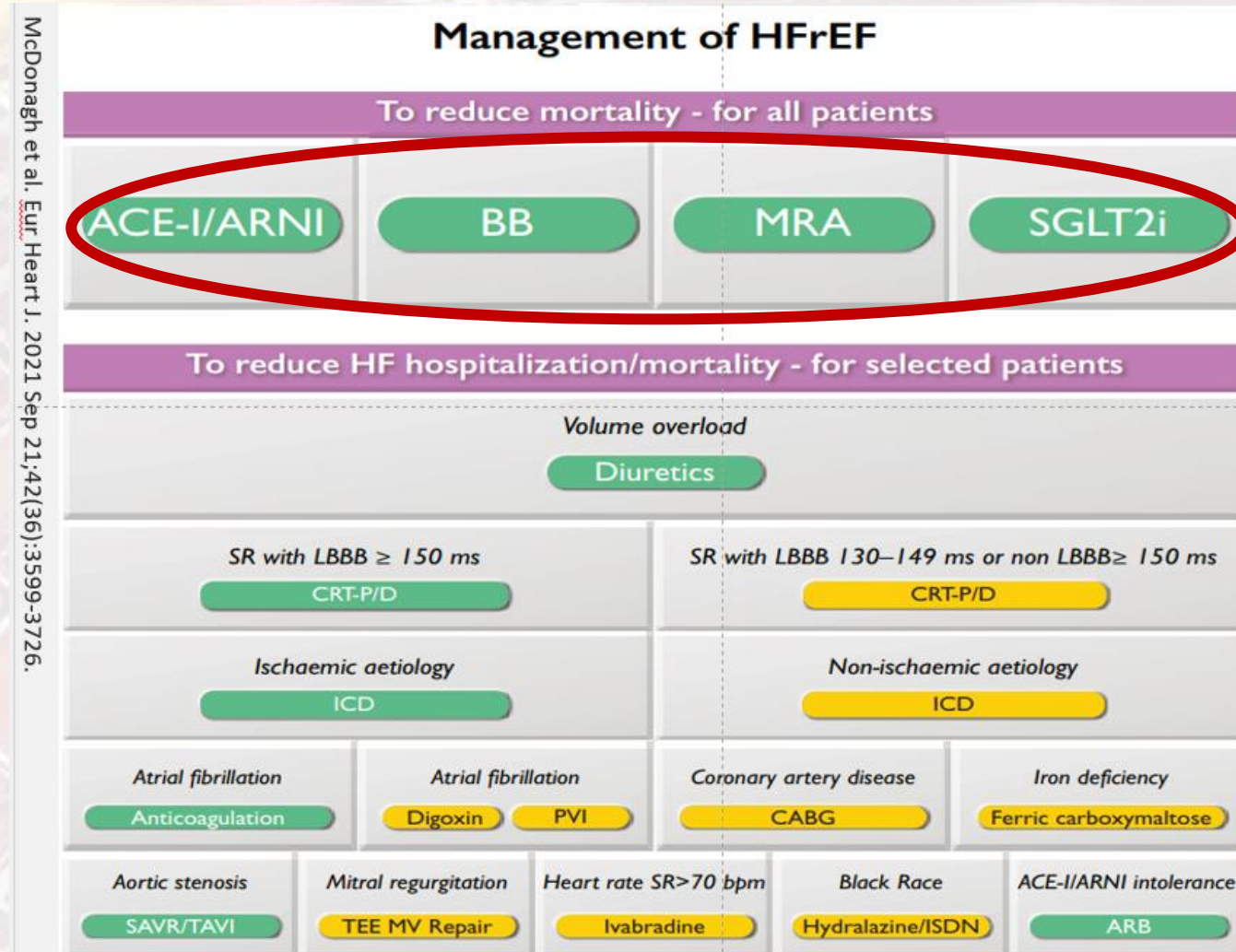
Diuretics are recommended in patients with HFrEF with signs and/or symptoms of congestion to alleviate HF symptoms, improve exercise capacity and reduce HF hospitalizations.

I

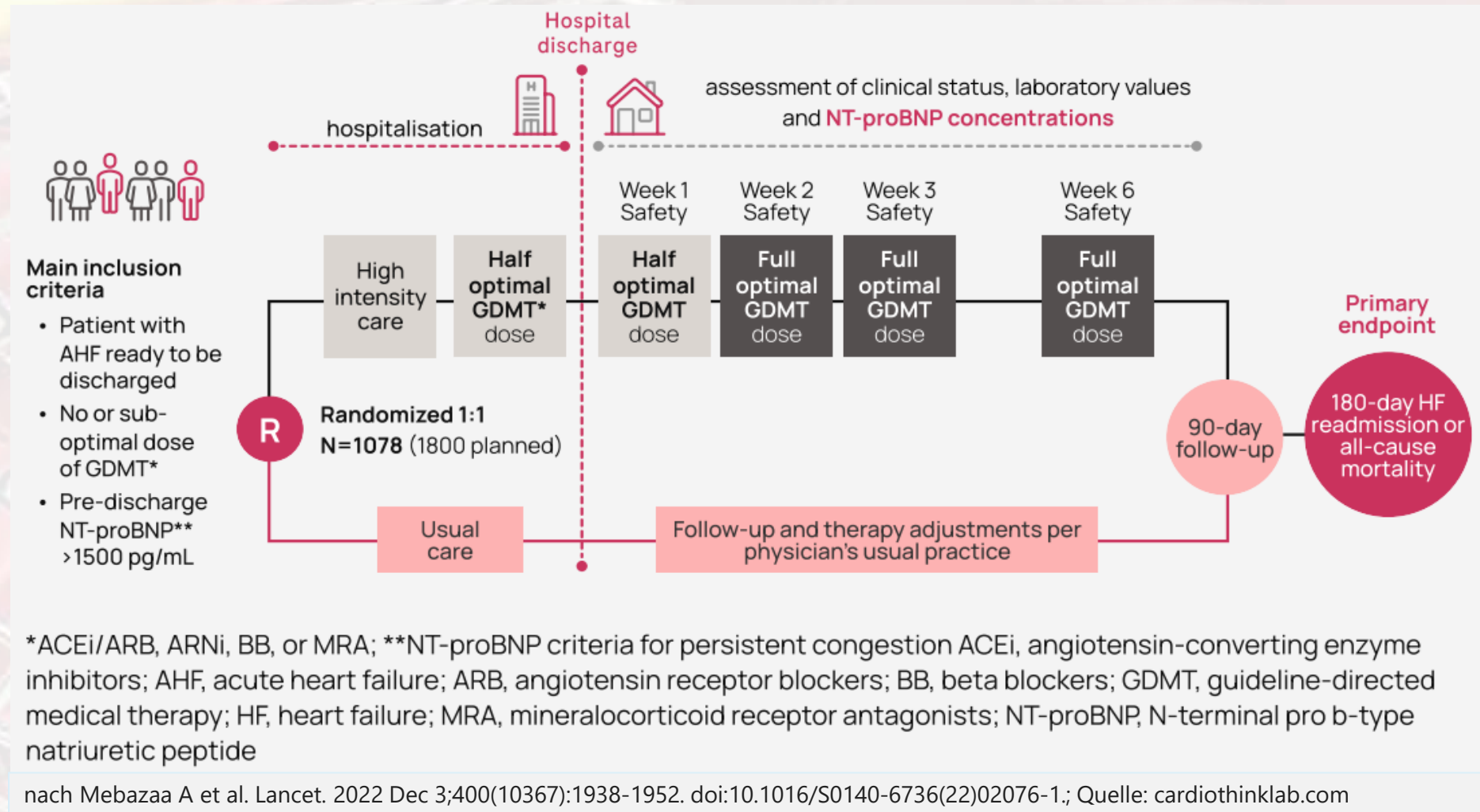
C

McDonagh et al. Eur Heart J. 2021 Sep 21;42(36):3599-3726.

HFrEF-Leitlinie 2021/2023: Die „Fantastischen Vier“



Warum gleichzeitig und schnell? STRONG-HF 2022



STRONG-HF: Ergebnisse

The high intensity care group: **34% relative** and **8.1% absolute risk reduction (ARR)** in the combination of death or heart failure readmission.¹⁴



CV (cardiovascular) death
26% lower

HF readmission
44% lower

All-cause death
16% lower

STRONG-HF study results demonstrated clear benefits for acute heart failure patients by adapting the strategy of care.

nach Mebazaa A et al. Lancet. 2022 Dec 3;400(10367):1938-1952. doi:10.1016/S0140-6736(22)02076-1; Quelle: cardiiothinklab.com

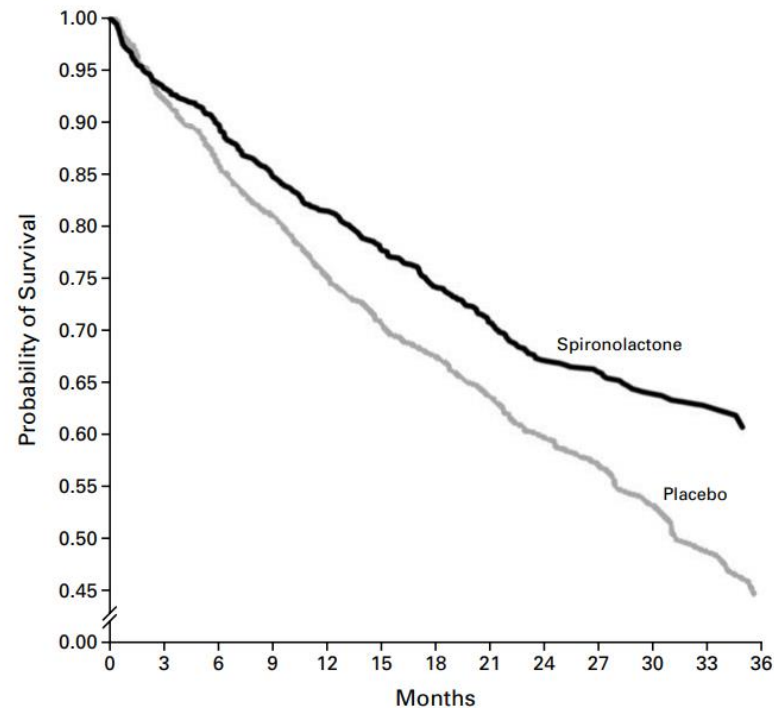
Recommendation	Class ^a	Level ^b
An intensive strategy of initiation and rapid up-titration of evidence-based treatment before discharge and during frequent and careful follow-up visits in the first 6 weeks following a HF hospitalization is recommended to reduce the risk of HF rehospitalization or death.^{c,d,e 16}	I	B
McDonagh et al. Eur Heart J. 2021 Sep 21;42(36):3599-3726.		

Schnelles Auftitrieren der HF-Therapie

Sharma A et al. JACC Basic Transl Sci. 2022 Mar 2;7(5):504-517

4 Therapies on Board in 4 Weeks					
Acute HF		Chronic HF		De Novo HF	
STOP	ACEI • ARB	STOP	ACEI • ARB	INITIATE	ARNI • β -blocker
CONTINUE	β -blocker	CONTINUE	β -blocker	INITIATE in 2-4 weeks	SGLT2i • MRA
INITIATE in hospital	ARNI • SGLT2i	INITIATE	ARNI • SGLT2i		
INITIATE at discharge	MRA	INITIATE in 2 weeks	MRA		
Start low dose ARNI/BB - Uptitrate over time to guideline-directed or maximally-tolerated doses after all 4 foundational therapies have been introduced					
Anticipate potential side effects					
Hypotension		Declining eGFR		Hyperkalemia	
a. Assess volume status and diuretic dose b. Consider spacing medications during the day c. Discontinue therapies that do not offer CV benefits (e.g. CCBs)		Anticipate an early decline in eGFR (~20%) that will recover and stabilize with time		Consider K ⁺ binders (e.g. patiomer and sodium zirconium cyclosilicate)	

Spironolacton-RALES 1999



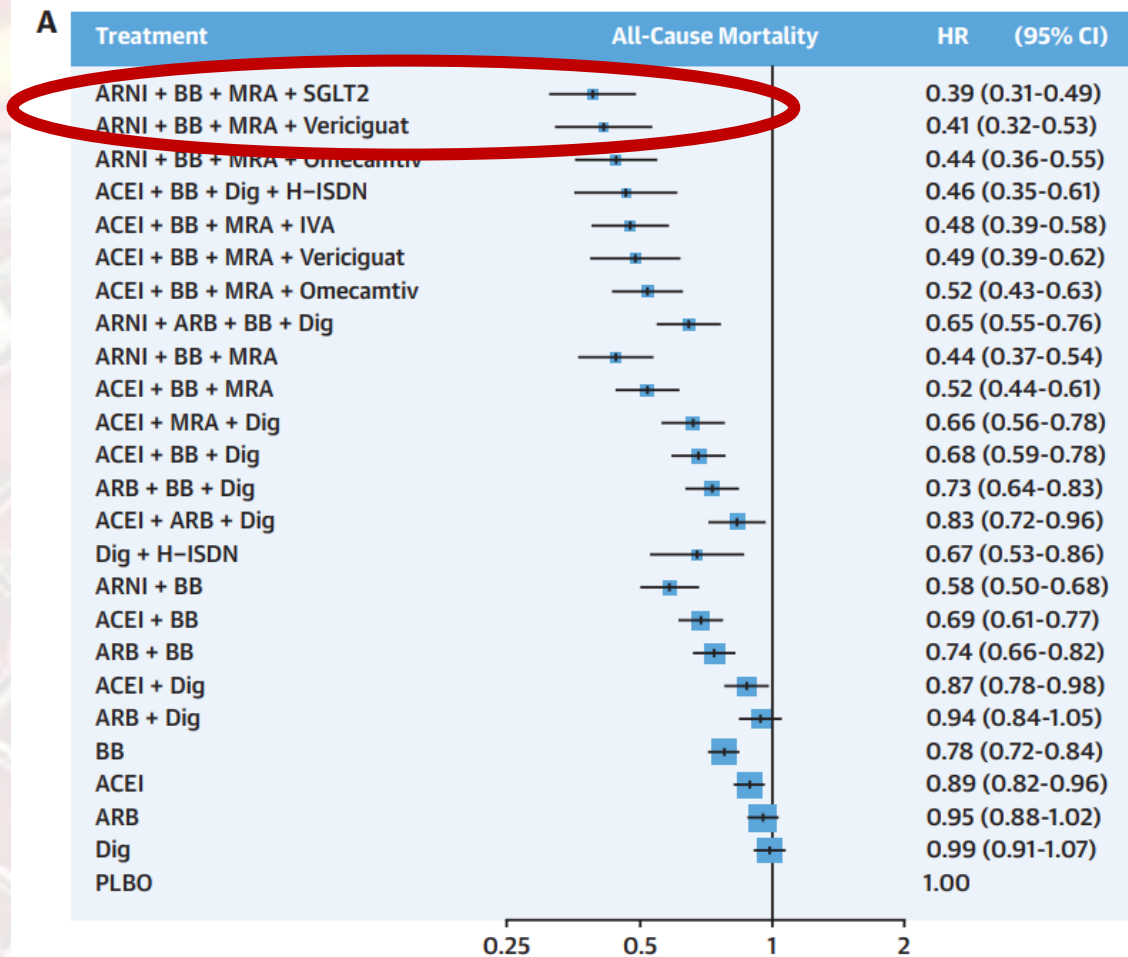
NO. AT RISK

Placebo	841	775	723	678	628	592	565	483	379	280	179	92	36
Spironolactone	822	766	739	698	669	639	608	526	419	316	193	122	43

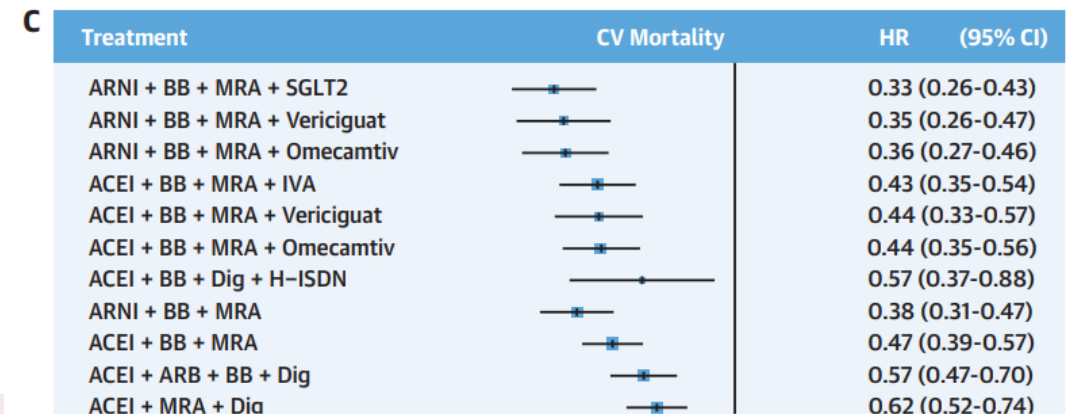
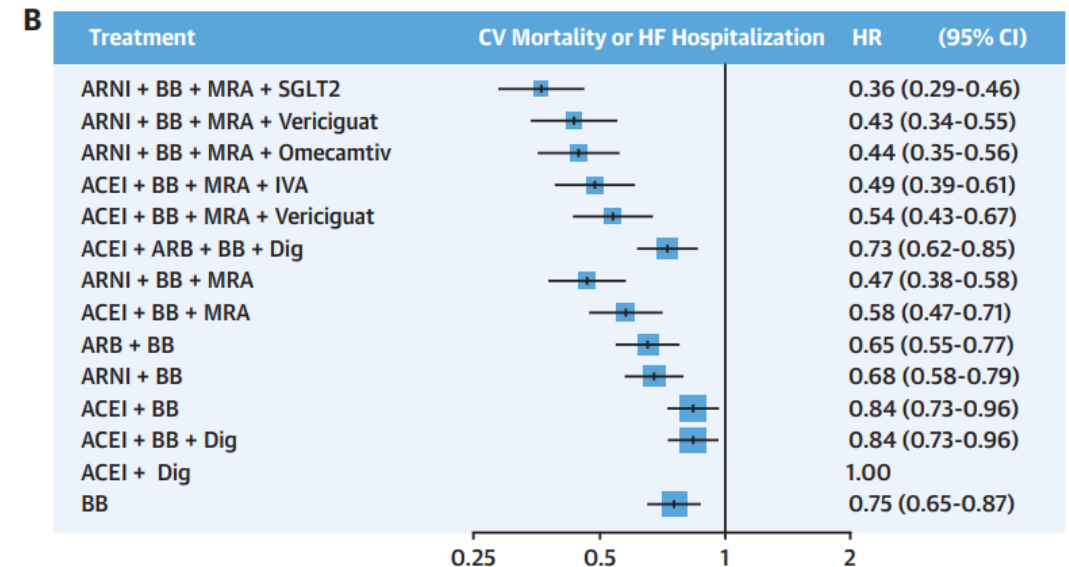
Pitt B et al. N Engl J Med. 1999 Sep 2;341(10):709-17.

- Sterblichkeit um 30% reduziert im Vergleich zu Placebo
- EF <35%
- Add on zu Enalapril

Metaanalyse: Vergleich der Therapiekombinationen

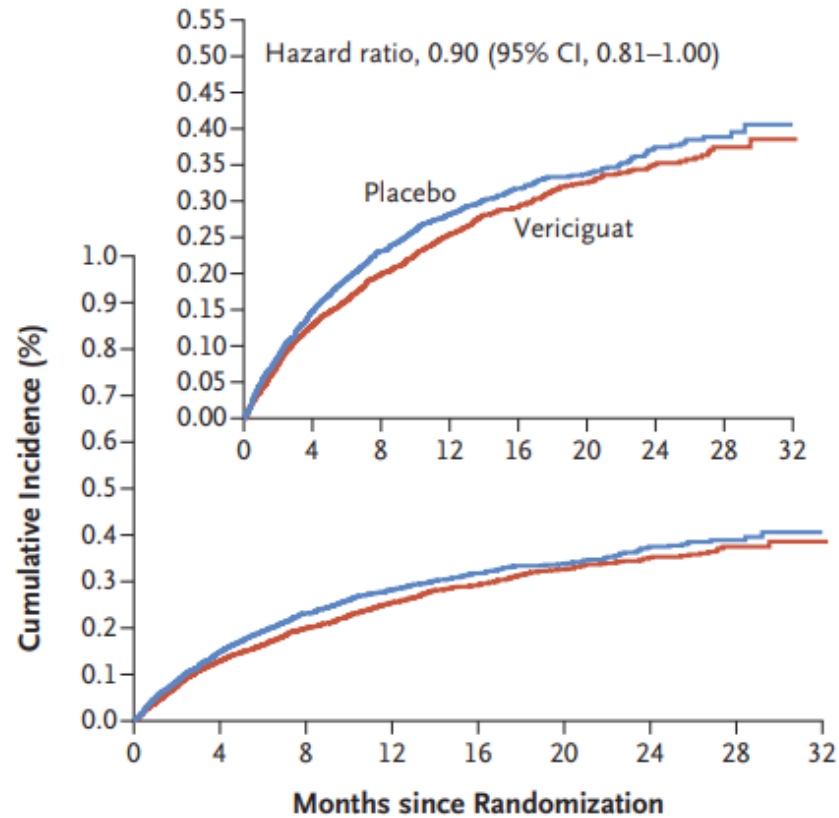


Tromp, J. et al. J Am Coll Cardiol HF. 2022;10(2):73-84.



Victoria: Vericiguat

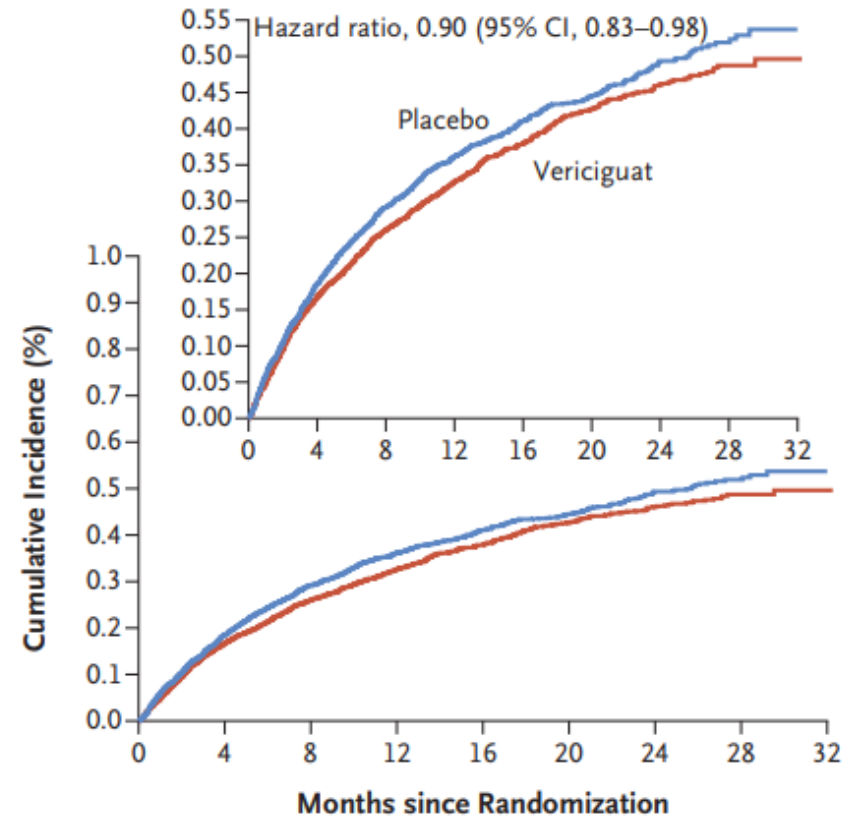
C Hospitalization for Heart Failure



No. at Risk

Placebo	2524	2052	1554	1096	771	558	323	110	0
Vericiguat	2526	2098	1620	1153	825	577	348	125	1

D Death from Any Cause or Hospitalization for Heart Failure



No. at Risk

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

Armstrong PW et al. N Engl J Med. 2020 May 14;382(20):1883-1893.

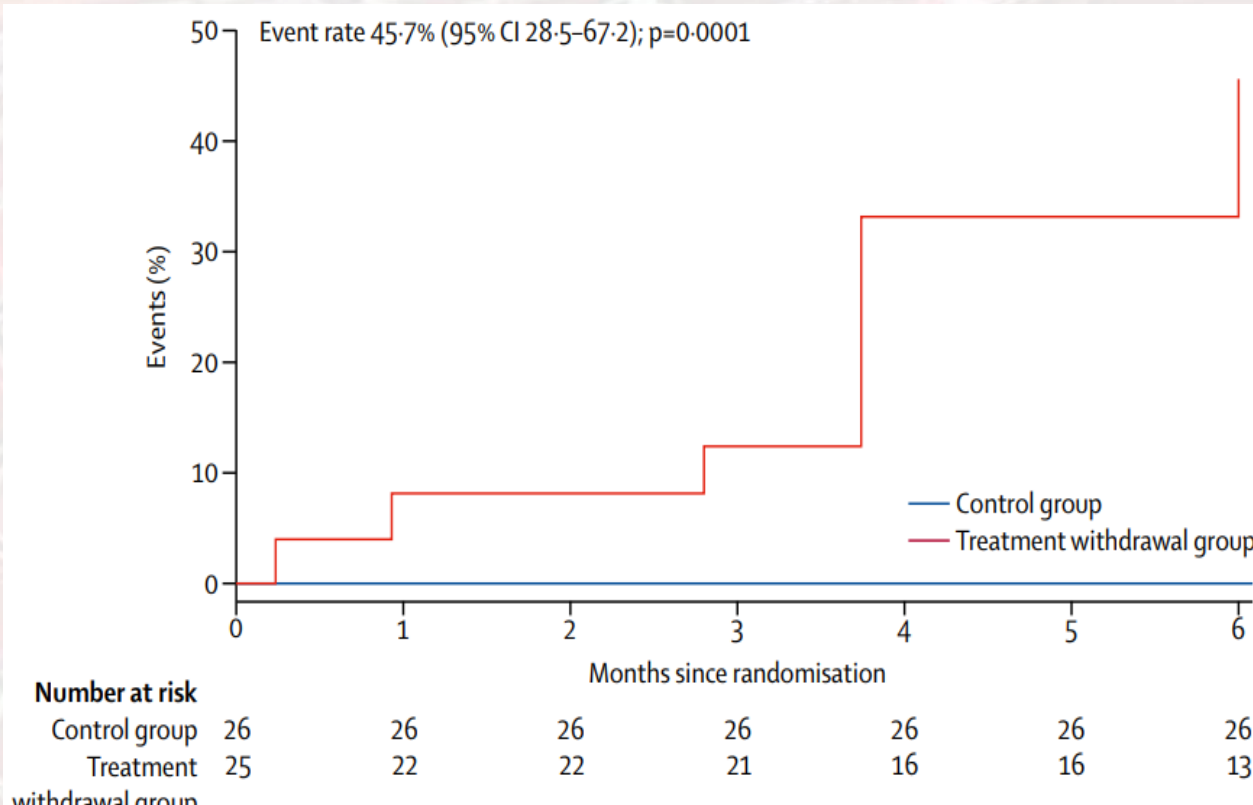
WHF (worsening HF): Vericiguat - Victoria 2020

- Klinische bzw. morphologische Verschlechterung der HF
- Erneute Dekompensation
- Konventionelle Therapie ausgeschöpft
- LVEF < 45%
- Primärer Endpunkt: 10%ige Reduktion (CV-Death+ HFH)
- Eventrate: abs. Risikoreduktion 4,3%/100 PY, NNT 24

→ Vericiguat als Add-On bzw. Alternative wenn eines der „Fab Four“ nicht möglich

HFimpEF:

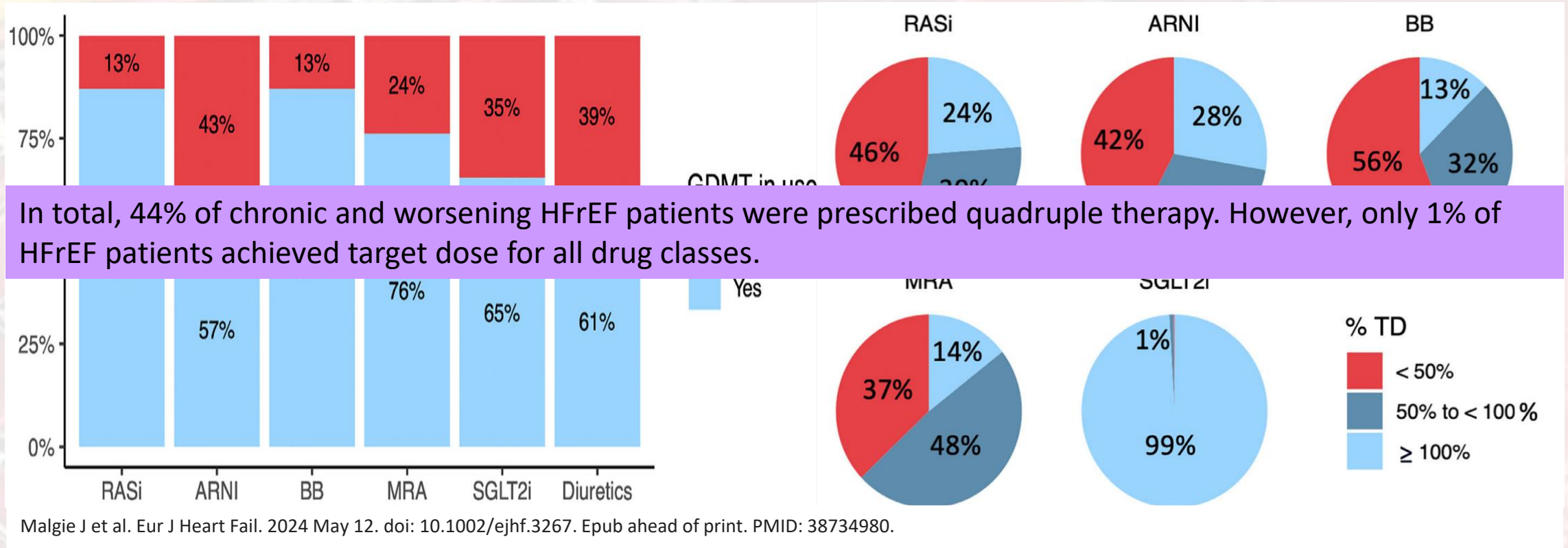
auf keinen Fall die „Fantastischen 4“ absetzen!!!



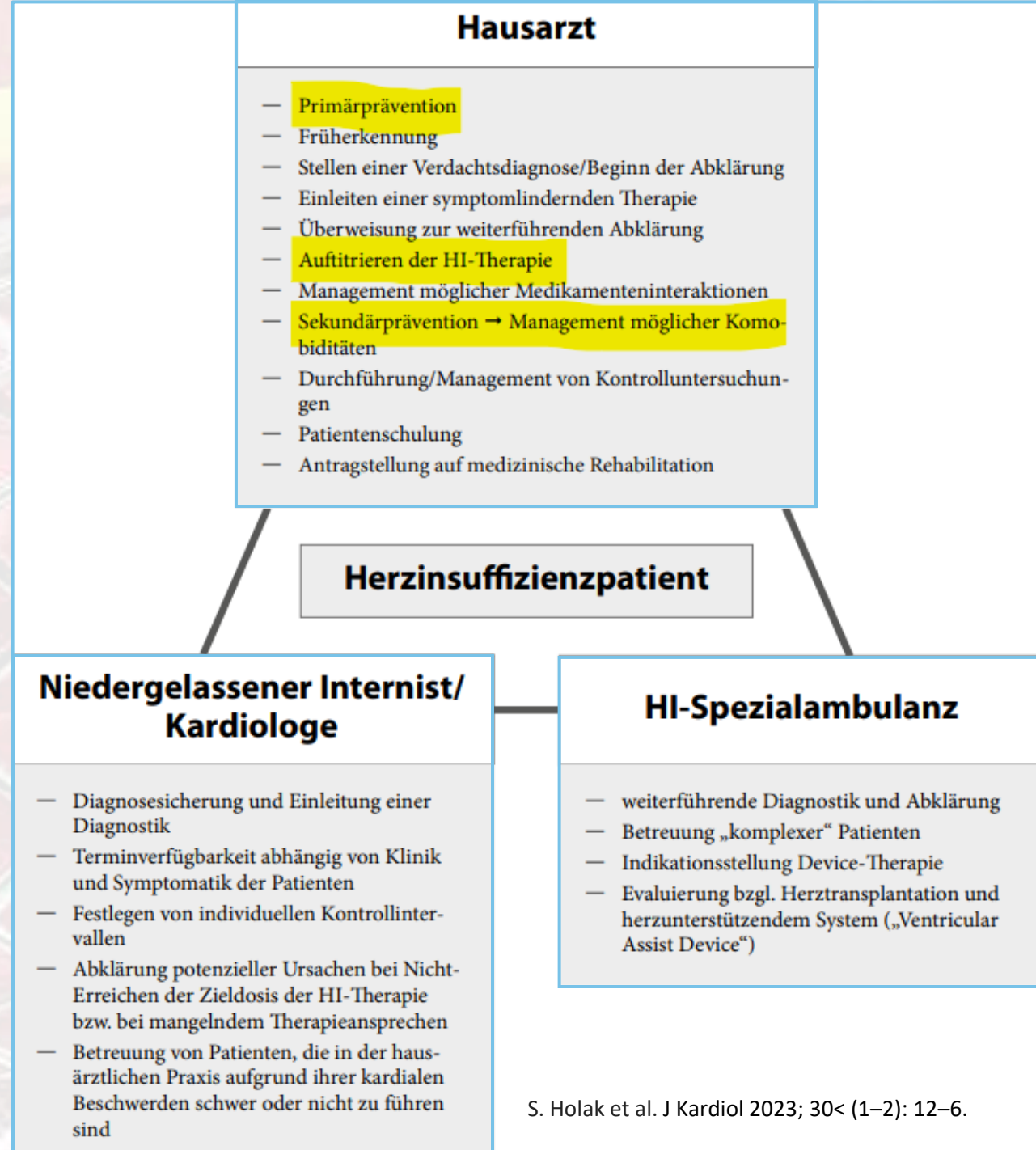
Halliday BP et al. Lancet. 2019 Jan 5;393(10166):61-73.

Rezidivrate nach TRED-HF-Studie **45%**, wenn die HI-Therapie abgesetzt wird, und zwar schon nach 6 (!) Monaten

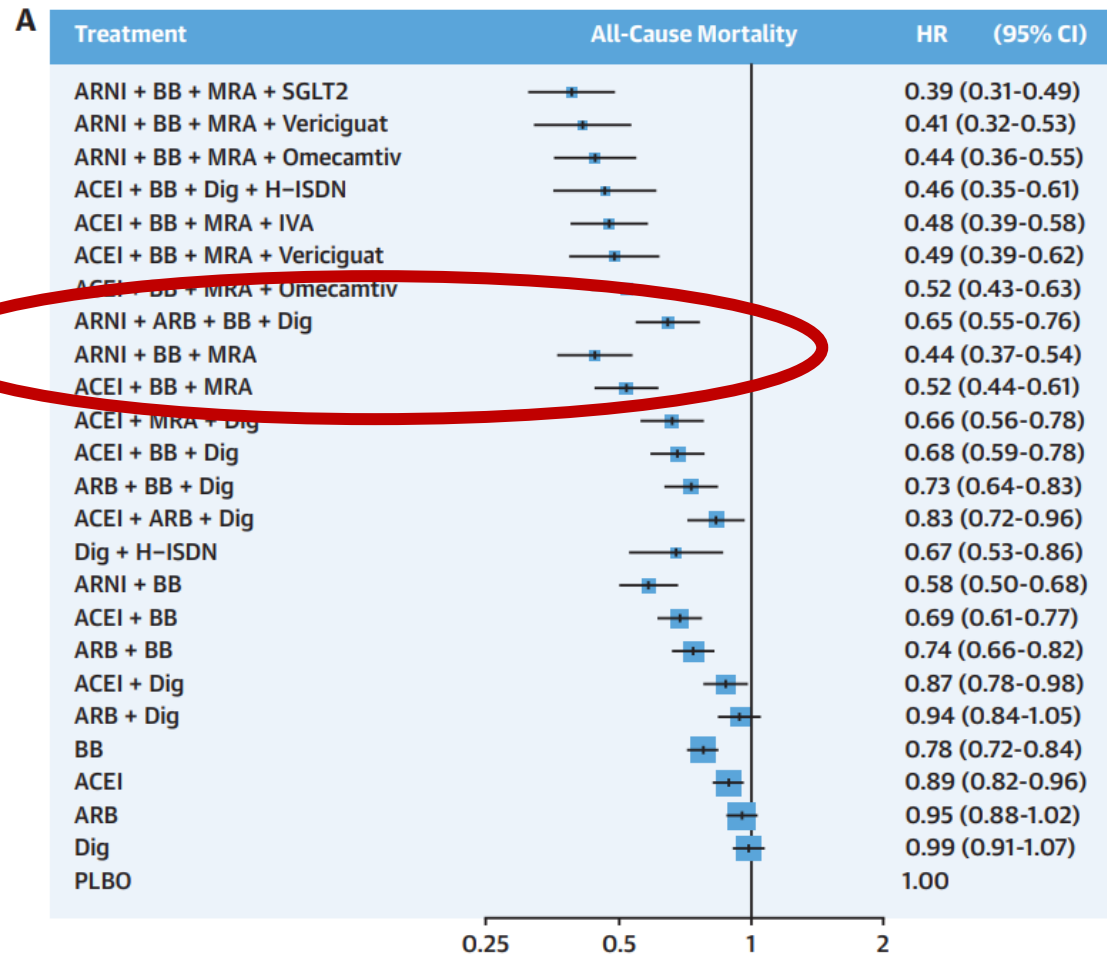
Setzen wir das im Alltag um? -> TITRATE-HF



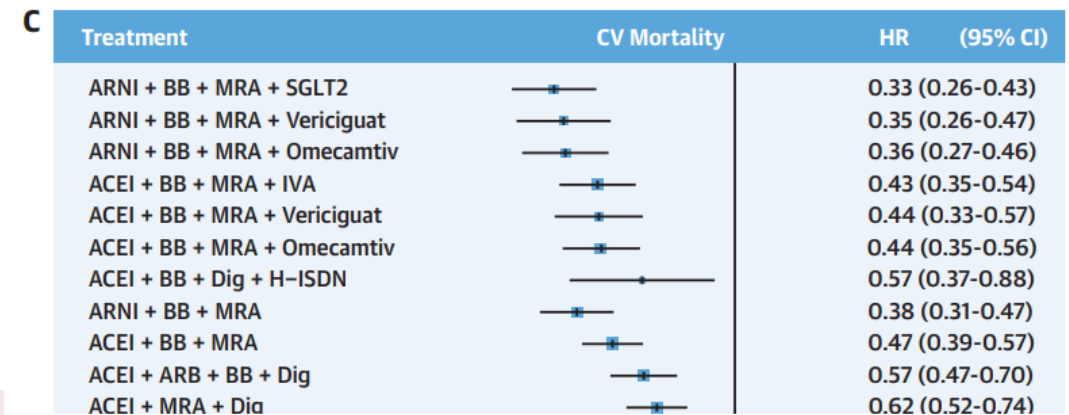
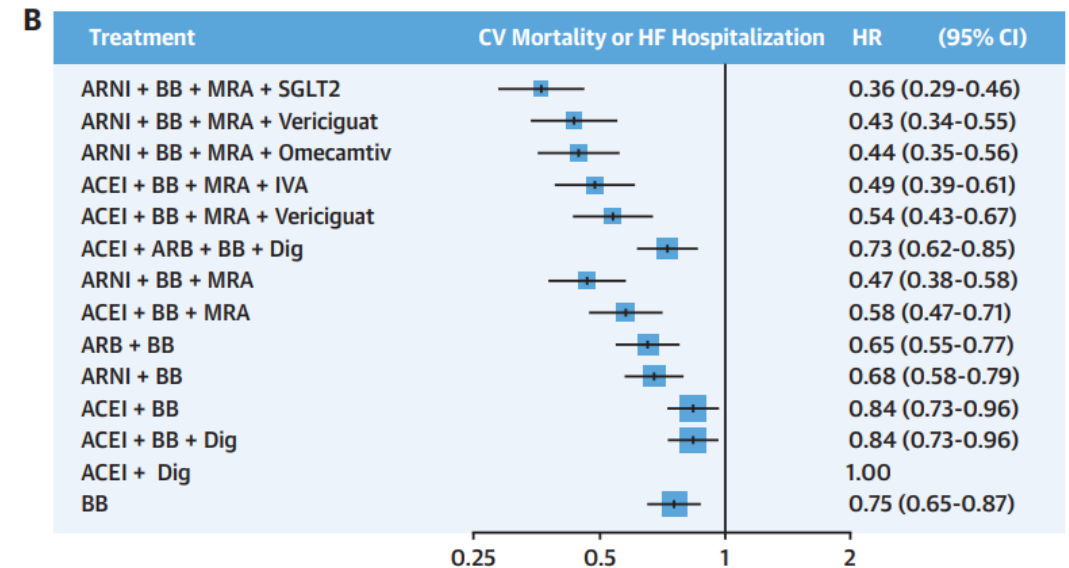
Schnittstellenmanagement HA-Kardiologe/in von besonderer Bedeutung: Positionspapier ÖGAM/ÖKG



Metaanalyse: Vergleich der Therapiekombinationen



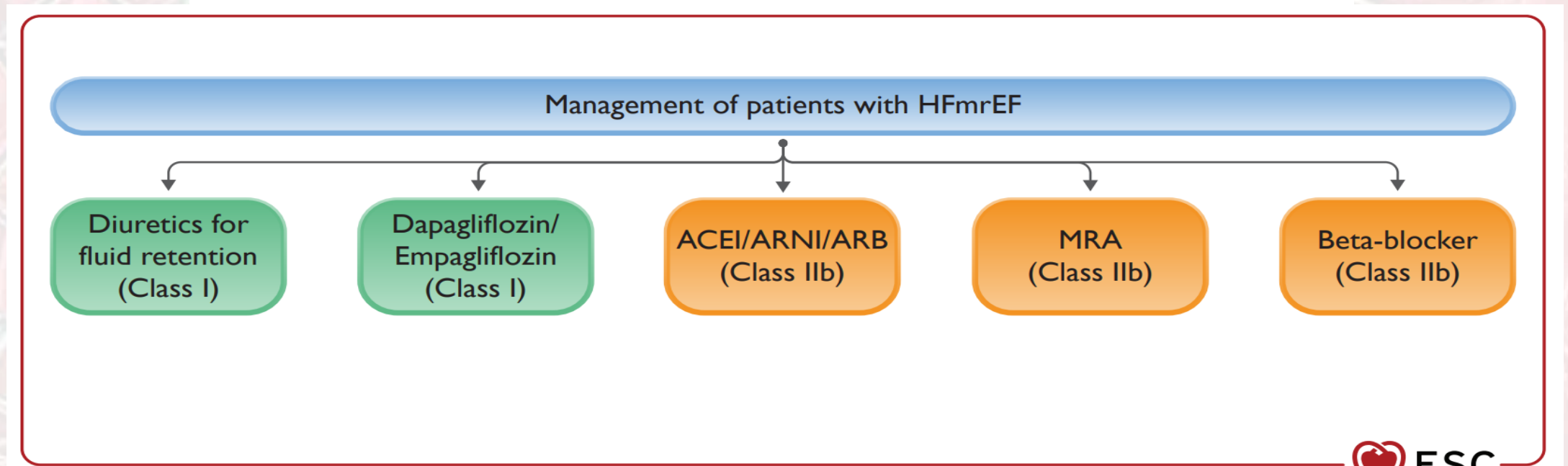
Tromp, J. et al. J Am Coll Cardiol HF. 2022;10(2):73-84.



Und was ist mit der HFmrEF? ESC 2023

Recommendation	Class ^a	Level ^b
An SGLT2 inhibitor (dapagliflozin or empagliflozin) is recommended in patients with HFmrEF to reduce the risk of HF hospitalization or CV death. ^{c 6,8}	I	A

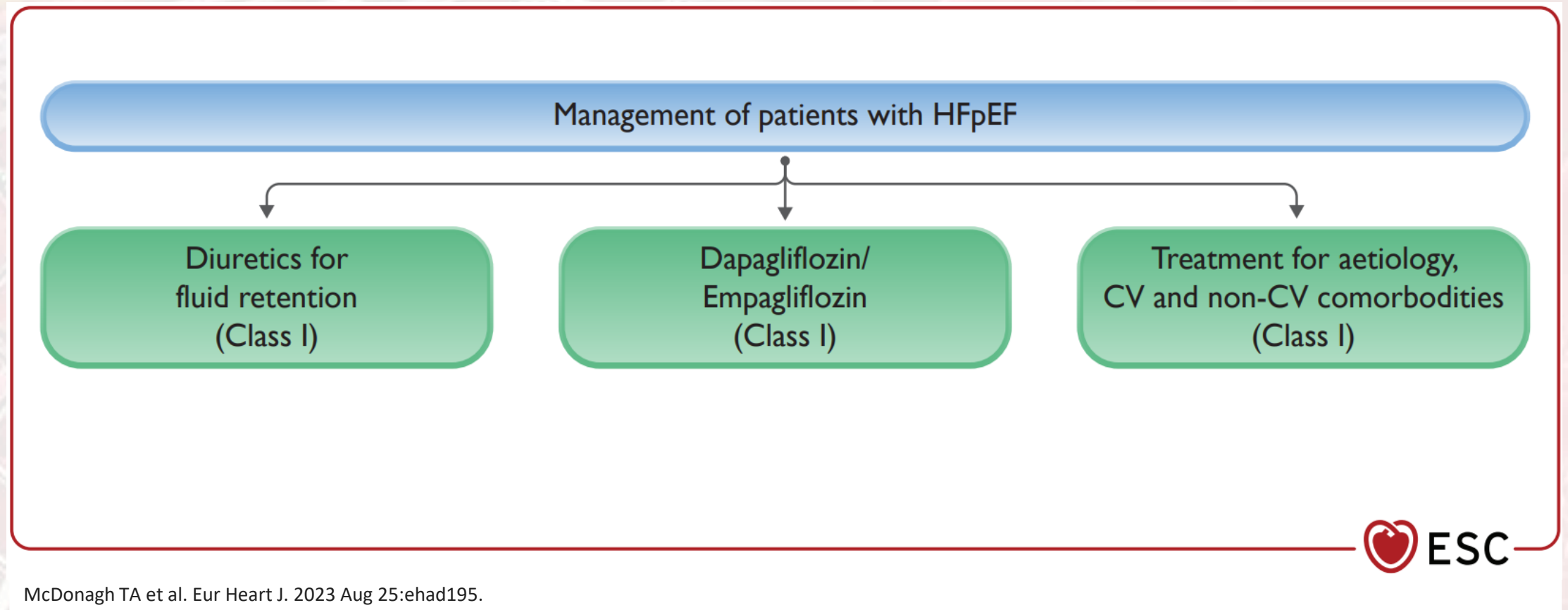
© ESC 2023



McDonagh TA et al. Eur Heart J. 2023 Aug 25;ehad195.

10.102024

Therapie der HFpEF: SGLT-Inh. + Prävention (ESC-Update 08/23)





The MOONRAKER trial programme will generate data for finerenone in more than 15,000 patients with HF across clinical settings



Efficacy and safety profile of finerenone in patients with symptomatic HF vs placebo (N=6016)



Population:
Patients with HF
(NYHA class II–IV)
and LVEF $\geq 40\%$



Primary outcome:
Total number of
CV deaths and
HF events



Efficacy and safety profile of finerenone when initiated early in patients hospitalised with HF vs placebo (N=5200)



Population:
Patients hospitalised
due to HF with
LVEF $\geq 40\%$



Primary outcome:
Total number of
CV deaths and
HF events



Efficacy and safety profile of early combination treatment in patients with HF independent of LVEF (finerenone + SGLT-2i vs usual care; N=1500)



Population*:
Patients hospitalised
due to HF
independent of LVEF



Primary outcome:
All-cause mortality,
total HF events, time to
first HF events and
KCCQ-TSS (win ratio)



Efficacy and safety profile of finerenone in patients with symptomatic HFrEF intolerant of or not eligible for steroidal MRAs (vs placebo; N=2600)



Population#:
Patients with
symptomatic HFrEF



Primary outcome:
Time to first
CV death or HF event

Je höher die UACR, umso höher das VHF-Risiko

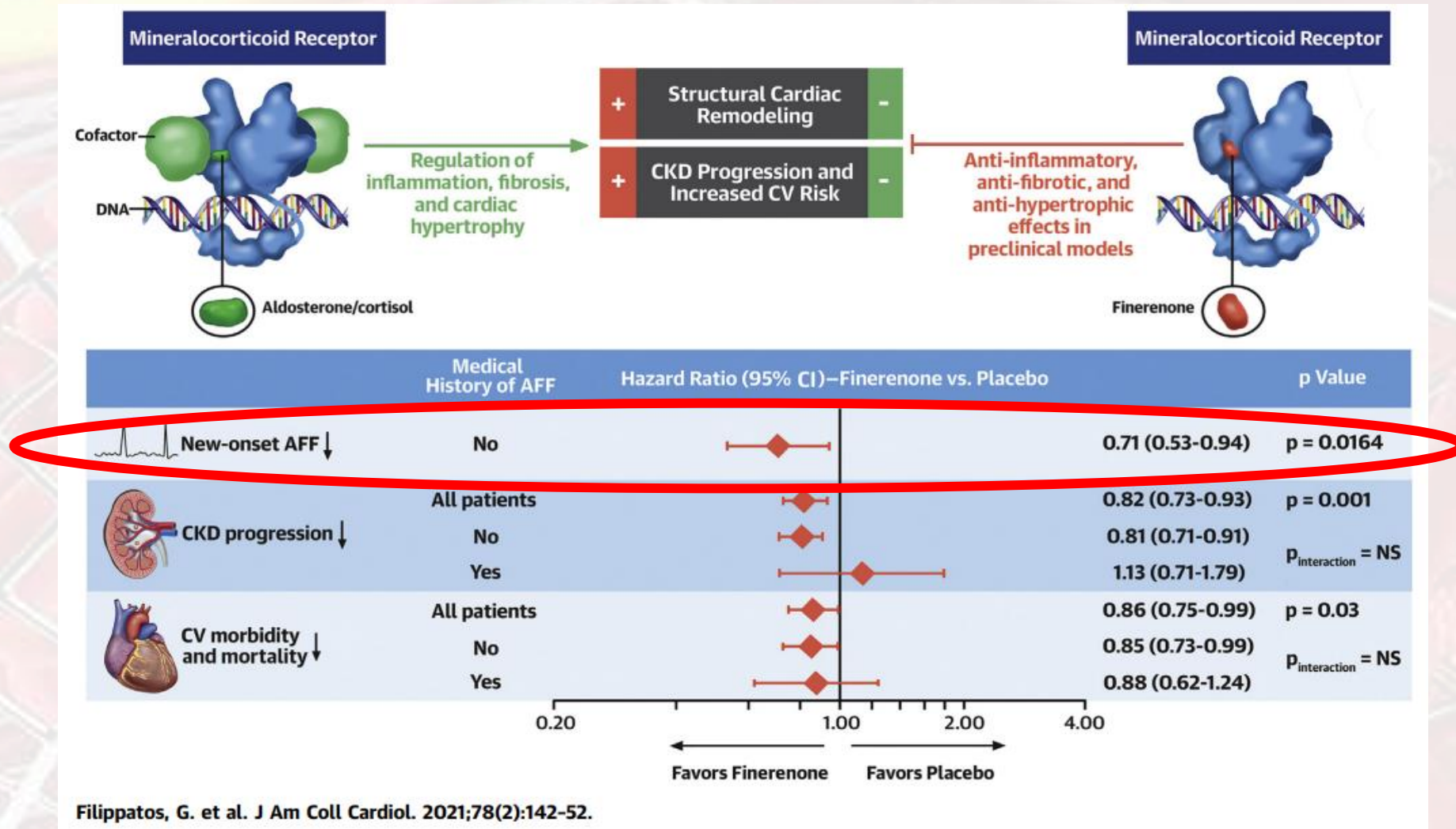
Overall eGFRcr	ACR (mg/g)				
	<10	10–29	30–299	300–999	1000+
105+	1.1	1.3	1.7	2.4	3.5
90–104	Ref	1.2	1.5	1.9	2.3
60–89	1.0	1.2	1.4	1.7	2.2
45–59	1.2	1.3	1.5	1.8	2.4
30–44	1.4	1.5	1.7	2.0	2.4
15–29	1.9	1.8	2.0	2.6	3.0
<15	2.6	2.5	3.1	3.6	4.2

Atrial fibrillation: 50 cohorts

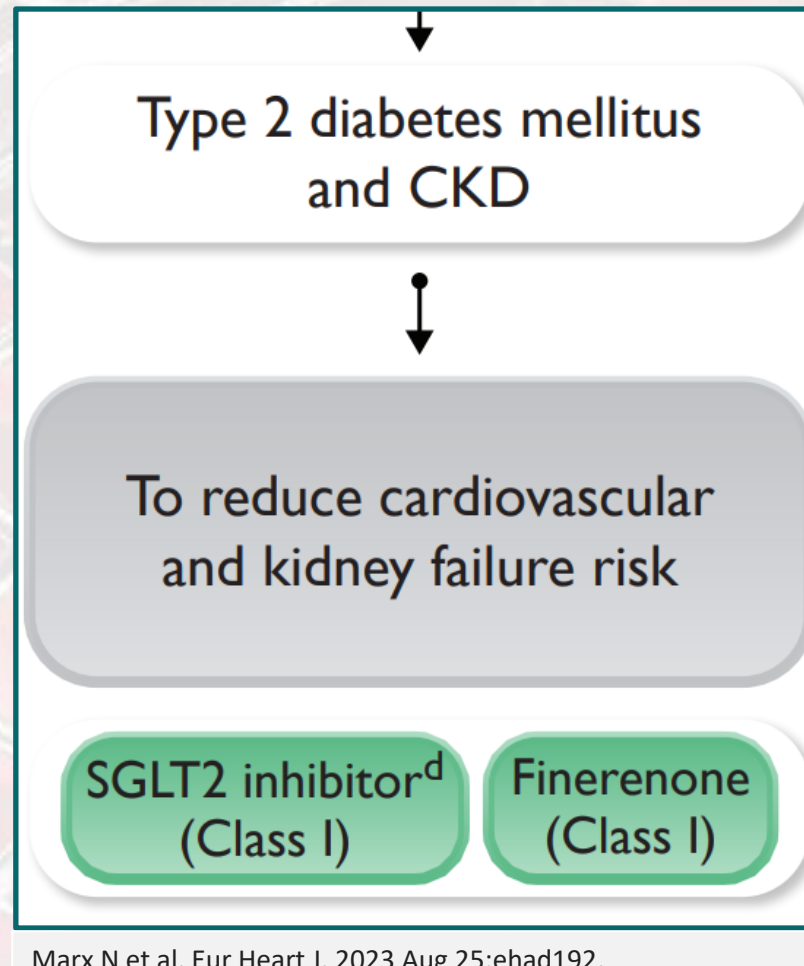
Study size = 22,886,642; events = 1,068,701

Grams ME et al. JAMA. 2023 Oct 3;330(13):1266-1277.

Finerenon-Vorhofflimmern



Diabetes mellitus Typ II+CKD,- MRA in Prävention (Kardioarenoprotektion)



Marx N et al. Eur Heart J. 2023 Aug 25;ehad192.

Ziel-LDL in Abh. von GFR und UACR ohne DM

	A1 (AKR: <30 mg/g)	A2 (AKR30-300mg/g)	A3 (AKR300-3000 mg/g)
G1 >90 ml/min	Score 2	Score 2	
G2 60 – 90 ml/min	Score 2	Score 2	
G3a 45-59 ml/min	Score 2		
G3b 30-44 ml/min			
G4 15-29 ml/min			
G5 <15 ml/min			

Nach Visseren FLJ et al. . Eur Heart J. 2021 Sep 7;42(34):3227-3337 und Mach F et al. Eur Heart J. 2020 Jan 1;41(1):111-188.

rot = hohes Risiko (Ziel-LDL < 70 mg/dl); hellrot = sehr hohes Risiko (Ziel-LDL < 55 mg/dl)

Ziel LDL bei CKD +in Abh. v. der UACR und der GFR

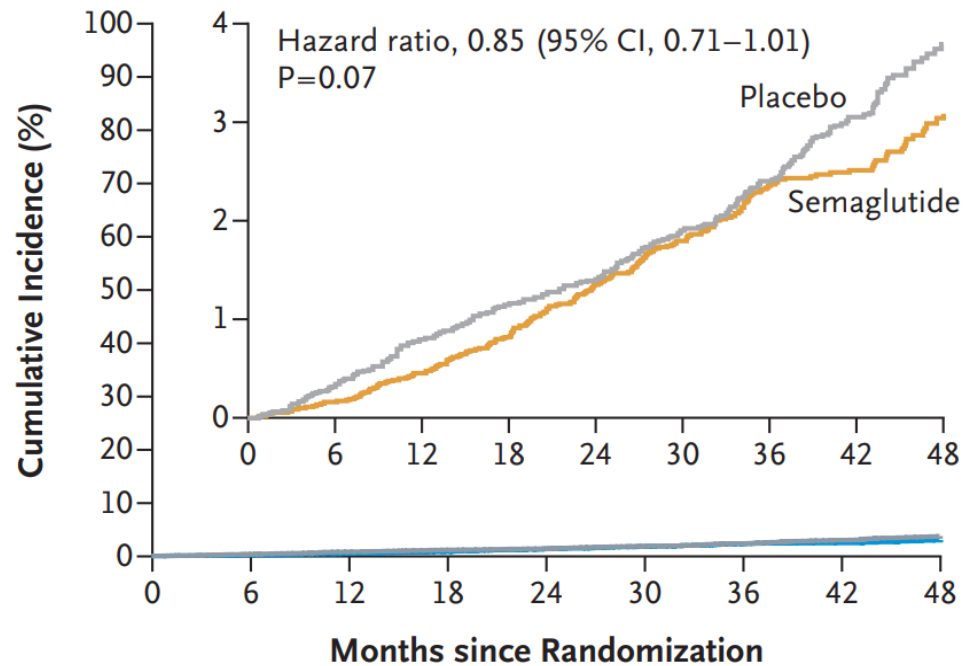
	A1 (AKR: <30 mg/g)	A2 (30-300mg/g)	A3 (300-3000 mg/g)	Endorgansch.
G1 >90 ml/min	Score 2-DM	Score 2-DM		
G2 60 – 90 ml/min	Score 2-DM	Score 2-DM		
G3a 45-59 ml/min	Score 2-DM			
G3b 30-44 ml/min				
G4 15-29 ml/min				
G5 <15 ml/min				

Nach Visseren FLJ et al. . Eur Heart J. 2021 Sep 7;42(34):3227-3337 und Mach F et al. Eur Heart J. 2020 Jan 1;41(1):111-188.

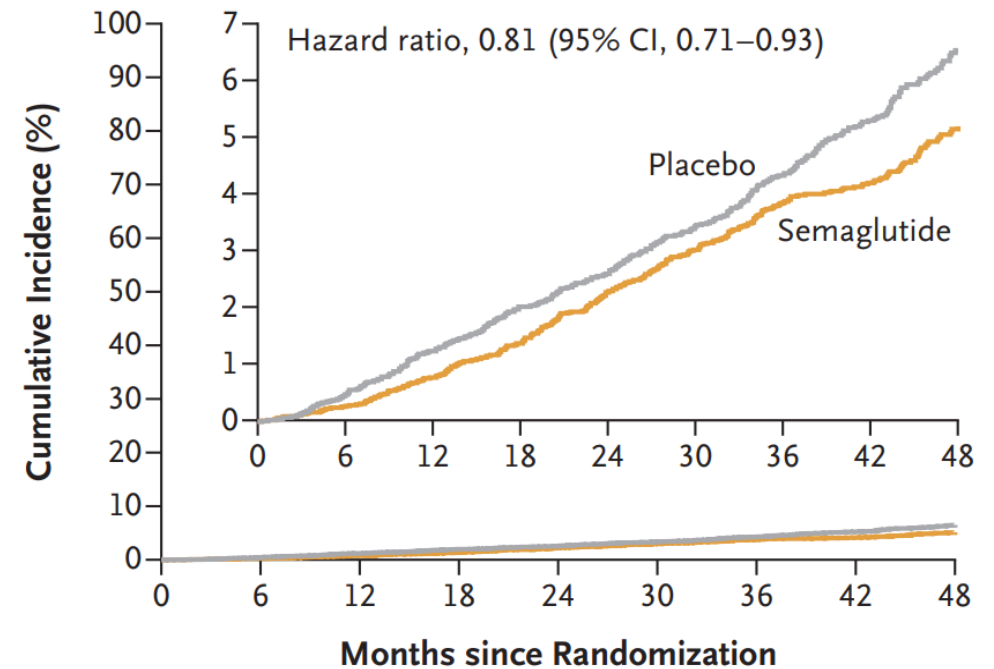
rot = hohes Risiko (Ziel-LDL < 70 mg/dl); hellrot = sehr hohes Risiko (Ziel-LDL < 55 mg/dl)

GLP1-RA als Bestandteil der HI-Prävention: Select

B Death from Cardiovascular Causes



D Death from Any Cause



Lincoff AM et al. N Engl J Med. 2023 Dec 14;389(24):2221-2232.

Optimale Kardioneuroprotektion bei CKD

- ACE-Hem
- SGLT2

Bestimmung der UACR zur
Festlegung der individuellen
Therapieziele bei PatientInnen mit
CKD zur Festlegung des individuellen
Therapieziels unerlässlich!

Zusammenfassung

- Proteinurie/Albuminurie ist unabhängiger kardioresnaler Risikofaktor.
- UACR muss bei PatientInnen mit CKD und/oder Diabetes bestimmt werden.
- Finerenon senkt das kardioresnale Risiko durch eine Verringerung der UACR (Klasse Ia-Empfehlung bei DM+CKD).
- Finerenon senkt Rate an HF-Events bei HFmrEF und HFpEF.
- Die 4 Säulen der HF-Therapie sollten innerhalb von 6 Wochen rasch aufdosiert werden.
- Daten zu Finerenon bei HFrEF folgen, in Zukunft möglicher Ersatz für steroidale MRAs.

The light at the end of the tunnel

