Intra-aortic balloon counterpulsation and infarct size in patients with acute anterior myocardial infarction without shock: The CRISP AMI Randomized Trial

Manesh R. Patel, MD, Richard W. Smalling, MD, PhD,
Holger Thiele, Prof Dr med, Huiman X. Barnhart, PhD, Yi Zhou, PhD,
Praveen Chandra, MD, Derek Chew, MD, Marc Cohen, MD,
John French, MB CHB, PhD, Divaka Perera, MD,E. Magnus Ohman, MD

European Society of Cardiology – Hotline Presentation August 30th 2011

Duke Clinical Research Institute

MAQUET
GETINGE GROUP

Background

- Despite improvements in STEMI care
  - The 6 month mortality remains high ~10%[1]
- Intra-aortic balloon counterpulsation
  - ↑Diastolic arterial pressure (coronary perfusion pressure)
  - ↓Simultaneously decrease afterload and left ventricular end diastolic pressure (LVEDP) - both work to decrease oxygen consumption
  - Decreases infarct expansion when placed prior to reperfusion in animal studies [2,3]

[1]Heart disease and stroke statistics--2009 update. Circulation 2009;119:e21-181.
[2]LeDoux JF et. al.. Catheterization & Cardiovascular Interventions 2008;72:513-21.
[3]Azevedo CF et. al. European Heart Journal 2005;26:1235-41.

Primary Objective

CRISP am counterpulsation reduces infarct size pre pci in acute myocardial infarction

To determine whether routine initiation of intra-aortic balloon counterpulsation (IABC) before mechanical reperfusion compared to standard of care (SOC) primary PCI decreases infarct size in patients with anterior ST-segment elevation myocardial infarction (STEMI) without cardiogenic shock

Study Design

CRISP am — counterpulsation reduces infarct size pre pci in acute myocardial infarction

Anterior STEMI without Shock

Inclusion Criteria
- Anterior STEMI
  2 mm in 2 contiguous leads or at least 4 mm in the anterior leads
- Planned Primary PCI within 6 hrs
- Adult able to consent

Intra-aortic Balloon Counterpulsation prior to PCI

Randomize
Open Label
(n ~ 300)

Standard of Care Primary PCI

At least 12 hours of IABC post PCI

Routine Post PCI care

Cardiac MRI performed day 3-5 post PCI

Primary Endpoint: Infarct Size on CMR
1. All Patients with CMR data
2. Patients with Prox LAD occlusion TIMI 0/1 flow

Clinical Events – 6 months

clinicaltrials.gov as # NCT00833612.
Also at controlled-trials.com #ISRCTN89012474

Exclusion Criteria

CRISP am counterpulsation reduces infarct size pre pci in acute myocardial infarction

- Known Contraindication to MRI
- Prior Thrombolytic Therapy for STEMI
- Cardiogenic Shock
- Prior MI, CABG, or ESRD
- Contraindications to IABC
  - Known Severe AI, AAA, or severe peripheral artery disease
  - >400 lbs of < 4 feet

Statistical Methodology

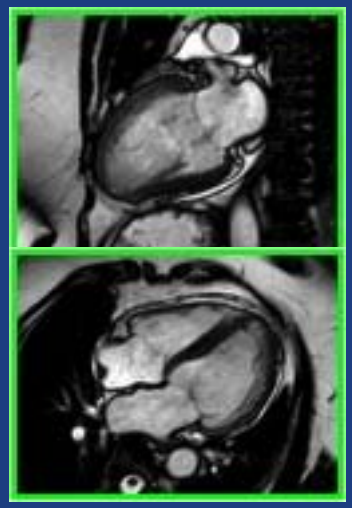
CRISP am counterpulsation reduces infarct size pre pci in acute myocardial infarction

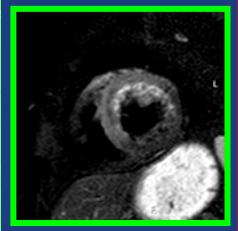
- **Sample Size**
  - Estimated Infarct size
    - All patients (25.3 -26.6% LV)[1,2] and (19.9 - 28.8% LV)[1,2] prox. LAD TIMI 0/1
  - 25% reduction (270 patients) 10% CMR data missing
  - >80% power, Type 1 error 0.025 (2-sided)
  - **~ 300 patients**
- **Primary Endpoint Evaluation:** Infarct Size on CMR
  - Modified ITT – all patients with CMR data
  - All CMR patients with proximal LAD occlusion TIMI 0/1
- **Primary Safety Evaluation:** Major vascular complications and Major bleeding
- **Clinical Outcomes:** 6-month rate all cause mortality, MACE

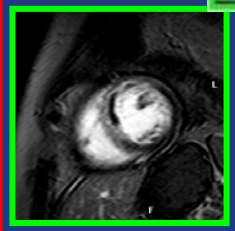
[1] Patel et al. Jacc: Cardiovascular Imaging 2010;3:52-60
[2] Thiele et al. Circulation 2008 Jul 1;118(1):49-57 Epub 2008 Jun 16

CMR Protocol

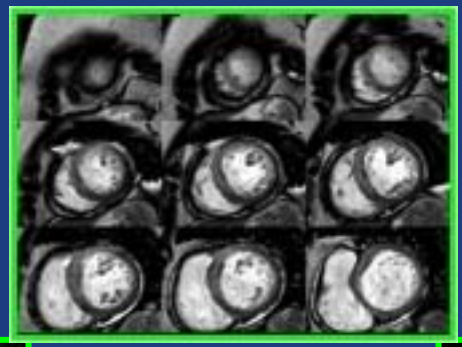
CRISP am — counterpulsation reduces infarct size pre pci in acute myocardial infarction

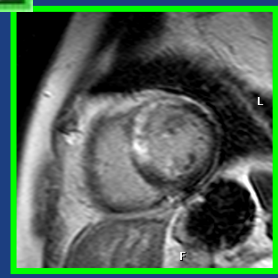


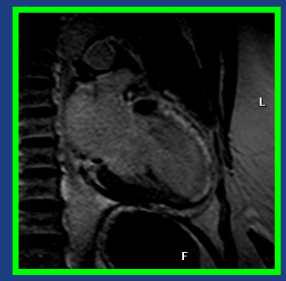


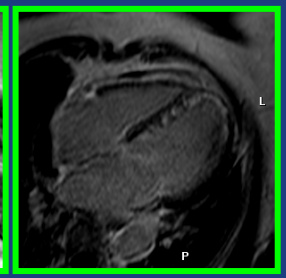


Contrast-injection 0.15 mmol/kg/KG Bolus Gadovist i.v.









0 5 10 15 20 25 30 35 40

Time (min)

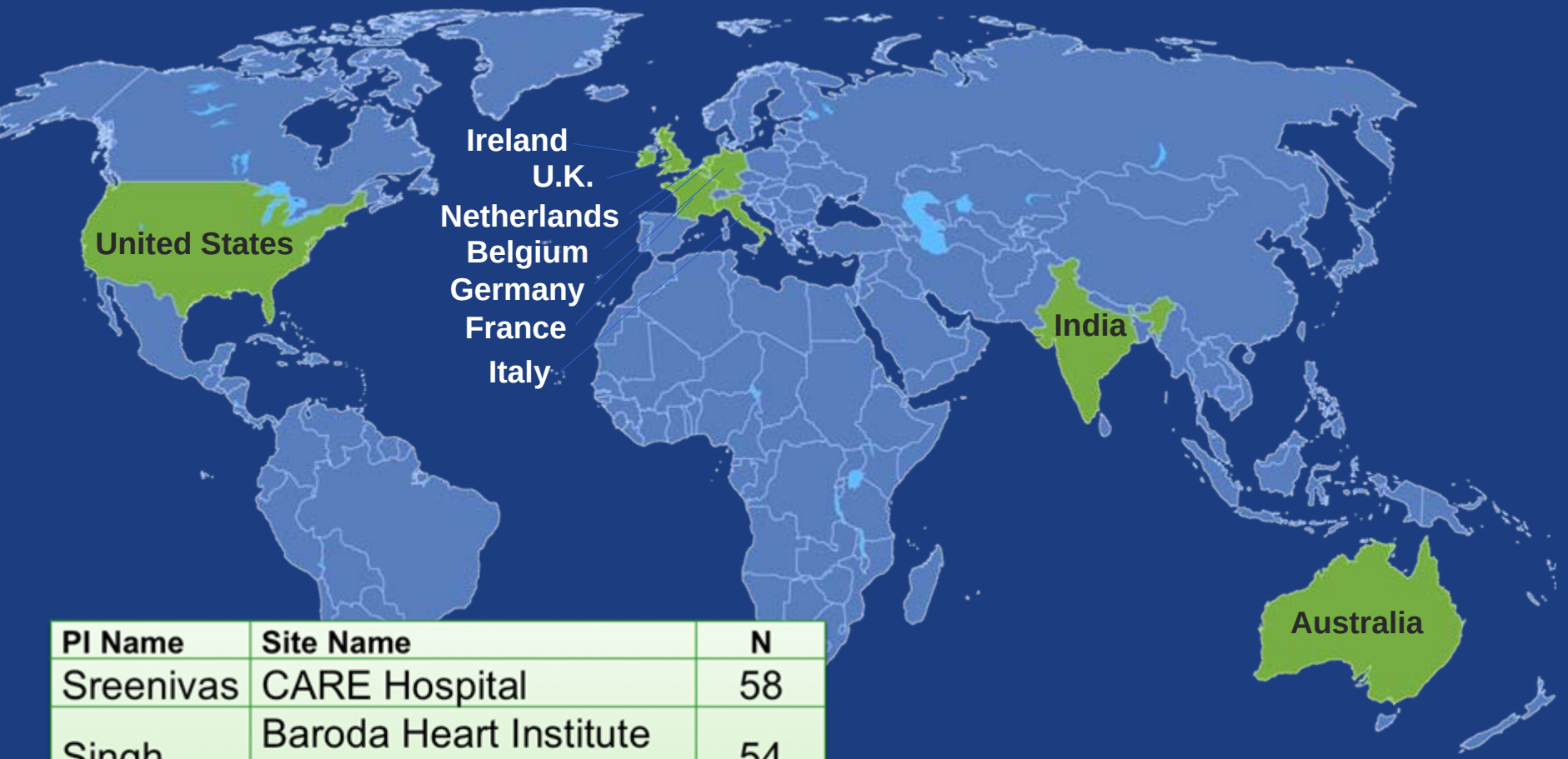
Survey

Function	Edema	Early enhancement	Function	Delayed enhancement	Delayed enhancement
4-chamber 2-chamber	3 short axes	Short axes Apex-Base	Short axes Apex-Base	Short axes Apex-Base	4-chamber 2-chamber
SSFP sequence (TR/TE/flip = 3.2ms/1.2ms/60°)	T2 STIR sequence (TR/TE/flip = 2 heart beats/80ms/90°) slice thickness: 8-10 mm	Inversion recovery gradient echo sequence (TR/TE/flip 2.8ms/1.1ms/15°) slice thickness: 8-10 mm, no gap	SSFP sequence (TR/TE/flip = 3.2ms/1.2ms/60°) slice thickness: 8-10 mm, no gap	Inversion recovery gradient echo sequence (TR/TE/flip 2.8ms/1.1ms/15°) slice thickness: 8-10 mm, no gap	

Enrollment

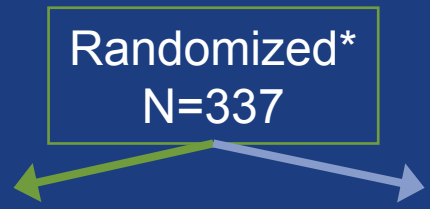
9 countries, 30 sites, 337 patients

CRISP am — counterpulsation reduces infarct size pre pci in acute myocardial infarction



PI Name	Site Name	N
Sreenivas	CARE Hospital	58
Singh	Baroda Heart Institute and Research Centre	54
Blaxill	Leeds General Infirmary	32
Pijls	Catherina Hospital	28
Mills	Duke Univ. Med Center	23

Study Conduct



	IABC N=161	SOC N=176
Received intervention	153 (95.03%)	161 (91.48%)
Withdrew	4	2
Lost to follow-up		
MRI not performed		
Died		
Unstable		
Metallic contraindication	3	1
Unable to tolerate	11	18
Other	6	0
MRI performed, not evaluable	**5**	**7**

Crossing over to IABC	**15**
Sustained hypotension/Cardiogenic shock	12
To prevent event post□vessel dissection	1
Failed PCI of IR vessel	1
Continued chest pain	1

Baseline Demographics

	All (N=337)	IABC (N=161)	SOC (N=176)
Age, median (25th, 75th), yrs	56.6 (48.4, 65.6)	56.1 (48.3, 64.3)	57.7 (48.6, 66.4)
Male, %	81.9	82.0	81.8
Race, %			
White	47.8	50.3	45.5
Asian	45.1	46.6	43.8
Black or African American	4.7	1.9	7.4
Other	2.1	1.2	2.8
Medical history, %			
Hypertension on drug tx.	29.4	24.2	34.1
Current nicotine use	31.8	33.1	30.7
Dyslipidemia on drug tx.	12.5	12.5	12.5
Diabetes mellitus	18.7	16.8	20.5

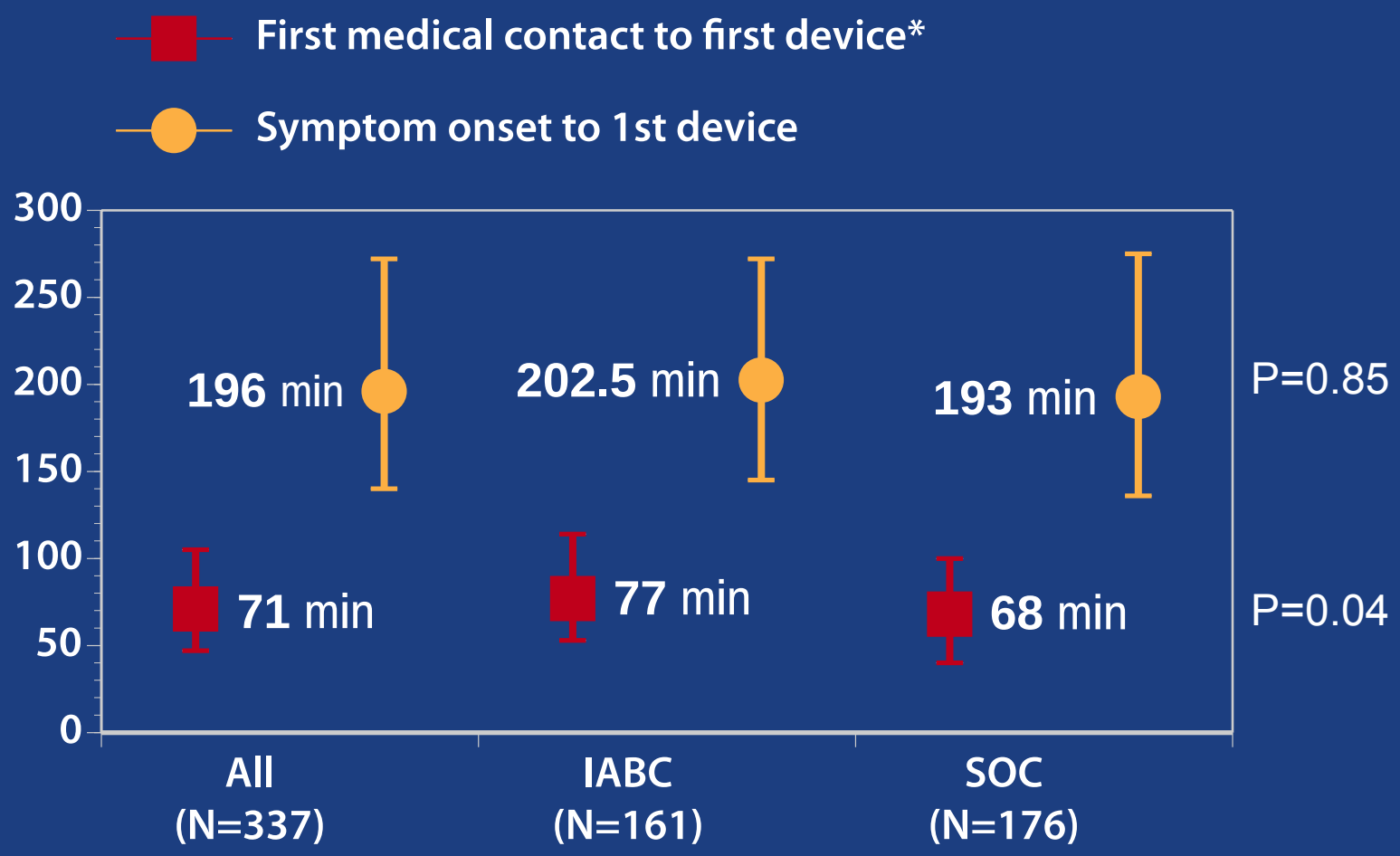
Baseline Demographics (cont.)

	All (N=337)	IABC (N=161)	SOC (N=176)
SBP, median (25th, 75th), mm Hg	131.0 (118.0, 150.0)	130.0 (113.0, 150.0)	135.0 (120.0, 151.0)
DBP, median (25th, 75th), mm Hg	80.0 (70.0, 92.0)	80.0 (70.0, 92.0)	80.0 (71.5, 92.0)
HR, median (25th, 75th), bpm	81.0 (71.0, 94.0)	81.0 (71.0, 93.0)	80.0 (70.0, 94.0)
ST ↑ in anterior leads, no. (%)			
0–<2 mm	0 (0.0)	0 (0.0)	0 (0.0)
2–<4 mm	1 (0.3)	0 (0.0)	1 (0.6)
4–<6 mm	135 (40.1)	61 (37.9)	74 (42.0)
≥6 mm	201 (59.6)	100 (62.1)	101 (57.4)

PCI Procedure

	All N=337	IABC N=161	SOC N=176
PCI			
PCI performed, %	94.3	96.3	92.6
Infarct-related artery			
Left anterior descending, %	97.6	99.4	96.0
Infarct-related artery stenosis location			
Proximal, %	62.9	64.8	61.2
Infarct-related artery TIMI flow pre-intervention			
Grade 0, %	65.3	66.0	64.7
Grade 1, %	10.3	11.3	9.4
Infarct-related artery final TIMI flow post-intervention			
Grade 3, %	94.2	92.9	95.3

Time to Treatment



Primary outcome

	All (N=337)	IABC (N=161)	SOC (N=176)	P Value
Primary endpoint				
Infarct size (% LV), modified ITT all patients with CMR data				**0.060**
N	275	133	142	
Mean	39.8	42.1	37.5	
Median	38.8	42.8	36.2	
Infarct size (% LV), modified ITT patients prox. LAD and TIMI flow 0/1				**0.110**
N	192	93	99	
Mean	44.4	46.7	42.3	
Median	42.1	45.1	38.6	

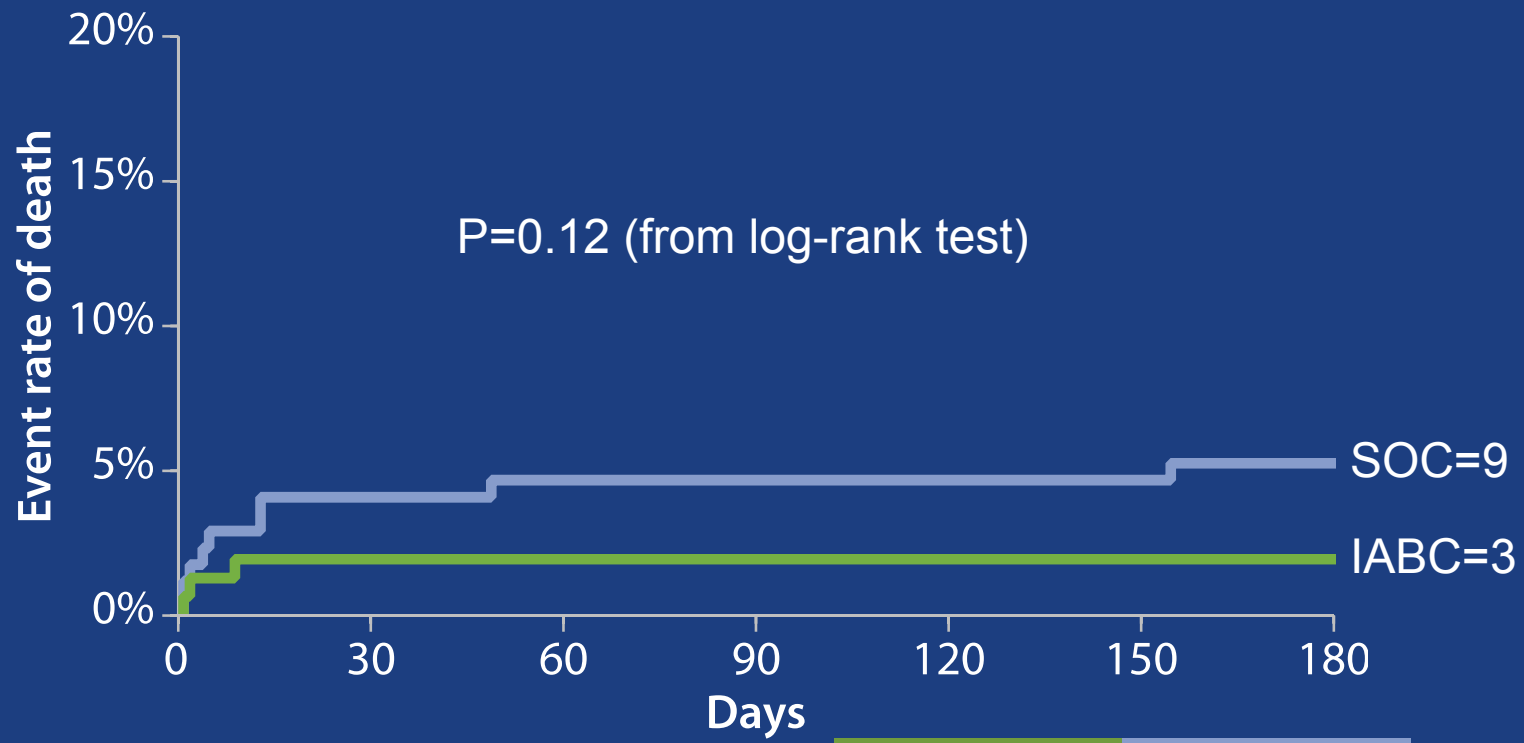
Co-primary endpoint: 2-sided p=0.025

30-day Clinical Events

	IABC (N=161)	SOC (N=176)	P Value
Death, %	1.9*	4.0*	0.26*
Stroke, %	1.9	0.6	0.35
Major bleed per GUSTO 1 definition or transfusion, %	3.1	1.7	0.49
Vascular complications, (n) %	7(4.3)	2 (1.1)	0.09
Major limb ischemia requiring operative intervention (n)	0	0	
Distal embolization (n)	0	0	
Major dissection (n)	2	0	
Pseudoaneurysm or AV fistula (n)	3	2	
Hematoma >5 cm (n)	3	0	

*From KM curves and log-rank test.

All Cause Death – 6 months



	IABC (N=161)	SOC (N=176)	P Value
Death, %	1.9*	5.2*	0.12*
Death/recurrent MI/new or worsening CHF, %	6.3*	10.9*	0.15*
Death/shock/new or worsening CHF, %†	5.0*	12.0*	0.03*

**From KM curves and log-rank test.* *†Exploratory analysis.*

Conclusion

CRISP am counterpulsation reduces infarct size pre pci in acute myocardial infarction

Among Patients with Acute Anterior STEMI without cardiogenic shock use of Intra-aortic counterpulsation prior to PCI compared to standard of care PCI:

1. Does not reduce infarct size
2. All cause mortality at 6 months was not different
3. Exploratory composite clinical endpoint favored of IABC

Lessons for Current and Future Care

CRISP am counterpulsation reduces infarct size pre pci in acute myocardial infarction

- These findings do not support the routine use of IABC prior to PCI in Anterior STEMI patients without cardiogenic shock,
- Clinicians should continue to be vigilant about identifying patients who are at risk for rapid deterioration or hypotension that may benefit from support, as seen with the cross-over in this trial (8.5%)
- Acute STEMI studies are feasible without significant increases in door-to-device times

Acknowledgements

CRISP Steering Committee
Manesh R. Patel, Holger Thiele, Richard W. Smalling, Praveen Chandra, Marc Cohen, Divaka Perera, Derek Chew, John French, E. Magnus Ohman

CRISP AMI investigators
Sreenivas Kumar A., Singh, Blaxill, Pijls, Mills, Thomas, Henriksen, Smalling, Passey, Bashir, McCann, Weintraub, Cohen, Vranckx, Thiele, Reddy, Schwab, Ling, Garg, Chandra, Sinhal, Casale, Banerjee, Khanna, Hillegass, Varghese, Satler, Strasser, Biederman, Shavelle, Valente, Lefevre, Kaluski, Carozza Jr.. Weeks. Bush. Saligrama, Bingi. Talwar, Diebele

DSMB
Eric Bates, David Holmes, Richard Trout

Global Coordinating Center
Duke Clinical Research Institute
•Pam Monds, Project Lead
•Dorothy J Wagstaff, Lead Clinical Data Specialist
•Joey Zhou, Huiman Barnhardt - Statistician
•Karen Ramsey, Lead CRA

MRI Core Lab
The Heart Center Leipzig -University Hospital
•Matthias Gutberlet – Director, Maren Redlich
•Fabian Juhrich,

Regional Centers groups
•Meredith Cooney, Flinders Coordinating Centre, Australia/NZ Lead
•Tanya Fawcett, MAQUET CV, Europe Lead
•Vaibhav S. Pawar, Jubilant Clinsys Ltd., India Lead


CRISP
ami
counterpulsation
reduces infarct
size pre pci in
acute myocardial
infarction