



**Ivabradine is associated with improved  
health related quality of life in patients with  
heart failure.**

**Results from the SHIFT substudy.**

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Jeffrey Borer, Ian Ford, Luigi Tavazzi, Karl Swedberg**



# Disclosures

Consultant: Servier

- Health related quality of life (HQoL) refers to the **subjective perception** of health
- Patients with heart failure have worse HQoL than patients with many other common chronic conditions
- Therefore, improving HQoL in heart failure is an important goal of therapy



## Background: quality of life in HF

- Current treatment goals in HF are to improve both survival and quality of life
- Therapies that have survival benefits have a modest effect (ACEIs) or no impact (BBs) on quality of life
- Some therapies that improve quality of life (e.g. inotropic agents) do not improve survival

# Ivabradine and outcomes in chronic heart failure (SHIFT): a randomised placebo-controlled study



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## Summary

**Background** Chronic heart failure is associated with high mortality and morbidity. Raised resting heart rate is a risk factor for adverse outcomes. We aimed to assess the effect of heart-rate reduction by the selective sinus-node inhibitor ivabradine on outcomes in heart failure.

**Methods** Patients were eligible for participation in this randomised, double-blind, placebo-controlled, parallel-group study if they had symptomatic heart failure and a left-ventricular ejection fraction of 35% or lower, were in sinus rhythm with heart rate 70 beats per min or higher, had been admitted to hospital for heart failure within the previous year, and were on stable background treatment including a  $\beta$  blocker if tolerated. Patients were randomly assigned by computer-generated allocation schedule to ivabradine titrated to a maximum of 7.5 mg twice daily or matching placebo. Patients and investigators were masked to treatment allocation. The primary endpoint was the composite of cardiovascular death or hospital admission for worsening heart failure. Analysis was by intention to treat. This trial is registered, number ISRCTN70429960.

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**Ivabradine led to significant reduction in the primary composite  
endpoint of cardiovascular mortality or hospitalization for  
worsening heart failure**

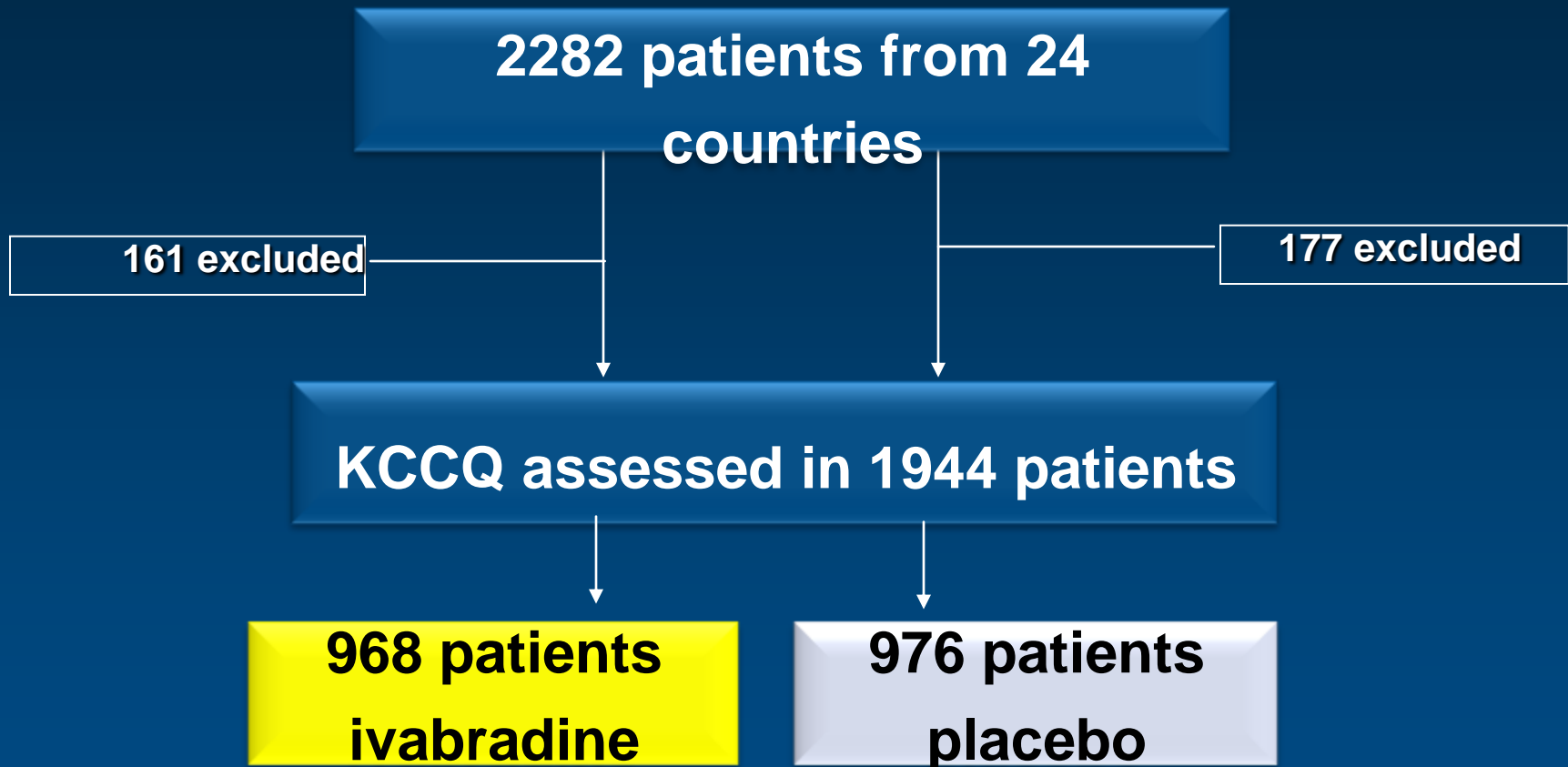
- **≥18 years**
- **Class II to IV NYHA heart failure**
- **Ischaemic/non-ischaemic aetiology**
- **LV systolic dysfunction (EF ≤35%)**
- **Heart rate ≥70 bpm**
- **Sinus rhythm**
- **Hospital admission for worsening heart failure ≤12 months**



## Patient-Reported Outcomes (PRO) HQoL Substudy

- Sub-study within SHIFT to assess the impact of heart rate slowing with ivabradine on HQoL using the disease-specific Kansas City Cardiomyopathy Questionnaire (KCCQ)
- KCCQ was measured at baseline, 4, 12 and 24 months after randomization

# Patients evaluated with KCCQ In PRO substudy



Median study duration: 22.9 months; maximum: 41.7 months



# Baseline characteristics of PRO Substudy

	Ivabradine N=968	Placebo N=976
Mean age, y	61	61
Male, %	75	77
BMI	28	28
Mean CHF duration, y	4	4
CHF Ischemic cause, %	65	63
NYHA II, %	59	57
NYHA III, %	40	42
NYHA IV, %	1	1
Mean LVEF, %	28	28
Mean HR, bpm	80	80



# Baseline treatments of PRO Substudy

	<b>Ivabradine N=968</b>	<b>Placebo N=976</b>
<b>Beta-blockers, %</b>	<b>90</b>	<b>91</b>
<b>ACE inhibitors, %</b>	<b>81</b>	<b>83</b>
<b>ARBs, %</b>	<b>16</b>	<b>15</b>
<b>Diuretics, %</b>	<b>85</b>	<b>83</b>
<b>Anti-aldosterone agents, %</b>	<b>67</b>	<b>64</b>
<b>Digitalis, %</b>	<b>19</b>	<b>19</b>
<b>Devices, %</b>	<b>5</b>	<b>7</b>

- **The clinical summary score (CSS):**  
mean of the physical limitation and total symptom domains scores
- **The overall summary score (OSS):**  
Clinical summary score (CSS) + quality of life and social limitation scores

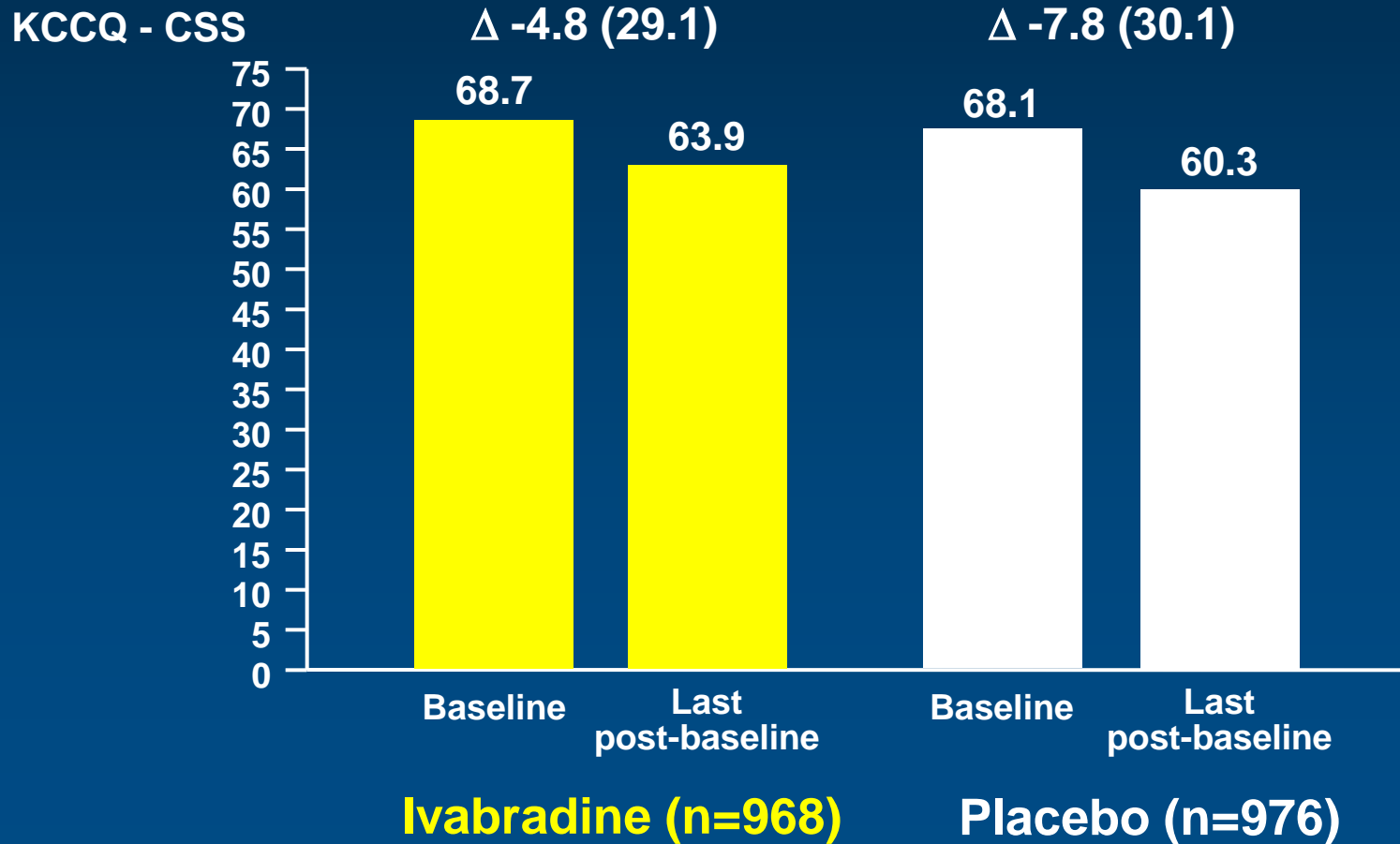


# Clinical summary score

Change from baseline to last assessment

Including scoring **death as 0**

Difference = 3.3 (1.3); **p = 0.012**





# Clinical summary score

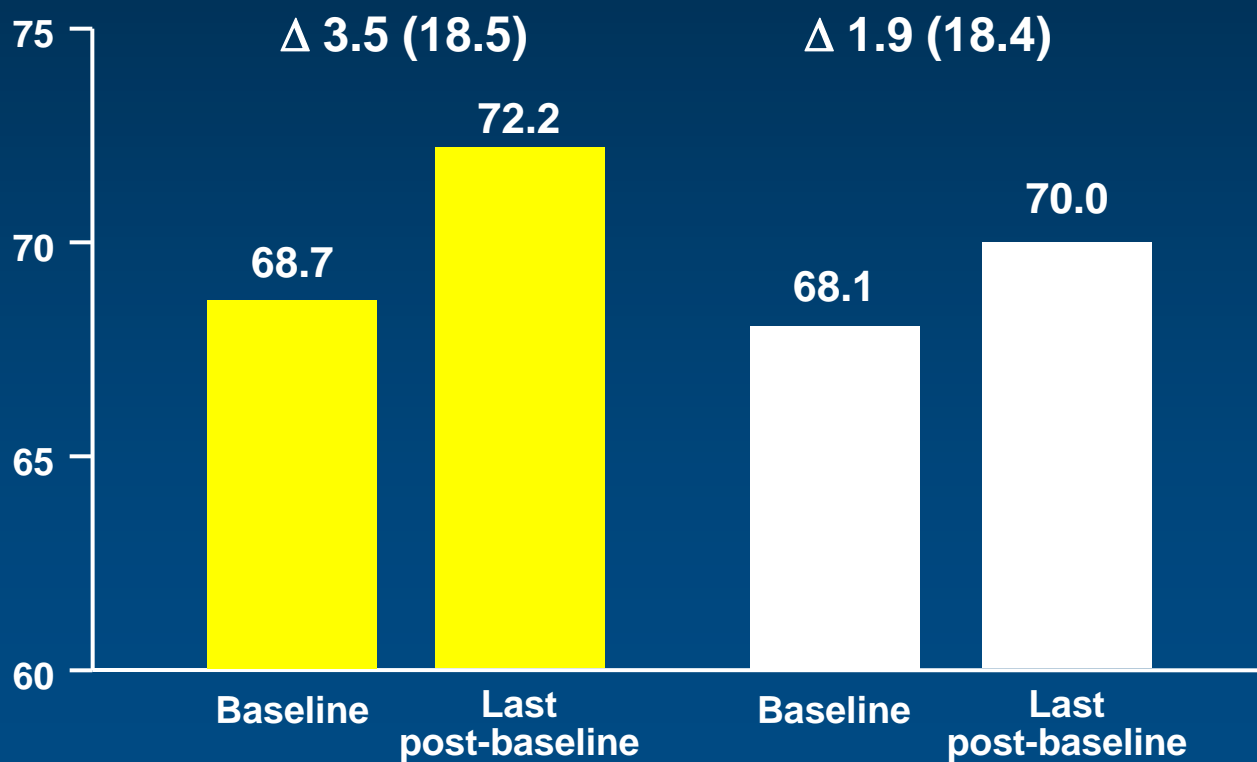
Change from baseline to last assessment

## Analysis of *surviving* patients

Difference = 1.9 (0.8), **p = 0.015**

KCCQ – CSS

“surviving”



**Ivabradine (n=968)**

**Placebo (n=976)**



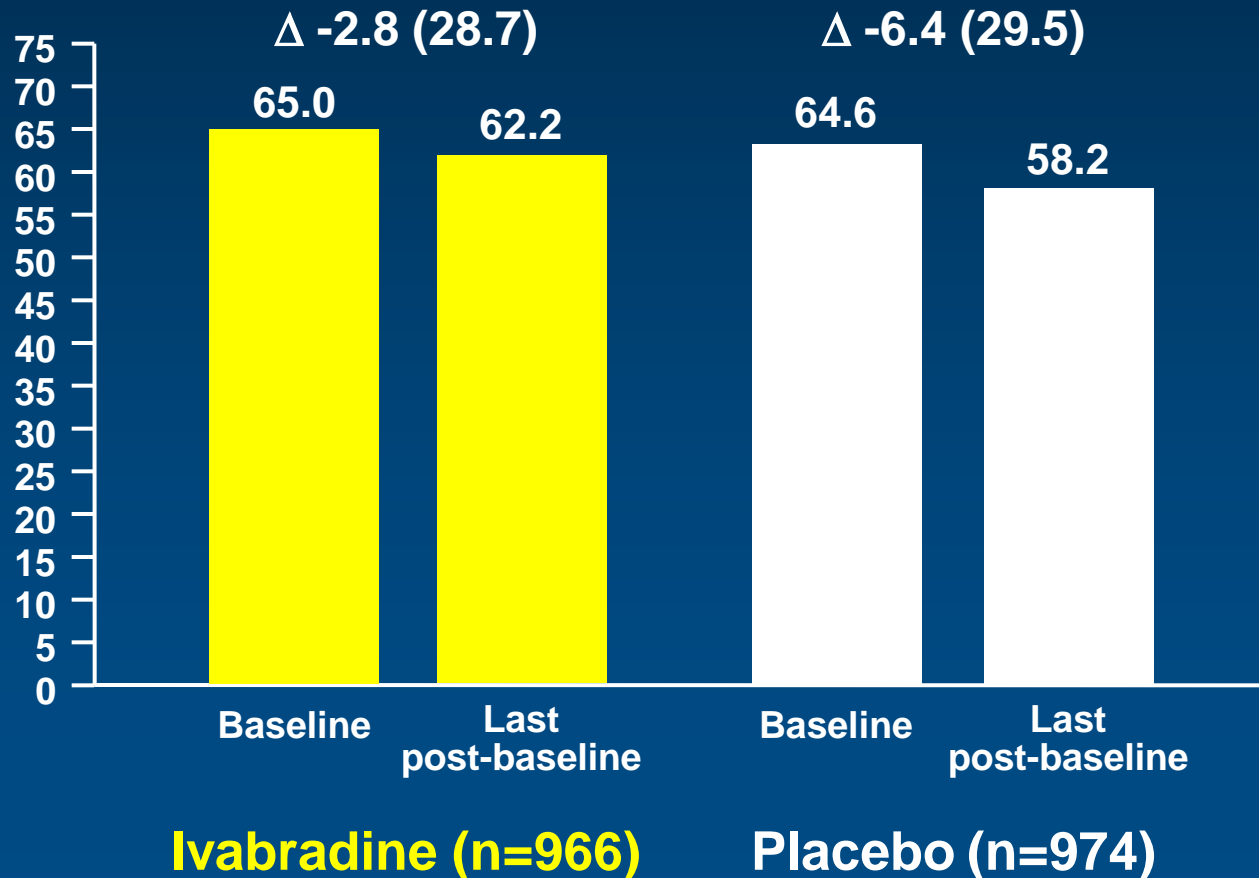
# Overall summary score

Change from baseline to last assessment

including scoring **death as 0**

Difference = 3.7 (1.3), **p = 0.004**

KCCQ – OSS





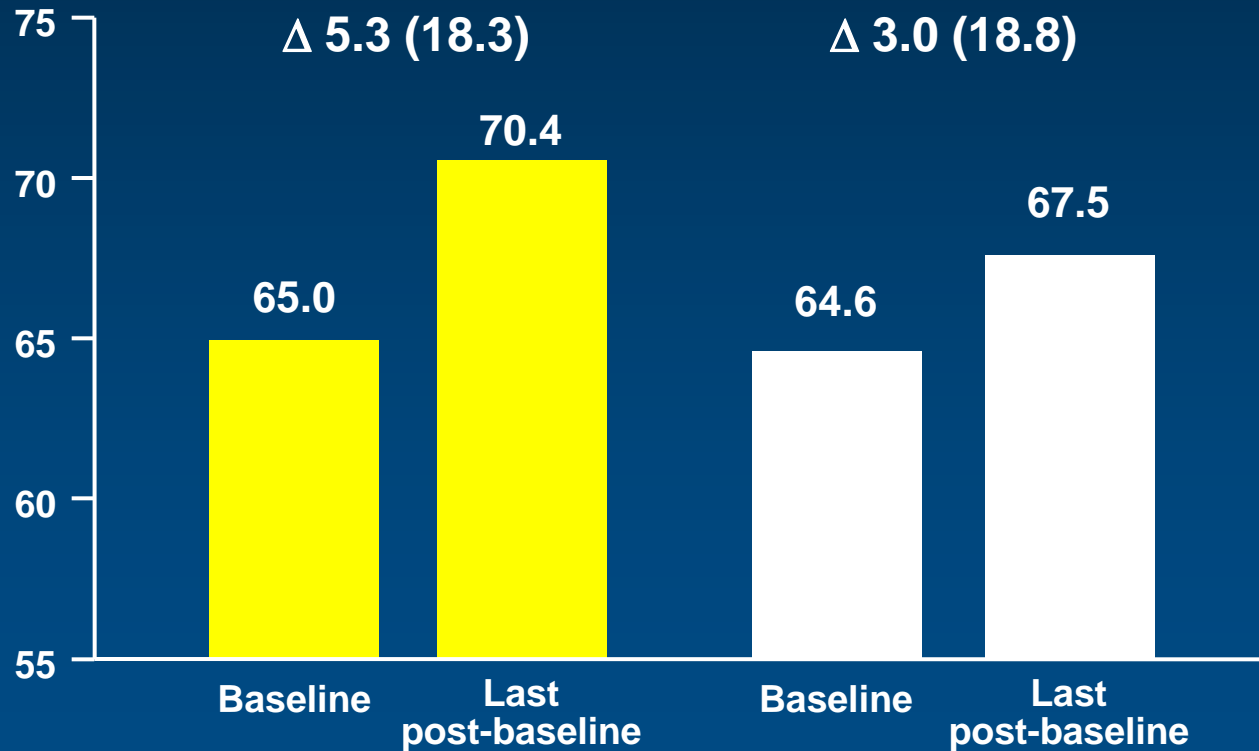
# Overall summary score

Change from baseline to last assessment

## Analysis of *surviving* patients

Difference = 2.6 (0.8),  $p < 0.001$

KCCQ – OSS  
“surviving”



Ivabradine (n=966)

Placebo (n=974)



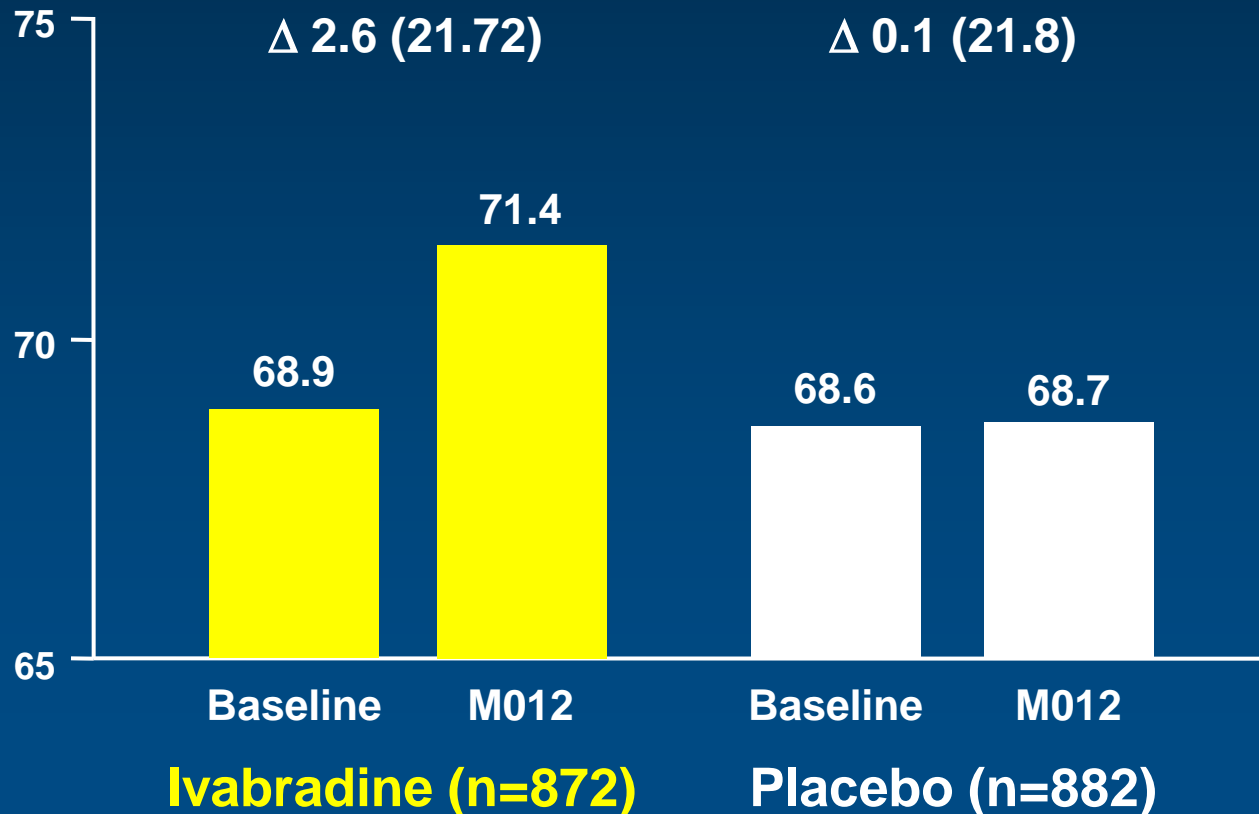
# Clinical summary score

Change from baseline to Month 12

Including scoring **death as 0**

Difference = 2.6 (0.9) [0.67; 4.53], **p = 0.008**

KCCQ – CSS





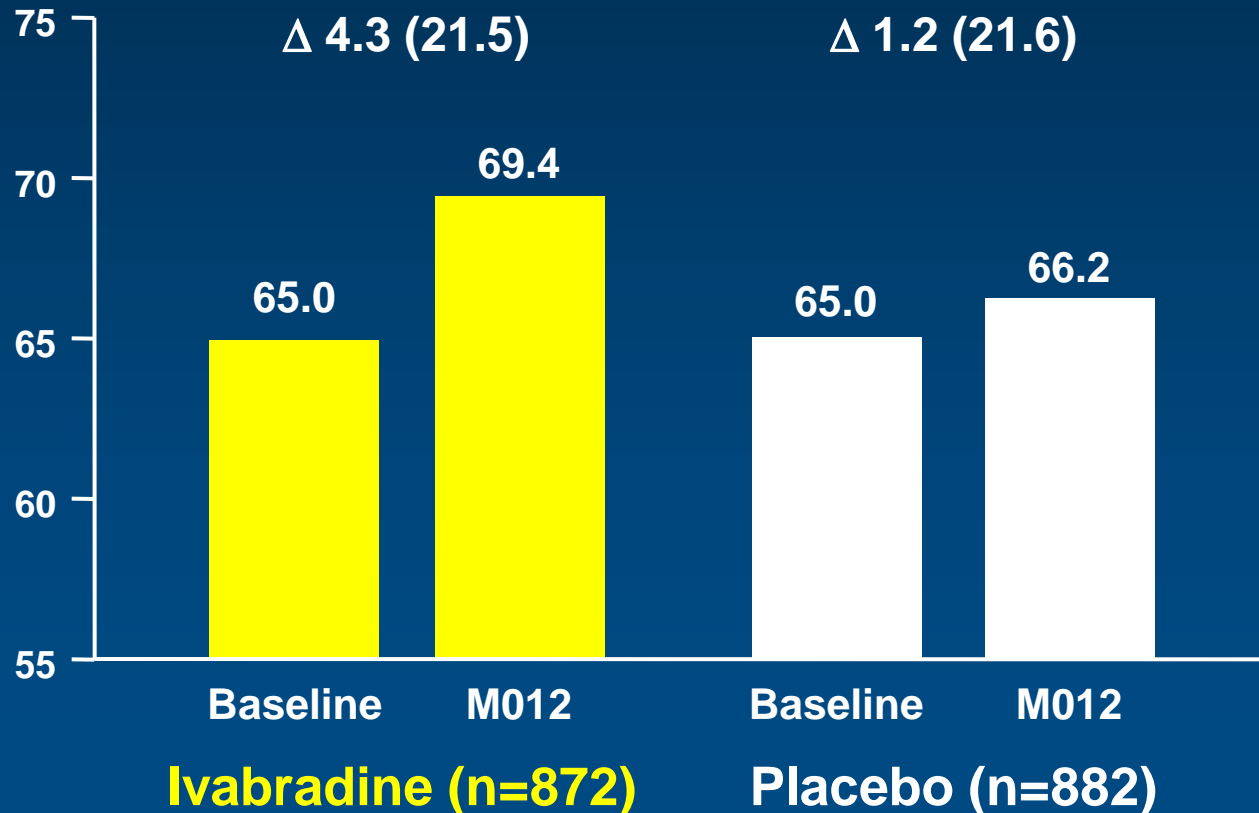
# Overall summary score

Change from baseline to Month 12

Including scoring **death as 0**

Difference = 3.2 (0.9) [1.25; 5.06], **p = 0.001**

KCCQ – CSS



- In patients with heart failure and systolic dysfunction who are in sinus rhythm with HR >70 bpm, heart rate reduction with ivabradine was associated with improved HQoL
- This HQoL benefit was seen in addition to reduction in the primary endpoint of cardiovascular death or hospitalization for worsening heart failure

- Three central components in care of patients with HF were achieved in SHIFT:
  - 1. Reduction in mortality (heart failure related)
  - 2. Reduction in morbidity (reduced hospitalization for worsening HF)
  - 3. Improved HQoL