הטיפול האופטימלי לאי ספיקת לב:
שיפור איכות החיים כמדד פרוגנוסטי

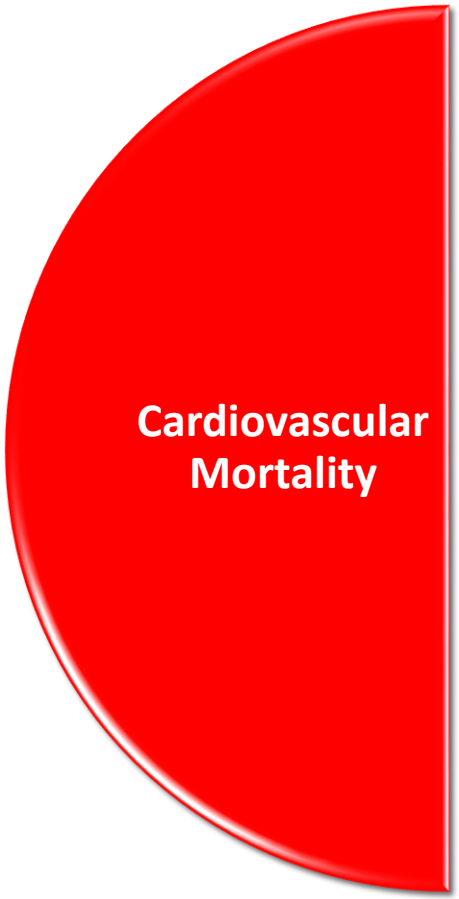
ד"ר אבישי גרופר
אחראי תחום אי ספיקת לב מתקדמת
המכון לאי ספיקת לב
מרכז הלב ע"ש לבייב, שיבא, תל השומר

ההרצאה בחסות

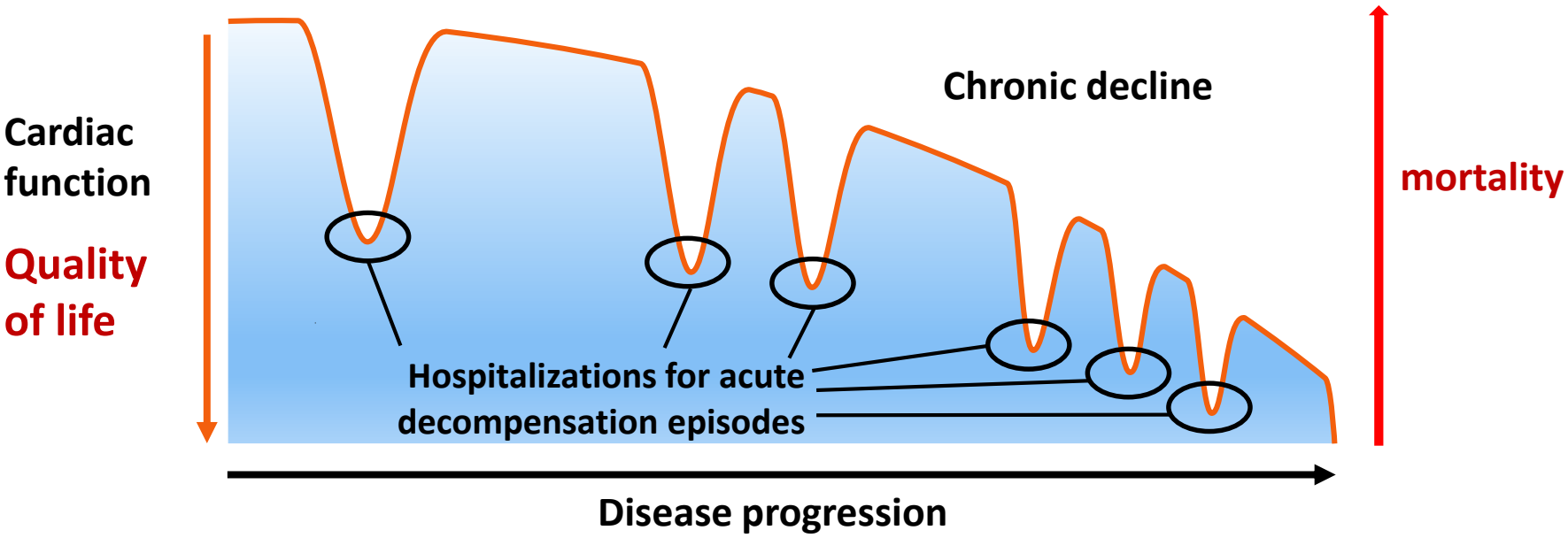
NOVARTIS

הכנס השנתי של החוג לשיקום חולי הלב 2019

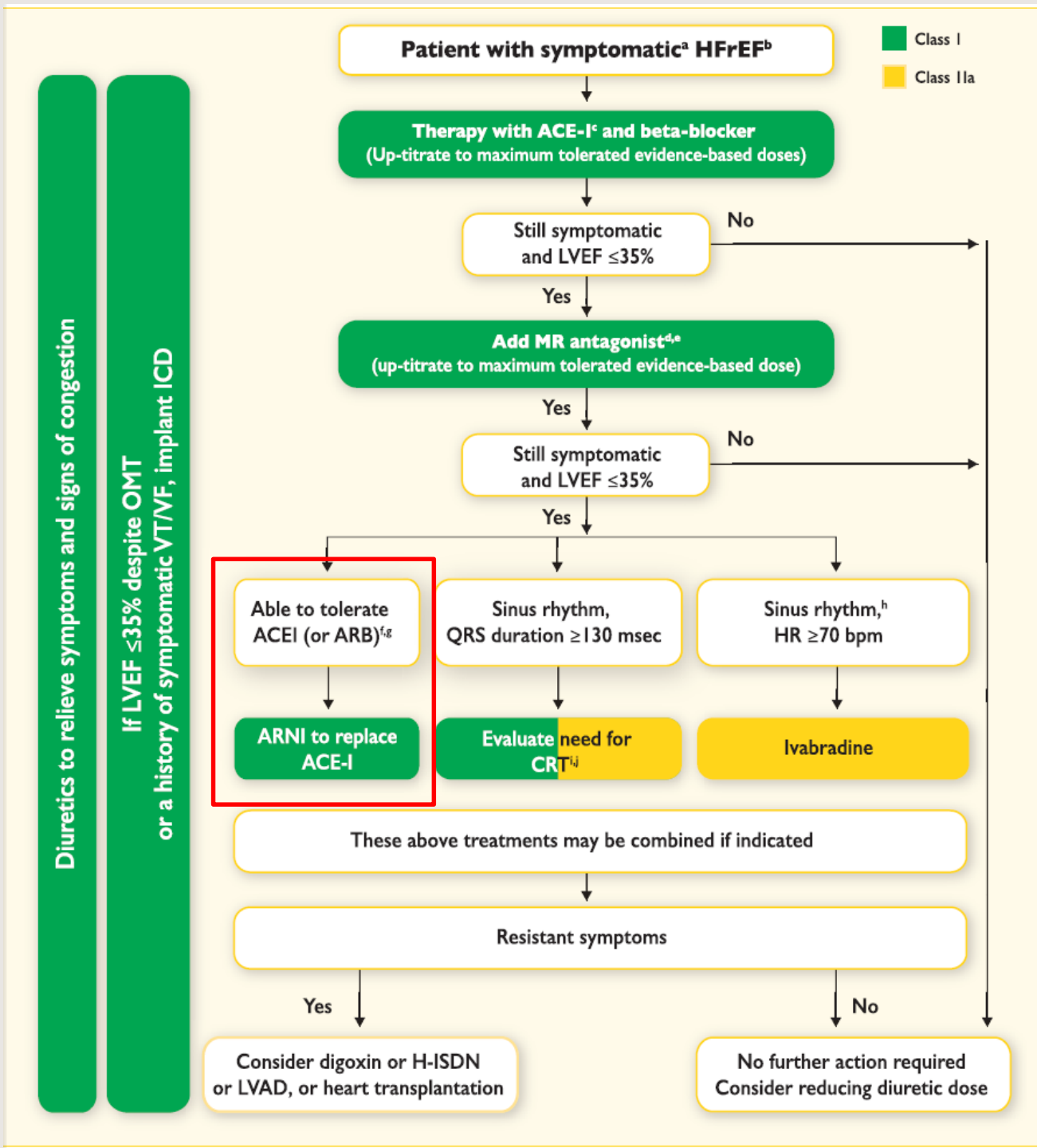
Heart Failure Treatment Goals



HF is a chronic condition interspersed with acute episodes

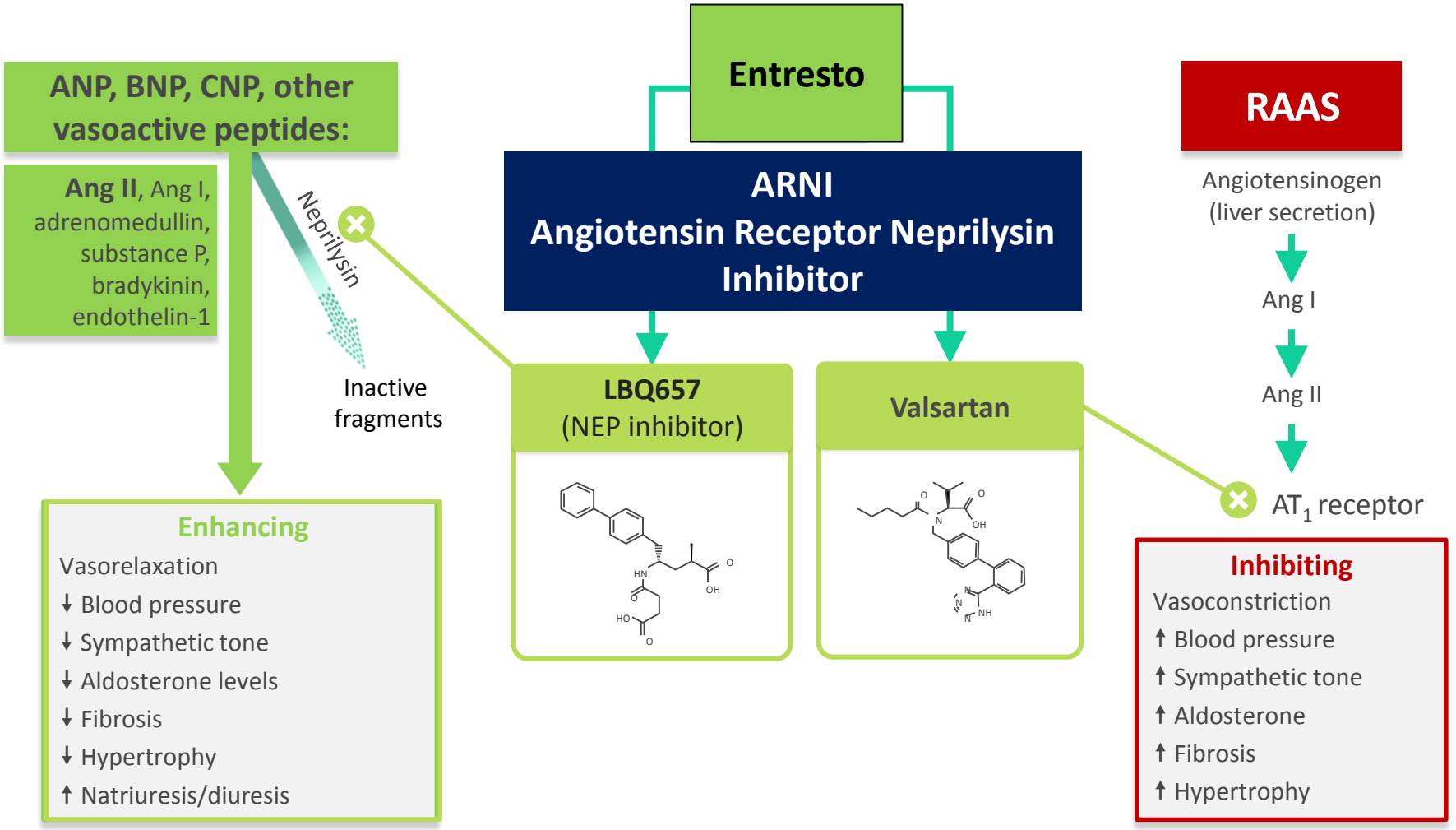


Therapeutic algorithm for a patient with symptomatic heart failure with reduced ejection fraction

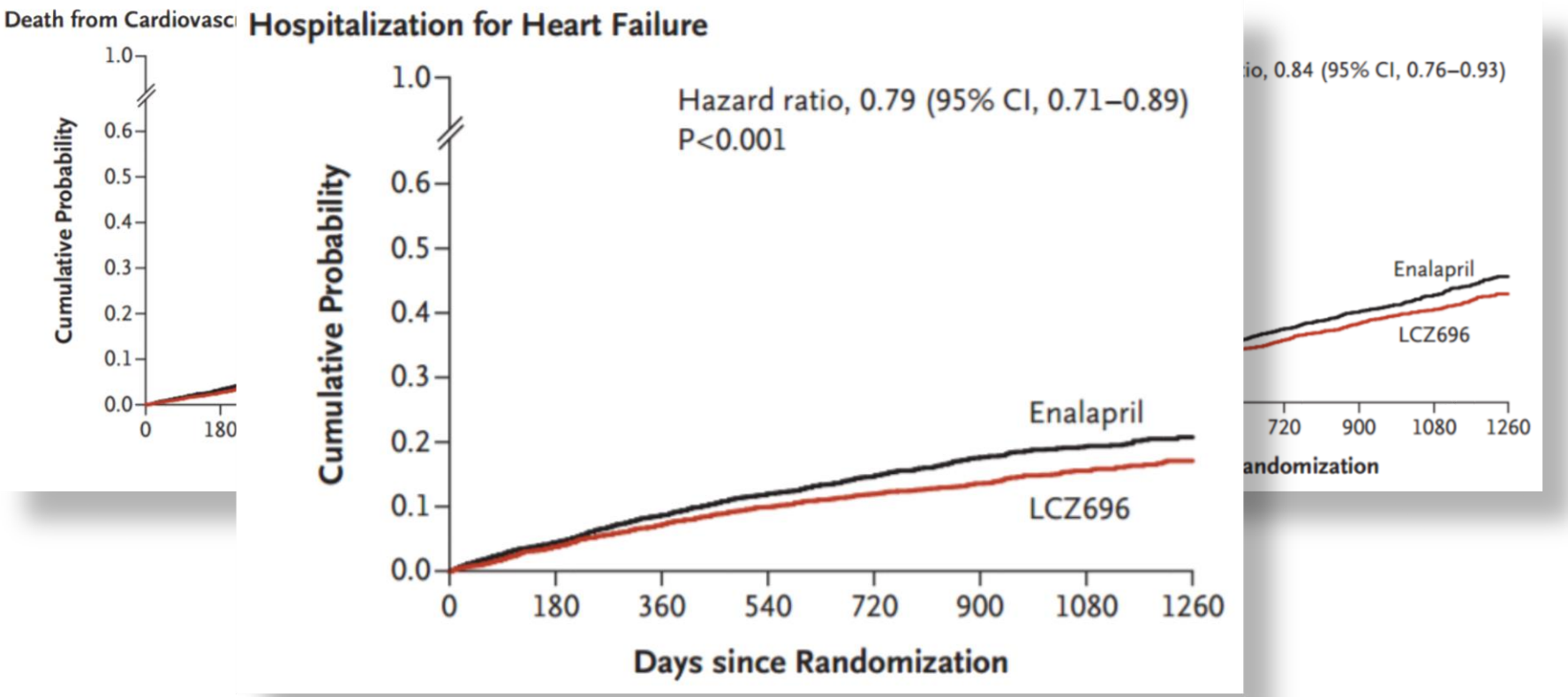


2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure,

Entresto simultaneously inhibits neprilysin (via sacubitril) and blocks AT_1 receptors (via valsartan)

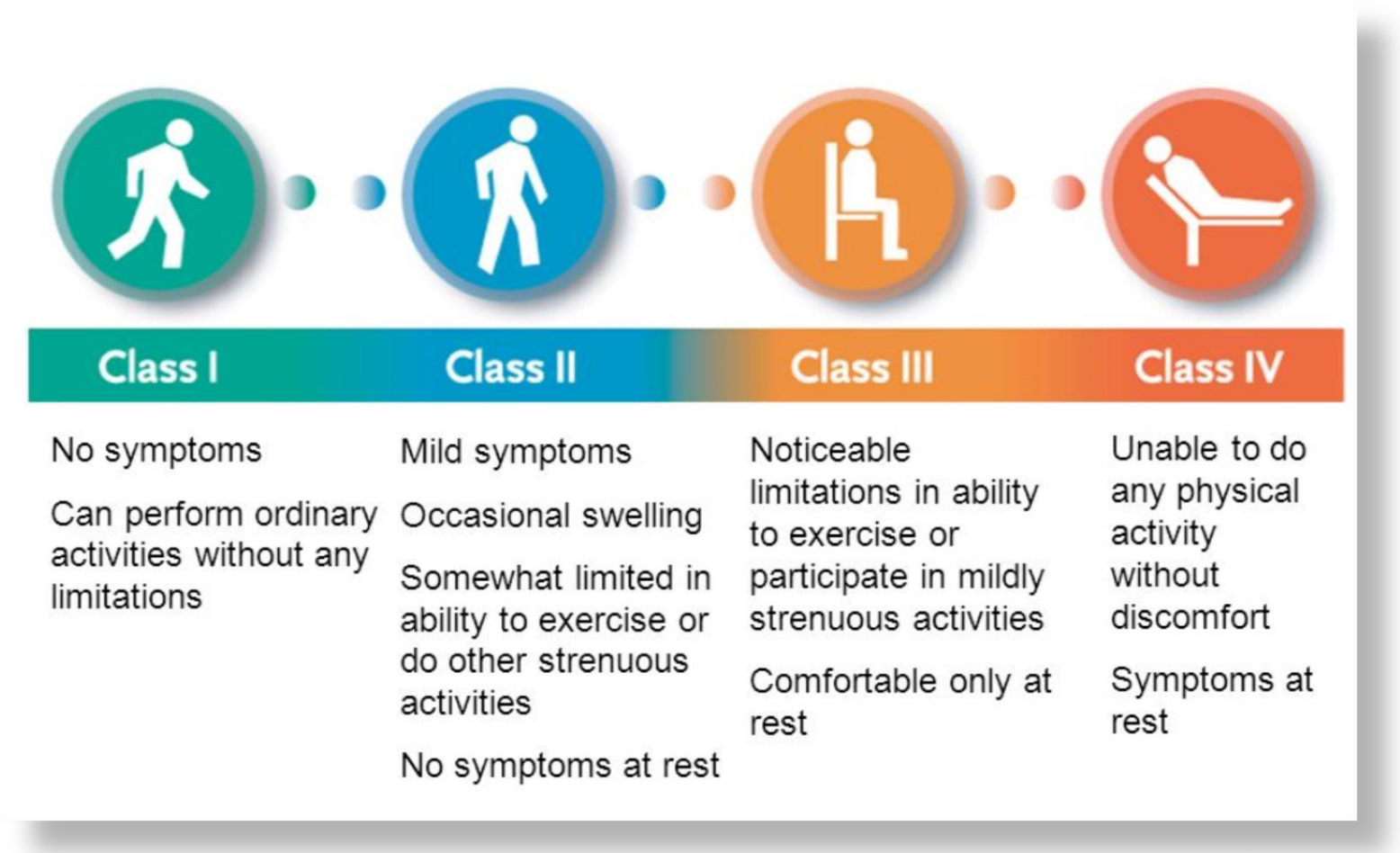


PARADIGM-HF: study outcomes



McMurray et al. NEJM 2014; 371:993–1004

New York Heart Association (NYHA) Class



PARADIGM-HF

Of the 8399 patients randomized in the PARADIGM-HF study, 3125 (37%) had no prior HF hospitalization.

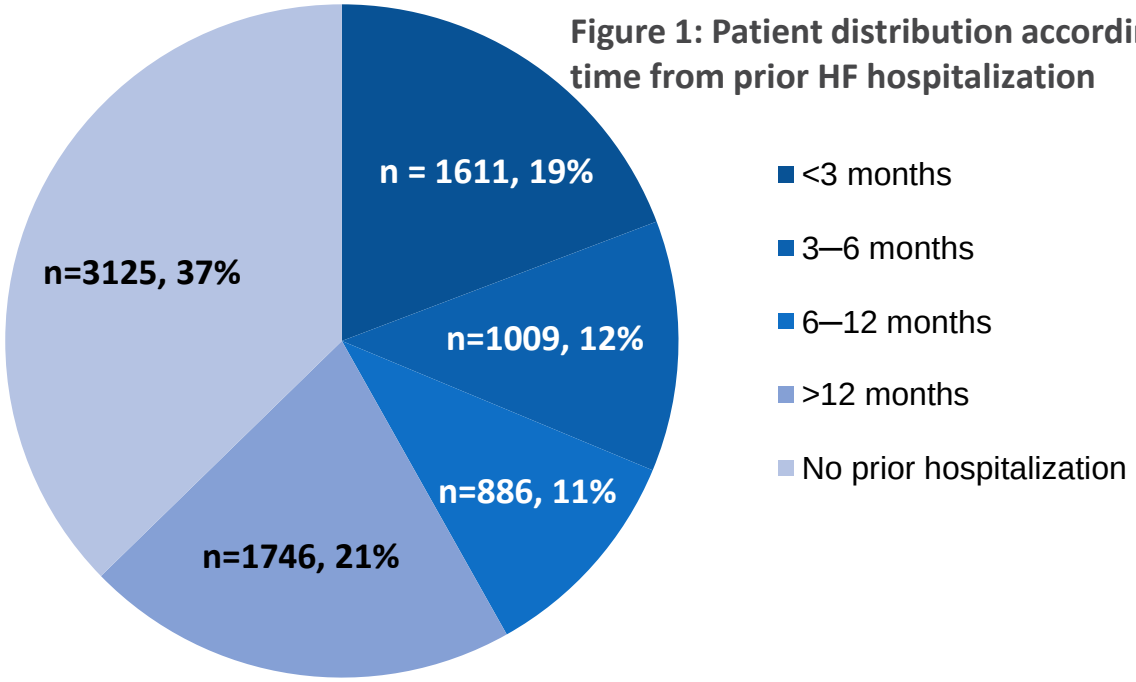
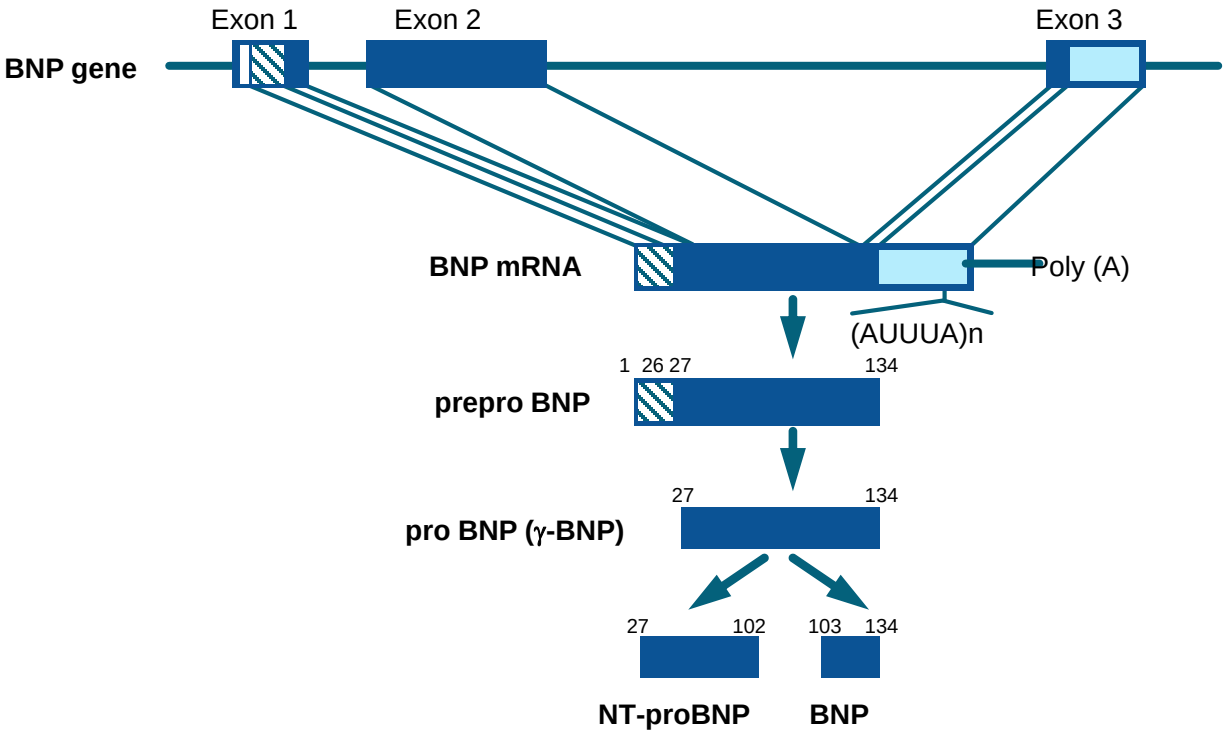


Figure 1: Patient distribution according to time from prior HF hospitalization

Solomon et al. JACC Heart Failure. 2016

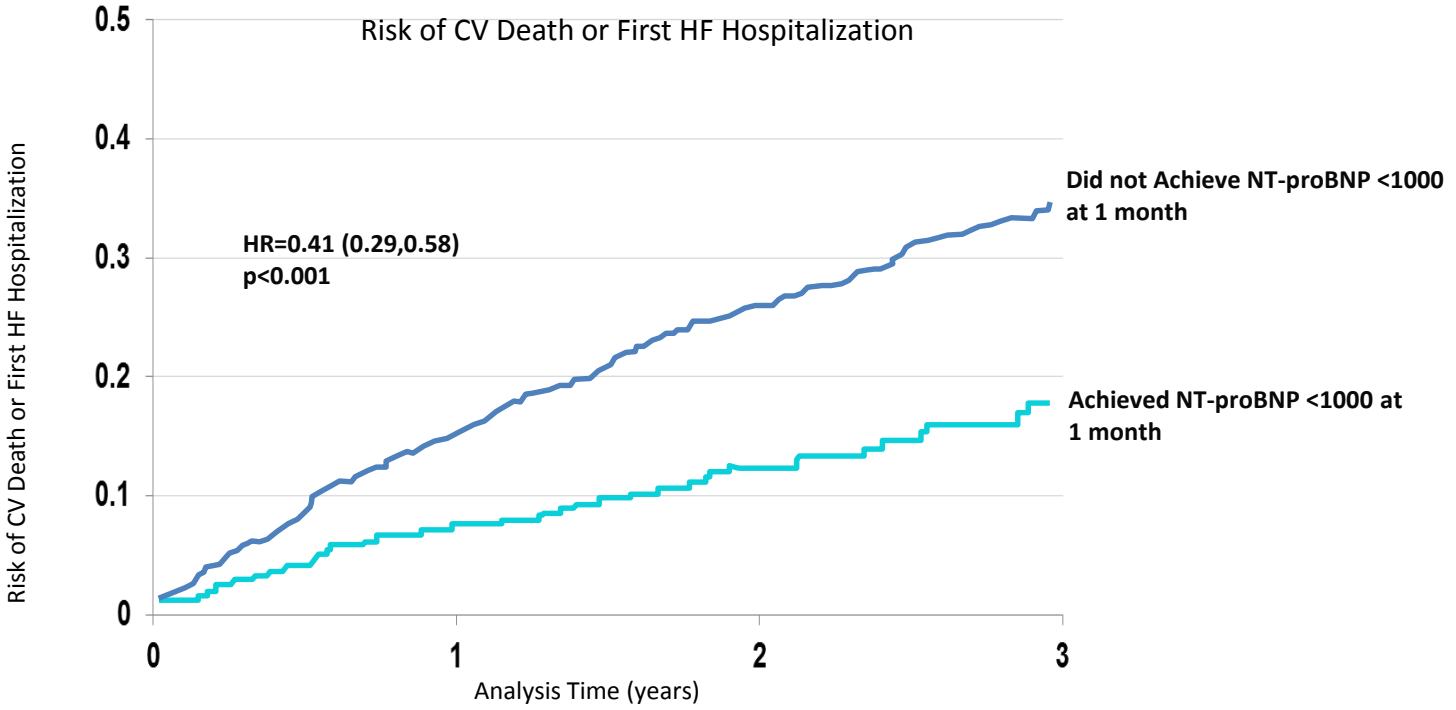
BNP and NT-proBNP are formed by cleavage of precursor molecules



Nishikimi et al. J Cardiol 2011;57:131–140

Relationship of NT-proBNP and Cardiovascular Events

Reduction in NT-proBNP Following HF Treatment is Associated with Reduction in CV Death and HF Hospitalization



Achieving levels of NT-proBNP <1000 as early as 1 month after randomization to HF therapy was associated with a significant reduction in risk of CV death or first HF hospitalization

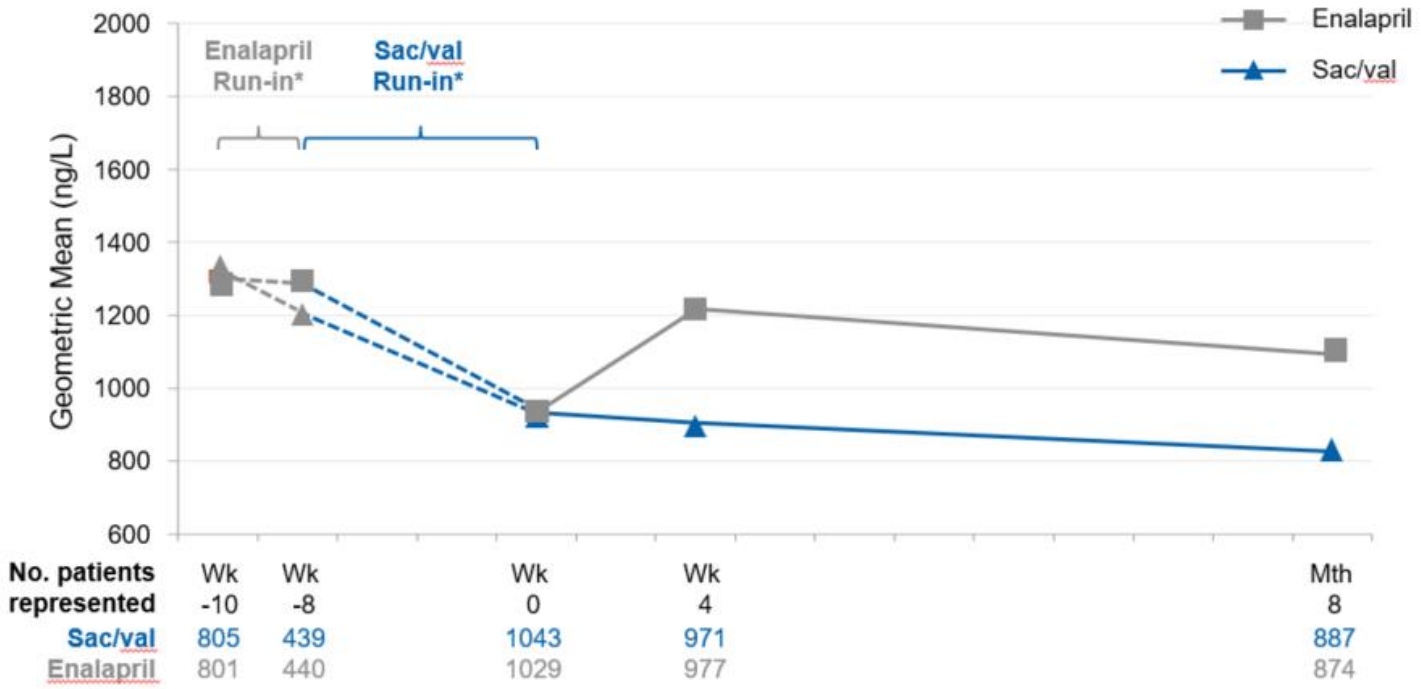
This was a post hoc analysis of PARADIGM-HF Study. Analytic variability (imprecision of the test) and biological variability (expected variability within the subject over time) may influence the accuracy of a predictive value of a change in biomarkers. The change from baseline data should therefore be interpreted in light of the influence of the biological variability known to be present in HFrEF patients.

NT-proBNP N-terminal pro–brain natriuretic peptide. HF, Heart Failure. CV, Cardiovascular

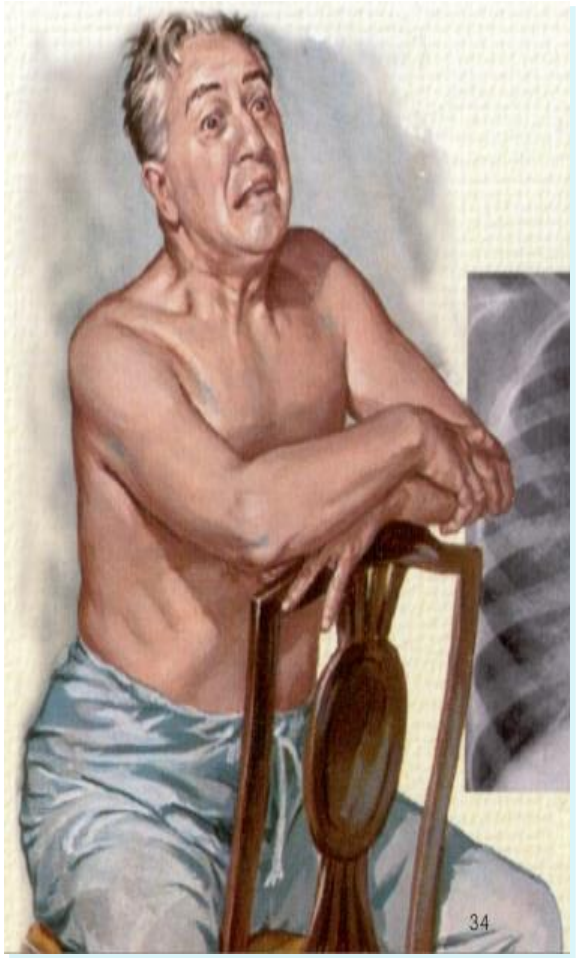
Zile MR, et al. J Am Coll Cardiol. 2016;68(22):2425–2436.

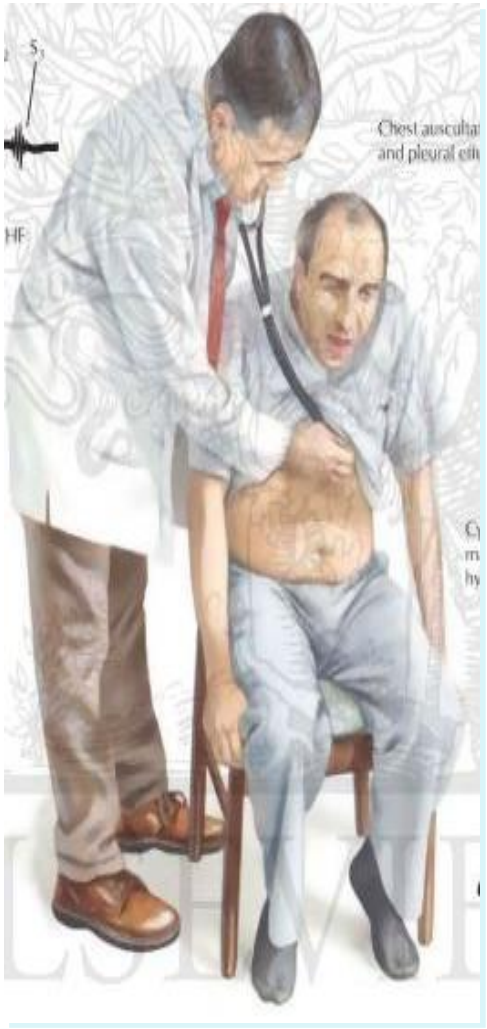
PARADIGM-HF

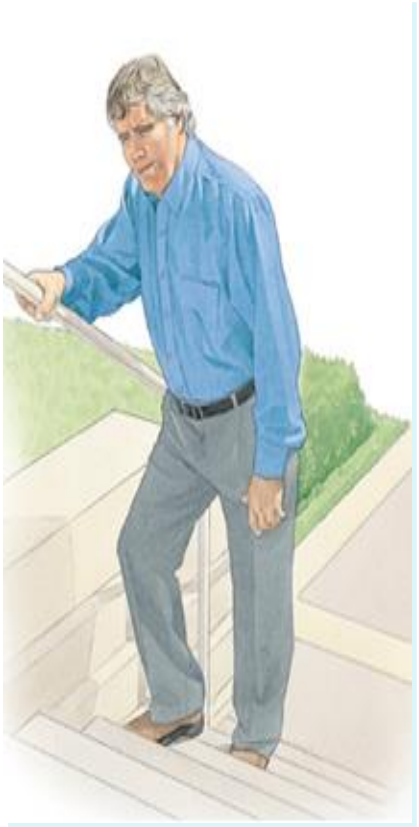
Effects of Sacubitril/Valsartan or Enalapril on NT-proBNP in Patients with HFrEF



This was an exploratory endpoint of the PARADIGM-HF trial, measured in a subset of the overall trial population
NT-proBNP N-terminal pro–brain natriuretic peptide
Patients in both groups received the same single-blind treatment
Packer M, et al. *Circulation.* 2015;131:54–61
Data on File, PARADIGM-HF Clinical Study Report, Novartis Pharmaceuticals Corp; October 2014

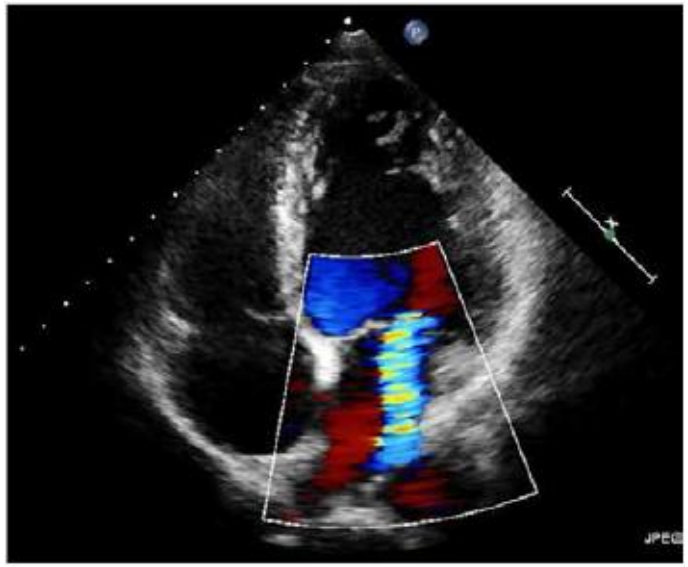

34


Chest auscultat
and pleural eff

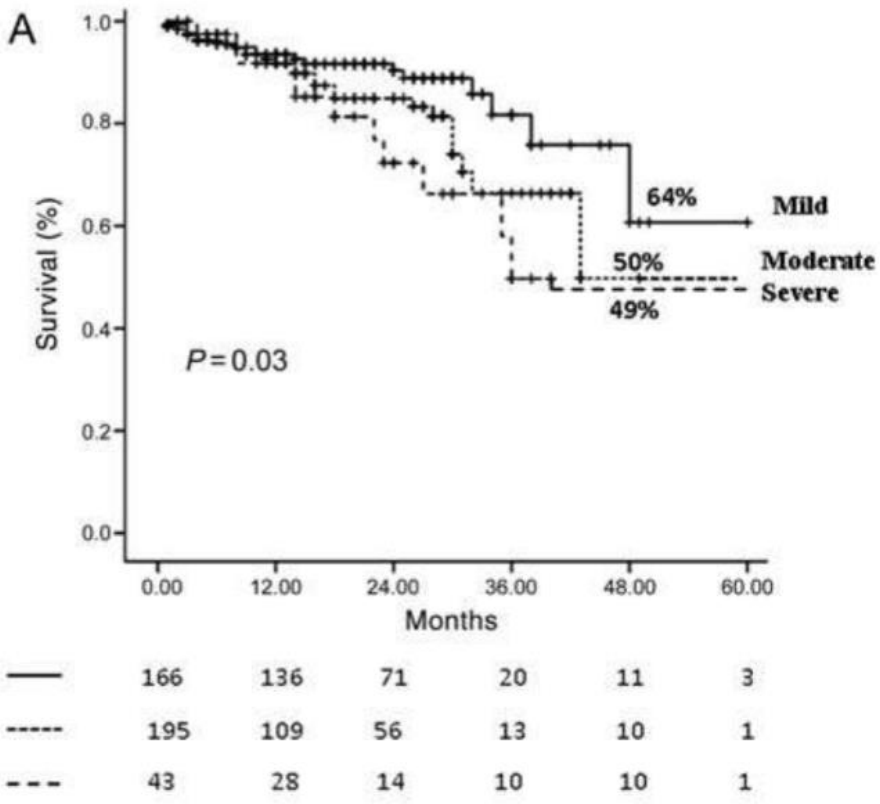


סימנים להחמרה באי ספיקת לב

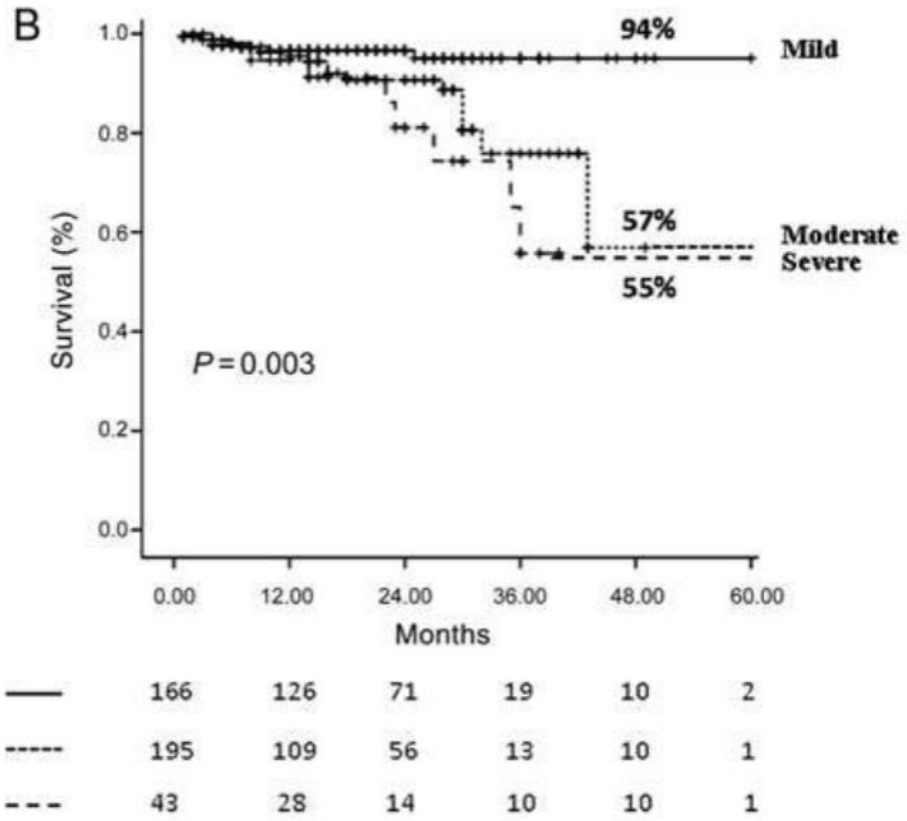
Mitral regurgitation



Survival free of **all-cause mortality** according to functional MR



Survival free of **cardiac death** according to functional MR



Agricola E, Ielasi A, Oppizzi M, Faggiano P, Ferri L, Calabrese A, Vizzardi E, Alfieri O, Margonato A. Long-term prognosis of medically treated patients with functional mitral regurgitation and left ventricular dysfunction. Eur J Heart Fail. 2009;11:581-587.

Circulation

ORIGINAL RESEARCH ARTICLE

Angiotensin Receptor Neprilysin Inhibitor for Functional Mitral Regurgitation

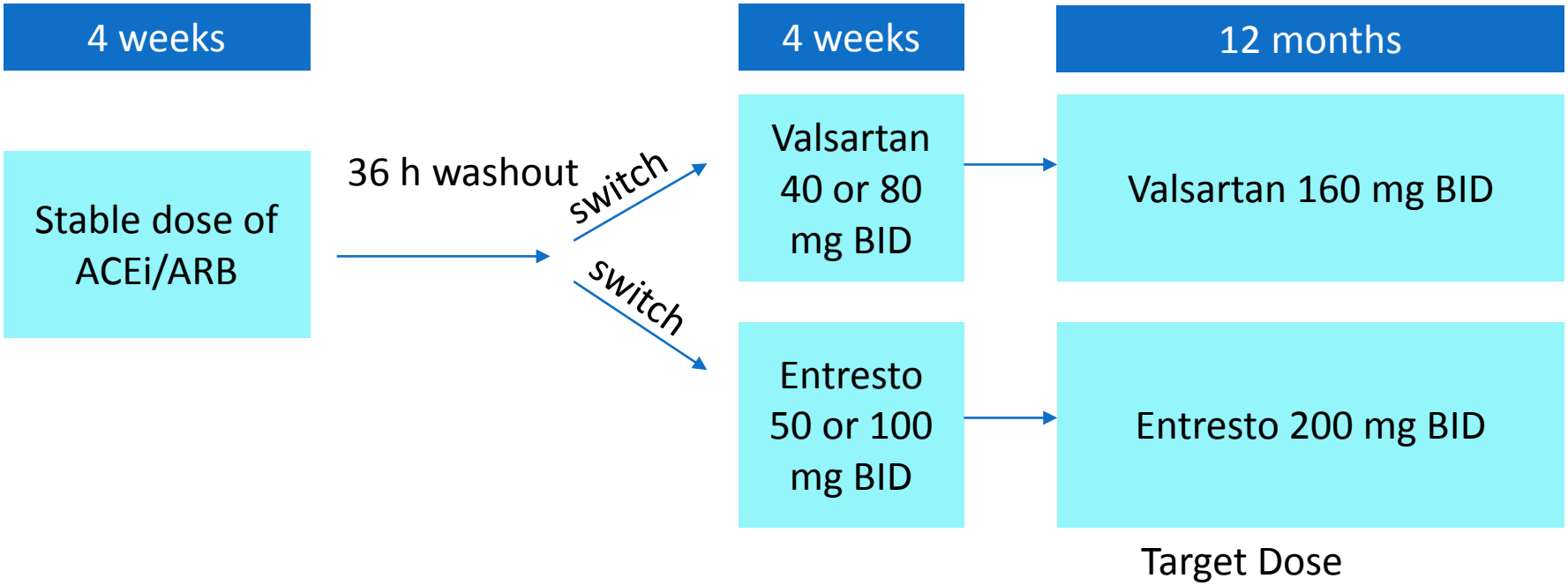
PRIME Study

Kang DH et al. *Circulation.* 2019;139:1354–1365.

Inclusion criteria:

- Age ≥ 20
- **Stable HF**, NYHA II-III
- **LVEF 25-50%**
- Significant functional MR ≥ 6 month:
  - Normal mitral valve leaflets and chords
  - Regional/global wall motion abnormalities if LV+ tethering of leaflet.
  - EROA > 0.1 cm^2 > 6 month , despite medical treatment with beta blockers + ACEi/ARB.
- On stable optimal dose of beta blockers and ACEi/ARB at least 4 weeks.

Study design



❑**Primary end point**:

Change in EROA of functional MR from baseline to 12 months follow-up.

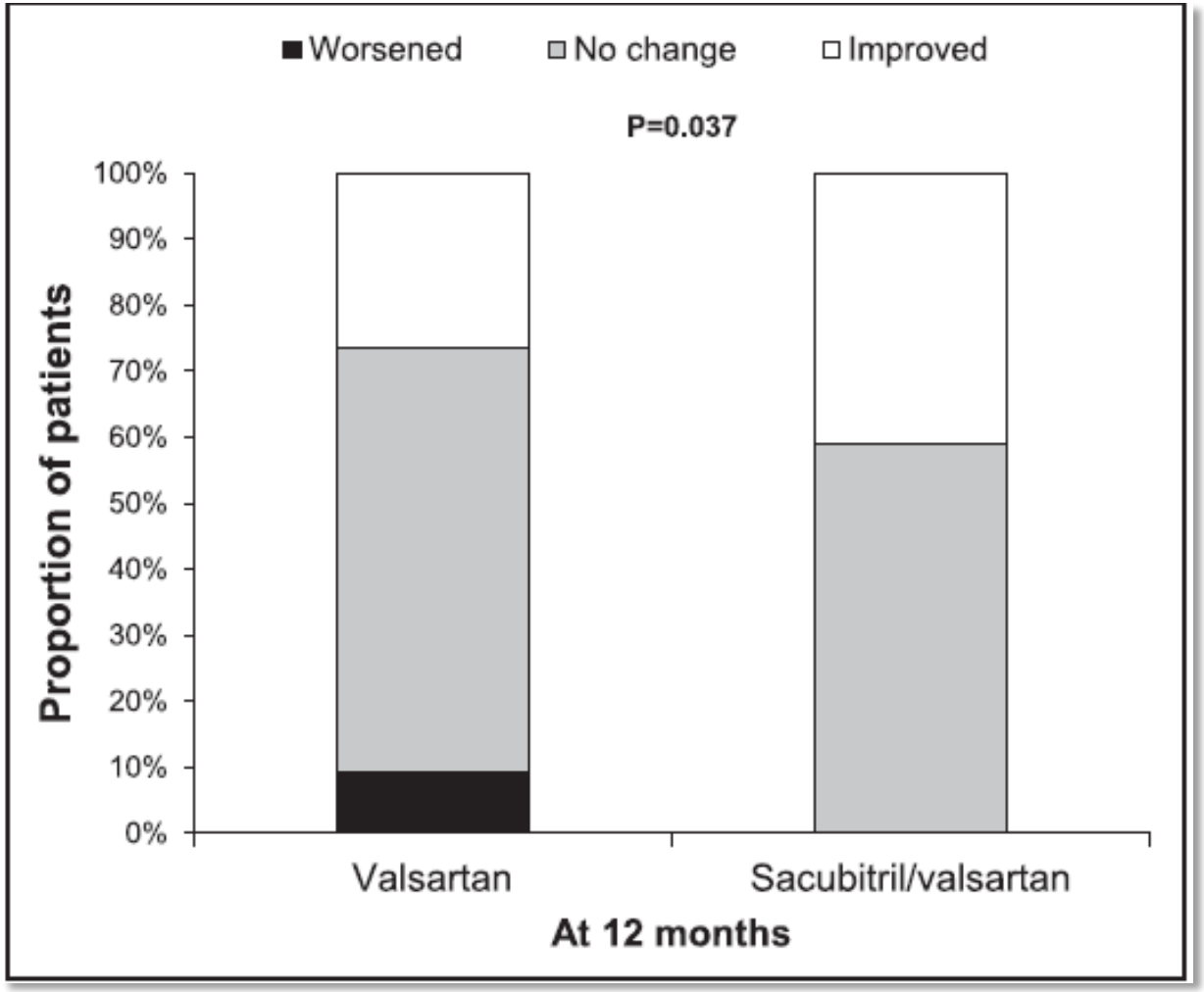
Kang et al. Circulation. 2019;139:1354–1365.

Baseline characteristics

- 118 patients: 60 sacubitril/valsartan, 58 valsartan.
- Mean age 62.6±11.2, 61% men
- 36%- ischemic cause of MR
- Mean LVEF 34±7%
- Mean ERO 0.20±0.10 cm^2
- Mean RV 35±16 ml

Kang et al. Circulation. 2019;139:1354–1365.

Significant change in MR at 12-month



Kang et al. Circulation. 2019;139:1354–1365.

Ventricular arrhythmia

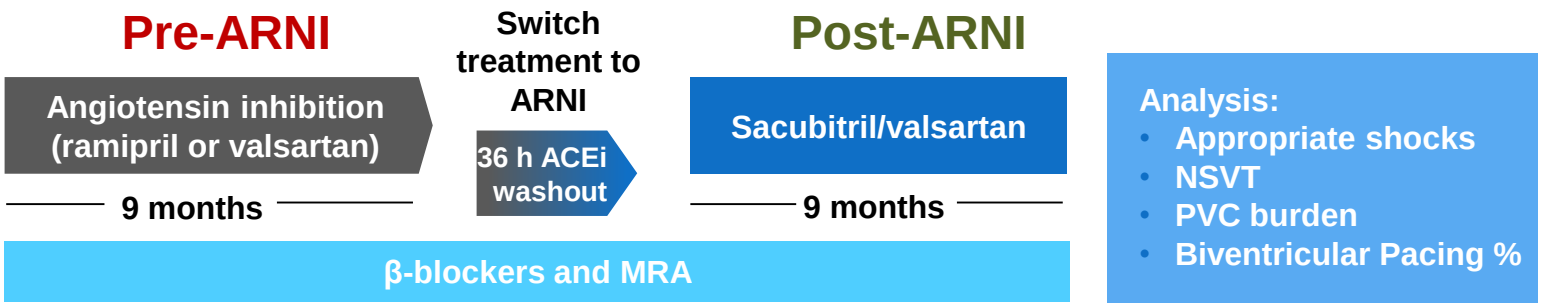
Effects of angiotensin-neprilysin inhibition compared to angiotensin inhibition on ventricular arrhythmias in reduced ejection fraction patients under continuous remote monitoring of implantable defibrillator devices

Carlos de Diego, MD, PhD,*† Luis González-Torres, MD,*† José María Núñez, MD,†
Raúl Centurión Inda, MD,* David A. Martin-Langerwerf, MD,† Antonio D. Sangio, MD,†
Piotr Chochowski, MD,* Pilar Casasnovas, MD,* Julio C. Blazquéz, MD,*
Jesús Almendral, MD, PhD‡

*From the *Hospital Universitario de Torrevieja, Alicante, Spain, †Hospital Universitario de Elche Vinalopó, Universidad Católica de Murcia, Alicante, Spain, and ‡Grupo HM Hospitales, Universidad CEU San Pablo, Madrid, Spain.*

de Diego et al. Heart Rhythm. 2018;15:395-402

Effects of angiotensin-neprilysin inhibition as compared to angiotensin inhibition on ventricular arrhythmias



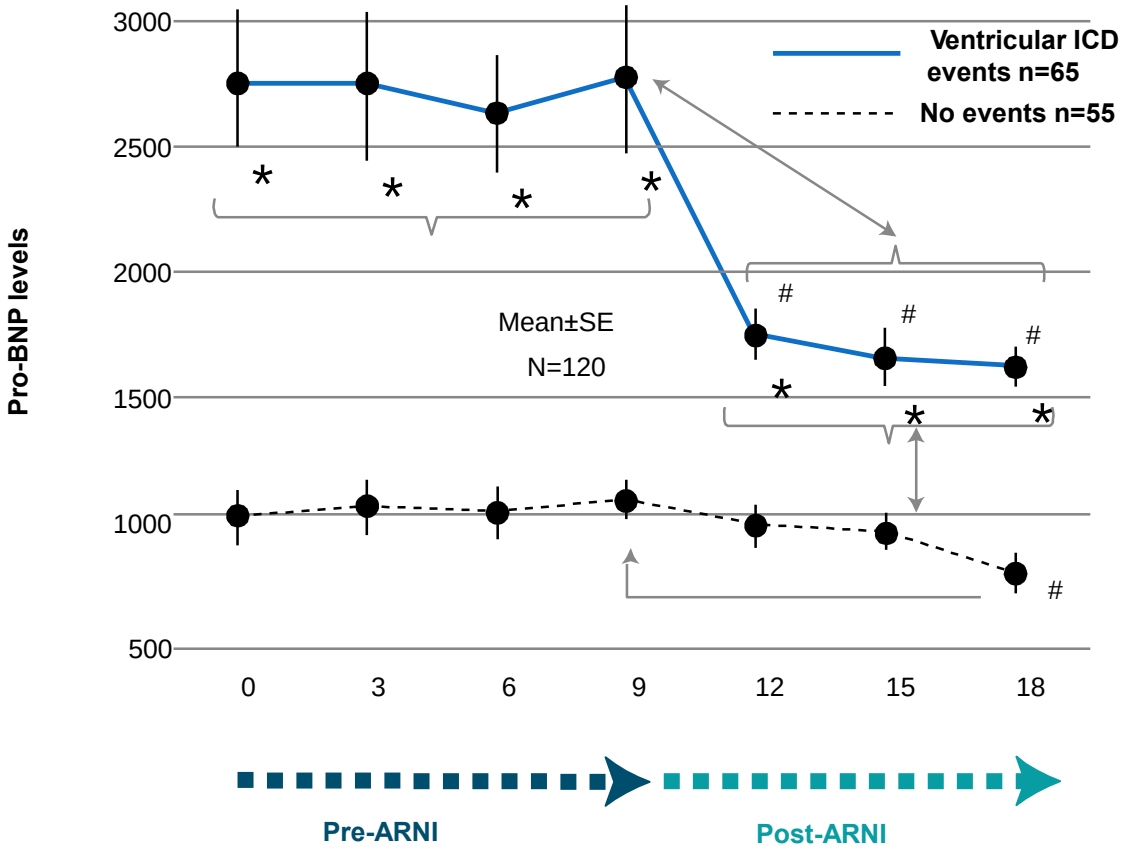
Patient population:
120 HFrEF patients with ICD or ICD-CRT referred to cardiology HF/arrhythmia outpatient clinic:

- HF symptoms with NYHA class ≥II despite optimal medical therapy, including initiation and titration of ACEi (ramipril) or ARB (valsartan), β-blockers, and MRA if tolerated
- LVEF ≤40%
- Under home monitoring of an ICD
- Patients serve as their own control by design

de Diego et al. Heart Rhythm. 2018;15(3):395-402

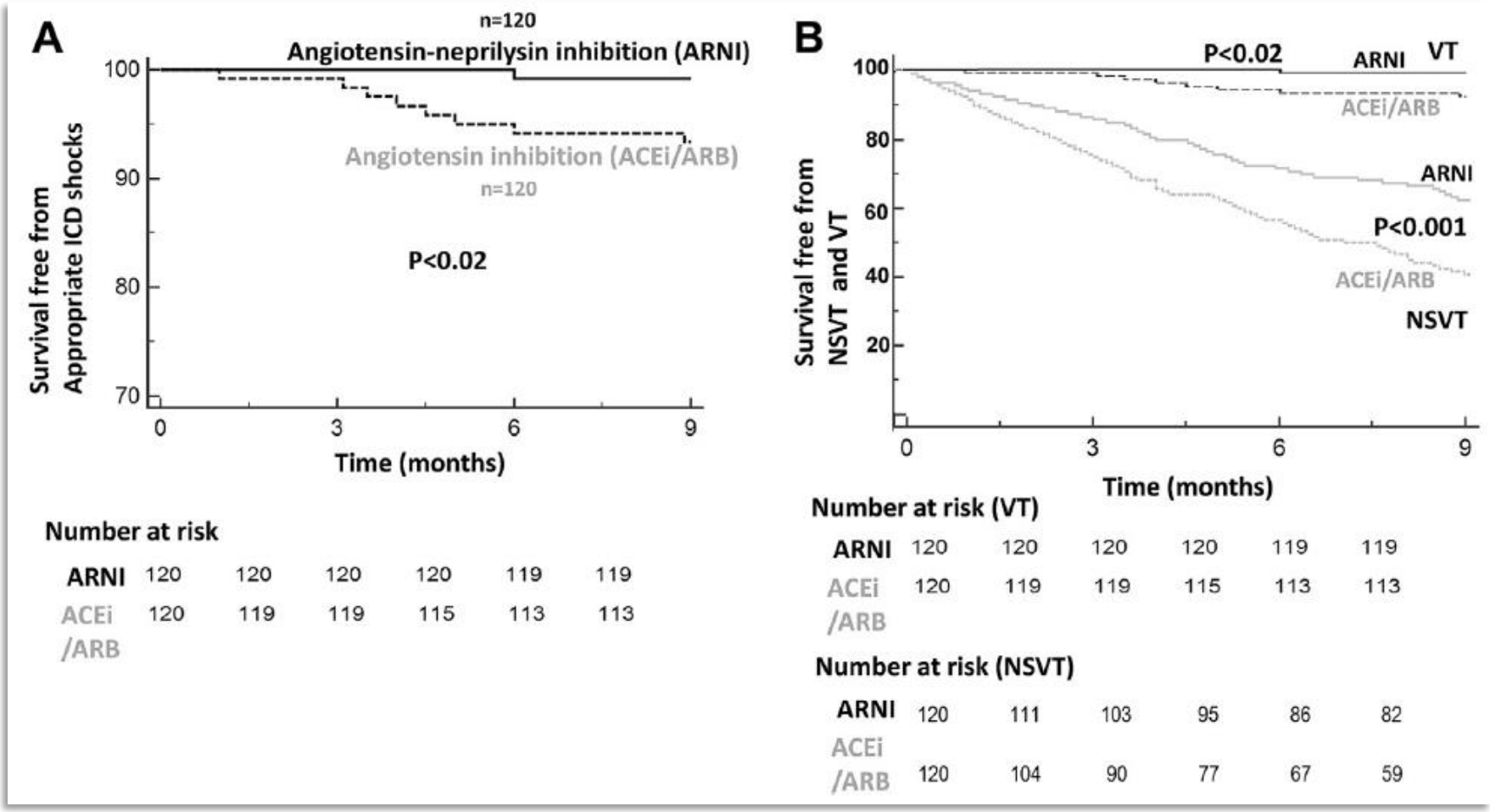
Entresto decreases pro-BNP in patients with VA ICD events

- Prior to switching to sacubitril/valsartan (pre-ARNI), pro-BNP levels were significantly elevated in patients with VA ICD events compared with patients without VA
- Following the switch to sacubitril/valsartan (post-ARNI), both groups experienced a decrease in pro-BNP levels, though this effect was more pronounced in the VA ICD group



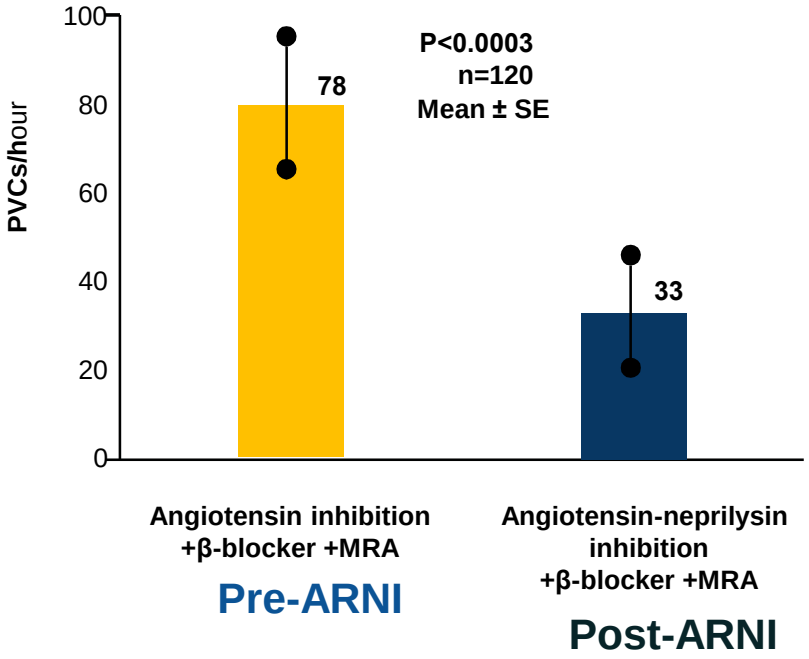
1. de Diego et al. Heart Rhythm. 2018;15(3):395-402

Ventricular arrhythmias and appropriate ICD shocks



De Diego et al. Heart Rhythm 2018;15:395–402

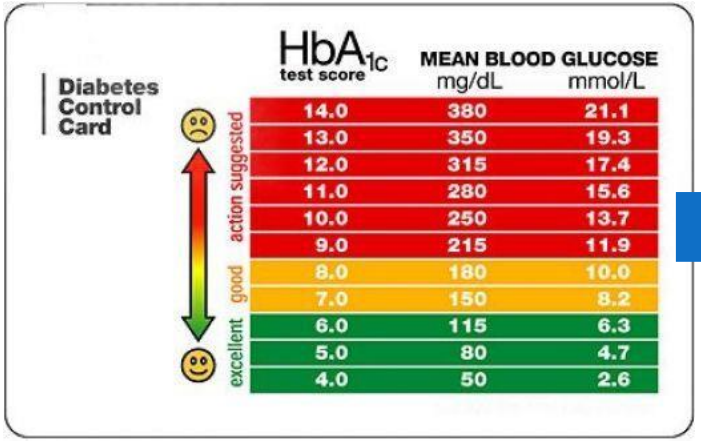
A decrease in PVC burden after Entresto was associated with an increase in biventricular pacing %, compared with ACEi/ARB



de Diego et al. Heart Rhythm. 2018;15(3):395-402

The change in the paradigm of antidiabetic treatment goals

SGLT2 inhibitors:
from glucocentricity to reduction of CV risk and mortality



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes

Bernard Zinman, M.D., Christoph Wanner, M.D., John M. Lachin, Sc.D., David Fitchett, M.D., Erich Bluhmki, Ph.D., Stefan Hantel, Ph.D.,

Primary endpoint:

MACE:

- **Cardiovascular death**
- **Non-fatal MI**
- **Non-fatal stroke**

primary outcome occurred in 490 of 4687 patients (10.5%) in the pooled empagliflozin group and in 282 of 2333 patients (12.1%) in the placebo group (hazard ratio in the empagliflozin group, 0.86; 95.02% confidence interval, 0.74 to 0.99; P=0.04 for superiority). There were no significant between-group differences in

posite cardiovascular outcome and of death from any cause when the study drug was added to standard care. (Funded by Boehringer Ingelheim and Eli Lilly; EMPA-REG OUTCOME ClinicalTrials.gov number, NCT01131676.)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Dapagliflozin and Cardiovascular Outcomes in Type 2 Diabetes

S.D. Wiviott, I. Raz, M.P. Bonaca, O. Mosenzon, E.T. Kato, A. Cahn, M.G. Silverman, T.A. Zelniker, J.F. Kuder, S.A. Murphy, D.L. Bhatt, L.A. Leiter, D.K. McGuire, J.P.H. Wilding, C.T. Ruff, I.A.M. Gause-Nilsson, M. Fredriksson, P.A. Johansson, A.-M. Langkilde, and M.S. Sabatine, for the DECLARE–TIMI 58 Investigators*

Co-primary endpoints:

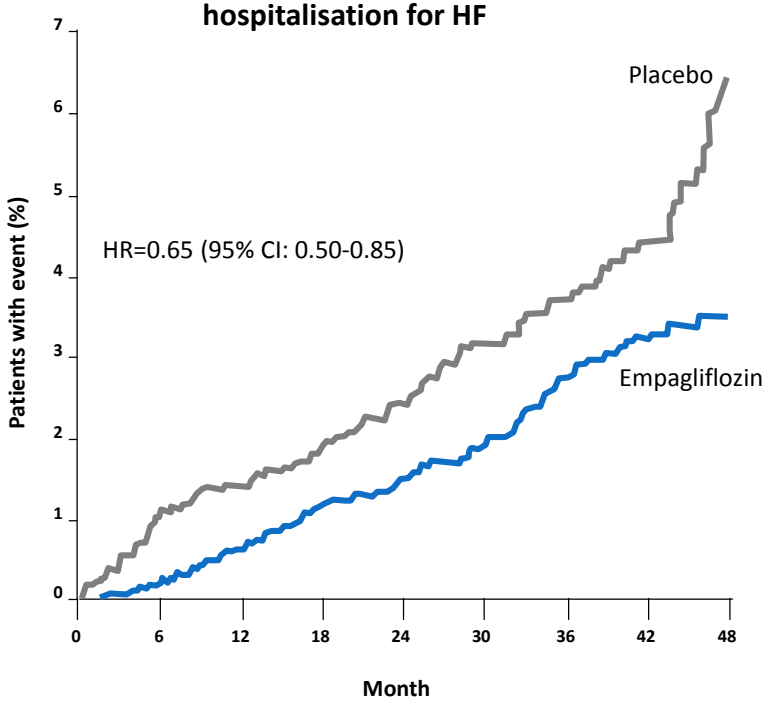
- **Composite of death or Heart Failure Hospitalization**

for noninferiority). In the two primary efficacy analyses, dapagliflozin did not result in a lower rate of MACE (8.8% in the dapagliflozin group and 9.4% in the placebo group; hazard ratio, 0.93; 95% CI, 0.84 to 1.03; P=0.17) but did result in a lower rate of cardiovascular death or hospitalization for heart failure (4.9% vs. 5.8%; hazard

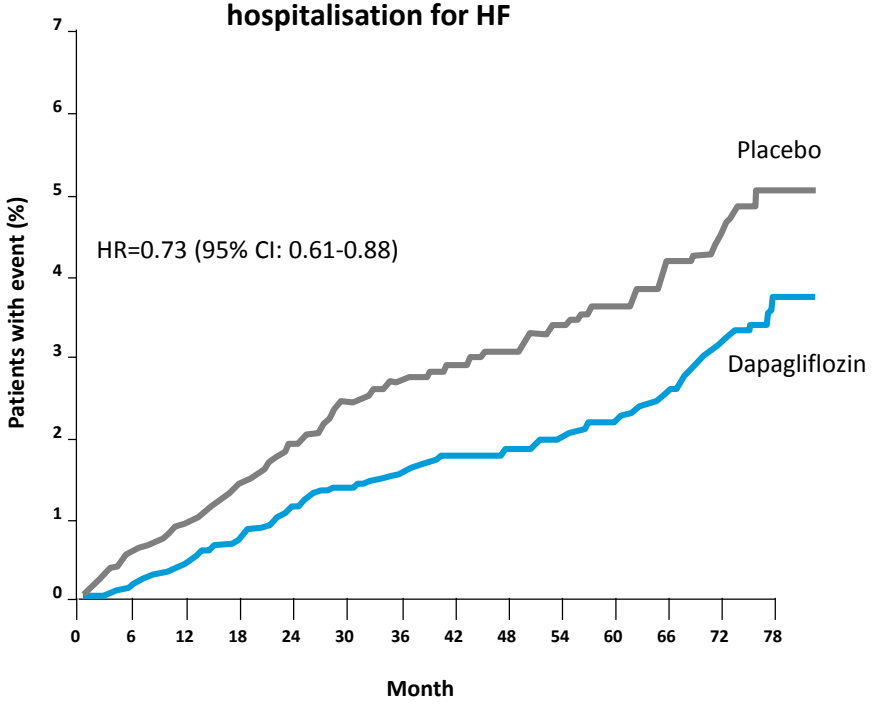
pitalization for heart failure, a finding that reflects a lower rate of hospitalization for heart failure. (Funded by AstraZeneca; DECLARE–TIMI 58 ClinicalTrials.gov number, NCT01730534.)

New insights into HF prevention have emerged from trials examining SGLT2 inhibitor use in T2D

EMPA-REG OUTCOME[1]
hospitalisation for HF



DECLARE[2]
hospitalisation for HF



CI, confidence interval; CV, cardiovascular; HF, heart failure; hHF, hospitalisation for heart failure; HR, hazard ratio; MACE, major adverse cardiovascular events; SGLT2, sodium-glucose cotransporter-2; T2D, type 2 diabetes.

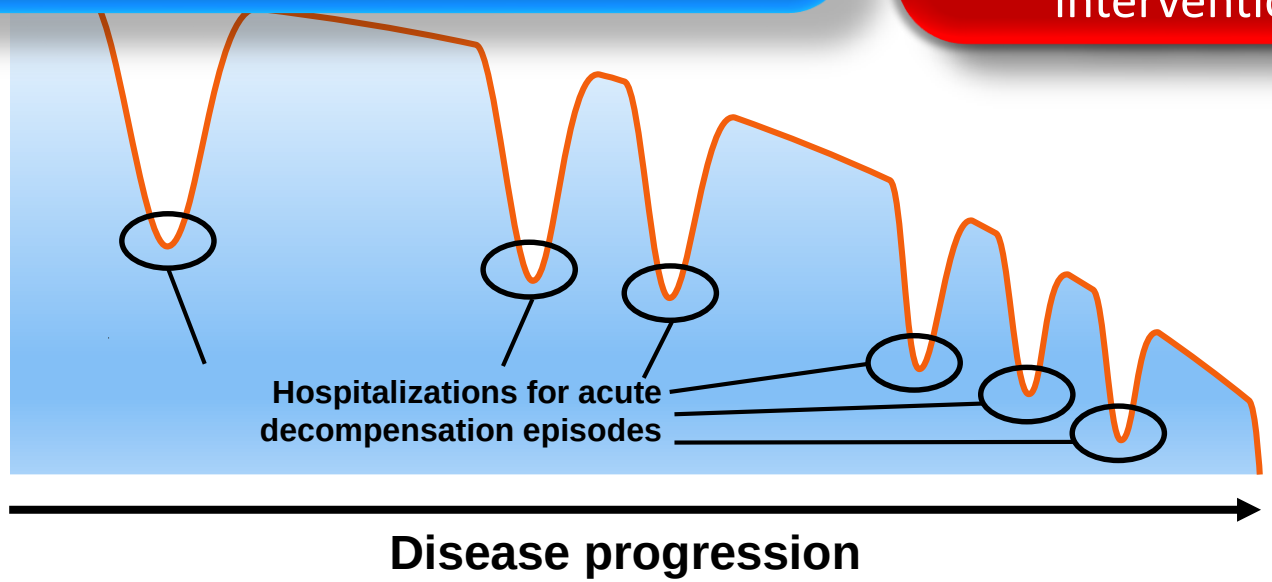
1. Zinman B, et al. *N Engl J Med.* 2015;373:2117–2128. 2. Wiviott S, et al. N Engl *J Med.* 2019;380:347-357.

Therapeutic Options:

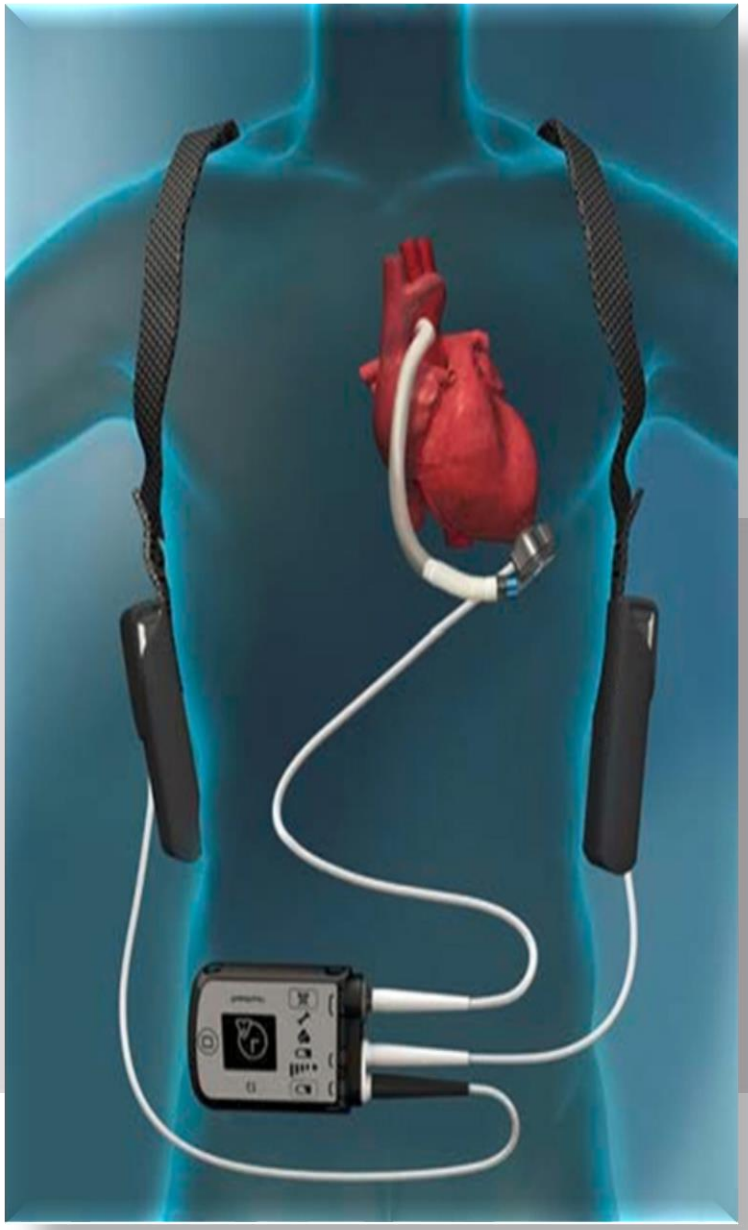
- Heart transplantation
- Chronic inotropes
- Long-term mechanical support

Advanced Heart Failure

Refractory HF requiring specialized interventions

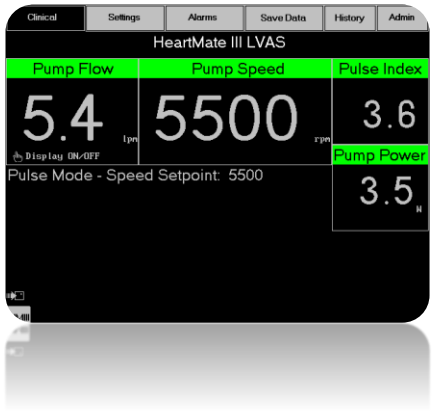


Heart Mate 3



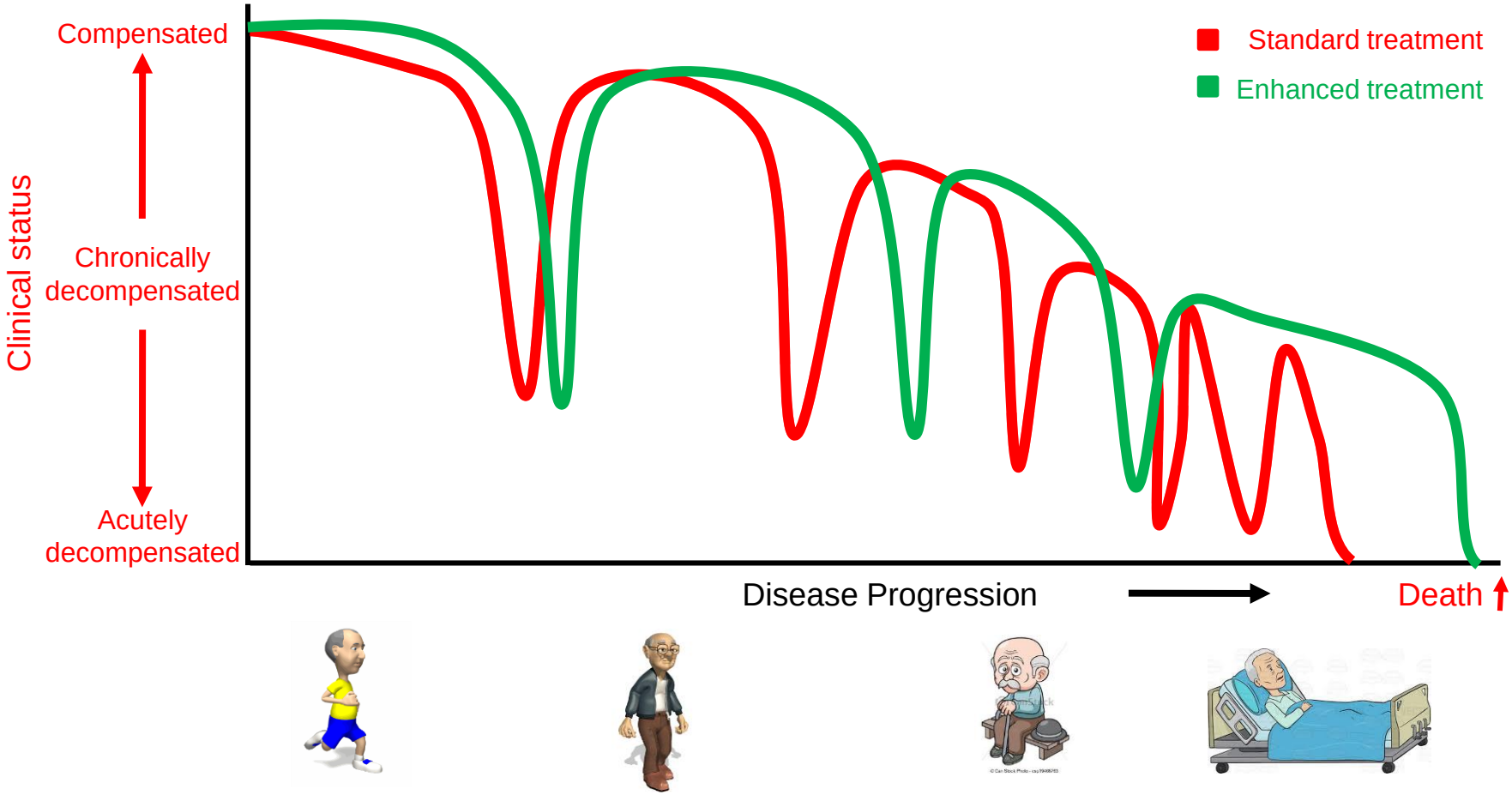
מעקב וניטור במטופל עם מכשיר LVAD

- מדדי המכשיר:
  - Speed
  - Flow
  - Power
  - Pulsatility Index



- ניטור קצב לב כרגיל (מוניטור, אק"ג)
- מדידת לחץ דם: Mean Arterial Pressure (MAP)
  - טווח מטרה 65-80 ממ"כ

HF is a progressive disease whereby cardiac structure and function continue to deteriorate



Adapted from Gheorghiade et al. 2005[2]

1. Ahmed et al. Am Heart J 2006;151:444–50; 2. Gheorghiade et al. Am J Cardiol 2005;96:11G–17G; 3. Gheorghiade, Pang. J Am Coll Cardiol 2009;53:557–73; 4. Holland et al. J Card Fail 2010;16:150–6; 5. Muntwyler et al. Eur Heart J 2002;23:1861–6; 6. McCullough et al. J Am Coll Cardiol 2002;39:60–9; 7. McMurray JJ. et al. Eur Heart J. 2012;33(14):1787–1847

תודה על ההקשבה

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