

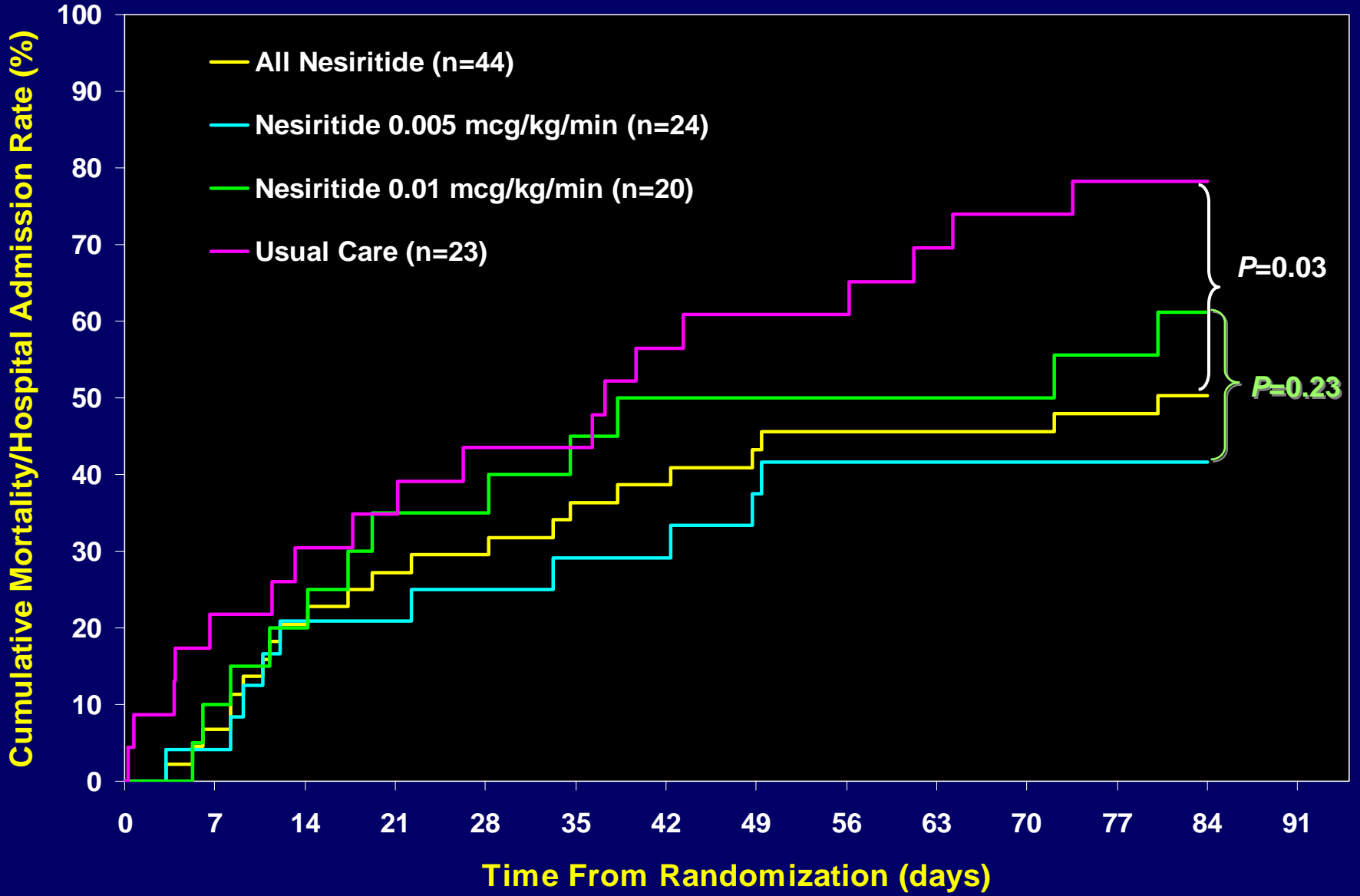
# **Results of the Follow-up Serial Infusions of Nesiritide for the Management of Patients With [Advanced] Heart Failure (FUSION II) Trial**

**American College of Cardiology  
56<sup>th</sup> Annual Scientific Session  
New Orleans, Louisiana  
March 25, 2007**

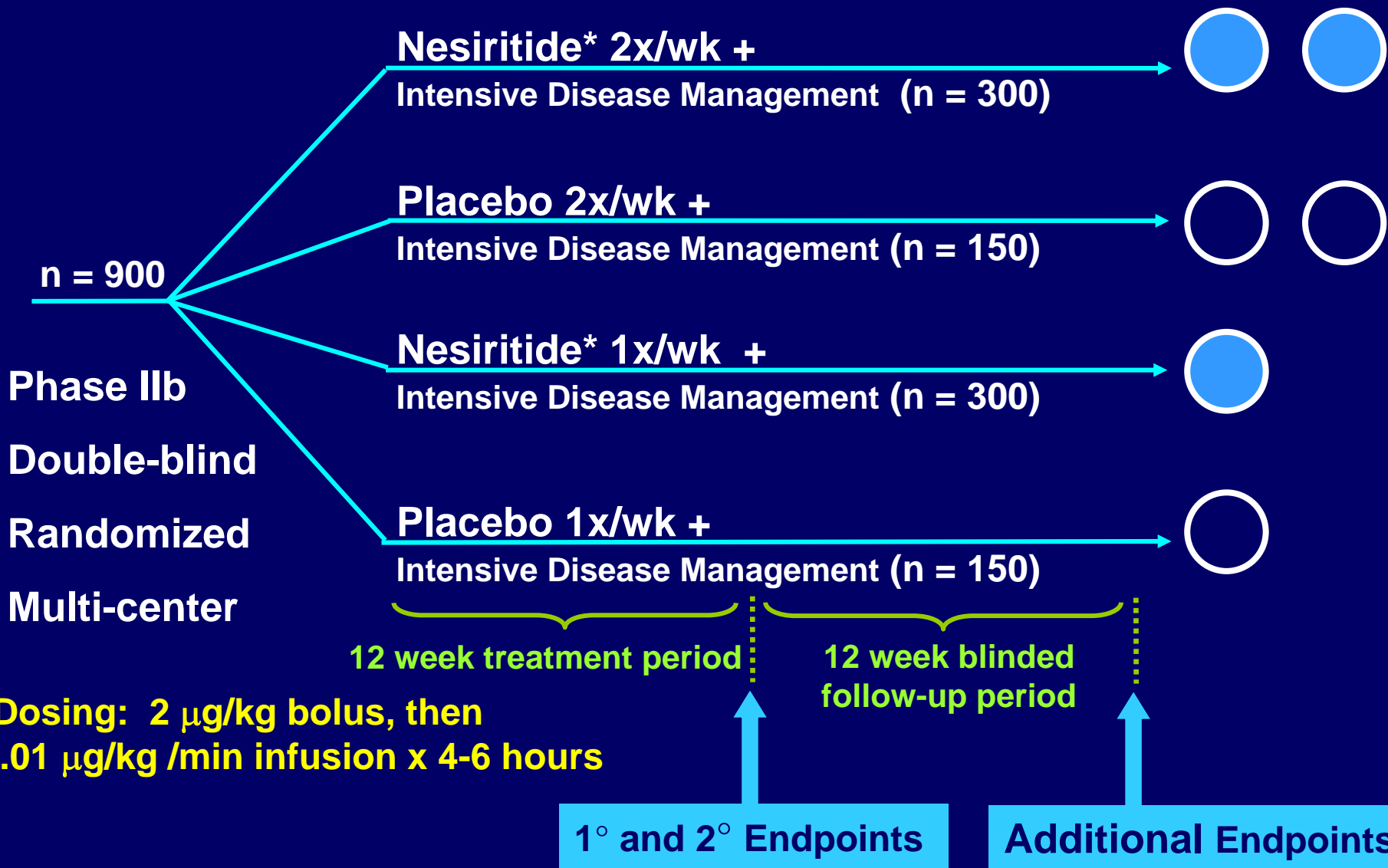
**Clyde W. Yancy, M.D.**

**on behalf of the FUSION II Steering Committee  
Henry Krum, MD; Barry M. Massie, MD;  
Marc A Silver, MD; Lynne W. Stevenson, MD  
and the FUSION II Investigators**

# FUSION I: Mortality & All-cause Hospitalization (High Risk Patients- ACC/AHA Stage D HF or 'CDHF')



# FUSION II Study Design



# Efficacy Endpoints

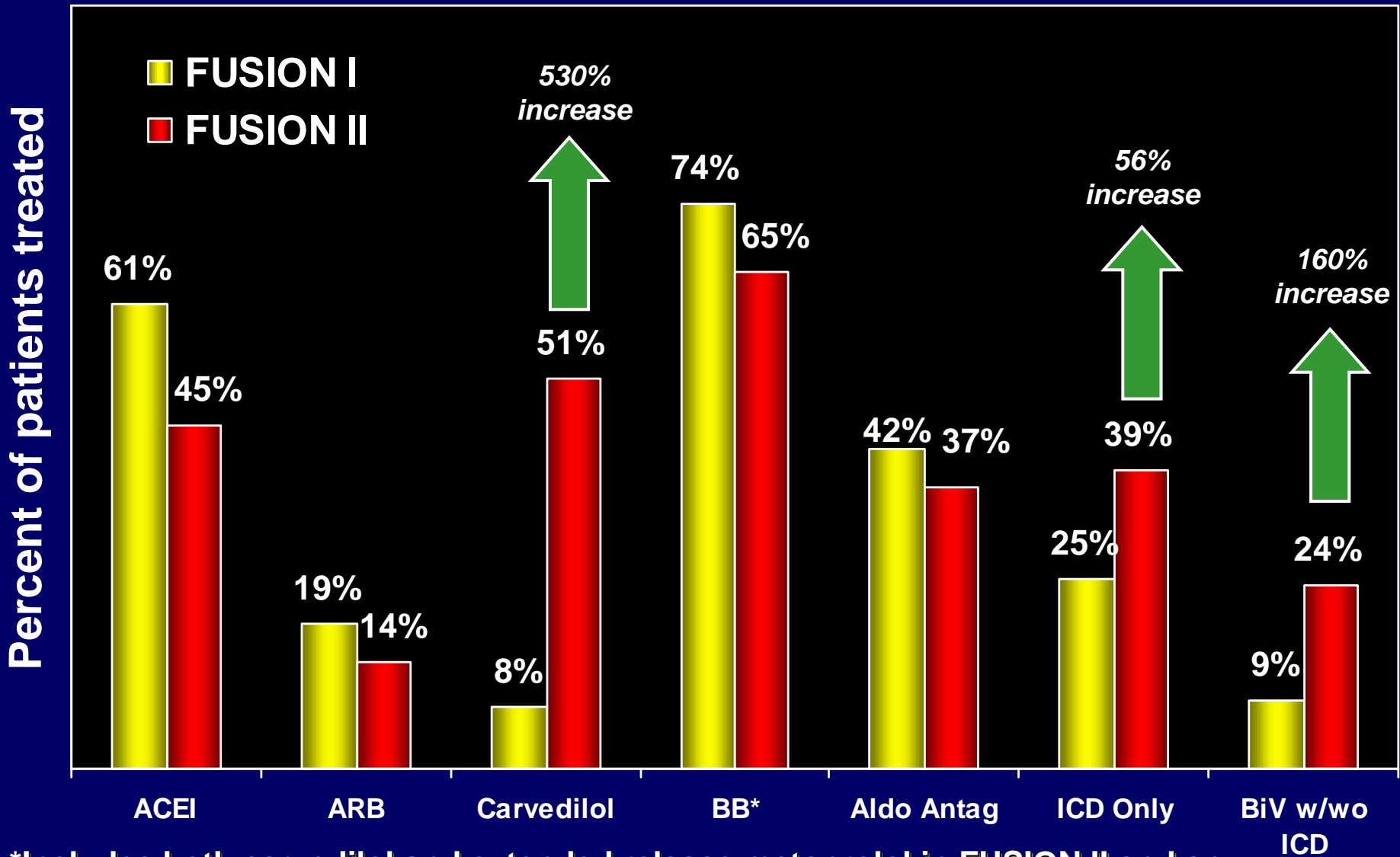
- **Primary**
  - Time to all cause death or first CV and/or renal hospitalization through Week 12
- **Secondary\***
  - Number of CV and/or renal hospitalizations adjusted for observation period duration
  - Days alive and out of hospital
  - Change in KCCQ summary score
  - Time to CV death

\*from day of randomization through week 12, or week 13 for KCCQ

# Demographics

	Placebo Combined Groups N=306	Nesiritide Combined Groups N=605
<b>Age, years, Mean <math>\pm</math> SD,</b>	<b>65 <math>\pm</math> 13</b>	<b>65 <math>\pm</math> 13</b>
<b>Male, (%)</b>	<b>72.2%</b>	<b>70.4%</b>
<b>Ethnicity, (%)</b>		
Caucasian	60.1%	64.8%
African American	23.5%	20.3%
Hispanic	6.2%	6.0%
Asian	6.5%	6.4%
<b>Ischemic etiology, (%)</b>		
Ischemic	63.4%	64%
Idiopathic	20.6%	18.7%
Hypertensive	4.2%	5.6%
<b>LVEF, Mean <math>\pm</math> SD</b>	<b>25% <math>\pm</math> 8%</b>	<b>25% <math>\pm</math> 8%</b>
<b>Body Mass Index, Mean <math>\pm</math> SD</b>	<b>28.9 <math>\pm</math> 7.1</b>	<b>28.3 <math>\pm</math> 6.8</b>
<b>NYHA class, (%)</b>		
III	46.1%	47.1%
IV	53.9%	52.9%

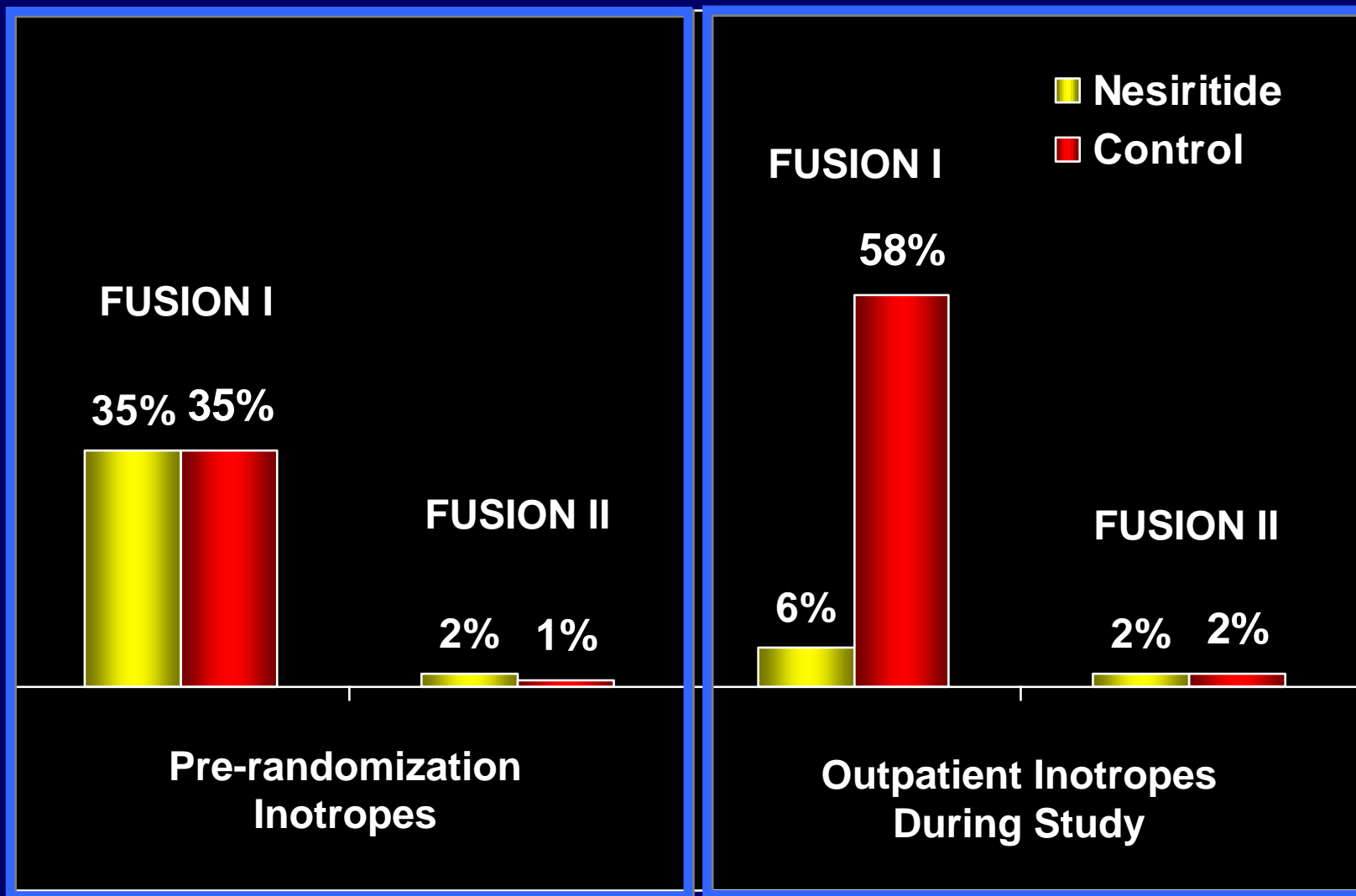
# Baseline Therapy FUSION I vs. FUSION II



\*Includes both carvedilol and extended release metoprolol in FUSION II and any beta-blocker in FUSION I

# Inotrope Infusions FUSION I vs FUSION II

Percent of patients treated



\*Refers to exposure to inotropes within 2 weeks of randomization

# FUSION II: Primary Composite Endpoint Through Week 12

	Placebo Combined N=306	Nesiritide Combined N=605	*P-value
All cause mortality and CV/renal hospitalization†	36.8%	36.7%	0.79
All Cause Mortality	9.6%	9.5%	0.98
CV/renal hospitalization	33.9%	32.9%	0.95

\*P value: NES vs. placebo stratified by dose group

†Modified ITT: all treated ITT patients

# FUSION II: Secondary Endpoints Week 12

	Placebo Combined N=306	Nesiritide Combined N=605	*P-value
Number of CV/renal Hospitalizations Mean $\pm$ SD	0.8 $\pm$ 1.88	1.0 $\pm$ 3.95	0.38
Days Alive and Out of Hospital	74.8 $\pm$ 17.5	72.5 $\pm$ 20.5	0.09
Change in KCCQ Mean $\pm$ SD	14.2 $\pm$ 21.1	13.0 $\pm$ 24.1	0.52
CV Mortality	9.2%	8.1%	0.68

\*P value nesiritide vs. placebo stratified by dose group

# SAFETY

## Any Adverse Event

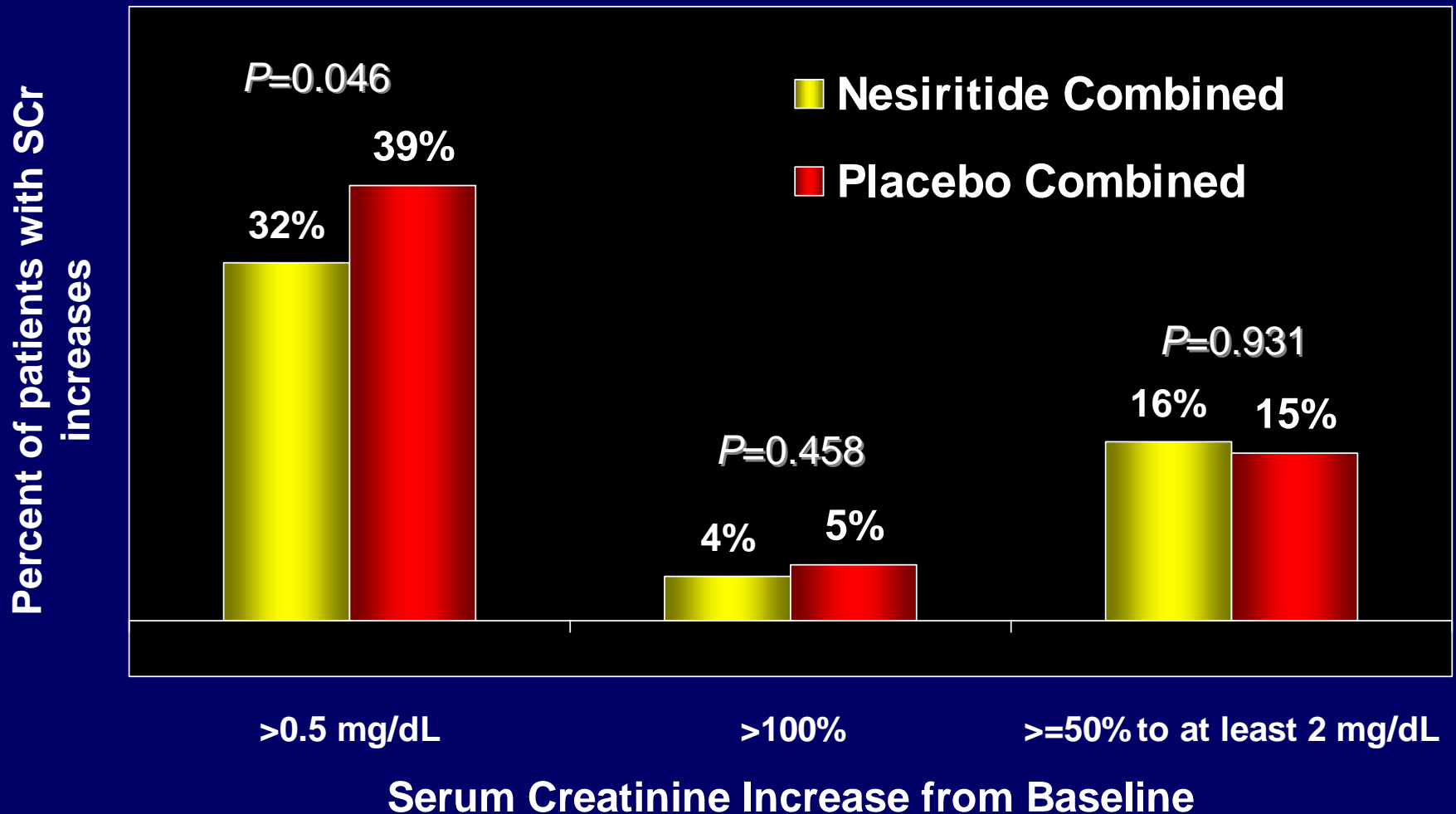
	Placebo Combined Groups N=306	Nesiritide Combined Groups N=605	P-value
All AEs	86.9%	88.7%	0.45
All drug-related AEs	27.5%	42.0%	<0.01
All SAEs	56.5%	60.4%	0.29
All drug-related SAEs	8.2%	8.0%	0.90
All AEs that caused permanent study drug discontinuation	25.5%	27.0%	0.63

**AE: Adverse event**

**SAE: Serious adverse event that results in death, is life-threatening, requires inpatient hospitalization, or prolongation of existing hospitalization, or results in persistent or significant disability/incapacity.**

# SAFETY

## Protocol Specified Changes in Serum Creatinine\*



\*Outpatient Clinic Visit Values Only

## **FUSION II – Conclusions**

- **In this patient population with advanced HF and serial infusions of nesiritide:**
  - **No evidence of drug induced renal harm compared to placebo**
  - **No evidence of increased mortality at pre-specified endpoints**

# FUSION II - Conclusions

- In the context of optimal adherence to evidence based medical and device therapies and in concert with excellent disease management, serial infusions of nesiritide did not result in a demonstrable clinical benefit over intensive outpatient management of patients with CDHF
- Adherence to guideline based therapy AND meticulous follow-up should be optimized for patients with CDHF