# Herzinsuffizienz

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Kardiologie, Campus Virchow Klinikum

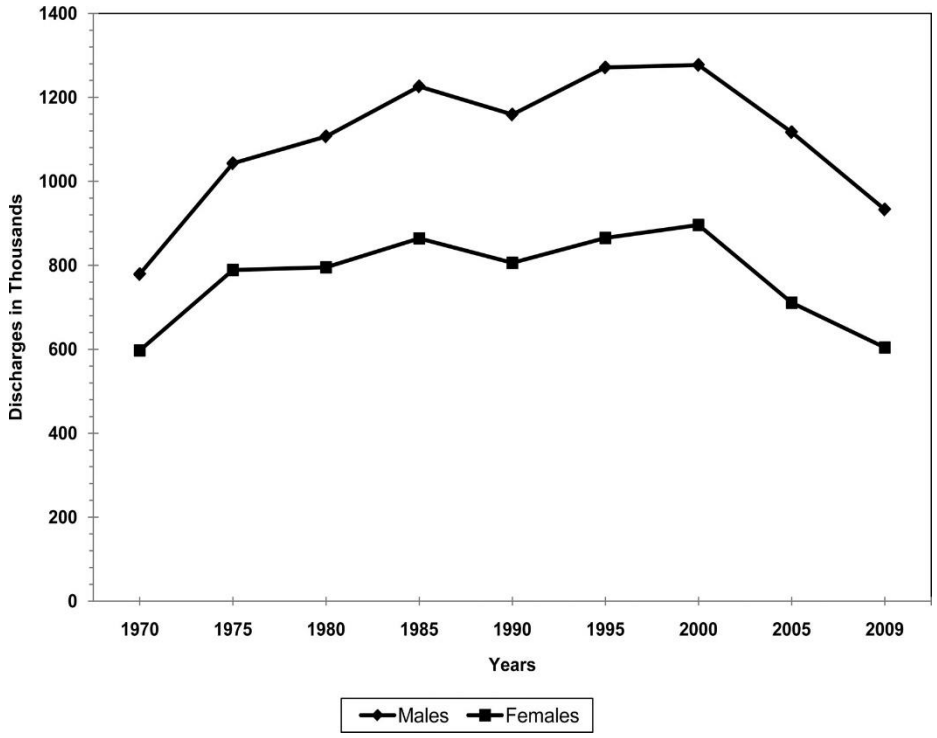
CHARITÉ

Berlin

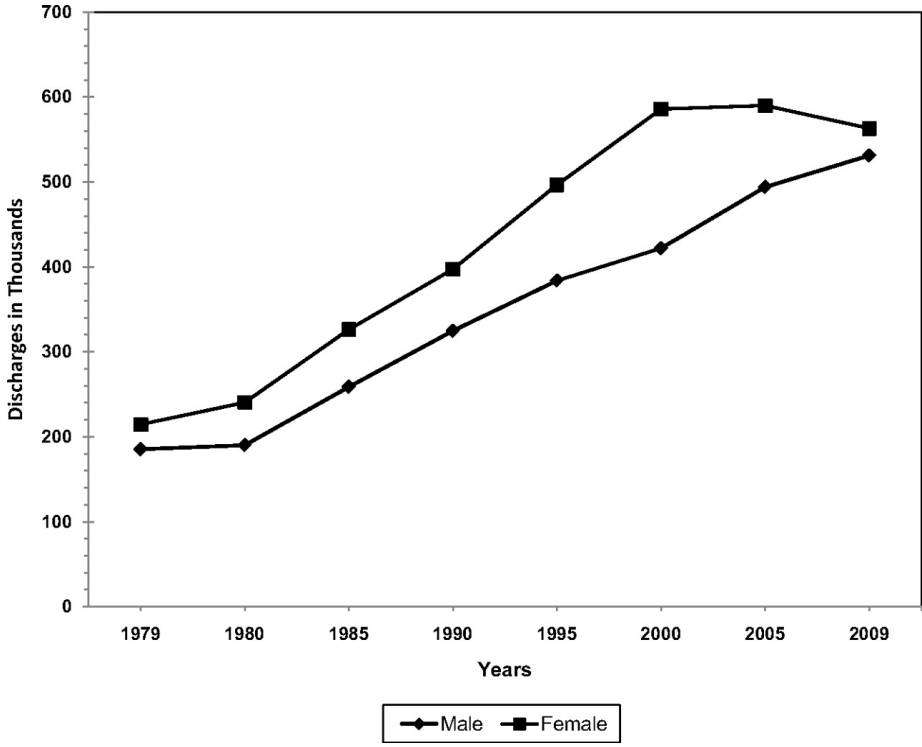
# Hospitalisationsrate der CHF

**(United States: 1979–2009)**

for coronary heart disease




for heart failure




Roger VL et al. Circulation 2012

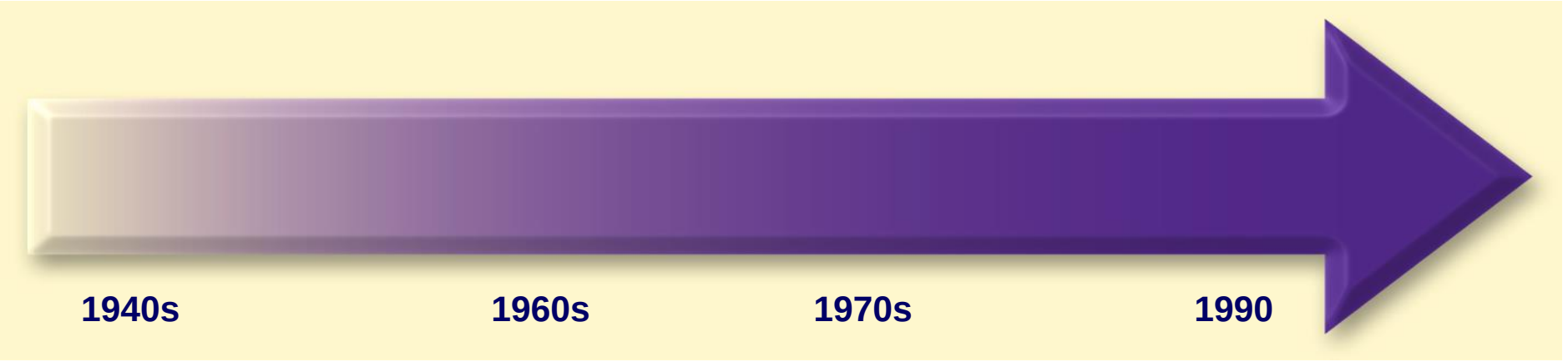
Prof. C. Tschöpe; Charite, Kardiologie Berlin

# Entwicklung der Herzinsuffizienz Modelle

**Kardiorenal**
Digitalis und
Diuretika
**-> Nierenperfusion**

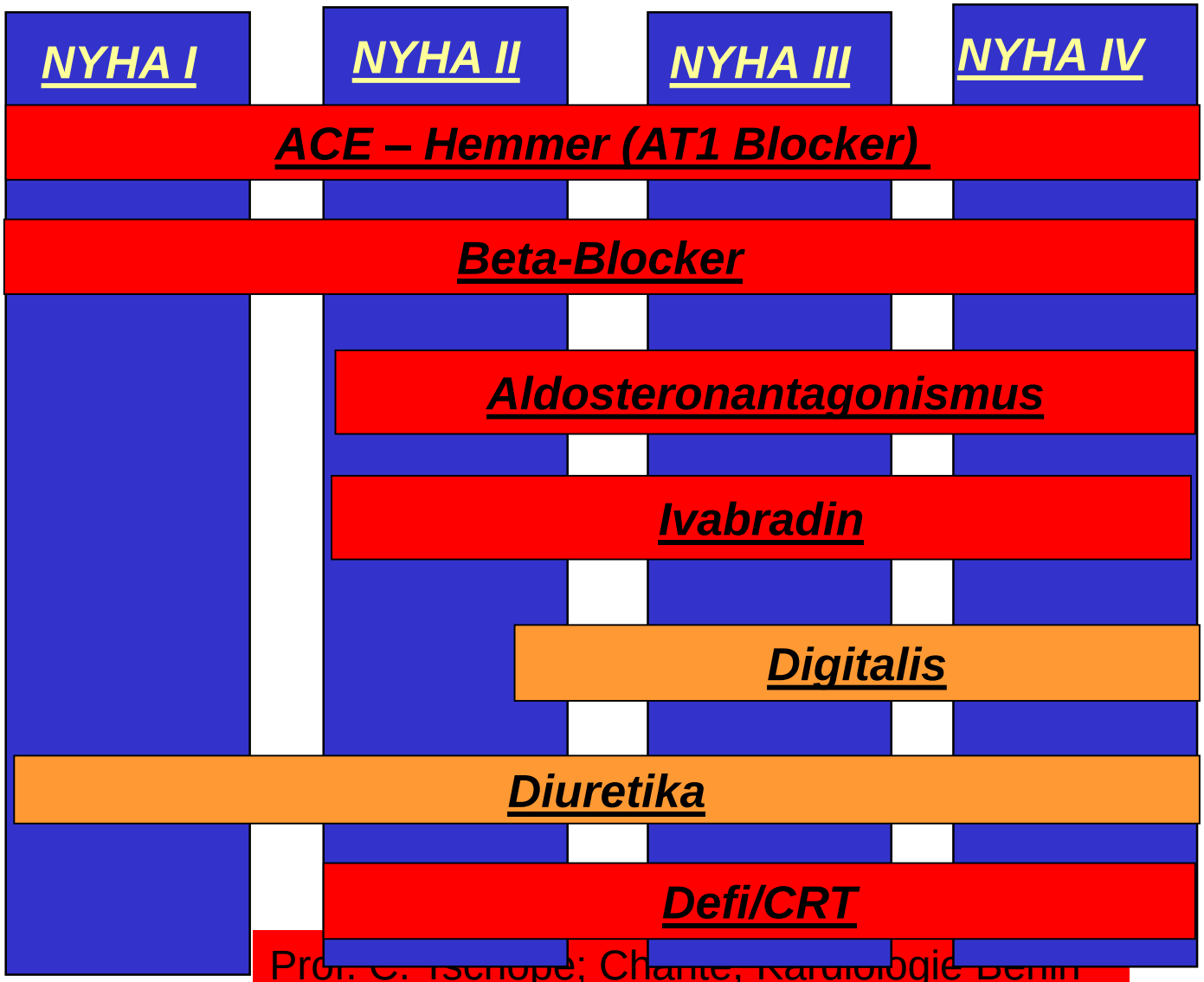
**Hämodynamik**
Vasodilatatoren
pos. inotrope Substanzen
- **> Wandstress-reduktion**

**Neurohormonal**
ACE Inhibitoren / AT1 Blocker
ß-Blocker
Aldosteronantagonisten
**CRT**
**- > Neurohormonale Inhibition**

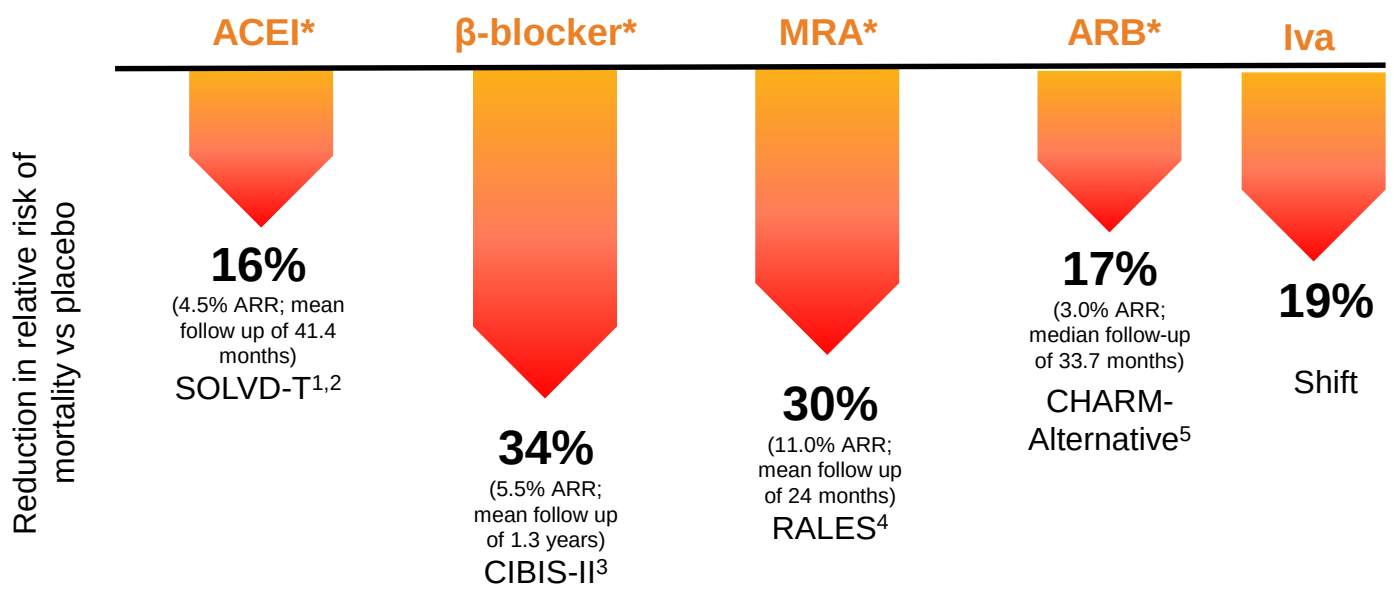



Pepper, *Arch Intern Med* 1999.

# Stadiengerechte Basistherapie 2012



# Weiterhin bestehende hohe Mortalität bei der Herzinsuffizienz




- However, significant mortality remains: ~50% of patients die within 5 years of diagnosis[6–8]

1. McMurray et al. Eur Heart J 2012;33:1787–847; 2. SOLVD Investigators. N Engl J Med 1991;325:293–302;
3. CIBIS-II Investigators. Lancet 1999;353:9–13; 4. Pitt et al. N Engl J Med 1999;341:709-17;–50;
5. Granger et al. Lancet 2003;362:772–6; 6. Go et al. Circulation 2014;129:e28-e292;
7. Yancy et al. Circulation 2013;128:e240–327; 8. Levy et al. N Engl J Med 2002;347:1397–402

European Heart Journal
doi:10.1093/eurheartj/ehw128



# 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

## The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

## Developed with the special contribution of the Heart Failure Association (HFA) of the ESC

**Authors/Task Force Members: Piotr Ponikowski* (Chairperson) (Poland), Adriaan A. Voors* (Co-Chairperson) (The Netherlands), Stefan D. Anker (Germany), Héctor Bueno (Spain), John G. F. Cleland (UK), Andrew J. S. Coats (UK), Volkmar Falk (Germany), José Ramón González-Juanatey (Spain), Veli-Pekka Harjola (Finland), Ewa A. Jankowska (Poland), Mariell Jessup (USA), Cecilia Linde (Sweden), Petros Nihoyannopoulos (UK), John T. Parissis (Greece), Burkert Pieske (Germany), Jillian P. Riley (UK), Giuseppe M. C. Rosano (UK/Italy), Luis M. Ruilope (Spain), Frank Ruschitzka (Switzerland), Frans H. Rutten (The Netherlands), Peter van der Meer (The Netherlands)**



Ponikowski P, et al. Eur J Heart Fail 2016 & EHJ 2016 (online available) 

# Recommendations for cardiac imaging in patients with suspected or established heart failure

| Recommendations | Class [a] | Level [b] |
|---|---|---|
| TTE is recommended for the assessment of m… with suspected HF in order to establish a diagnosis of either HFrEF, HFmrEF or HFpEF. | I | C |
| TTE is recommended to assess LVEF in order … suitable for evidence-based pharmacological and device (ICD, CRT) treatm… | I | C |
| TTE is recommended for the assessment of valve disease, … ventricular function and pulmonary arterial pressure in patients with an already established diagnosis of either HFrEF, HFmrEF or HFpEF in order to identify those suitable for correction of valve disease. | I | C |
| TTE is recommended for the assessment of myocardial structure and function in subjects to be exposed to treatment which potentially can damage myocardium (e.g. chemotherapy). | I | C |
| Other techniques (including systolic tissue Doppler velocities and deformation indices, i.e. strain and strain rate), should be considered in a TTE protocol in subjects at risk of developing HF in order to identify myocardial dysfunction at the preclinical stage. | IIa | C |
| CMR is recommended for the assessment of myocardial structure and function (including right heart) in subjects with poor acoustic window and patients with complex congenital heart diseases (taking account of cautions/contra-indications to CMR). | I | C |
| CMR with LGE should be considered in patients with dilated cardiomyopathy in order to distinguish between ischaemic and non-ischaemic myocardial damage in case of equivocal clinical and other imaging data (taking account of cautions/contra-indications to CMR). | IIa | C |
| CMR is recommended for the characterization of myocardial tissue in case of suspected myocarditis, amyloidosis, sarcoidosis, Chagas disease, Fabry disease non-compaction cardiomyopathy, and haemochromatosis (taking account of cautions/contra-indications to CMR). | I | C |

HFrEF
HFmrEF
HfpEF

Prof. C. Tschöpe; Charite, Kardiologie Berlin

# Definition of heart failure with preserved (HFpEF), mid-range (HFmrEF) & reduced ejection fraction (HFrEF)

| Type of HF | | HFrEF | HFmrEF | HFpEF |
|---|---|---|---|---|
| CRITERIA | 1 | Symptoms ± Signs[a] | Symptoms ± Signs[a] | Symptoms ± Signs[a] |
| | 2 | LVEF <40% | LVEF 40–49% | LVEF ≥50% |
| | 3 | – | 1. Elevated levels of natriuretic peptides[b];<br>2. At least one additional criterion:<br>a. relevant structural heart disease (LVH and/or LAE),<br>b. diastolic dysfunction (for details see Section 4.3.2). | 1. Elevated levels of natriuretic peptides[b];<br>2. At least one additional criterion:<br>a. relevant structural heart disease (LVH and/or LAE),<br>b. diastolic dysfunction (for details see Section 4.3.2). |

Prof. C. Tschöpe; Charite, Kardiologie Berlin

# Recommendations for treatment of patients with HF with preserved ejection fraction and heart failurewith mid-range ejection fraction

| Recommendations | Class [a] | Level [b] |
|---|---|---|
| it is recommended to screen patients with HFpEF or HFmrEF for both cardiovascular and non-cardiovascular comorbidities, which, if present, should be treated provided safe and effective interventions exist to improve symptoms, well-being and/or prognosis. | I | C |
| Diuretics are recommended in congested patients with HFpEF or HFmrEF in order to alleviate symptoms and signs. | I | B |

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# Recommendations for diagnostic tests in patients with heart failure

| Recommendations | Class [a] | Level [b] |
|---|---|---|
| The following diagnostic tests are recommended/should be considered for initial assessment of a patient with newly diagnosed HF in order to evaluate the patient's suitability for particular therapies, to detect reversible/treatable causes of HF and co-morbiditi | | |
| - haemo | I | C |
| - sodiu | | |
| - liver f | | |
| - glucos | | |
| - lipid p | | |
| - TSH | | |
| - ferritin, TSAT = TIBC | | |
| - natriuretic peptides | IIa | C |
| Additional diagnostic tests aiming to identify other HF aetiologies and comorbidities should be considered in individual patients with HF when there is a clinical suspicion of a particular pathology (see Table 3.4 on HF aetiologies). | IIa | C |
| A 12-lead ECG is recommended in all patients with HF in order to determine heart rhythm, heart rate, QRS morphology, and QRS duration, and to detect other relevant abnormalities. This information is needed to plan and monitor treatment. | I | C |
| Exercise testing in patients with HF: | | |
| - is recommended as a part of the evaluation for heart transplantation and/or mechanical circulatory support (cardiopulmonary exercise testing); | I | C |
| - should be considered to optimize prescription of exercise training (preferably cardiopulmonary exercise testing); | IIa | C |
| - should be considered to identify the cause of unexplained dyspnoea (cardiopulmonary exercise testing). | IIa | C |
| - may be considered to detect reversible myocardial ischaemia. | IIb | C |

Eisenkapazität

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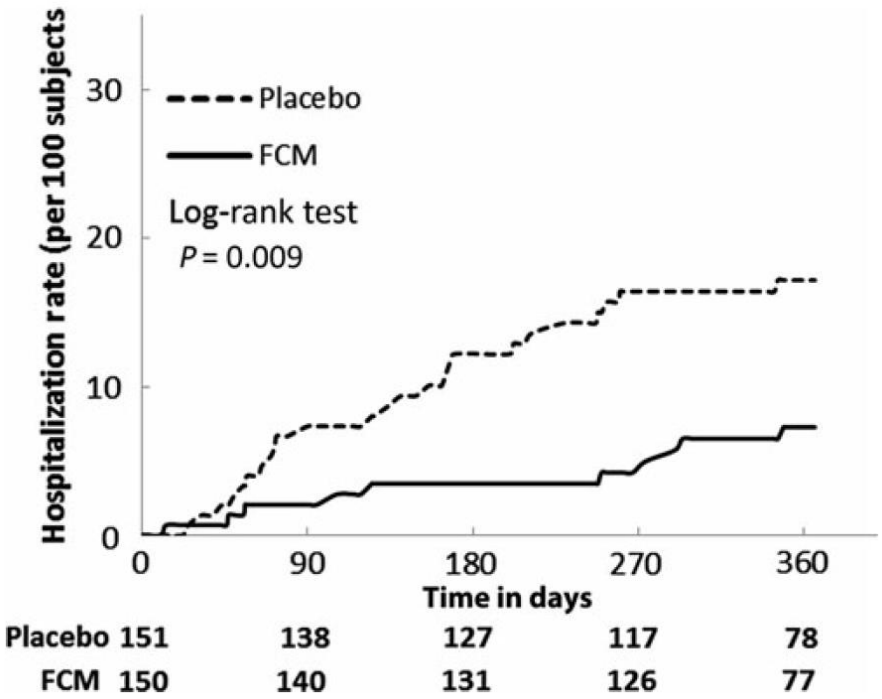
# II a - Indikation Eisendefizienz

## CONFIRM-HF

**Effekt von iv Eisengaben**




Ponikowski et al EHF 2015

Prof. C. Tschöpe; Charite, Kardiologie Berlin

HEART FAILURE NETWORK

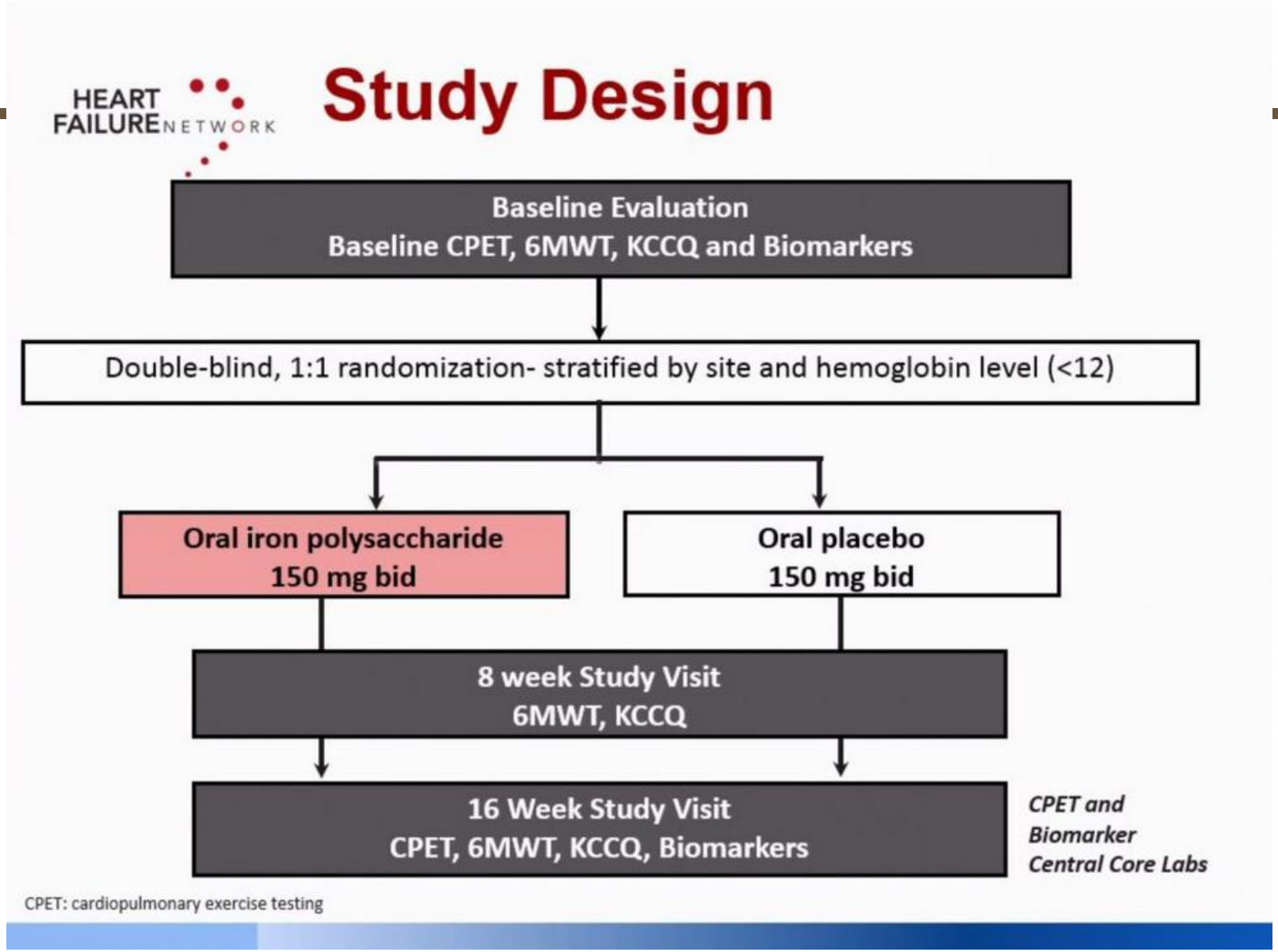
# Oral Iron Repletion effects on Oxygen UpTake in Heart Failure (IRONOUT)

*Gregory D. Lewis, M.D.*
*on behalf of*
*The NHLBI Clinical Heart Failure Network*

U.S. Department of Health and Human Services
National Institutes of Health

National Heart Lung and Blood Institute
People Science Health

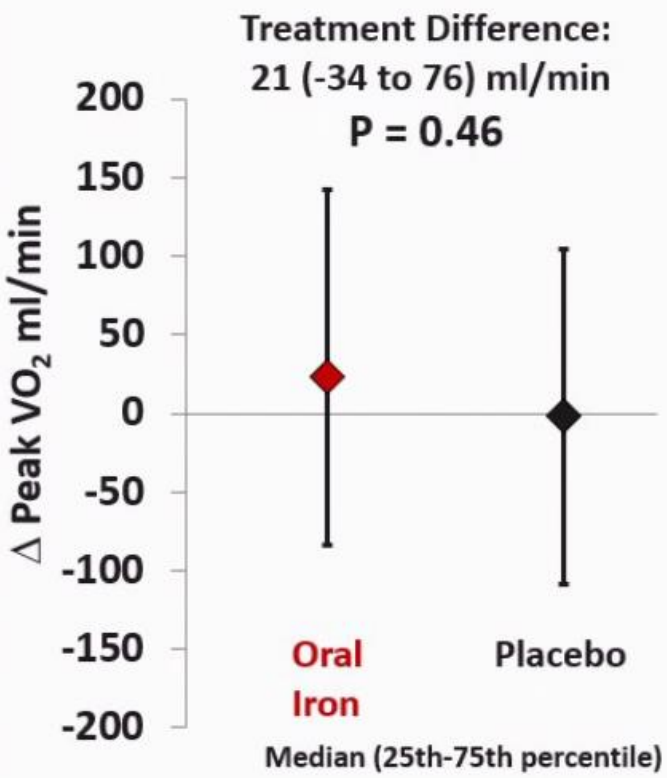
Prof. C. Tschöpe; Charite, Kardiologie Berlin

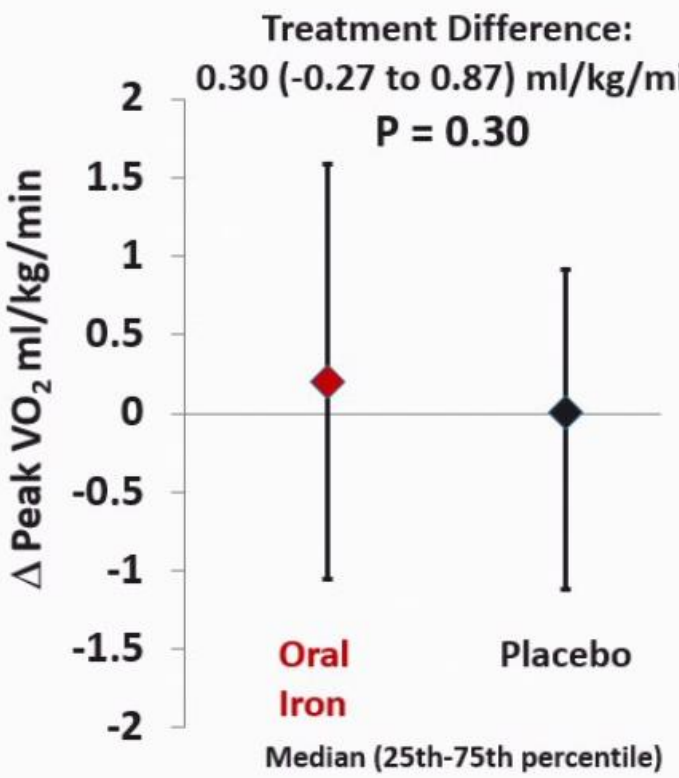



Prof. C. Tschöpe; Charite, Kardiologie Berlin

Gregory Lewis, presented at AHA Scientific Sessions 2016

# Results: Primary Endpoint

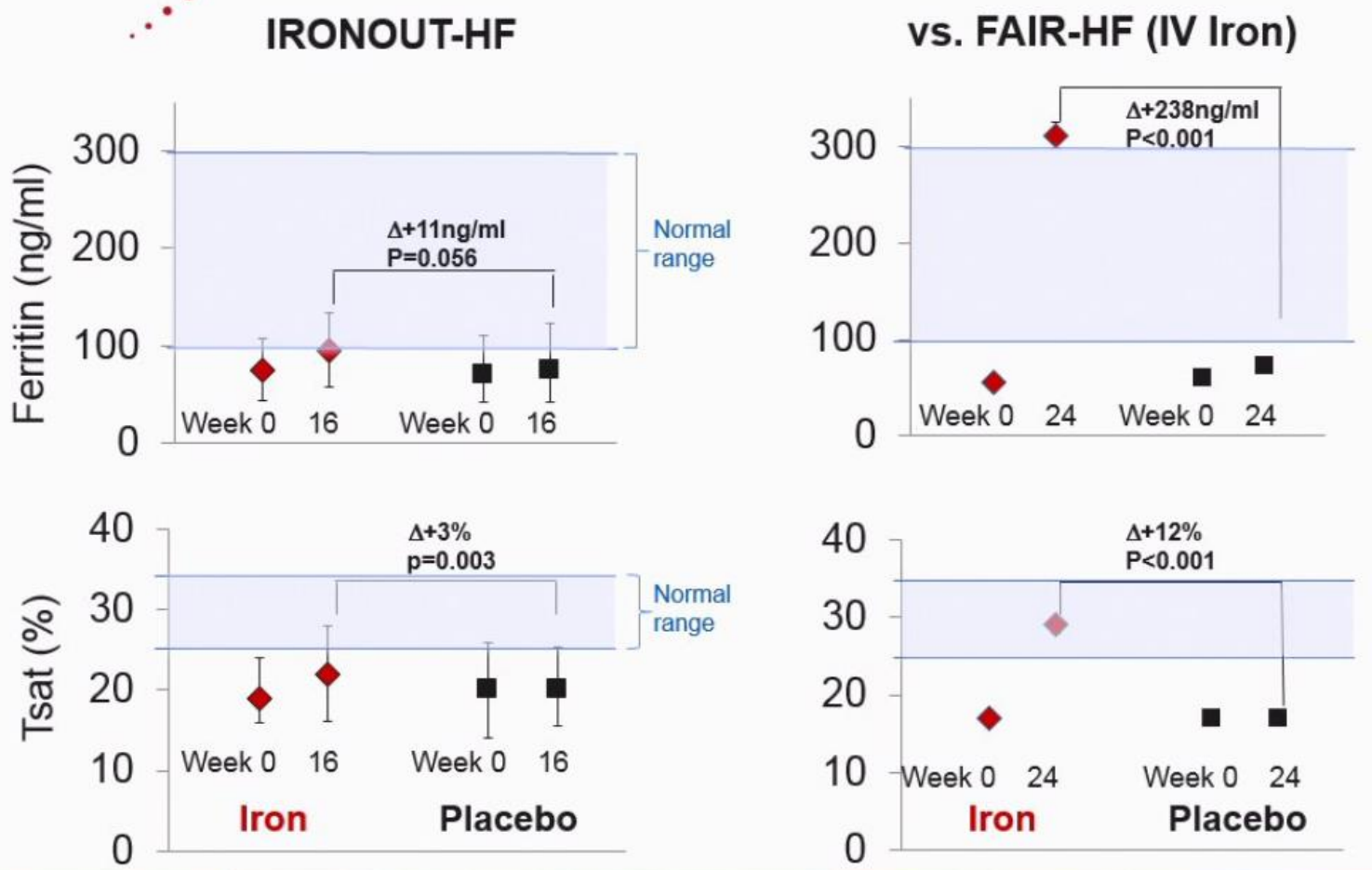



Prof. C. Tschöpe; Charite, Kardiologie Berlin

Gregory Lewis, presented at AHA Scientific Sessions 2014

# Results: Δ Iron Studies




Prof. C. Tschöpe; Charite, Kardiologie Berlin

Gregory Lewis, presented at AHA Scientific Sessions 2016

# Recommendations to prevent or delay the development of overt heart failure or prevent death before the onset of symptoms

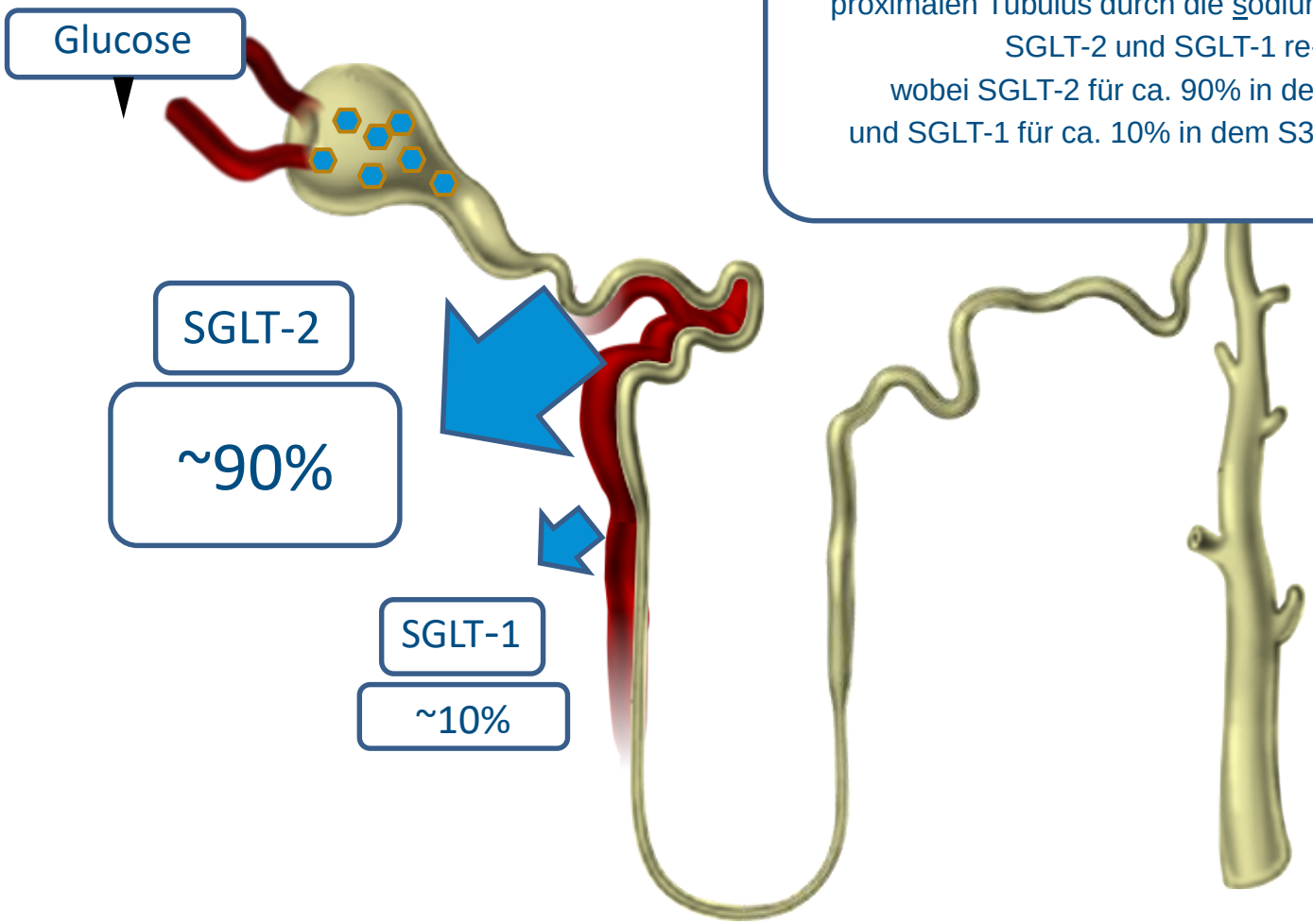
| Recommendations | Class [a] | Level [b] |
|---|---|---|
| Treatment of hypertension is recommended to prevent or d | I | A |
| Treatment with statins is recommended in patients with or a dysfunction, in order to prevent or delay the onset of HF an | I | A |
| Counselling and treatment for smoking cessation and alcohol consume excess alcohol in order to prevent or delay the onse | I | C |
| Treating other risk factors of HF (e.g. obesity, dysglycaemia) IF. | IIa | C |
| Empagliflozin should be considered in patients with type 2 diabetes in order to prevent or delay the onset of HF and prolong life. | IIa | B |
| ACE-I is recommended in patients with asymptomatic LV systolic dysfunction and a history of myocardial infarction in order to prevent or delay the onset of HF and prolong life. | I | A |
| ACE-I is recommended in patients with asymptomatic LV systolic dysfunction without a history of myocardial infarction, in order to prevent or delay the onset of HF. | I | B |
| ACE-I should be considered in patients with stable CAD even if they do not have LV systolic dysfunction, in order to prevent or delay the onset of HF. | IIa | A |
| Beta-blocker is recommended in patients with asymptomatic LV systolic dysfunction and a history of myocardial infarction, in order to prevent or delay the onset of HF or prolong life. | I | B |
| ICD is recommended in patients:<br>a) with asymptomatic LV systolic dysfunction (LVEF ≤30%) of ischaemic origin, who are at least 40 days after acute myocardial infarction,<br>b) with asymptomatic non-ischaemic dilated cardiomyopathy (LVEF ≤30%), who receive OMT therapy,<br><br>in order to prevent sudden death and prolong life. | I | B |

1. Metformin
2. Metformin plus Empagliflozin

Ziel Hba1c bei DM und HF
> 7%

# SGLT-2 Hemmer - Renale Glucose Re-Absorption wird blockiert

Fast die gesamte gefilterte Glucose wird im proximalen Tubulus durch die sodium glucose co-transporter SGLT-2 und SGLT-1 re-absorbiert, wobei SGLT-2 für ca. 90% in dem S1+S2 Segment, und SGLT-1 für ca. 10% in dem S3 Segment zuständig ist

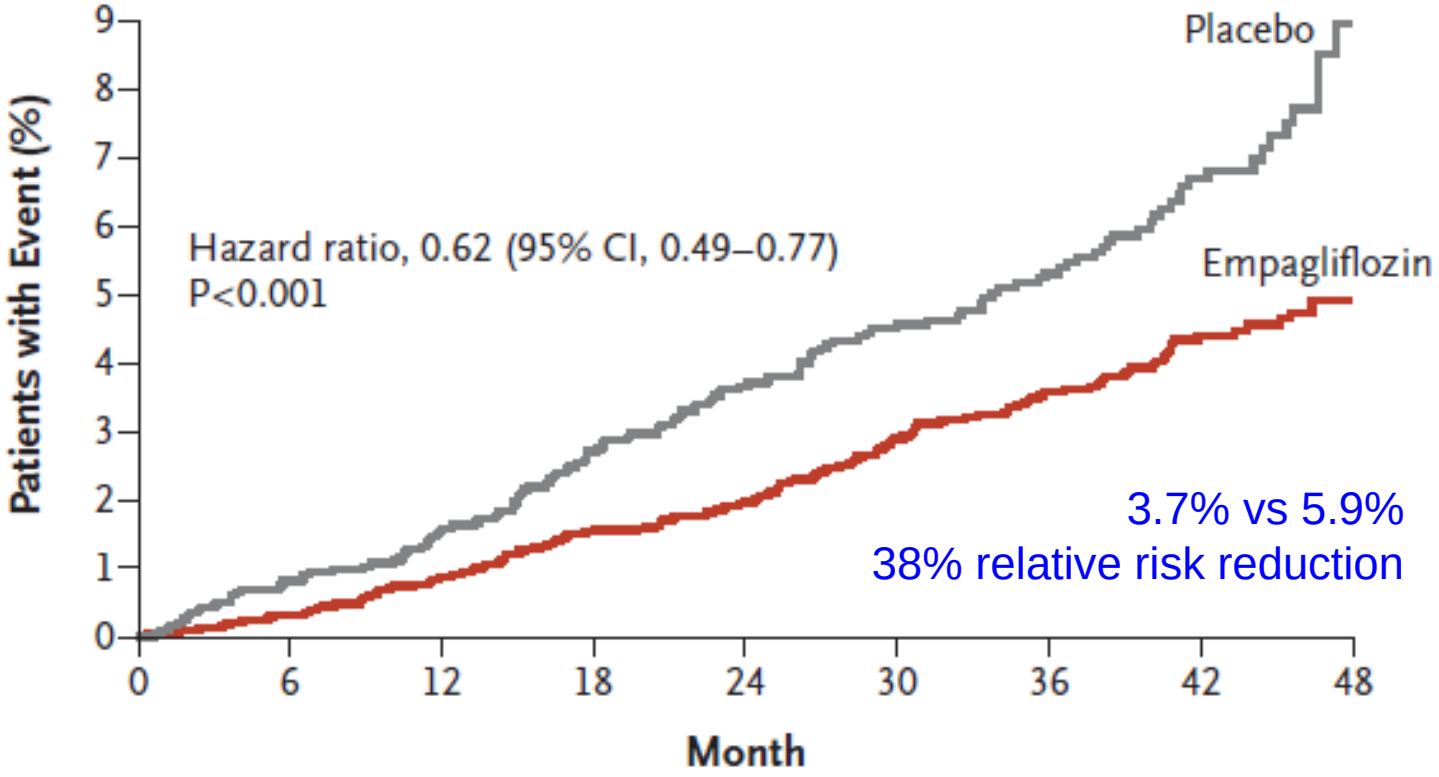



Prof. C. Tschöpe; Charite, Kardiologie Berlin

Lee YJ, Han HJ. Kidney Int Suppl 2007

# Cardiovascular Death

**Death from Cardiovascular Causes**




**No. at Risk**

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Empagliflozin | 4687 | 4651 | 4608 | 4556 | 4128 | 3079 | 2617 | 1722 | 414 |
| Placebo | 2333 | 2303 | 2280 | 2243 | 2012 | 1503 | 1281 | 825 | 177 |

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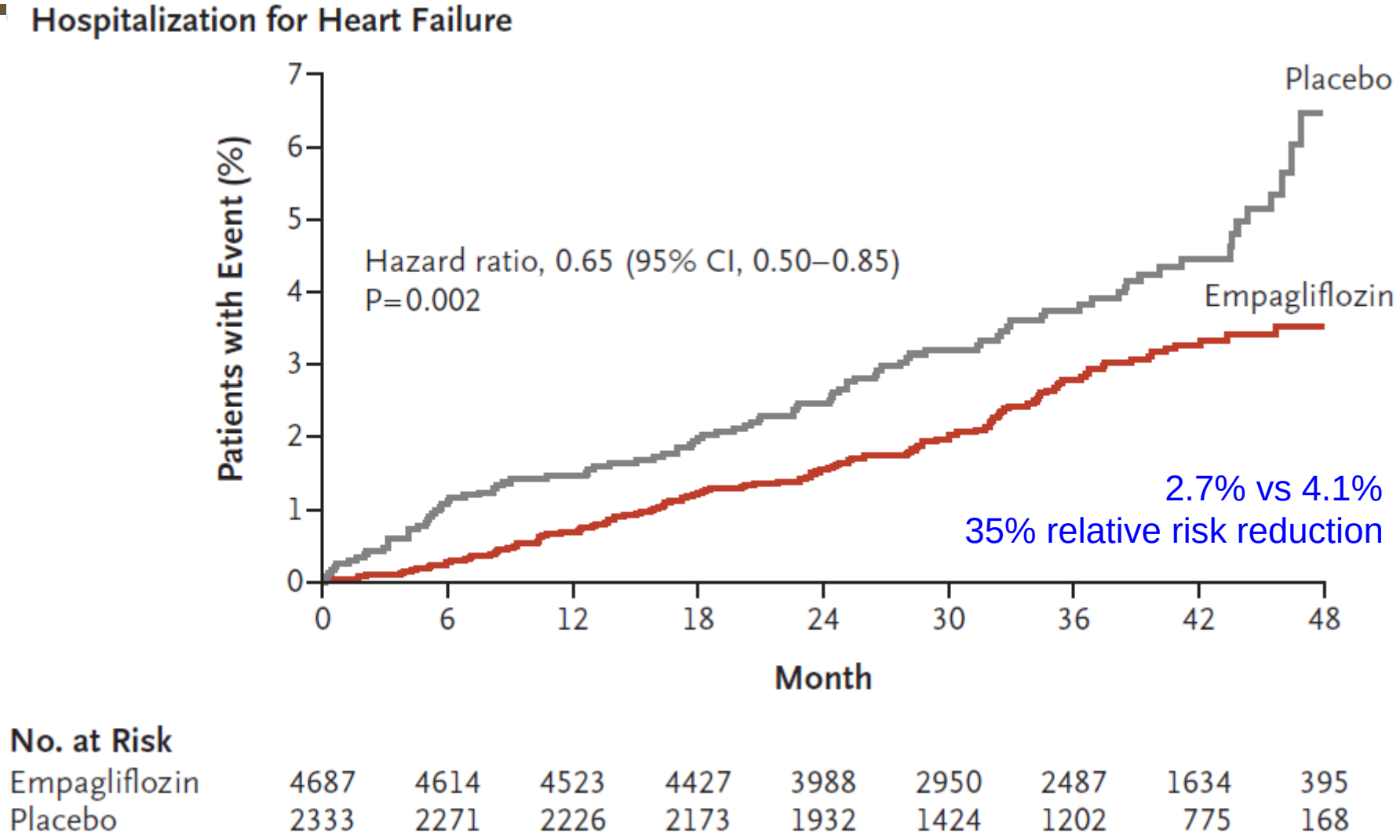
EMPA-REG, NEJM 2015

# Hospitalization for Heart Failure



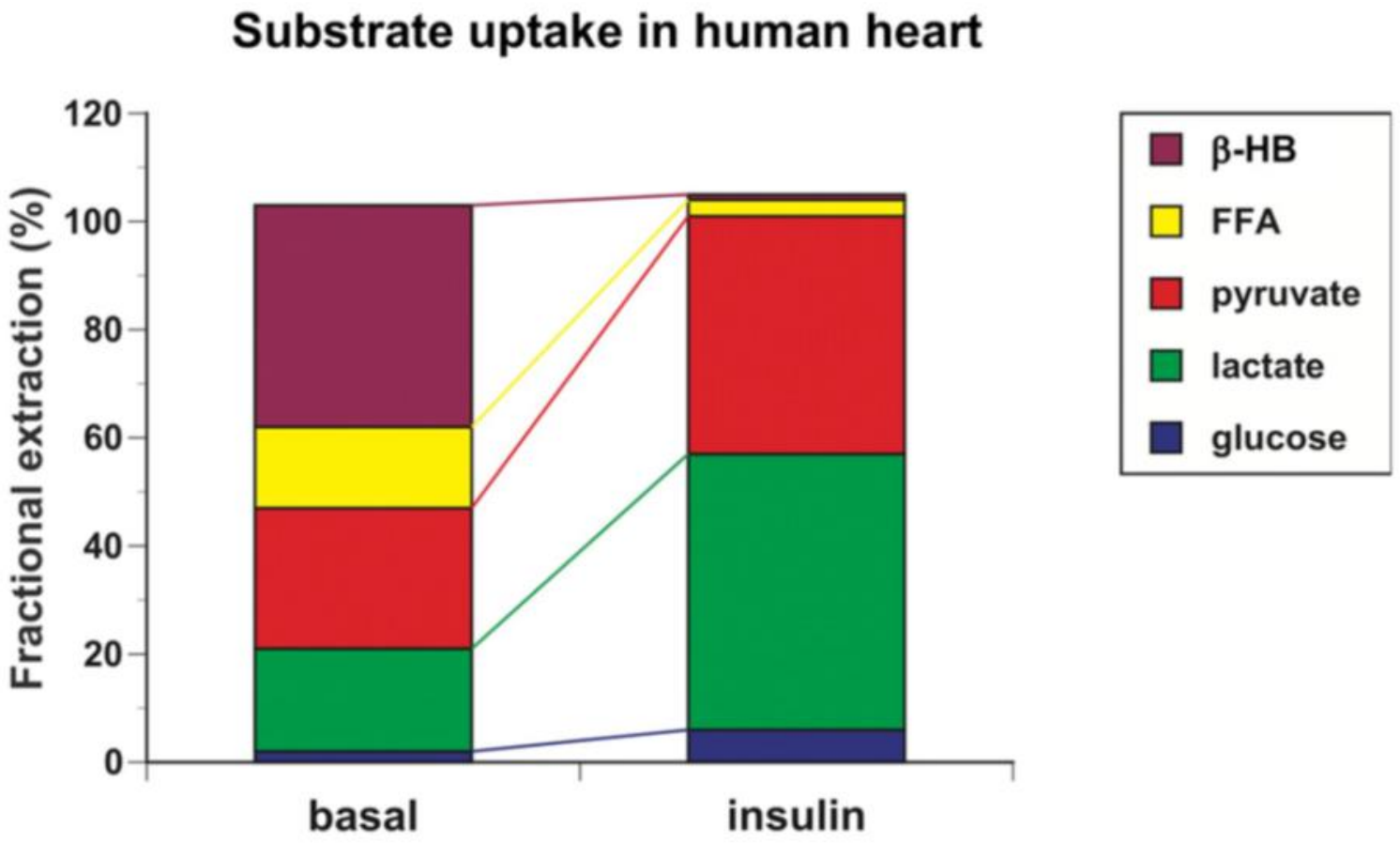

Prof. C. Tschöpe; Charite, Kardiologie Berlin

EMPA-REG, NEJM 2015

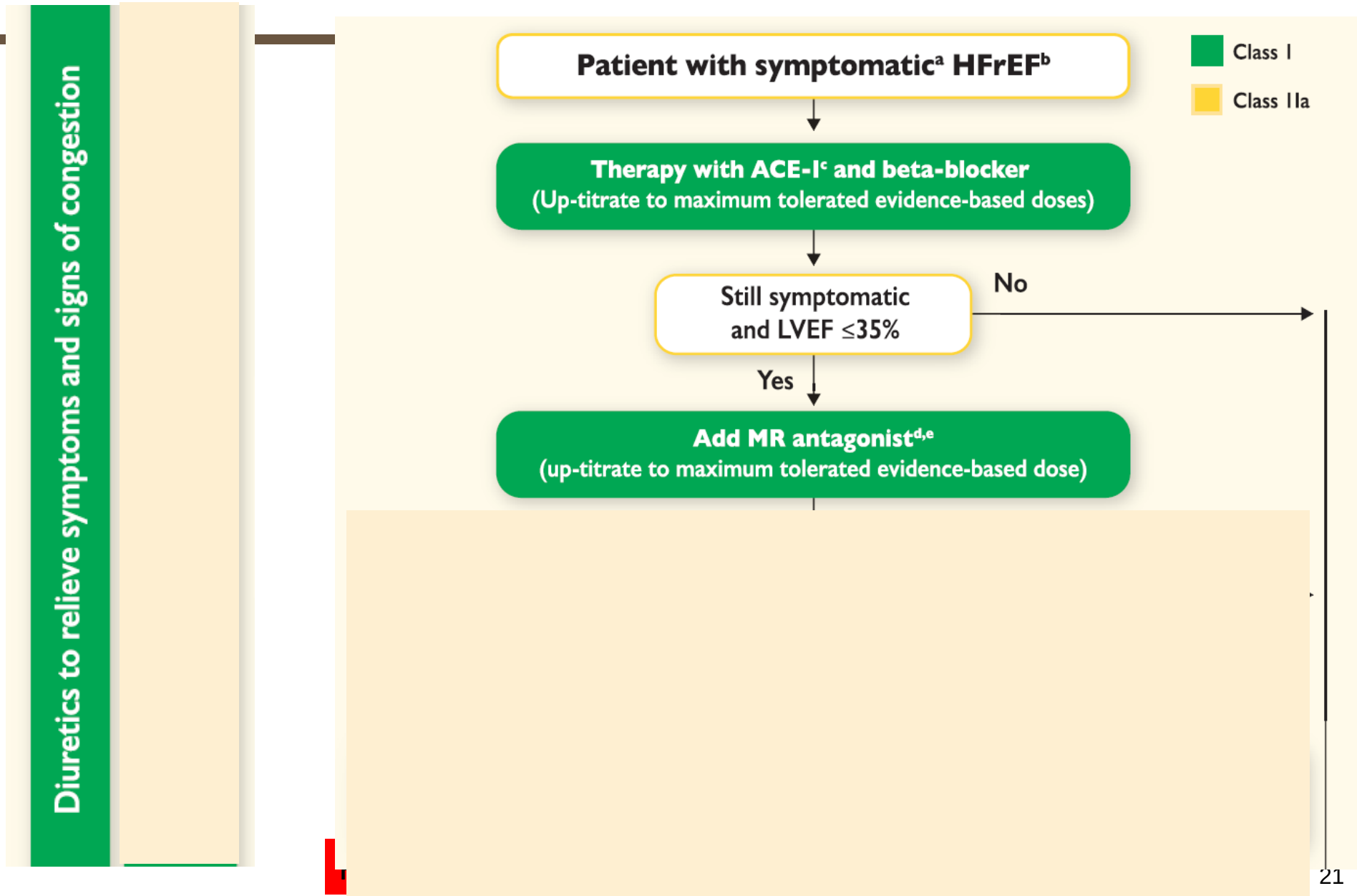
# CV Protection in the EMPA-REG OUTCOME Trial: A "Thrifty Substrate" Hypothesis

*Ele Ferrannini,[1] Michael Mark,[2] and Eric Mayoux[2]*

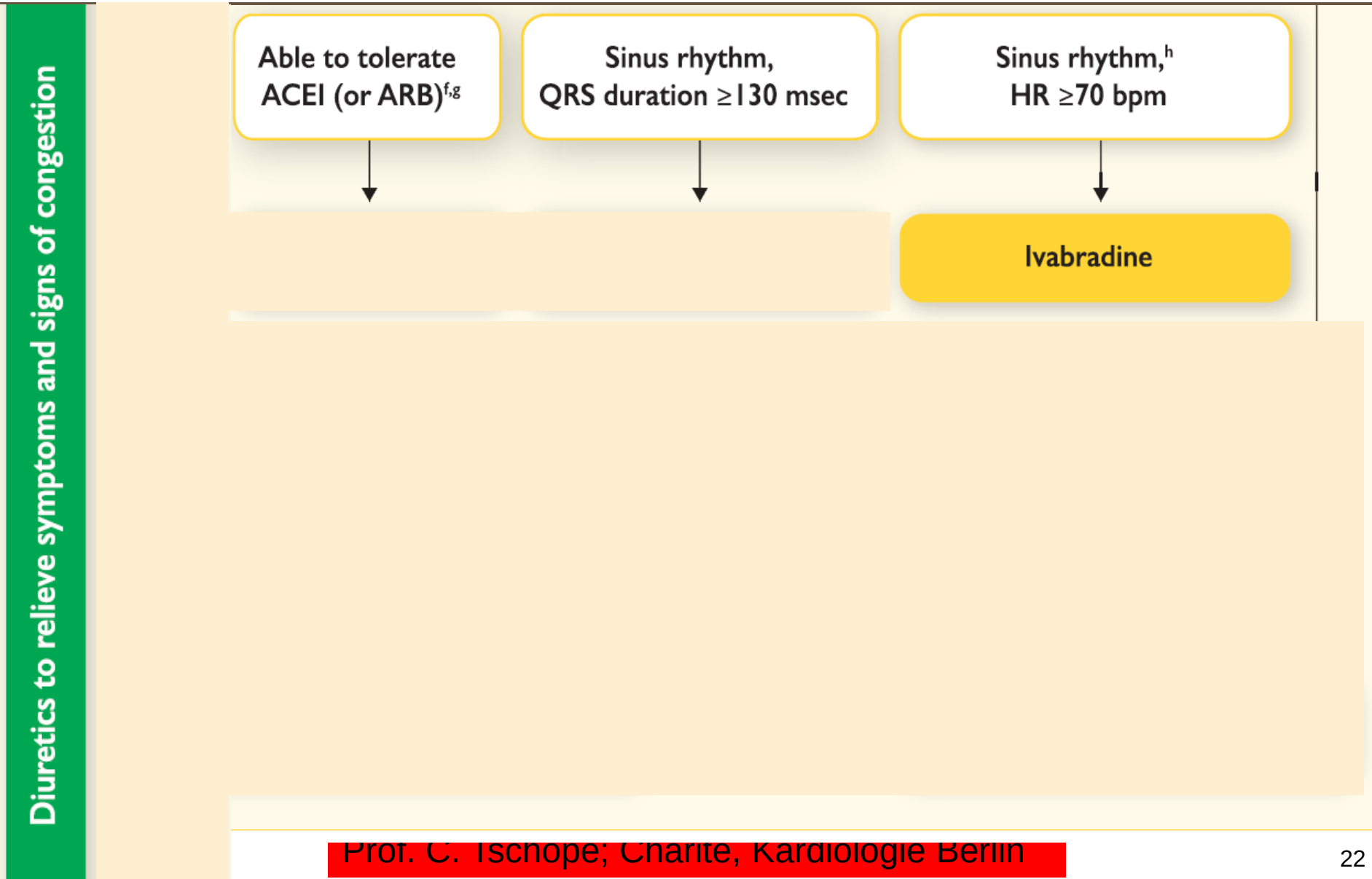
*Diabetes Care 2016;39:1108–1114 | DOI: 10.2337/dc16-0330*



# Medikamentöse Therapie bei HFrEF

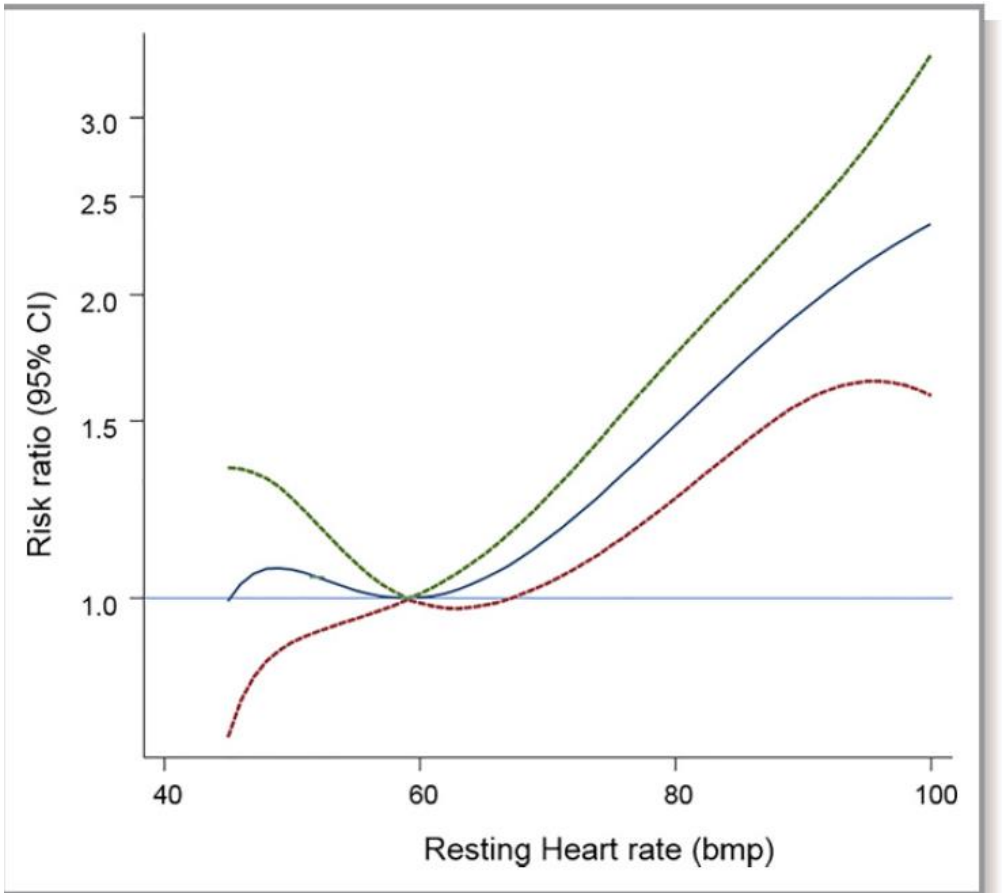


# Medikamentöse Therapie bei HFrEF



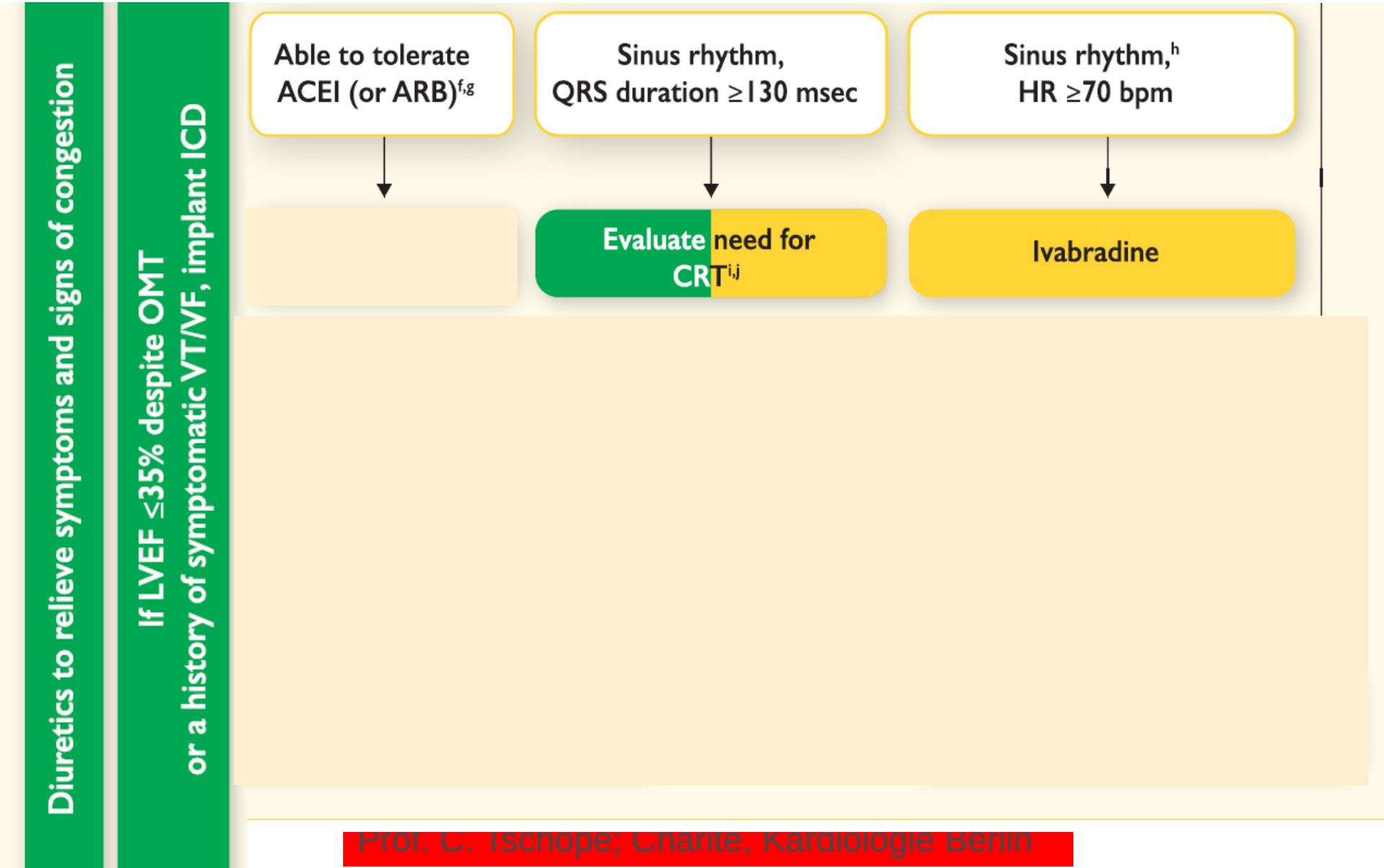
# Nicht-linearer Zusammenhang zwischen Ruheherzfrequenz und Auftreten von Herzinsuffizienz

Metaanalyse: Ruheherzfrequenz als Risikofaktor für Auftreten von Herzinsuffizienz; n = 7.073 (1.181 x Inzidenz Herzinsuffizienz)

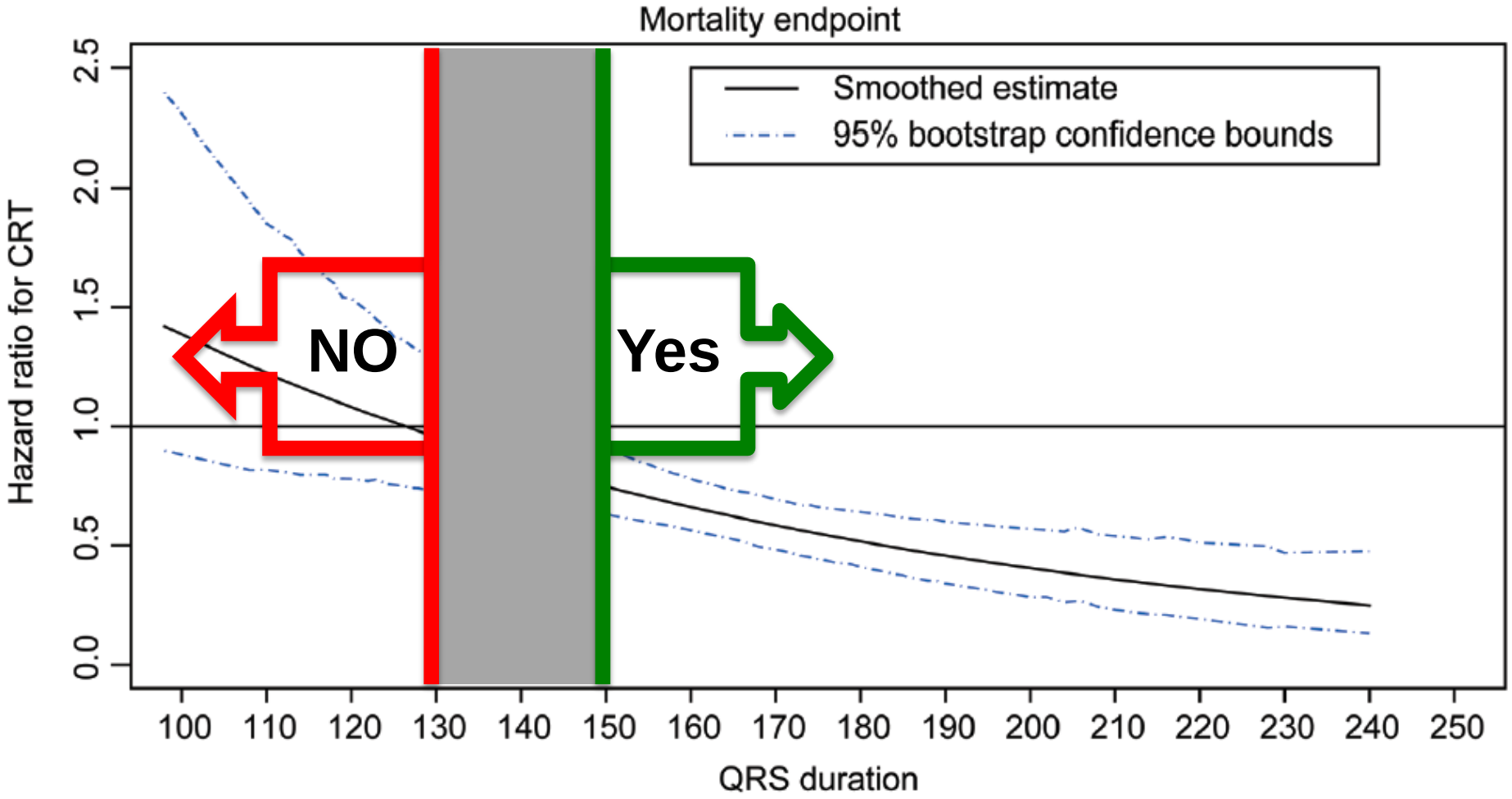



Kahn et al., J Am Heart Assoc. 2015;4:e001364

# Therapeutic algorithm for a patient with symptomatic HF with reduced ejection fraction. (cont.)



# The Do`s and Don`ts of CRT




Ruschitzka HFA 2016
mod. Cleland EHJ 2013

# Gaps in evidence



## 15.5 Devices

**Defi in DCM**
**II A (ESC)**
**IB (USA)**

# DANISH

DANish study to assess the efficacy of Implantable cardioverter defibrillator in patients with nonischemic Systolic Heart failure on mortality

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

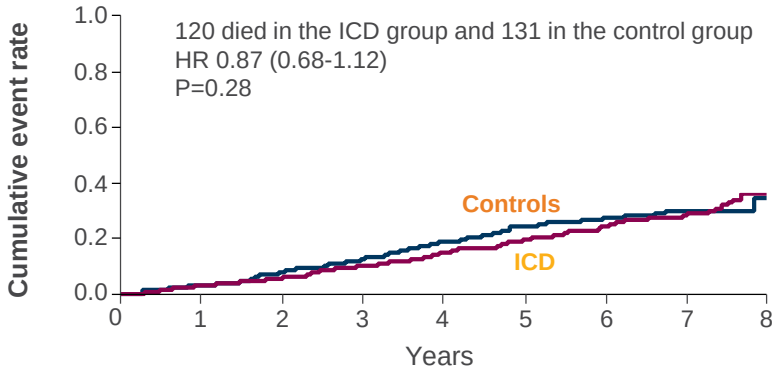
## Defibrillator Implantation in Patients with Nonischemic Systolic Heart Failure

Lars Køber, M.D., D.M.Sc., Jens J. Thune, M.D., Ph.D., Jens C. Nielsen, M.D., D.M.Sc., Jens Haarbo, M.D., D.M.Sc., Lars Videbæk, M.D., Ph.D., Eva Korup, M.D., Ph.D., Gunnar Jensen, M.D., Ph.D., Per Hildebrandt, M.D., D.M.Sc., Flemming H. Steffensen, M.D., Niels E. Bruun, M.D., D.M.Sc., Hans Eiskjær, M.D., D.M.Sc., Axel Brandes, M.D., Anna M. Thøgersen, M.D., Ph.D., Finn Gustafsson, M.D., D.M.Sc., Kenneth Egstrup, M.D., D.M.Sc., Regitze Videbæk, M.D., Christian Hassager, M.D., D.M.Sc., Jesper H. Svendsen, M.D., D.M.Sc., Dan E. Høfsten, M.D., Ph.D., Christian Torp-Pedersen, M.D., D.M.Sc., and Steen Pehrson, M.D., D.M.Sc., for the DANISH Investigators*

# DANISH

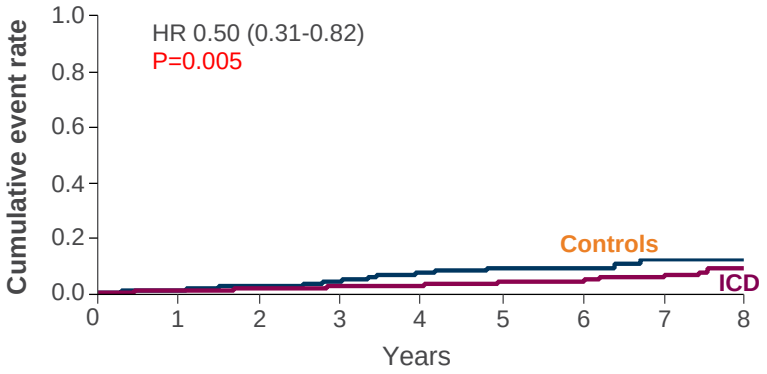
## Results – primary and secondary outcome

**Primary outcome**
All-cause mortality




| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Controls | 560 | 540 | 517 | 438 | 344 | 248 | 169 | 88 | 12 |
| ICD | 556 | 540 | 526 | 451 | 358 | 272 | 186 | 107 | 17 |

**Secondary outcome**
Sudden cardiac death

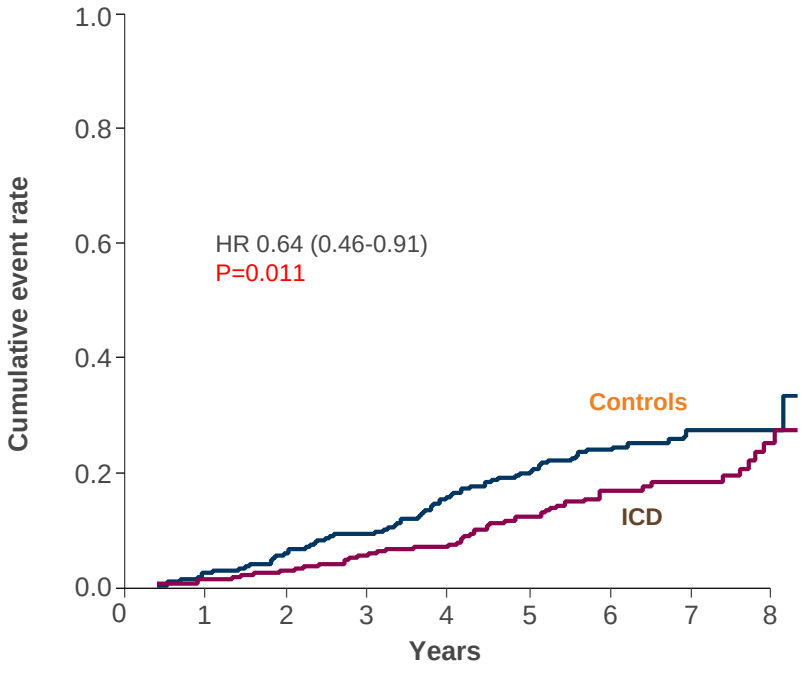



| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Controls | 560 | 540 | 517 | 438 | 344 | 248 | 169 | 88 | 12 |
| ICD | 556 | 540 | 526 | 451 | 358 | 272 | 186 | 107 | 17 |

DANISH

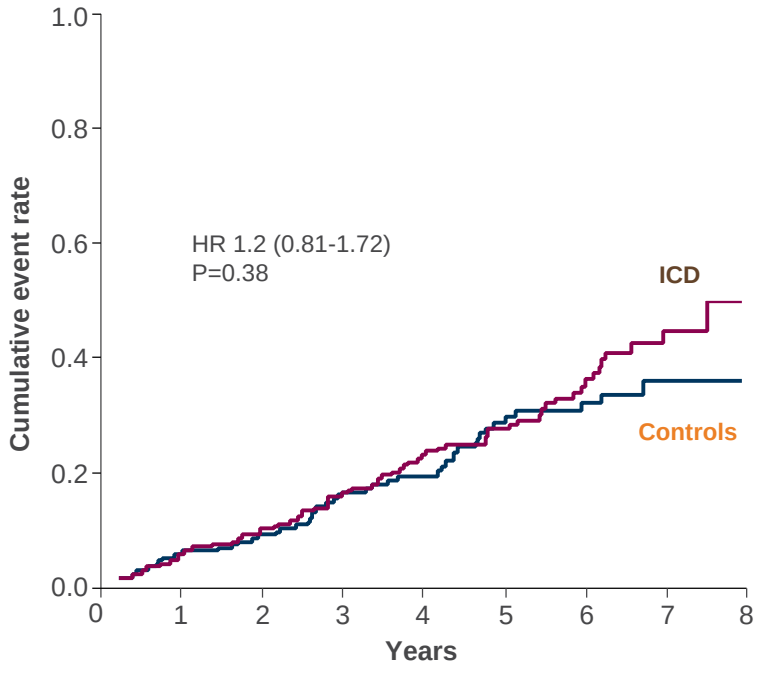
# Results – all-cause mortality by age

**Age** – youngest two tertiles – age <68 years



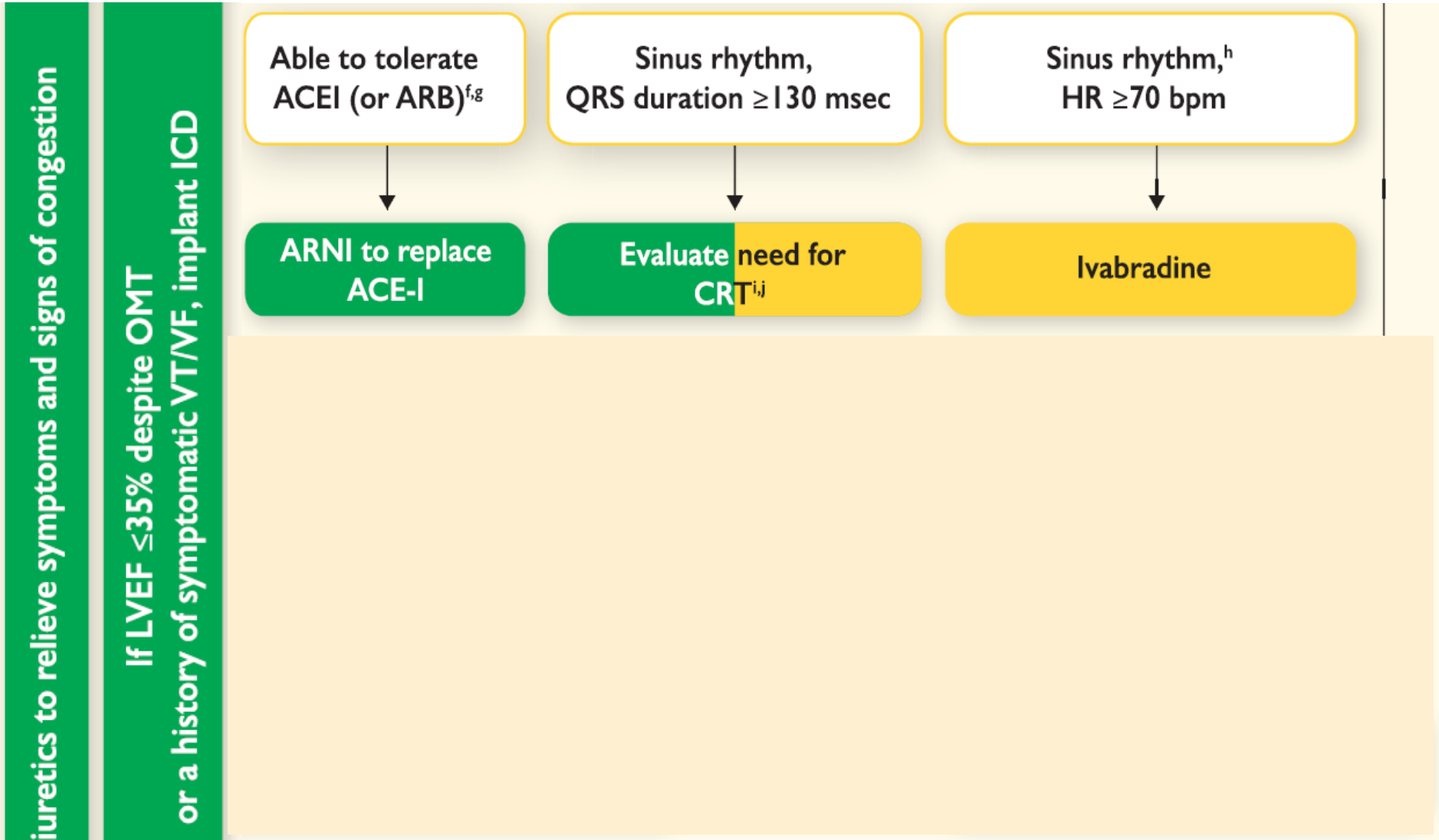

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Controls | 383 | 372 | 354 | 308 | 241 | 176 | 123 | 64 | 10 |
| ICD | 340 | 336 | 330 | 294 | 237 | 179 | 132 | 82 | 15 |

**Age** – oldest tertile – age ≥ 68 years




| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Controls | 177 | 166 | 163 | 130 | 103 | 72 | 46 | 24 | 2 |
| ICD | 216 | 204 | 196 | 157 | 121 | 93 | 54 | 25 | 2 |

# Therapeutic algorithm for a patient with symptomatic HF with reduced ejection fraction. (cont..)



# Therapeutic algorithm for a patient with symptomatic HF with reduced ejection fraction.

- ESC-HF guidelines provide **strong Class I** recommendation for sacubitril/valsartan
- Endorsement showing in section 7.3.2 of 2016 Guidelines, discussed in light of PARADIGM-HF

**Pharmacological treatments indicated in patients with symptomatic (NYHA Class II-IV) HFrEF**

| Recommendations | Class | Level |
|---|---|---|
| An **ACEi** is recommended, in addition to a beta blocker, for symptomatic patients with HFrEF to reduce the risk of HF hospitalization and death | I | A |
| A **beta blocker** is recommended, in addition an ACEi, for patients with stable, symptomatic HFrEF to reduce the risk of HF hospitalization and death | I | A |
| An **MRA** is recommended for patients with HFrEF, who remain symptomatic despite treatment with an ACEi and a beta-blocker, to reduce the risk of HF hospitalization and death | I | A |
| **Sacubitril/valsartan** is recommended as a **replacement for an ACEi** to further reduce the risk of HF hospitalization and death in ambulatory patients with HFrEF who remain symptomatic despite optimal treatment with an ACEi, a beta-blocker and an MRA* | I | B |

**Patient should have elevated natriuretic peptides (plasma BNP ≥150 pg/mL or plasma NT-proBNP ≥600 pg/mL, or if HF hospitalization within the last 12 months, plasma BNP ≥100 pg/mL or plasma NT-proBNP ≥400 pg/mL) and able to tolerate enalapril 10 mg b.i.d.*

ACC, American College of Cardiology; AHA, American Heart Association; ACEI, angiotensin-converting-enzyme inhibitor; ARB, angiotensin II receptor blocker, ARNI, angiotensin receptor neprilysin inhibitor; CV, cardiovascular; ESC, European Society of Cardiology; HF, heart failure; HFSA, Heart Failure Society of America; HFrEF, HF with reduced ejection fraction; NYHA, New York Heart Association

Ponikowski et al. Eur Heart J. 21 May 2016. doi:10.1093/eurheartj/ehw128
Yancy et al. *J Am Coll Cardiol*. Published 21 May 2016. doi:10.1016/j.jacc.2016.05.011;

# Therapeutic algorithm for a patient with symptomatic HF with reduced ejection fraction.

| CLASS (STRENGTH) OF RECOMMENDATION |
|---|
| **CLASS I (STRONG)** — **Benefit >>> Risk** |
| Suggested phrases for writing recommendations:<br>▪ Is recommended<br>▪ Is indicated/useful/effective/beneficial<br>▪ Should be performed/administered/other<br>▪ Comparative-Effectiveness Phrases†:<br>○ Treatment/strategy A is recommended/indicated in preference to treatment B<br>○ Treatment A should be chosen over treatment B |

| LEVEL (QUALITY) OF EVIDENCE‡ |
|---|
| **LEVEL A** |
| ▪ High-quality evidence‡ from more than 1 RCT<br>▪ Meta-analyses of high-quality RCTs<br>▪ One or more RCTs corroborated by high-quality registry studies |
| **LEVEL B-R** — **(Randomized)** |
| ▪ Moderate-quality evidence‡ from 1 or more RCTs<br>▪ Meta-analyses of moderate-quality RCTs |

| Recommendations for Renin-Angiotensin System Inhibition With ACE Inhibitor or ARB or ARNI | | |
|---|---|---|
| **COR** | **LOE** | **Recommendations** |
| I | ACE: A | The clinical strategy of inhibition of the renin-angiotensin system with ACE inhibitors *(Level of Evidence: A)* (9-14), OR ARBs *(Level of Evidence: A)* (15-18), OR ARNI *(Level of Evidence: B-R)* (19) in conjunction with evidence-based beta blockers (20-22), and aldosterone antagonists in selected patients (23, 24), is recommended for patients with chronic HF*r*EF to reduce morbidity and mortality. |
| | ARB: A | |
| | ARNI: B-R | |



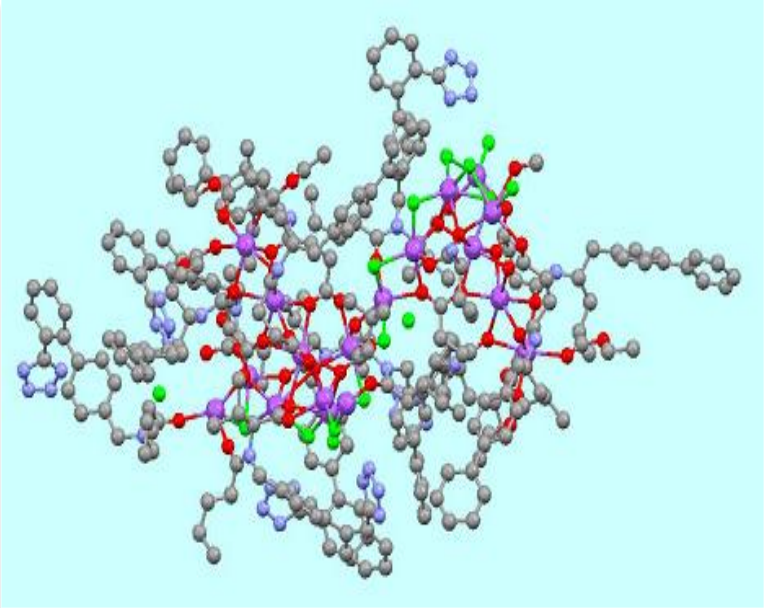


Yancy et al JACC 2016

# LCZ696 ist der erste Angiotensin Rezeptor Neprilysin Inhibitor (ARNI)

- LCZ696 is a salt complex that comprises the two active moieties:[2,3]
  - sacubitril (AHU377) – a pro-drug; further metabolized to the neprilysin inhibitor LBQ657, and
  - valsartan – an $AT_1$ receptor blocker

  in a 1:1 molar ratio

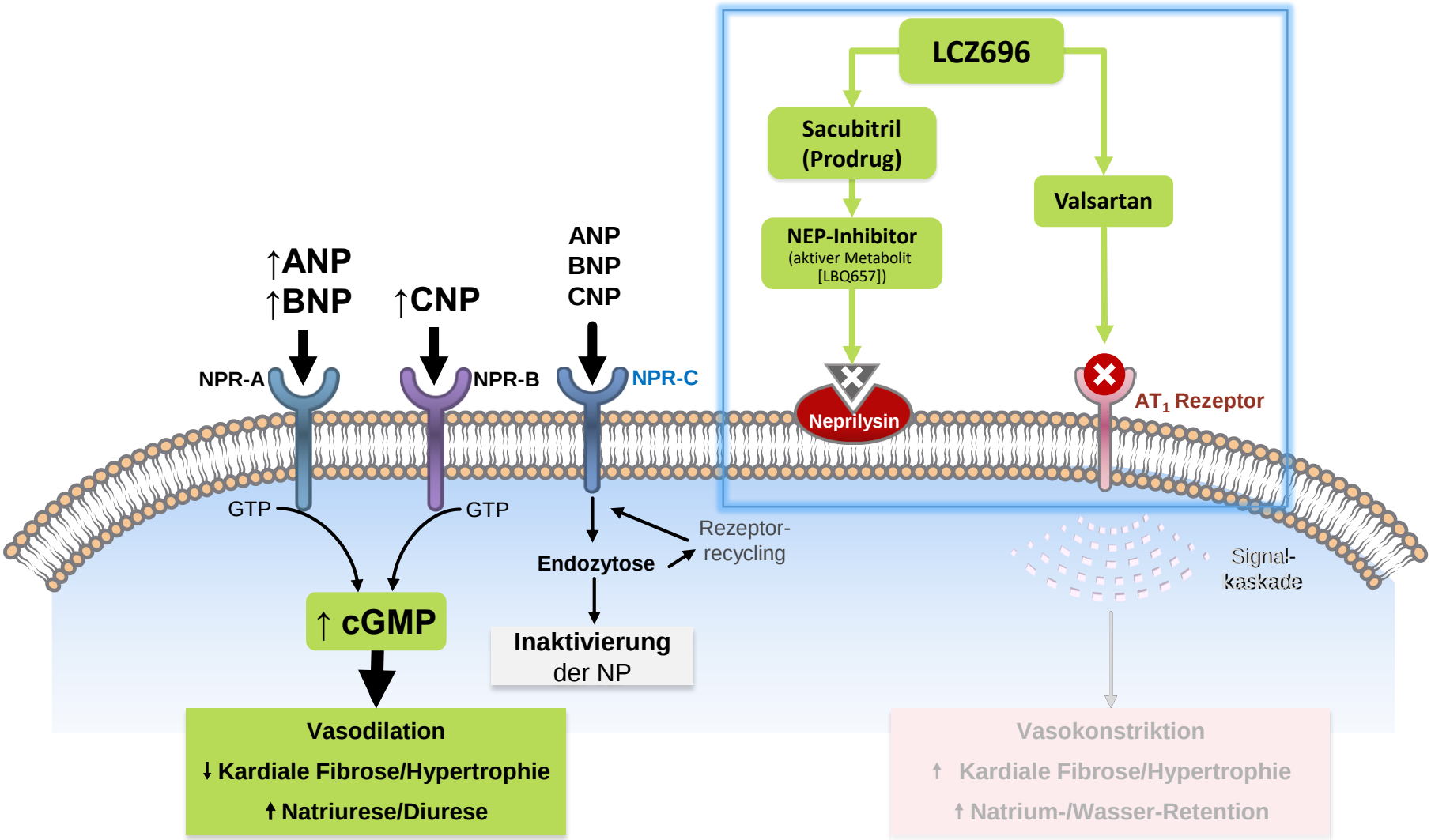


*3D LCZ696 structure*[2]



1. Bloch, Basile. J Clin Hypertens 2010;12:809–12; 2. Gu et al. J Clin Pharmacol 2010;50:401–14; 3. Langenickel & Dole. Drug Discov Today Ther Strateg 2012;9:e131–9

# LCZ696 verstärkt die vorteilhaften Effekte des NP Systems und hemmt gleichzeitig nachteilige Effekte des RAAS




# PARADIGM-HF Study

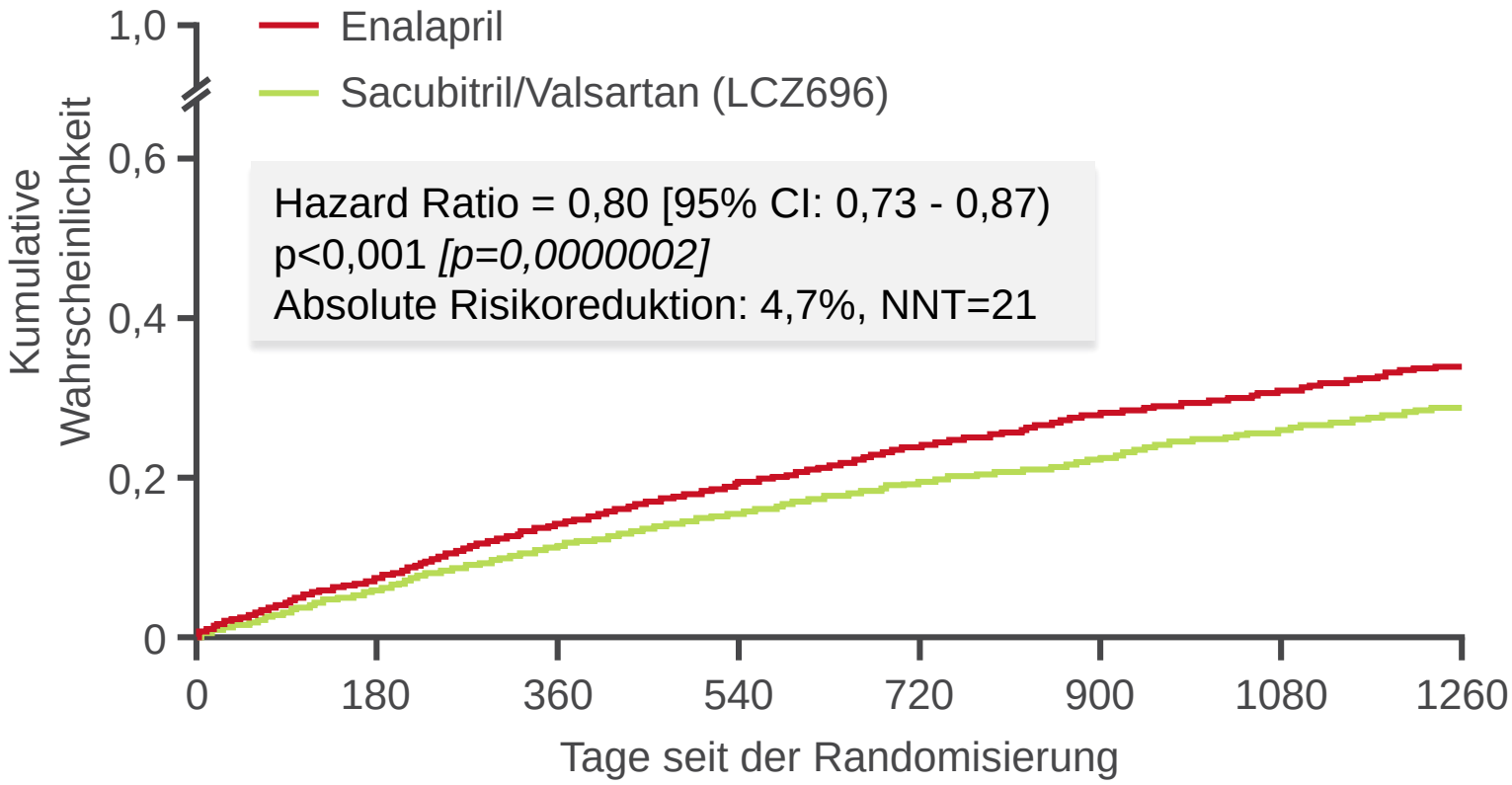
## Prospective comparison of ARNI with ACEI to Determine Impact on Global Mortality and morbidity in Heart Failure

A multicenter, randomized, double-blind, parallel-group, active-controlled study to evaluate the efficacy and safety of LCZ696 compared with enalapril on morbidity and mortality in patients with chronic HF and reduced ejection fraction

August 2014/GMCC_NP4 request 275741/expiry August 2015

Prof. C. Tschöpe; Charite, Kardiologie Berlin

# Primärer Endpunkt: CV-bedingter Tod oder erste Hospitalisierung wg. Herzinsuffizienz



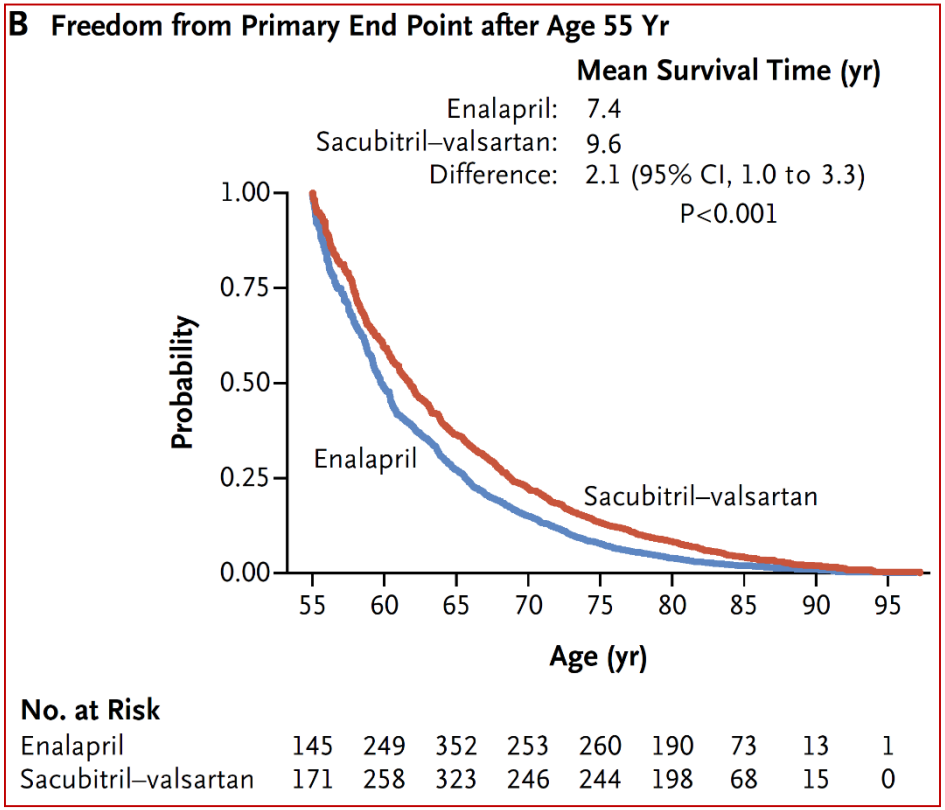

| Anz. mit Risiko | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Sacubitril-Vals. | 4.187 | 3.922 | 3.663 | 3.018 | 2.257 | 1.544 | 896 | 249 |
| Enalapril | 4.212 | 3.883 | 3.579 | 2.922 | 2.123 | 1.488 | 853 | 236 |

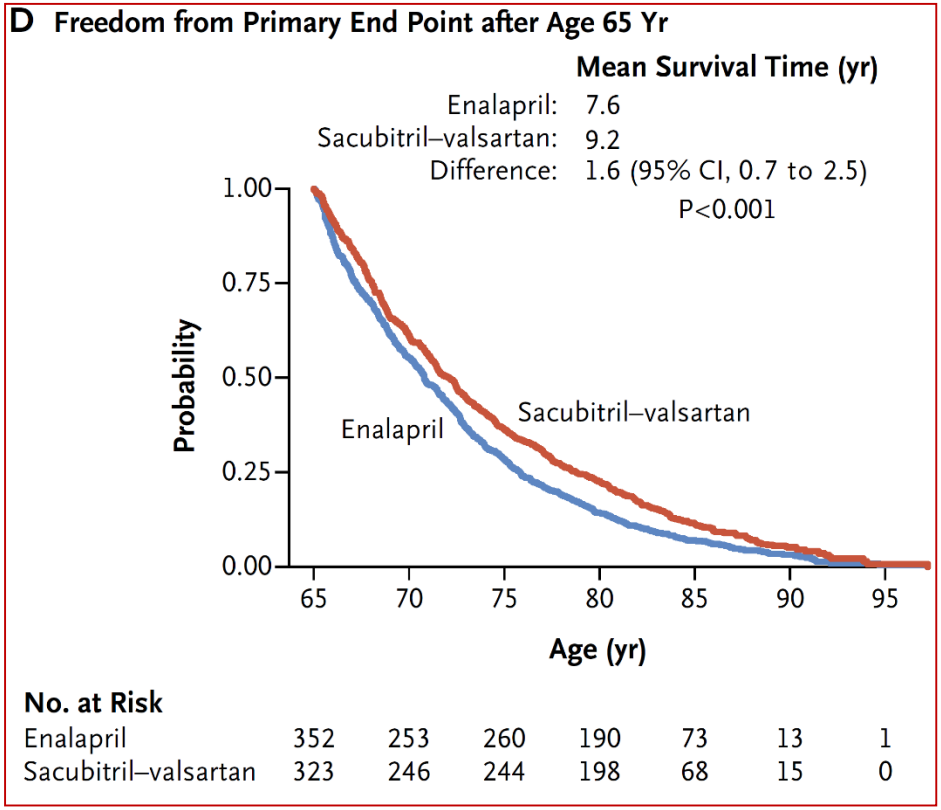


McMurray et al. N Engl J Med 2014;371(11):993-1004.

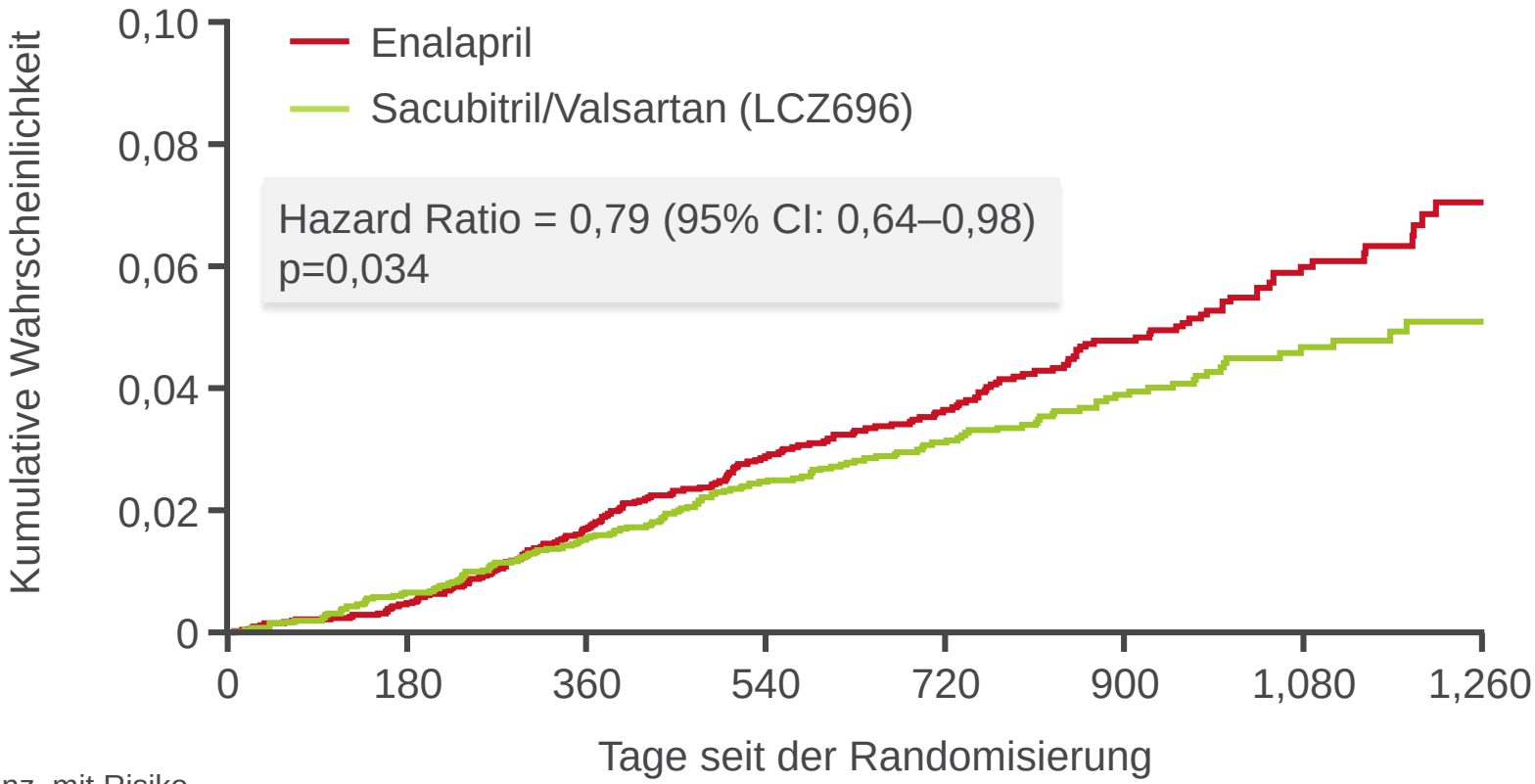
# Lebenverlängerung: 1.5-2 Jahre

*Claggett et al., NEJM 2015; 373: 2289*



# „Mode of Death“ - Herzinsuffizienzverschlechterung



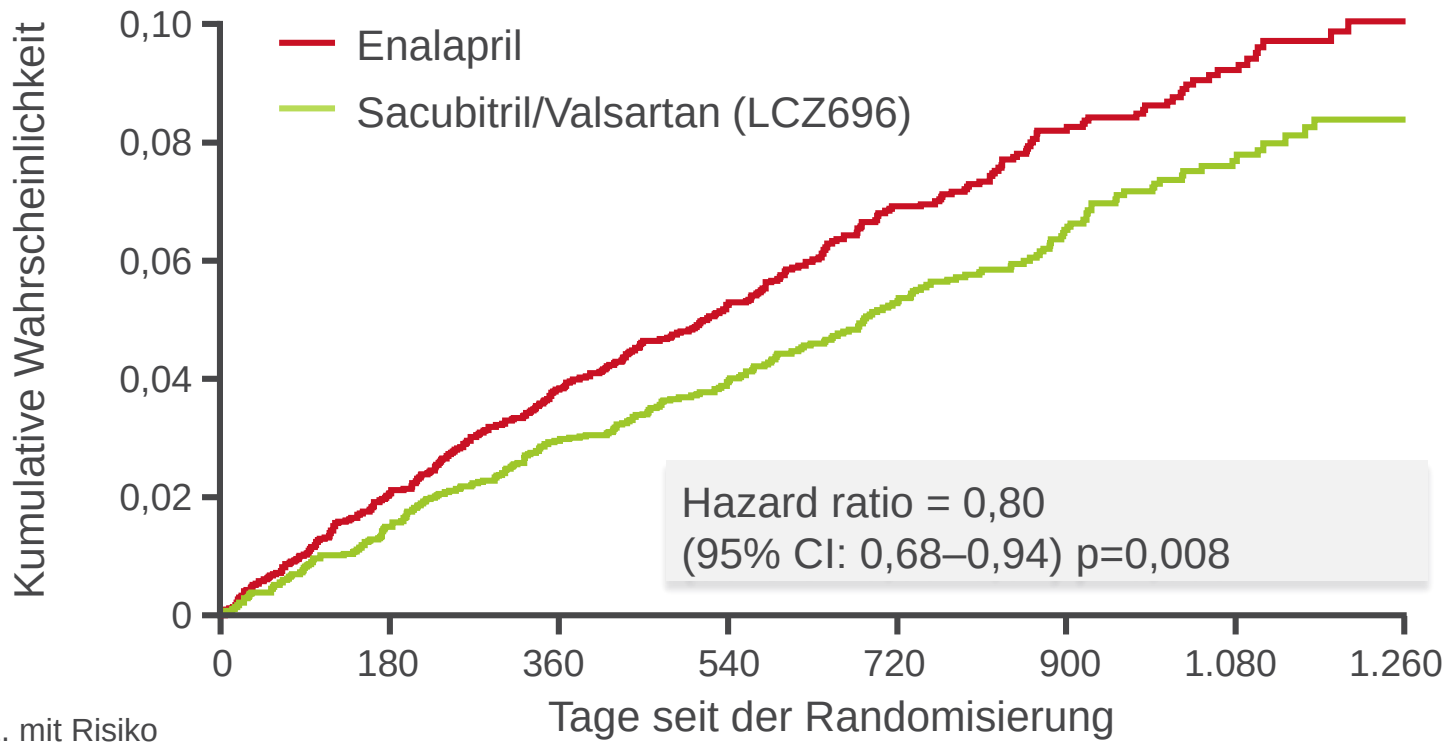

| Anz. mit Risiko | | | | |
|---|---|---|---|---|
| Sacubitril/Vals. | 4.187 | 3.891 | 2.478 | 1.005 |
| Enalapril | 4.212 | 3.860 | 2.410 | 994 |



CI=confidence interval

Desai et al. Eur Heart J 2015;36(30):1990-7

# „Mode of Death“ – Plötzlicher Herztod



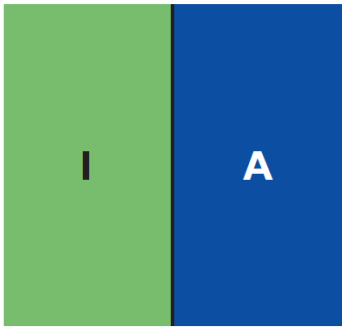

| Anz. mit Risiko | | | | |
|---|---|---|---|---|
| Sacubitril/Vals. | 4.187 | 3.891 | 2.478 | 1.005 |
| Enalapril | 4.212 | 3.860 | 2.410 | 994 |



Desai et al. Eur Heart J 2015;36(30):1990-7;
Data on file, Clinical Study Protocol CLCZ696B2314

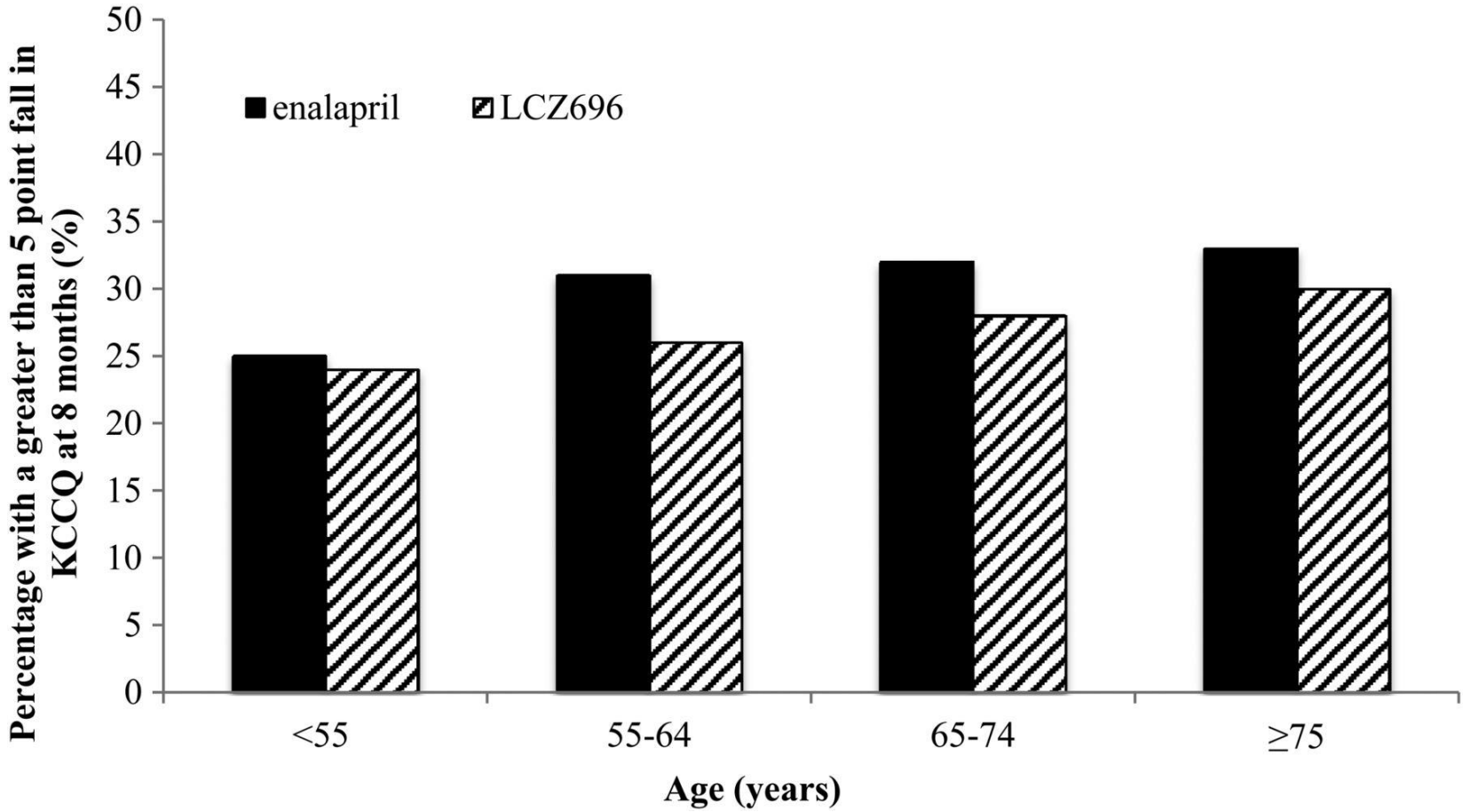
# VT and CHF

- **Treatment with beta-blocker, MRA and sacubitril/valsartan reduces the risk of sudden death and is recommended for patients with HFrEF and ventricular arrhythmias (as for other patients).**



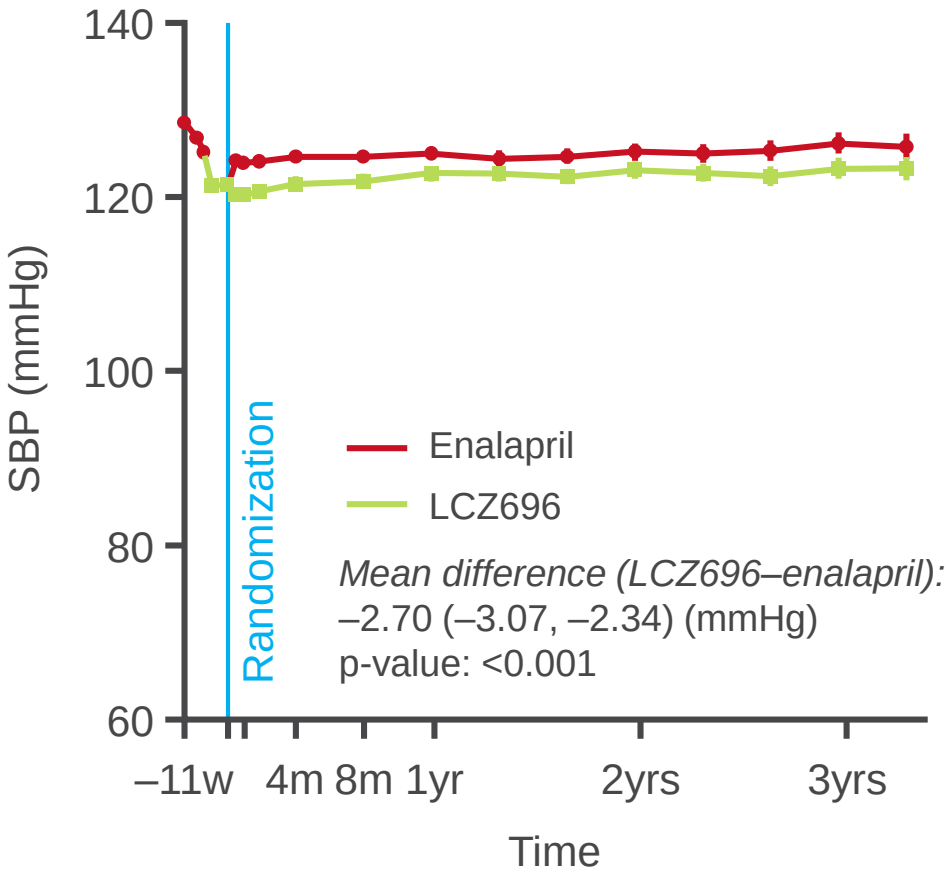

**2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure**

**Proportion of patients with a five-point or greater fall (deterioration) in Kansas City Cardiomyopathy Questionnaire at 8 months by age category and treatment.**




Pardeep S. Jhund et al. Eur Heart J 2015;36:2576-2584

# Systolischer Blutdruck vor und nach Randomisierung




- Compared with the randomization level, the mean SBP at 8 months was 3.2 ± 0.4 mmHg lower in the LCZ696 group than in the enalapril group (p<0.001)
- When modeled as a time-dependent covariate, the difference in BP was not a determinant of the incremental benefits of LCZ696



McMurray, et al. N Engl J Med 2014; ePub ahead of print; DOI: 10.1056/NEJMoa1409077. (Supplementary appendix)

# Umsetzung

## Mögliches Problem?

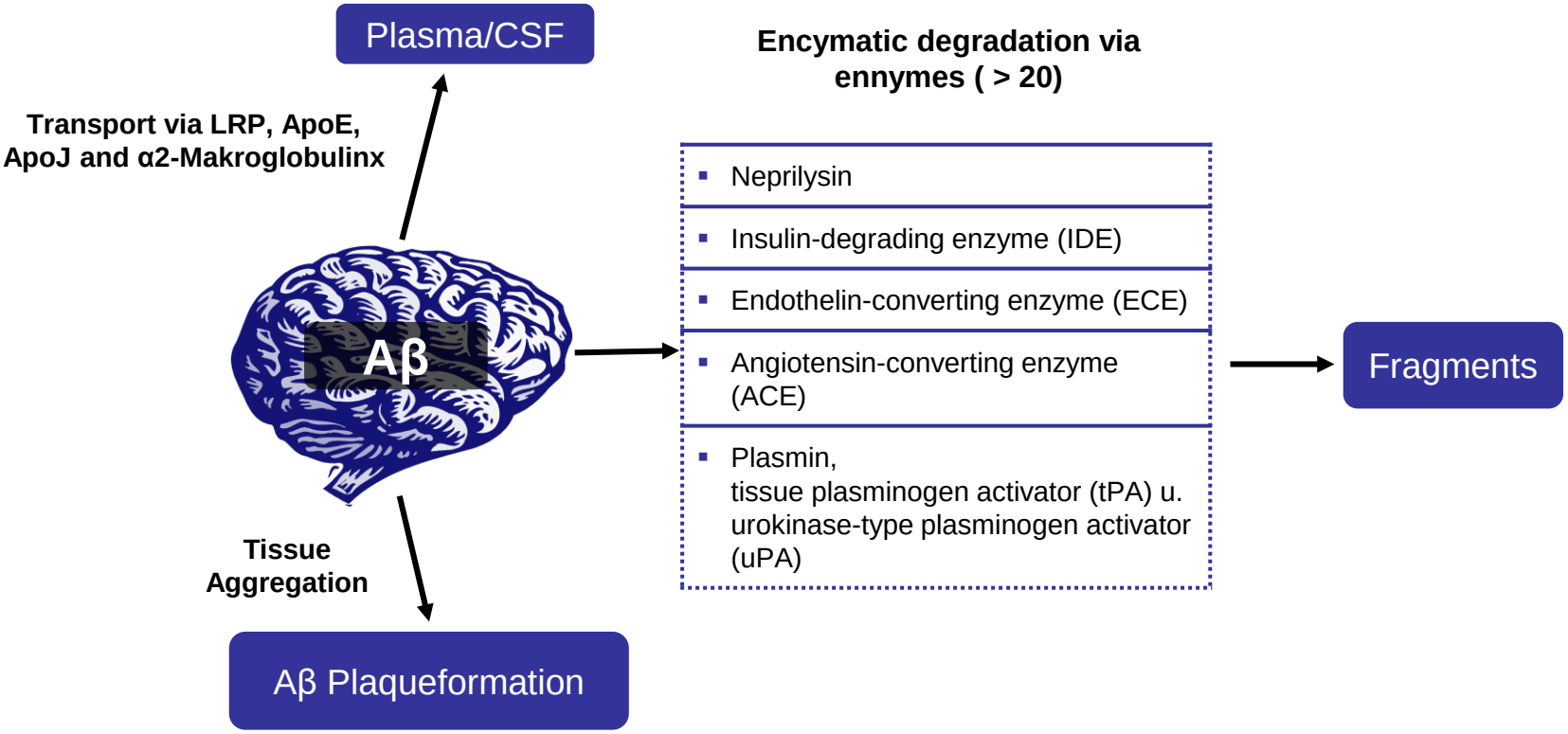
## Zunahme von M. Alzheimer

***-> Neurologische Gesellschaft warnt***



McMurray, et al. N Engl J Med 2014; ePub ahead of print: DOI: 10.1056/NEJMoa1409077.

# β Amyloid Metabolism




Aβ=Amyloid-β; ApoE=Apolipoprotein E; ApoJ=Apolipoprotein J; CSF=Cerebrospinal fluid; LRP=Low density lipoprotein receptor-related protein.





Wang et al. J Biomed Biotechnol 2006;58406

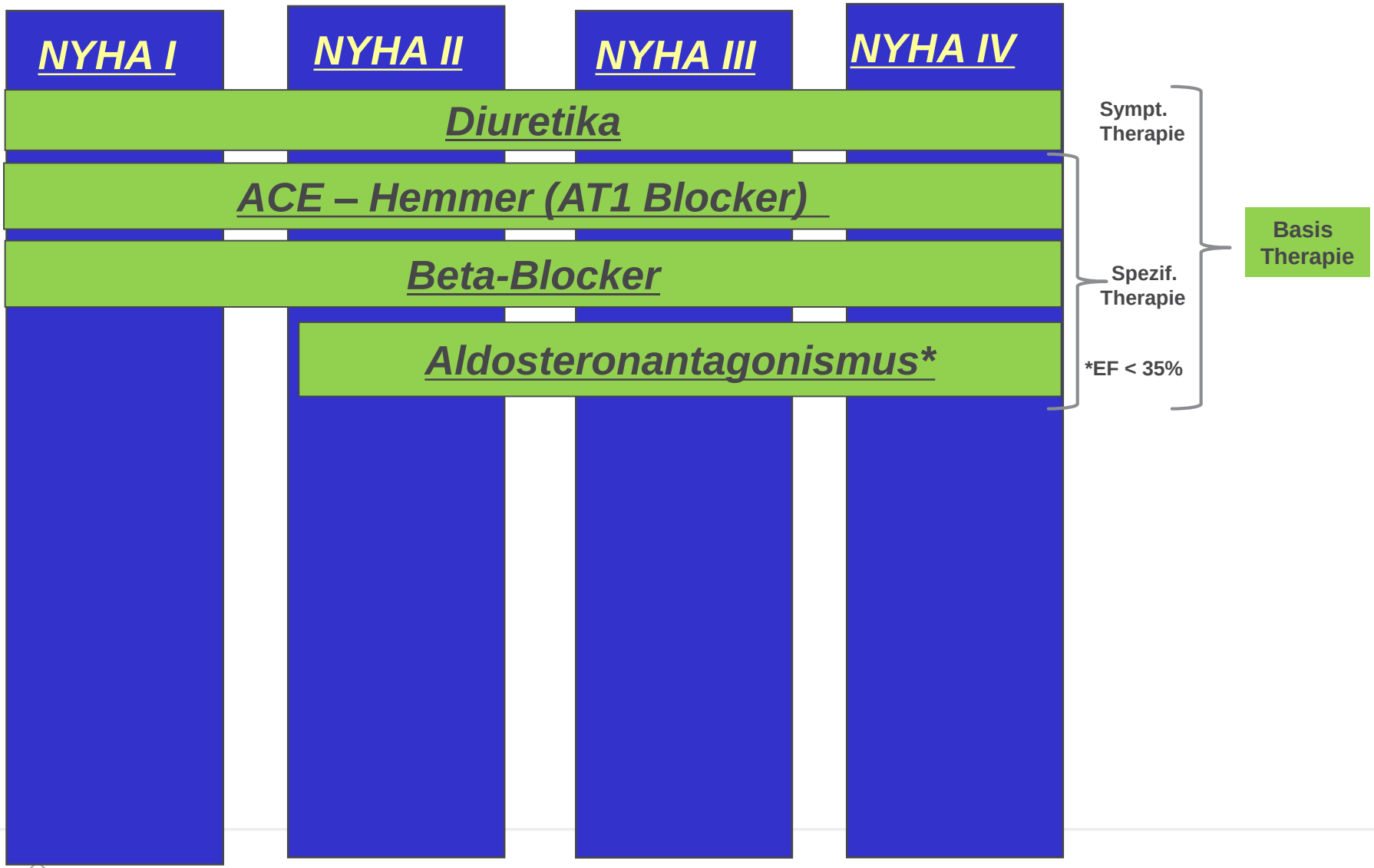
# PARADIGM-HF: LCZ696 was not associated with a increase in dementia-related AEs (narrow SMQs) compared with enalapril

| Dementia-related AE | LCZ696 n=4,203 | Enalapril n=4,229 | Hazard ratio (95% CI) |
|---|---|---|---|
| ***Narrow search terms for SMQ dementia*** | | | |
| Total, n (%) | **12 (0.29)** | **15 (0.35)** | **0.79 (0.37–1.70)** |
| Dementia | 6 (0.14) | 10 (0.24) | |
| Dementia Alzheimer's type | 2 (0.05) | 2 (0.05) | |
| Vascular dementia | 2 (0.05) | 1 (0.02) | |
| Hippocampal sclerosis | 1 (0.02) | 0 (0.00) | |
| Presenile dementia | 1 (0.02) | 0 (0.00) | |
| Senile dementia | 0 (0.00) | 2 (0.05) | |

AE=adverse event; CI=confidence interval;
PARADIGM-HF=Prospective comparison of ARNI with ACEI to Determine Impact on Global Mortality and morbidity in Heart Failure;
SMQ=standardized MedRA query

Cannon et al. Eur J Heart Fail 2015;17(Suppl 1):49–50 (Abstract P242 and poster)

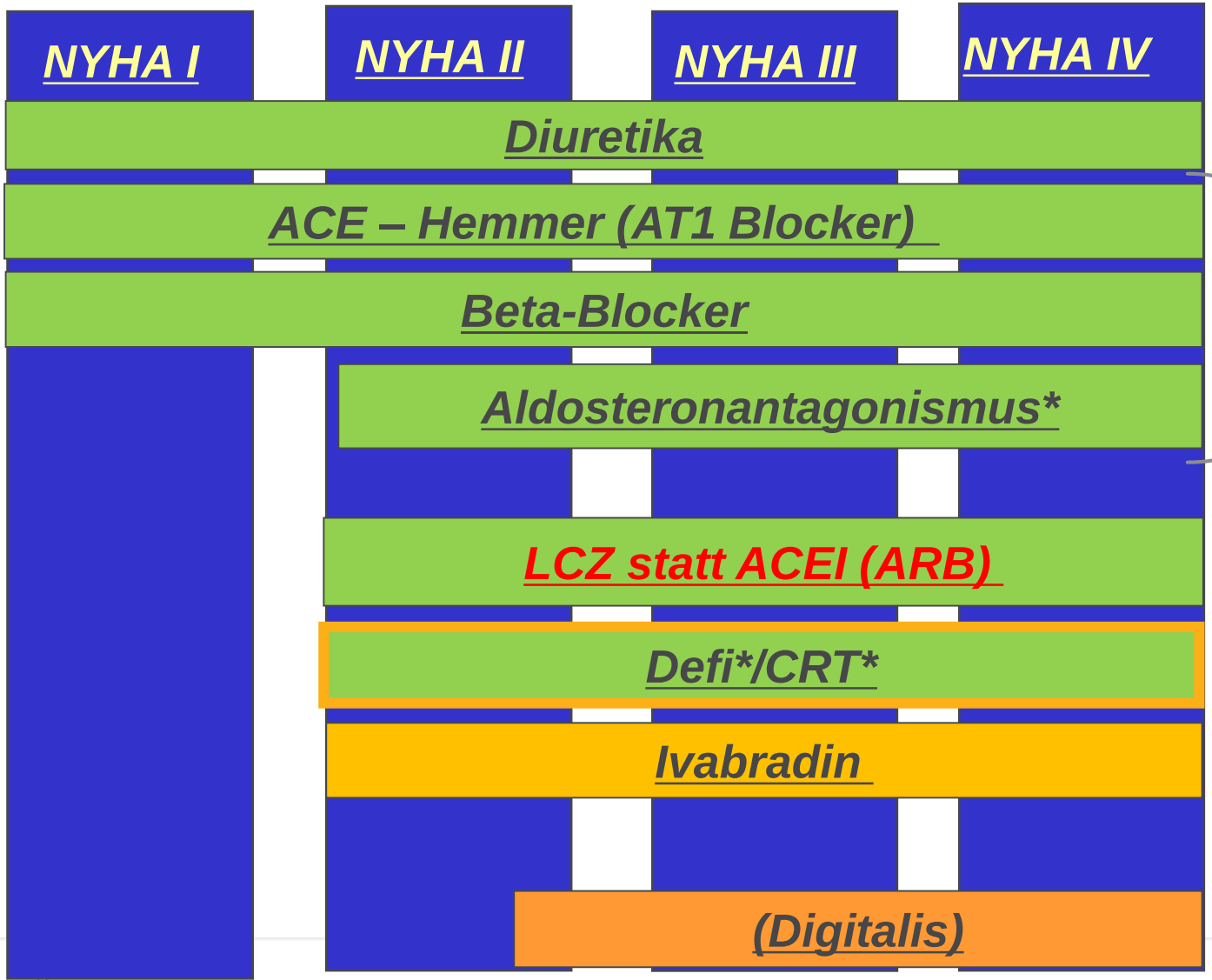
# Stadiengerechte Basistherapie 2017






Prof. C. Tschöpe; Charite, Kardiologie Berlin

# Stadiengerechte Basistherapie 2017






Prof. C. Tschöpe; Charite, Kardiologie Berlin

# Zusammenfassung

- **Prognose der CHF ist sehr schlecht**

- **Standard Therapie: ACE-I/ARBs, BBs, MRA, IVA und Devices; Prognose weiterhin schlecht**

- **CRT: 1a Indikation bei LSB /QRS > 150ms**

**Sacubitril/Valsartan: 1b Indikation, EF < 35% und Symptomatik (NYHA II !) trotz Standardtherapie nach Absetzten von ACEI/ARB**