1

2

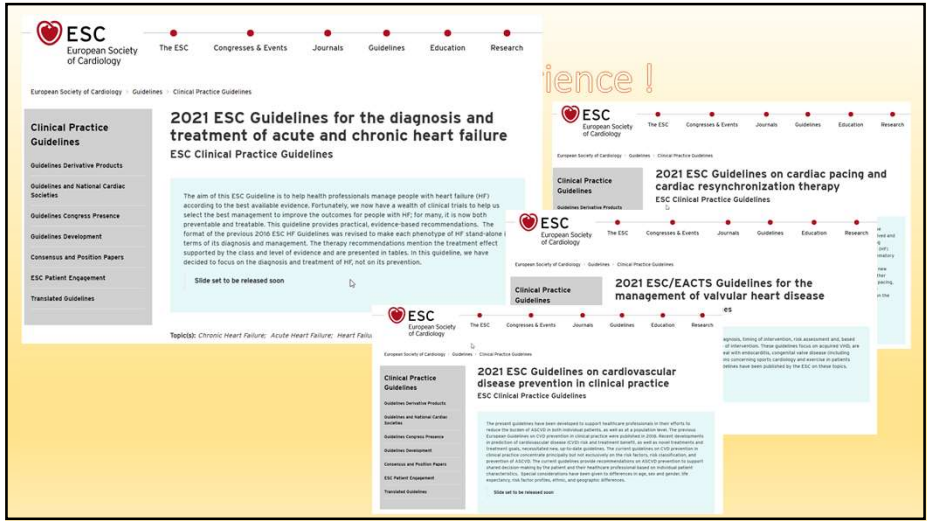
Management Herzinsuffizienz im Spital und in der Praxis

Dr. Michael Neuhaus
Leitender Artz Kardiologie
STGAG Frauenfeld

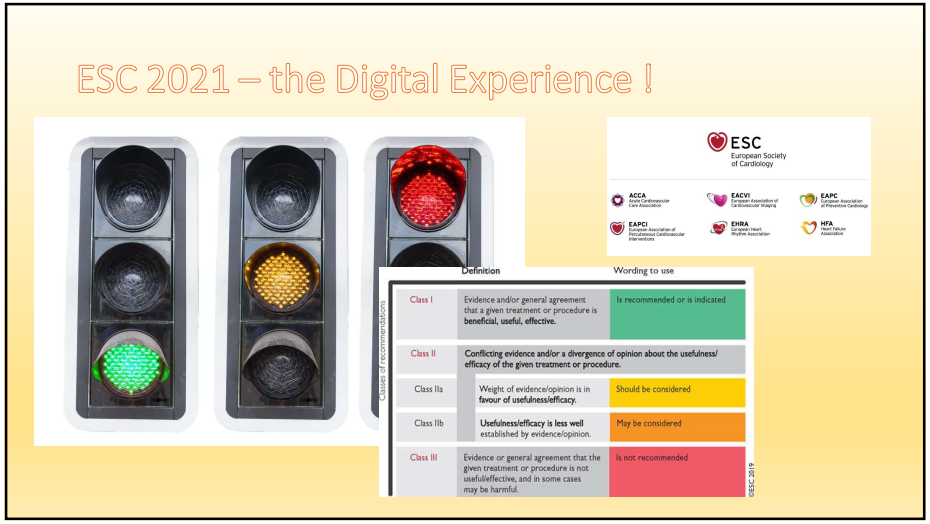
3

All you need to know....

4


ESC
European Society of Cardiology
The ESC
Congresses & Events
Journals
Guidelines
Education
Research
Clinical Practice Guidelines
Guidelines Derivative Products
Guidelines and National Cardiac Societies
Guidelines Congress Presence
Guidelines Development
Consensus and Position Papers
ESC Patient Engagement
Translated Guidelines
2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure
ESC Clinical Practice Guidelines
Slide set to be released soon
2021 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy
ESC Clinical Practice Guidelines
2021 ESC/EACTS Guidelines for the management of valvular heart disease
2021 ESC Guidelines on cardiovascular disease prevention in clinical practice
ESC Clinical Practice Guidelines

5


ESC 2021 – the Digital Experience !
ESC
European Society of Cardiology
ACCA
EACVI
EAPC
EAPCI
EHRA
HFA
Definition
Wording to use
Class I
Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.
Is recommended or is indicated
Class II
Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.
Class IIa
Weight of evidence/opinion is in favour of usefulness/efficacy.
Should be considered
Class IIb
Usefulness/efficacy is less well established by evidence/opinion.
May be considered
Class III
Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.
Is not recommended
Classes of recommendations
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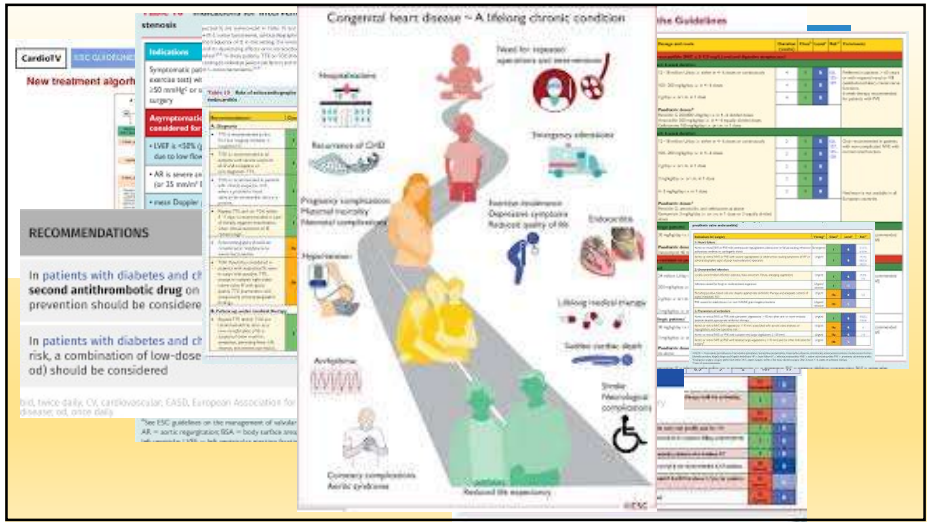
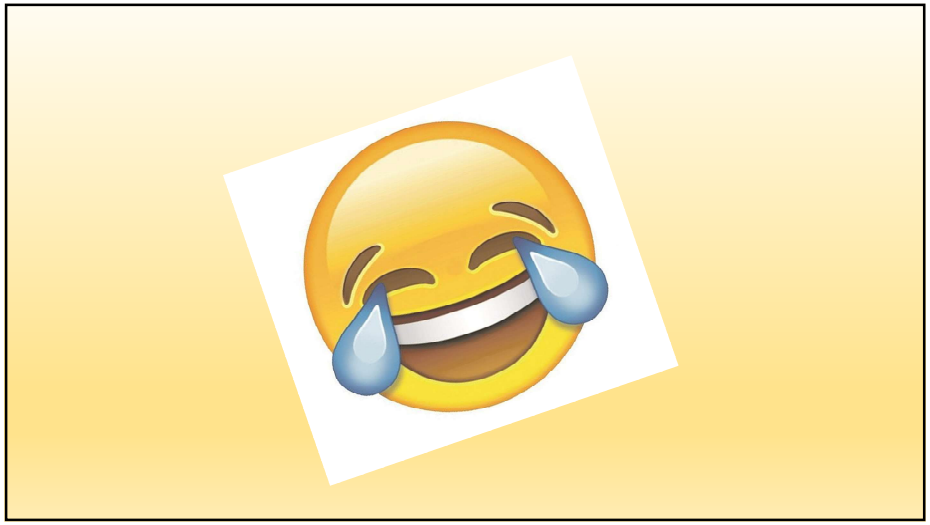
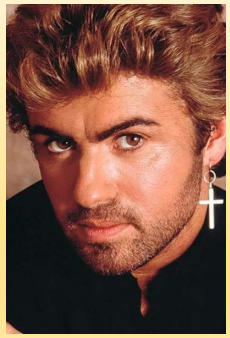

CardioTV
New treatment algorithm
RECOMMENDATIONS
Congenital heart disease ~ A lifelong chronic condition
Need for repeated interventions and reintervention
Hospitalizations
Recurrence of CHD
Emergency admissions
Pregnancy complications
Maternal mortality
Fetomaternal complications
Exercise incompetence
Depressive symptoms
Reduced quality of life
Endocarditis
Heart failure
Lifelong medical therapy
Sudden cardiac death
Arrhythmia
Stroke
Neurological complications
Coronary complications
Aortic dilatation
Reduced life expectancy

7



8

49 jähriger Patient mit DCMP



- Akute Dyspnoe über die letzten 7 Tage
- Orthopnoe, Nykturie 2x
- Beinödeme
- Keine Angina pectoris
- Gewichtszunahme ca. 7 Kg in letzten 2 Monaten

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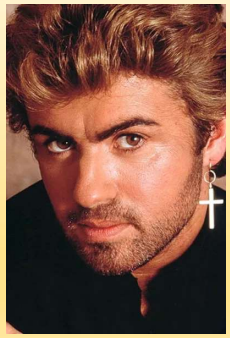
49 jähriger Patient mit DCMP



- Z.n. Myokarditis vor 10 Jahren
- Z.n. Pneumonie vor 7 Jahren
- Z.n. Hospitalisation bei Herzinsuffizienz vor 2 Jahren
- Raucher
- Regelmässiger C2-Konsum
- Keine familiären Herzleiden
- Normaler Blutdruck bisher
- Kein Diabetes

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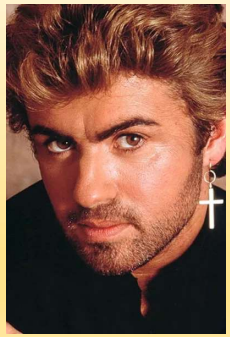
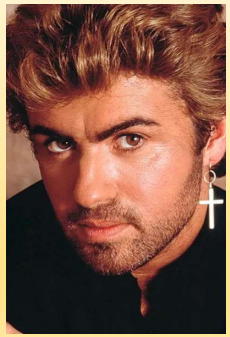
49 jähriger Patient mit DCMP



- Bisherige Medikation:
- Concor 2.5mg 1-0-0
- Zestril 5mg 1-0-0
- Torasemid 5mg 1-0-0

11

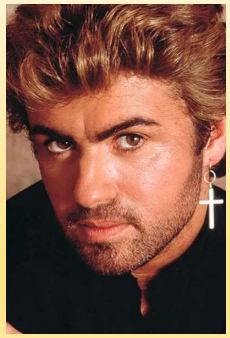
49 jähriger Patient mit DCMP



- Feuchte RG's beidseits, Unterschenkelödeme
- BD 137/83, Puls 91/min, regelmässig
- 2/6 Decreschendo Systolicum apical
- HJR positiv

12

49 jähriger Patient mit DCMP



- NT-pro-BNP 7983 ng/l
- Hs Troponin T 22ng/l, nach 1 Stunde 24 ng/l
- eGFR CKD-EPI 55 ml/min/1.73m2
- K+ 4.4 mmol/l
- O2 Sättigung 90% bei Raumluft

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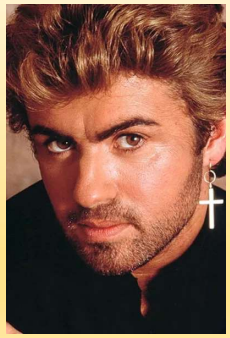
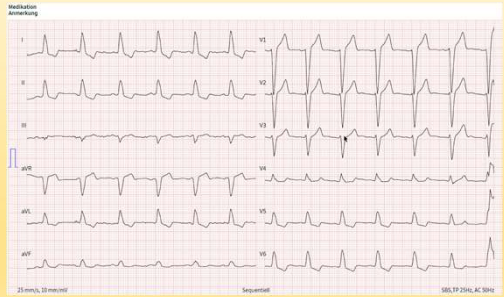
49 jähriger Patient mit DCMP





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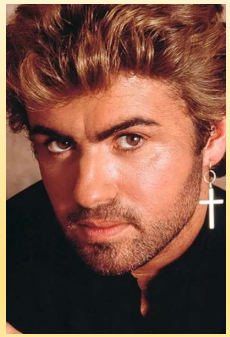
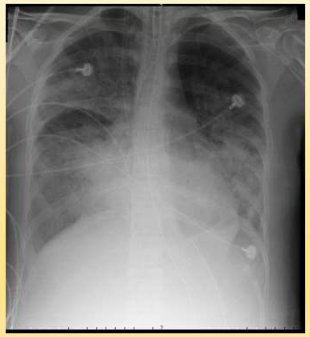
49 jähriger Patient mit DCMP





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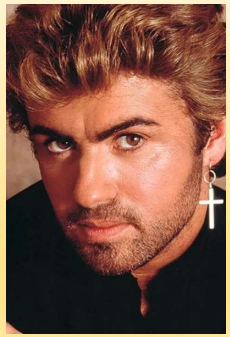
49 jähriger Patient mit DCMP



- 40mg Lasix i.v.
- 2 Liter O2 nasal
- Verbesserung der Symptomatik
- Stationär

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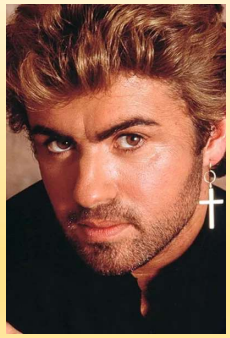
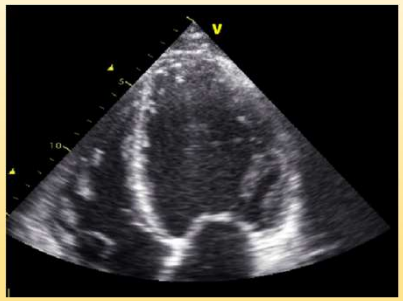
49 jähriger Patient mit DCMP





LVEF 20 %

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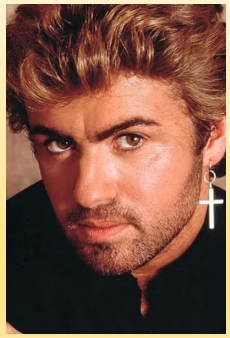
49 jähriger Patient mit DCMP



- Keine Koronarangiographie (schon bei letzter Hospitalisation erfolgt)
- Rekompensation (-7kg)
- Medikamentöser Ausbau
- Demissio

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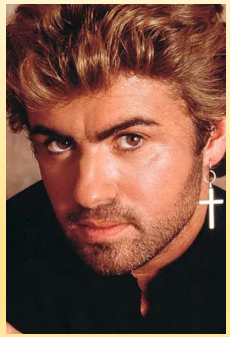
49 jähriger Patient mit DCMP



Austrittsmedikation:

Concor 5mg 1-0-0
Zestril 10mg 1-0-0
Aldactone 100mg 1-0-0
Torasemid 10mg 1-0-0

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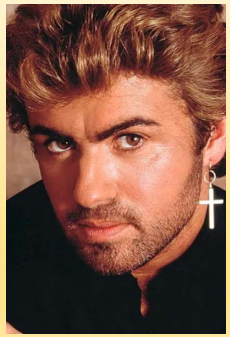
49 jähriger Patient mit DCMP



Patient soll Körpergewicht täglich kontrollieren

Hausarzt:

Verlaufskontrolle Elektrolyte und Kreatinin (Austritts eGFR 68ml/min/1.73m2)

Ausbau der Herzinsuffizienztherapie

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The new universal definition of heart failure classifies the different phenotypes according to LVEF

LVEF	≤40%	41–49%	≥50%
	HF with reduced EF (HFrEF)	HF with mildly reduced EF (HFmrEF)	HF with preserved EF (HFpEF)
		HF with improved EF (HFimpEF) HF with a baseline LVEF ≤40%, a ≥10-point increase from baseline LVEF, and a second measurement of LVEF >40%	

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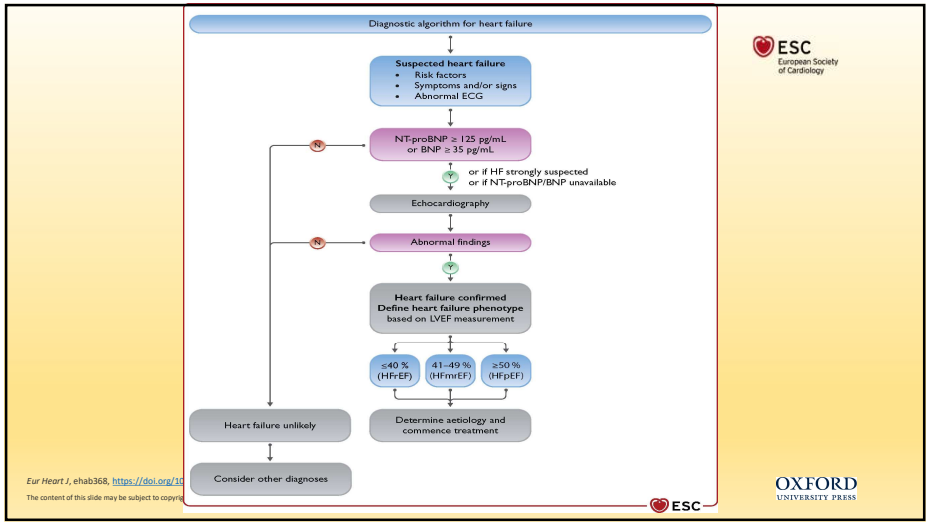

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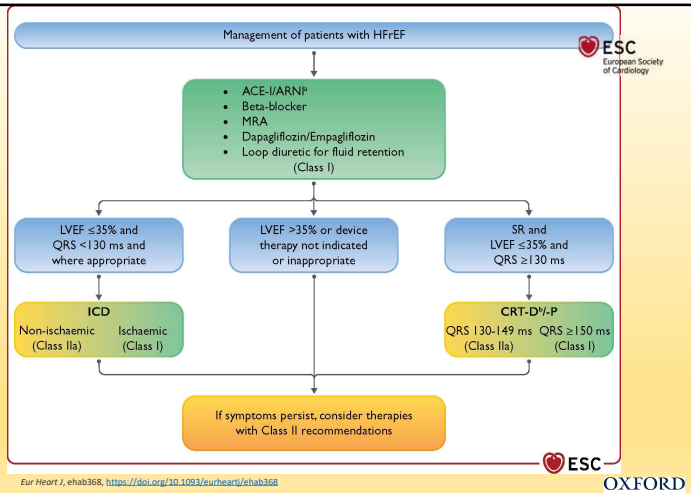

Eur Heart J, ehab368, https://doi.org/10.1093/eurheartj/ehab368

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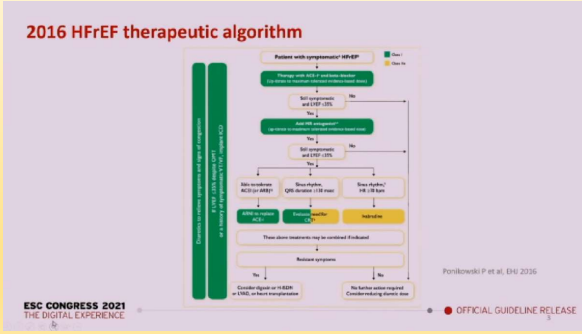

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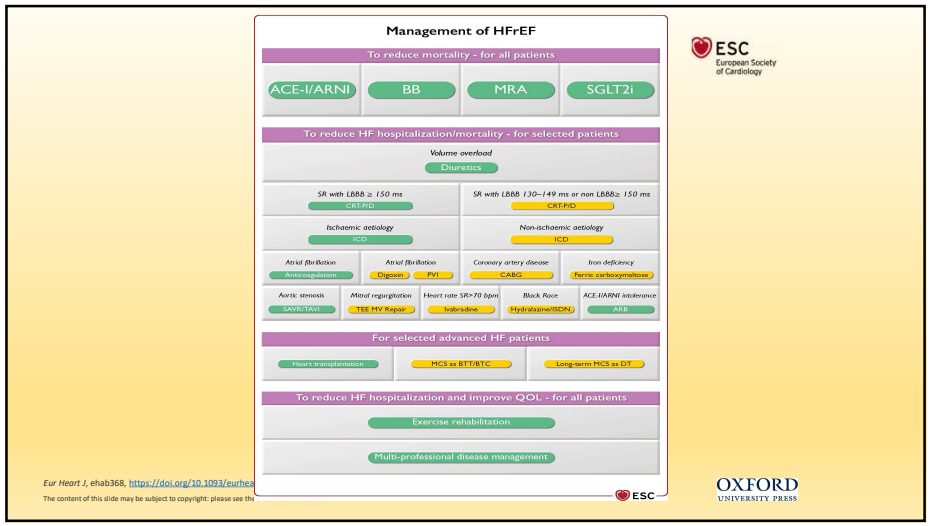

Eur Heart J, ehab368, https://doi.org/10.1093/eurhea

25

Key changes to HFrEF treatment in 2021

- New class I recommended therapy for HFrEF: the SGLT2 inhibitors dapagliflozin and empagliflozin
- The 4 key drug therapies should be initiated as quickly and safely as possible
- Importance of tailored management
- Primary prevention ICD in non-ischaemic cardiomyopathy now IIa
- Emphasis on broad LBBB in selecting patients for CRT

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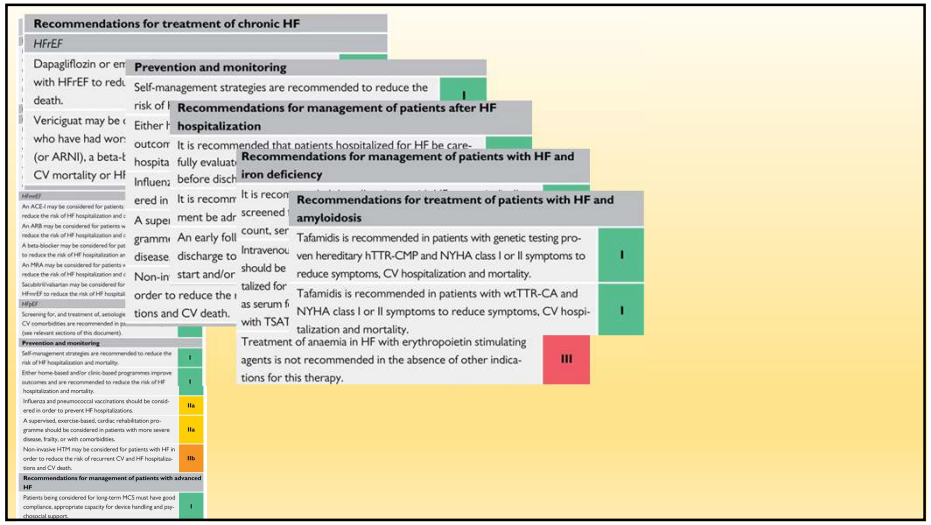

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Recommendations	Class[a]	Level[b]
Loop diuretics		
Diuretics are recommended in patients with HFrEF with signs and/or symptoms of congestion to alleviate HF symptoms, improve exercise capacity, and reduce HF hospitalizations.[137]	I	C
ARB		
An ARB[c] is recommended to reduce the risk of HF hospitalization and CV death in symptomatic patients unable to tolerate an ACE-I or ARNI (patients should also receive a beta-blocker and an MRA).[138]	I	B
I_f-channel inhibitor		
Ivabradine should be considered in symptomatic patients with LVEF ≤35%, in SR and a resting heart rate ≥70 b.p.m. despite treatment with an evidence-based dose of beta-blocker (or maximum tolerated dose below that), ACE-I/(or ARNI), and an MRA, to reduce the risk of HF hospitalization and CV death.[139]	IIa	B
Ivabradine should be considered in symptomatic patients with LVEF ≤35%, in SR and a resting heart rate ≥70 b.p.m. who are unable to tolerate or have contraindications for a beta-blocker to reduce the risk of HF hospitalization and CV death. Patients should also receive an ACE-I (or ARNI) and an MRA.[140]	IIa	C
Soluble guanylate cyclase receptor stimulator		
Vericiguat may be considered in patients in NYHA class II–IV who have had worsening HF despite treatment with an ACE-I (or ARNI), a beta-blocker and an MRA to reduce the risk of CV mortality or HF hospitalization.[141]	IIb	B

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Vericiguat (Verquvo®): VICTORIA Study Data

Zulassung Schweiz voraussichtlich 24.9.2021

The use of Vericiguat is[illegible]zerland – these slides are meant to provide scie[illegible]tional sGC stimulator Vericiguat in p[illegible]ith HFrEF

MA-M_VER-CH-0013_01.2021

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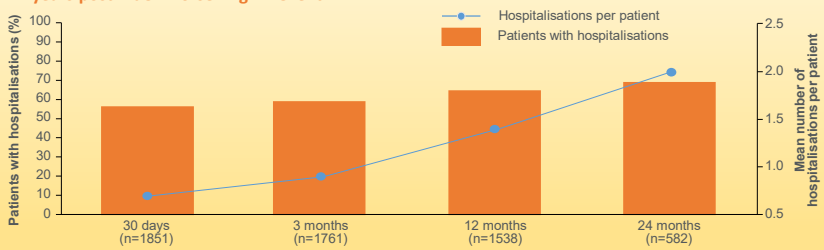
More Than Half of Patients with Chronic HF may Require Rehospitalisation Within a Month of a Worsening HF Event

Patients with hospitalisations and number of hospitalisations per patient through 2 years post index worsening HF event



56% of patients were re-hospitalised within 30 days of the worsening HF event and the number of HF-related hospitalisations increased over time

HF, heart failure
Butler J et al. *J Am Coll Cardiol.* 2019;73:935–944

30

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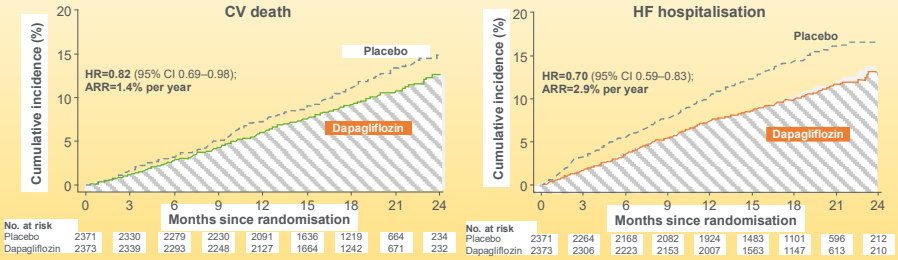
DAPA-HF: Patients in the Dapagliflozin Group Are Still at Risk of CV Death or HF hospitalisation

DAPA-HF: Kaplan–Meier curves for components of primary outcome



Primary composite outcome: 16.3% of patients in the dapagliflozin group experienced CV death or worsening HF* over a median follow-up of 18.2 months

*Defined as hospitalisation or an urgent visit resulting in intravenous therapy for HF
ARR, absolute risk reduction; CI, confidence interval; CV, cardiovascular; HF, heart failure; HR, hazard ratio
McMurray JJV et al. *N Engl J Med.* 2019;381:1995–2008

31

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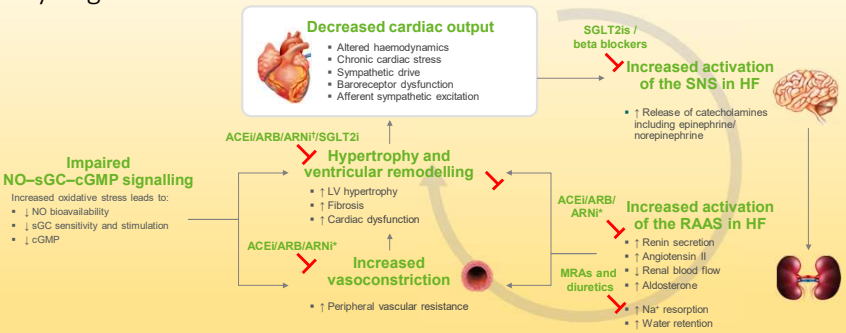
Currently Available HF Treatments Target Several Pathways Dysregulated in HF[1–8]



*RAAS inhibitor component of ARNi; †Neprilysin inhibitor component of ARNi
ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNi, angiotensin receptor-neprilysin inhibitor; cGMP, cyclic guanosine monophosphate; HF, heart failure; LV, left ventricular; MRA, mineralocorticoid receptor antagonist; NO, nitric oxide; RAAS, renin-angiotensin-aldosterone system; sGC, soluble guanylate cyclase; SGLT2i, sodium-glucose co-transporter 2 inhibitor; SNS, sympathetic nervous system
1. Gheorghiade M et al. *Heart Fail Rev.* 2013;18:123–134 ;2. Ponikowski P et al. *Eur Heart J.* 2016;37:2129–2200; 3. Breitenstein S et al. *Handb Exp Pharmacol.* 2017;243:235–247; 4. Klabunde RE. *Pathophysiology of Heart Failure.* In: Cardiovascular Physiology Concepts. Available at: https://cvphysiology.com/Heart%20Failure/HF003. Accessed July 2020; 5.

32

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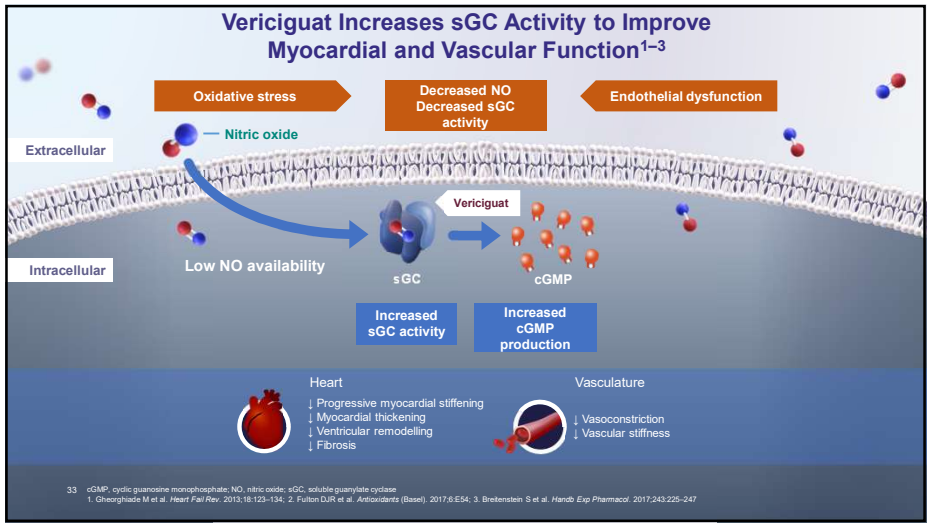

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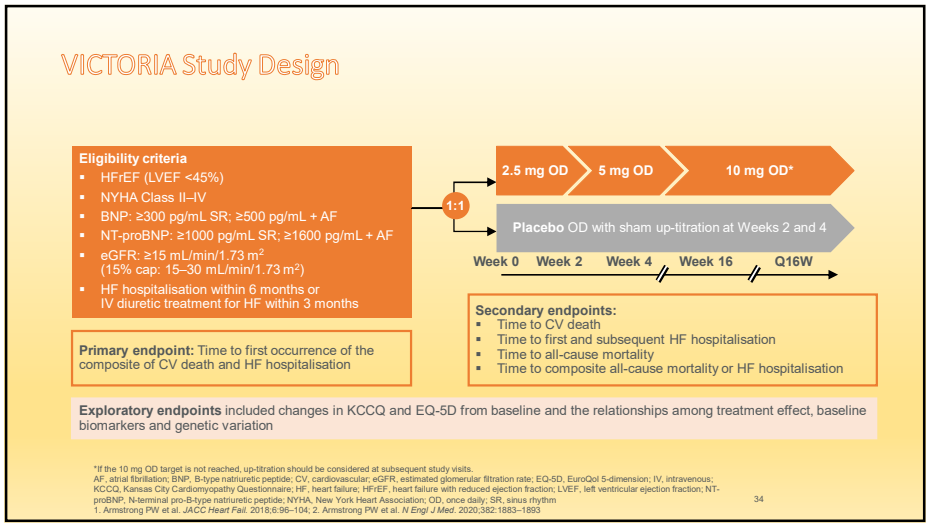

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HF Medications in VICTORIA

Characteristic	Vericiguat (N=2521)	Placebo (N=2519)
Standard-of-care treatment, n (%)		
Beta blocker	2349 (93.2%)	2342 (93.0%)
ACEi/ARB	1847 (73.3%)	1853 (73.6%)
MRA	1747 (69.3%)	1798 (71.4%)
ARNi (sacubitril/valsartan)	360 (14.3%)	371 (14.7%)
Triple therapy	1480 (58.7%)	1529 (60.7%)
Standard-of-care device treatment, n (%)		
Implantable cardioverter defibrillator	696 (27.6%)	703 (27.9%)
Biventricular pacemaker	370 (14.7%)	369 (14.6%)

Armstrong PW et al. *N Engl J Med*. 2020;382:1883–1893

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Index Events in VICTORIA

Characteristic	Vericiguat (N=2526)	Placebo (N=2524)
Index event, n (%)		
Hospitalisation for HF in previous 3 months	1673 (66.2)	1705 (67.6)
Hospitalisation for HF in previous 3–6 months	454 (18.0)	417 (16.5)
IV diuretic for HF (without hospitalisation) in previous 3 months	399 (15.8)	402 (15.9)
Mean time from initial HFrEF diagnosis to randomisation, years ±SD	4.7±5.5	4.8±5.4

HF, heart failure; HFrEF, heart failure with reduced ejection fraction; IV, intravenous; SD, standard deviation
Armstrong PW et al. *N Engl J Med*. 2020;382:1883–1893

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The VICTORIA Trial Targeted a Distinct Patient Population in Contrast to Other Contemporary HF Trials

VICTORIA patients have the largest medical need due to persistently elevated event rates, resulting in a much higher baseline-risk patient population

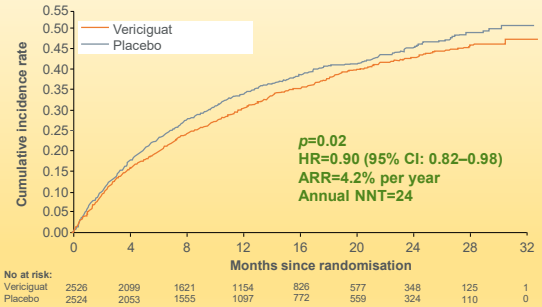
	DAPA-HF[1,2]	PARADIGM-HF[3–5]	VICTORIA[6,7]
Median NT-proBNP (pg/mL)	1437	1608	2816
HFH within 6 months (%)	16.4	31	84
NYHA Class III/IV at baseline (%)	32	25	41
Primary outcome (Events in comparator arms per 100-PY)	15.6*	13.2	37.8
HFH	9.8	7.7	29.1
CV death	7.9	7.5	13.9

Note: this is not intended as a direct comparison of the different studies.
*The primary endpoint for DAPA-HF was CV death or hospitalisation or urgent visit resulting in IV therapy for HF. Primary endpoints for PARADIGM-HF and VICTORIA were CV death or first HFH
CV, cardiovascular; HF, heart failure; HFH, heart failure hospitalisation; IV, intravenous; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; PY, patient-years
1. McMurray JJV et al. *Eur J Heart Fail.* 2019;21:1402–1411; 2. McMurray JJV et al. *N Engl J Med.* 2019;381:1995–2008; 3. McMurray JJV et al. *Eur J Heart Fail.* 2014; 16:817–825; 4. Solomon SD et al. *JACC Heart Fail.* 2016;4:816–822; 5. McMurray JJV et al. *Eur Heart J.* 2015;36:434–439; 6. Armstrong PW et al. *N Engl J Med.* 2020;382:1883–1893; 7. Pieske B et al. *Eur J Heart Fail.* 2019;21:1596–1604
37

37

Vericiguat Significantly Reduced the Annualised Absolute Risk of the Primary Composite Outcome by 4.2%

Time to CV death or first HF hospitalisation



No at risk:

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

- Median follow-up period: **10.8 months**
- Event rate per 100 patient-years was **33.6%** for **vericiguat** vs **37.8%** for **placebo**

ARR, absolute risk reduction; CI, confidence interval; CV, cardiovascular; HF, heart failure; HR, hazard ratio; NNT, number needed to treat
Armstrong PW et al. *N Engl J Med.* 2020;382:1883–1893
38

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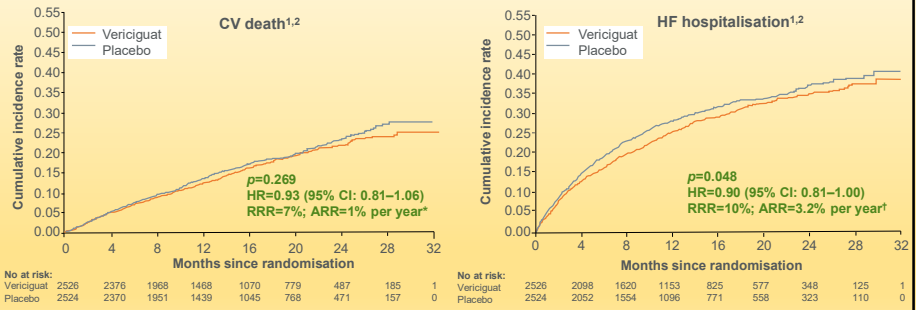
Cumulative Incidence Rates of Primary Endpoint Components

HF hospitalisation drives primary endpoint; CV death is directionally consistent



No at risk:

Vericiguat	2526	2376	1968	1468	1070	779	487	185	1
Placebo	2524	2370	1951	1439	1045	768	471	157	0

No at risk:

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

*Annual ARR: 13.9-12.9=1%; †Annual ARR: 29.1-25.9=3.2%
ARR, absolute risk reduction; CI, confidence interval; HFH, heart failure hospitalisation; HR, hazard ratio; RRR, relative risk reduction
1. Armstrong PW et al. *N Engl J Med.* 2020;382:1883–1893; 2. Armstrong PW et al. Oral Presentation at *ACC* 2020
39

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Conclusion Vericiguat and VICTORIA

Mechanism of action[1,2]
- Vericiguat enhances the cGMP pathway leading to improved cardiovascular function in HF

Patient population[2]
- VICTORIA included patients with symptomatic chronic HF (LVEF <45%) who had a previous worsening HF event despite currently available HF therapies

Efficacy[2,3]
- Vericiguat significantly reduced the annualised absolute risk of the VICTORIA composite outcome of time to HFH or CV death by 4.2%
- The effect of vericiguat on the primary outcome was consistent across most prespecified subgroups
- Vericiguat reduced the primary endpoint and its components across a range of NT-proBNP levels up to 8000 pg/mL

Safety[2,4]
- Overall AE profile of vericiguat comparable to placebo
- Electrolytes or renal function similar between groups
- Symptomatic hypotension and syncope tended to be more common with vericiguat
- Despite decreases in SBP occurring early in the titration phase, no further clinically relevant reductions in BP were subsequently observed

AE, adverse event; cGMP, cyclic guanosine monophosphate; CV, cardiovascular; cGMP, cyclic guanosine monophosphate; HF, heart failure; HFH, heart failure hospitalisation; NT-proBNP, N-terminal pro-B-type natriuretic peptide; SBP, systolic blood pressure
1. Gheorghiade M et al. *Heart Fail Rev.* 2013;18:123; 2. Armstrong PW et al. *N Engl J Med.* 2020;382:1883–1893; 3. Ezekowitz JA et al. Oral Presentation at *HFA Discoveries* 2020; 4. Armstrong PW et al. Oral Presentation at *ACC* 2020
40

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Preis pro Jahr für 1 verhinderte Hospitalisation wegen Herzinsuffizienz

24‘500 CHF

Tagespreis 2.80 CHF

41

The importance of screening for albuminuria to prevent CV disease in patients with CKD and T2D: The FIDELITY analysis

Rajiv Agarwal and Gerasimos Filippatos
Bertram Pitt, Stefan D. Anker, Peter Rossing, Amer Joseph, Peter Kolkhof, Christina Nowack, Martin Gebel, Luis M. Ruilope, George L. Bakris, on behalf of the FIDELIO-DKD and FIGARO-DKD Investigators

28 August 2021

FIDELITY

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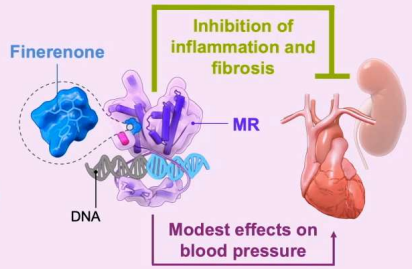
Finerenone is a selective nonsteroidal MRA that interacts with the MR in a different way to steroidal MRAs

- Finerenone blocks MR overactivation, which contributes to inflammation and fibrosis, leading to kidney and CV damage[1,2]
- Finerenone has a unique binding mechanism and distribution vs steroidal MRAs, which results in high potency, selectivity and a differential effect on MR cofactor binding[1,2]
- In FIDELIO-DKD, finerenone slowed CKD progression and improved CV outcomes in patients with CKD and T2D[3]
  - The incidence of hyperkalaemia leading to permanent discontinuation was low



DNA, deoxyribonucleic acid; MR, mineralocorticoid receptor; MRA, mineralocorticoid receptor antagonist

1. Agarwal R, *et al. Eur Heart J* 2021;42:152–161; 2. Agarwal R, *et al. Nephrol Dial Transplant* 2020; doi: 10.1093/ndt/gfaa294; 3. Bakris GB, *et al. N Engl J Med* 2020;383:2219–2229

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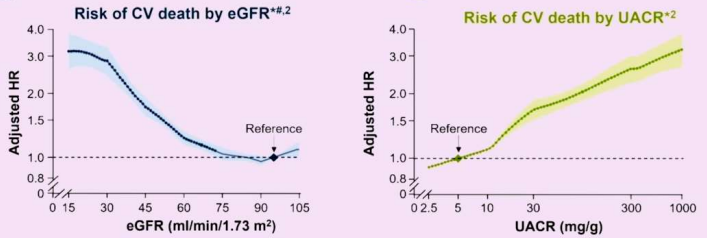
CV risk in patients with CKD and T2D increases as eGFR falls and as UACR rises

CKD = eGFR <60 ml/min/1.73 m² for >3 months[1]

and OR

CKD = albuminuria UACR >30 mg/g for >3 months[1]



*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; #Figure adapted from Matsushita K, *et al.* 2015

CKD, chronic kidney disease; CV, cardiovascular; eGFR, estimated glomerular filtration rate; HR, hazard ratio; T2D, type 2 diabetes; UACR, urine albumin-to-creatinine ratio

1. Kidney Disease Improving Global Outcomes. *Kidney Int* 2013;3:1–150; 2. Matsushita K, *et al. Lancet Diabetes Endocrinol* 2015;3:514–525

44

FIDELITY is a large individual patient data pooled analysis of FIDELIO-DKD[1] and FIGARO-DKD[2]

48 countries

13,171 patients randomised

3 years' median follow-up

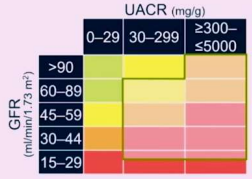
R

Finerenone 10 or 20 mg od*

Placebo

Key eligibility criteria

- ✓ T2D
- ✓ CKD
- ✓ On single RASi
- ✓ Serum [K+] ≤4.8 mmol
- ✗ Symptomatic HFrEF



Key outcomes

CV composite

Time to CV death, non-fatal MI, non-fatal stroke, or HHF

57% eGFR kidney composite

Time to kidney failure,# sustained ≥57% decrease in eGFR from baseline, or renal death

*10 mg if screening eGFR 25–<60 ml/min/1.73 m². 20 mg if ≥60 ml/min/1.73 m². up-titration encouraged from month 1 if serum [K+] ≤4.8 mEq/l and eGFR stable. #kidney failure defined as either ESKD (initiation of chronic dialysis for ≥90 days or kidney transplant) or sustained decrease in eGFR <15 ml/min/1.73 m². ESKD, end-stage kidney disease; GFR, glomerular filtration rate; HHF, hospitalisation for heart failure; HFrEF, heart failure with reduced ejection fraction; [K+], potassium concentration; MI myocardial infarction; RASi, renin–angiotensin system inhibitor; od, once daily.

1. Bakris GB, *et al. N Engl J Med* 2020;383:2219–2229. 2. Pitt B, presented at ESC congress 2021

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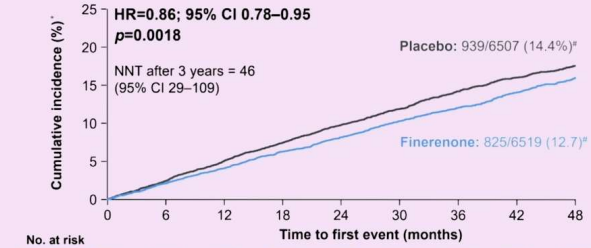
On top of optimised RAS blockade, finerenone significantly reduced the risk of the composite CV outcome by 14%

Time to CV death, non-fatal MI, non-fatal stroke, or hospitalisation for HF



No. at risk									
Finerenone	6519	6360	6202	6009	5273	4207	3065	2187	1087
Placebo	6507	6330	6125	5938	5184	4147	2969	2135	1082

*Cumulative incidence calculated by Aalen–Johansen estimator using deaths due to other causes as competing risk. #number of patients with an event over a median of 3.0 years of follow-up
CI, confidence interval; HR, hazard ratio; NNT, number needed to treat

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FIDELITY summary and conclusions

In patients with CKD stage 1–4 with moderate-to-severely elevated albuminuria (UACR ≥30 mg/g) and T2D, well-controlled blood pressure and HbA1c, no symptomatic HFrEF, and treated with a optimised RASi, finerenone:

Reduced the risk of CV morbidity and mortality by 14% (NNT 46)

The CV benefit of finerenone was primarily driven by a rapid and consistent 22% reduction in HHF, and was consistent regardless of baseline eGFR or UACR, and use of SGLT-2is or GLP-1RAs

Reduced the risk of CKD progression by 23% (NNT 60)

Finerenone significantly reduced the incidence of all non-fatal components of the kidney endpoint, including a 20% reduction in ESKD

Safety profile of finerenone was consistent with that seen in FIDELIO-DKD[1] and FIGARO-DKD[2]

The increase in hyperkalaemia with finerenone was manageable, and routine potassium monitoring minimised its clinical impact

1. Bakris GB, *et al. N Engl J Med* 2020;383:2219–2229. 2. Pitt B, presented at ESC congress 2021

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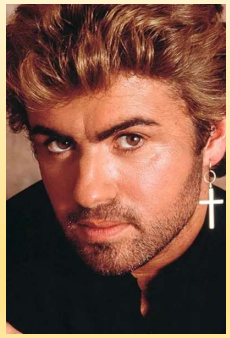
Preis pro Jahr für 1 verhinderte Hospitalisation wegen Herzinsuffizienz

957'000 $
(Tagespreis 19 $)

49

49 jähriger Patient mit DCMP

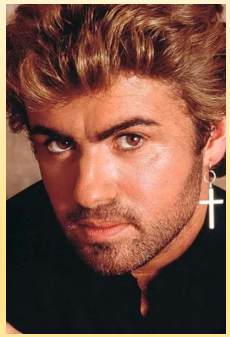


Austrittsmedikation:

Concor 5mg 1-0-0
Zestril 10mg 1-0-0
Aldactone 100mg 1-0-0
Torasemid 10mg 1-0-0

50

49 jähriger Patient mit DCMP

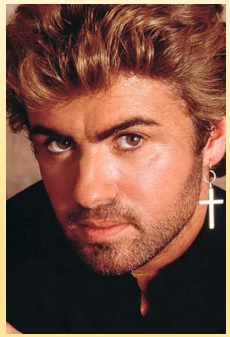


Austrittsmedikation sollte sein:

Concor 5mg 1-0-0
Entresto 50mg 1-0-1
Aldactone 100mg 1-0-0
Forxiga 10mg 1-0-0
Torasemid 5mg nach Körpergewicht

51

49 jähriger Patient mit DCMP

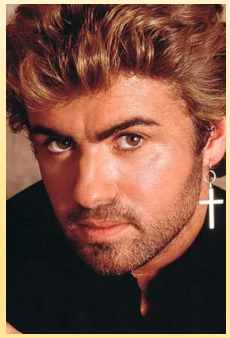


Austrittsempfehlung sollte sein:

Ambulante Kardiale Rehabilitation
Klare Zielgewichtsdefinition

52

49 jähriger Patient mit DCMP



Hausarztvisite nach 1-2 Wochen

Blutdruck

- wenn normotensiv: Ausbau ARNI

Puls (wenn >60/min)

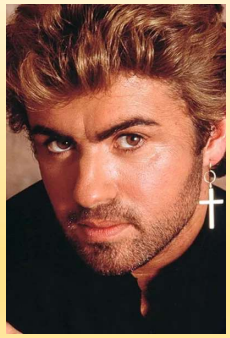
- Ausbau Betablocker

Elektrolyte

- Wenn K+ > 5.5 -> Partiromer

53

49 jähriger Patient mit DCMP



Kreatinin Clearance

- ein initialer Abfall unter SGLT-2 Inhibitor ist normal !

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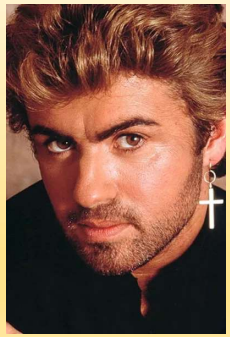
49 jähriger Patient mit DCMP



Hausarztvisite nach 1-2 Wochen

Blutbild / Eisenstatus (wenn im Spital vergessen gegangen…)

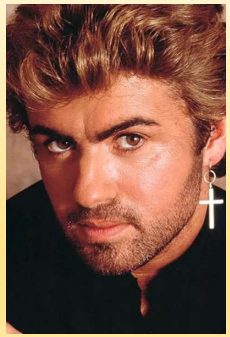
- Eisensubstitution

Check GI-Infektionen

Check Impfstatus (Pneumokokken/Influenza/Covid)

55

49 jähriger Patient mit DCMP



Hausarztvisite nach 1 Monat

Ausdosieren Herzinsuffizienzmedikation zur maximalen Dosis

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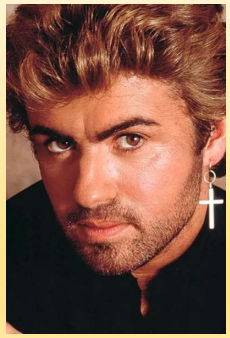
49 jähriger Patient mit DCMP



Kardiologische Kontrolle nach 2-3 Monaten

EKG (LSB)

Verlaufs-TTE (LVEF, Klappeninsuffizienzen, PA-Druck)

-> Indikation ICD/CRT

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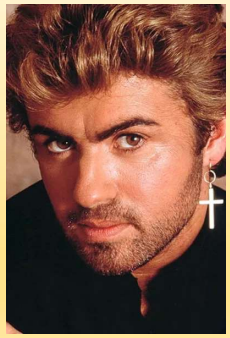
49 jähriger Patient mit DCMP



Falls Rezidiv Dekompensation:

Vericiguat (Verquvo) 10mg 1-0-0

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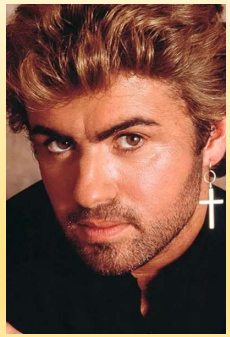
49 jähriger Patient mit DCMP



Kosten dieser Patient / Jahr

Medikamente 1750 CHF

Verquvo: zusätzlich 1022 CHF

Plus HA – Visiten, Kardiologie-Visiten, Labor ca. 1500 CHF

CRT: 10’000 CHF ICD/CRT 25’000 CHF

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Recommendations for the treatment of patients with heart failure with preserved ejection fraction

Recommendations	Class[a]	Level[b]
Screening for, and treatment of, aetiologies, and cardiovascular and non-cardiovascular comorbidities is recommended in patients with HFpEF (see relevant sections of this document).	I	C
Diuretics are recommended in congested patients with HFpEF in order to alleviate symptoms and signs.[137]	I	C

HFpEF = heart failure with preserved ejection fraction.

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The new universal definition of heart failure classifies the different phenotypes according to LVEF

LVEF	≤40%	41–49%	≥50%
	HF with reduced EF (HFrEF)	HF with mildly reduced EF (HFmrEF)	HF with preserved EF (HFpEF)
		HF with improved EF (HFimpEF): HF with a baseline LVEF ≤40%, a ≥10-point increase from baseline LVEF, and a second measurement of LVEF >40%	

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EMPEROR-Preserved: Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria

• Age ≥18 years
• Chronic HF NYHA class II–IV
• **LVEF >40%**
• **NT-proBNP:**
  • **>300 pg/mL** in patients without AF
  • **>900 pg/mL** in patients with AF
• **Structural changes in the heart** (increases in left atrial size or left ventricular mass) **or HHF within 12 months of screening**
	• MI, coronary artery bypass graft surgery or other major CV surgery, stroke or TIA ≤90 days before visit
	• Heart transplant recipient, or listed for heart transplant
	• Acute decompensated HF
	• SBP ≥180 mmHg at randomization
	• Symptomatic hypotension and/or SBP <100 mmHg
	• eGFR <20 mL/min/1.73 m^2 or requiring dialysis

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EMPEROR-Preserved study design

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)

EMPEROR-Preserved
LVEF >40%
5988 patients

- Empagliflozin 10 mg OD
- Placebo

Median follow-up 26.2 months

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 S *et al. N Engl J Med.* 2021;XX:XXX.

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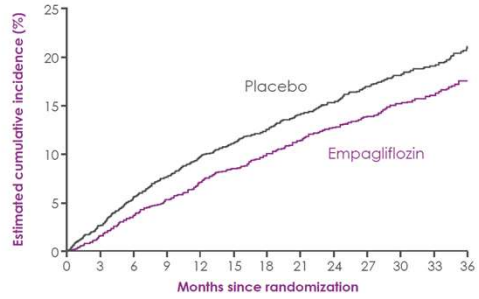
Empagliflozin demonstrated a clinically meaningful 21% RRR in the composite primary endpoint of CV death or HHF



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;XX:XXX.

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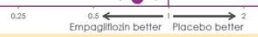
EMPEROR-Preserved is the first and only study to demonstrate a consistent, clinically meaningful benefit across all prespecified subgroups (2/3)

	Empagliflozin n with event/N analysed	Placebo n with event/N analysed	HR (95% CI)
Overall	415/2997	511/2991	0.79 (0.69, 0.90)
Baseline LVEF			
<50%	145/995	193/988	0.71 (0.57, 0.88)
≥50% to <60%	138/1028	173/1030	0.80 (0.64, 0.99)
≥60%	132/974	145/973	0.87 (0.69, 1.10)
Baseline diabetes status			
Diabetes	239/1466	291/1472	0.79 (0.67, 0.94)
No diabetes	176/1531	220/1519	0.78 (0.64, 0.95)
Baseline eGFR (CKD-EPI)			
≥60 mL/min/1.73 m²	152/1493	189/1505	0.81 (0.65, 1.00)
<60 mL/min/1.73 m²	263/1504	321/1484	0.78 (0.66, 0.91)
Baseline NYHA class			
II	275/2435	361/2452	0.75 (0.64, 0.87)
III/IV	140/562	150/539	0.86 (0.68, 1.09)
HF hospitalization in ≤12 months			
No	258/2298	319/2321	0.81 (0.68, 0.95)
Yes	157/699	192/670	0.73 (0.59, 0.90)
Cause of HF			
Ischaemic	157/1079	177/1038	0.85 (0.69, 1.06)
Non-Ischaemic	258/1917	334/1953	0.75 (0.64, 0.89)



Anker S et al. N Engl J Med. 2021;XX:XXX.

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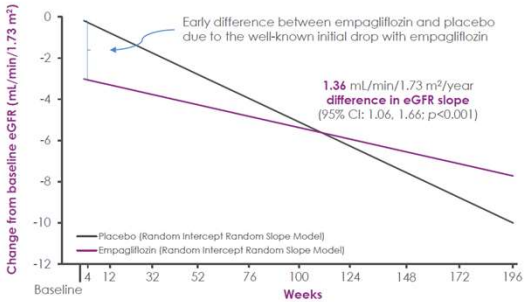
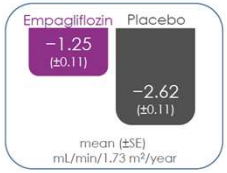
Empagliflozin protected the kidney by significantly slowing the decline in kidney function



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;XX:XXX.

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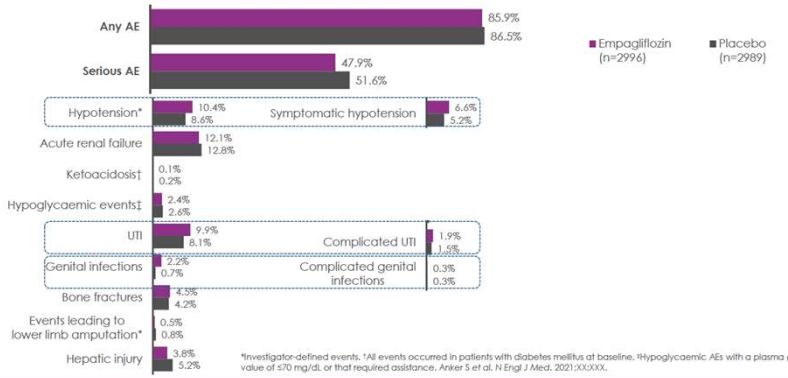
EMPEROR-Preserved: Selected adverse events of interest



*Investigator-defined events. †All events occurred in patients with diabetes mellitus at baseline. ‡Hypoglycaemic AEs with a plasma glucose value of ≤70 mg/dL or that required assistance. Anker S et al. N Engl J Med. 2021;XX:XXX.

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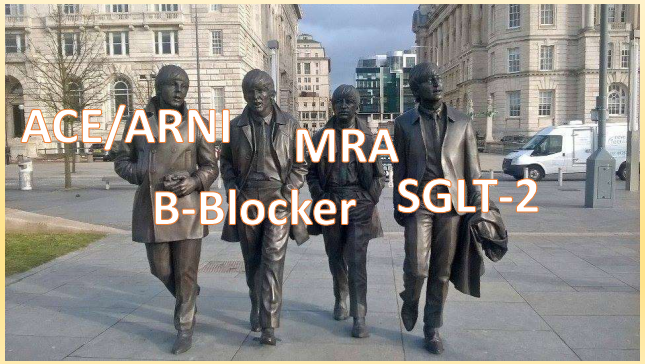
Preis pro Jahr für 1 verhinderte Hospitalisation wegen Herzinsuffizienz

47'500 CHF

Tagespreis 1.90 CHF

68

The fabulous Four !



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