

# Heart Failure and Cardiomyopathies

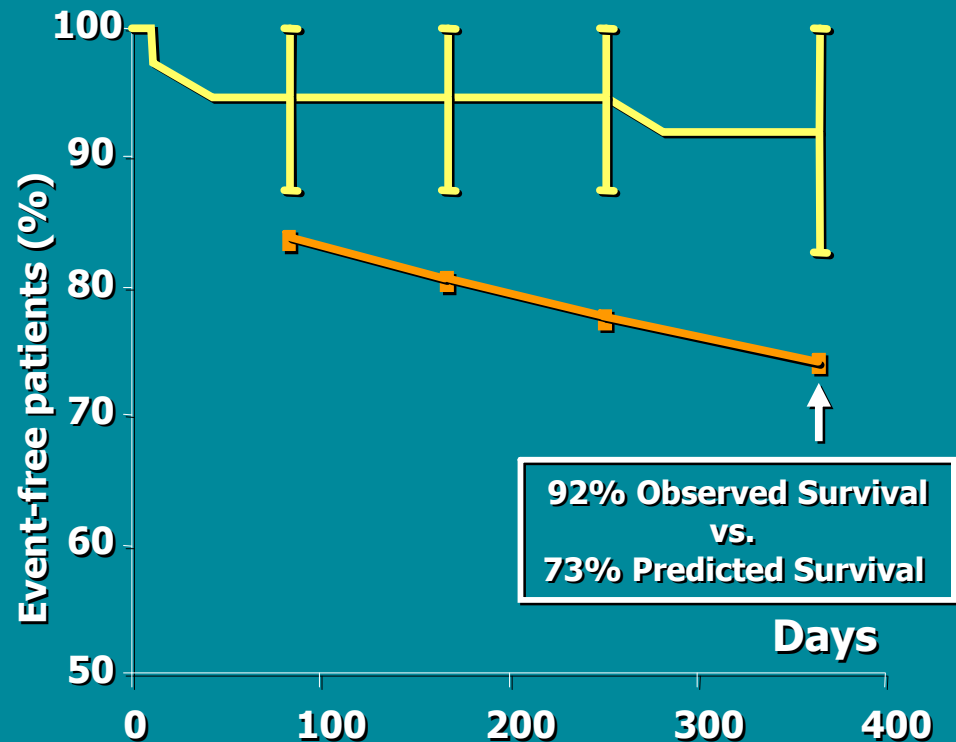
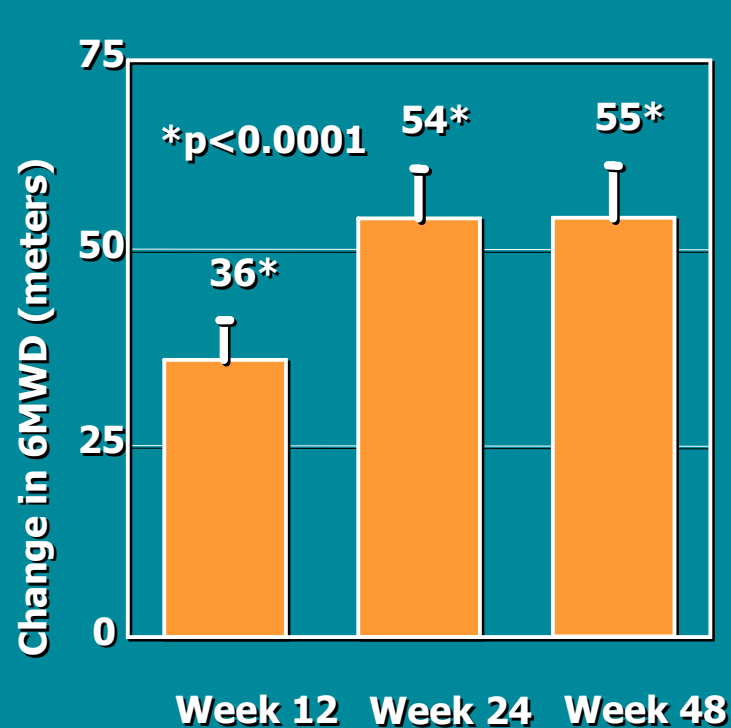
P Ponikowski (Wroclaw, PL)

*ESC CONGRESS 2005*



1. Pulmonary arterial hypertension
2. Acute heart failure
3. Chronic heart failure

# Long-term benefits of ambrisentan in patients with pulmonary arterial hypertension



- Ambrisentan had a durable benefit on exercise capacity
- It may also have a beneficial effect on mortality

*N Galie, IT; 762*

## AHF with Systolic Dysfunction

Oxygen, CPAP  
Furosemide ± Vasodilator  
Clinical evaluation (leading to mechanistic therapy)

**Congestion and low perfusion at rest ?**

**SBP > 100 mmHg**

Vasodilator  
(NTG, SNP, BNP)

Good response  
Oral therapy  
Furosemide, ACEi

**SBP 85 -100 mmHg**

Vasodilator and/or inotropic  
(dobutamine, PDEi,  
levosimendan)

**SBP < 85 mmHg**

Volume loading ?  
Inotrope and/or  
DA >5 µg/kg/min  
and/or NE

No response  
Reconsider mechanistic therapy  
Inotropic agents

# Treatment and outcome of CV in the female population in Europe – Results of the Euro Heart Survey Programme



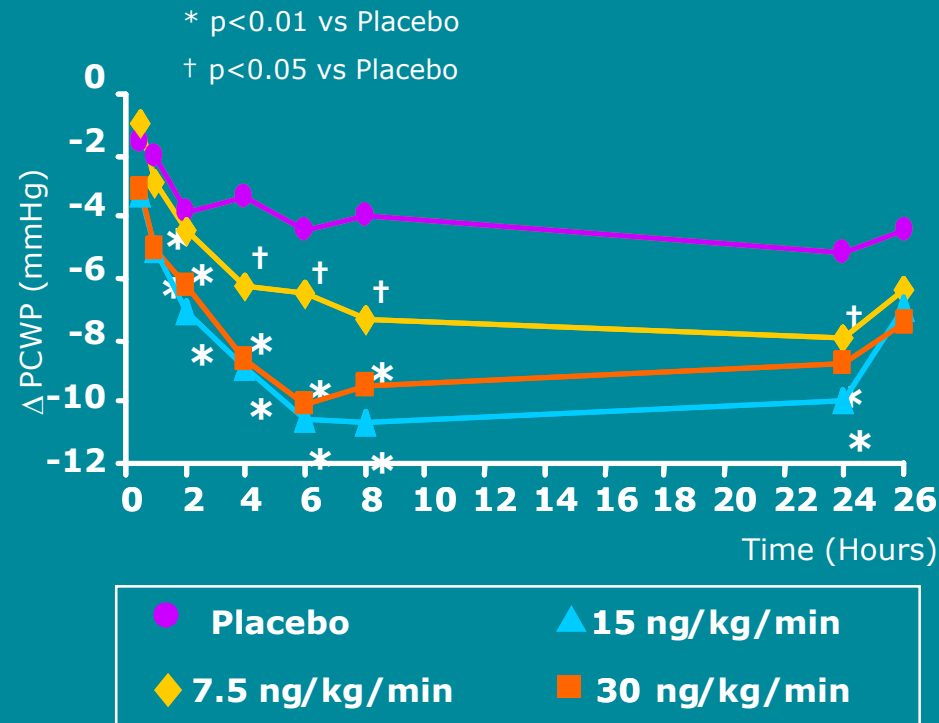
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## Treatment and outcome of CV in the female population in Europe – Results of the Euro Heart Survey Programme

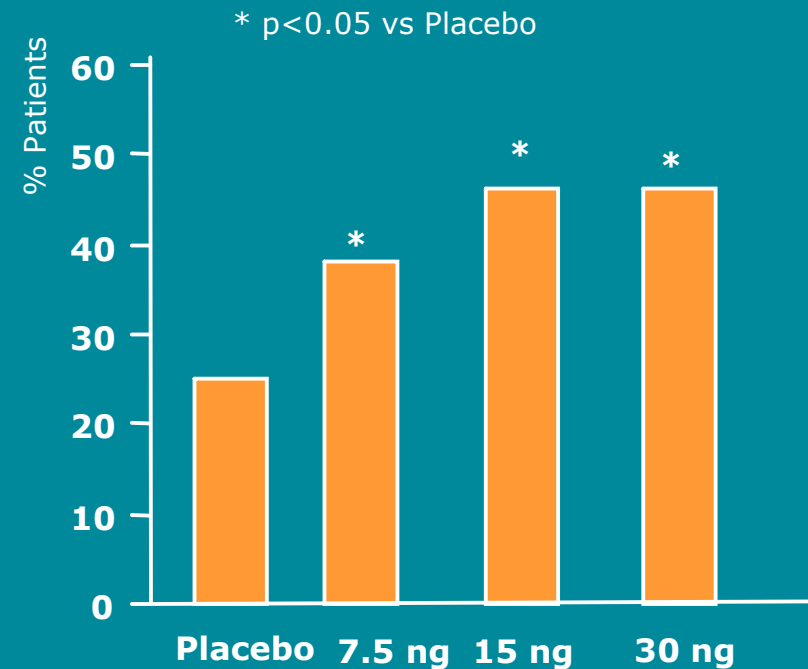
	Male (61%)	Female (39%)	p
Age, y	68 ± 8	73 ± 7	***
Acute denovo %	36	44	***
LVEF (%)	35	43	***
CAD %	61	44	***
Hypertension %	59	67	***
Renal failure %	19	12	***
Anemia %	10	17	***
Diabetes %	31	35	*
Dead at discharge %	6,4	8,4	

*M. Nieminen, FI;120*

# SIRIUS II: Safety and efficacy of an Intravenous placebo controlled Randomised Infusion of Ularitide in a prospective double-blind Study in patients with symptomatic, decompensated chronic heart failure



## Patient-assessed dyspnea at 6 hrs: moderately or markedly better



Ularitide is haemodynamically active and has beneficial clinical effects in patients with symptomatic decompensated HF

*V Mitrovic, DE; 132*

# From the guidelines perspective: when might inotrope support be necessary?

## Positive inotropic drugs in CHF: 2005 ACC/AHA Guidelines

### Long term infusion

- May be harmful and is not recommended as routine therapy
- May be considered for palliation of symptoms in patients with refractory end-stage HF who cannot be weaned from intravenous to oral therapy.

### Routine intermittent infusions

Are not recommended for pts with refractory end-stage HF

## Positive Inotropic Therapy: 2005 ESC Guidelines on CHF

### Oral inotropic agents

- Repeated or prolonged treatment increases mortality and **is not recommended in CHF**

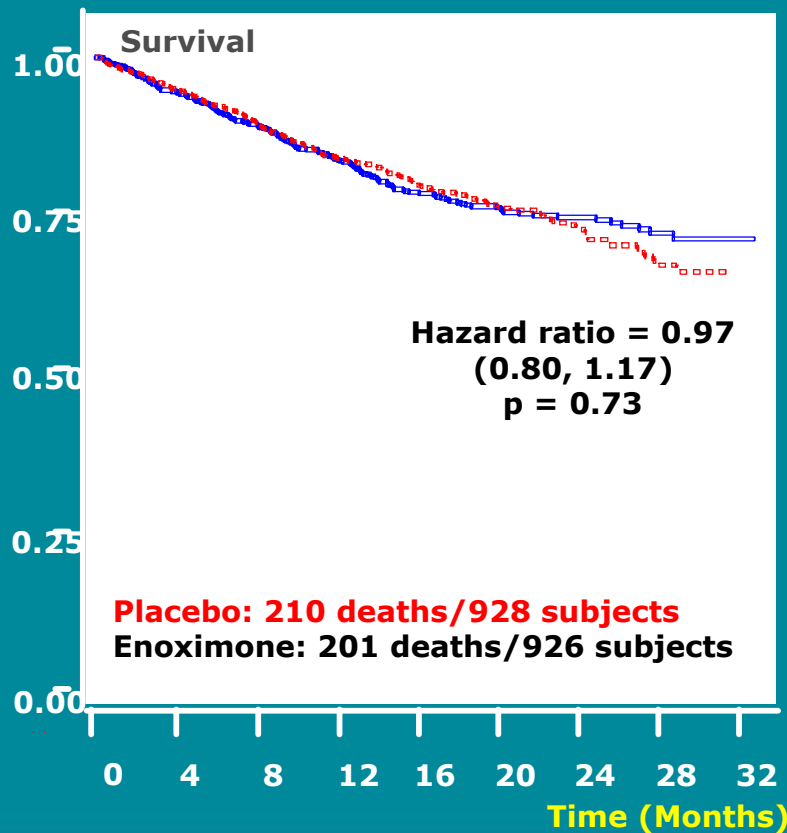
### Intravenous inotropic agents

- ...treatment-related complications may occur and their effect on prognosis is uncertain.

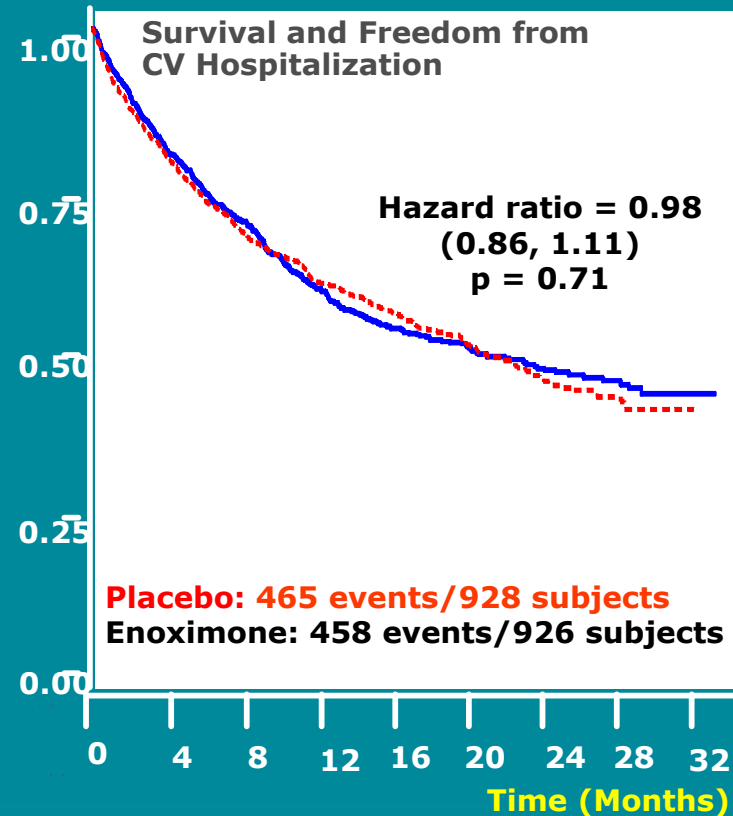
*M Metra, IT; 812*

# ESSENTIAL: The Studies of Oral Enoximone Therapy in Advanced Heart Failure (MY-021/MY-026 Combined)

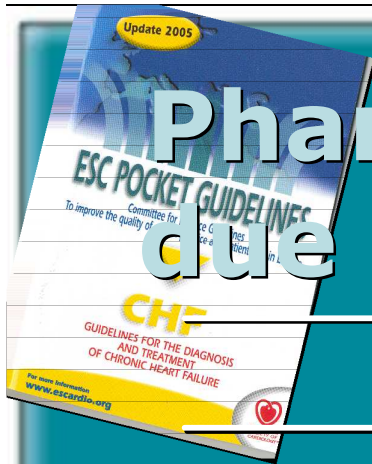
## Time to All-Cause Mortality



## Time to All-Cause Mortality or CV Hospitalization



M Metra II, 124



# Pharmacological therapy of HF due to LV Systolic Dysfunction

**For survival/morbidity  
mandatory therapy**

**For symptoms**

**NYHA I**

Cont. ACE inhibitor/ARB if ACE inhibitor intolerant, continue aldosterone antagonist if post-MI add beta-blocker if post-MI

reduce / stop diuretic

**NYHA II**

ACE inhibitor as first-line treatment/ARB if ACE inhibitor intolerant add beta-blocker and aldosterone antagonist if post MI

+/- diuretic depending on fluid retention

**NYHA III**

ACE inhibitor plus ARB or ARB alone if ACE intolerant beta-blocker add aldosterone antagonist

+ diuretics + digitalis  
If still symptomatic

**NYHA IV**

Continue ACE inhibitor/ARB beta-blocker Aldosterone antagonist

+diuretics + digitalis  
+ consider temporary inotropic support

*K Swedberg, SE; 787*

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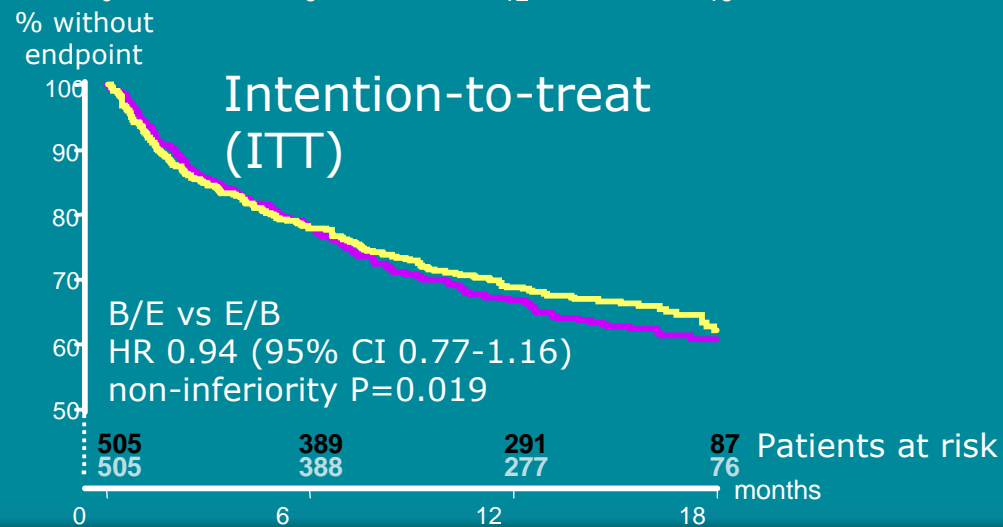
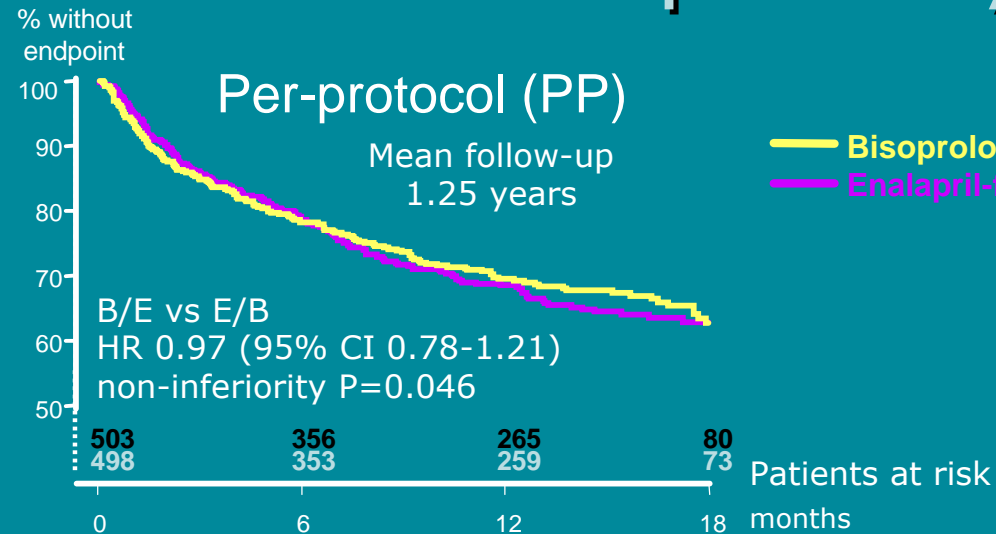
# ACE inhibitor or $\beta$ -blocker?

What is the optimal order of initiation of therapy?



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# CIBIS III - primary endpoint



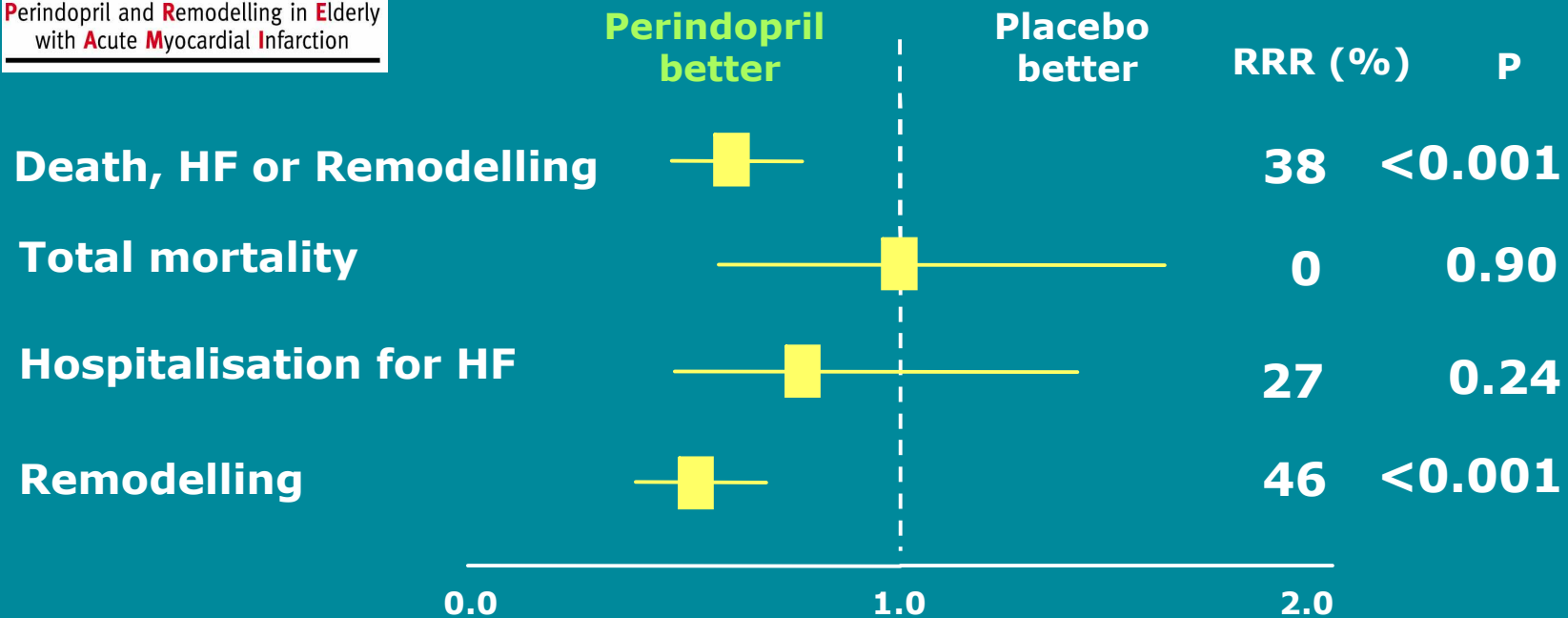
## CIBIS III: clinical implication

it supports a free choice  
of initial treatment for CHF –  
enalapril or bisoprolol -  
based on the physician's  
individual judgment

*R Willenheimer, SE; 126*

# PREAMI

Perindopril and Remodelling in Elderly with Acute Myocardial Infarction



Perindopril in elderly post-AMI patients with normal EF:

- reduction of the combined primary end-point of death, HF hosp and remodelling
- the 8 mg/day regimen – well tolerated, may be suggested as a standard treatment in this clinical setting

*R Ferrari, IT; 128*

# CHF and renal failure – a fateful alliance

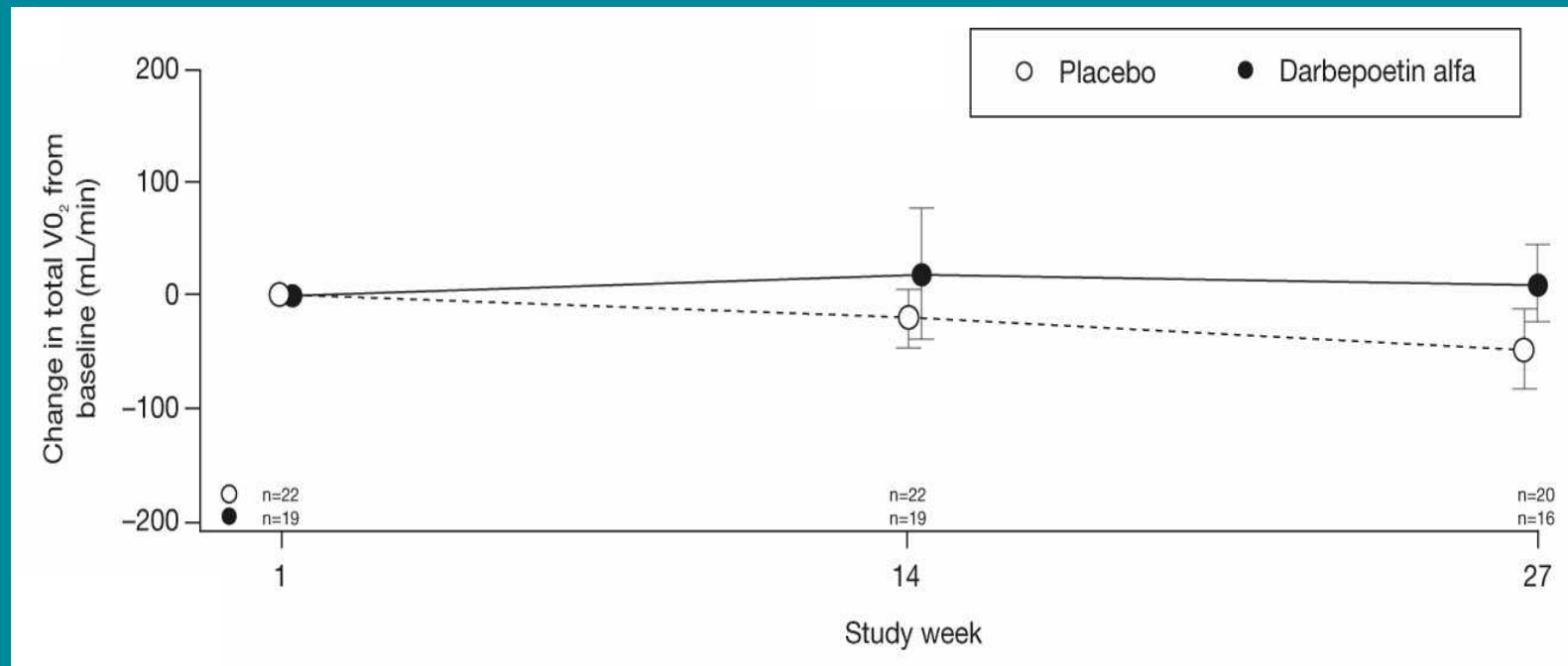
## Conclusions

- In patients with HF, renal dysfunction
  - is common
  - under-recognised
  - has multiple aetiologies
  - deteriorates progressively
  - may worsen with ACEi / ARB / ARA
- Only patients with severe renal dysfunction excluded by most clinical trials
  - Interaction with ACEi on outcome unknown !!
  - No evidence of adverse interaction on outcome with ARB
  - Possibly greater benefit on outcome with beta-blockers
  - Possibly less benefit on outcome with ARAs
  - No evidence of adverse interaction on outcome with CRT

*M Komajda, FR, 1950 and JGF Cleland, UK, 1953*

# Effect of darbepoetin alfa on Exercise Tolerance in Anaemic Patients With Symptomatic Chronic Heart Failure: A Randomised, Double-blind, Controlled Trial

Difference in adjusted\* mean (95% CI) change of absolute peak  $\text{VO}_2$  from baseline to week 27 between darbepoetin alfa and placebo groups:  
50 mL/min (-33 to 133);  $P = 0.23$

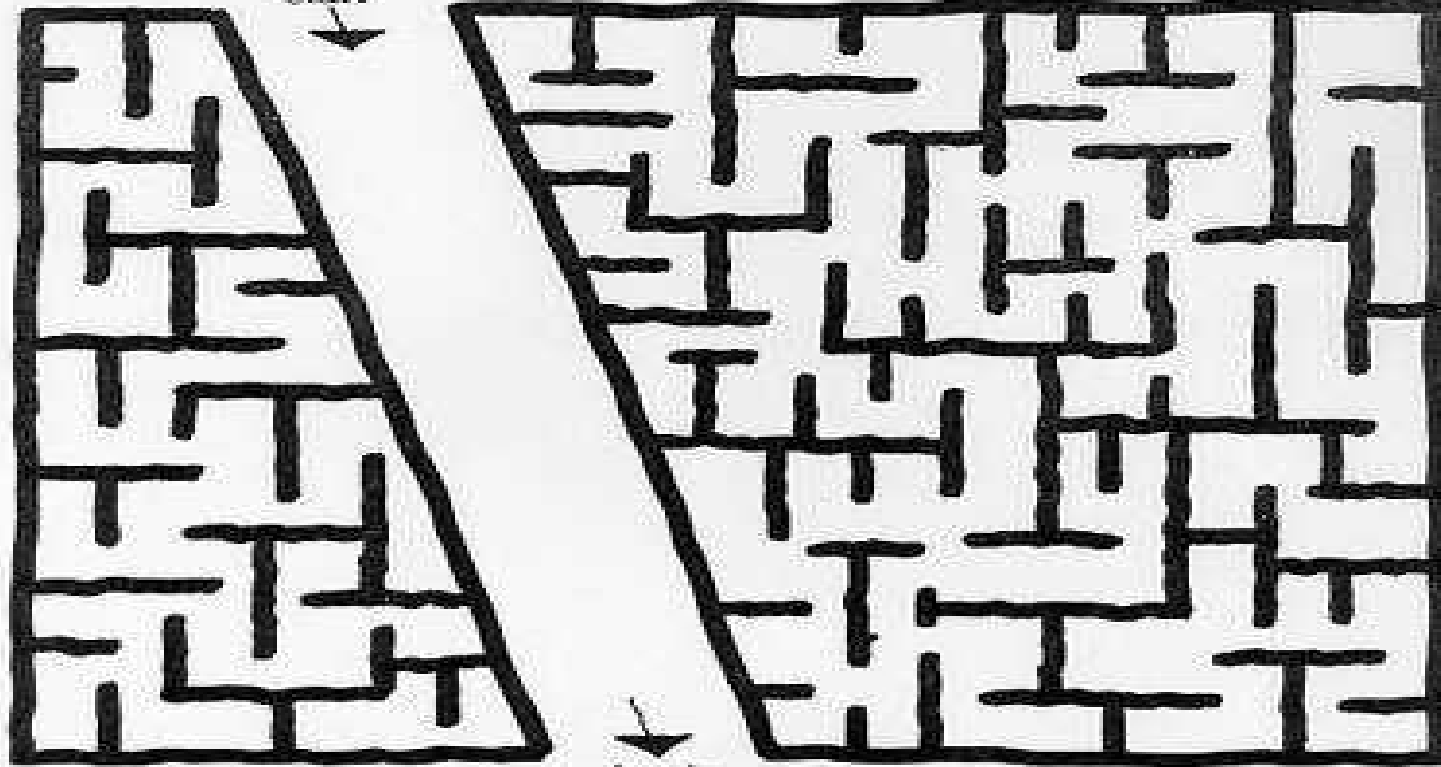


*P Ponikowski, PL, 1956*

# get through the **MAZE!**

**ESC 2005**

start



finish

**ESC 2006**

see if you can find your way through this perplexing maze...

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