1

Hart & Herzlich am See - Updates 2021

Dr. Michael Neuhaus
Leitender Artz Kardiologie
STGAG Frauenfeld

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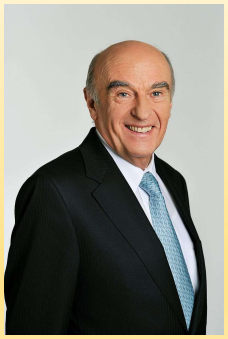
79 jähriger Patient mit KHK und HI



- 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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79 jähriger Patient mit KHK und HI

- Z.n. Herz-Kreislauf-Stillstand 2008
- 5-fach AKB 2008 (Inselspital)
- Z.n. Hospitalisation bei Herzinsuffizienz vor 2 Jahren
- Nichtraucher
- Keine familiären Herzleiden
- Arterielle Hypertonie (ED 2006)
- Kein Diabetes
- Dyslipidämie

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79 jähriger Patient mit KHK und HI

- Bisherige Medikation:
- Aspirin cardio 100mg 1-0-0
- Concor 2.5mg 1-0-0
- Zestril 5mg 1-0-0
- Sortis 20mg 0-0-1
- Torasemid 5mg 1-0-0

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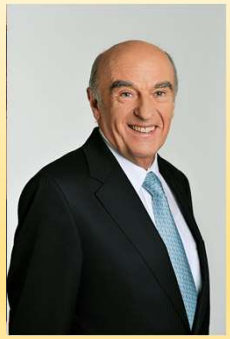
79 jähriger Patient mit KHK und HI



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

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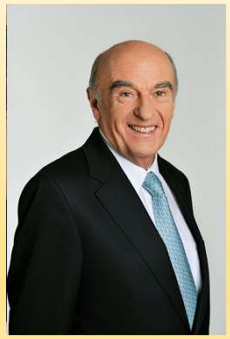
79 jähriger Patient mit KHK und HI



- 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
- Cholesterin 4.3mmol/l, HDL 1.1mmol/l, LDL 2.7 mmol/l
- O2 Sättigung 90% bei Raumluft

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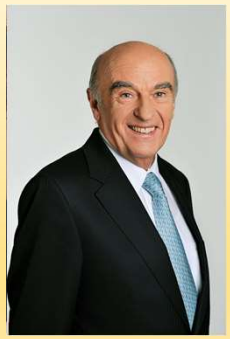
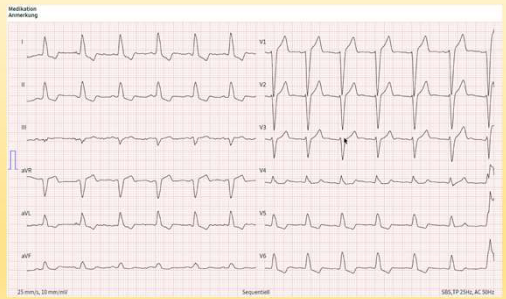
79 jähriger Patient mit KHK und HI





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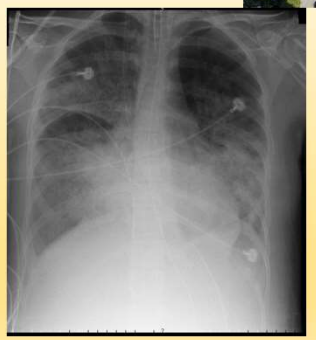
79 jähriger Patient mit KHK und HI



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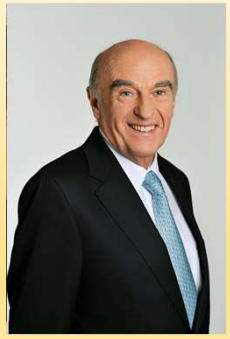
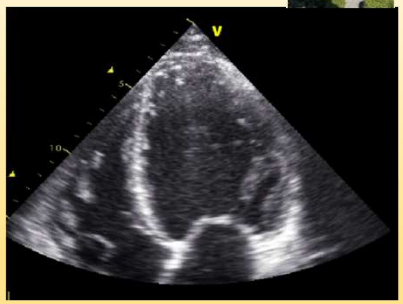
79 jähriger Patient mit KHK und HI



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

11

79 jähriger Patient mit KHK und HI



LVEF 30 %

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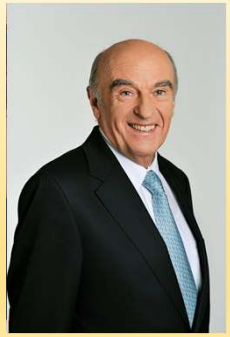
79 jähriger Patient mit KHK und HI



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

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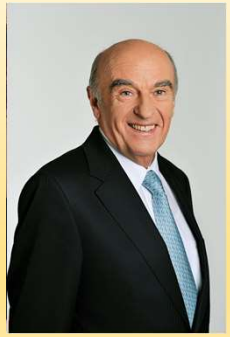
79 jähriger Patient mit KHK und HI



Austrittsmedikation:

- Aspirin cardio 100mg 1-0-0
- Concor 5mg 1-0-0
- Zestril 10mg 1-0-0
- Aldactone 100mg 1-0-0
- Sortis 40mg 0-0-1
- Torasemid 5mg 1-0-0

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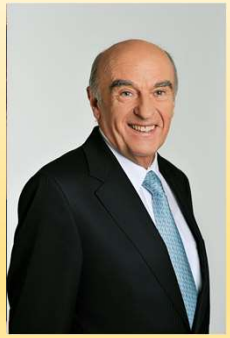
79 jähriger Patient mit KHK und HI



Patient soll Körpergewicht täglich kontrollieren

Hausarzt:

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

Ausbau der Herzinsuffizienztherapie

15

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

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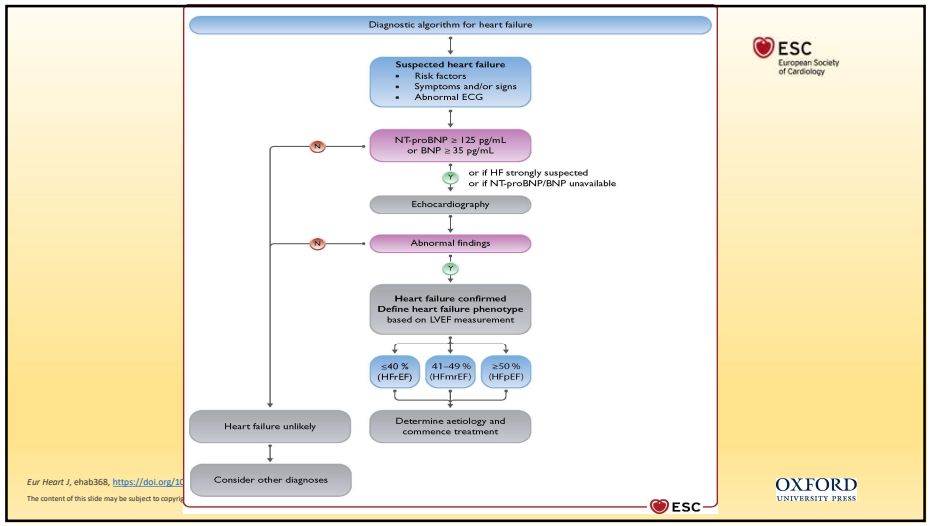

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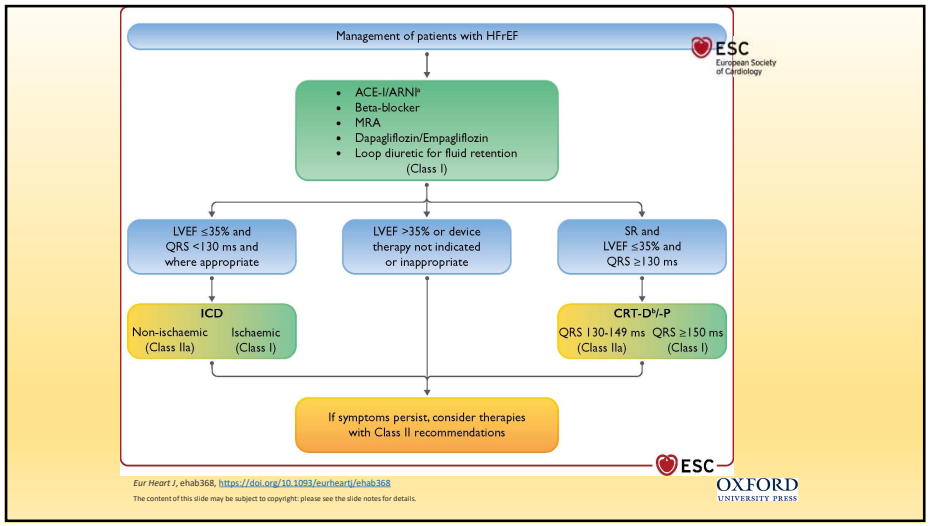

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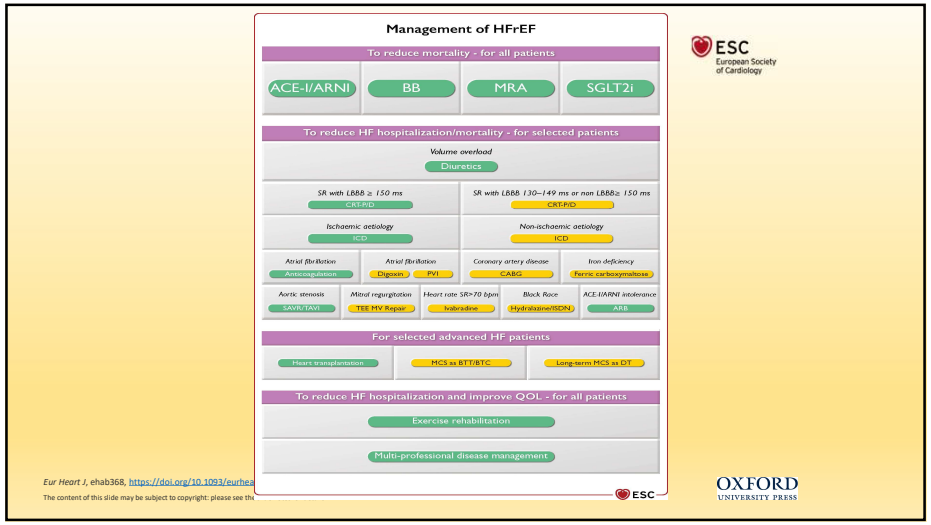

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Key changes to HFrEF treatment in 2021

- 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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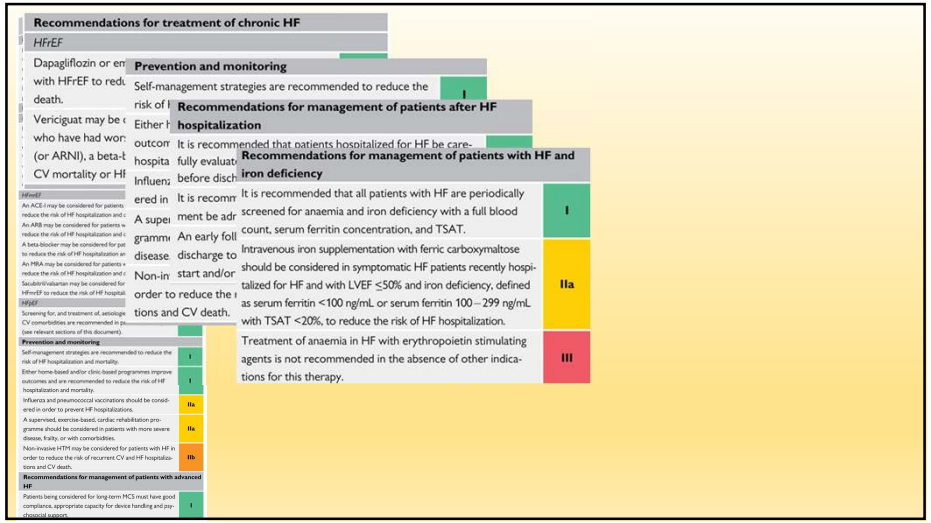

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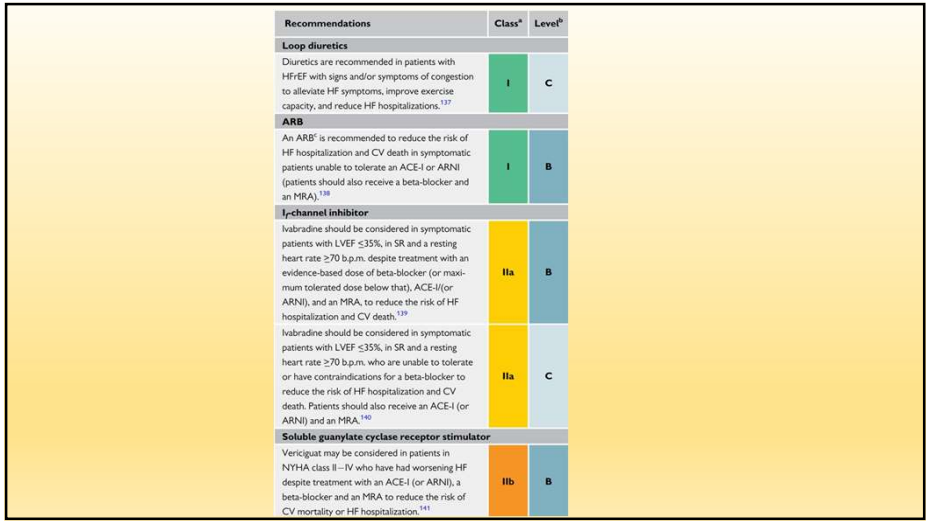

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Vericiguat (Verquvo®): VICTORIA Study Data

Zulassung Schweiz voraussichtlich 24.9.2021

The use of Vericiguat is… …erland – these slides are meant to provide scie… …ional sGC stimulator Vericiguat in p… …th HFrEF

MA-M_VER-CH-0033_01.2021

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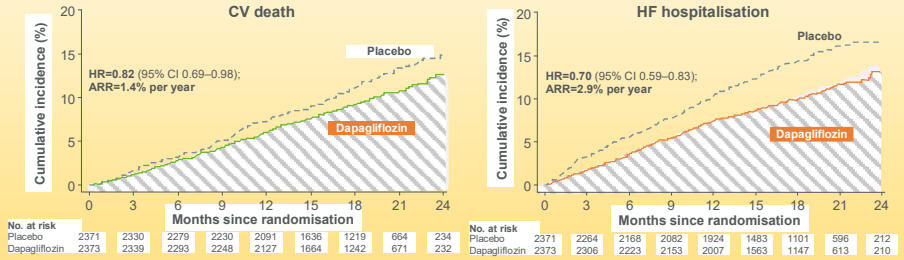
DAPA-HF: Patients in the Dapagliflozin Group Are Still at Risk of CV Death or HF hospitalisation

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

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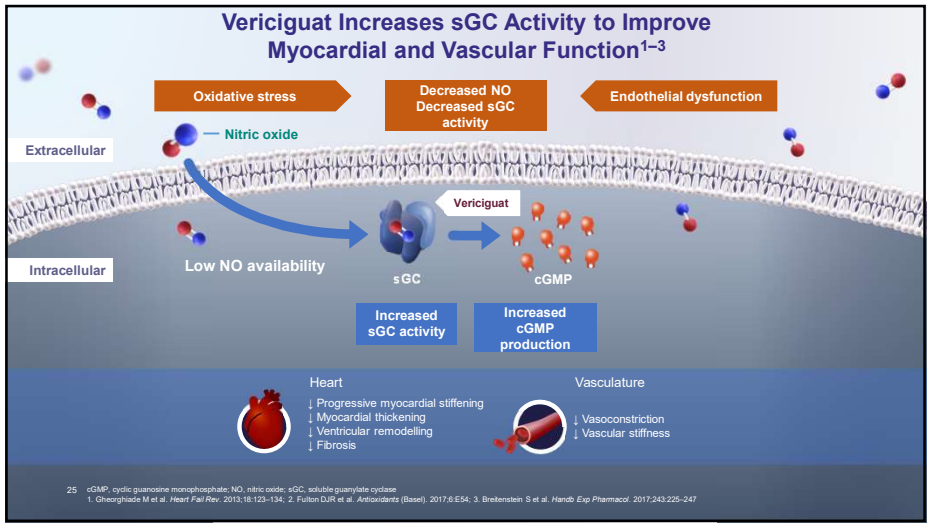
Vericiguat Increases sGC Activity to Improve Myocardial and Vascular Function[1–3]
Oxidative stress
Decreased NO
Decreased sGC activity
Endothelial dysfunction
Nitric oxide
Extracellular
Intracellular
Low NO availability
Vericiguat
sGC
cGMP
Increased sGC activity
Increased cGMP production
Heart
↓ Progressive myocardial stiffening
↓ Myocardial thickening
↓ Ventricular remodelling
↓ Fibrosis
Vasculature
↓ Vasoconstriction
↓ Vascular stiffness
25 cGMP, cyclic guanosine monophosphate; NO, nitric oxide; sGC, soluble guanylate cyclase
1. Gheorghiade M et al. Heart Fail Rev. 2013;18:123–134; 2. Fulton DJR et al. Antioxidants (Basel). 2017;6:E54; 3. Breitenstein S et al. Handb Exp Pharmacol. 2017;243:225–247

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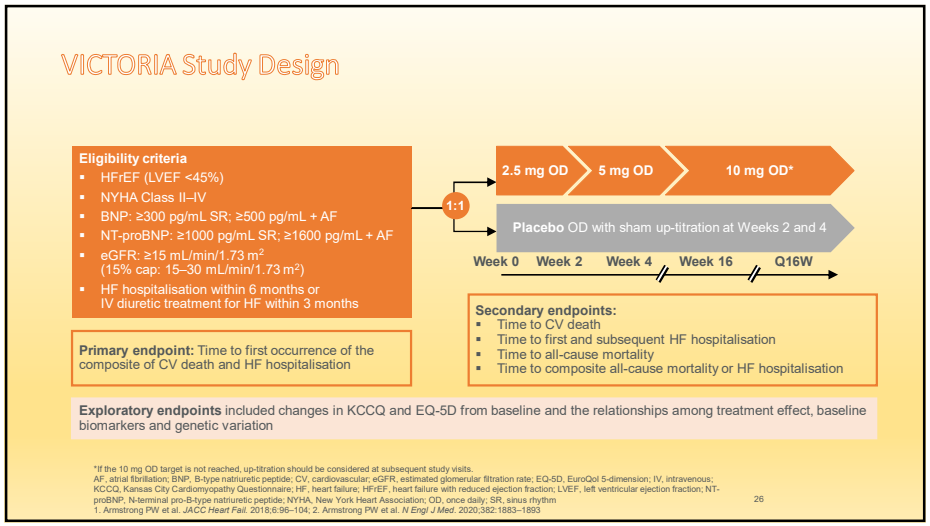
VICTORIA Study Design
Eligibility criteria
HFrEF (LVEF <45%)
NYHA Class II–IV
BNP: ≥300 pg/mL SR; ≥500 pg/mL + AF
NT-proBNP: ≥1000 pg/mL SR; ≥1600 pg/mL + AF
eGFR: ≥15 mL/min/1.73 m²
(15% cap: 15–30 mL/min/1.73 m²)
HF hospitalisation within 6 months or IV diuretic treatment for HF within 3 months
1:1
2.5 mg OD
5 mg OD
10 mg OD*
Placebo OD with sham up-titration at Weeks 2 and 4
Week 0
Week 2
Week 4
Week 16
Q16W
Primary endpoint: Time to first occurrence of the composite of CV death and HF hospitalisation
Secondary endpoints:
Time to CV death
Time to first and subsequent HF hospitalisation
Time to all-cause mortality
Time to composite all-cause mortality or HF hospitalisation
Exploratory endpoints included changes in KCCQ and EQ-5D from baseline and the relationships among treatment effect, baseline biomarkers and genetic variation
*If the 10 mg OD target is not reached, up-titration should be considered at subsequent study visits.
AF, atrial fibrillation; BNP, B-type natriuretic peptide; CV, cardiovascular; eGFR, estimated glomerular filtration rate; EQ-5D, EuroQol 5-dimension; IV, intravenous; KCCQ, Kansas City Cardiomyopathy Questionnaire; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; OD, once daily; SR, sinus rhythm
1. Armstrong PW et al. JACC Heart Fail. 2018;6:96–104; 2. Armstrong PW et al. N Engl J Med. 2020;382:1883–1893

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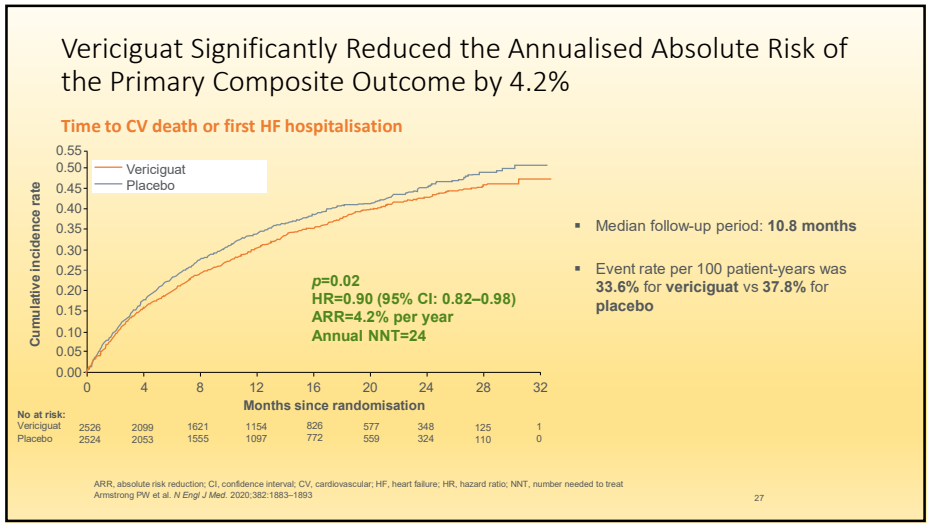
Vericiguat Significantly Reduced the Annualised Absolute Risk of the Primary Composite Outcome by 4.2%
Time to CV death or first HF hospitalisation
Vericiguat
Placebo
Cumulative incidence rate
p=0.02
HR=0.90 (95% CI: 0.82–0.98)
ARR=4.2% per year
Annual NNT=24
Months since randomisation
No at risk:
Vericiguat 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

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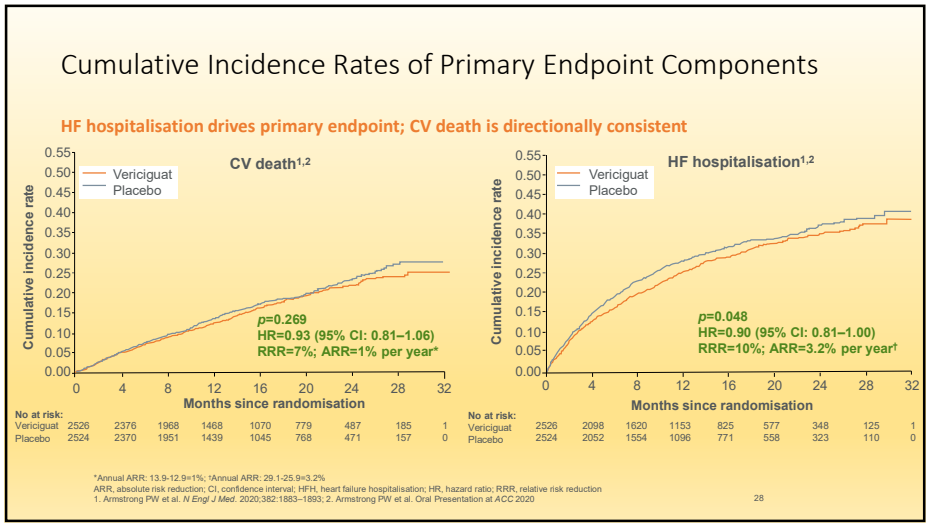
Cumulative Incidence Rates of Primary Endpoint Components
HF hospitalisation drives primary endpoint; CV death is directionally consistent
CV death[1,2]
Vericiguat
Placebo
Cumulative incidence rate
p=0.269
HR=0.93 (95% CI: 0.81–1.06)
RRR=7%; ARR=1% per year*
Months since randomisation
No at risk:
Vericiguat 2526 2376 1968 1468 1070 779 487 185 1
Placebo 2524 2370 1951 1439 1045 768 471 157 0
HF hospitalisation[1,2]
Vericiguat
Placebo
Cumulative incidence rate
p=0.048
HR=0.90 (95% CI: 0.81–1.00)
RRR=10%; ARR=3.2% per year†
Months since randomisation
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

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Preis pro Jahr für 1 verhinderte Hospitalisation wegen Herzinsuffizienz

24‘500 CHF

Tagespreis 2.80 CHF

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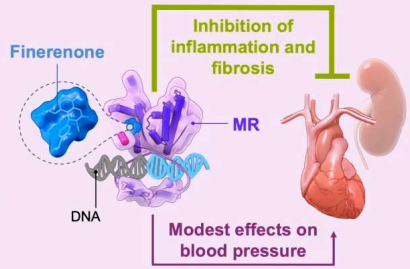
Finerenone is a selective nonsteroidal MRA that interacts with the MR in a different way to steroidal MRAs

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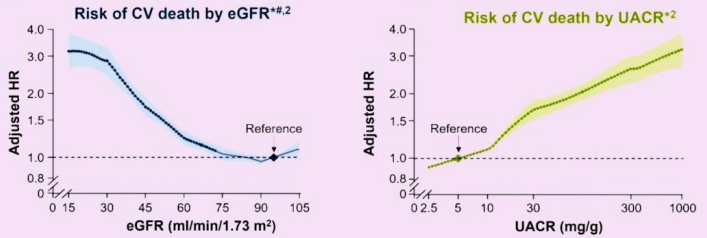
CV risk in patients with CKD and T2D increases as eGFR falls and as UACR rises

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

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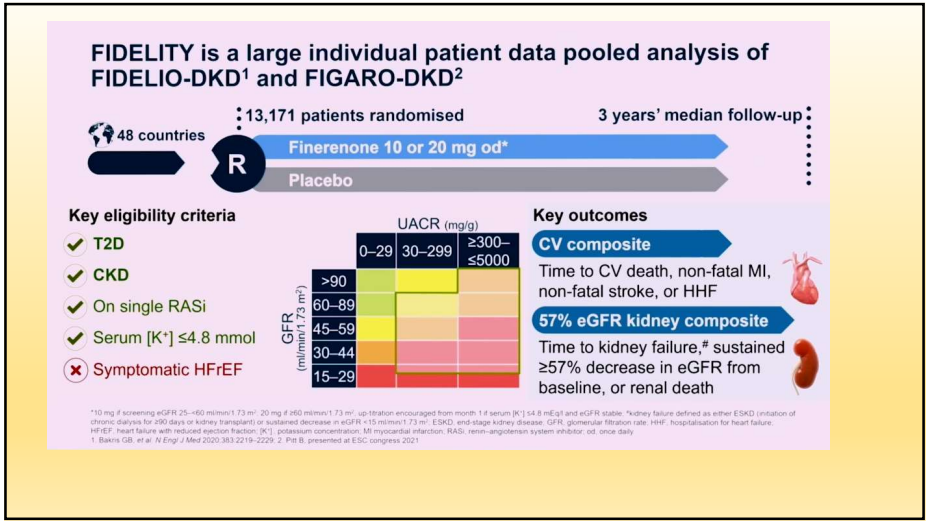
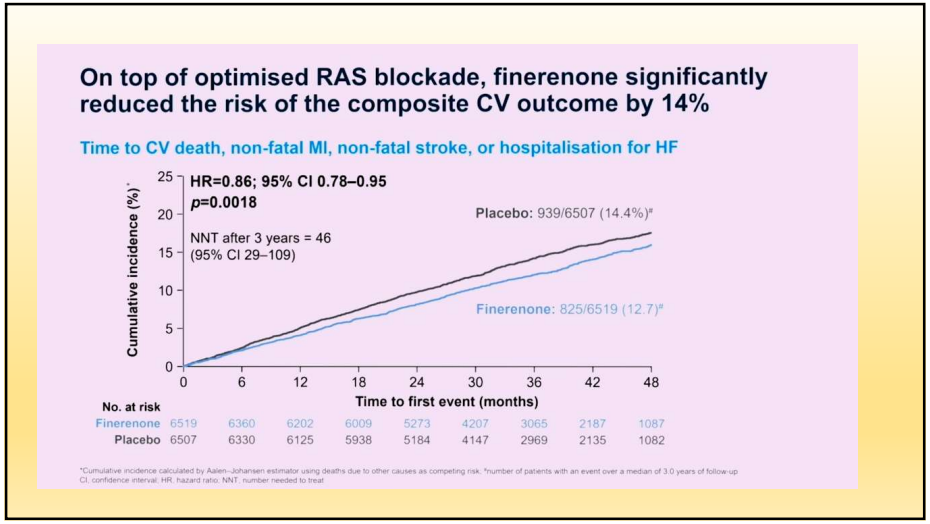


33



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Preis pro Jahr für 1 verhinderte Hospitalisation wegen Herzinsuffizienz

957'000 $

(Tagespreis 19 $)

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HFpEF – endlich!

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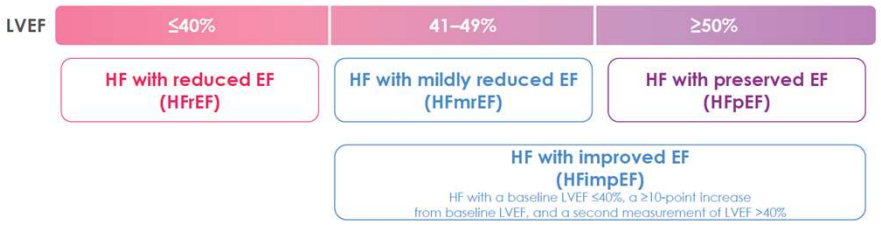
The new universal definition of heart failure classifies the different phenotypes according to LVEF



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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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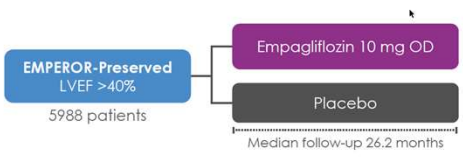
EMPEROR-Preserved study design

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)



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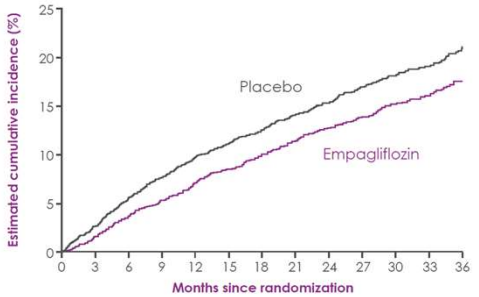
Empagliflozin demonstrated a clinically meaningful 21% RRR in the composite primary endpoint of CV death or HHF



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

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

*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)

0.25 0.5 1 2
Empagliflozin better | Placebo better

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

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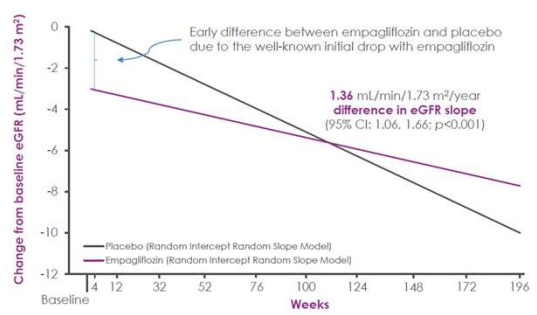
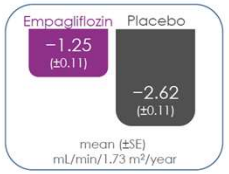
Empagliflozin protected the kidney by significantly slowing the decline in kidney function



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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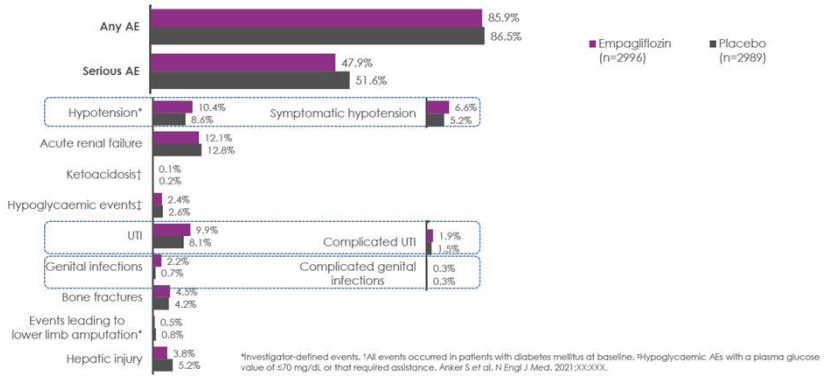
EMPEROR-Preserved: Selected adverse events of interest



45

Preis pro Jahr für 1 verhinderte Hospitalisation wegen Herzinsuffizienz

47‘500 CHF

Tagespreis 1.90 CHF

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Kardiale Amyloidose

Recommendations for treatment of patients with HF and amyloidosis	
Tafamidis is recommended in patients with genetic testing proven hereditary hTTR-CMP and NYHA class I or II symptoms to reduce symptoms, CV hospitalization and mortality.	I
Tafamidis is recommended in patients with wtTTR-CA and NYHA class I or II symptoms to reduce symptoms, CV hospitalization and mortality.	I

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Transthyretin-assoziierte Amyloidose mit Kardiomyopathie (ATTR-CM)[1,2]

- ATTR-CM ist lebensbedrohlich und wird oft übersehen[1]
- Verursacht durch Ablagerungen von Transthyretin (TTR)-Amyloidfibrillen[2]
- Verspätete oder falsche Diagnose verschlechtert Prognose der Patienten[1]
- Mediane Überlebensdauer ab Diagnose unbehandelt:[2]
  - Hereditäre ATTR-CM (hATTR-CM): ca. 2.5 Jahre bei *Val122Ile*-Mutation
  - ATTR-CM vom Wildtyp (wtATTR-CM): ca. 3.5 Jahre

1. Witteles RM et al. Screening for Transthyretin Amyloid Cardiomyopathy in Everyday Practice. JACC Heart Fail. 2019 Aug;7(8):709-716.
2. Rubergi FL et al. Transthyretin Amyloid Cardiomyopathy: JACC State-of-the-Art Review. J Am Coll Cardiol. 2019 Jun 11;73(22):2872-2891.

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Die Pathogenese von ATTR-CM[1]

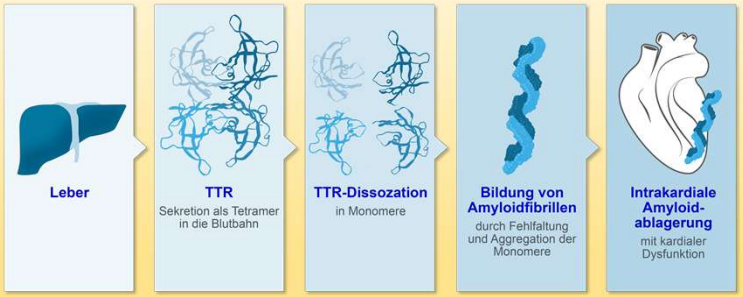

Abbildung adaptiert nach Ref. 1

[1] Ruberg FL et al. Transthyretin Amyloid Cardiomyopathy: JACC State-of-the-Art Review. J Am Coll Cardiol. 2019 Jun 11;73(22):2872-2891.

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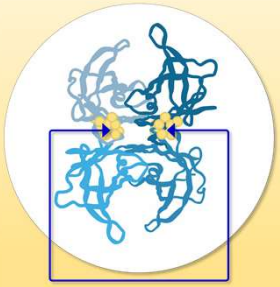
Der Wirkmechanismus von Tafamidis[1–3]

- Tafamidis bindet an TTR an den beiden Thyroxin-Bindungsstellen und stabilisiert das Tetramer.[1]
- Die Stabilisierung des TTR-Tetramers verhindert die Dissoziation in Monomere.[2,3]



Bindungsstellen von Tafamidis[1]

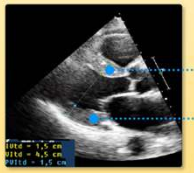
[1] Vyndaqel® (Tafamidis): aktuelle Fachinformation unter www.swissmedicinfo.ch
[2] Maneli LAS et al. Cardiac amyloidosis: An underdiagnosed/underappreciated disease. Eur J Intern Med. 2019 Sep;67:1-13.
[3] Ruberg FL et al. Transthyretin Amyloid Cardiomyopathy: JACC State-of-the-Art Review. J Am Coll Cardiol. 2019 Jun 11;73(22):2872-2891.

50

Echokardiographie[1–4]

- Nachweis einer erhöhten LV-Wanddicke (>12 mm)[1]
- Ohne eindeutig feststellbare Ursache wie z.B. Hypertonie[1,2]

Transthorakale Echokardiogramme, die eine erhöhte LV-Wanddicke zeigen:[3,4]

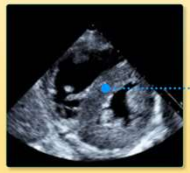


Parasternale Langachsenansicht[3]

Erhöhte enddiastolische LV-Wanddicke des interventrikulären Septums

Erhöhte enddiastolische posteriore LV-Wanddicke

Abbildung aus Ref. 3 mit Genehmigung von Oxford University Press und European Society of Cardiology



Parasternale Kurzachsenansicht[4]

Erhöhte enddiastolische LV-Wanddicke des interventrikulären Septums

Abbildung aus Ref. 4 mit Genehmigung von Elsevier

[1] Maurer MS et al. Expert Consensus Recommendations for the Suspicion and Diagnosis of Transthyretin Cardiac Amyloidosis. Circ Heart Fail. 2019 Sep;12(9):e006075.
[2] Narotsky DL et al. Wild-Type Transthyretin Cardiac Amyloidosis: Novel Insights From Advanced Imaging. Can J Cardiol. 2016 Sep;32(9):1166.e1-1166.e10.
[3] González-López E et al. Wild-type transthyretin amyloidosis as a cause of heart failure with preserved ejection fraction. Eur Heart J. 2015 Oct 7;36(38):2585-94.
[4] Siddiqi OK, Ruberg FL. Cardiac amyloidosis: An update on pathophysiology, diagnosis, and treatment. Trends Cardiovasc Med. 2018 Jan;28(1):10-21.

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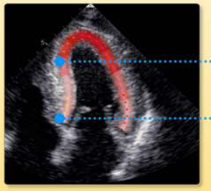
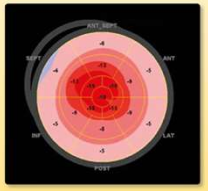
Strain-Echokardiogramme mit «Apical Sparing»[1]



«Apical Sparing» des longitudinalen Strains

Eingeschränkter longitudinaler Strain im mittleren Wandbereich

Eingeschränkter longitudinaler Strain in den basalen Segmenten



«Bull's Eye»-Ansicht eines longitudinalen Strains, der ein «Apical Sparing» zeigt.

Dieses Muster wird auch häufig als «Cherry on Top»-Muster bezeichnet.

Abbildungen aus Ref. 1 mit Genehmigung von Elsevier

[1] Narotsky DL et al. Wild-Type Transthyretin Cardiac Amyloidosis: Novel Insights From Advanced Imaging. Can J Cardiol. 2016 Sep;32(9):1166.e1-1166.e10.

52

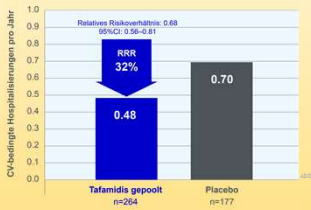
Tafamidis reduzierte signifikant das Mortalitätsrisiko und die Häufigkeit CV-bedingter Hospitalisierung[1]

Individuelle Patientendaten aus den Studien ATTR-ACT und ATTR-ACT Extension

Gesamtmortalität nach 30 Monaten*

Patienten (n) bei Baseline
Tafamidis gepoolt 264
Placebo 177

Häufigkeit CV-bedingter Hospitalisierungen im Verlauf von 30 Monaten



Abbildungen adaptiert nach Ref. 1

HR: hazard ratio; CI: confidence interval; RRR: Relative risk reduction
* Herztransplantation, kombinierte Herz- und Lebertransplantation, Implantation einer mechanischen Herz-Kreislauf-Unterstützung werden in dieser Analyse gleichgesetzt mit Tod.

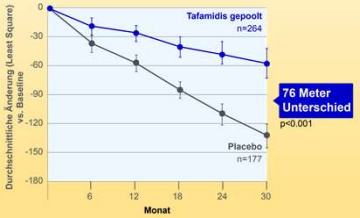
1 Maurer MS et al. Tafamidis Treatment for Patients with Transthyretin Amyloid Cardiomyopathy. N Engl J Med. 2018 Sep 13;379(11):1007-1016.

53

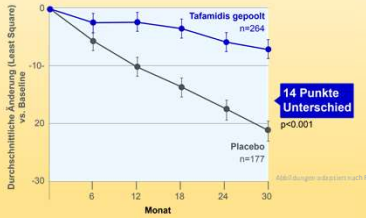
Tafamidis zeigte einen signifikanten Nutzen in Bezug auf Leistungsfähigkeit und Lebensqualität[1]

Sekundäre Hauptendpunkte von ATTR-ACT

Veränderung der 6-Minuten-Gehdistanz von Baseline bis Monat 30



Veränderung im KCCQ-OS-Score von Baseline bis Monat 30*



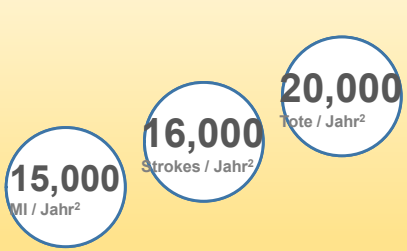
Abbildungen adaptiert nach Ref. 1

* Beurteilung der Lebensqualität mit folgenden Domänen: Gesamtsymptome (Häufigkeit, Belastung), körperliche Einschränkung, Lebensqualität und soziale Einschränkung

1 Maurer MS et al. Tafamidis Treatment for Patients with Transthyretin Amyloid Cardiomyopathy. N Engl J Med. 2018 Sep 13;379(11):1007-1016.

54

CVD ist die führende Todesursache in der Schweiz, verantwortlich für 1/3 aller Todesfälle[1#f]



10.1 Mrd CHF³*

Totale jährliche Kosten bezogen auf kardio-vaskuläre Erkrankungen

1. Taschenstatistik Gesundheit Schweiz 2019, Bundesamt für Statistik (BFS), #Cancer <1/3; Respiratory, infectious disease, accident. 2.Bundesamt für Statistik (Herz- und Kreislauf-Erkrankungen). https://www.bfs.admin.ch/bfs/de/home/statistiken/kataloge-datenbanken/publikationen/uebersichtsdarstellungen/taschenstatistik-schweiz.assetdetail.7767423.html (online access 05/2019) https://www.bfs.admin.ch/bfs/de/home/statistiken/gesundheit/gesundheitszustand/krankheiten/herz-kreislauf-erkrankungen.html (online access 05/2019)
3. Wieser et al.: How much does the treatment of each major disease cost? A decomposition of Swiss National Health Accounts. The Journal of Health Economics (2018) 19: 1146-1161. * Cardiovascular diseases stood out as the most expensive disease category (15.6% of total spending). Split into 10% health goods (20% medicinal products, 80% medication), 90% patient care. MI = myocardial infarction.

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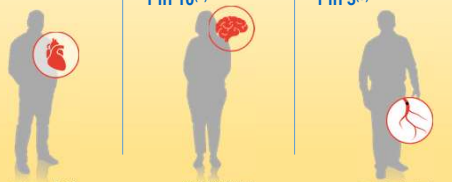
Jeder 5. MI-Patient wird ein neues Ereignis haben innerhalb eines Jahres [1-3]

After MI:
Risk of recurrence within a year
1 in 5(1)

After Stroke:
Risk of recurrence in 5 years
1 in 10(2)

Symptomatic PAD:
Risk of recurrence within a year
1 in 5(3)

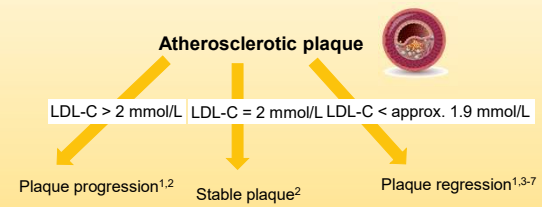


SC-CH-AMG145-00641

1. Jernberg T et al. Cardiovascular risk in post-myocardial infarction patients: nationwide real world data demonstrate the importance of a long-term perspective. Eur Heart J. 2015;36(19):1163-70. 2. Amarenco P et al. High-dose atorvastatin after stroke or transient ischemic attack. N Engl J Med. 2006;355(6):549-59. 3. Steg PG, Bhatt DL, Wilson PW, D'Agostino R Sr, Ohman EM, Röther J, Liau CS, Hirsch AT, Mas JL, Ikeda Y, Pencina MJ, Goto S; REACH Registry Investigators. MI = myocardial infarction

56

Plaque Dynamik abhängig vom Plasma- LDL-C Wert



Atherosclerotic plaques are dynamic[8]

1. Bogiatzi et al., Stroke. 2012. 2. Nissen et al., J Am Med Assoc 2004. 3. Nissen et al., J Am Med Assoc 2006. 4. Nicholls et al., NEJM 2011. 5. Räber et al., Eur Heart J 2015. 6. Lee et al., Am J Cardiol 2012. 7. Tsujita et al., J Am Coll Cardiol 2015. 8. Grundy SM, et al. J Clin Lipidol. 2014;8:2s-6s.

57

Assessing the Impact of PCSK9 Inhibition on Coronary Plaque Phenotype with Optical Coherence Tomography: Primary results of the HUYGENS Study

Stephen J Nicholls, Thomas Hucko, Steven E. Nissen, Francesco Prati, Stephan Windecker, Yu Kataoka, Rishi Puri, Bei Wang, Julie Butters, Giuseppe Di Giovanni, Stephen Jones and Peter J Psaltis.

MONASH University | MONASH VICTORIAN HEART INSTITUTE | MONASHHEART MonashHealth

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This study was funded by Amgen Inc. ClinicalTrials.gov: NCT03570697

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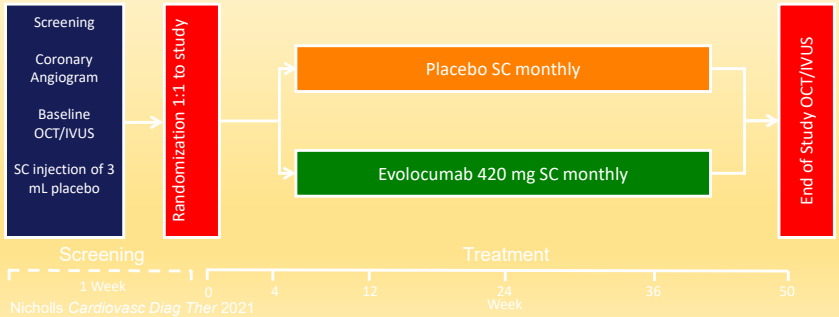
HUYGENS Study Design

161 patients with (i) NSTEMI, (ii) angiographic CAD, (iii) LDL-C ≥60 mg/dL on high-intensity, ≥80 mg/dL on low/moderate-intensity or ≥130 mg/dL on no statin at screening, (iv) subsequently treated with maximally tolerated statin and (v) target segment on OCT containing at least one image with a FCT <120 µm and one image with lipid arc >90°



Nicholls *Cardiovasc Diag Ther* 2021

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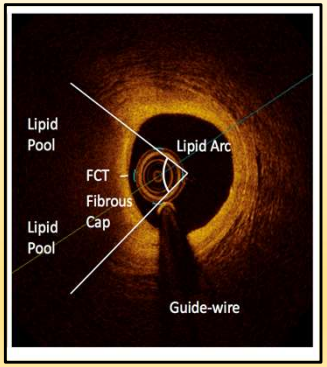
Imaging Analysis



- OCT analysis on images 0.2-mm apart in a segment defined by proximal and distal side branches
- Primary endpoint: change in minimum FCT anywhere in the segment
- Secondary endpoints
  - Percent change in minimum FCT
  - Change in average minimum FCT
  - Change in maximum lipid arc
- Plaque analysis: regions containing FCT ≤120µm and lipid arc >90° for ≥3 consecutive images

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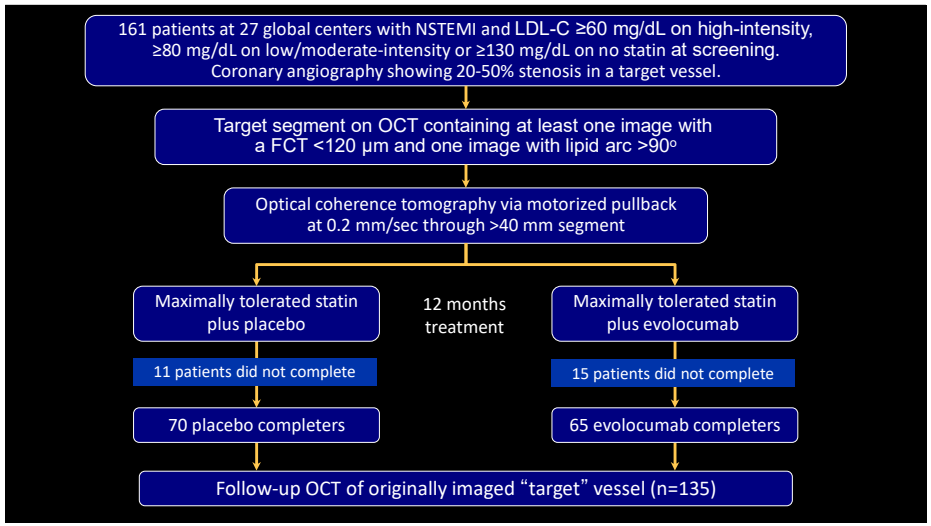
161 patients at 27 global centers with NSTEMI and LDL-C ≥60 mg/dL on high-intensity, ≥80 mg/dL on low/moderate-intensity or ≥130 mg/dL on no statin at screening. Coronary angiography showing 20-50% stenosis in a target vessel.
Target segment on OCT containing at least one image with a FCT <120 µm and one image with lipid arc >90°
Optical coherence tomography via motorized pullback at 0.2 mm/sec through >40 mm segment
Maximally tolerated statin plus placebo
12 months treatment
Maximally tolerated statin plus evolocumab
11 patients did not complete
15 patients did not complete
70 placebo completers
65 evolocumab completers
Follow-up OCT of originally imaged "target" vessel (n=135)

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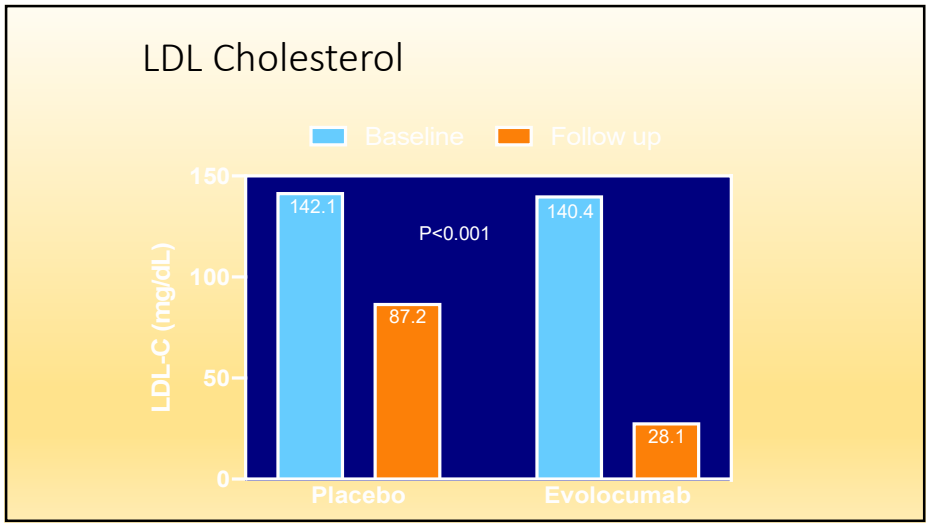
LDL Cholesterol
Baseline
Follow up
LDL-C (mg/dL)
150
100
50
0
142.1
87.2
P<0.001
140.4
28.1
Placebo
Evolocumab

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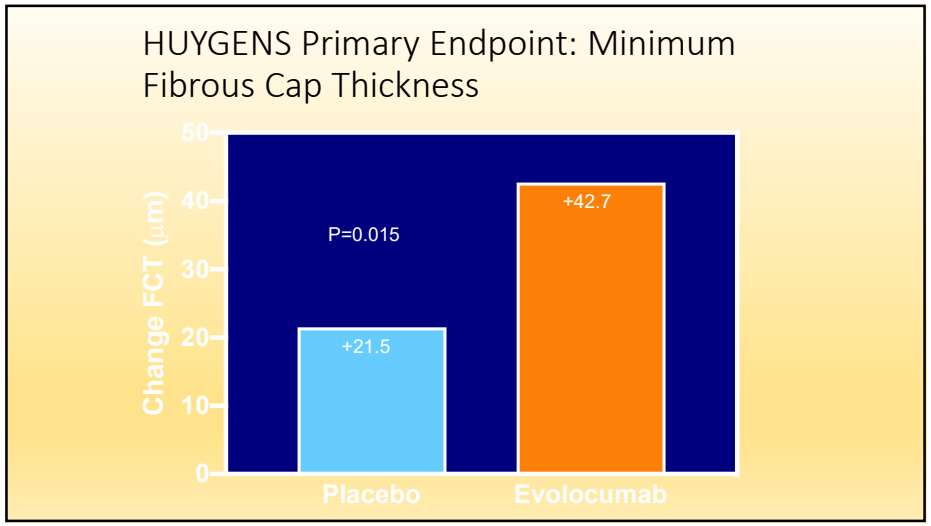
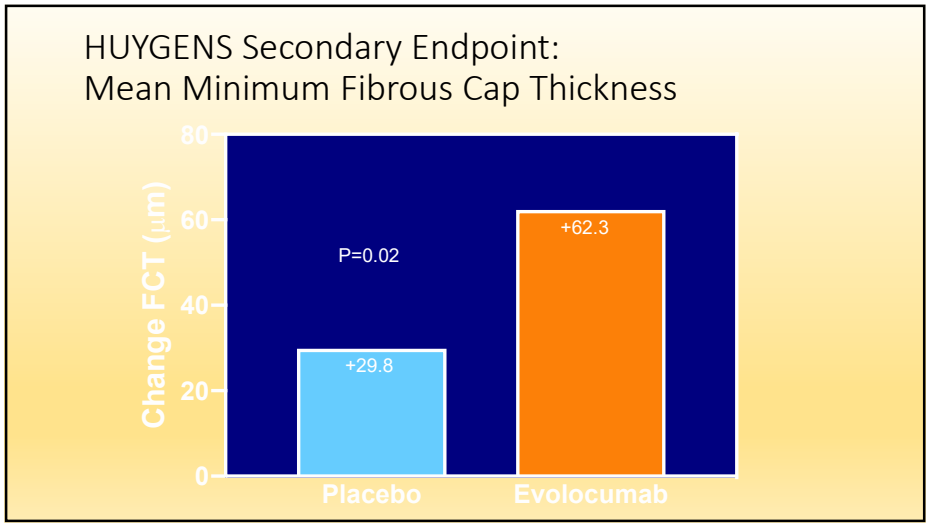

HUYGENS Primary Endpoint: Minimum Fibrous Cap Thickness
Change FCT (µm)
50
40
30
20
10
0
P=0.015
+21.5
+42.7
Placebo
Evolocumab

63


HUYGENS Secondary Endpoint: Mean Minimum Fibrous Cap Thickness
Change FCT (µm)
80
60
40
20
0
P=0.02
+29.8
+62.3
Placebo
Evolocumab

64

Adverse Clinical Events and Safety Findings

Event	Placebo (N=81)	Evolocumab (N=80)
Death	1.2%	0%
Nonfatal MI	3.7%	0%
Injection site reactions	1.2%	0%
Myalgia	7.4%	6.3%
Discontinuation from treatment	12.2%	4.9%

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Was ist der ideale LDL- Cholesterin-Spiegel?

Ein idealer LDL-Cholesterin Spiegel liegt bei:
1.2 – 1.8 mmol/L
Human newborns < 0.6 mmol/L

O'Keefe et al. JACC 2004;43:2142-2146
Chandar V, Med J Armed Forces India. 1994 Apr; 50(2): 101-104.

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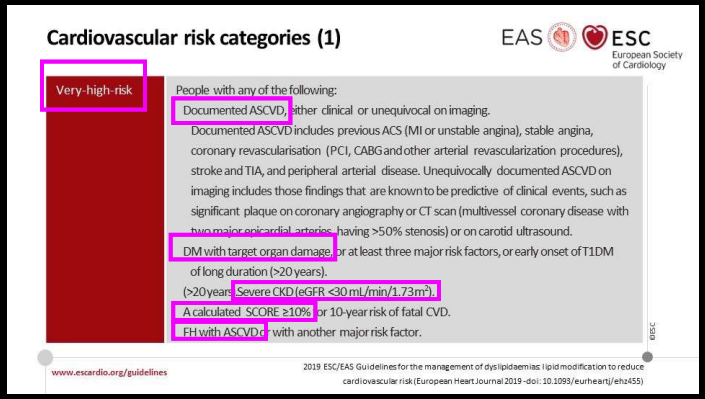

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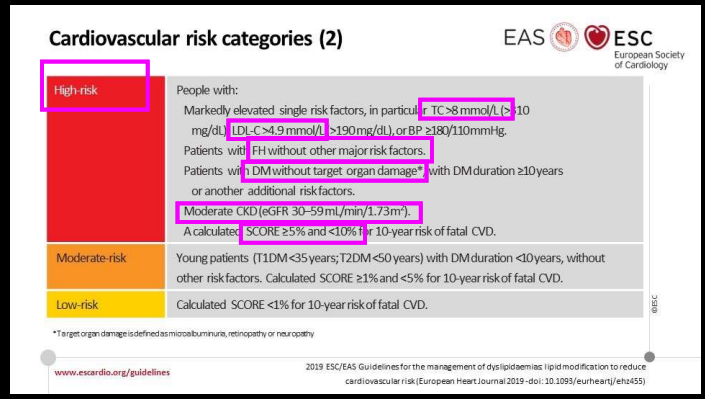

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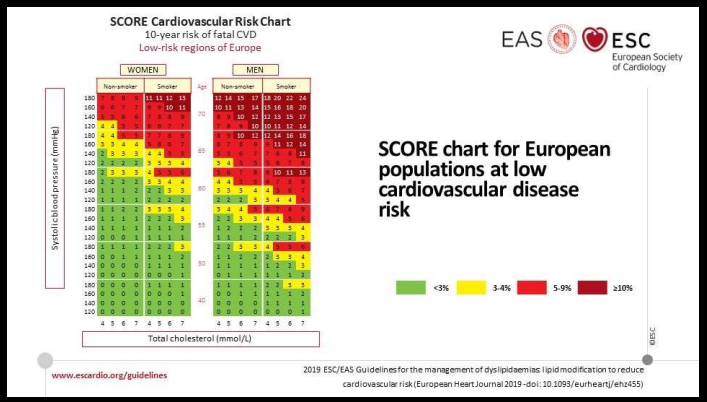
SCORE Cardiovascular Risk Chart
10-year risk of fatal CVD
Low-risk regions of Europe
WOMEN
MEN
Non-smoker
Smoker
Systolic blood pressure (mmHg)
Total cholesterol (mmol/L)
SCORE chart for European populations at low cardiovascular disease risk
<3%
3-4%
5-9%
≥10%
EAS
ESC
European Society of Cardiology
www.escardio.org/guidelines
2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

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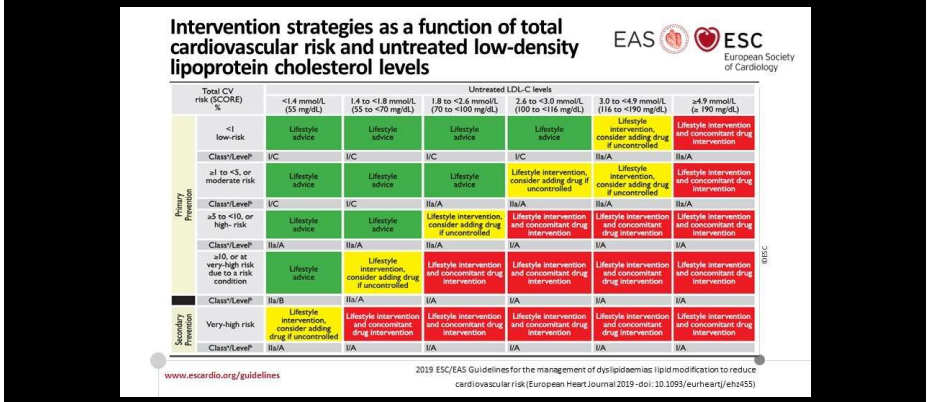
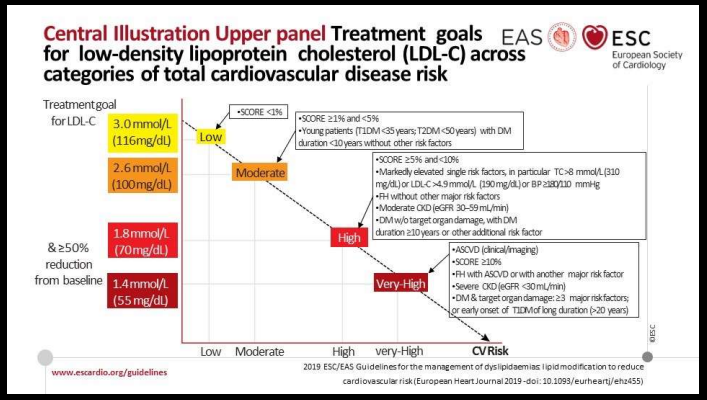
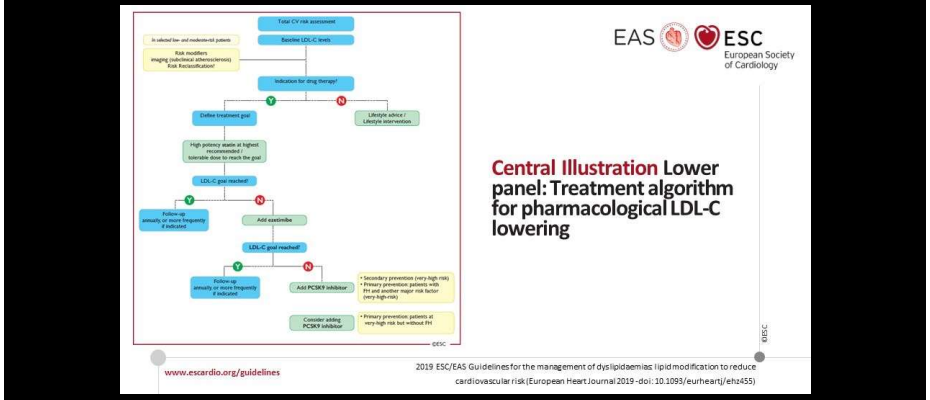

Intervention strategies as a function of total cardiovascular risk and untreated low-density lipoprotein cholesterol levels
EAS
ESC
European Society of Cardiology
Total CV risk (SCORE) %
Untreated LDL-C levels
<1.4 mmol/L (55 mg/dL)
1.4 to <1.8 mmol/L (55 to <70 mg/dL)
1.8 to <2.6 mmol/L (70 to <100 mg/dL)
2.6 to <3.0 mmol/L (100 to <116 mg/dL)
3.0 to <4.9 mmol/L (116 to <190 mg/dL)
≥4.9 mmol/L (≥ 190 mg/dL)
Primary Prevention
Secondary Prevention
<1 low-risk
≥1 to <5, or moderate risk
≥5 to <10, or high- risk
≥10, or at very-high risk due to a risk condition
Very-high risk
Lifestyle advice
Lifestyle intervention, consider adding drug if uncontrolled
Lifestyle intervention and concomitant drug intervention
Class[a]/Level[b]
I/C
IIa/A
IIa/B
I/A
www.escardio.org/guidelines
2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

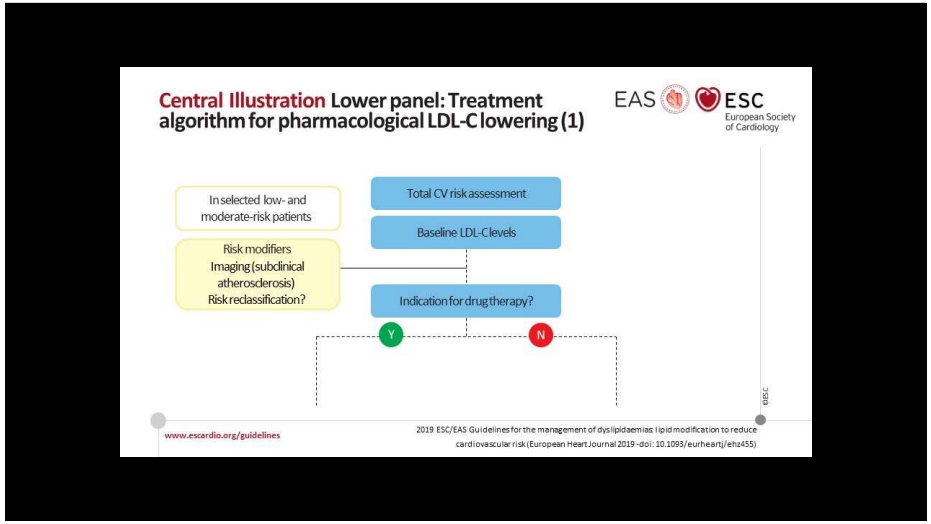
70


Central Illustration Upper panel Treatment goals for low-density lipoprotein cholesterol (LDL-C) across categories of total cardiovascular disease risk
EAS
ESC
European Society of Cardiology
Treatment goal for LDL-C
3.0 mmol/L (116 mg/dL)
2.6 mmol/L (100 mg/dL)
1.8 mmol/L (70 mg/dL)
1.4 mmol/L (55 mg/dL)
& ≥50% reduction from baseline
Low
Moderate
High
Very-High
•SCORE <1%
•SCORE ≥1% and <5%
•Young patients (T1DM <35 years; T2DM <50 years) with DM duration <10 years without other risk factors
•SCORE ≥5% and <10%
•Markedly elevated single risk factors, in particular TC >8 mmol/L (310 mg/dL) or LDL-C >4.9 mmol/L (190 mg/dL) or BP ≥180/110 mmHg
•FH without other major risk factors
•Moderate CKD (eGFR 30–59 mL/min)
•DM w/o target organ damage, with DM duration ≥10 years or other additional risk factor
•ASCVD (clinical/imaging)
•SCORE ≥10%
•FH with ASCVD or with another major risk factor
•Severe CKD (eGFR <30 mL/min)
•DM & target organ damage: ≥3 major risk factors; or early onset of T1DM of long duration (>20 years)
CV Risk
www.escardio.org/guidelines
2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

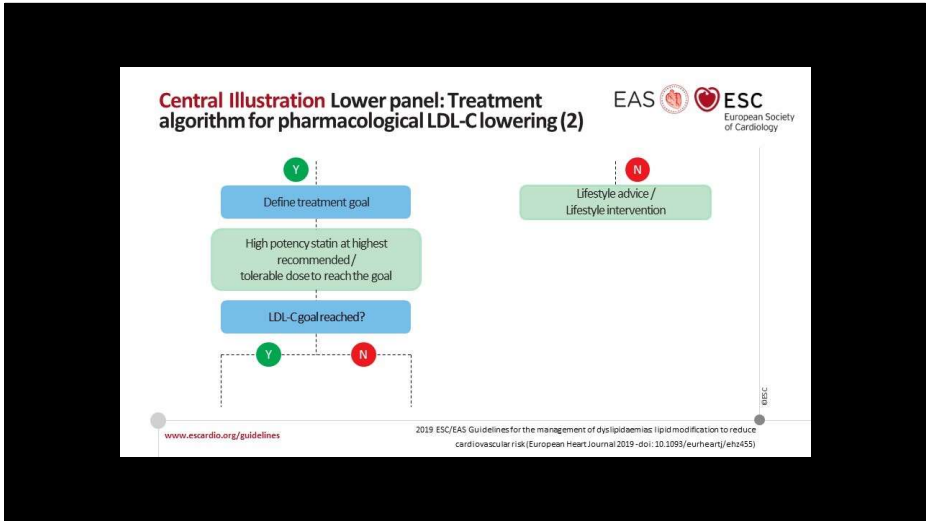
71


EAS
ESC
European Society of Cardiology
Central Illustration Lower panel: Treatment algorithm for pharmacological LDL-C lowering
www.escardio.org/guidelines
2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

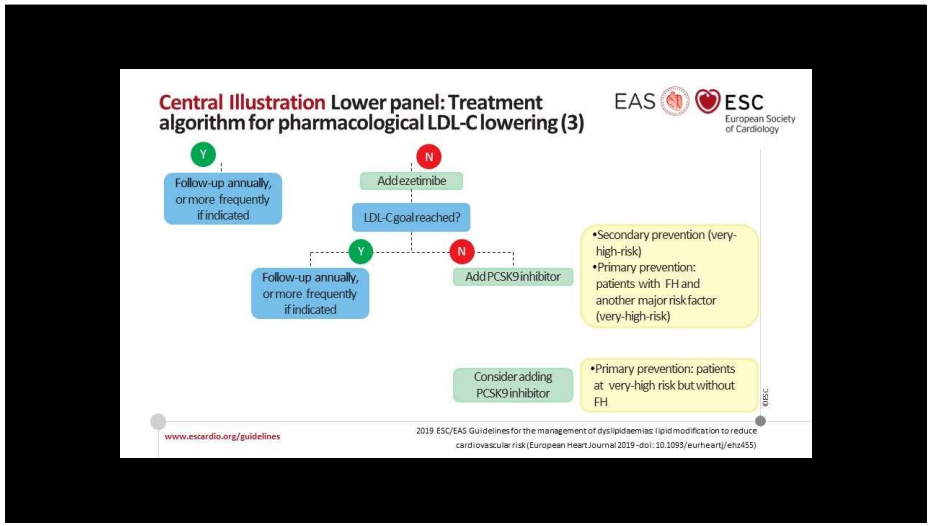
72


Central Illustration Lower panel: Treatment algorithm for pharmacological LDL-C lowering (1)
EAS ESC European Society of Cardiology
In selected low- and moderate-risk patients
Risk modifiers Imaging (subclinical atherosclerosis) Risk reclassification?
Total CV risk assessment
Baseline LDL-C levels
Indication for drug therapy?
Y
N
www.escardio.org/guidelines
2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 - doi: 10.1093/eurheartj/ehz455)

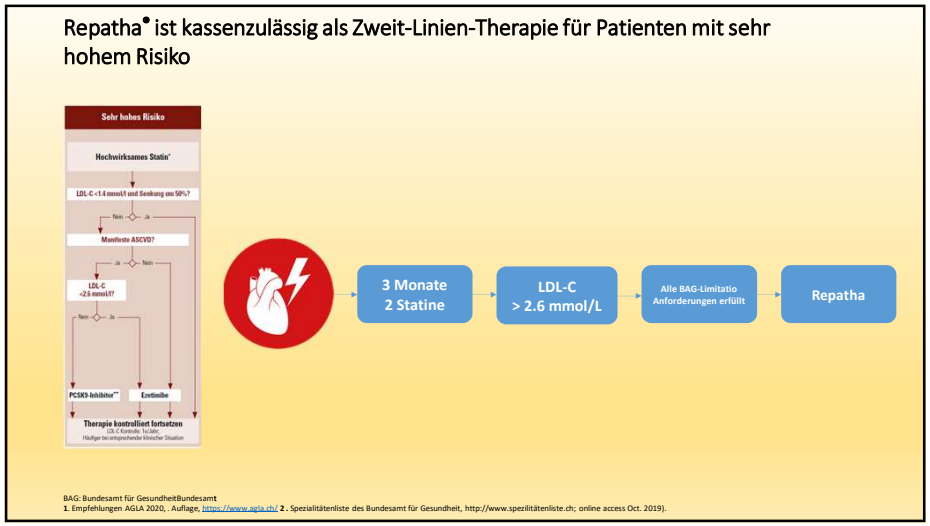
73


Central Illustration Lower panel: Treatment algorithm for pharmacological LDL-C lowering (2)
EAS ESC European Society of Cardiology
Y
Define treatment goal
High potency statin at highest recommended / tolerable dose to reach the goal
LDL-C goal reached?
Y
N
N
Lifestyle advice / Lifestyle intervention
www.escardio.org/guidelines
2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 - doi: 10.1093/eurheartj/ehz455)

74


Central Illustration Lower panel: Treatment algorithm for pharmacological LDL-C lowering (3)
EAS ESC European Society of Cardiology
Y
Follow-up annually, or more frequently if indicated
N
Add ezetimibe
LDL-C goal reached?
Y
Follow-up annually, or more frequently if indicated
N
Add PCSK9 inhibitor
•Secondary prevention (very-high-risk)
•Primary prevention: patients with FH and another major risk factor (very-high-risk)
Consider adding PCSK9 inhibitor
•Primary prevention: patients at very-high risk but without FH
www.escardio.org/guidelines
2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 - doi: 10.1093/eurheartj/ehz455)

75


Repatha® ist kassenzulässig als Zweit-Linien-Therapie für Patienten mit sehr hohem Risiko
Sehr hohes Risiko
Hochwirksames Statin*
Manifeste ASCVD?
Therapie kontrolliert fortsetzen
3 Monate 2 Statine
LDL-C > 2.6 mmol/L
Alle BAG-Limitatio Anforderungen erfüllt
Repatha
BAG: Bundesamt für GesundheitBundesamt
1. Empfehlungen AGLA 2020, . Auflage, https://www.agla.ch/ 2. Spezialitätenliste des Bundesamt für Gesundheit, http://www.spezilitätenliste.ch; online access Oct. 2019).

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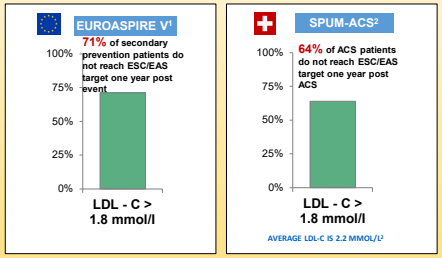
LDL-C Ziel* Erreichung bei very high-risk CV Patienten ist ungenügend[1-2]



In Switzerland two thirds of post-ACS patients do not reach the ESC/EAS 2016 target.

1. De Backer G, EAS2018 Late Breaking Clinical Trial Online May 8, 2018: https://www.eas-society.org/news/399857/EAS2018-Late-Breaking-Clinical-Trial-EUROASPIRE-V.htm
2. Gencer, Koskinas et al. J Am Heart Association 2017;6:e006537. Data from SPUM-ACS: A prospective, multi-center cohort study of consecutive patients hospitalized with ACS in Switzerland. *If target defined as <1.8 mmol/L. SPUM-ACS = Special Program University Medicine-Acute Coronary Syndromes / Participating academic centers from Switzerland: Bern, Geneva, Lausanne, and Zurich. EUROASPIRE = Survey in secondary prevention (1 year post-index event); EUROASPIRE VI: N=7998, year 2012–2013. EUROASPIRE V: N=8261, year 2016. ACS = Acute Coronary Syndrome; SPUM-ACS = (Special Program University Medicine-Acute Coronary Syndromes).

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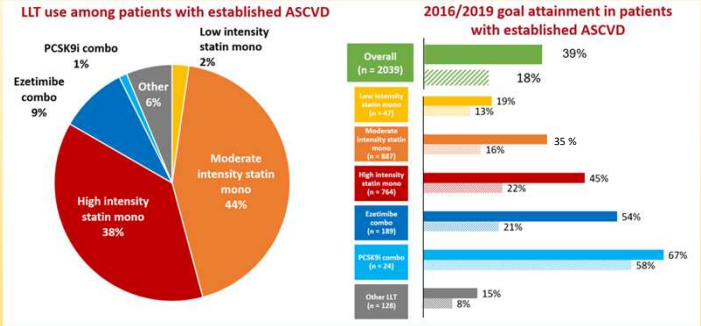
DAVINCI: Bei Patienten mit sehr hohem Risiko und bestehender ASCVD wurde das Ziel häufiger von denjenigen erreicht, die eine Kombinationstherapie erhielten



Patienten mit sehr hohem Risiko erreichten den 2019 Zielwert (1,4 mmol/l) im Vergleich zum 2016 Zielwert nur etwa zur Hälfte (18 % vs. 39 %).

Das Tortendiagramm zeigt den Prozentanteil der Patienten, die bei der LDL-C-Messung die jeweilige LLT erhielten. Das Balkendiagramm zeigt den Prozentanteil der Patienten, die die LDL-C-Ziele 2016 (durchgezogene Balken) bzw. 2019 (schraffierte Balken) erreichten. ASCVD, atherosklerotische kardiovaskuläre Erkrankung; combo, Kombinationstherapie; LDL-C, Low-Density-Lipoprotein-Cholesterin; LLT, lipidsenkende Therapie; mono, Monotherapie; PCSK9i; Proprotein-Convertase-Subtilisin/Kexin-Typ-9-Inhibitor.
Ray KK, Does Evolocumab use in Europe match 2019 ESC/EAS lipid guidelines? Results from the HEYMANS study. European Society of Cardiology Congress 2020, The Digital Experience, Sunday 30 August 2020, Rapid Fire Abstracts
Ray KK et al., EU-Wide Cross-Sectional Observational Study of Lipid-Modifying Therapy Use in Secondary and Primary Care: the DAVINCI study. *European Journal of Preventive Cardiology* 2020 doi:10.1093/eurjpc/zwaa047

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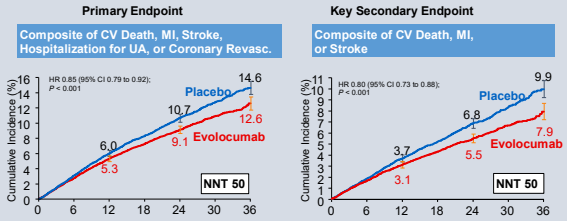
FOURIER STUDIE

MANIFESTE KARDIOVASKULÄRE ERKRANKUNG (MI, ISCHÄMISCHER SCHLAGANFALL ODER SYMPTOMATISCHE PAVK) UNTER STATINTHERAPIE[1]

1. Sabatine MS, et al. N Engl J Med. 2017;376:1713-1722.
CI = confidence interval; CV = cardiovascular; HR = hazard ratio; MI = myocardial infarction; UA = unstable angina; NNT = Number needed to treat.
NNT over 3 years; N = 22'351.

80

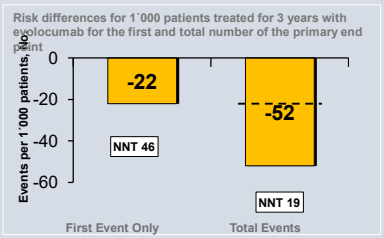
EVOLOCUMAB REDUZIERT MAJOR CARDIOVASCULAR EVENTS[1]



1. Sabatine MS, et al. N Engl J Med. 2017;376:1713-1722.
CI = confidence interval; CV = cardiovascular; HR = hazard ratio; MI = myocardial infarction; UA = unstable angina; NNT = Number needed to treat.
NNT over 3 years; N = 22'351.

81

EVOLOCUMAB REDUZIERT TOTALE EREIGNISSE STÄRKER ALS LEDIGLICH ERSTEREIGNISSE[1]



Driven by reductions in myocardial infarction, stroke and coronary revascularization (MACE).

For every 1´000 patients treated for 3 years, 22 first and 52 total primary end point events were prevented with evolocumab.

1. Murphy SA et al. Effect of the PCSK9 Inhibitor Evolocumab on Total Cardiovascular Events in Patients With Cardiovascular Disease: A Prespecified Analysis From the FOURIER Trial. JAMA Cardiology. Published Online May 22, 2019.
NNT over 3 years; NNT = Number needed to treat.

82

Jahreskosten Repatha

- 8'100 CH
- NNT 50 über 3 Jahre für Verhinderung 1 MACE
- 1'200'000 CHF für Verhinderung 1 MACE / Jahr

83

The ODYSSEY OUTCOMES Trial: Topline Results

Alirocumab in Patients After Acute Coronary Syndrome

Gregory G. Schwartz, Michael Szarek, Deepak L. Bhatt, Vera Bittner, Rafael Diaz, Jay Edelberg, Shaun G. Goodman, Corinne Hanotin, Robert Harrington, J. Wouter Jukema, Guillaume Lecorps, Angèle Moryusef, Robert Pordy, Matthew Roe, Harvey D. White, Andreas Zeiher, **Ph. Gabriel Steg**
On behalf of the ODYSSEY OUTCOMES Investigators and Committees

American College of Cardiology – 67th Scientific Sessions
March 10, 2018

ClinicalTrials.gov: NCT01663402

ODYSSEY OUTCOMES

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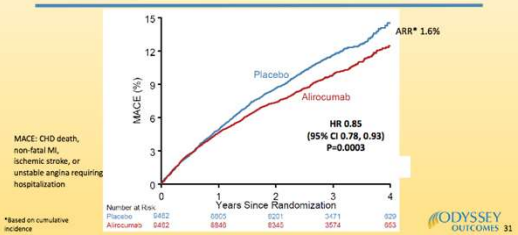
ACC.18

Primary Efficacy Endpoint: MACE



MACE: CHD death, non-fatal MI, ischemic stroke, or unstable angina requiring hospitalization

*Based on cumulative incidence

ODYSSEY OUTCOMES 31

85

EVOLOCUMAB UND ALIROCUMAB GELTEN ALS EFFEKTIV UND OEKONOMISCH TRAGBAR IN EINER DEFINIERTEN POPULATION GEMÄSS BAG[1]

Repatha® and Praluent ® are reimbursed accompanying a diet and in addition to a maximally tolerated dose of LDL-C lowering therapy* for the treatment of:

Secondary Prevention ASCVD After a clinically apparent atherosclerotic ischemic cardiovascular event**	**LDL-C > 2.6 mmol/l**
Primary Prevention Severe familial hypercholesterolaemia***	**LDL-C > 5.0 mmol/l or LDL-C > 4.5 mmol/l with at least one add. risk factor****

1. Spezialitätenliste des Bundesamt für Gesundheit (BAG), http://www.spezialitätenliste.ch; (online access Oct. 2019).
After cost approval by the health insurer after prior consultation of the statutory health insurance physician. *2nd or 3rd line, after max. tolerated statins +/- ezetimibe or statin intolerance and ezetimibe; **Adults with hypercholesterolaemia, HeFH, and HoFH (adults and adolescent from age of 12 years). ***Adults with severe HeFH, and for 5.0 mmol/l, HoFH (adults and adolescent from age of 12 years). ****Diabetes mellitus, increased lipoprotein (a)> 50 mg / dl, pronounced arterial hypertension. ASCVD, atherosclerotic cardiovascular disease; HoFH = Homozygous Familial hypercholesterolaemia; HeFH = heterozygous familial hypercholesterolaemia; LDL-C = low-density lipoprotein cholesterol; SI = statin intolerance.

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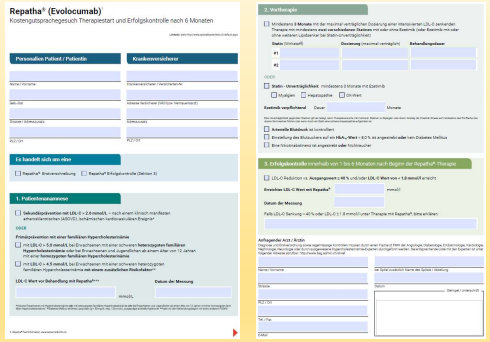
Kostengutsprache Gesuch



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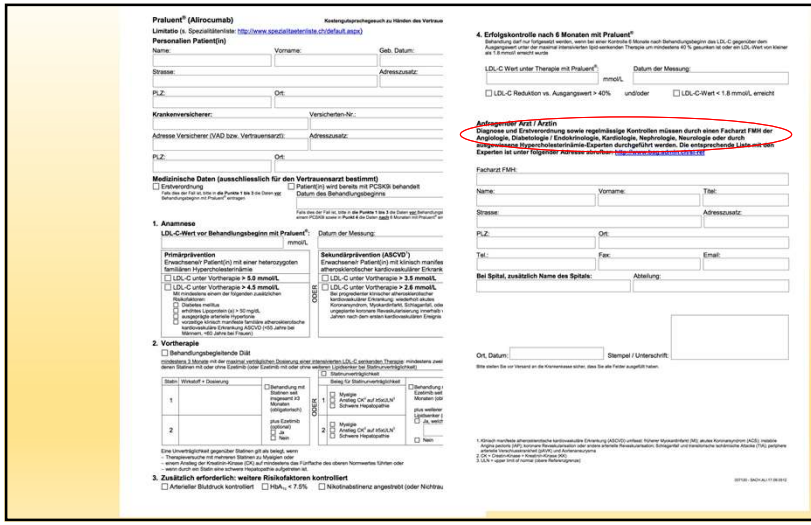

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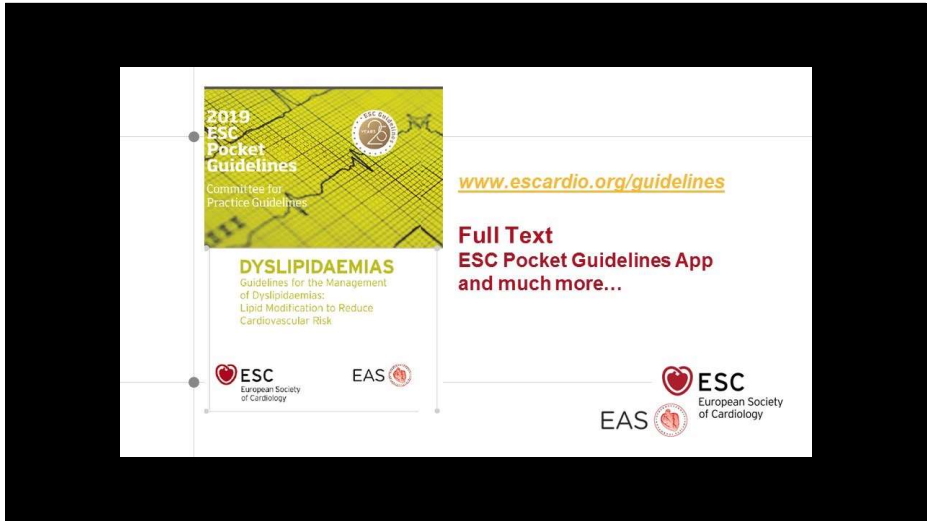


89

79 jähriger Patient mit KHK und HI

Austrittsmedikation:

- Aspirin cardio 100mg 1-0-0
- Concor 5mg 1-0-0
- Zestril 10mg 1-0-0
- Aldactone 100mg 1-0-0
- Sortis 20mg 0-0-1
- Torasemid 5mg 1-0-0

90

79 jähriger Patient mit KHK und HI

Austrittsmedikation sollte sein:

- Aspirin cardio 100mg 1-0-0
- Concor 5mg 1-0-0
- Entresto 50mg 1-0-1
- Aldactone 100mg 1-0-0
- Forxiga 10mg 1-0-0
- Atozet 80/10mg 0-0-1
- Torasemid 5mg 1-0-0

91

79 jähriger Patient mit KHK und HI

Austrittsempfehlung sollte sein:

Ambulante Kardiale Rehabilitation

Klare Zielgewichtsdefinition

92

79 jähriger Patient mit KHK und HI

Hausarztvisite nach 1-2 Wochen

Blutdruck

wenn normotensiv:
Ausbau ARNI

Puls (wenn >60/min)

Ausbau Betablocker

Elektrolyte

Wenn K+ > 5.5 -> Partiromer

93

79 jähriger Patient mit KHK und HI

Kreatinin Clearance

ein initialer Abfall unter
SGLT-2 Inhibitor ist normal !

94

79 jähriger Patient mit KHK und HI

Hausarztvisite nach 1-2 Wochen

Blutbild / Eisenstatus (wenn im Spital vergessen gegangen…)

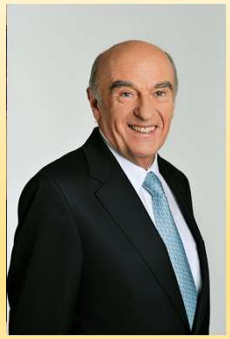
Eisensubstitution

Check GI-Infektionen

Check Impfstatus
(Pneumokokken/Influenza/Covid)

95

79 jähriger Patient mit KHK und HI



Hausarztvisite nach 1 Monat

Ausdosieren
Herzinsuffizienzmedikation zur maximalen Dosis

96

79 jähriger Patient mit KHK und HI

Kardiologische Kontrolle nach 2-3 Monaten

EKG (LSB)

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

-> Indikation ICD/CRT

LDL > 2.6mmol/l

-> PCSK9-Inhibitor

97

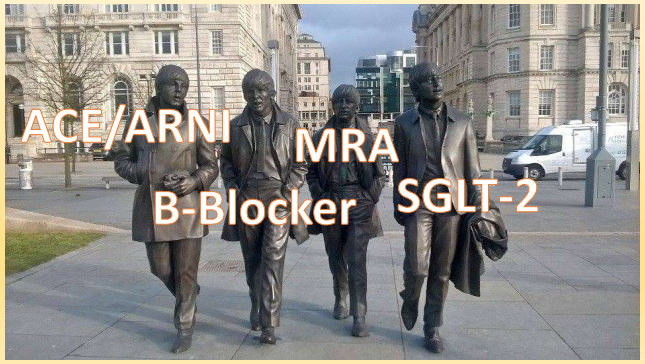
79 jähriger Patient mit KHK und HI

Falls Rezidiv Dekompensation:

Vericiguat (Verquovo) 10mg 1-0-0

98

The fabulous Four !



99

100