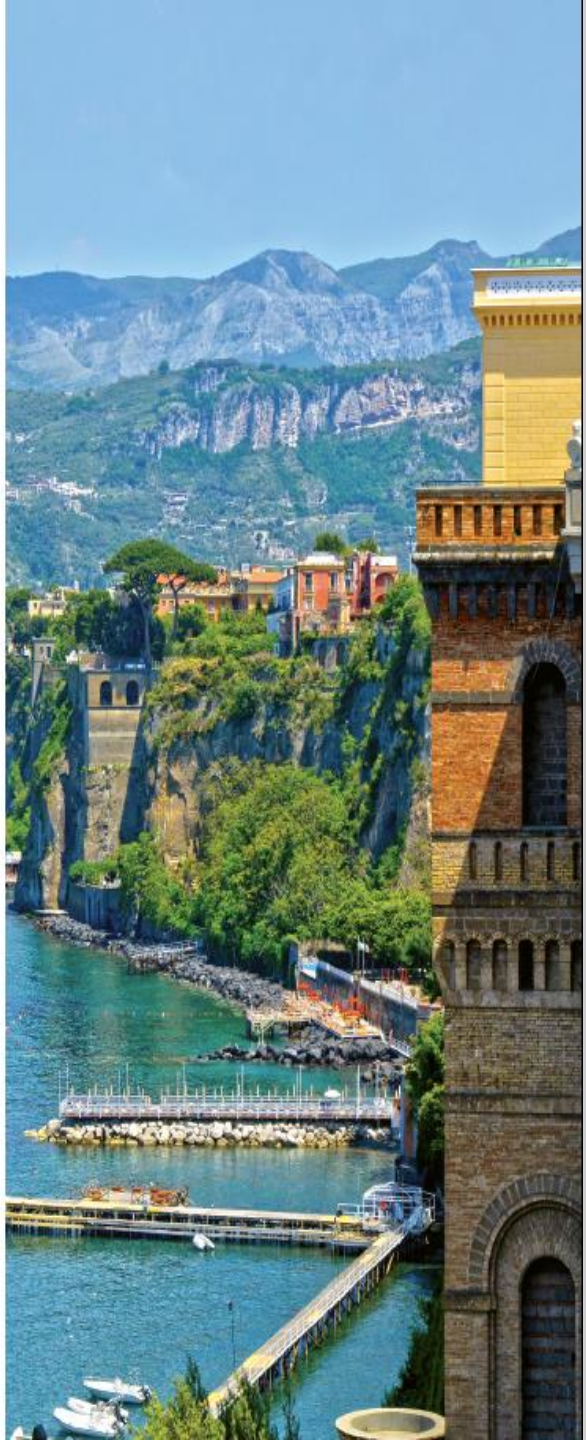
ANCE
Cardiologia Italiana del Territorio

XXIX
CONGRESSO
NAZIONALE
ANCE

PROGRAMMA



10 - 13 OTTOBRE 2019

Centro Congressi
Hilton Sorrento Palace
Sorrento (NA)

Evidenze cliniche di miglioramento della capacità funzionale nello scompenso cardiaco a frazione di eiezione ridotta (HFrEF)

F.M. Sarullo M.D.

Responsabile U.O. di Cardiologia Riabilitativa

Ospedale Buccheri La Ferla Fatebenefratelli

Palermo

HF is a major and growing public health problem in Italy

- In Italy HF affects ~600.000 patients and it is estimated that the prevalence doubles every decade (about 10% after 65 years of age)[1]
  - 8 days is the hospitalization median time during acute[2]
  - 4-7% of patients do not survive to the initial acute episode[2,3]
  - About 20% of patients die within 1 year[4]
  - About 50% of patients die within 5 years[5,6]
- It is supposed that during the next decades the number of HF patients will undergo a substantial increase as a result of the growing risk factors prevalence, the ageing of the population and the improved MI survival[10]
- In most of European Countries HF management takes up about 2% of the health-care budget[8]. Costs include:[9]
  - 6-8% medical check-ups
  - 8-9% outpatient care
  - 11-18% pharmacological tratments
  - 70% Hospitalizations

1. Ministero della Salute. “Scompenso cardiaco”; **2.** Maggioni et al. Eur J Heart Fail 2010;12:1076-84.; **3.** Cleland et al. Eur Heart J 2003;24:442-636. **4.** Maggioni et al. Eur J Heart Fail 2013;15:808-17. **5.** Roger et al. JAMA 2004;292:344-50. **6.** Levy et al. N Engl J Med 2002;347:1397-402. **8.** Dickstein et al. Eur Heart J 2008;29:2388-442. **9.** Neumann et al. Dtsch Arztebl Int 2009;106:269-75. **10.** Hunt et al. J Am Coll Cardiol 2009;53:e1–90;

(R)evolution of Heart Failure Treatment

Palliative Drugs | **Neurohormonal Drugs** | **Devices** | **ARNI**

Pre-1980 → 1980s → 1990s → 2000s → 2010s → 2016

Digitalis
Diuretics

ACE-I

ICDs

β-Blockers

Transplantation

CRT, CRT-D

LVAD

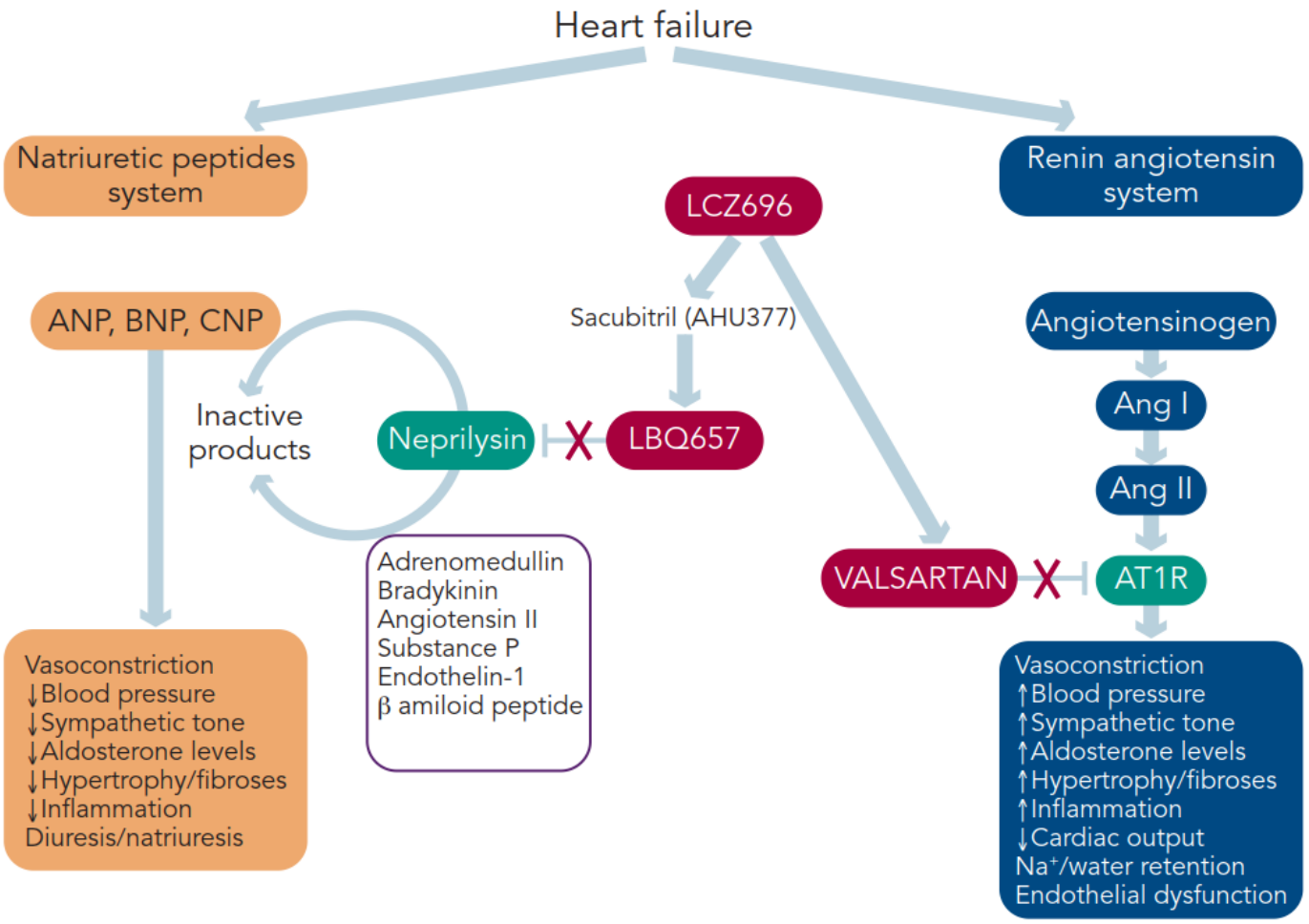
MR-Antagonists

Ivabradine

Sensing Devices

ARNI

Angiotensin II receptor – Neprilisin Inhibition (ARNI)



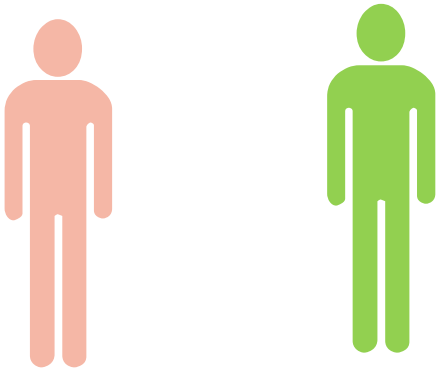
PARADIGM-HF: study design

Primary objective

- To evaluate the effect of LCZ696 97/103 mg BID compared with enalapril 10 mg BID, in addition to conventional HFrEF treatment, in delaying **time to first occurrence** of either **CV death** or **HF hospitalization**[1]

Key Inclusion Criteria:

- Chronic HF NYHA FC II–IV with LVEF ≤35%*
- BNP (or NT-proBNP) levels as follows:
  - ≥150 (or ≥600 pg/mL), or
  - ≥100 (or ≥400 pg/mL) and a hospitalization for HFrEF within the last 12 months
- eGFR >30 mL/min/1.73
- SBP >100
- ≥4 weeks' stable treatment with an ACEI or an ARB[#], and a β-blocker
- Aldosterone antagonist should be considered for all patients (with treatment with a stable dose for ≥4 weeks, if given)



LCZ696 97/103 mg BID[§]

Enalapril 10 mg BID[#]

On top of standard HFrEF therapy (BB/Diuretic/MRA...) **(excluding ACEIs and ARBs)**

*Enalapril 5 mg BID (10 mg TDD) for 1–2 weeks followed by enalapril 10 mg BID (20 mg TDD) as an optional starting run-in dose for those patients who are treated with ARBs or with a low dose of ACEI; ‡200 mg TDD; §400 mg TDD; #20 mg TDD

ACEI: angiotensin-converting-enzyme inhibitor; ARB: angiotensin receptor blocker; ARNI: angiotensin receptor neprilysin inhibitor; BID: twice daily; HFrEF: heart failure with reduced ejection fraction; PARADIGM-HF: Prospective comparison of ARNI with ACEI to Determine Impact on Global Mortality and morbidity in Heart Failure; TDD: total daily dose

McMurray et al. Eur J Heart Fail. 2013;15:1062–73; McMurray et al. Eur J Heart Fail 2014;16:817–25; McMurray et al. N Engl J Med 2014;371:993–1004

PARADIGM-HF: Key inclusion and Exclusion criteria

Key inclusion criteria

- Age > 18 years old
- Chronic HF NYHA FC II–IV
- LVEF ≤35%*
- BNP (or NT-proBNP) levels as follows:
  - ≥150 (or ≥600 pg/mL), or
  - ≥100 (or ≥400 pg/mL) and a hospitalization for HFrEF within the last 12 months
- ≥4 weeks' stable treatment with an ACEI or an ARB[#], and a β-blocker

Key Exclusion criteria

- eGFR <30 mL/min/1.73 m^2 at screening,
- Serum potassium >5.4 mmol/L at the end of the run-in
- SBP <100 mmHg at screening, OR SBP <95 mmHg at randomization
- Requirement for treatment with both ACEI and ARBs
- Current acute decompensated HF
- History of severe pulmonary disease
- History of angioedema
- SCA, stroke, TIA, major CV surgery, PCI, or carotid angioplasty within the 3 months prior to screening

*The ejection fraction entry criteria was ≤40% in the original protocol
[#]Dosage equivalent to enalapril ≥10 mg/day

McMurray et al. Eur J Heart Fail. 2013;15:1062–73

Baseline patient profile and treatments

Characteristic	PARADIGM-HF (N=8442)
Age (mean), years	64
Female sex, % of patients	22
NYHA class, % of patients	
I	5
II	70
III	24
IV	1
Heart rate (mean), bpm	72
BP (mean), mmHg	
Systolic	121
Diastolic	74
LVEF (mean), %	29

Concomitant treatments at randomization, n (%)	LCZ696 (n=4187)	Enalapril (n=4212)
Diuretics	3363 (80.3)	3375 (80.1)
Digitalis	1223 (29.2)	1316 (31.2)
β-blockers	3899 (93.1)	3912 (92.9)
Mineralocorticoid antagonists	2271 (54.2)	2400 (57.0)
ICD	623 (14.9)	620 (14.7)
CRT	292 (7.0)	282 (6.7)

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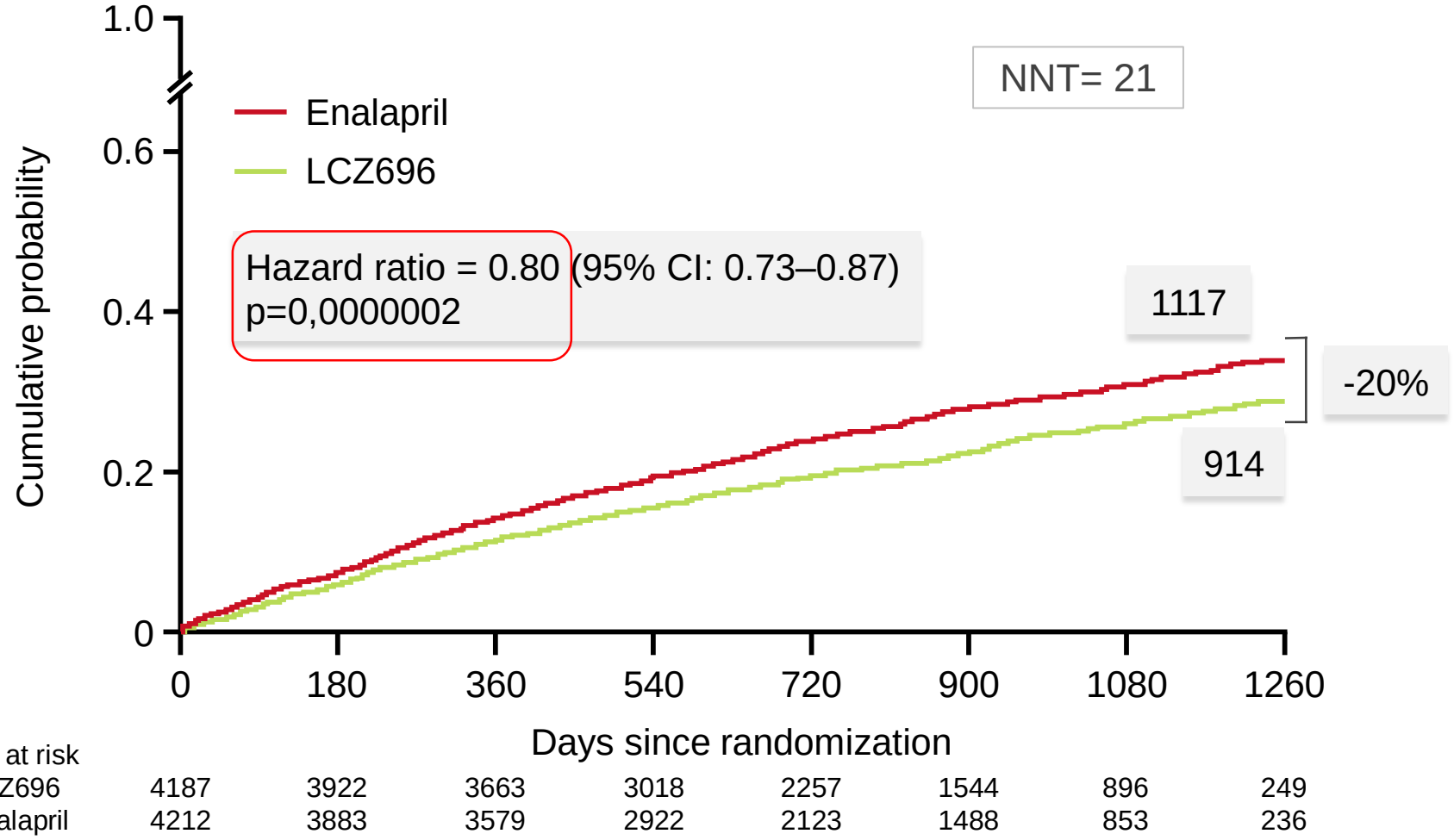
BP=blood pressure; bpm=beats per minute; LVEF=left ventricular ejection fraction; NYHA=New York Heart Association

McMurray et al. Eur J Heart Fail. 2014;16:817–25

PARADIGM-HF: RESULTS

Primary endpoint:

Death from CV causes or first hospitalization for HF



No at risk								
LCZ696	4187	3922	3663	3018	2257	1544	896	249
Enalapril	4212	3883	3579	2922	2123	1488	853	236

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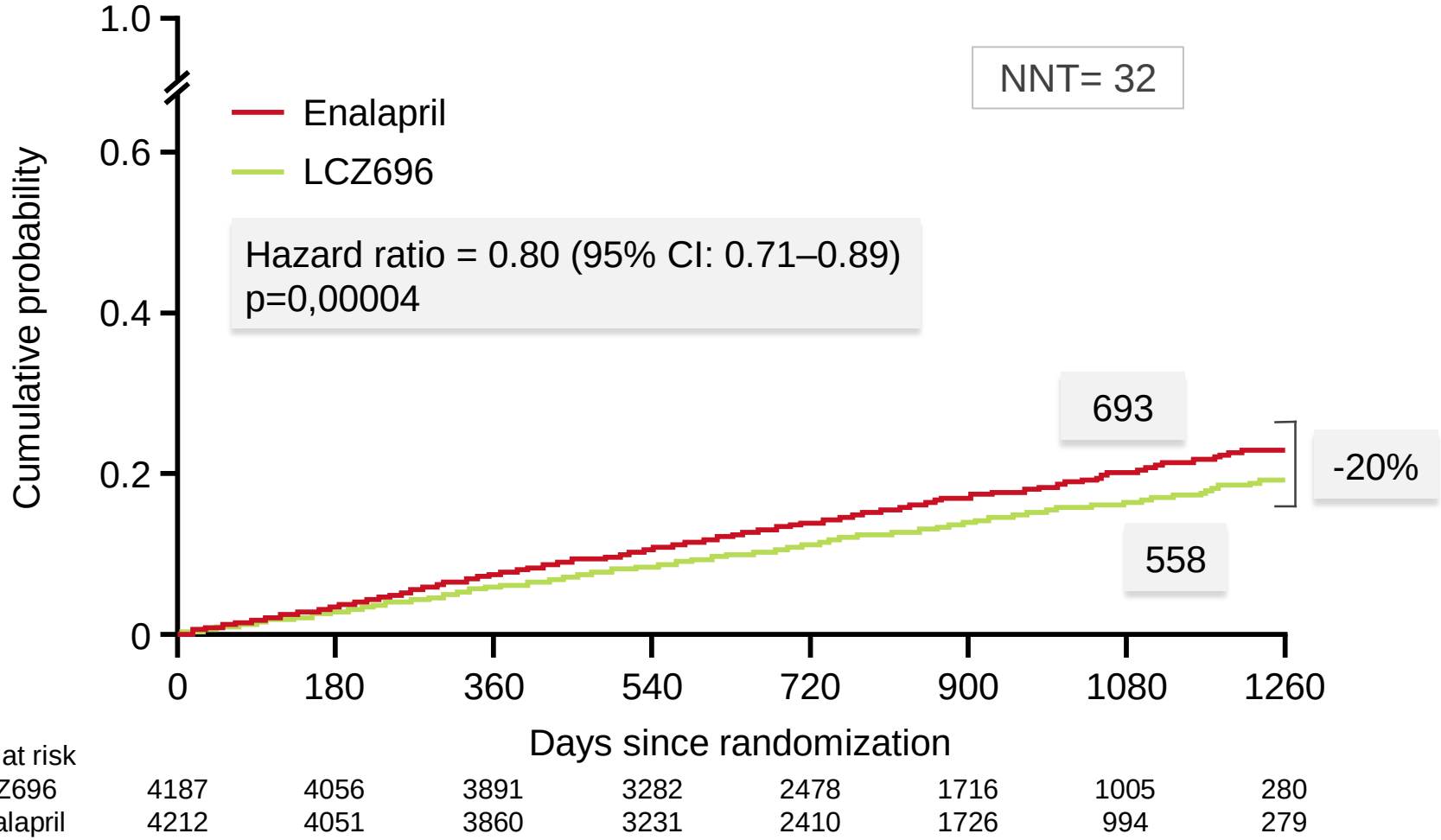
McMurray, et al. N Engl J Med 2014;

ESC GL objective: Reduce Mortality
PARADIGM HF RESULTS: Death from CV causes



No at risk								
LCZ696	4187	4056	3891	3282	2478	1716	1005	280
Enalapril	4212	4051	3860	3231	2410	1726	994	279

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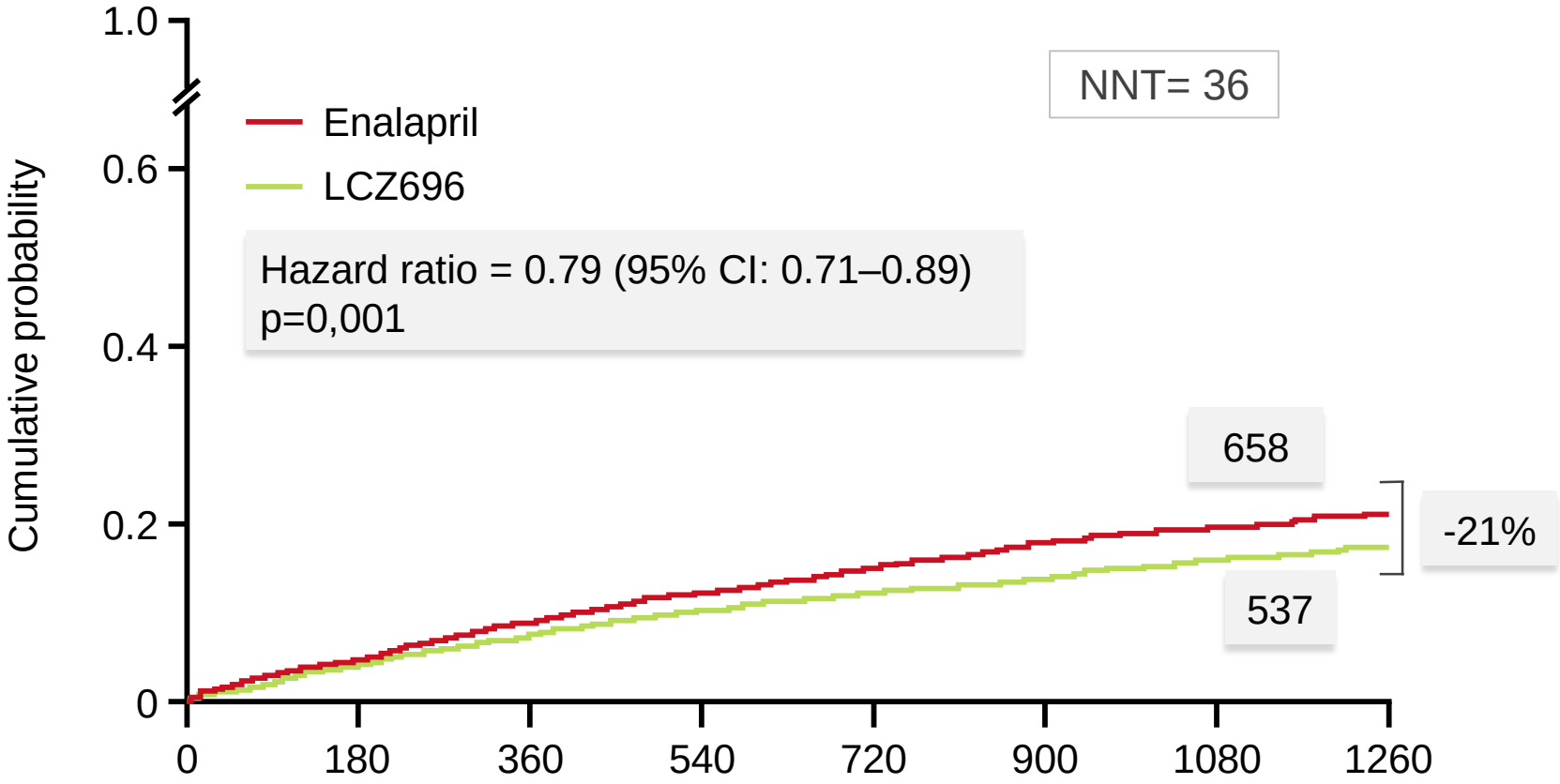
McMurray, et al. N Engl J Med 2014

ESC GL objective: Prevent hospital admission
PARADIGM HF RESULTS: First hospitalization for HF



No at risk								
LCZ696	4187	3922	3663	3018	2257	1544	896	249
Enalapril	4212	3883	3579	2922	2123	1488	853	236

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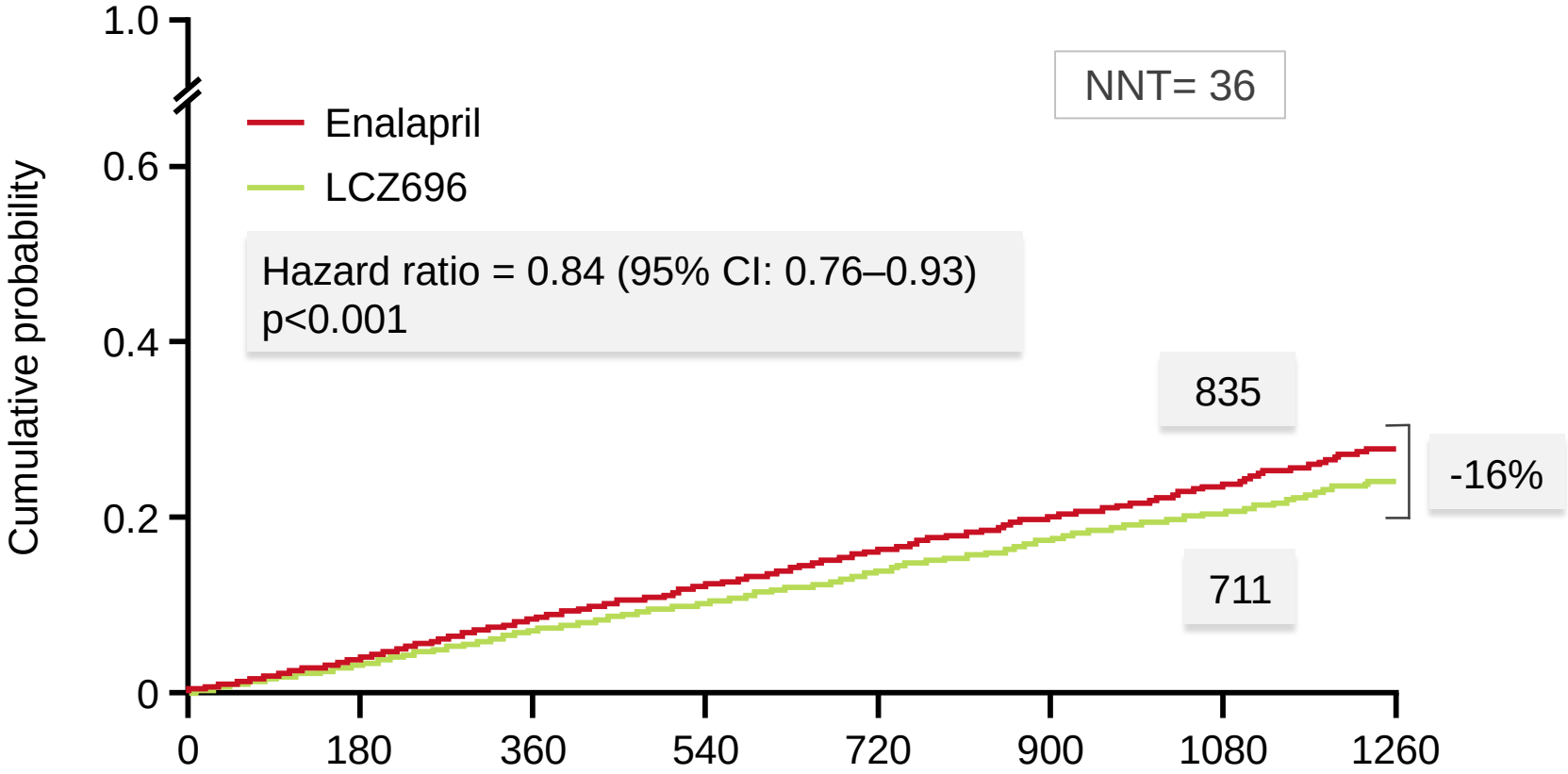
McMurray, et al. N Engl J Med 2014

ESC GL objective: Reduce Mortality

Death from any cause



No at risk								
LCZ696	4187	4056	3891	3282	2478	1716	1005	280
Enalapril	4212	4051	3860	3231	2410	1726	994	279

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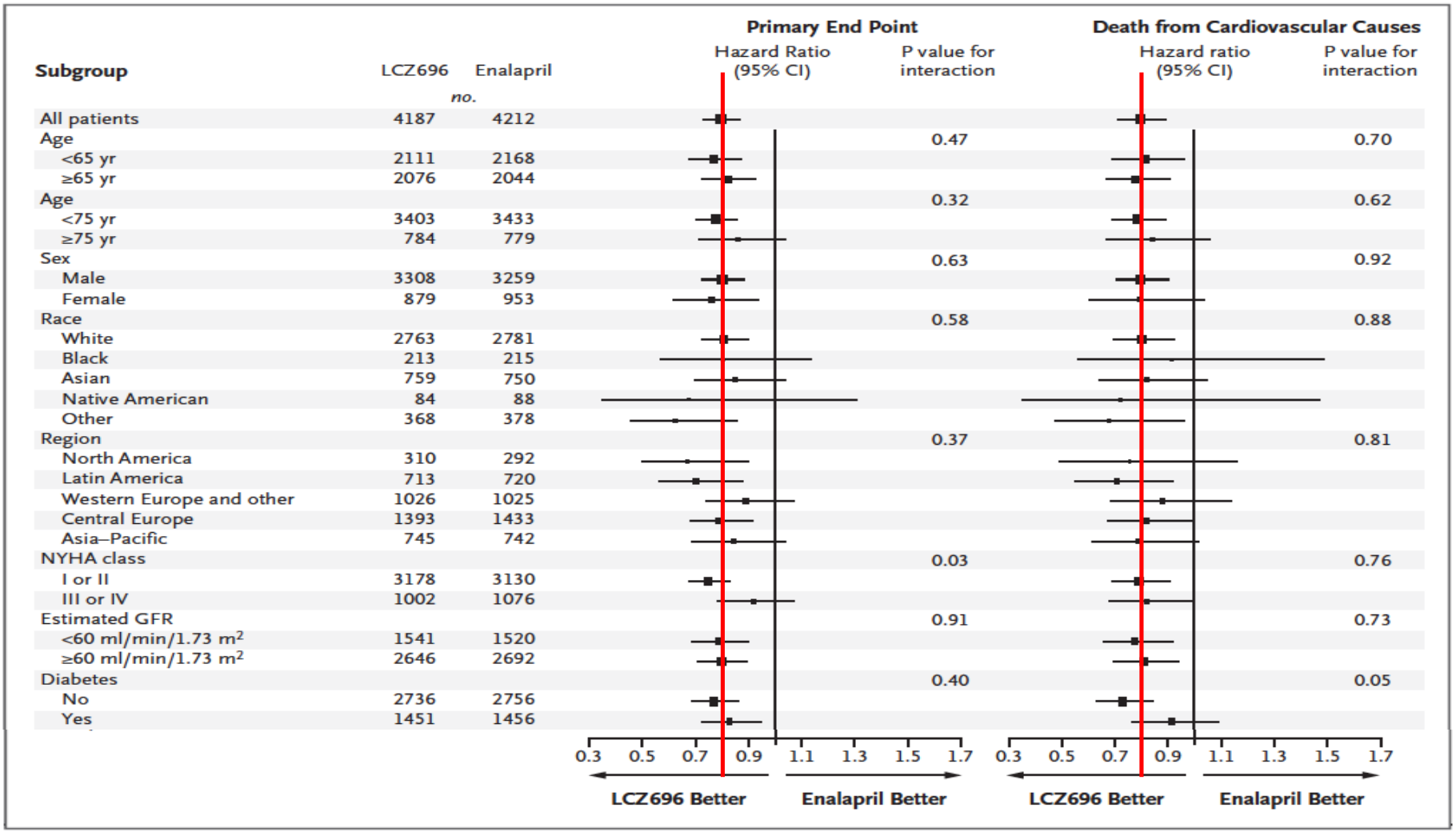
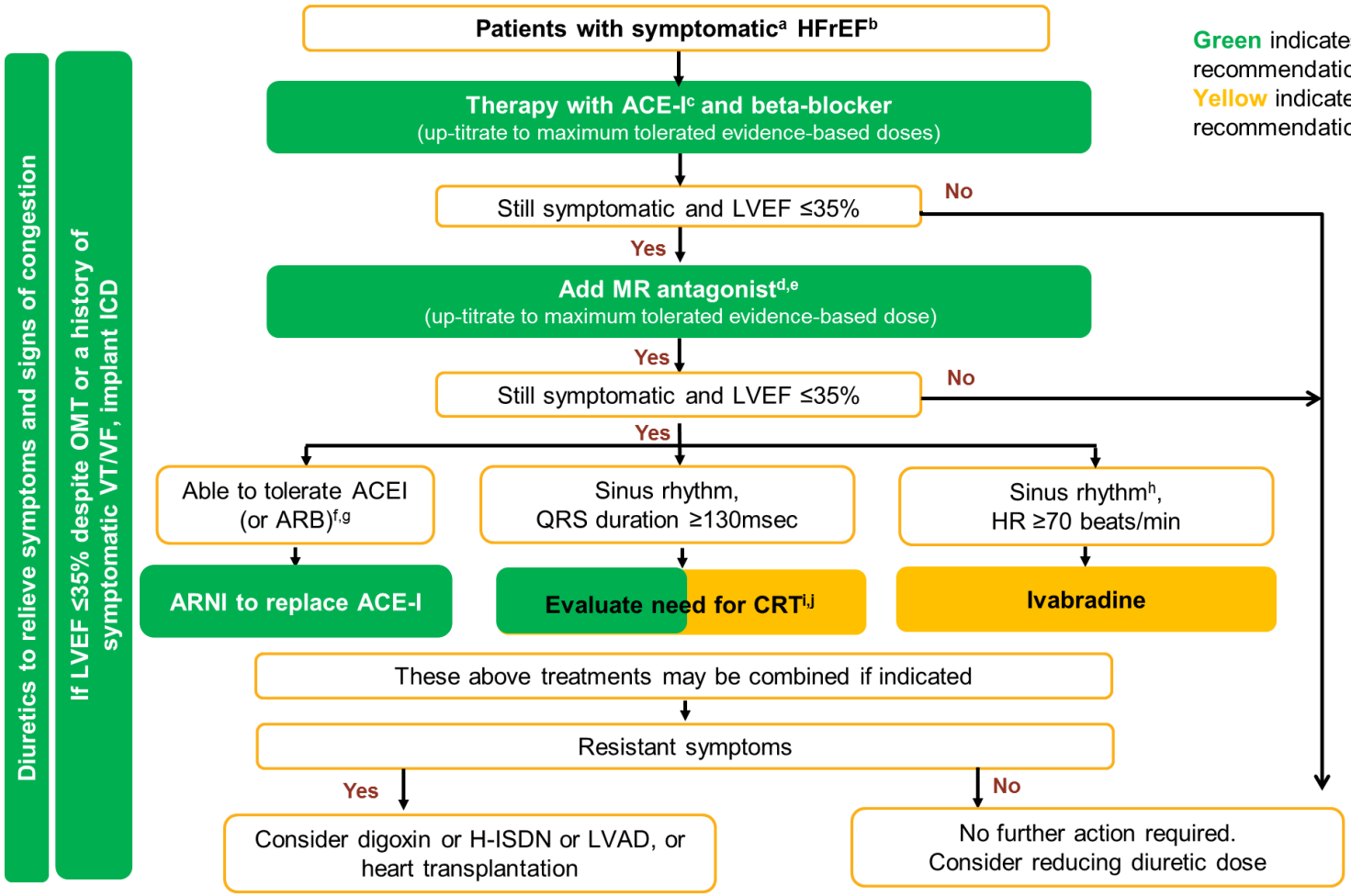
McMurray, et al. N Engl J Med 2014

PARADIGM HF – Results of the subgroups analysis 1



McMurray, et al. N Engl J Med 2014

2016 ESC HFrEF Guideline
Treatment Algorithm



Green indicates a **class I** recommendation;
Yellow indicates a **class IIa** recommendation.

[a]Symptomatic=NYHA Class II-IV; [b]HFrEF=LVEF<40%; [c]If ACEI not tolerated/contra-indicated, use ARB; [d]If MR antagonist not tolerated/contra-indicated, use ARB; [e]With a hospital admission for HF within the last 6 months or with elevated natriuretic peptides (BNP >250 pg/ml or NTproBNP >500 pg/ml in men and 750 pg/ml in women); [f]With an elevated plasma NP level (BNP ≥150 pg/mL or plasma NT-proBNP ≥ 600 pg/mL, or if HF hospitalization within recent 12 months plasma BNP ≥ 100 pg/mL or plasma NT-proBNP ≥ 400 pg/mL); [g]In doses equivalent to enalapril 10 mg *b.i.d.*; [h]With a hospital admission for HF within the previous year; [i]CRT is recommended if QRS ≥ 130 msec and LBBB (in sinus rhythm); [j]CRT should/may be considered if QRS ≥ 130 msec with non-LBBB (in a sinus rhythm) or for patients in AF provided a strategy to ensure bi-ventricular capture in place (individualized decision)

Ponikowski P et al. Eur Heart J. 21 May 2016.

Sacubitril-valsartan in heart failure and multimorbidity patients

R R Fraile et al - ESC - Heart Fail 2018 Oct;5(5):956-959

Sacubitril–valsartan in heart failure and multimorbidity patients

Raquel Rodil Fraile[1]*, Vincenzo Malafarina[2,3] and Gregorio Tiberio López[1]

[1]*Internal Medicine Department, Chronic-Multimorbidity Unit, Complejo Hospitalario de Navarra, Irunlarrea, 34, 31008, Pamplona, Spain;* [2]*Geriatric Department, Chronic-Multimorbidity Unit, Complejo Hospitalario de Navarra, Irunlarrea, 34, 31008, Pamplona, Spain;* [3]*Department of Nutrition, Food Science and Physiology, Faculty of Pharmacy and Nutrition, University of Navarra, 31008, Pamplona, Spain*

Abstract

Aims The poor control of symptoms in patients with advanced heart failure with reduced ejection function (HFrEF) can limit the functionality of patients. Sacubitril–valsartan, compared with enalapril, has been shown to reduce mortality and hospitalization, and nowadays, there is still little evidence about the improvement on functionality. The aim of our study is to analyse the improvement of the functional class and the 6 min walking test (6MWT) in patients with multiple pathologies and advanced heart failure.

Methods and results From September 2016 to March 2018, 65 multimorbidity patients with severe symptomatic HFrEF were initiated to receive sacubitril–valsartan. Mean age was 78.6 ± 7.4 years, and 68% were male. The Charlson co-morbidity index was 8 points. Seventy-four per cent had New York Heart Association (NYHA) Functional Class IV. After the treatment, patients were able to achieve 55.68 m or more on 6MWT, and 91% presented an improvement in the NYHA functional class.

Conclusions Sacubitril–valsartan relieves symptoms and improves functional class prognostic risk of patients with advanced HFrEF and co-morbidity.

RR Fraile et al; ESC Heart Fail. 2018 Oct;5(5):956-959

In pazienti comorbidi e anziani miglioramento sintomatologico e funzionale dopo 286 gg di trattamento medio

Table 2 Comparison of the analytical and clinical characteristics before and after the start of sacubitril–valsartan

Characteristics[a]	Before	After	*P*
Clinical			
Blood pressure (mmHg)	125.8 ± 18.8	127.7 ± 21.7	0.43
6 min walking test (m)	223.44 ± 93.55	279.12 ± 104.81	<0.001
NYHA scale, *n* (%)			0.002
Class II	1 (1)	33 (51)	
Class III	16 (25)	26 (40)	
Class IV	48 (74)	6 (9)	
MAGGIC score, *n* (%)	38.14	28.75	<0.001
MAGGIC score Risk Group 1	1 (1)	2 (3)	
MAGGIC score Risk Group 2	1 (1)	3 (4)	
MAGGIC score Risk Group 3	1 (1)	9 (14)	
MAGGIC score Risk Group 4	11 (16)	17 (26)	
MAGGIC score Risk Group 5	13 (20)	16 (25)	
MAGGIC score Risk Group 6	38 (61)	18 (28)	
Treatment (mg/dL)			
Mineralocorticoid agonist	29.01	26.34	
Diuretic	78.77	96.62	
Analytics			
Serum creatinine (mg/dL)	1.62 ± 0.58	1.66 ± 0.58	0.53
Serum troponin T (pg/mL)	45.07 ± 48.17	36.22 ± 30.45	0.03
Serum HbA1c (%)	7.18 ± 1.7	7.04 ± 1.6	0.83
Serum albumin (mg/dL)	3.89 ± 0.43	3.87 ± 0.36	0.44
Serum BNP (pg/mL)	565.5 ± 579.49	654.21 ± 1292.2	0.36

BNP, brain natriuretic peptide.
[a]Plus–minus values are means ± SD.

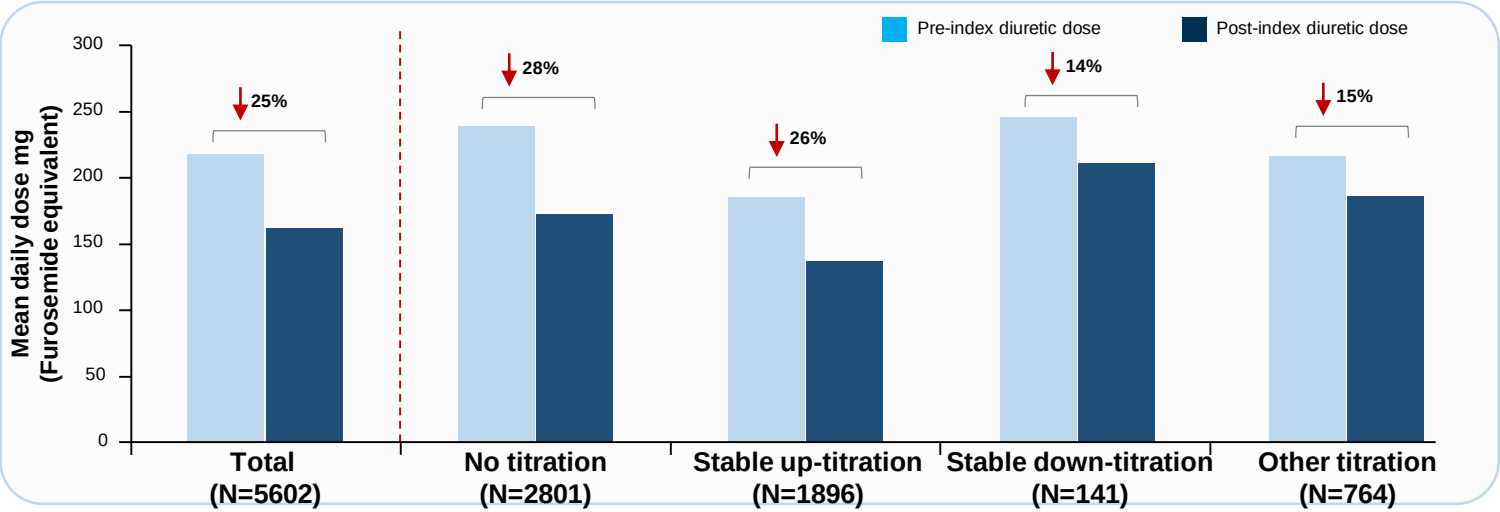
RR Fraile et al; ESC Heart Fail. 2018 Oct;5(5):956-959

Concomitant use of heart failure medication amongst 10,556 patients with sacubitril/valsartan therapy in Germany

R. Wachter et al ESC - Heart Fail 2018; 20 (S1): 5-638; 1547

Utilizzo del diuretico in una coorte di 10,556 pazienti trattati con sacubitril/valasartan (database Tedesco)

- ***Oral diuretics*** were prescribed in 77% of patients during pre-index and in 73% patients at 6 months post-index (P<0.001)
- ***GPs*** prescribed ***47% higher doses*** of diuretics compared with cardiologists (p<0.001) at post-index
- ***Mean furosemide equivalent dose*** was ***218 mg/day*** during the 6 months pre-index and ***163 mg/day*** at 6 months post-index (P<0.001)



- Lower diuretic doses and frequent reductions in diuretic doses after sacubitril/valsartan initiation was observed in patients with sacubitril/valsartan uptitration vs downtitration

*Common oral diuretics evaluated during pre- and post-index were furosemide, torasemide, hydrochlorothiazide and xipamide GP, general physician

R Wachter et al., EJHF, 2018, 20 (S1): 5-638; 1547

Sacubitril/Valsartan to Reduce Secondary Mitral Regurgitation

Refinement of Guideline-Directed Medical Therapy?

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Kang DH et al; Circulation. 2019;139:1354–1365.
DOI: 10.1161/CIRCULATIONAHA.118.03707

Caratteristiche dello studio

- Prospective, multicenter, double-blind, randomized, active-controlled trial: acubitril/valsartan (n=60) versus valsartan (n=58) alone in reducing functional, ischemic MR in 118 patients with HF, chronic MR secondary to LV dysfunction and LV ejection fraction (LVEF) between 25% and 50%.
- Objectiive: change from baseline to 12 months follow-up on
  - Primary: Change in effective regurgitant orifice area (EROA) of functional MR.
  - Secondary: Changes in regurgitant volume, LV end-systolic volume and end-diastolic volume, and incomplete mitral leaflet closure area.
- Compared with valsartan, **sacubitril/valsartan significantly decreased**:
  - EROA (−0.058 ± 0.095 versus −0.018 ± 0.105 cm^2; P=0.032).
  - Regurgitant volume (mean difference of change −7.3 mL, 95% confidence interval [CI] −12.6 to −1.9; P=0.009).
  - Ratio of mitral inflow velocity to mitral annular relaxation velocity (E/E') (mean difference of change −2.7, 95% CI −5.1 to −0.2; P=0.037).
  - Left atrial volume index (mean difference of change −8.9 mL/m^2, 95% CI −14.6 to −3.3; P=0.002).
  - Arterial impedance (mean difference of change −1.82 $mmHg/mL/m^2$, 95% CI −3.37 to −0.26; P=0.023).
- There were no significant between-group differences in incomplete mitral leaflet closure area and LV volumes except LV end-diastolic volume index (−7.0 mL/m^2, 95% CI −13.8 to −0.2; P=0.044).
- Reductions in blood pressure and the incidence of serious adverse events were similar in the two treatment groups.

Kang DH et al; Circulation. 2019;139:1354–1365. DOI: 10.1161/CIRCULATIONAHA.118.03707

L'ottimizzazione del trattamento con sac/vals migliora il deficit funzionale mitralico vs valsartan

The authors prospectively included symptomatic patients with heart failure with a baseline LVEF between 25% and 50%

Clinical Perspective

What Is New?

- PRIME trial (Pharmacological Reduction of Functional, Ischemic Mitral Regurgitation) has demonstrated that an angiotensin receptor neprilysin inhibitor is more effective in improving functional mitral regurgitation associated with heart failure than an angiotensin receptor blocker.
- In comparison with valsartan, sacubitril/valsartan further reduces the effective regurgitant orifice area, left ventricular end-diastolic volume index, left atrial volume index, and the ratio of mitral inflow velocity to mitral annular relaxation velocity (E/E′).

What Are the Clinical Implications?

- Angiotensin receptor-neprilysin inhibitor may be considered for optimal medical therapy of stable patients with heart failure and functional mitral regurgitation.

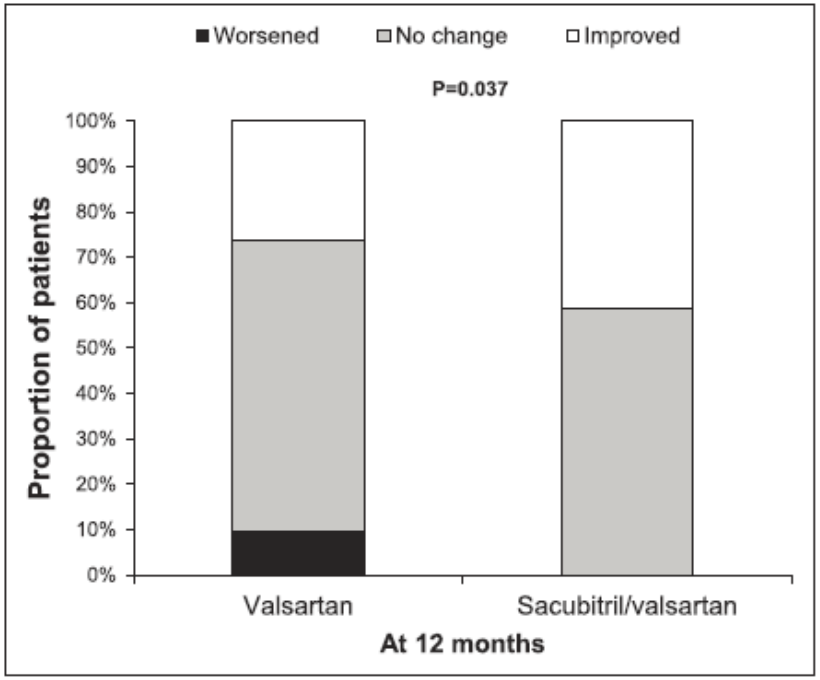
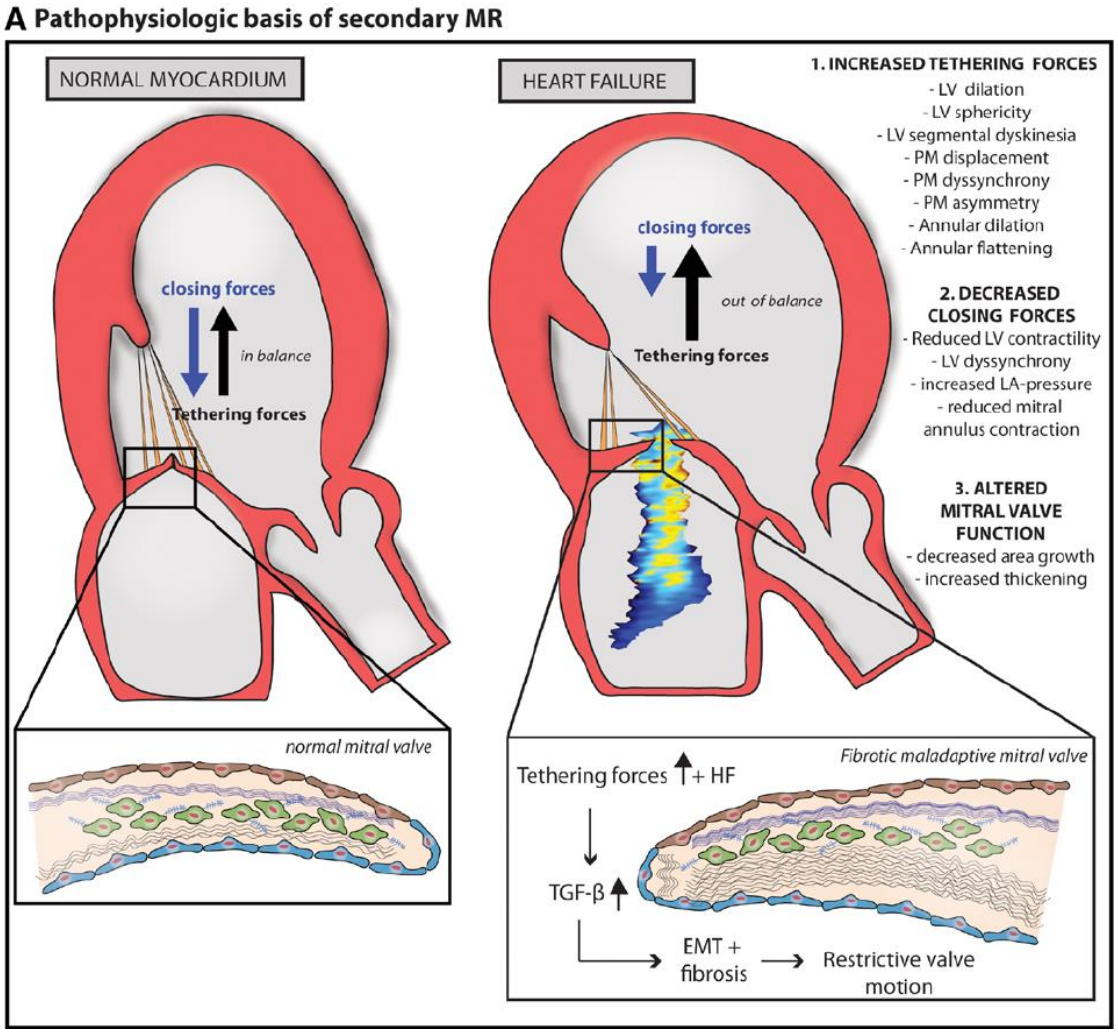


Figure 3. Significant changes in MR.
Percentage of patients who have significantly worsened, remained unchanged, or significantly improved at the 12-month follow-up. MR indicates mitral regurgitation.

Kang DH et al; Circulation. 2019;139:1354–1365. DOI: 10.1161/CIRCULATIONAHA.118.03707

L'ottimizzazione del trattamento con sac/vals migliora il deficit funzionale mitralico vs valsartan



perhaps indicate that patient selection (severe MR without advanced LV dilation) is important (see Figure B).[9] Indeed, once the LV has remodeled significantly, it is well established that the presence of severe MR loses its prognostic relation with poor outcome.[15] As such, percutaneous interventions targeting secondary MR in that setting might be futile in reverting the progressed disease, thereby underscoring the importance of adequate follow-up of patients under uptitration of guideline-directed medical therapy and assessment of eligibility for additional percutaneous interventions. Clearly, further analysis of the COAPT and MITRA-FR trials and the finalization of the RESHAPE-HF2 trial (A Clinical Evaluation of the Safety and Effectivieness of the MitraClip System in the Treatment of Clinically Significant Functional Mitral Regurgitation; NCT02444338) will help to understand the precise place of percutaneous techniques to reduce the degree of MR and improve clinical outcome. However, for now, it is clear that, before contemplating these percutaneous interventions, guideline-directed medical therapy should always be optimized first. This intrinsically includes the prescription of the class I lifesaving therapy sacubitril/valsartan.

W. Mullens, P Martens - Circulation 2019 Mar 12;139(11):1366-1370

Hospitalization cost reduction with sacubitril-valsartan implementation in a cohort of patients from the Daunia Heart Failure Registry

M. Correale et al, IJC Heart & Vasculature 22 (2019) 102–104

Hospitalization cost reduction with sacubitril-valsartan implementation in a cohort of patients from the Daunia Heart Failure Registry

Michele Correale [a], Ilenia Monaco [a], Armando Ferraretti [a], Lucia Tricarico [a], Giuseppina Padovano [a], Ennio Sascia Formica [a], Valeria Tozzi [a], Davide Grazioli [b], Matteo Di Biase [c], Natale Daniele Brunetti [a,*]

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ABSTRACT

Introduction: Aim of this study was to assess the impact of the introduction of new class of drugs (ARNI: angiotensin receptor-neprilysin inhibitor) on hospital related costs in a real world cohort of patients with chronic heart failure (CHF).

Methods: Seventy-three consecutive patients with CHF and systolic dysfunction eligible for the treatment with ARNIs from the Daunia Heart Failure Registry were enrolled. Incidence of hospitalizations before and after treatment with ARNI, costs for drug and hospitalization for HF were recorded, indexed per year and compared.

Results: Indexed mean number of hospitalizations per year was 0.93 ± 1.70 before and 0.19 ± 0.70 after introduction of ARNI ($p < 0.001$, −80%), 2.26 ± 1.95 before and 0.38 ± 1.2 after ARNI in the subgroup of patients with at least one hospitalization for HF in the year before treatment with ARNI ($p < 0.001$, −83%).

Mean indexed cost for hospitalization was 2067 ± 3715 euros before and 1847 ± 1549 after ARNI (p n.s., −11%); in the subgroup with at least one hospitalization for HF 5175 ± 4345 before and 2311 ± 2308 after ARNI ($p < 0.001$, −55%). Cost reduction increased with the number of indexed hospitalization per year before ARNI from 11% to 66%.

Conclusion: In a real world scenario, treatment with ARNI is associated with lower indexed rates of hospitalizations and hospitalization related costs. Cost reduction increases with at least one indexed hospitalization for heart failure before treatment with ARNI.

Correale M. et al, IJC Heart & Vasculature 22 (2019) 102–104

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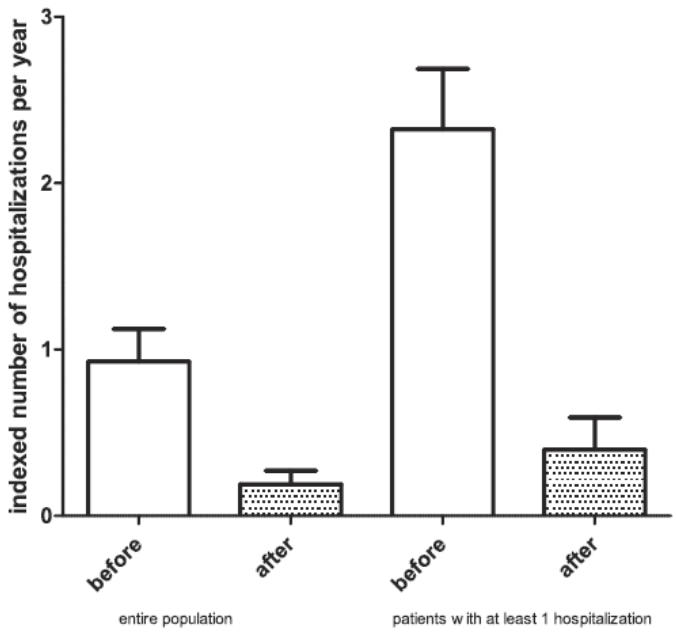


Fig. 1. Number of indexed hospitalizations for heart failure before and after treatment with ARNI ($p < 0.001$): left, whole population; right, patients with at least one indexed hospitalization for heart failure in the year before treatment.

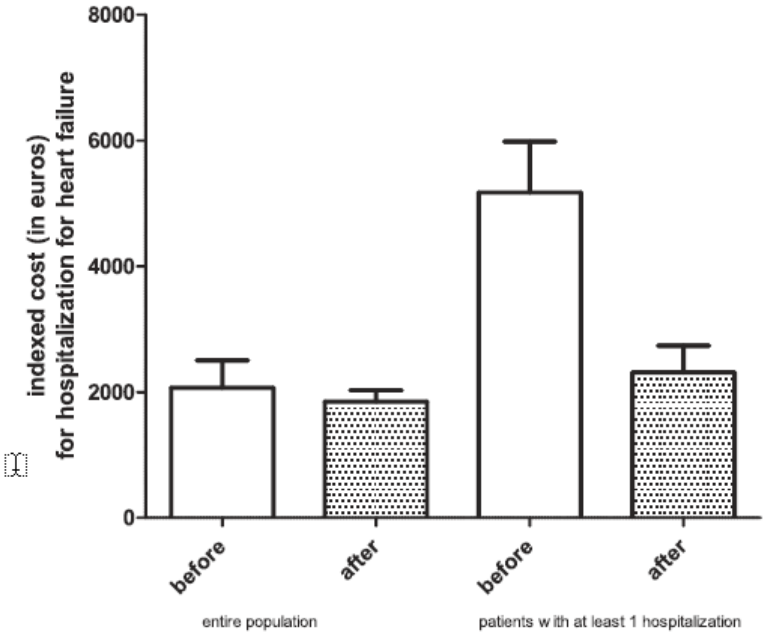


Fig. 2. Mean indexed costs for hospitalizations for heart failure before and after treatment with ARNI: left, whole population (p n.s.); right, patients with at least one indexed hospitalization for heart failure in the year before treatment ($p < 0.001$).

Correale M. et al, IJC Heart & Vasculature 22 (2019) 102–104

Sacubitril/valsartan reduces ventricular arrhythmias in parallel with left ventricular reverse remodeling in heart failure with reduced ejection fraction

Mertens P. et al, Clin Res Cardiol. 2019 Feb 20.

doi: 10.1007/s00392-019-01440-y. [Epub ahead of print]

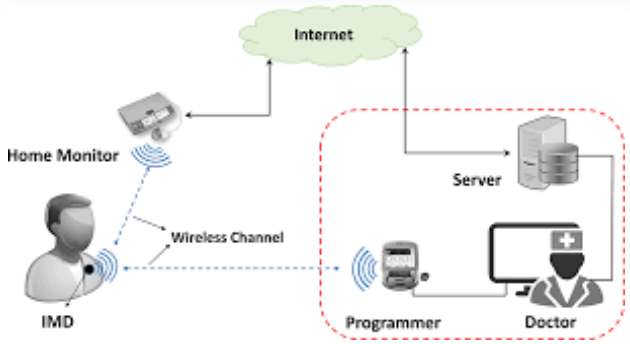
Caratteristiche dello studio

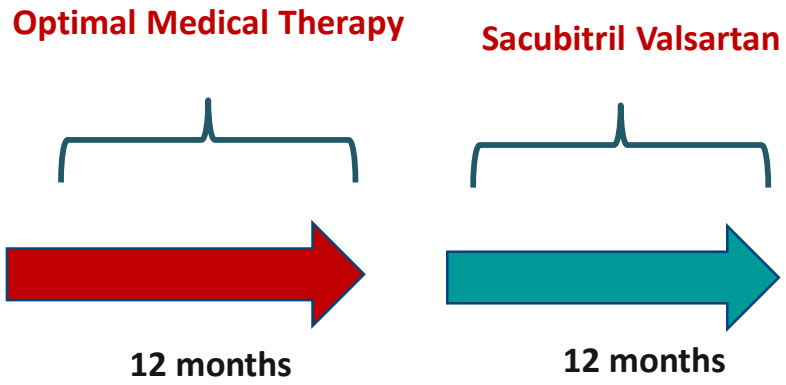
151 patients with HF-rEF (FE 29%)
NYHA II/III

ICD (30%), CRT-D (51%), CRT-P (18,6%)

Optimal medical therapy

Home monitoring



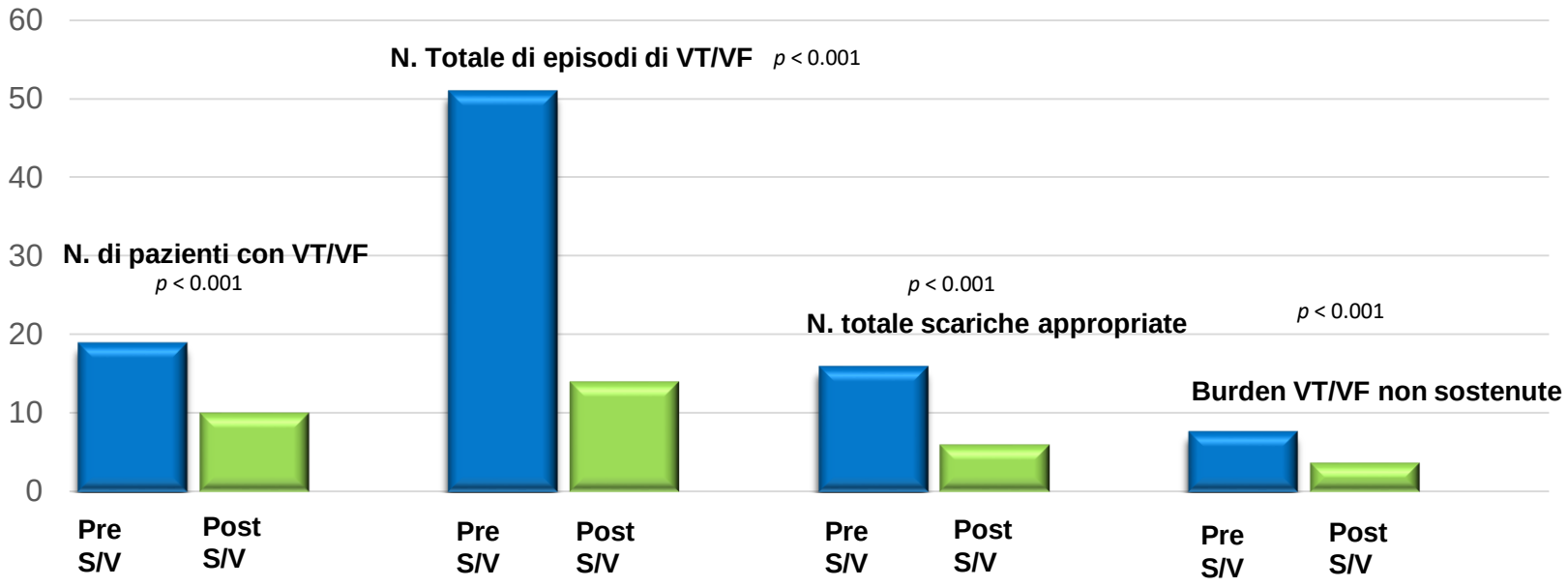


Guideline-directed heart failure therapy	
ACE-I or ARB	151 (100%)
Beta-blocker	143 (95%)
Aldosterone antagonist	130 (86%)
Loop diuretic	73 (48%)
Ivabradine	17 (11%)
Digoxin	13 (9%)
Amiodarone	49 (33%)

P. Martens et al, Clinical Research in Cardiology feb 20, 2019

VT/VF burden prima e dopo l'introduzione di sacubitril valsartan

Initiation of sacubitril/valsartan is associated with a lower degree of VT/VF, resulting in less ICD-interventions. This beneficial effect on ventricular arrhythmias might be related to cardiac reverse remodeling



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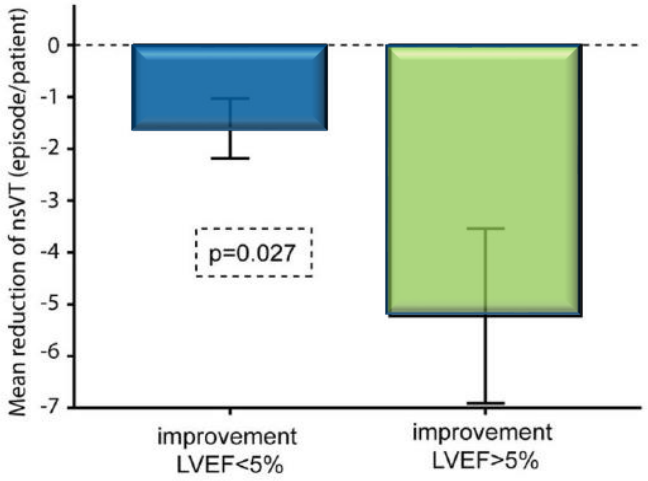
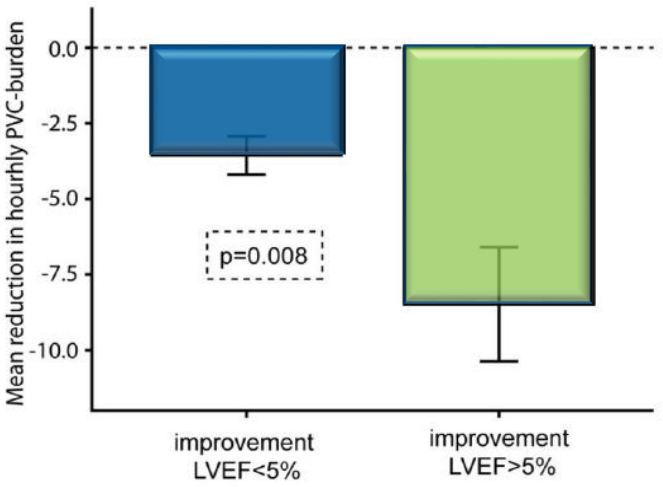
Effetto sul ventricolo sx

sacubitril/valsartan reduces ventricular arrytmias in parallel with left ventricular reverse remodeling in heart failure with reduced ejection fraction

Riduzione delle nsVT vs reverse remodeling



Riduzione del burden PVC orario vs reverse remodeling



P. Martens et al, Clinical Research in Cardiology feb 20, 2019

P. Martens et al, Clinical Research in Cardiology feb 20, 2019

“Early Effects of Sacubitril/Valsartan on Exercise Tolerance in Patients with Heart Failure with Reduced Ejection Fraction”

G. Vitale, ... F.M. Sarullo, J. Clin. Med. 2019, 8, 262; doi:10.3390/jcm8020262

Caratteristiche dei pazienti al basale

DEMOGRAPHICS	
Age, year, mean ± SD	58.7 ± 9.3
Female sex, no. (%)	14 (14)
SBP, mmHg, mean ± SD	117 ± 14
DBP, mmHg, mean ± SD	72 ± 10
Heart rate, beats/min, mean ± SD	67 ± 11
Body mass index, kg/m^2, mean ± SD	28.1 ± 4.2
MEDICAL HISTORY	
Hypertension, no. (%)	51 (51)
Diabetes, no. (%)	34 (34)
Atrial fibrillation, no. (%)	17 (17)
COPD, no. (%)	10 (10)
eGFR, mL/min/1.73m^2, mean ± SD	67.8 ± 23.7
Nt-pro-BNP, median (IQ range)	1200 (446–2120)
LVEF (%), mean ± SD	27 ± 6
LVEDV, mL, mean ± SD	218 ± 57
LVESV, mL, mean ± SD	153 ± 56
Ischemic cardiomyopathy, no. (%)	51 (51)
Non-ischemic cardiomyopathy, no. (%)	48 (49)
NYHA functional class II, no. (%)	62 (63)
NYHA functional class III, no. (%)	37 (37)
NYHA functional class IV, no. (%)	0 (0)
MEDICAL THERAPY	
Furosemide, no. (%)	88 (89)
Furosemide dosage, mean ± SD	102 ± 105
Antialdosterone, no. (%)	87 (88)
ACE-inhibitors, no. (%)	62 (63)
ARBs, no. (%)	25 (25)
Beta-blockers, no. (%)	93 (94)
Ivabradine, no. (%)	20 (20)
Digoxin, no. (%)	7 (7)
Implantable cardioverter defibrillator, no. (%)	76 (77)
Cardiac resynchronization therapy, no. (%)	22 (22)

ACE: angiotensin-converting enzyme; ARB: angiotensin receptor inhibitor; COPD: chronic obstructive pulmonary disease; DBP, diastolic blood pressure; eGFR: estimated glomerular filtration rate (as assessed by MDRD formula); IQ: inter-quartile; LVEDV: left ventricular end-diastolic volume; LVEF: left ventricular ejection fraction; LVESV: left ventricular end-systolic volume; Nt-pro-BNP: N-terminal pro–B-type natriuretic peptide; NYHA: New York Heart Association; SBP: systolic blood pressure; SD: standard deviation.

Vitale G. et al, J. Clin. Med. 2019, 8, 262; doi:10.3390/jcm8020262

Caratterizzazione dei pazienti in funzione del dosaggio

	Sacubitril/Valsartan 24/26 mg 28 pts	Sacubitril/Valsartan 97/103 mg 34 pts	*P* value
BASELINE CHARACTERISTICS			
Age, year, mean ± SD	57.8 ± 10.8	57.4 ± 8.6	0.87
Female sex, no. (%)	7 (25)	2 (6)	0.06
Ischemic cardiomyopathy, no. (%)	14 (50)	18 (53)	0.99
NYHA II, no. (%)	14 (50)	27 (79)	0.018
NYHA III, no. (%)	14 (50)	7 (21)	0.018
Diabetes, no. (%)	7 (25)	10 (29)	0.77
Atrial fibrillation, no. (%)	6 (21)	2 (6)	0.12
eGFR (MDRD), ml/min/1.73m^2, mean ± SD	63.3 ± 21.6	72.6 ± 16.7	0.07
Furosemide dose, mean ± SD	108 ± 126	63 ± 95	0.03
Implantable cardioverter defibrillator, no. (%)	22 (78)	24 (70)	0.56
Cardiac resynchronization therapy, no. (%)	8 (28)	8 (23)	0.77
SBP, NT-PRO-BNP, EDV, ESV, AND LVEF (BASELINE AND FOLLOW-UP DATA)			
SBP, mmHg, mean ± SD (Baseline)	114.3 ± 12.1	120.5 ± 14.7	0.07
SBP, mmHg, mean ± SD (Follow-up)	96 ± 11	105 ± 12	0.004
Nt-pro-BNP, median (IQ range) (Baseline)	1623.5 (477-2947)	815 (358-1929)	0.013
Nt-pro-BNP, median (IQ range) (Follow-up)	1065 (376-1739)	394.5 (195-952)	0.01
LVEDV, ml, mean ± SD (Baseline)	208 ± 54	222 ± 55	0.31
LVEDV, ml, mean ± SD (Follow-up)	209 ± 56	209 ± 59	0.98
LVESV, ml, mean ± SD (Baseline)	147 ± 57	161 ± 48	0.29
LVESV, ml, mean ± SD (Follow-up)	146 ± 57	143 ± 50	0.89
LVEF (%), mean ± SD (Baseline)	28.1 ± 5.7	28.3 ± 5.1	0.88
LVEF (%), mean ± SD (Follow-up)	28.6 ± 6.3	32.3 ± 6.6	0.026

eGFR: estimated glomerular filtration rate (as assessed by MDRD formula); IQ: inter-quartile; LVEDV: left ventricular end-diastolic volume; LVEF: left ventricular ejection fraction; LVESV: left ventricular end-systolic volume; Nt-pro-BNP: N-terminal pro–B-type natriuretic peptide; NYHA: New York Heart Association; SBP: systolic blood pressure; SD: standard deviation.

G. Vitale, .. F.M. Sarullo, J. Clin. Med. 2019, 8, 262; doi:10.3390/jcm8020262

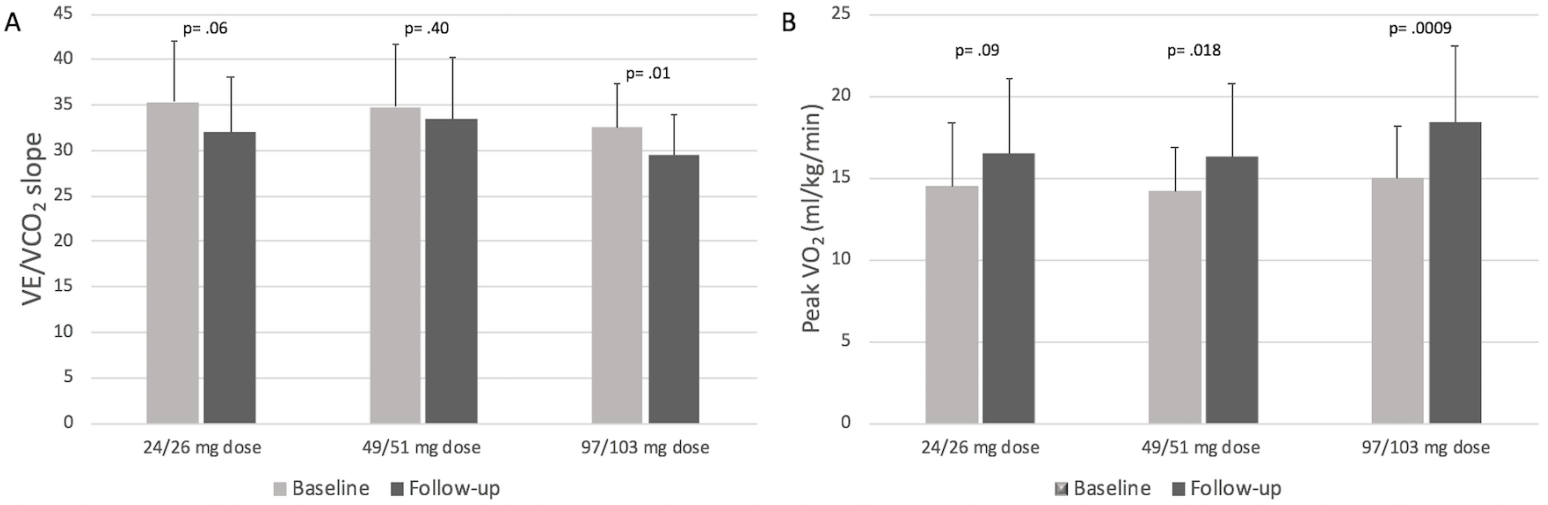
Journal of Clinical Medicine

MDPI

Article

Early Effects of Sacubitril/Valsartan on Exercise Tolerance in Patients with Heart Failure with Reduced Ejection Fraction

Giuseppe Vitale [1], Giuseppe Romano [2], Antonino Di Franco [3], Giuseppa Caccamo [1], Cinzia Nugara [1,4], Laura Ajello [2], Salvo Storniolo [5], Silvia Sarullo [5], Valentina Agnese [2], Francesco Giallauria [6], Giuseppina Novo [5], Francesco Clemenza [2] and Filippo M. Sarullo [1,*]



J. Clin. Med. **2019**, *8*(2), 262; https://doi.org/10.3390/jcm8020262

Sacubitril/Valsartan in Real-Life Practice: Experience in Patients with Advanced Heart Failure and Systematic Review

C Moliner-Abos et al. Cardiovasc Drugs Ther. 2019 Feb 28. doi: 10.1007/s10557-019-06858-0. [Epub ahead of print]

Valutazione retrospettica di 108 pazienti con scompenso avanzato

	Study population ($n = 108$)	PARADIGM-HF drug arm ($n = 4187$)	p value
Age, years, $\bar{x}$ (SD)	64 (11)	64 (11)	1.000
Males, n (%)	85 (79)	3308 (79)	0.939
Ischemic etiology, n (%)	59 (55)	2506 (60)	0.275
Atrial fibrillation, n (%)	42 (39)	1517 (36)	0.571
LVEF, $\bar{x}$ (SD)	30 (7)	30 (6)	1.000
NYHA functional class, n (%)			
II	65 (60)	2998 (72)	< 0.001
III	43 (40)	969 (23)	
Previous HF admission, n (%)	43 (40)	2607 (62)	< 0.001
NT-proBNP, ng/L, median (IQR)	1164 (698–3678)	1631 (885–3154)	< 0.001
Serum creatinine, mg/dL, $\bar{x}$ (SD)	1.1 (0.3)	1.1 (0.3)	1.000
Serum potassium, mmol, $\bar{x}$ (SD)	4.5 (0.5)	4.5 (0.5)	1.000
Systolic BP, mmHg, $\bar{x}$ (SD)	123 (19)	122 (15)	0.589
Beta-blockers, n (%)	105 (97)	3899 (93)	0.094
ACEI/ARB, n (%)	108 (100)	4185 (100)	1.000
MRA, n (%)	100 (93)	2271 (54)	< 0.001
ICD, n (%)	58 (54)	623 (15)	< 0.001
CRT, n (%)	20 (19)	292 (7)	< 0.001
Waiting list for heart transplantation	8 (7)	0	–

HF heart failure, $\bar{x}$ mean, *SD* standard deviation, *LVEF* left ventricular ejection fraction, *NYHA* New York Heart Association, *ng* nanograms, *L* liter, *IQR* interquartile range, *mg* milligrams, *dL* deciliter, *mmol* milimoles, *BP* blood pressure, *mm* millimeters, *ACEI* angiotensin converter enzyme inhibitors, *ARB* aldosterone receptor blockers, *MRA* mineralocorticoed receptor antagonist, *ICD* implantable cardiac defibrillator, *CRT* cardiac resynchronization therapy

C Moliner-Abos et al Cardiovasc Drugs Ther. 2019 Feb 28. doi: 10.1007/s10557-019-06858-0. [Epub ahead of print]

Variazioni osservate dopo 6 mesi medi di trattamento

Riduzione delle ospedalizzazioni (23% vs. 8%, $p < 0.05$) , miglioramento della classe NYHA,

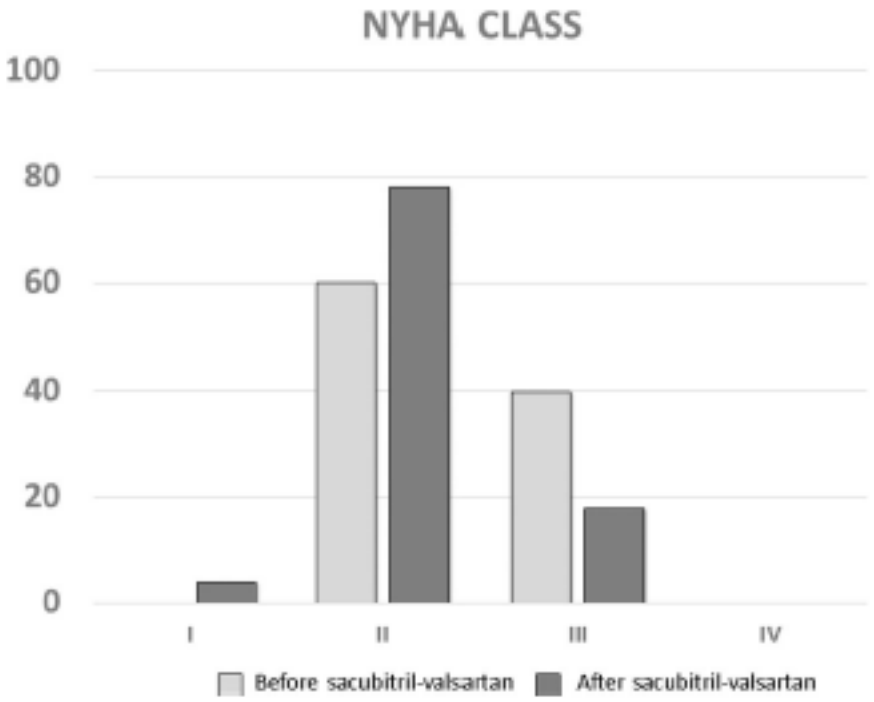
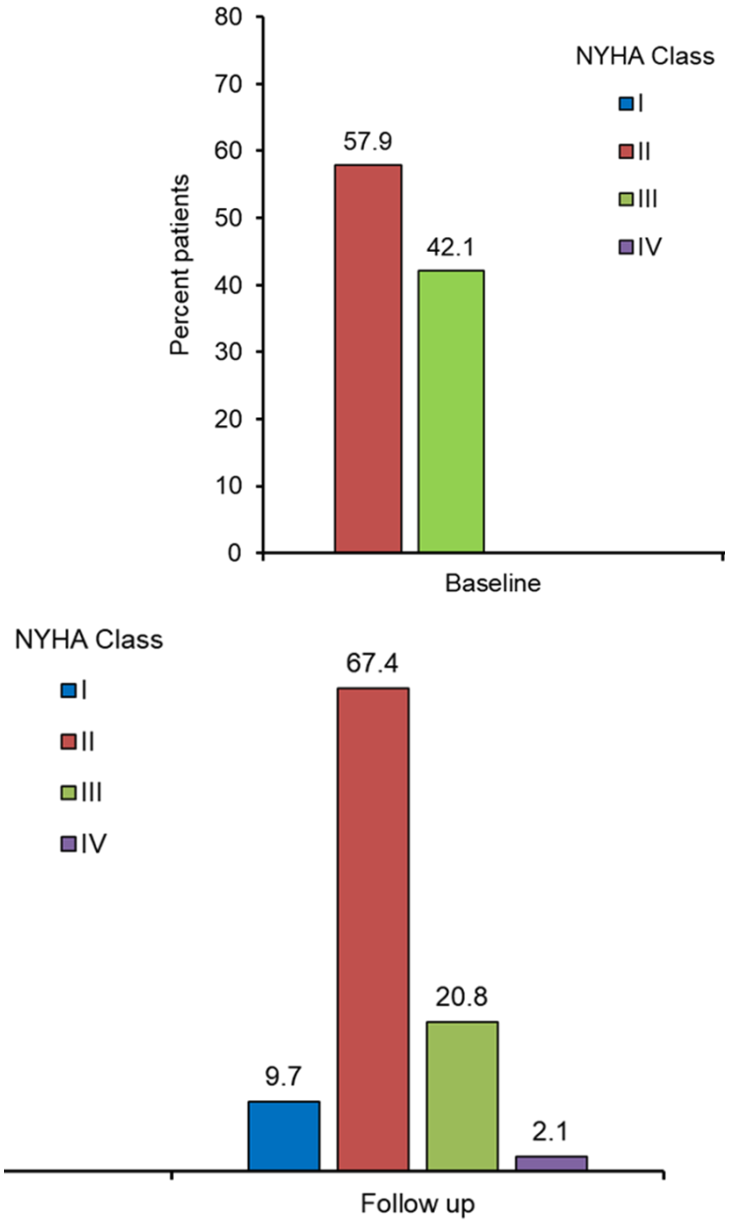


Fig. 1 NYHA class before and after the treatment with sacubitril/valsartan. Results are expressed in percentage of patients. NYHA, New York Heart Association

C Moliner-Abos et al Cardiovasc Drugs Ther. 2019 Feb 28. doi: 10.1007/s10557-019-06858-0. [Epub ahead of print]

	Patients (n=175)
Age, yr, mean ± SD	58.6 ± 9.8
Female sex, no. (%)	27 (15.4)
Systolic blood pressure, mmHg, mean ± SD	118 ± 15.5
eGFR, mL/min/1.73m^2, median (range)	66.2 (24–155)
Serum potassium, mEq/L, median (range)	4.2 (3-5.5)
Nt-pro-BNP, median (range)	1252 (78-15147)
NYHA functional class, no. (%)	
II	106 (60.6)
III	68 (38.9)
Treatment at randomization, no. (%)	
Furosemide	155 (88.6)
Furosemide dose, mean ± SD	137 ± 161.2
Antialdosterone	146 (83.4)
Antialdosterone dose, mg, mean ± SD	28.7 ± 8.3
ACE-inhibitors	113 (64.6)
Sartans	55 (31.4)
Beta-blockers	162 (92.6)
Ivabradine	33 (18.9)
Digoxin	15 (8.6)
Implantable cardioverter defibrillator	139 (79.9)
Cardiac resynchronization therapy	44 (25.1)



ISMETT – Osp. Buccheri La Ferla Fatebenefratelli

GRAZIE

Il vero viaggio di scoperta non consiste nel cercare nuove terre, ma nell'avere nuovi occhi

(Marcel Proust)