

H

Kardiologischer Workshop

Hart&Herzlich Bad Horn, 14.09.2023

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Leitender Arzt
Klinik für Kardiologie KSSG



www.kssg.ch

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Fall – weiblich, 66 Jahre

Anamnese:

- Vorstellung wegen progredienter Dyspnoe, NYHA II-III
- Leichte US-Ödeme beidseits seit 3 Wochen
- Keine weiteren neuen Beschwerden, keine AP, keine Orthopnoe

Bisherige Diagnosen und cvRF

- Koronare 1-Gefässerkrankung mit PTCA RIVA Mitte vor 3 Jahren
- Chron. Niereninsuffizienz mit Baseline GFR um 40ml/min/1.73m²
- Art. Hypertonie, Dyslipidämie, Adipositas (BMI 32kg/m²)

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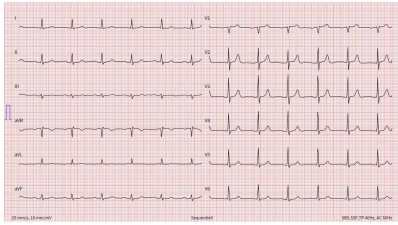
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Fall – weiblich, 66 Jahre

Status:

- BMI 32kg/m²
- BD 147/96mmHg
- HF 70/min
- Reine Herztöne, 2/6 Systolikum
- Leichte Ödeme bds bis Mitte US
- Feine basale RGS pulmonal bds
- Pos. HJR



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Fall – weiblich, 66 Jahre

Labor:

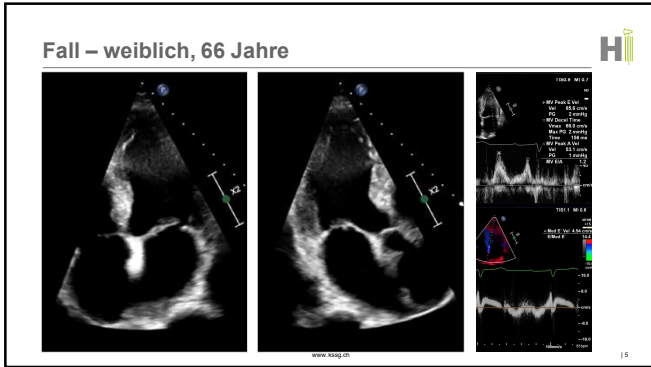
- GFR 39ml/min/1.73m²
- Na 138mmol/l
- K 4.6mmol/l
- Hb 132g/l
- TSH normwertig
- ASAT/ALAT normwertig
- LDL-Chol. 2.6mmol/l
- NT-proBNP 520ng/l

Bisherige Medikation:

- ASS cardio 100mg
- Bisoprolol 2.5mg
- Atorvastatin 40mg
- Perindopril 5mg
- Amlodipin 5mg

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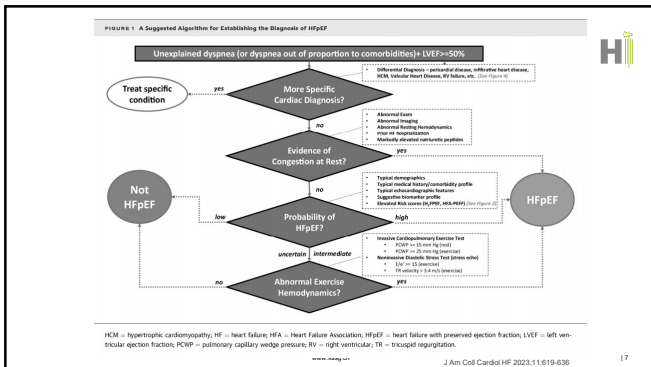
Definition HFpEF ESC

Type of HF	HFREF	HFmrEF	HFpEF
Criteria 1	Symptoms ± signs*	Symptoms ± signs*	Symptoms ± signs*
Criteria 2	LVEF ≤40%	LVEF 41–49%†	LVEF ≥50%‡
Criteria 3	–	–	Objective evidence of cardiac structural and/or functional abnormalities consistent with the presence of LV diastolic dysfunction/raised LV filling pressures, including raised natriuretic peptides§

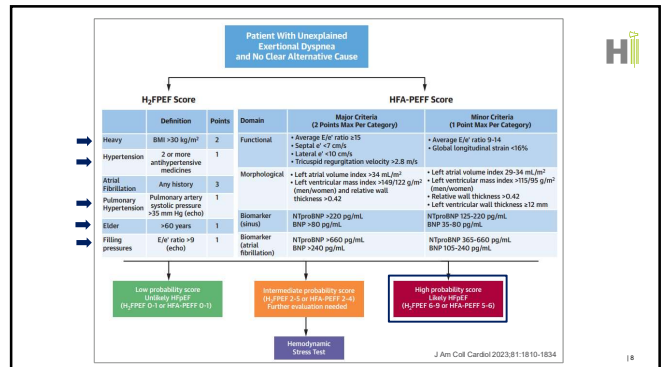
HF, heart failure; HFmrEF, heart failure with mildly reduced ejection fraction; HFREF, heart failure with preserved ejection fraction; HFpEF, heart failure with reduced ejection fraction; LV, left ventricle; LVEF, left ventricular ejection fraction.
 *Signs may not be present in the early stages of HF (especially in HFpEF) and in optimally treated patients.
 †For the diagnosis of HFmrEF, the presence of other evidence of structural heart disease (e.g. increased left atrial size, LV hypertrophy, or echocardiographic measures of impaired LV filling) makes the diagnosis more likely.
 ‡For the diagnosis of HFpEF, the greater the number of abnormalities present, the higher the likelihood of HFpEF.

www.kisp.ch | Eur Heart J (2023) 44, 1–13 | 6

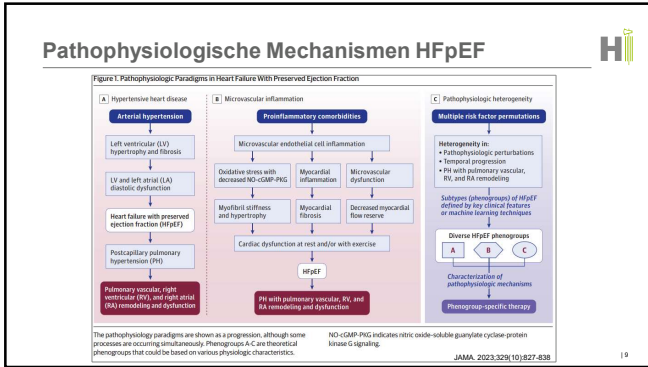
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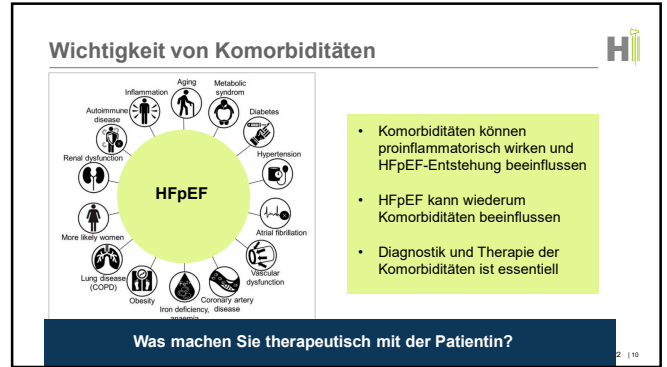
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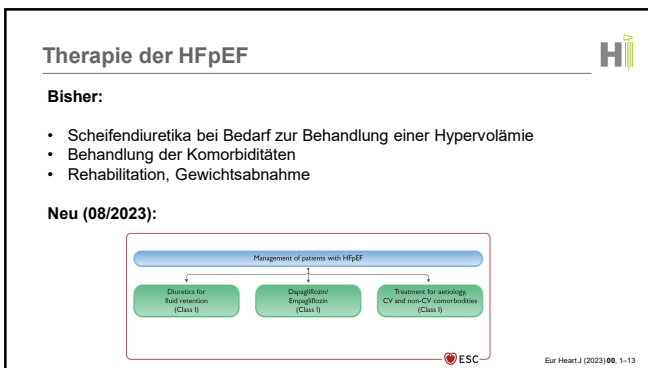
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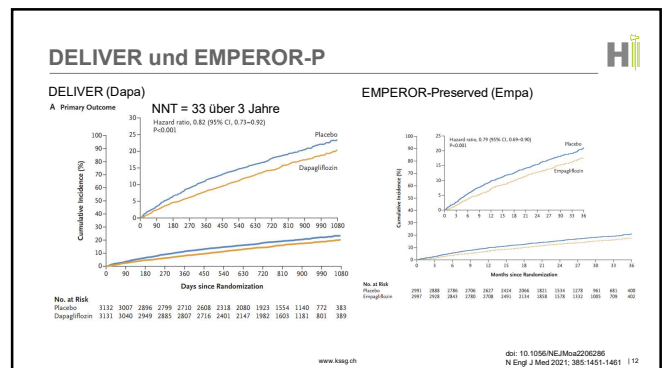
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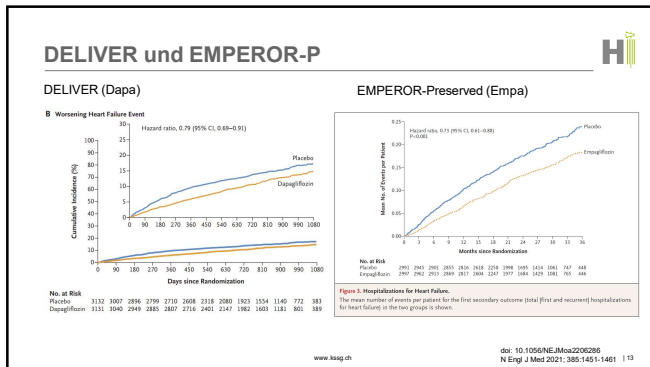
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Therapie HFmrEF

Type of HF	HF+EF	HFmrEF	HFpEF
Criteria 1	Symptoms a sign ^a	Symptoms a sign ^a	Symptoms a sign ^a
Criteria 2	LVEF ≥50%	LVEF 41–49%	LVEF ≥50%
Criteria 3	–	–	Objective evidence of cardiac structural and/or functional abnormalities consistent with the presence of LV diastolic dysfunction ^b or LV filling pressures, including raised mitral E/A ratio ^c

HF: Heart failure; HFmrEF: heart failure with mildly reduced ejection fraction; HFpEF: heart failure with preserved ejection fraction; HF+EF: heart failure with reduced ejection fraction; LV: left ventricle; LVEF: left ventricular ejection fraction.
^aSigns may not be present in the early stages of HF (especially in HFpEF) and in optimally treated patients.
^bIncludes the presence of HFmrEF, the presence of other causes of structural heart disease, increased mitral area, LV hypertrophy, or echocardiographic measures of impaired LV filling.
^cFrom the highest mitral E/A.
 For the diagnosis of HFpEF, the greater the number of abnormalities present, the higher the likelihood of HFpEF.

Management of patients with HFmrEF

Diuretics for fluid retention (Class I)

Dapagliflozin/ Empagliflozin (Class I)

ACEI/ARNI/ARB (Class IIb)

MRA (Class IIb)

Beta-blocker (Class IIb)

ESC | 14

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Aktuelle SL-Limitatio für HFpEF/HFmrEF

Empagliflozin bisher einziger SGLT2-Inhibitor auf SL-Liste

Herzinsuffizienz mit erhaltener oder mittlerer Ejektionsfraktion (HFpEF / HFmrEF)
 Zur individuell optimierten Standardtherapie gemäss aktuellen Empfehlungen in geeigneter Kombination mit anderen Arzneimitteln zur Behandlung der Herzinsuffizienz für die Behandlung erwachsener Patientinnen oder Patienten mit chronischer Herzinsuffizienz der NYHA-Klassen I-IV seit mindestens 3 Monaten, deren Ejektionsfraktion der linken Herzkammer (LVEF) vor Behandlung mit Empagliflozin 10 mg >40% betrug. Die Patientinnen und Patienten müssen mindestens eines der folgenden Anzeichen einer Herzinsuffizienz aufweisen:
 - Strukturelle Herzveränderung (Vergrößerung des linken Vorhofs und/oder linksventrikuläre Hypertrophie)
 - Hospitalisierung aufgrund der Herzinsuffizienz (HHF) innerhalb der letzten 12 Monate

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Fall – weiblich, 66 Jahre

Labor:

- GFR 39ml/min/1.73m²
- Na 138mmol/l
- K 4.6mmol/l
- Hb 132g/l
- TSH normwertig
- ASAT/ALAT normwertig
- LDL-Chol. 2.6mmol/l
- NT-proBNP 520ng/l

Bisherige Medikation:

- ASS cardio 100mg
- Bisoprolol 2.5mg
- Atorvastatin 40mg
- Perindopril 5mg
- Amlodipin 5mg
- Torasemid 10mg
- Empagliflozin 10mg

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Zielwerte Lipide

Risikokategorie	Zielwerte	LDL-Cholesterin*	Non-HDL-Cholesterin*	ApoB*	Therapiestrategie	Medikamentöse Therapie**
Sehr Hoch	< 1,4 mmol/l und 50% Reduktion	< 2,2 mmol/l	< 0,65 g/l	1. Potentes Statin 2. PCSK9-Hemmer, Ezetimibe, Bempedoinsäure		
Hoch	< 1,8 mmol/l und 50% Reduktion	< 2,6 mmol/l	< 0,8 g/l	1. Potentes Statin 2. PCSK9-Hemmer, Ezetimibe, Bempedoinsäure		
Intermediär	< 2,6 mmol	< 3,5 mmol/l	< 1,0 g/l	• Statin		
niedrig				• keine		

Was würden Sie an der Therapie der Pat. ändern?

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Wirkungspotenz versch. Therapeutika

Intervention	Cholesterin ↓	LDL-C ↓	HDL-C ↑	TG ↓
Statine	- 15-40%	- 20-55%	+ 5-15%	- 10-30%
Ezetimibe	- 18-20%	- 15-20%	ca. + 3%	ca. - 8%
PCSK9-Ak/siRNA	- 40-50%	- 50-70%	+ 5-10%	- 10-20%
Fibrate	- 10-25%	- 5-20%	+ 10-25%	- 20-50%
Bempedoinsäure	- 15%	- 22%	- 6%	- 1,5%

Tab. 8: Prozentuale Senkung bzw. Erhöhung einzelner Lipide durch verschiedene Lipidsenker

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Atherogene Lipoproteine

The Apolipoprotein B-Containing Lipoprotein Family: Atherogenic and Modifiable

APO B soll insbesondere immer bei D.M., gemischten Hyperlipidämien und Hypertriglyceridämien mitbestimmt werden

Lp(a) als wichtiger Risikoindikator einmalig mitbestimmen → Diesbzgl. Therapieansätze in klin. Studienphase

www.kssg.ch | Eur Heart J 2022;43:3198-3208 | 19

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Evolution der möglichen Therapien

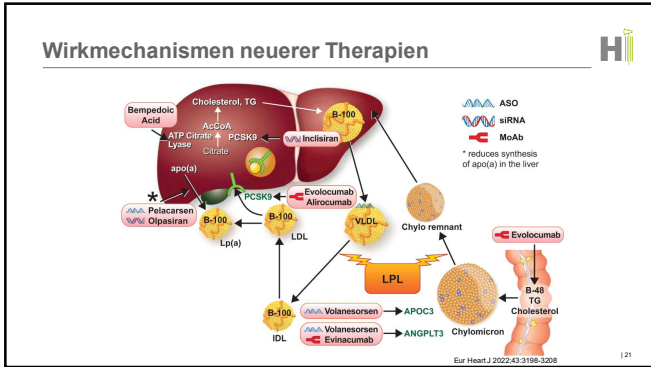
Evolution of Lipid Lowering Therapies:

Statins → Oral combination → MoAb → ASO → siRNA → Vaccination → Gene editing

LDL-C Main target | **Non-HDL (including remnants) Secondary target** | **Lp (a) New target**

*Therapies shown to decrease CV events | www.kssg.ch | Eur Heart J 2022;43:3198-3208 | 20

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Outcome-Daten PCSK9-Inhib.

Evolocumab (FOURIER)

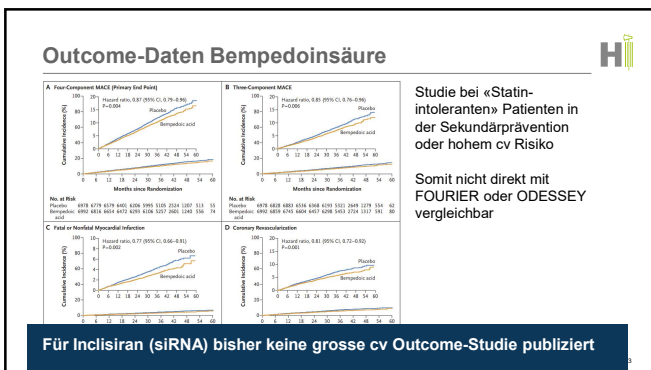
Outcome	Evolocumab (N=13,766)	Placebo (N=13,766)	Hazard Ratio (95% CI)	P Value*
Primary end point (cardiovascular death, myocardial infarction, stroke, hospitalization for unstable angina, or coronary revascularization)	1344 (9.7%)	1843 (13.4%)	0.68 (0.70-0.67)	<0.001
Key secondary end point (cardiovascular death, myocardial infarction, or stroke)	818 (5.9%)	1053 (7.6%)	0.68 (0.70-0.68)	<0.001
Other end points				
Cardiovascular death	251 (1.8%)	340 (2.5%)	1.06 (0.98-1.15)	0.41
Death from myocardial infarction	19 (0.14%)	30 (0.22%)	0.64 (0.49-0.84)	0.006
Death from stroke	91 (0.66%)	119 (0.86%)	0.66 (0.58-0.76)	<0.001
Other cardiovascular death	166 (1.2%)	177 (1.3%)	1.03 (0.90-1.18)	0.61
Death from cancer	444 (3.2%)	426 (3.1%)	1.04 (0.93-1.16)	0.54
Myocardial infarction	448 (3.2%)	539 (3.9%)	0.73 (0.65-0.82)	<0.001
Hospitalization for unstable angina	286 (2.1%)	399 (2.9%)	0.69 (0.63-0.76)	0.001
Stroke	307 (2.2%)	342 (2.5%)	0.79 (0.72-0.87)	0.001
Ischemic	171 (1.2%)	236 (1.7%)	0.70 (0.62-0.80)	0.001
Ischemic stroke	18 (0.13%)	27 (0.20%)	1.15 (0.68-1.96)	0.61
Unlabeled	13 (0.09%)	14 (0.10%)	0.59 (0.34-1.07)	0.09
Coronary revascularization	728 (5.3%)	980 (7.1%)	0.76 (0.72-0.80)	<0.001
Urgent	409 (3.0%)	547 (4.0%)	0.70 (0.64-0.78)	0.001
Elective	619 (4.5%)	533 (3.9%)	0.68 (0.63-0.73)	<0.001
Cardiovascular death or hospitalization for myocardial infarction, stroke or transient ischemic attack	228 (1.7%)	295 (2.1%)	0.77 (0.69-0.86)	0.001
OTC (not used in EU)	771 (5.6%)	1022 (7.4%)	0.68 (0.71-0.66)	<0.001

Alirocumab (ODYSSEY Outcome)

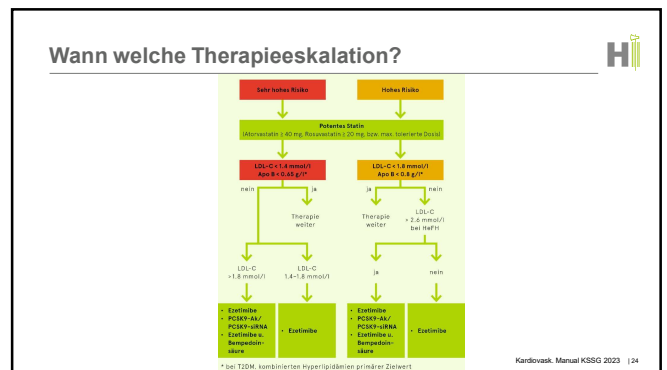
End Point	Alirocumab (N=1945)	Placebo (N=1945)	Hazard Ratio (95% CI)	P Value
Primary end point (composite of death from coronary heart disease, stroke, hospitalization for unstable angina, or coronary revascularization)	900 (9.5%)	1022 (11.1%)	0.81 (0.78-0.85)	<0.001
Key secondary end point (cardiovascular death, myocardial infarction, or stroke)	577 (10.3%)	644 (7.9-8.3%)	0.84 (0.79-0.89)	<0.001
Other end points				
Major secondary end points, in order of hierarchical testing				
Any coronary heart disease event*	1194 (12.7%)	1349 (14.3%)	0.84 (0.81-0.87)	0.001
Major coronary heart disease event†	790 (8.4%)	899 (9.5%)	0.88 (0.85-0.90)	0.006
Any cardiovascular event‡	1326 (13.7%)	1476 (15.6%)	0.87 (0.85-0.89)	<0.001
Composite of death from any cause, nonfatal myocardial infarction, or hospitalization for heart failure	975 (10.3%)	1124 (11.9%)	0.84 (0.79-0.89)	<0.001
Death from coronary heart disease	209 (2.2%)	222 (2.3%)	0.81 (0.76-1.11)	0.198
Death from cardiovascular causes	240 (2.5%)	271 (2.8%)	0.88 (0.78-1.00)	0.04
Death from any cause	344 (3.5%)	391 (4.1%)	0.81 (0.78-0.84)	0.001
Other end points§				
Nonfatal myocardial infarction	426 (4.4%)	472 (4.9%)	0.86 (0.77-0.96)	0.001
Fatal or nonfatal ischemic stroke	111 (1.1%)	122 (1.3%)	0.77 (0.67-0.89)	0.001
Unstable angina requiring hospitalization	37 (0.4%)	40 (0.4%)	0.81 (0.41-0.92)	0.001
Ischemic stroke, coronary revascularization, procedure	721 (7.4%)	820 (8.6%)	0.88 (0.79-0.97)	0.001
Hospitalization for congestive heart failure	176 (1.8%)	179 (1.9%)	0.98 (0.79-1.20)	0.92

N Engl J Med 2017; 376: 1713-1722 | www.kegg.ch | N Engl J Med 2018; 379:2097-2107

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Behandlung der Hypercholesterinämie in der Sekundärprophylaxe

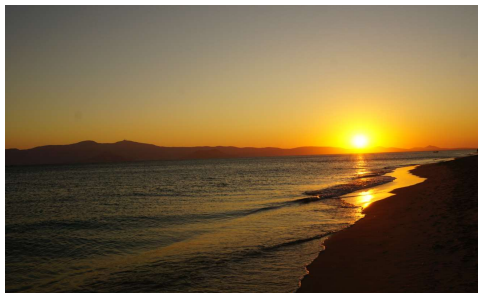
LDL >1.8mmol/l unter maximal verträglicher Statindosis (mindestens 2 Statine versucht) +/- Ezetimib

Therapieausbau mit Bempedoinsäure p.o. (Nilemdo) Rezept durch FA Kardo Termin nach ca. 5 Monaten im Ambi zur Bestimmung des Lipidprofils und Hämät. durch FA Kardo Wenn LDL Reduktion mind. 10%, Weiterführung der Therapie. Weitere Verordnung kann durch	Therapieausbau mit PCSK9-Inhibitor (Repatha, Praluent) Rezept durch FA Kardo Termin für Patientenschulung und 1. Injektion kard. Ambi durch PA Injektion durch Patient alle 2 (-4) Wochen Termin nach ca. 5 Monaten im Ambi zur Bestimmung Lipidprofil durch PA	Therapieausbau mit PCSK9-Senker (Leqvio) Rezept durch FA Kardo Termin für Patientenschulung und 1. Injektion kard. Ambi durch PA Termin nach 3 Monaten im Ambi für 2. Injektion und Lipidprofil (wenn geforderte Lipidwerte noch nicht erreicht, Wiederholung Labor nach weiteren 3 Monaten)
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Bei unserer Patientin: Therapie mit Repatha alle 2 Wochen s.c.
Lipidstatus nach 5 Monaten: LDL 1.3mmol/l

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Vielen Dank!



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Dapagliflozin in HFmrEF und HFpEF (DELIVER)

Einschlusskriterien:

- >40 Jahre alt, mit und ohne Diabetes mellitus
- Stabilisierte HI (stat. oder amb.) mit LVEF >40% (oder verbesserte LVEF >40%) und nachgewiesener LV Hypertrophie +/oder LA Vergrößerung
- Erhöhtes NT-proBNP (>300ng/l, bei VHF >600mg/l)

Studie:

- Randomisierung zu Dapagliflozin 10mg versus Placebo

Primärer Endpunkt:

- CV Todesfall oder sich verschlechternde HI (Hospitalisation oder dringende Kontrolle)

www.knog.ch doi: 10.1056/NEJoa2206286 1/27

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STEP-HFpEF

Semaglutide vs Placebo in Patienten mit HFpEF und Adipositas (BMI >30kg/m²)

Key inclusion Criteria:
HFpEF mit LVEF >45%, NYHA II-IV, KCCQ <90, 6MWT >100m, zusätzlich noch echokardiographische Hinweise auf diast. Dysfunktion oder gemessene erhöhte LVEDP oder HF-Hosp. <12 Monate

Key exclusion Criteria:
Bekannter Diabetes mellitus oder HbA1c >6.5%

www.knog.ch European Heart Journal, ehaj091 1/28

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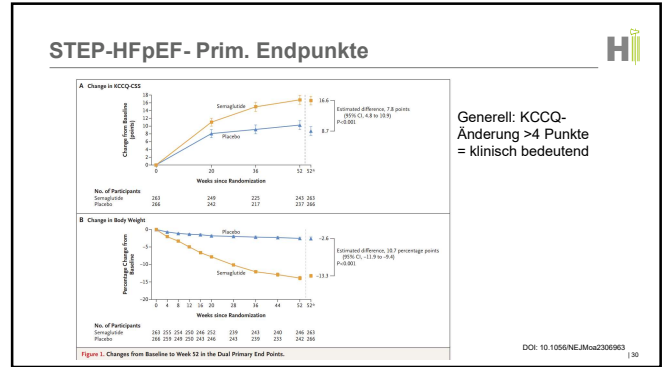
STEP-HFpEF

Table 1. Baseline Demographic and Clinical Characteristics of the Participants.*

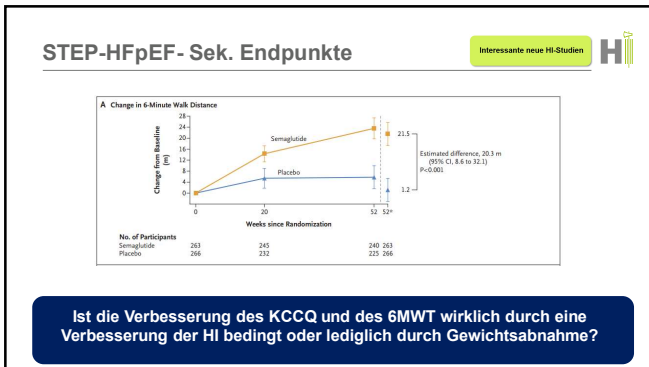
	Semaglutide (N=263)	Placebo (N=266)	Total (N=529)
Characteristics			
Female sex — no. (%)	149 (56.7)	148 (55.6)	297 (56.1)
Median age (IQR) — yr	70 (62–75)	69 (62–75)	69 (62–75)
Median body weight (IQR) — kg	104.7 (95.4–120.1)	105.3 (95.4–122.0)	105.1 (95.4–120.8)
Median BMI (IQR)	37.2 (33.9–41.1)	36.9 (33.3–41.4)	37.0 (33.7–41.4)
BMI status — no. (%)			
30 to <35	89 (33.8)	91 (34.2)	180 (34.0)
≥35	174 (66.2)	175 (65.8)	349 (66.0)
Median waist circumference (IQR) — cm	119.0 (115.3–127.1)	120.0 (115.3–128.0)	119.4 (115.3–128.0)
Median systolic blood pressure (IQR) — mm Hg	133 (122–145)	132 (120–142)	133 (121–144)
Median NT-proBNP level (IQR) — pg/mL	414.4 (252–1054.0)	498.8 (264.7–1025.0)	450.8 (238.2–1015.0)
Median CRP level (IQR) — mg/L	3.8 (1.9–7.0)	3.9 (2.0–6.4)	3.8 (1.9–7.1)
Median LVEF (IQR) — %	57.0 (50.0–60.0)	57.0 (50.0–60.0)	57.0 (50.0–60.0)
LVEF status — no. (%)			
HF with HFrEF	37 (14.1)	40 (15.0)	77 (14.5)
HF with HFpEF	115 (43.0)	102 (38.3)	217 (40.6)
HFpEF	112 (42.0)	124 (46.4)	236 (44.9)
Median KCCQ CSS (IQR) — points	58.4 (42.7–72.9)	58.3 (40.5–72.9)	58.3 (42.7–72.9)
Median 5-minute walk distance (IQR) — m	316.0 (215.5–388.0)	325.8 (222.4–392.0)	320.9 (245.5–389.0)
Hospitalization for heart failure within 1 year — no. (%)	42 (15.6)	59 (22.2)	101 (19.1)
Coexisting conditions at screening — no. (%)			
Atrial fibrillation	135 (51.3)	140 (52.6)	275 (51.9)
Hypertension	216 (82.1)	217 (81.4)	433 (81.7)
Coronary artery disease	53 (20.2)	45 (16.9)	98 (18.5)
NIHAF Functional Class — no. (%)			
I	33 (12.5)	167 (62.8)	200 (37.7)
II or III	80 (30.4)	99 (37.3)	179 (33.8)
Concomitant medication — no. (%)			
Diuretic	207 (78.7)	220 (82.7)	427 (80.7)
Loop diuretic	158 (60.1)	171 (64.3)	329 (62.2)
Thiazide	49 (18.6)	50 (18.8)	99 (18.9)
MRA	89 (33.8)	95 (35.7)	184 (34.8)
ACE, ARB, or ARNI	230 (87.6)	243 (91.4)	473 (89.5)
Beta-blocker	201 (76.4)	217 (81.6)	418 (79.0)
SCN5A inhibitor	8 (3.0)	11 (4.1)	19 (3.6)

DOI: 10.1056/NEJMoa2306963, 29

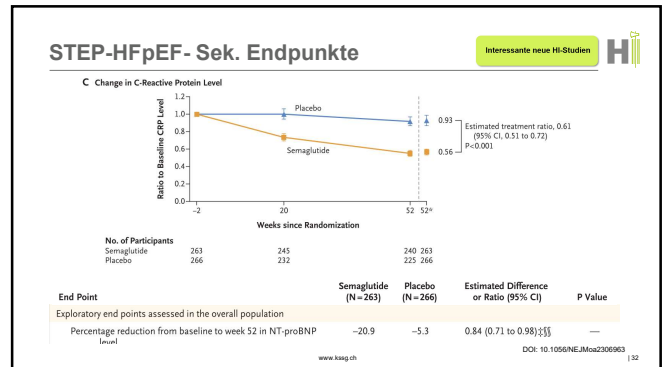
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