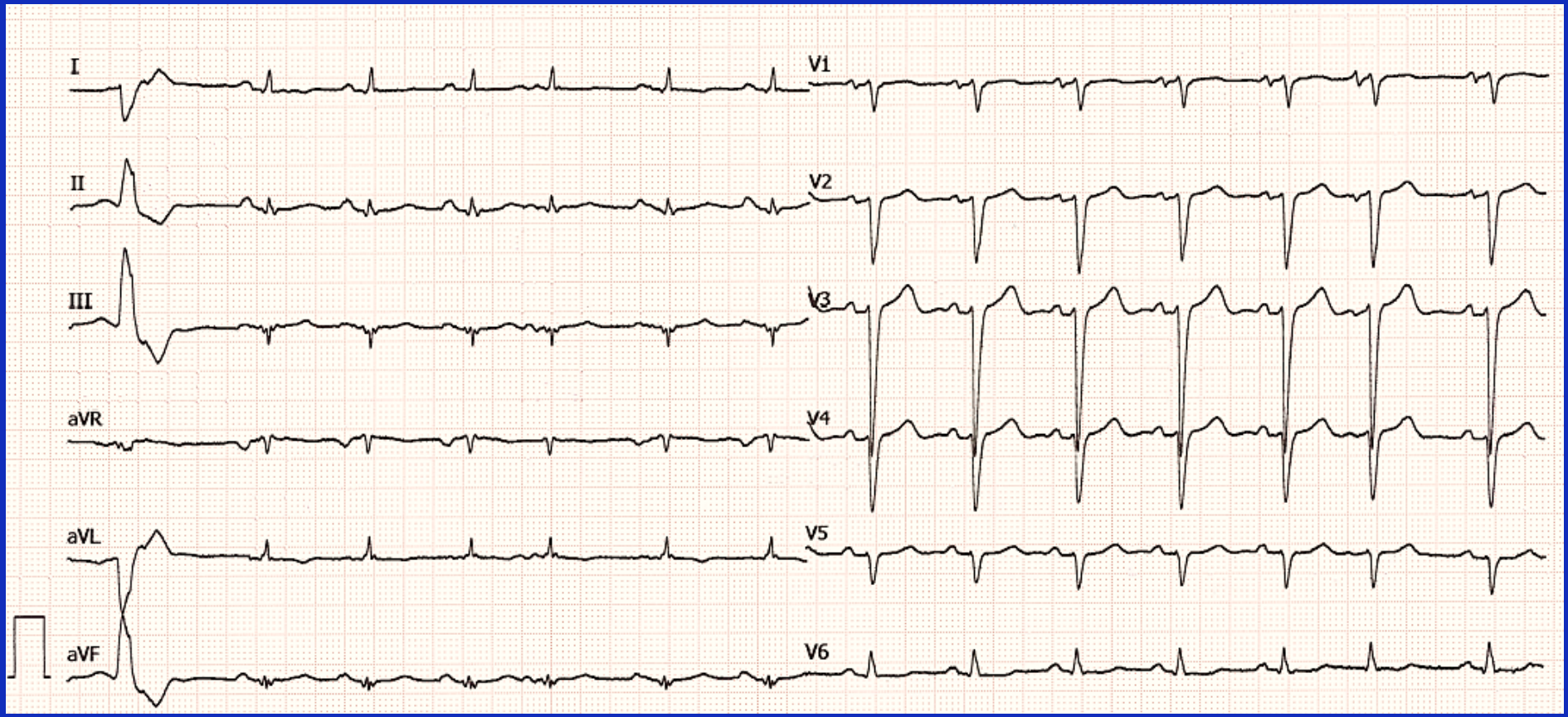
Le traitement de l'insuffisance cardiaque en 2016

Dr Philippe Meyer
Médecin adjoint agrégé
Service de cardiologie
Hôpitaux Universitaires de Genève
philippe.meyer@hcuge.ch

Colloque – FER – 10.11.2016

Vignette clinique: Monsieur A. C. 65 ans

AP	• S/P infarctus du myocarde en 1995 avec échec de thrombolyse et de PTCA de l'IVA • Hyperplasie bénigne de la prostate
AA	• Dyspnée progressive depuis mai 2015, stade NYHA III, orthopnée, OMI, Ø DRS
FRCV	• Ancien tabagisme, ancienne HTA, dyslipidémie
Médic.	• Aspirine 100 mg 1-0-0 • Crestor 5 mg 0-0-1 • Pradif 400 µg 1-0-0
Status	• TA 112/64 mmHg, FC régulière 90 bpm • TJ, déplacement latéral du choc de pointe, OMI → genoux ddc • Souffle holosystolique 3/6 apex, Ø B3. Auscult. pulmonaire sp
Labo	• Na 134, K 4.2, créat 98 (eGFR 62), NT-proBNP 7140


I
II
III
aVR
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aVF
V1
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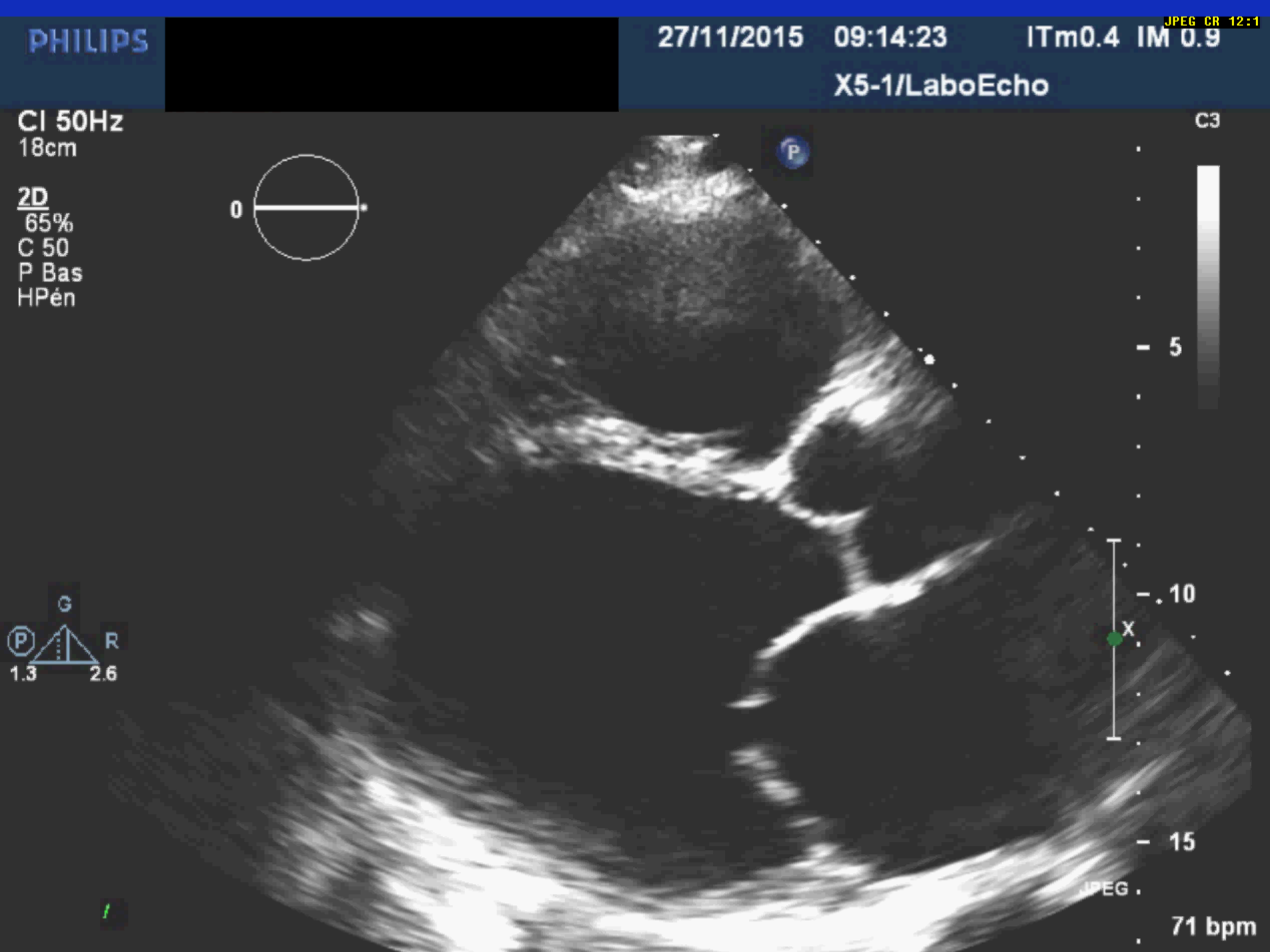
V6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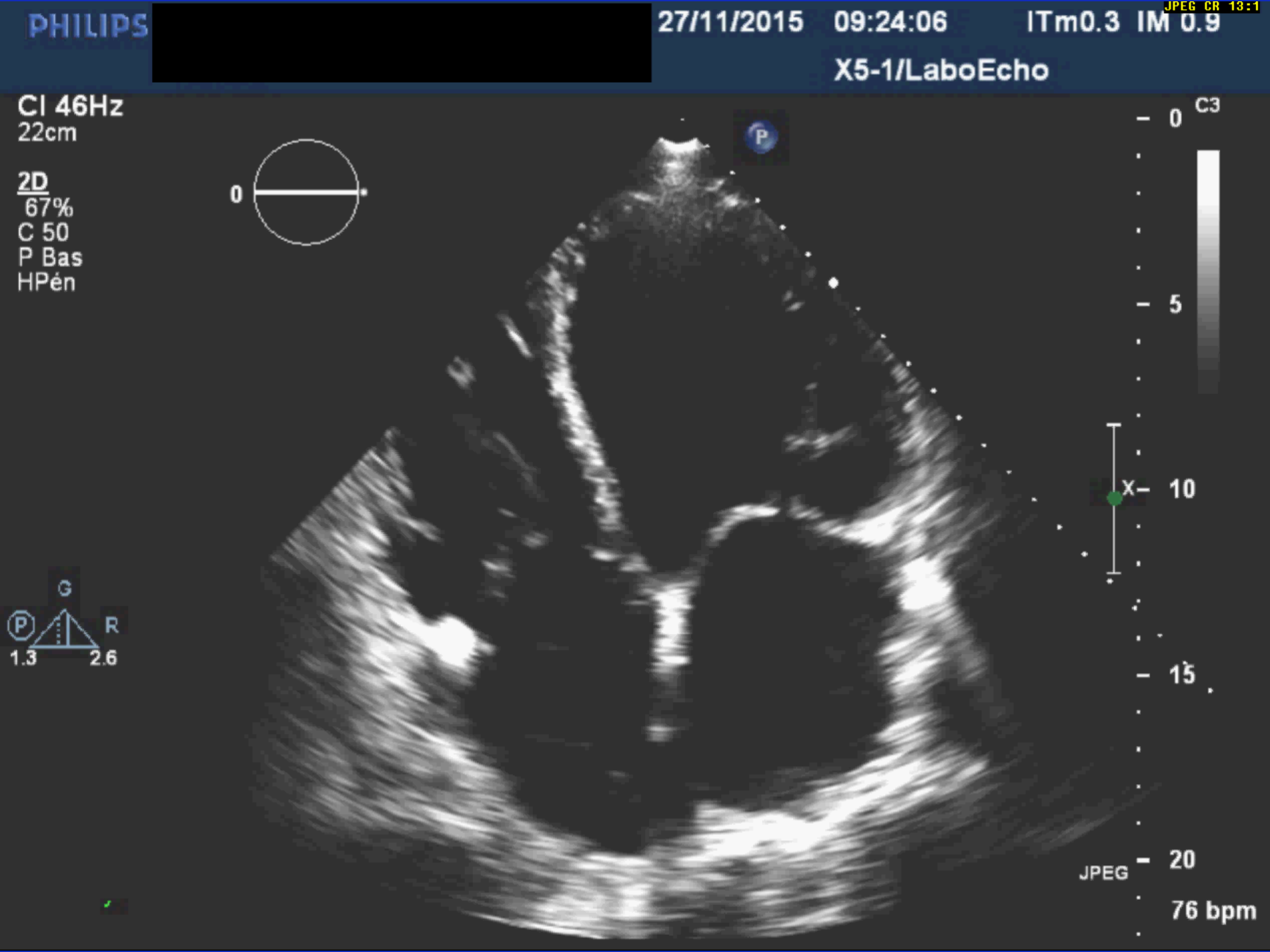
71 bpm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2.6
JPEG
76 bpm

Comment traiter ce patient en 2016?

European Heart Journal Advance Access published May 20, 2016

European Heart Journal
doi:10.1093/eurheartj/ehw128

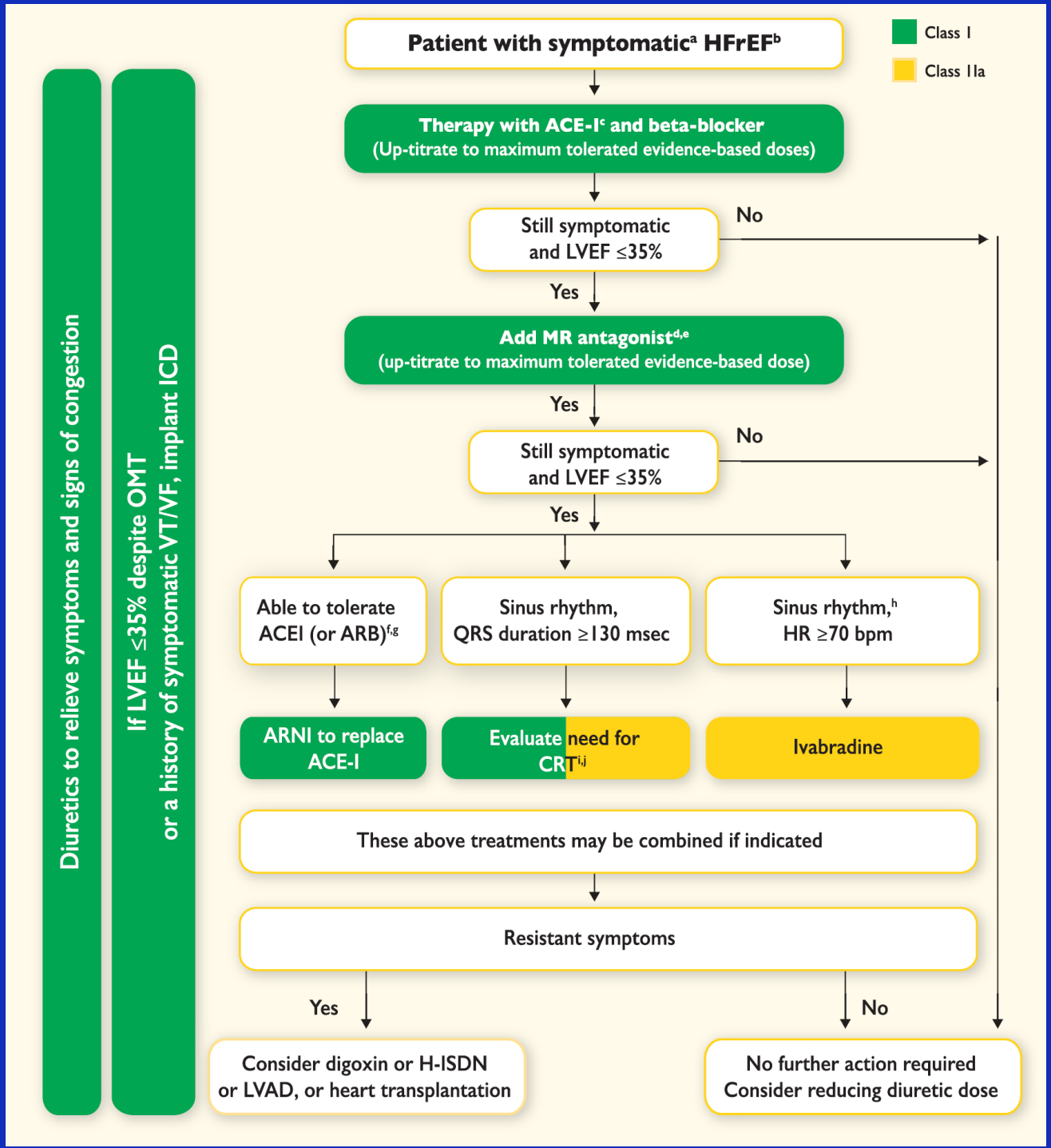
ESC GUIDELINES

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)

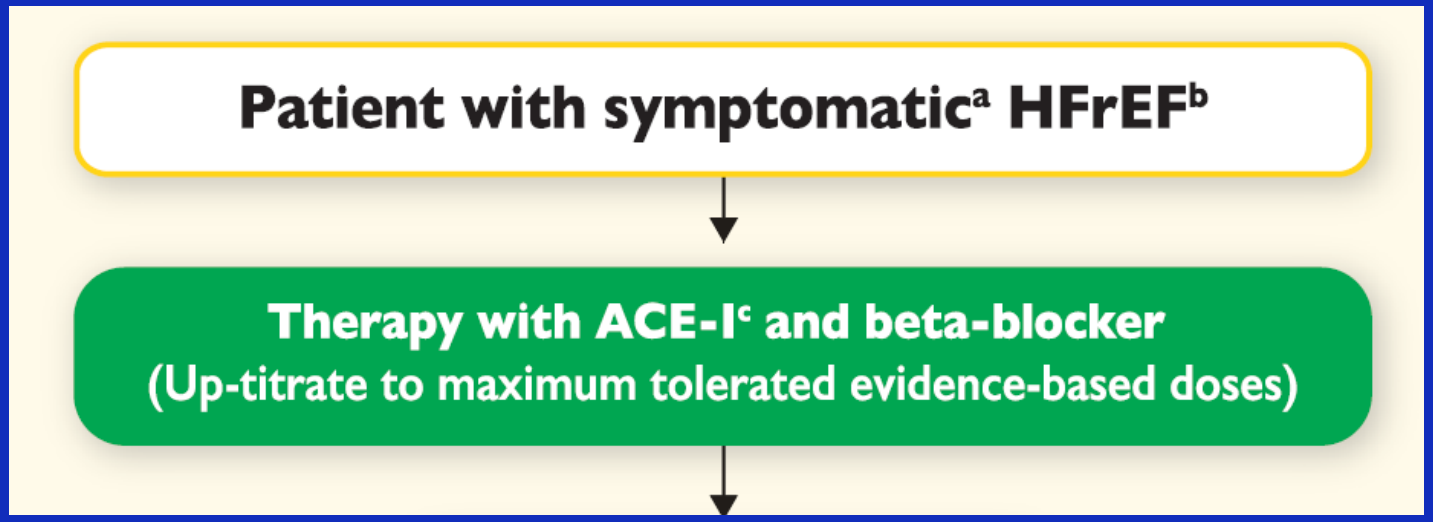
Developed with the special contribution of the Heart Failure Association (HFA) of the ESC

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)


Class I
Class IIa
Patient with symptomatic[a] HFrEF[b]
Therapy with ACE-I[c] and beta-blocker
(Up-titrate to maximum tolerated evidence-based doses)
Still symptomatic and LVEF ≤35%
No
Yes
Add MR antagonist[d,e]
(up-titrate to maximum tolerated evidence-based dose)
Yes
Still symptomatic and LVEF ≤35%
No
Yes
Able to tolerate ACEI (or ARB)[f,g]
Sinus rhythm, QRS duration ≥130 msec
Sinus rhythm,[h] HR ≥70 bpm
ARNI to replace ACE-I
Evaluate need for CRT[i,j]
Ivabradine
These above treatments may be combined if indicated
Resistant symptoms
Yes
No
Consider digoxin or H-ISDN or LVAD, or heart transplantation
No further action required
Consider reducing diuretic dose
Diuretics to relieve symptoms and signs of congestion
If LVEF ≤35% despite OMT or a history of symptomatic VT/VF, implant ICD

1ère ligne: diurétiques + IEC + BB

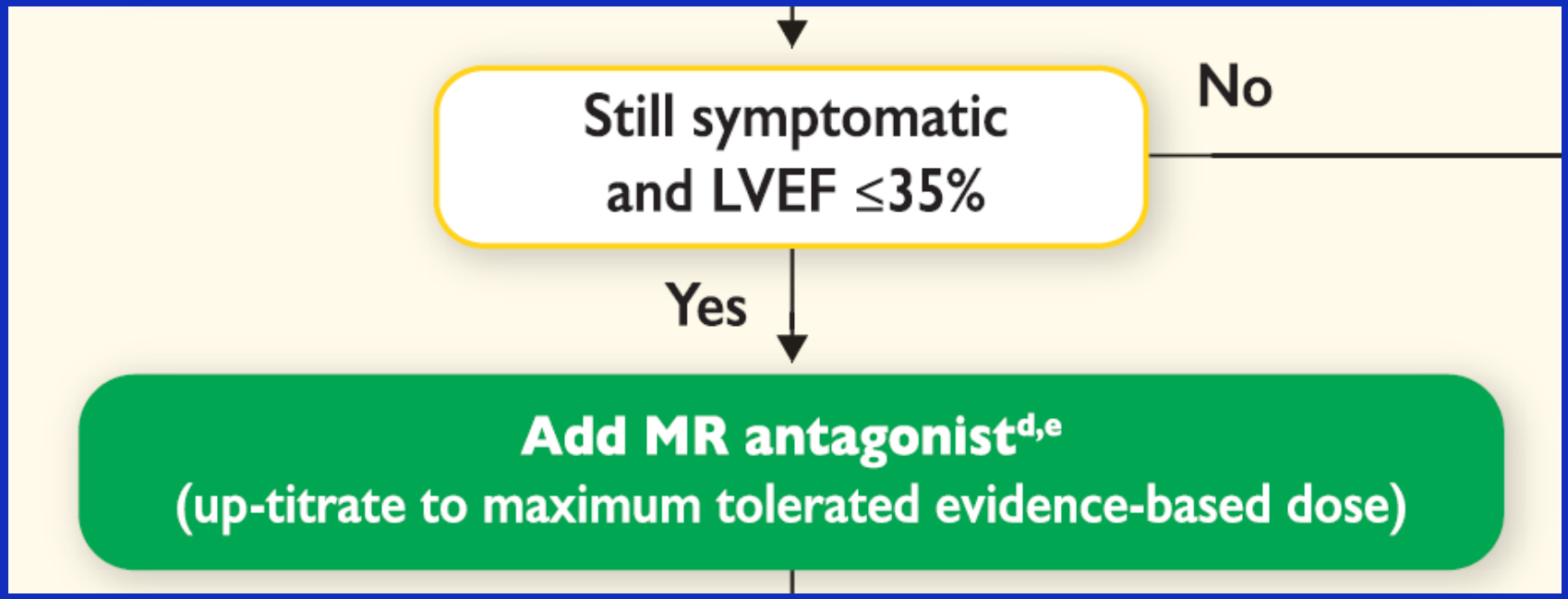
Diuretics to relieve symptoms and signs of congestion



Diurétiques, IEC et BB en pratique clinique

- Congestion persistante = symptômes persistants + **inefficacité des autres médicaments**
- **« Start low, go slow, AIM HIGH »**
- N'utiliser que les **bétabloquants «validés»**

2ème ligne: antagonistes de l'aldostérone



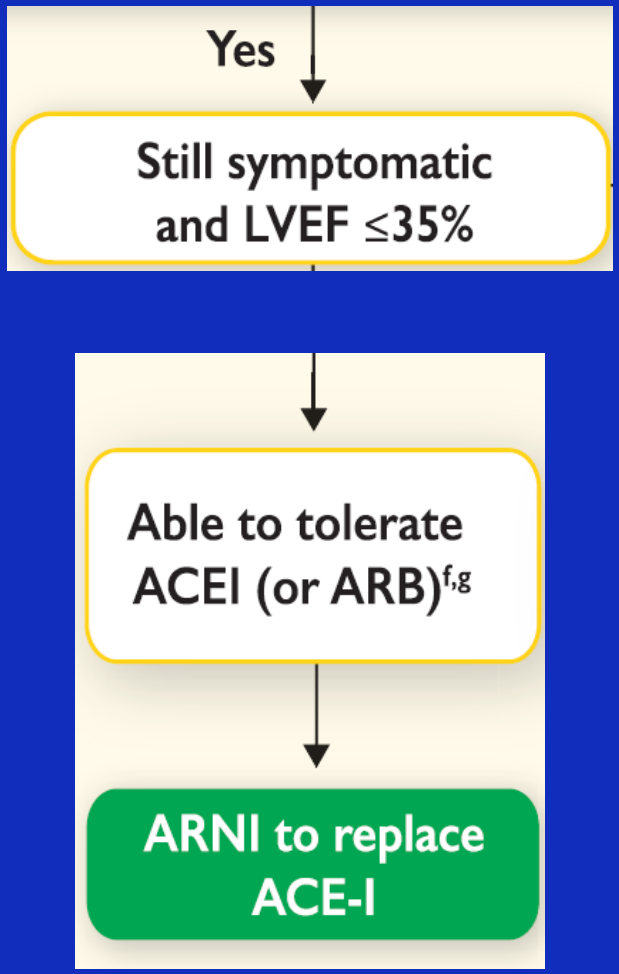
Antag. aldo. en pratique clinique:

- **Attention à l'hyperkaliémie!**
- **Eplérénone si gynécomastie**

Vignette clinique: Monsieur A. C. 65 ans (2 mois plus tard)

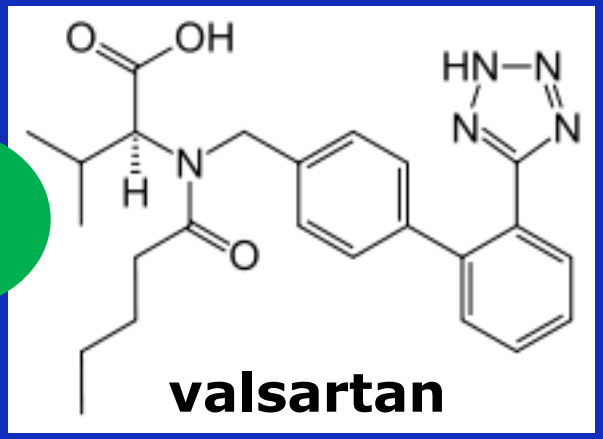
AA	• Dyspnée persistante, stade II-III, légers vertiges orthostatiques
Médic.	Aspirine 100 mg 1-0-0 Enalapril 2.5 mg 1-0-1 Aldactone 25 mg 1-0-0 Crestor 5 mg 0-0-1 Torem 5 mg 1-0-0 Pradif 400 µg 1-0-0 Beloc zok 50 mg 1-0-0
Status	• TA 92/64 mmHg, FC régulière 68 bpm • TJ, déplacement latéral du choc de pointe, OMI malléolaires • Souffle holosystolique 3/6 apex, Ø B3. Auscult. pulmonaire sp
Labo	• Na 136, K 4.6, créat 110 (eGFR 56), NT-proBNP 6452

3ème ligne: remplacer IEC par ARNI



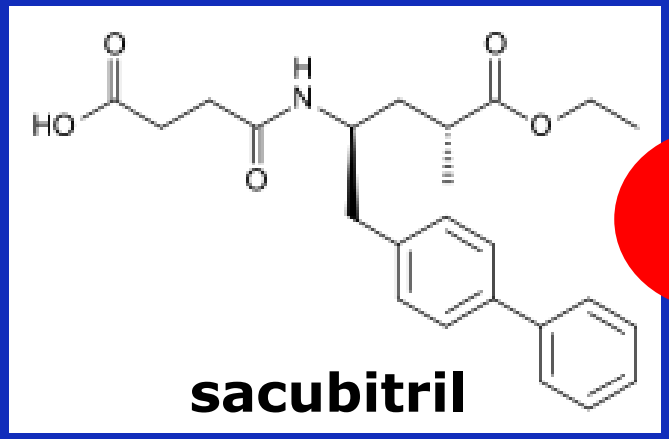
ARNI = Angiotensin receptor-neprilysin inhibitor

AR



valsartan

+



sacubitril

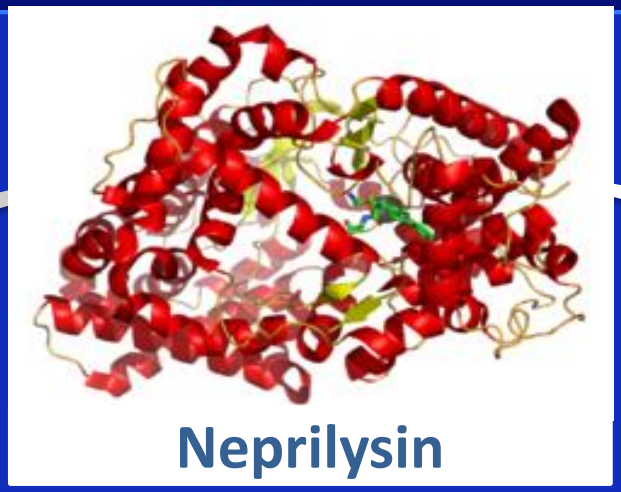
NI

ARB

Neprilysin inhibitor
(via LBQ657)

LCZ-696

Neprilysin inhibition



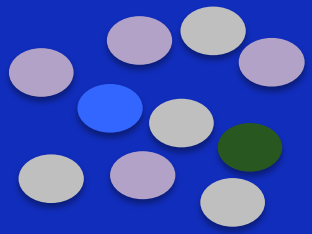
ET-1

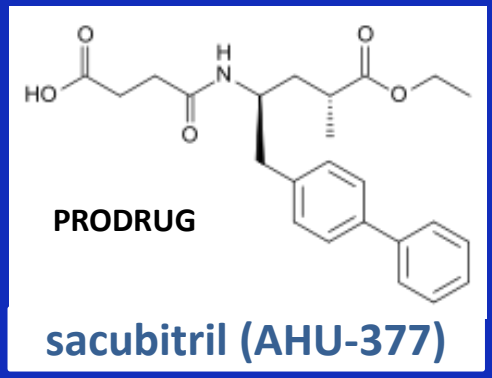
ANP

AT-2

BNP

BK





LBQ-657

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 11, 2014 VOL. 371 NO. 11

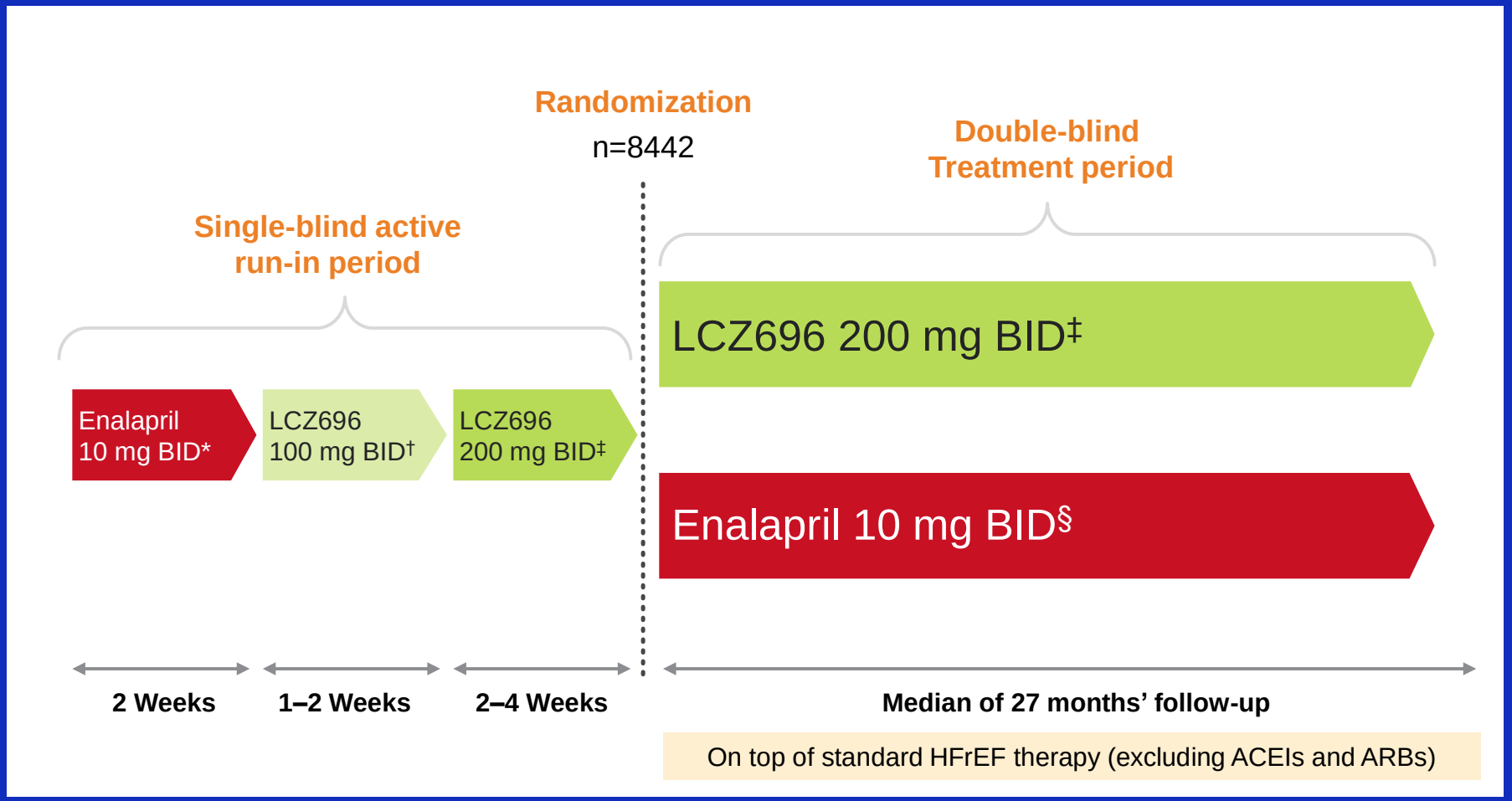
Angiotensin–Neprilysin Inhibition versus Enalapril in Heart Failure

John J.V. McMurray, M.D., Milton Packer, M.D., Akshay S. Desai, M.D., M.P.H., Jianjian Gong, Ph.D., Martin P. Lefkowitz, M.D., Adel R. Rizkala, Pharm.D., Jean L. Rouleau, M.D., Victor C. Shi, M.D., Scott D. Solomon, M.D., Karl Swedberg, M.D., Ph.D., and Michael R. Zile, M.D., for the PARADIGM-HF Investigators and Committees*

Prospective comparison of **ARNI** with **A**CEI to **D**etermine **I**mpact on **G**lobal **M**ortality and morbidity in **H**eart **F**ailure

New Engl J Med 2014;371:993-1004.

Design de l'étude PARADIGM-HF

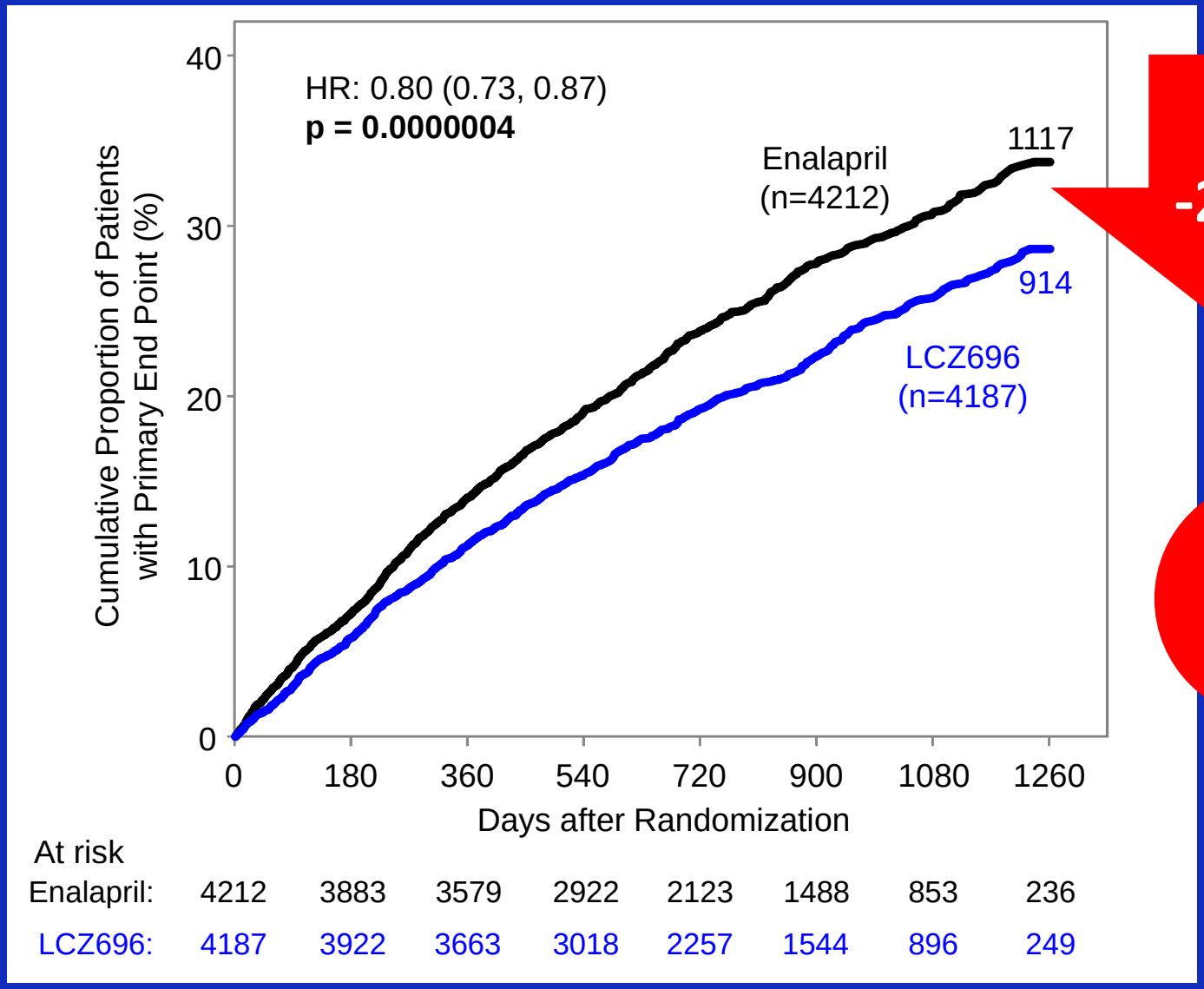


*Enalapril 5 mg BID (10 mg TDD) for 1–2 weeks followed by enalapril 10 mg BID (20 mg TDD) as an optional starting run-in dose for those patients who are treated with ARBs or with a low dose of ACEI; †200 mg TDD; ‡400 mg TDD; §20 mg TDD.

Main inclusion criteria

- **CHF NYHA Class II–IV and LVEF ≤ 40%**
  - BNP ≥ 150 pg/ml (NT-proBNP ≥600 pg/ml) ***OR***
  - BNP ≥ 100 pg/ml (NT-proBNP ≥400 pg/ml) and a hospitalization for HF within the last 12 months
- **Must be taking ACEI or ARB: i) dose equivalent to enalapril ≥10 mg/d ii) stable dose for at least 4 weeks**
- **Must be taking a β-blocker: unless contraindicated or not tolerated; stable dose for at least 4 weeks**
- **MRA (aldosterone antagonist) where indicated: e.g. RALES type patient**
- **Individually optimized dosing of background HF medications**

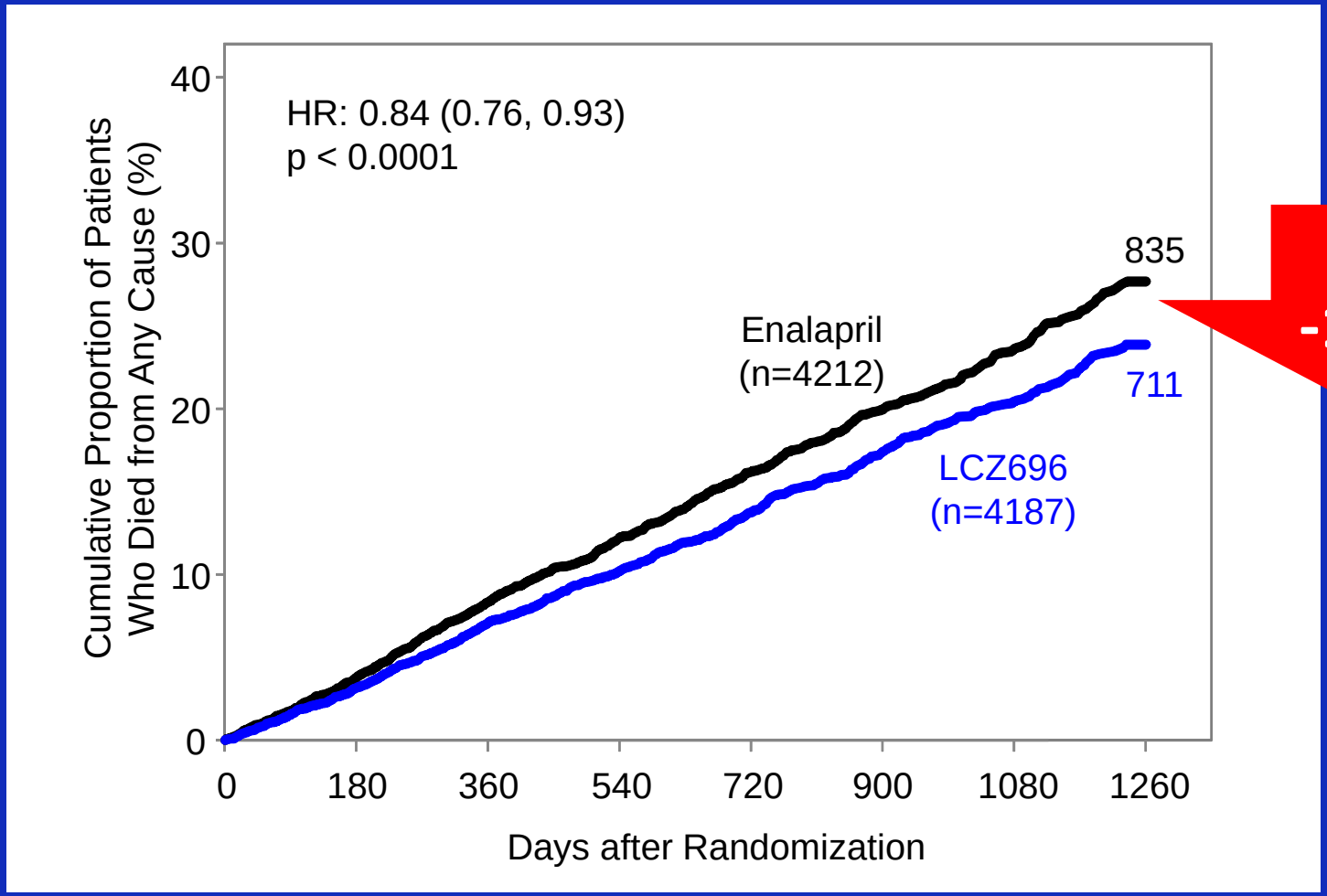
Primary endpoint: CV mortality + HF hospitalizations



RR
-20%

NNT
21

Secondary endpoint: all-cause mortality



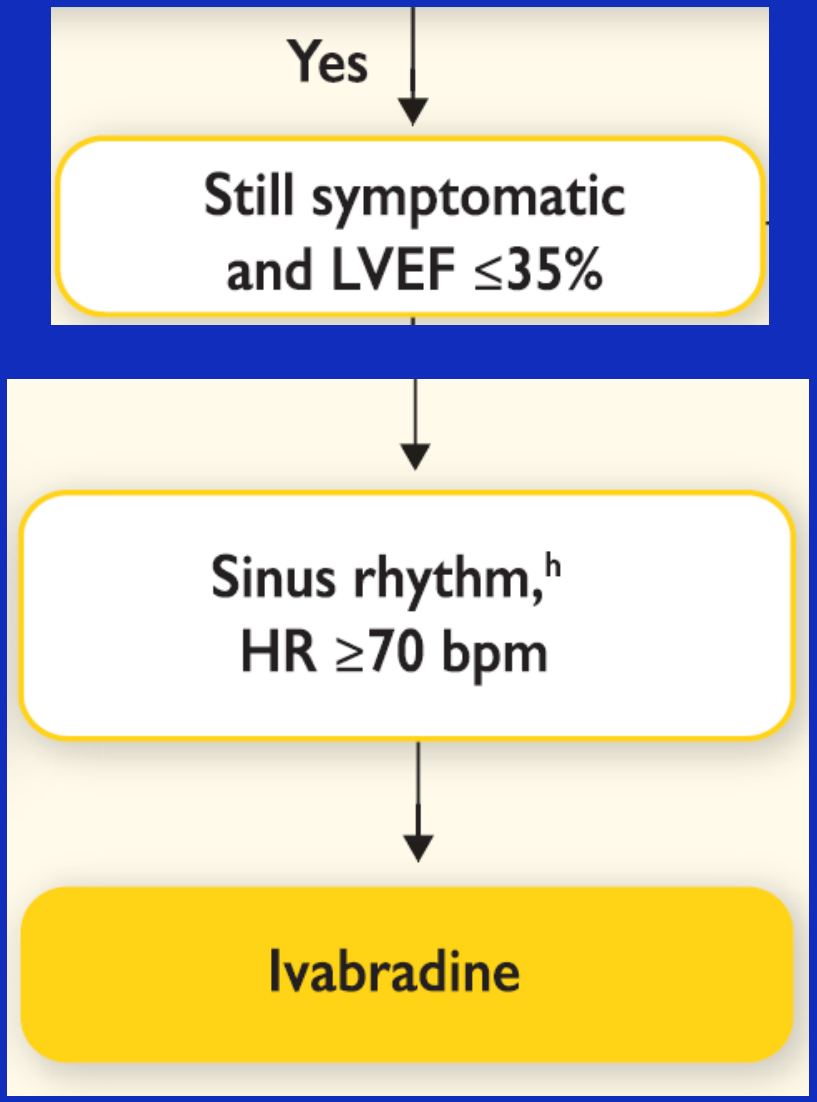
Safety

	LCZ696 (n=4187)	Enalapril (n=4212)	p value
Hypotension (%)			
symptoms	14.0	9.2	< 0.001
symptoms and SBP < 90 mmHg	2.7	1.4	<0.001
Renal impairment (%)			
Cr ≥ 2.5 mg/dl	3.3	4.5	0.007
Cr ≥ 3.0 mg/dl	1.5	2.0	0.10
Hyperkalaemia (%)			
K^+ > 5.5 mmol/l	16.2	17.4	0.15
K^+ > 6.0 mmol/l	4.3	5.6	0.007
Cough (%)	11.3	14.3	< 0.001

Le LCZ 696 en pratique clinique

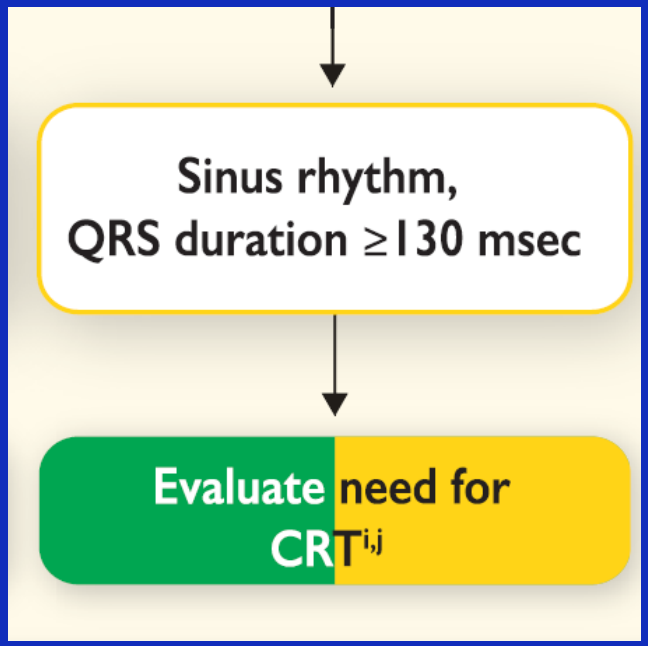
- Commencer à **50 mg 2x/j** si patient «**naïf d'IEC/sartans**» ou si sous des faibles doses d'IEC, équivalentes à **10 mg/j d'énalapril**
- « **Wash-out » de 36 heures** après l'arrêt des IEC (risque d'angiœdème)
- Titrer à la hausse (**doubler**) toutes les **2-4 sem**
- **Contrôler créatinine and électrolytes** 1-2 sem après début traitement et changement de doses.

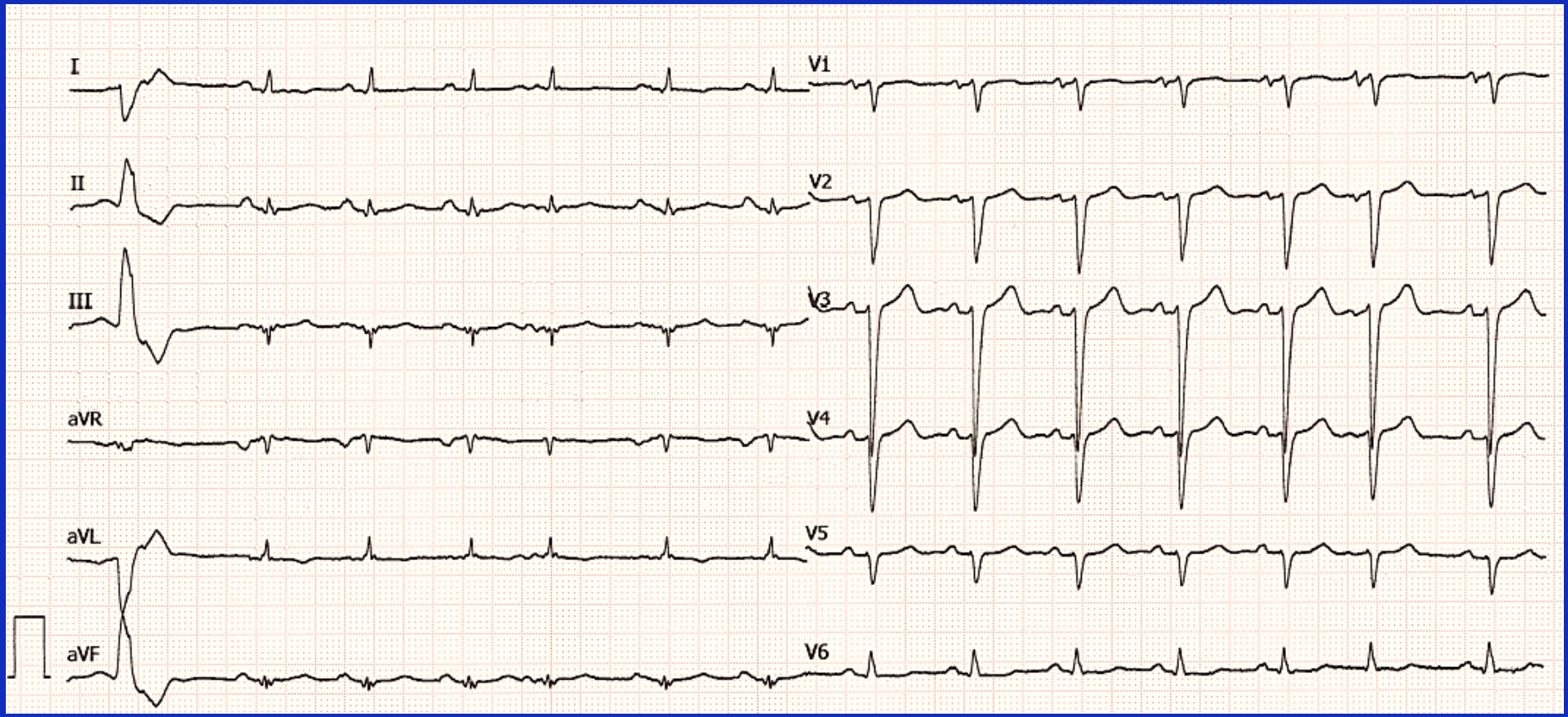
3ème ligne: considérer l'ivabradine



3ème ligne: considérer défibrillateur et/ou CRT

If LVEF ≤35% despite OMT
or a history of symptomatic VT/VF, implant ICD




I
II
III
aVR
aVL
aVF
V1
V2
V3
V4
V5
V6

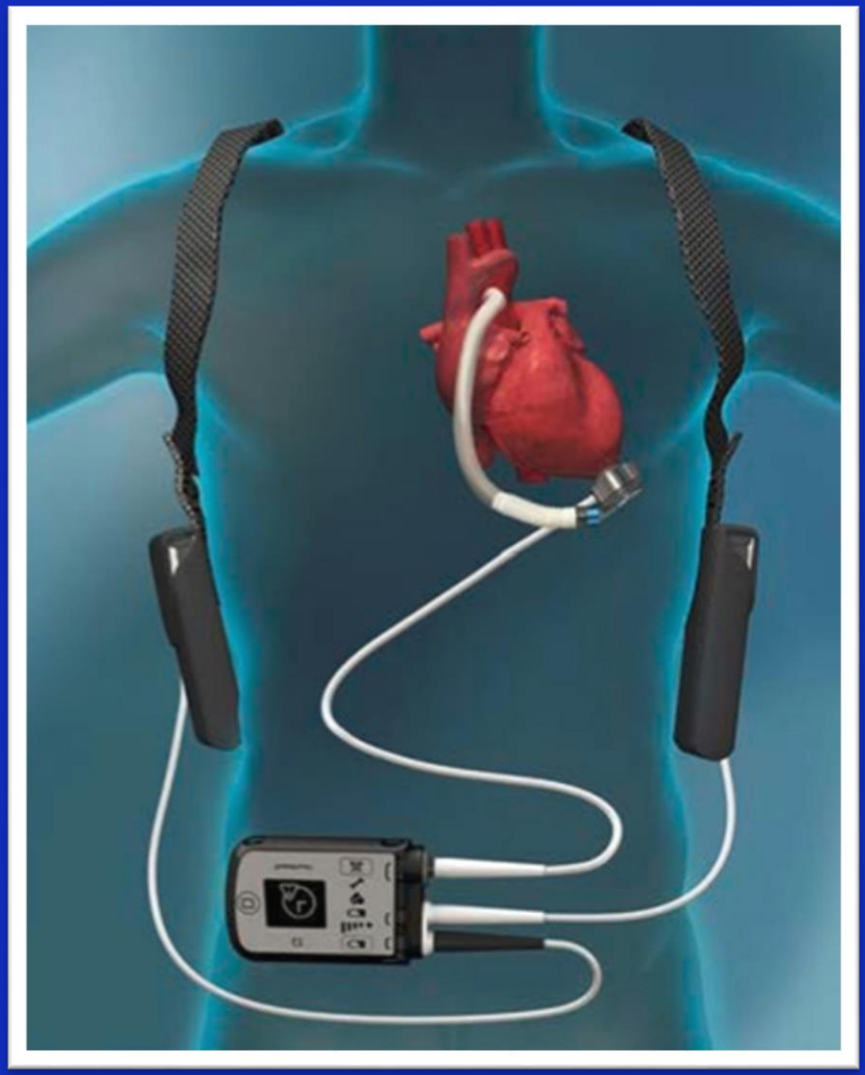
Vignette clinique: Monsieur A. C. 65 ans (suite)

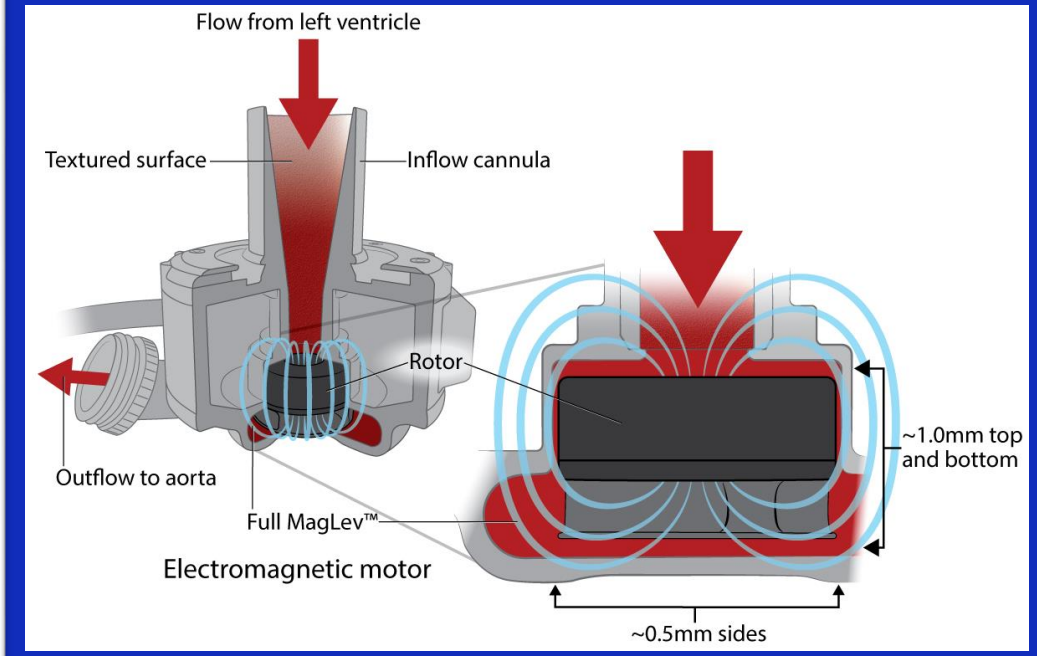
AA	• Dyspnée persistante, stade II-III, légers vertiges orthostatiques
Médic.	Aspirine 100 mg 1-0-0 Enalapril 2.5 mg 1-0-1 Aldactone 25 mg 1-0-0 Crestor 5 mg 0-0-1 Torem 5 mg 1-0-0 Pradif 400 µg 1-0-0 Beloc zok 50 mg 1-0-0
Status	• TA 92/64 mmHg, FC régulière 68 bpm • TJ, déplacement latéral du choc de pointe, OMI malléolaires • Souffle holosystolique 3/6 apex, Ø B3. Auscult. pulmonaire sp
Labo	• Na 136, K 4.6, créat 110 (eGFR 56), NT-proBNP 6452
Défib.	• Octobre 2015

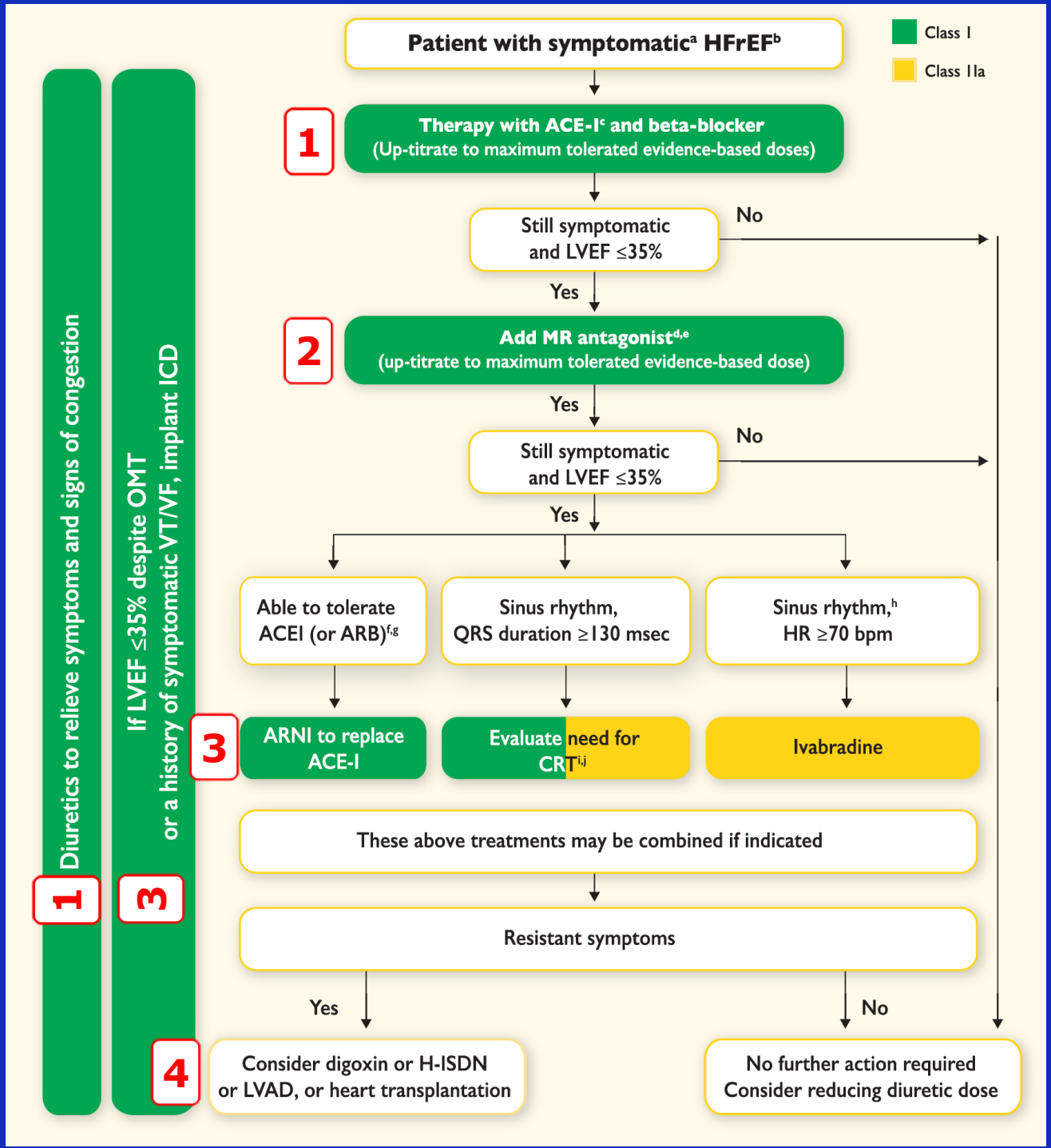
4ème ligne: considérer l'implantation d'une assistance ventriculaire et/ou la transplantation

Consider digoxin or H-ISDN
or LVAD, or heart transplantation

LVAD : HeartMate III implanté le 16.03.2016 en « bridge to transplant »






Class I
Class IIa
Patient with symptomatic[a] HFrEF[b]
1
Therapy with ACE-I[c] and beta-blocker
(Up-titrate to maximum tolerated evidence-based doses)
Still symptomatic and LVEF ≤35%
No
Yes
2
Add MR antagonist[d,e]
(up-titrate to maximum tolerated evidence-based dose)
Yes
Still symptomatic and LVEF ≤35%
No
Yes
Able to tolerate ACEI (or ARB)[f,g]
Sinus rhythm, QRS duration ≥130 msec
Sinus rhythm,[h] HR ≥70 bpm
3
ARNI to replace ACE-I
Evaluate need for CRT[i,j]
Ivabradine
These above treatments may be combined if indicated
Resistant symptoms
Yes
No
4
Consider digoxin or H-ISDN or LVAD, or heart transplantation
No further action required
Consider reducing diuretic dose
1 Diuretics to relieve symptoms and signs of congestion
3 If LVEF ≤35% despite OMT or a history of symptomatic VT/VF, implant ICD

UNIVERSITÉ DE GENÈVE
FACULTÉ DE MÉDECINE

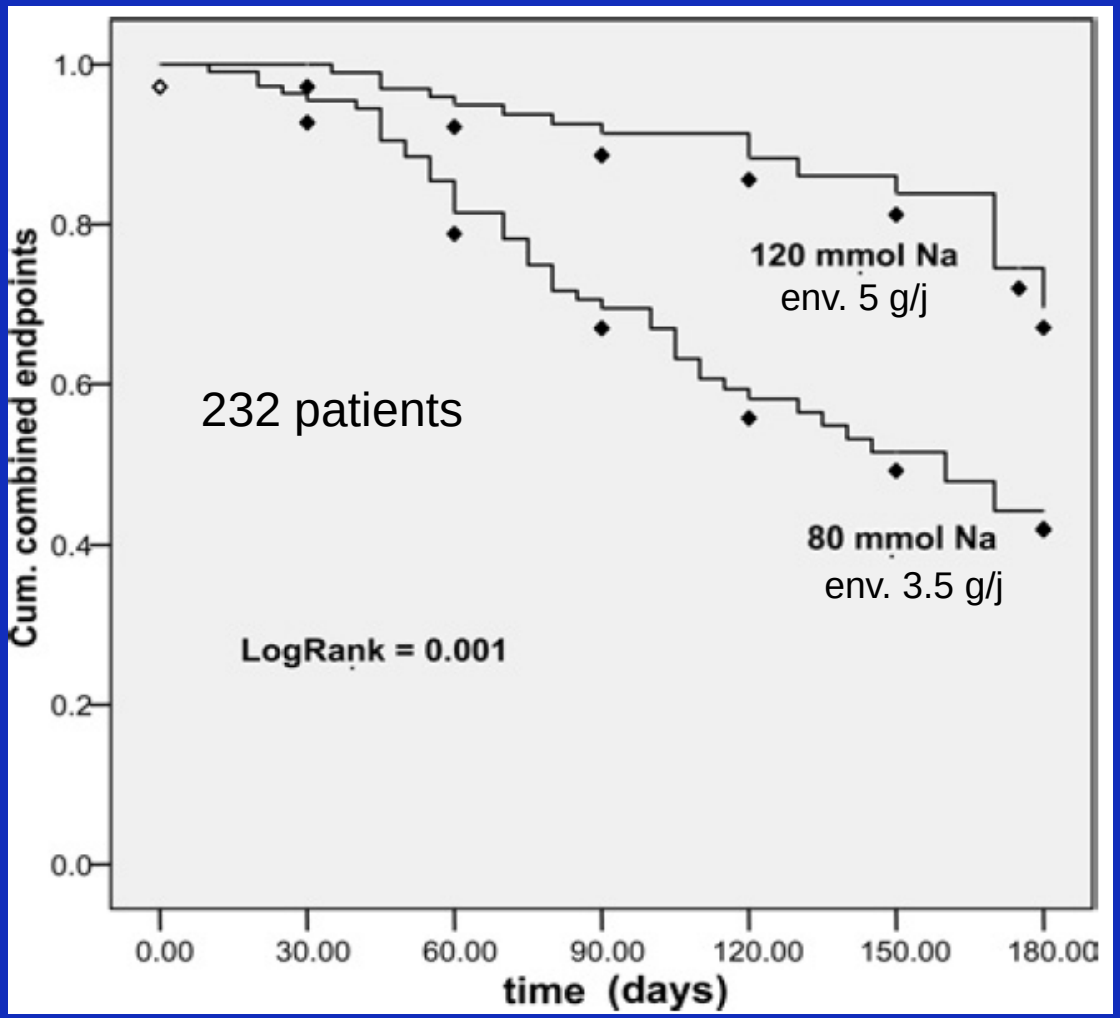
Hôpitaux Universitaires Genève

Merci !

Dr Philippe Meyer
Médecin adjoint agrégé
Service de cardiologie
Hôpitaux Universitaires de Genève
Philippe.meyer@hcuge.ch

Colloque – FER – 11.10.2016

RCT of "low" vs. "normal" sodium diet in systolic CHF



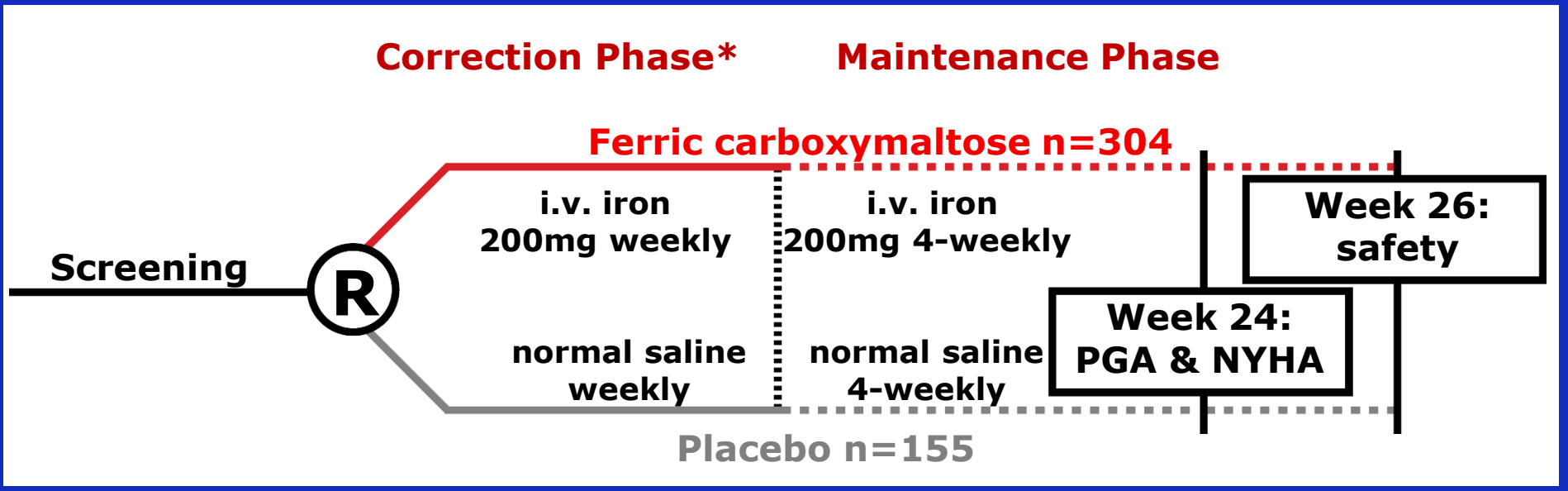
6 deaths
9 hospitalisations

15 deaths
30 hospitalisations

Clinical Science (2008) **114**, 221–230

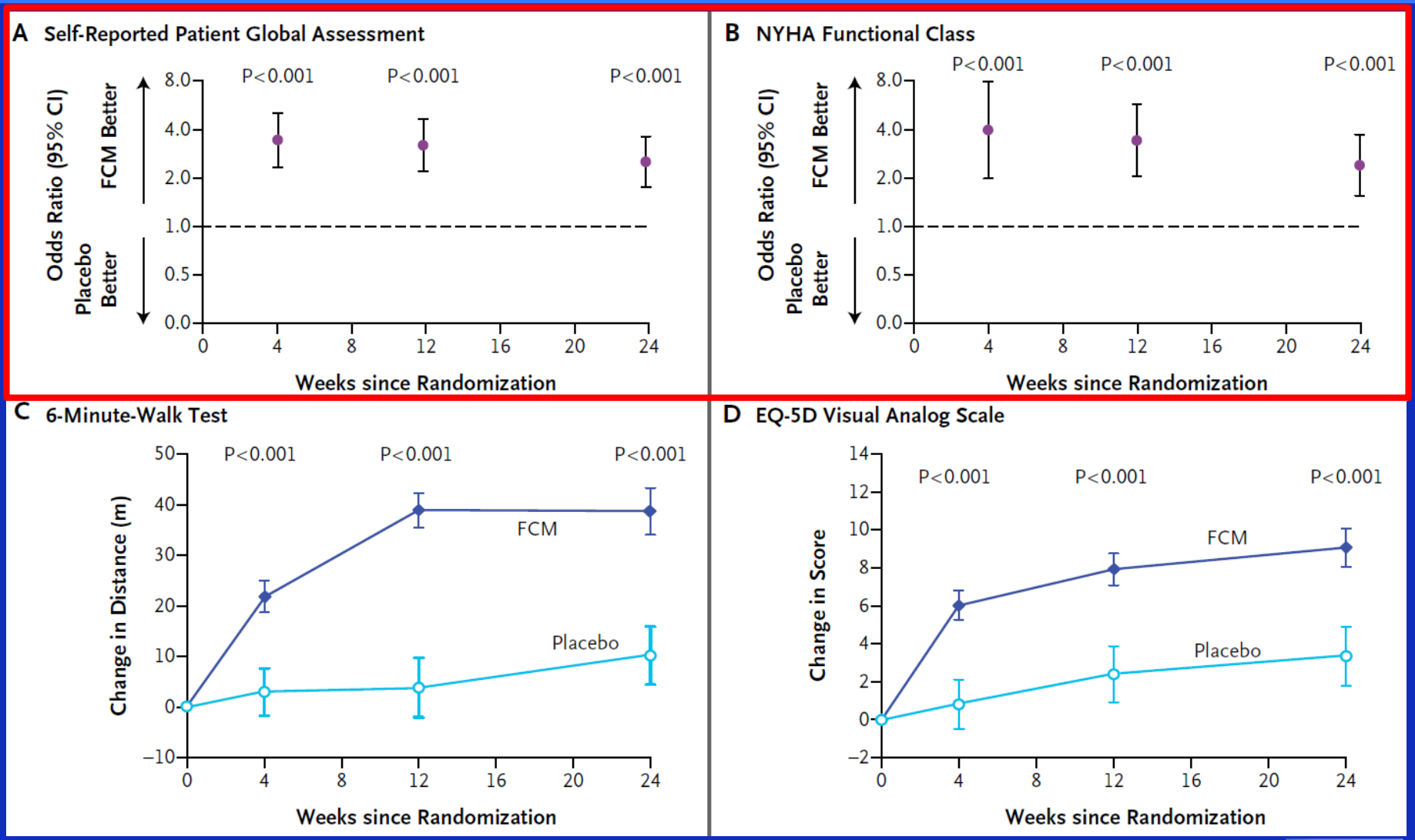
Ferric Carboxymaltose in Patients with Heart Failure and Iron Deficiency

- 459 patients with chronic heart failure
- NYHA class II / III, LVEF ≤40% (NYHA II) or ≤45% (NYHA III)
- Hb: 95–135 g/L
- Iron deficiency: serum ferritin <100 µg/L or <300 µg/L, if TSAT <20%
- Clinical staff: blinded and unblended personnel



Anker S et al. N Engl J Med 2009;361:2436-48

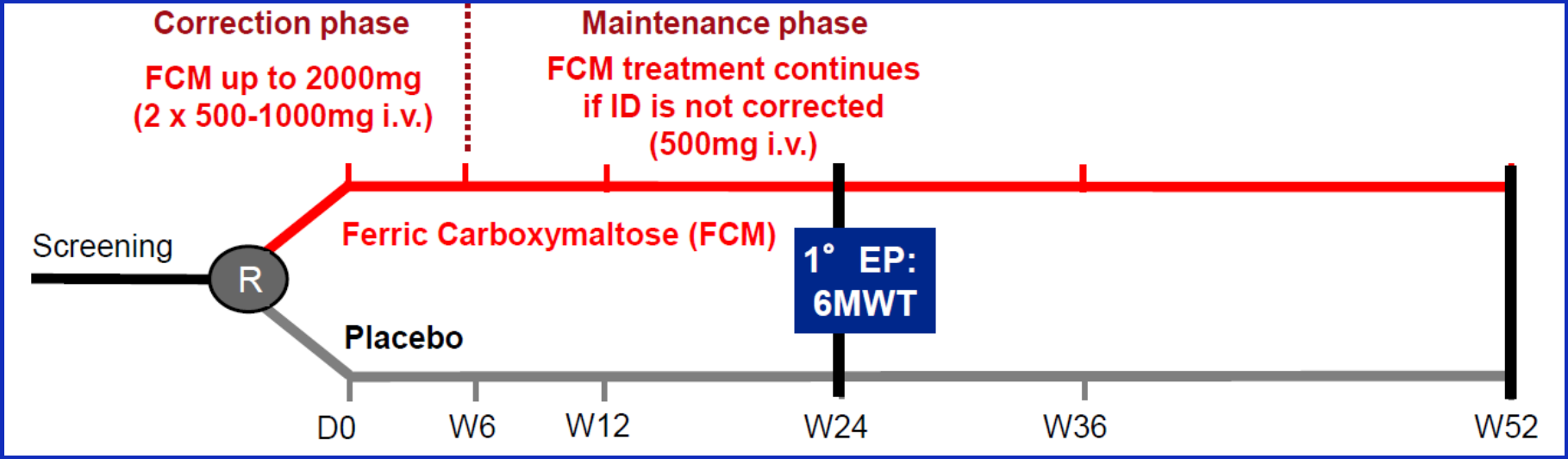
Ferric carboxymaltose improves symptoms, functional capacity and quality of life



Anker S et al. N Engl J Med;361:2436-48

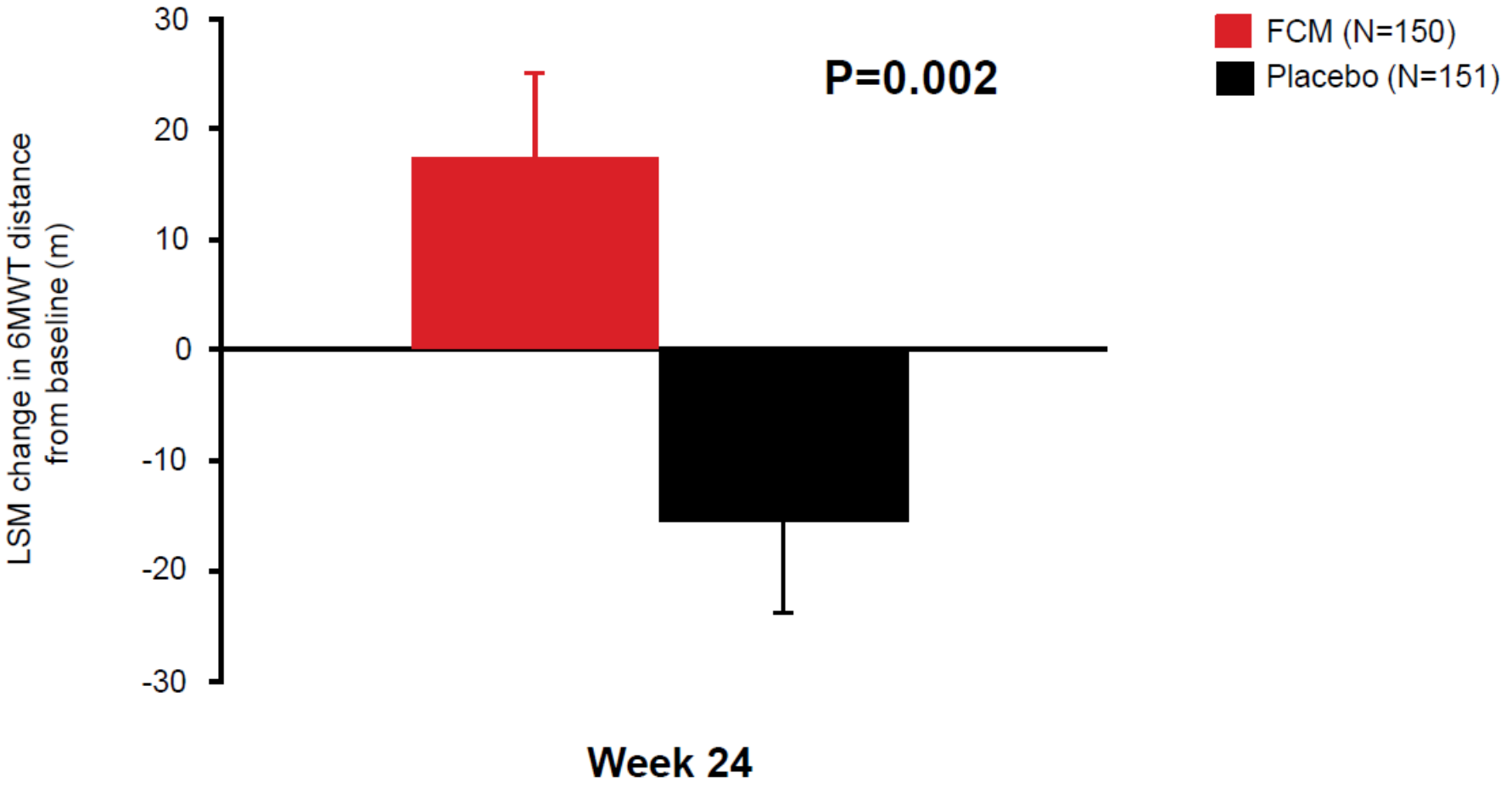
Beneficial effects of long-term intravenous iron therapy with ferric carboxymaltose in patients with symptomatic heart failure and iron deficiency†

- 304 patients with ambulatory heart failure
- NYHA class II / III, LVEF ≤45%
- BNP > 100 pg/mL or NT-proBNP > 400 pg/mL
- Iron deficiency: serum ferritin <100 ng/mL or 100-300 ng/mL if TSAT <20%
- Hb < 150 g/L



Ponikowski P et al. Eur Heart J 2014 Epub ahead of print

Ferric carboxymaltose improved 6MWT by 33 meters compared to placebo



Ponikowski P et al. Eur Heart J 2014 Epub ahead of print