Randomized comparison of intraaortic balloon counterpulsation versus optimal medical therapy in addition to early revascularization in acute myocardial infarction complicated by cardiogenic shock

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on behalf of the **IABP-SHOCK II Trial** Investigators

University of Leipzig – Heart Center

Disclosures

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IABP in Cardiogenic Shock

IABP SHOCK II RANDOMIZED CLINICAL TRIAL

History:

1962 Animal studies

Moulopoulos et al. Am Heart J 1962;63:669-675

1968 First clinical description in shock

Kantrowitz et al. JAMA 1968;203:135-140

1973 Hemodynamic effects in shock, Mortality unchanged

Scheidt et al. NEJM 1973;288:979-984

> 40 years > 1 Million patients treated, low complication rate, Benchmark registry

Ferguson et al. JACC 2001;38:1456-1462

Guidelines

IABP SHOCK II RANDOMIZED CLINICAL TRIAL

IABP in AMI complicated by cardiogenic shock

ACC/AHA

American Heart Association

AMERICAN COLLEGE OF CARDIOLOGY

Class IB

ESC

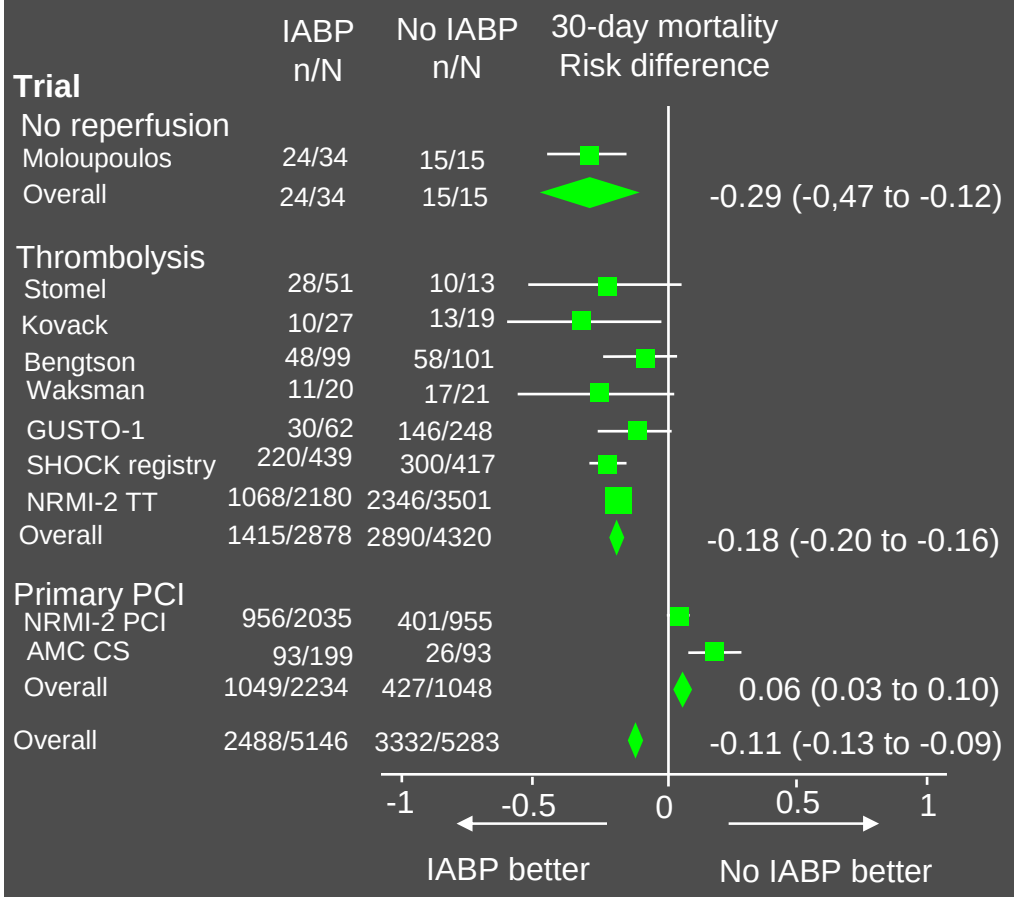
EUROPEAN SOCIETY OF CARDIOLOGY

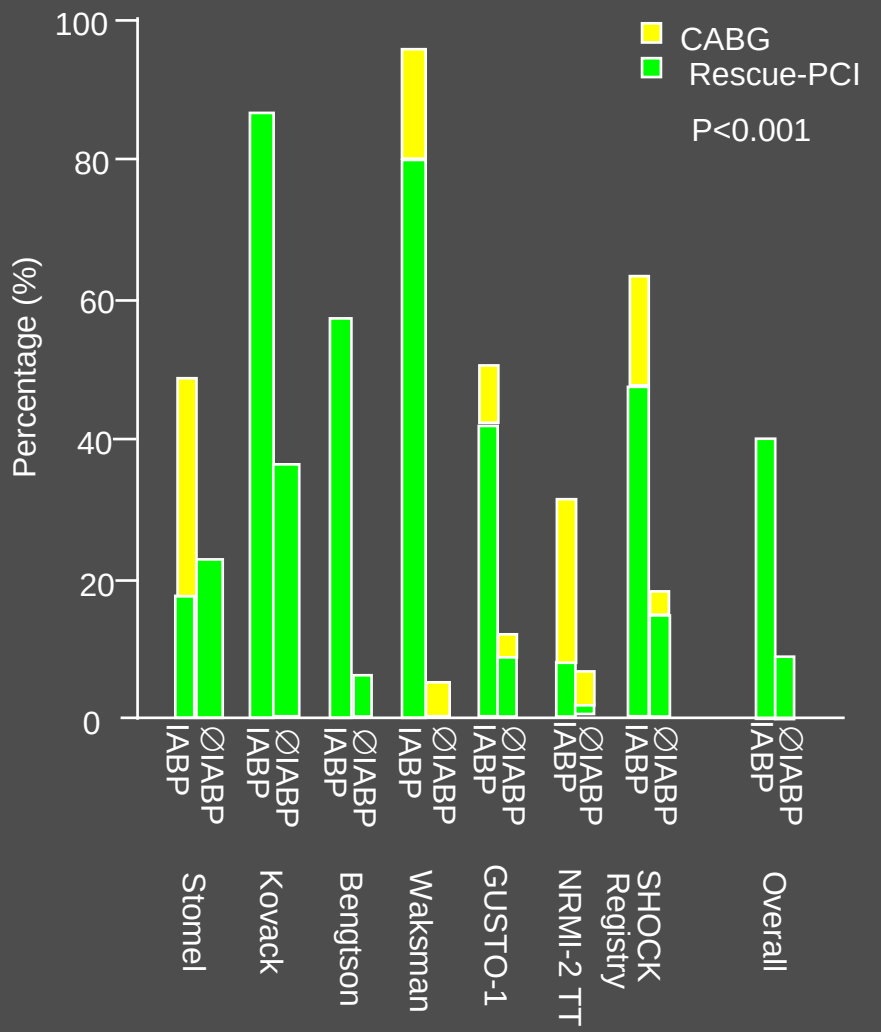
Class IC

Antman et al. Circulation 2004;110:82-292
Van de Werf et al. Eur Heart J 2008;29:2909-2945
Wijns et al. Eur Heart J 2010;31:2501-2555

Background

Mortality IABP vs no IABP - Metaanalysis

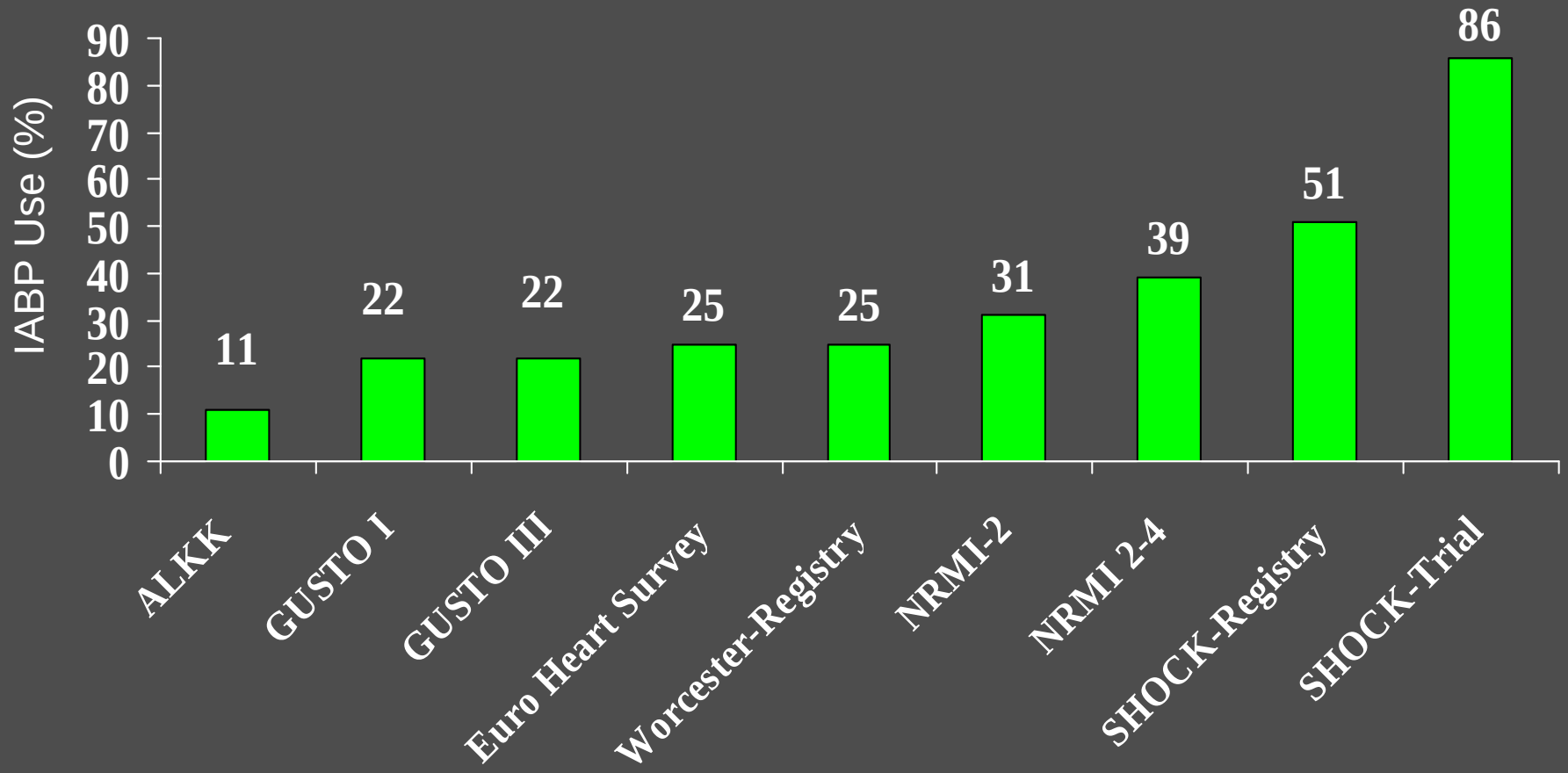




Sjauw et al. Eur Heart J 2009;30:459-468

Background

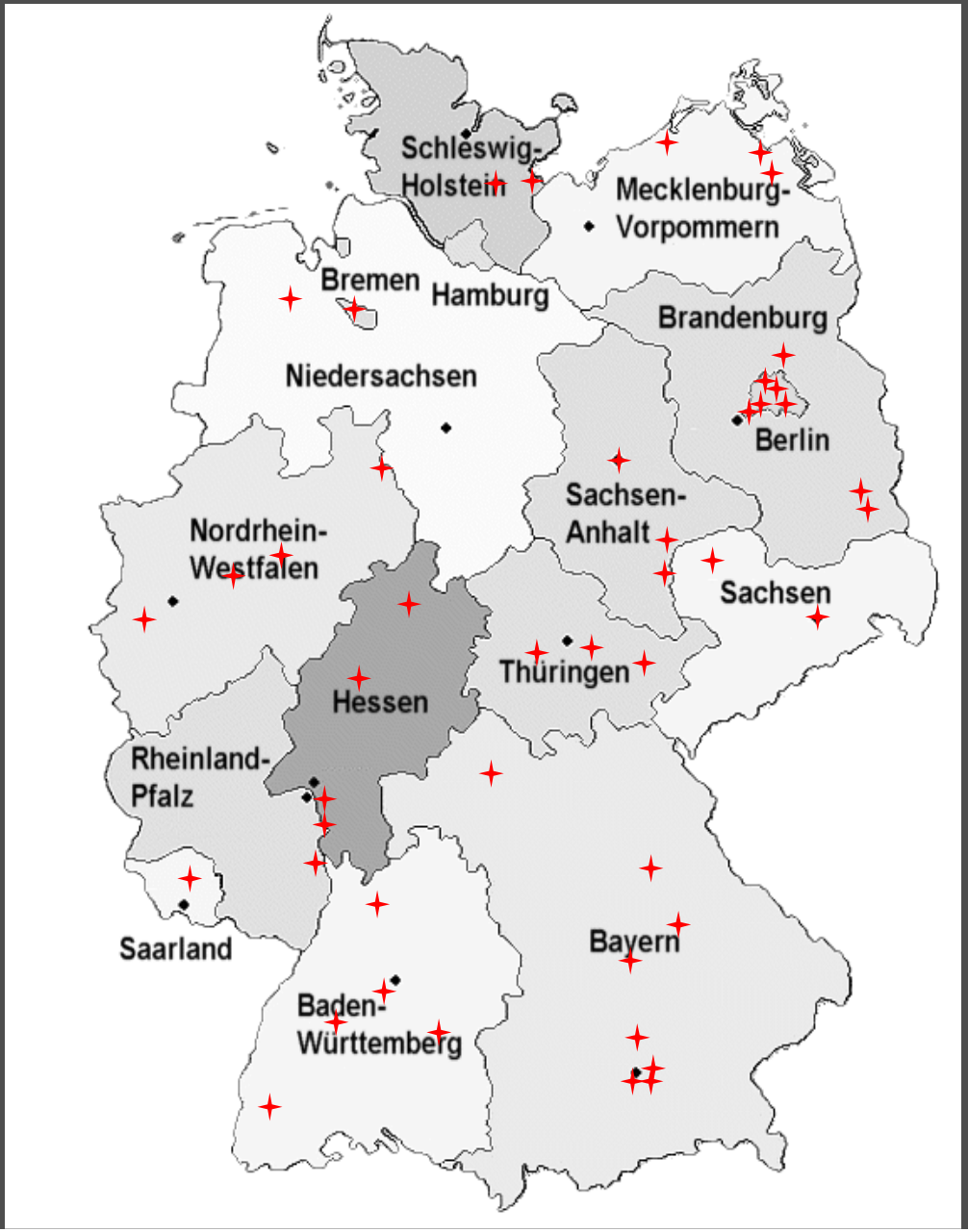
IABP-Use in Cardiogenic Shock



Thiele et al. Eur Heart J 2010,31:1828-1835

Methods

Study Sites and Organisation



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Support + Patronage:

DEUTSCHE GESELLSCHAFT FÜR KARDIOLOGIE - HERZ- UND KREISLAUFFORSCHUNG e.V.
GERMAN CARDIAC SOCIETY

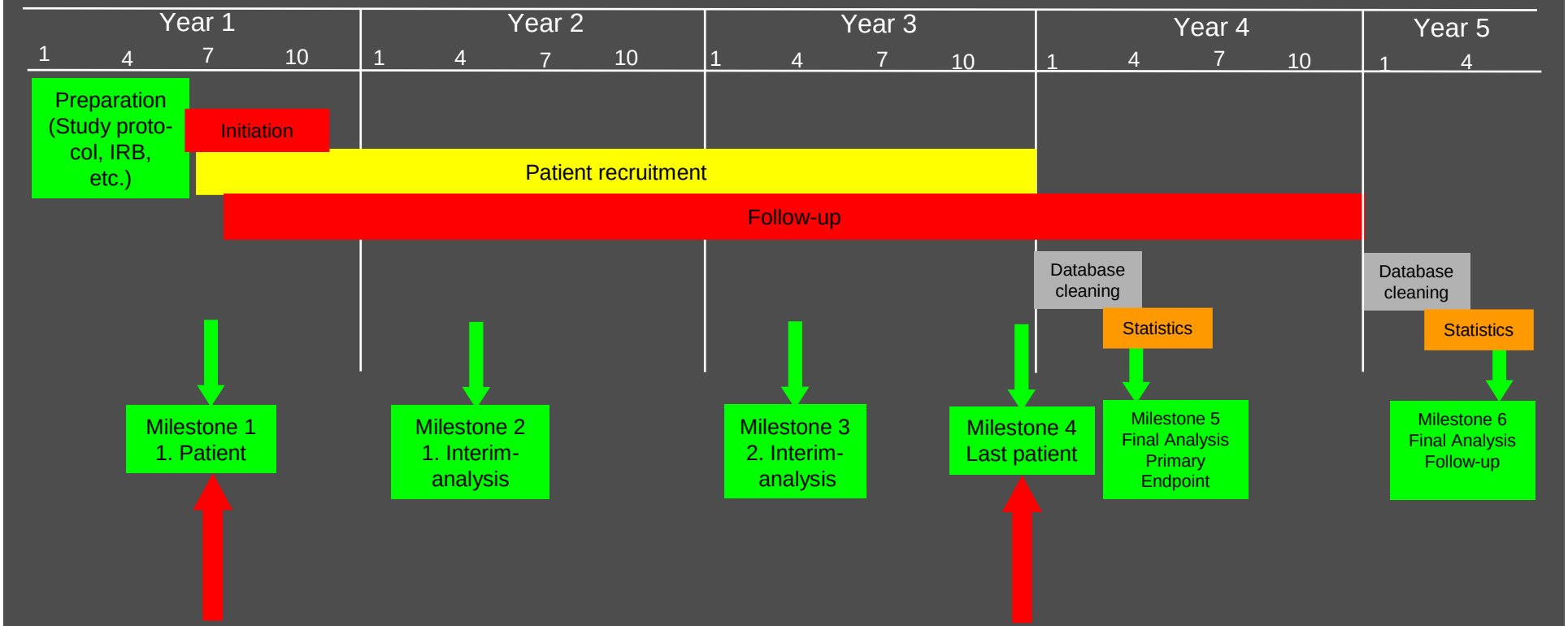
Deutsche Herzstiftung

ALKK Arbeitsgemeinschaft Leitender Kardiologischer Krankenhausärzte e.V.

DFG Deutsche Forschungsgemeinschaft

Methods

IABP-Shock-II Trial – Timelines



Statistical Methodology

IABP SHOCK II RANDOMIZED CLINICAL TRIAL

Sample Size

– Estimated 12% absolute difference in survival rates
– Sequential statistical design with 2 interim analyses (33% and 66% of patients)
– Significance level 0.0005 at 1st or 0.014 at 2nd interim analysis.
Final analysis at α-level 0.044 → 564 patients
– To compensate losses in follow-up and putative center effect → 600 patients

Primary Study Endpoint:

30-day all-cause mortality

Secondary Study Endpoints:

- Hemodynamic parameters (mean BP, heart rate pre and post revascularization)
- Time until stabilization
- Catecholamine dose and duration
- Inflammatory reaction (CRP)
- Serum-lactate (every 8 h for 48 h)
- Requirement for LVAD-implantation or HTx
- Serial creatinine-level and creatinine-clearance (Cockcroft-Gault-formula)
- Requirement for renal replacement therapy
- SAPS-2 Score
- Length of ICU-stay
- Length of mechanical ventilation
- Mortality after 6 and 12 months

Safety:

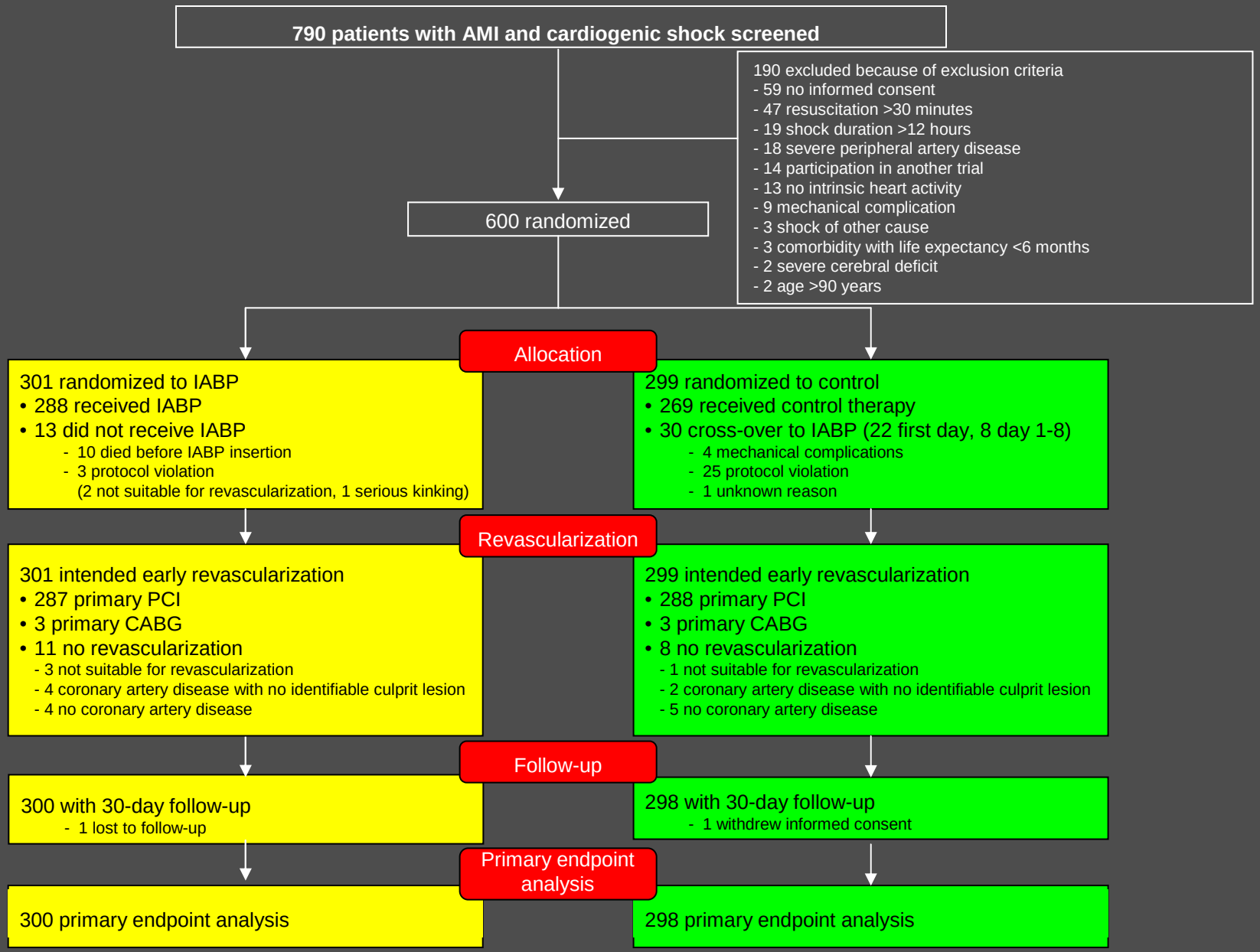
- GUSTO bleeding (severe/Life-Threatening and moderate)
- Peripheral ischemic complications
- Sepsis
- Stroke

Sjauw et al. Eur Heart J 2009;30:459-468
Thiele et al. Am Heart J 2012;163:938-45

Results

Trial Flow and Treatment

IABP SHOCK II RANDOMIZED CLINICAL TRIAL



Results

Patient Characteristics

IABP SHOCK II RANDOMIZED CLINICAL TRIAL

	IABP (n=301)	Control (n=299)
Age (years); median (IQR)	70 (58-78)	69 (58-76)
Male sex; n (%)	202 (67.1)	211 (70.6)
Current Smoking; n/total (%)	96/295 (32.5)	108/299 (36.1)
Hypertension; n/total (%)	213/296 (72.0)	199/299 (66.6)
Hypercholesterolemia; n/total (%)	122/295 (41.4)	105/299 (35.1)
Diabetes mellitus; n/total (%)	105/297 (35.4)	90/299 (30.1)
Body mass index (kg/m^2); median (IQR)	27.5 (24.7-30.1)	26.9 (24.7-29.4)
Prior myocardial infarction; n/total n (%)	71/300 (23.7)	61/299 (20.4)
Prior PCI; n/total n (%)	63/299 (21.1)	52/299 (17.4)
Prior CABG; n/total (%)	20/300 (6.7)	12/299 (4.0)
Fibrinolysis < 24 h before randomization; n/total (%)	28/301 (9.3)	20/299 (6.7)
STEMI/LBBB; n/total (%)	200/300 (66.7)	212/298 (71.1)
NSTEMI; n/total (%)	96/300 (32.0)	81/298 (27.2)
Resuscitation before randomization; n/total (%)	127/301 (42.2%)	143/299 (47.8)
Signs of impaired organ perfusion; n/total (%)		
Altered mental status	215/300 (71.7)	232/299 (77.6)
Cold, clammy skin and extremities	257/300 (85.7)	245/299 (81.9)
Oliguria	90/300 (30.0)	99/299 (33.1)
Serum lactate >2.0 mmol/l	226/300 (75.3)	218/298 (73.2)
Creatinine clearance (ml/min); median (IQR)	60.7 (43.4-86.6)	56.8 (39.7-78.1)
Infarct related artery; n/total (%)		
LAD	132/293 (45.1)	121/293 (41.3)
LCX	55/293 (18.8)	57/293 (19.5)
RCA	73/293 (24.9)	79/293 (27.0)
Left main	26/293 (8.9)	28/293 (9.6)
Bypass graft	7/293 (2.4)	8/293 (2.7)
Multivessel disease; n/total (%)	235/296 (79.4)	228/293 (77.9)
Left ventricular ejection fraction (%); median (IQR)	35 (25-45)	35 (25-45)

Results

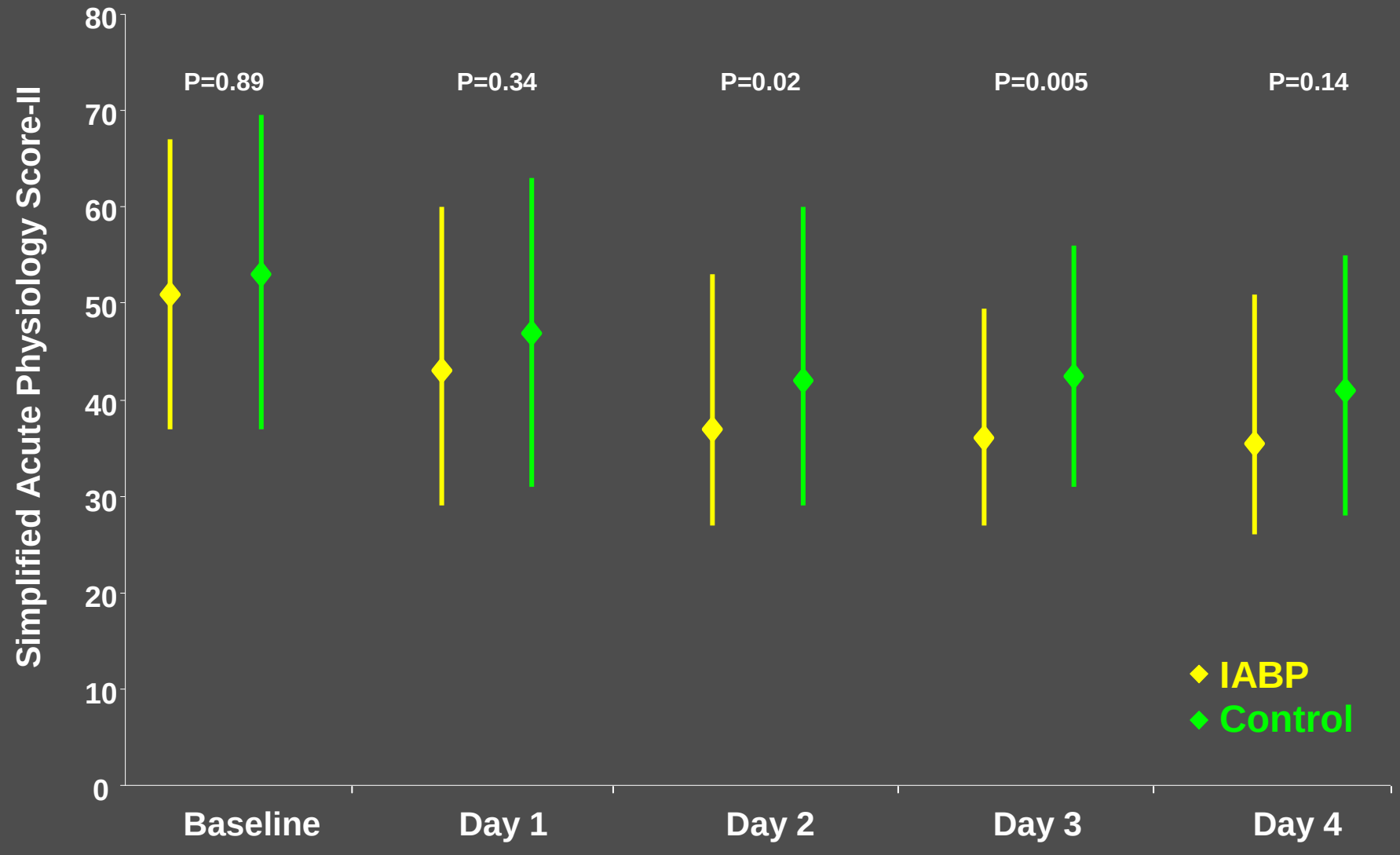
Treatment

IABP SHOCK II RANDOMIZED CLINICAL TRIAL

Variable	IABP (n=301)	Control (n=299)	p
Primary PCI; n/total (%)	287/301 (95.3)	288/299 (96.3)	0.55
Stent implanted; n/total (%)	273/301 (90.7)	266/299 (89.0)	0.48
Drug-eluting stent; n/total (%)	126/301 (41.9)	123/299 (41.1)	0.86
Immediate PCI of non-culprit lesions; n/total (%)	90/301 (29.9)	81/299 (27.1)	0.45
Immediate bypass surgery; n/total (%)	8/301 (2.7)	10/299 (3.3)	0.62
Staged bypass surgery; n/total (%)	3/301 (1.0)	4/299 (1.3)	0.72
Active left ventricular assist device; n/total (%)	11/301 (3.7)	22/299 (7.4)	0.05
Mild hypothermia; n/total (%)	106/301 (35.2)	120/299 (40.1)	0.21
Mechanical ventilation; n/total (%)	240/301 (79.7)	252/299 (84.3)	0.15
Duration of mechanical ventilation (days); median (IQR)	3.0 (1.0-8.0)	3.0 (1.0-8.0)	0.44
Duration of intensive care treatment (days); median (IQR)	6.0 (3.0-12.0)	6.0 (3.0-13.0)	0.34
Renal replacement therapy; n/total (%)	62/301 (20.6)	47/299 (15.7)	0.12
Antiplatelets and anticoagulation; n/total (%)	293/299 (98.0)	284/298 (95.3)	0.07
Aspirin	216/299 (72.2)	206/298 (69.1)	0.40
Clopidogrel	80/299 (26.8)	76/298 (25.5)	0.73
Prasugrel	19/234 (8.1)	15/228 (6.6)	0.52
Ticagrelor*	138/299 (46.2)	143/298 (48.0)	0.63
Glycoprotein IIb/IIIa-inhibitors	288/299 (96.3)	275/298 (92.3)	0.03
Unfractionated heparin	60/299 (20.1)	59/298 (19.8)	0.94
Low molecular weight heparin	29/299 (9.7)	36/298 (12.1)	0.34
Bivalirudin			
Catecholamines (µg/kg per minute); median (IQR)			
Dopamine	2.0 (1.2-3.6)	2.0 (1.0-2.6)	0.46
Norepinephrine	0.12 (0.04-0.33)	0.11 (0.04-0.28)	0.13
Epinephrine	0.10 (0.04-0.26)	0.08 (0.03-0.19)	0.045
Dobutamine	3.0 (1.5-6.1)	3.1 (1.5-6.8)	0.70
Duration of catecholamines (days), median (IQR)	3.0 (1.0-5.0)	3.0 (1.0-6.0)	0.81
Time to hemodynamic stabilization (days); median (IQR)	3.0 (1.0-5.0)	3.0 (1.0-6.0)	0.50

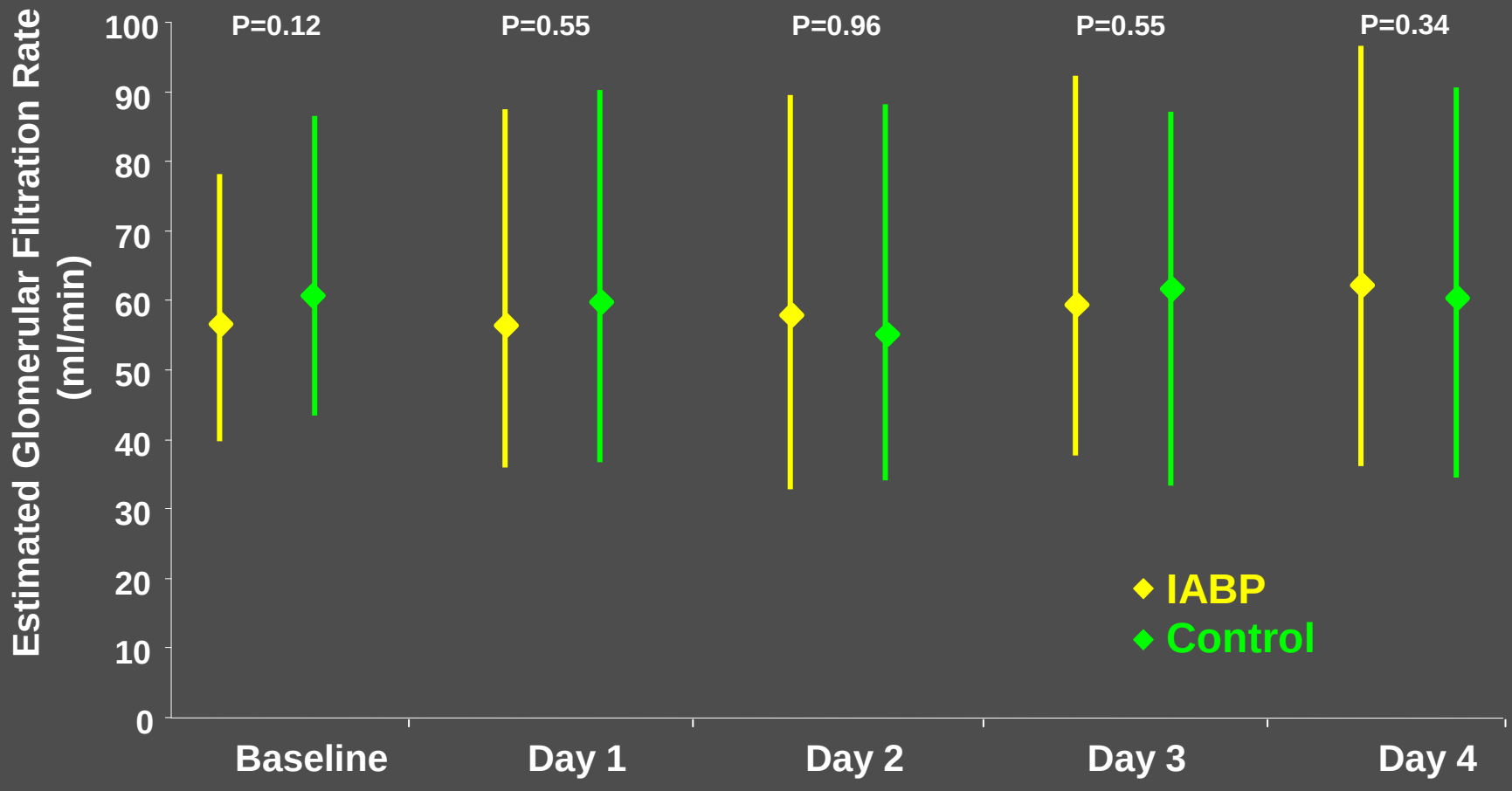
Results

Simplified Acute Physiology Score-II



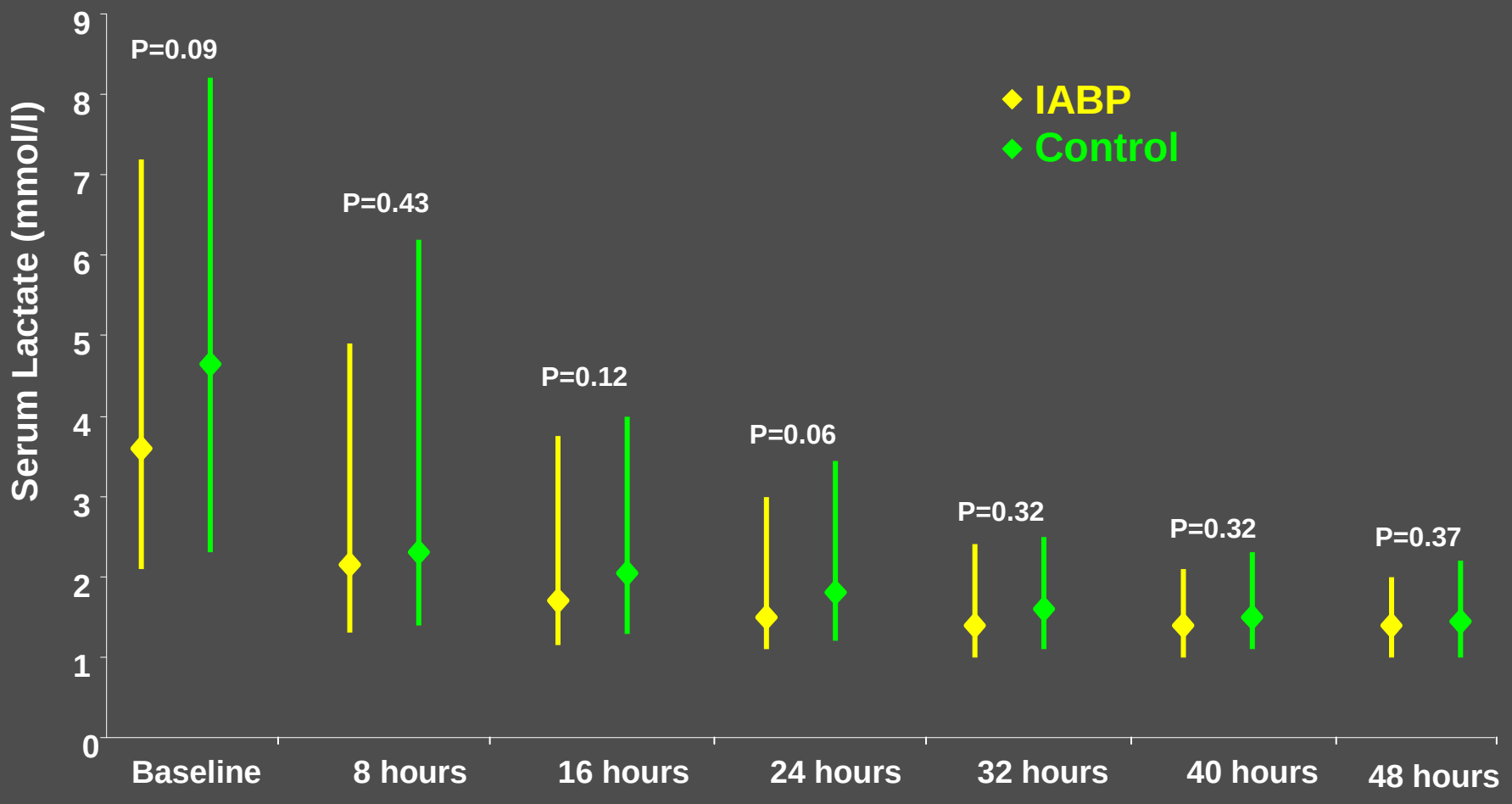
Results

Renal Function (eGFR)



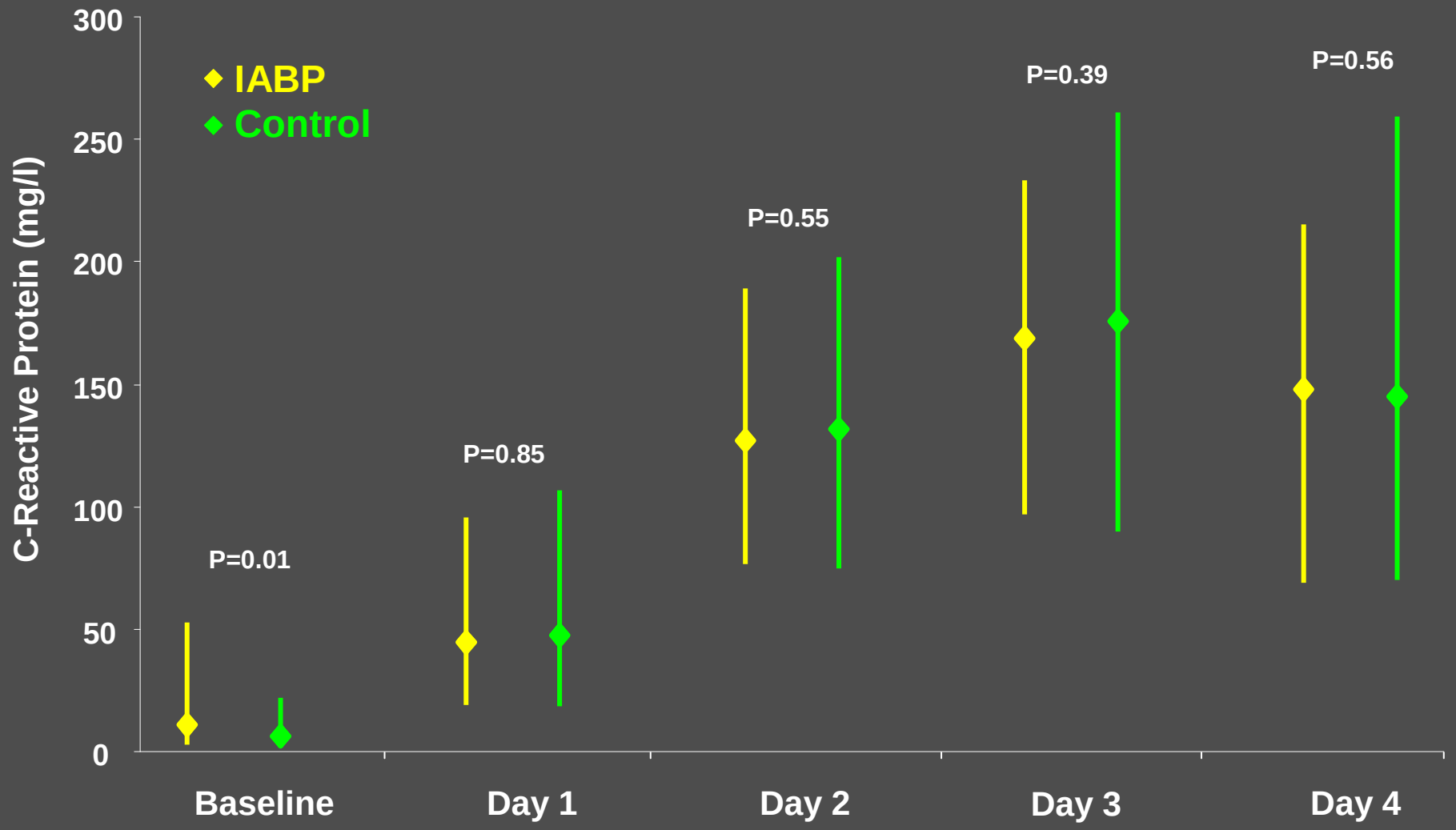
Results

Microcirculation (Serum Lactate)



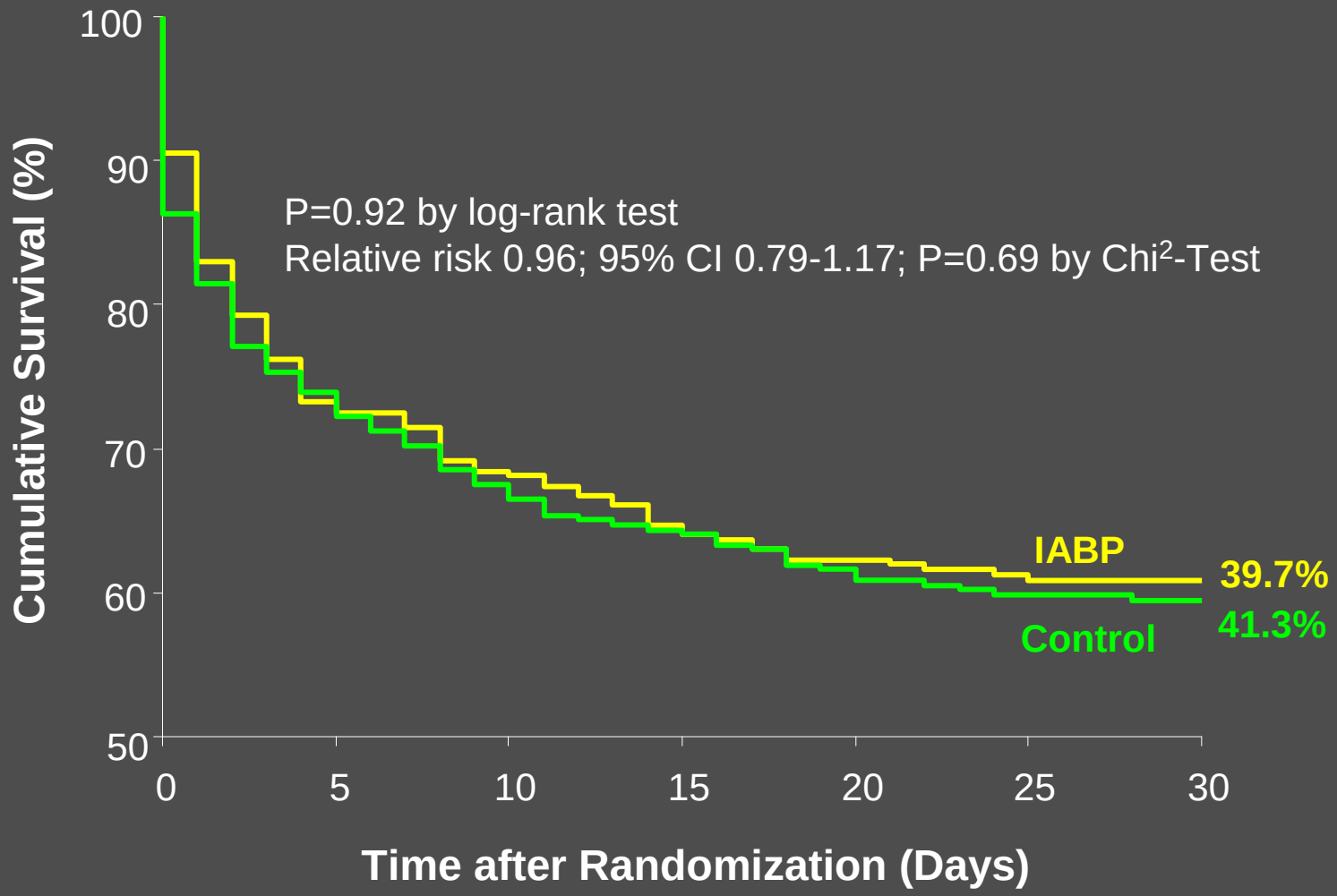
Results

Inflammatory Reaction (CRP)



Results

Primary Study Endpoint (30-Day Mortality)

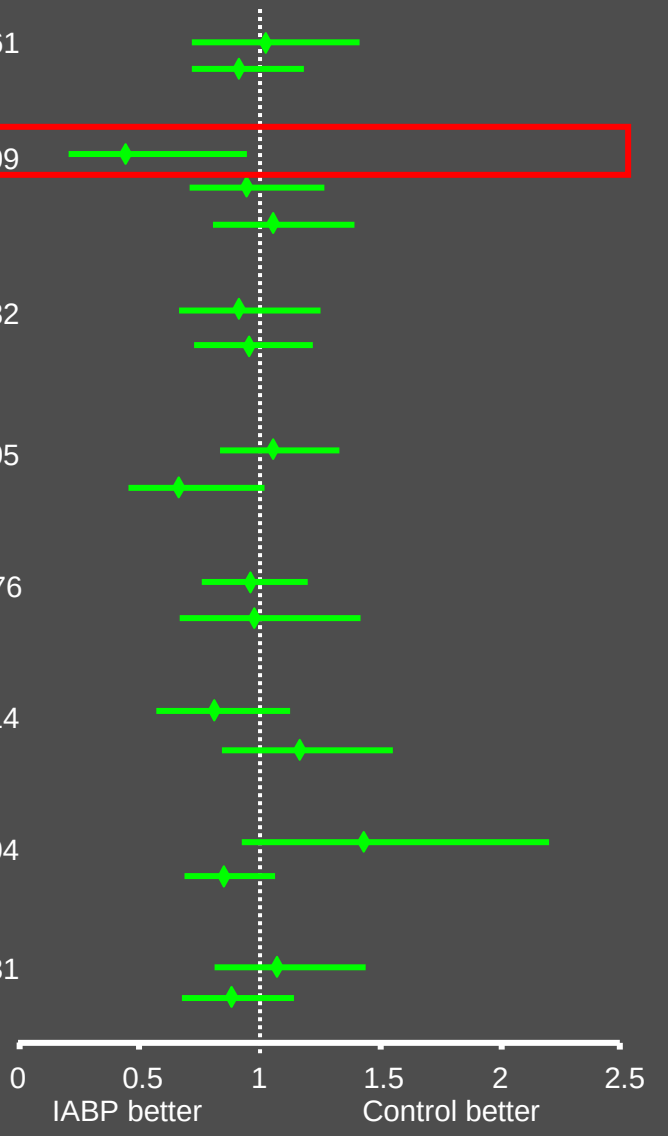


Results

Subgroups (30-Day Mortality)

IABP SHOCK II RANDOMIZED CLINICAL TRIAL

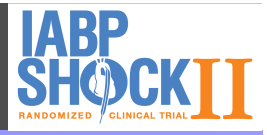
Baseline Variable	N	30-Day Mortality (%) IABP	30-Day Mortality (%) Control	Relative Risk (95% CI)	P-Value for Interaction
Female	187	44.4	43.2	1.03 (0.74-1.43)	0.61
Male	411	37.3	40.5	0.92 (0.72-1.18)	
Age <50 years	70	19.4	44.1	0.44 (0.21-0.95)	0.09
Age 50-75 years	334	34.6	36.5	0.95 (0.71-1.27)	
Age >75 years	194	53.7	40.0	1.07 (0.81-1.41)	
Diabetes	195	42.9	46.7	0.92 (0.67-1.26)	0.82
No diabetes	399	37.2	38.9	0.96 (0.74-1.23)	
Hypertension	410	42.9	40.4	1.06 (0.84-1.34)	0.05
No hypertension	183	28.9	43.0	0.67 (0.45-1.01)	
STEMI/LBBB	412	41.0	42.9	0.96 (0.77-1.21)	0.76
NSTEMI	177	37.5	38.3	0.98 (0.67-1.43)	
Anterior STEMI	216	35.4	43.7	0.81 (0.58-1.13)	0.14
Non-anterior STEMI	196	48.3	42.2	1.16 (0.85-1.57)	
Previous infarction	131	47.9	33.3	1.44 (0.93-2.21)	0.04
No previous infarction	466	37.3	43.3	0.86 (0.69-1.07)	
Hypothermia	226	48.1	44.2	1.09 (0.82-1.44)	0.31
No hypothermia	372	35.1	39.3	0.89 (0.68-1.16)	



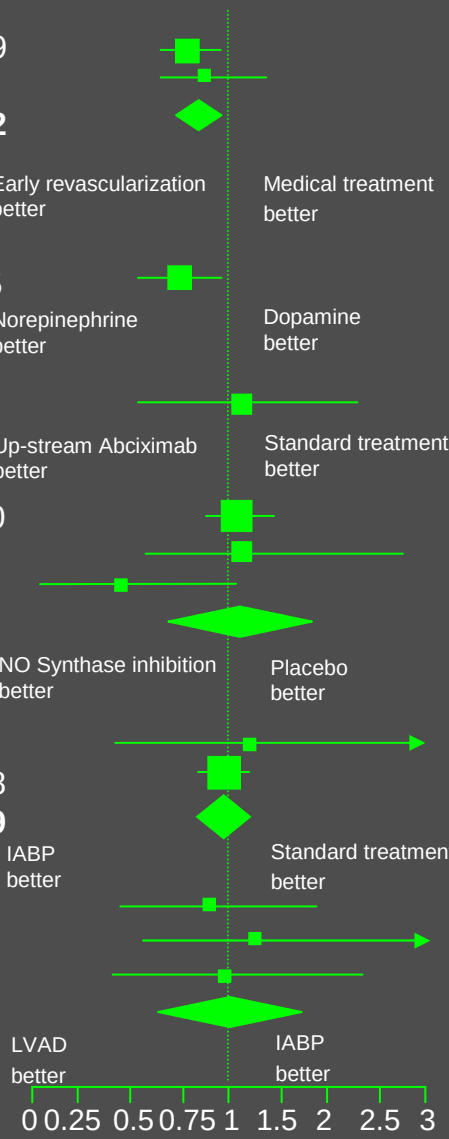
Safety

	IABP (n=300)	Control (n=298)	P
Stroke in-hospital n/total (%)	2/300 (0.7)	5/298 (1.7)	0.28
GUSTO bleeding; n/total n (%)			
Life-threatening/severe	10/300 (3.3)	13/298 (4.4)	0.51
Moderate	52/300 (17.3)	49/298 (16.4)	0.77
Peripheral ischemic complication requiring intervention; n/total n (%)	13/300 (4.3)	10/298 (3.4)	0.53
Sepsis; n/total n (%)	47/300 (15.7)	61/298 (20.5)	0.15

Randomized Studies in Cardiogenic Shock



Trial	Follow-up	n/N	n/N	Relative Risk 95% CI	Relative Risk 95% CI
Revascularization (PCI/CABG)					
SHOCK	1-year	76/152	83/149		0.80 (0.66;0.98)
SMASH	30 days	22/32	18/23		0.87 (0.66;1.29)
Total		**103/184**	**117/172**		**0.82 (0.70;0.98)**
Catecholamines					
SOAP II (CS Subgroup)	28 days	64/145	50/135		0.75 (0.55;0.93)
Glycoprotein IIb/IIIa-Inhibitors					
PRAGUE-7	In-hospital	15/40	13/40		1.15 (0.59;2.27)
NO Synthase Inhibitors					
TRIUMPH	30 days	97/201	76/180		1.14 (0.91;1.45)
SHOCK-2	30 days	24/59	7/20		1.16 (0.59;2.69)
Cotter et al	30 days	4/15	10/15		0.40 (0.13;1.05)
Total		**125/275**	**93/215**		**1.05 (0.85;1.29)**
IABP					
IABP-SHOCK I	30 days	7/19	6/21		1.28 (0.45;3.72)
IABP-SHOCK II	30 days	119/300	123/298		0.96 (0.79;1.17)
Total		**126/319**	**129/319**		**0.98 (0.81;1.18)**
LVAD					
Thiele et al	30 days	9/21	9/20		0.95 (0.48;1.90)
Burkhoff et al	30 days	9/19	5/14		1.33 (0.57-3.10)
Seyfarth et al	30 days	6/13	6/13		1.00 (0.44-2.29)
Total		**24/53**	**20/47**		**1.06 (0.68-1.66)**



Updated from Thiele et al. Eur Heart J 2010,31:1828-1835

Summary + Conclusions

- IABP support in cardiogenic shock is safe without significant inherent complications.
- However, IABP support did not reduce 30-day mortality in this large, randomized, multicenter trial in cardiogenic shock patients complicating myocardial infarction undergoing early revascularization.
- The primary study endpoint results are supported by a lack of benefit in secondary endpoints.

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IABP-SHOCK II Investigators from 37 German Sites

Steering Committee

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K. Werdan
U. Zeymer

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