Intracoronary Compared with Intravenous Bolus Abciximab Application During Primary Percutaneous Coronary Intervention

Cardiac Magnetic Resonance Substudy of the AIDA STEMI trial

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on behalf of the AIDA STEMI Investigators

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Disclosures

Off-label use of IC abciximab

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Potential Conflict of Interest:

Research Funding:
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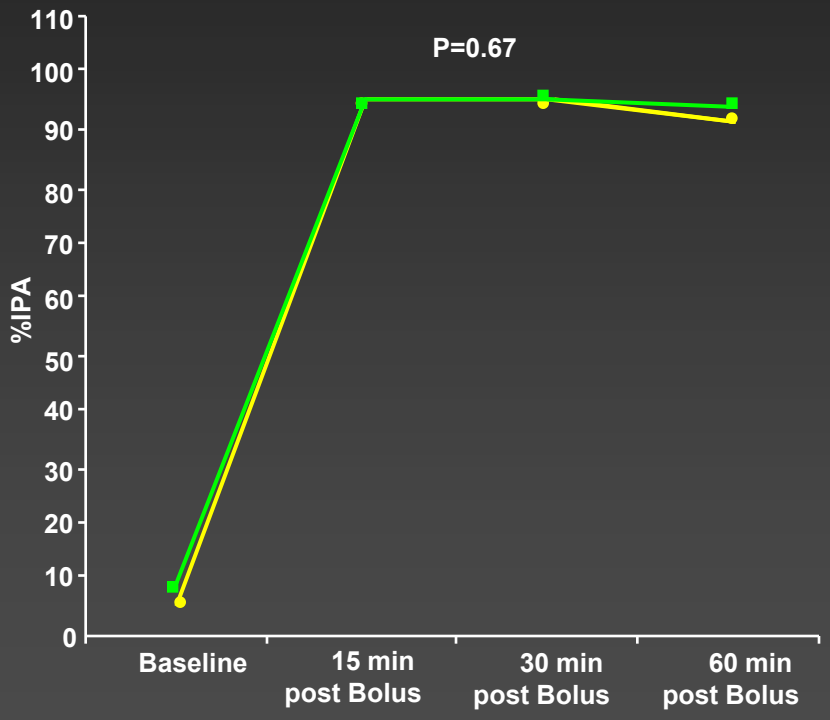
Consulting:
Maquet Cardiovascular, Avidal

Speaker Honoraria:
Lilly, Astra Zeneca, Daiichi Sankyo, Boehringer Ingelheim, Maquet Cardiovascular, Medicines Company

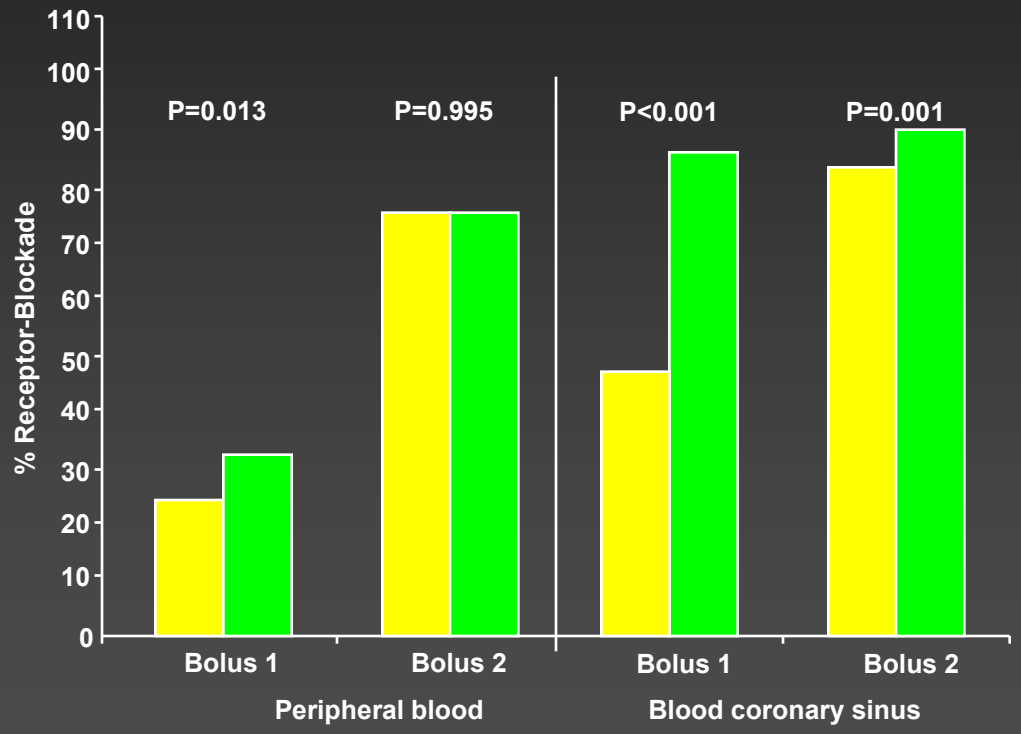
GP IIb/IIIa IC versus IV

2 x Bolus within 10 min. 180 µg/kg eptifibatide IC versus IV, subsequently 2 µg/kg^{-1} .min^{-1} continuous infusion i.v. for 18 h

IPA Periphery (20 µmol/L ADP)



GpIIb/IIIa Receptor-Blockade



IC Eptifibatide n=21

IV Eptifibatide n=19

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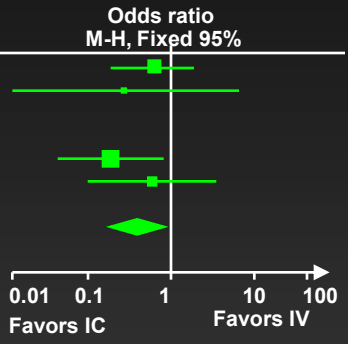
Deibele et al. Circulation 2010;121:784-791

Abciximab IC versus IV

30-day Mortality

Study or Subgroup	Intracoronary abciximab Events	Total	Intravenous abciximab Events	Total	Weight	Odds ratio M-H, Fixed 95%
CICERO 2010	5	271	7	263	33.7%	0.69
CRYSTAL AMI 2010	0	25	1	23	7.4%	0.29 (0.01;7.59)
Dominguez-Rodriguez 2009	0	25	0	25		Not estimable
EASY-MI 2010	0	53	0	52		Not estimable
Iversen 2011	2	185	9	170	44.8%	0.20 (0.04;0.92)
Thiele 2008	2	77	3	77	14.1%	0.66 (0.11;4.05)
Total (95%)		636		610	100.0%	0.43 (0.20;0.94)
Total events	9		20			

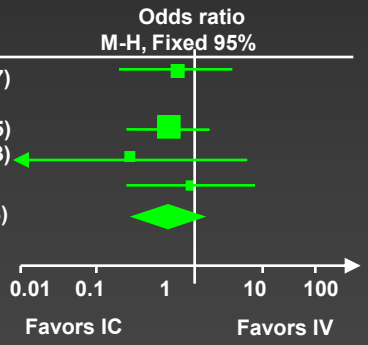
Heterogeneity: Chi^2 =1.88, df=3 (P=0.60);I^2=0%
Test for overall effect: Z=2.11 (P=0.03)



30-day Myocardial Infarction

Study or Subgroup	Intracoronary abciximab Events	Total	Intravenous abciximab Events	Total	Weight	Odds ratio M-H, Fixed 95%
CICERO 2010	3	271	4	263	27.5%	0.72 (0.16;3.27)
EASY-MI 2010	0	53	0	52		Not estimable
Iversen 2011	5	185	8	170	55.5%	0.56 (0.18;1.75)
Thiele 2008	0	77	2	77	17.0%	0.19 (0.01;4.13)
Total (95%)		586		562	100.0%	0.54 (0.23;1.28)
Total events	8	636	14			

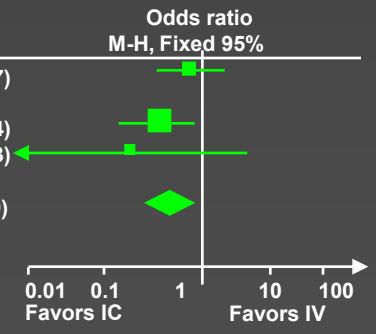
Heterogeneity: Chi^2 =0.58, df=2 (P=0.75);I^2=0%
Test for overall effect: Z=1.39 (P=0.17)



30-day Target Vessel Revascularization

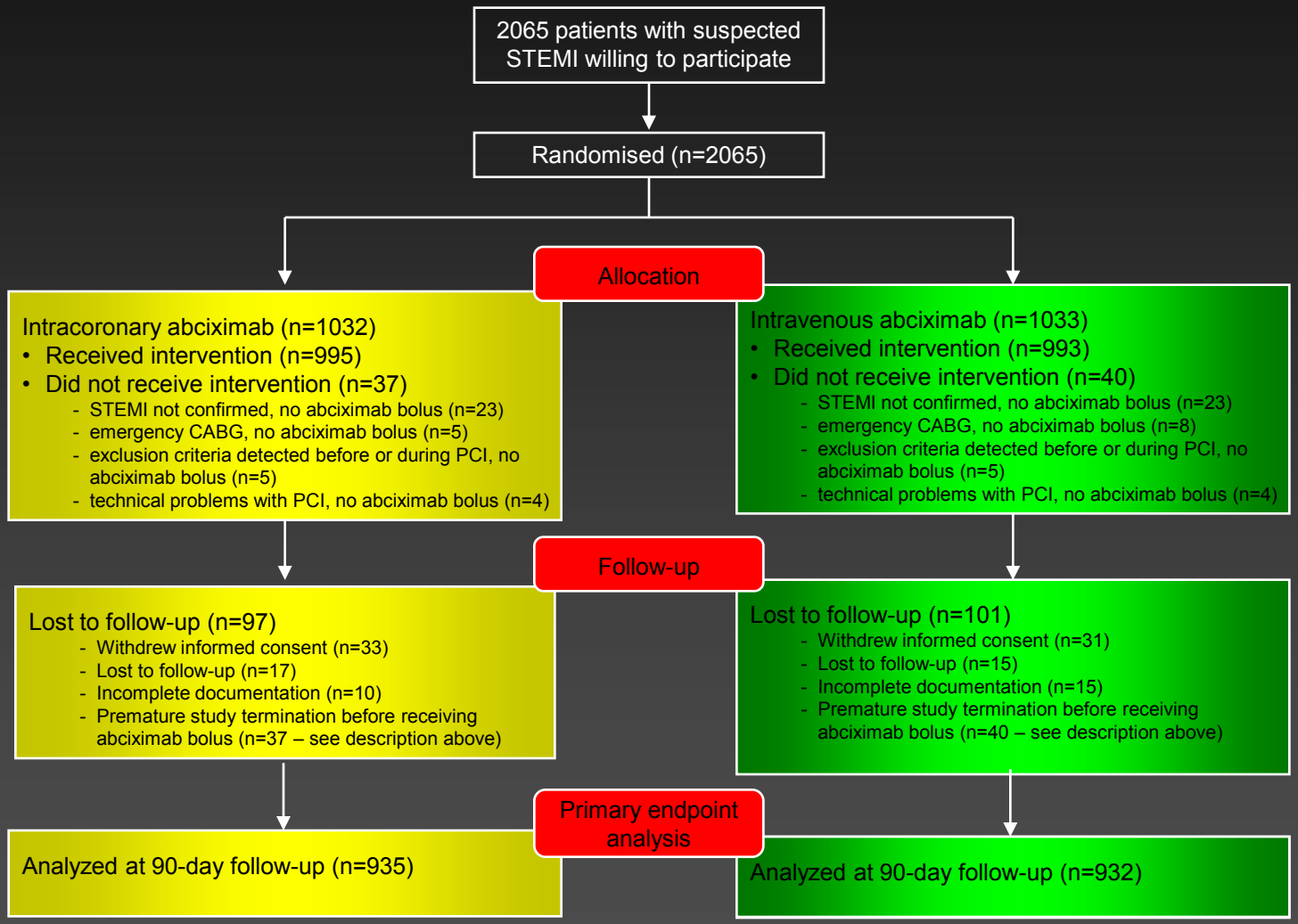
Study or Subgroup	Intracoronary abciximab Events	Total	Intravenous abciximab Events	Total	Weight	Odds ratio M-H, Fixed 95%
CICERO 2010	9	271	10	263	27.5%	0.87 (0.35;2.17)
EASY-MI 2010	0	53	0	52		Not estimable
Iversen 2011	7	185	16	170	55.5%	0.38 (0.15;0.94)
Thiele 2008	0	77	2	77	17.0%	0.19 (0.01;4.13)
Total (95%)		586		562	100.0%	0.53 (0.29;0.99)
Total events	16	636	28			

Heterogeneity: Chi^2 =2.58, df=2 (P=0.36);I^2=2%
Test for overall effect: Z=2.00 (P=0.05)



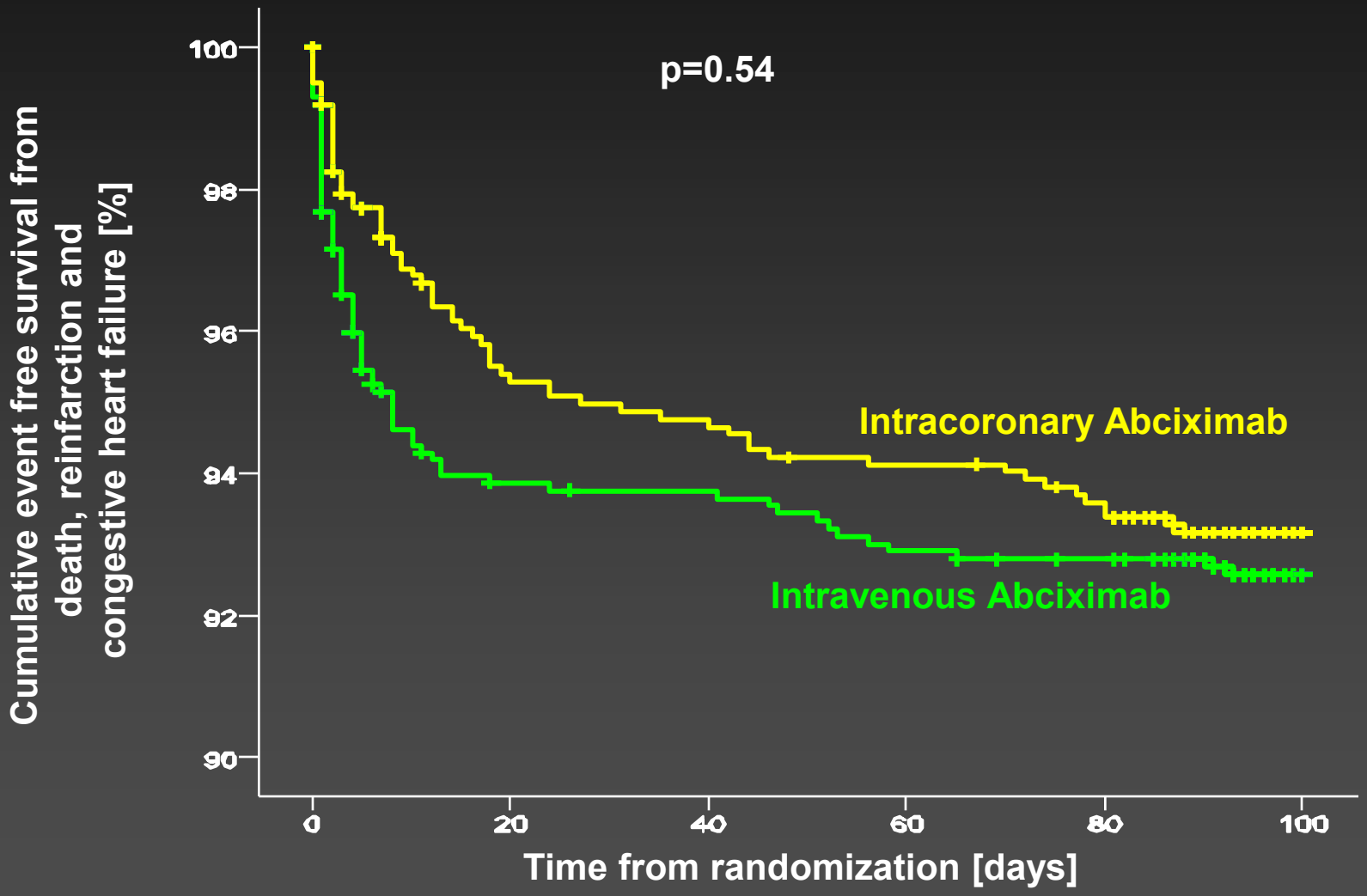
Navarese et al. Platelets 2011;1-8

Study Design, Flow, and Compliance



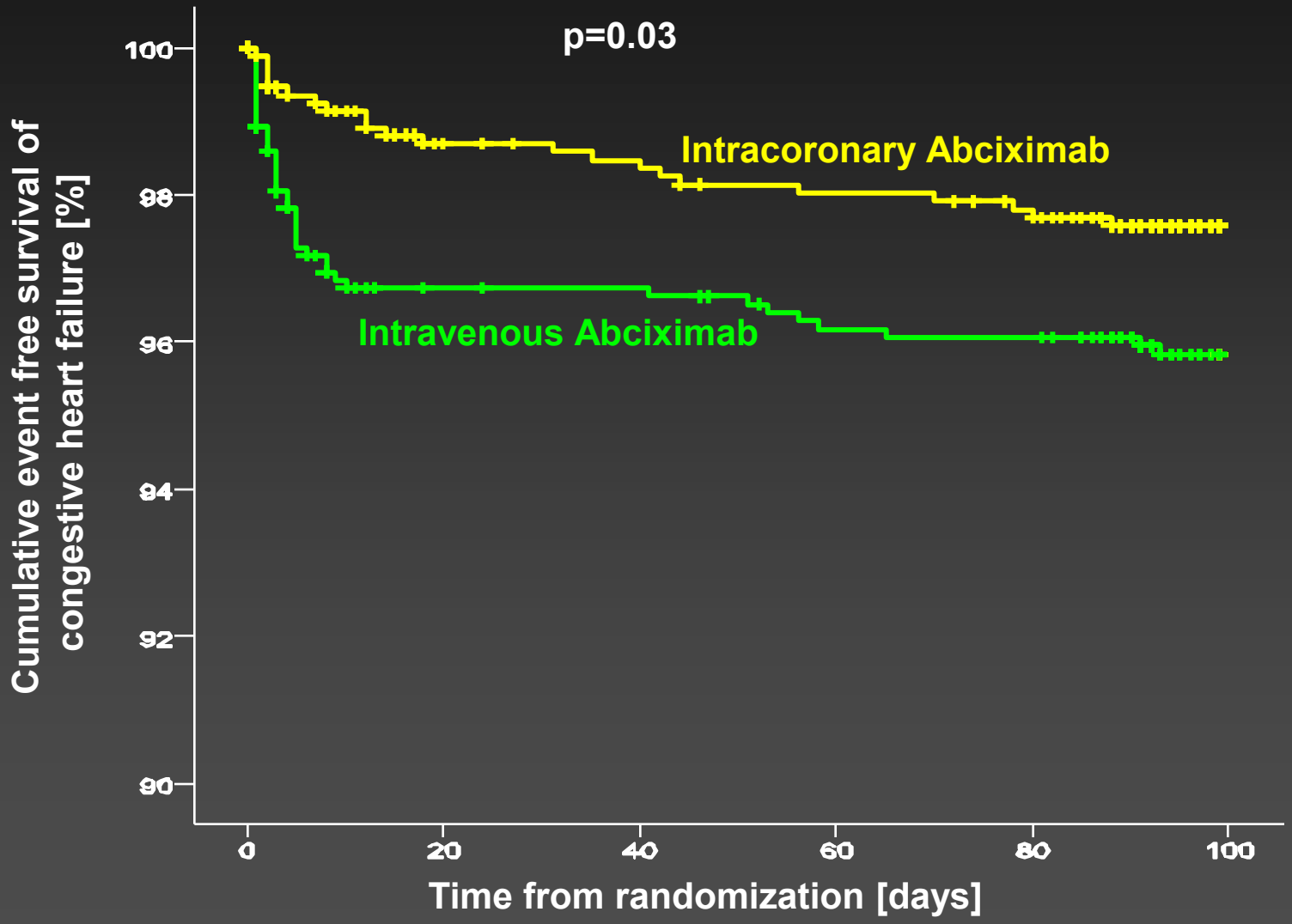
Thiele et al. Lancet 2012;379:923-31

Combined Clinical Endpoint



Thiele et al. Lancet 2012;379:923-31

Congestive Heart Failure



Thiele et al. Lancet 2012;379:923-31

AIDA STEMI CMR Substudy

- CMR enables investigation of mechanistic and pathophysiological effects of intracoronary + intravenous abciximab application on myocardial damage and reperfusion injury.

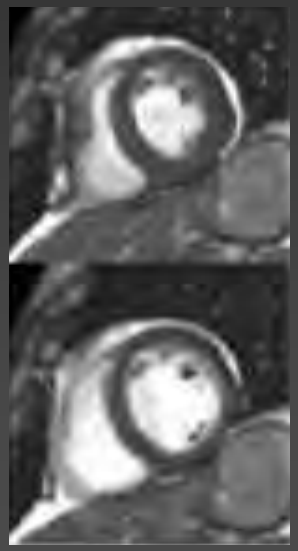
- To determine potential benefits of intracoronary abciximab application on infarct size, myocardial salvage, microvascular obstruction and ventricular function to further evaluate the benefit with respect to congestive heart failure.

Thiele et al. Am Heart J 2010;159:547-554

CMR Prognostic Implications

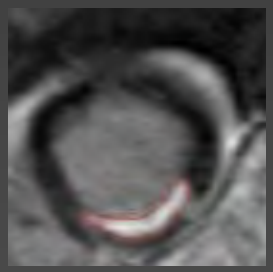
Prognostic relevance

Prognostic relevance validated



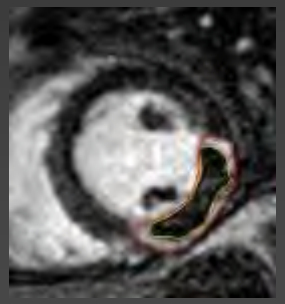
LV Volumes + Ejection fraction

Prognostic relevance validated



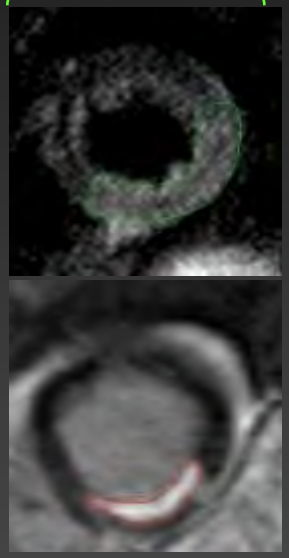
Infarct size

Prognostic relevance validated



Microvascular obstruction

Prognostic relevance partly validated



Myocardial salvage

Prognostic relevance partly validated

Hemorrhage

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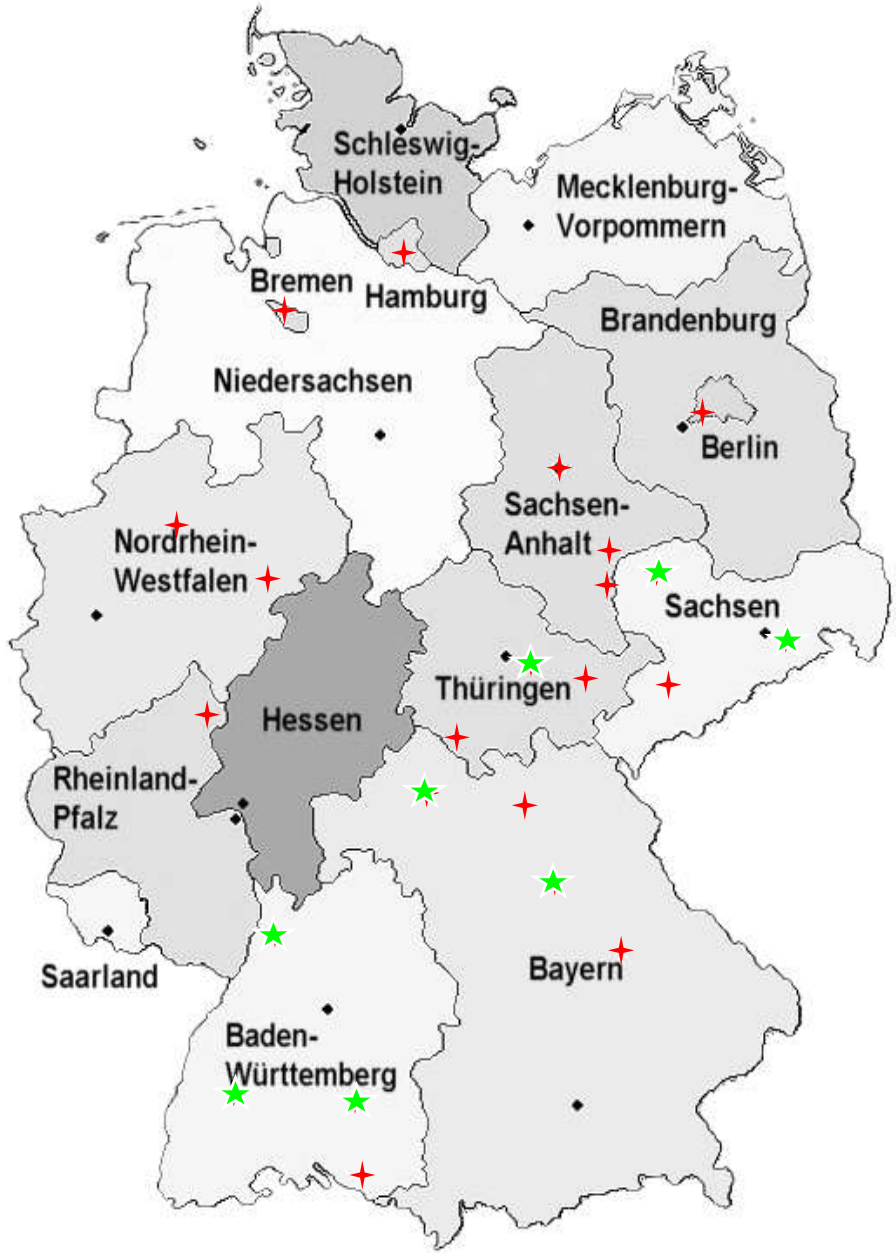
Desch et al. Trials 2011:12:e204-215

Study Organization and Study Sites



Investigator Initiated Trial

22 study sites in Germany

8 CMR study sites

CMR core laboratory:

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Henning Sünkel
Holger Thiele

DSMB:

Uwe Zeymer
Hans-Richard Arntz
Christoph Bode
Karl Wegscheider

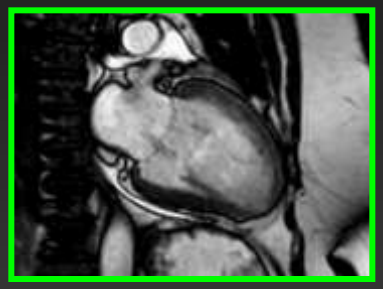
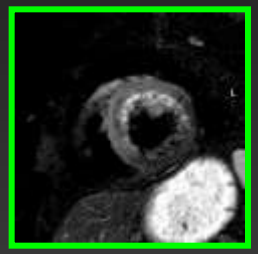
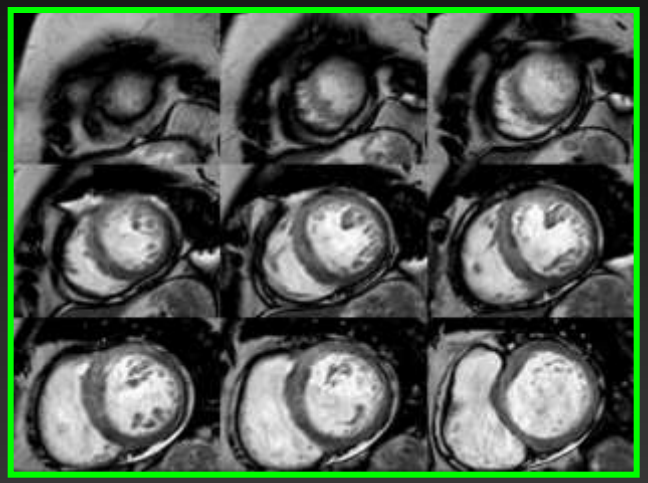
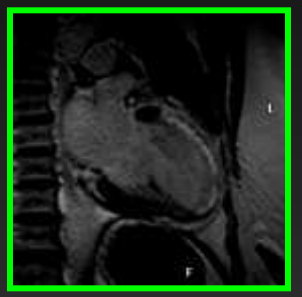
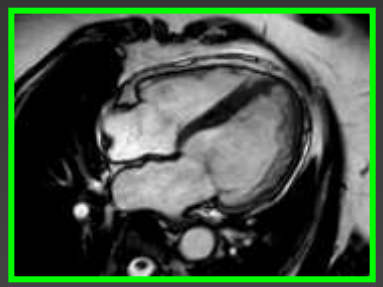
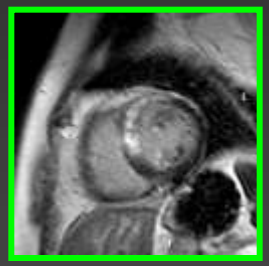
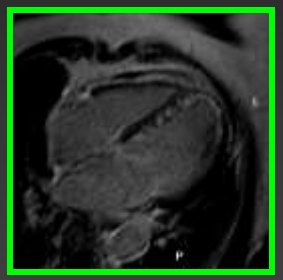
Steering Committee:

Holger Thiele
Jochen Wöhrle
Oana Brosteanu
Gerhard Schuler

CRO:

Clinical Trial Center Leipzig

CMR Protocol

Contrast-Injection 1,5 mmol/kg/BW

Bolus Gd i.v.

0 5 10 15 20 25 30 35 40

Time (min)

Survey	Function 4CH+2 CH	T2 SA	Function Short axes	Delayed enhancement 4CH + 2CH + SA

Area at risk + Hemorrhage

EF, EDV, ESV

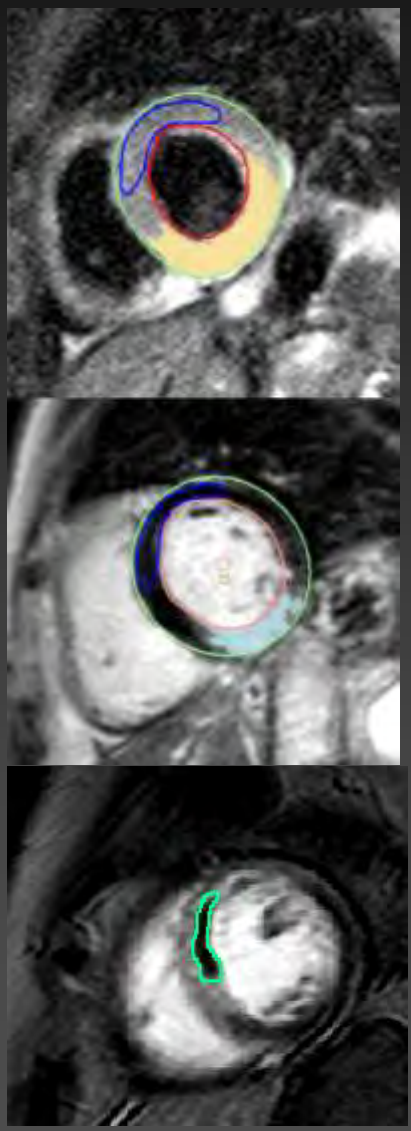
late MO + Infarct size

Thiele et al. Am Heart J 2010;159:547-554

CMR Image Analysis

Core laboratory assessed by blinded observers:

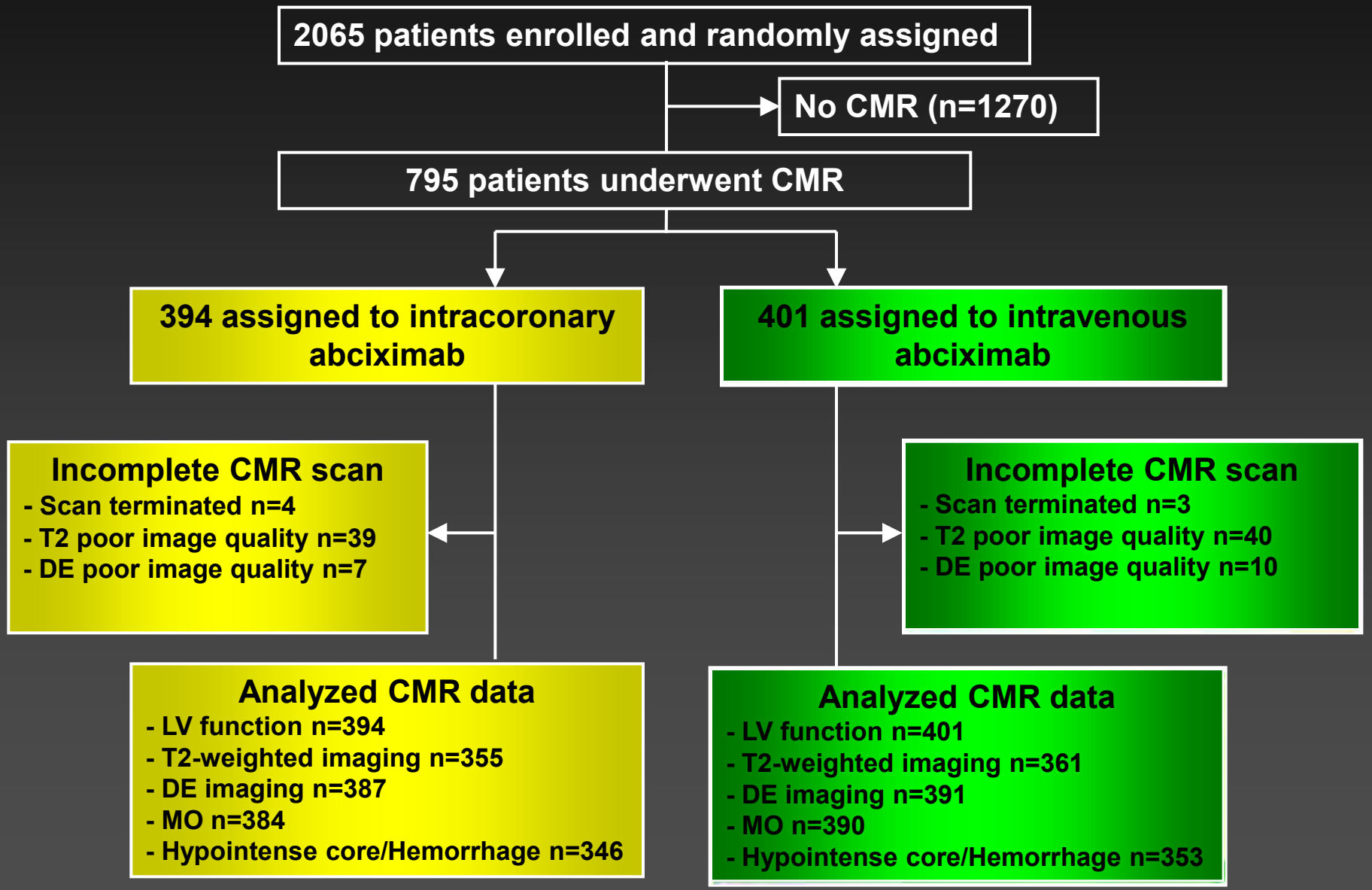
- Edema
- Hemorrhage
- Endocardial contours
- Epicardial contours
- Infarct
- Microvascular obstruction



Area at risk = Volume Edema/Volume LV mass
%Infarct Size = Volume Infarct/Volume LV mass
%MO = MO-Volume/Volume LV mass
%Hemorrhage = T2 hypointense core/Volume LV mass
Myocardial salvage = Edema-Infarct Size
Myocardial salvage index = Edema-Infarct Size/Edema

Thiele et al. JACC 2010; 2010;55:2201-2209
Eitel et al. JACC 2010; 55:2470–2479

Study Design, Flow, and Compliance



Patient Characteristics

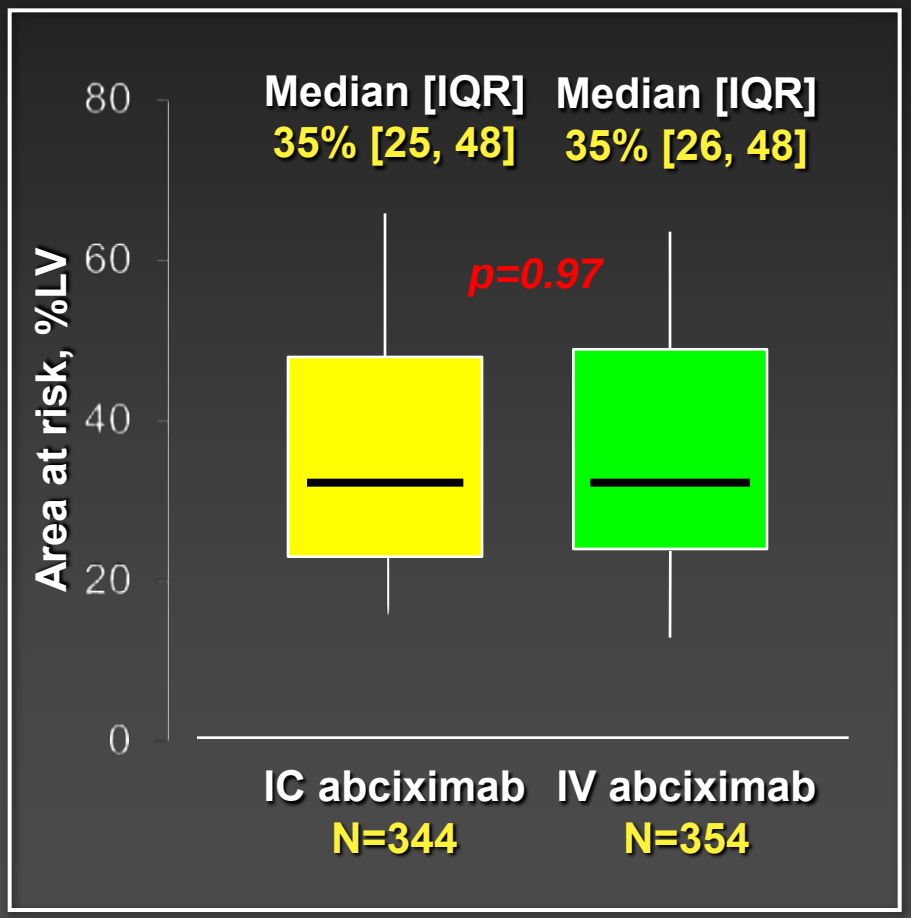
	IC Abciximab (n=394)	IV Abciximab (n=401)
Age (years); median (IQR)	63 (51-71)	61 (51-71)
Male sex; n (%)	287 (73)	316 (79)
Current Smoking; n/total n (%)	161/364 (44)	178/363 (49)
Hypertension; n/total n (%)	284/393 (72)	256/399 (64)
Hypercholesterolemia; n/total n (%)	147/391 (38)	157/396 (40)
Diabetes mellitus; n/total n (%)	87/392 (22)	73/400 (18)
Body mass index (kg/m^2); median (IQR)	27.4 (24.9-30.1)	27.3 (24.8-30.5)
Prior myocardial infarction; n/total n (%)	23/393 (6)	25/401 (6)
Prior PCI; n/total n (%)	35/394 (9)	32/401 (8)
Prior CABG; n/total n (%)	2/394 (1)	9/401 (2)
Anterior myocardial infarction; n/total n (%)	180/382 (47)	183/376 (49)
Creatinine clearance (ml/min); median (IQR)	92 (72-120)	96 (74-117)
Symptom-onset - PCI hospital, median (IQR)	164 (108-300)	190 (110-335)
Door-to-balloon-time; median (IQR)	30 (22-43)	29 (22-42)
Killip-class on admission; n/total n (%)		
1	341/394 (87)	358/401 (89)
2	35/394 (9)	24/401 (6)
3	11/394 (3)	9/401 (2)
4	7/394 (2)	10/401 (3)

Study Procedures and Medications

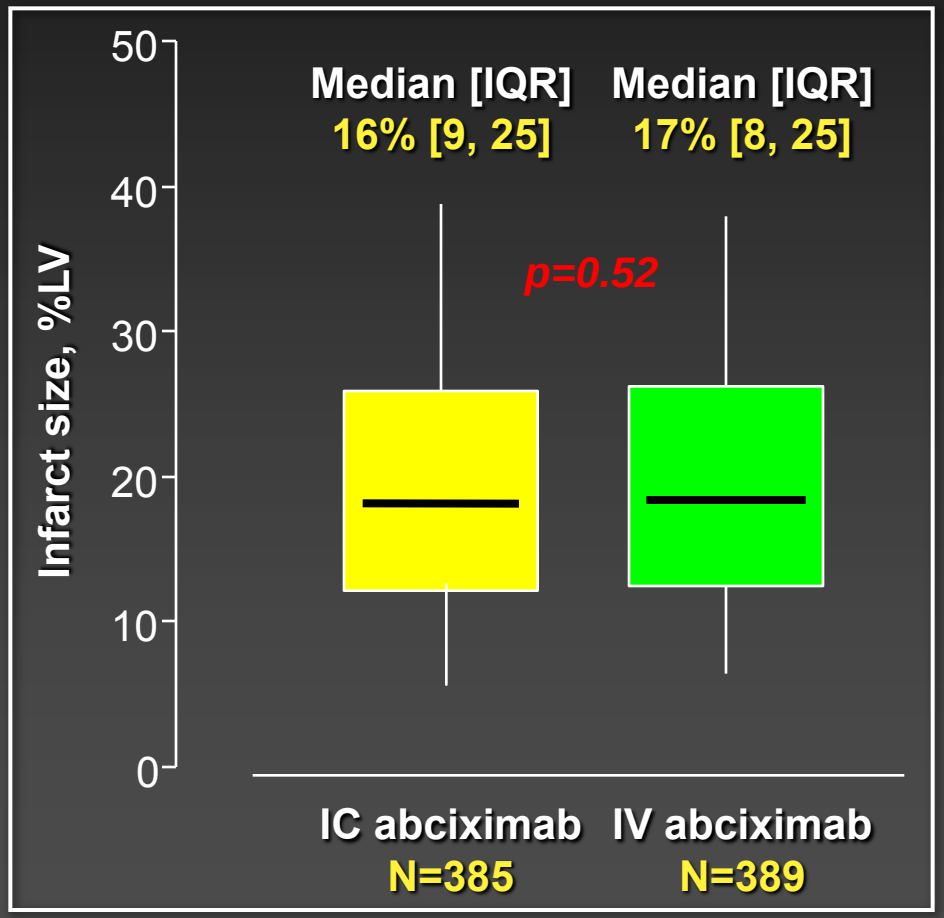
	IC Abciximab (n=394)	IV Abciximab (n=401)	p
Infarct-related artery; n/total n (%)			0.85
LAD	166/394 (42)	181/401 (45)	
LCX	51/394 (13)	46/401 (12)	
RCA	175/394 (44)	169/401 (42)	
Left main	2/394 (1)	3/401 (1)	
Bypass graft	0/394 (0)	2/401 (1)	
Thrombectomy; n/total n (%)	99/394 (25)	91/401 (23)	0.42
Drug-eluting stent; n/total n (%)	164/392 (42)	171/401 (43)	0.77
Bare metal stent; n/total n (%)	234/392 (60)	235/401 (59)	0.81
IABP; n/total n (%)	17/394 (4)	18/401 (5)	0.91
TIMI-flow III post PCI; n/total n (%)	343/394 (87)	358/400 (90)	0.59
Concomitant medications; n/total n (%)			
Beta-blocker	373/393 (95)	386/400 (97)	0.27
ACE-inhibitor/AT-1-antagonist	372/393 (95)	382/400 (96)	0.58
Aspirin	394/394 (100)	401/401 (100)	
Clopidogrel	330/381 (87)	348/387 (90)	0.15
Prasugrel	92/310 (30)	87/298 (29)	0.90
Clopidogrel and/or Prasugrel	385/385 (100)	390/390 (100)	
Statin	367/393 (93)	385/400 (96)	0.07
Aldosterone-antagonist	49/393 (13)	42/400 (11)	0.39
Completion of 12 h abciximab infusion	370/393 (94)	378/401 (94)	0.94

Area at Risk + Infarct Size

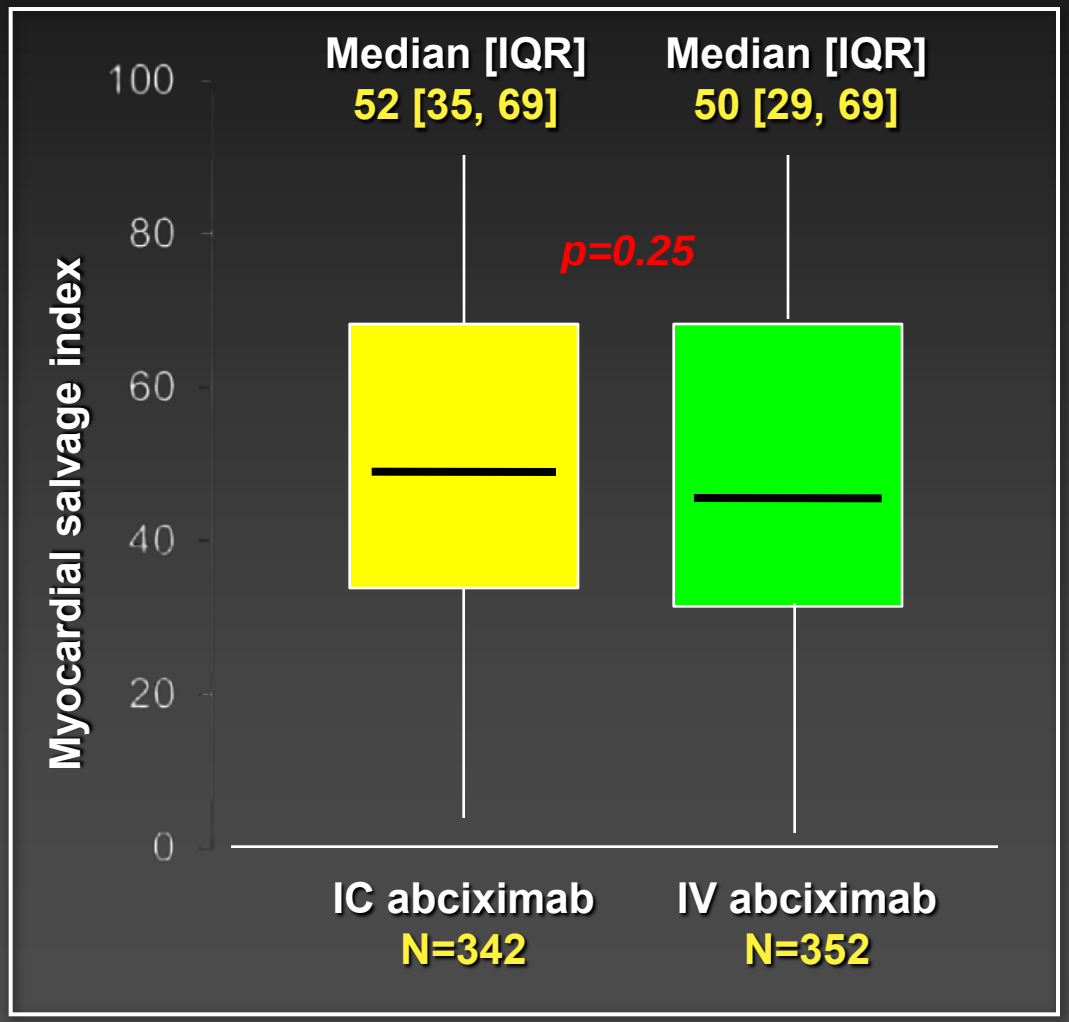
Area at risk



Infarct size

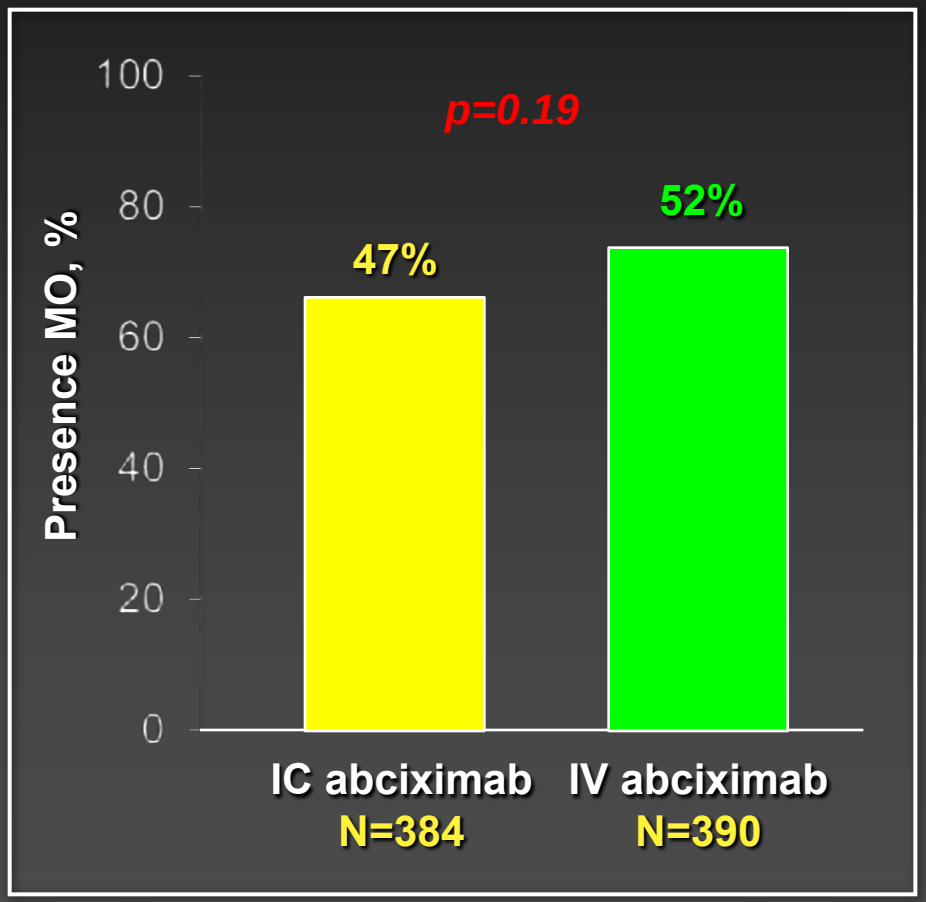


Myocardial Salvage Index

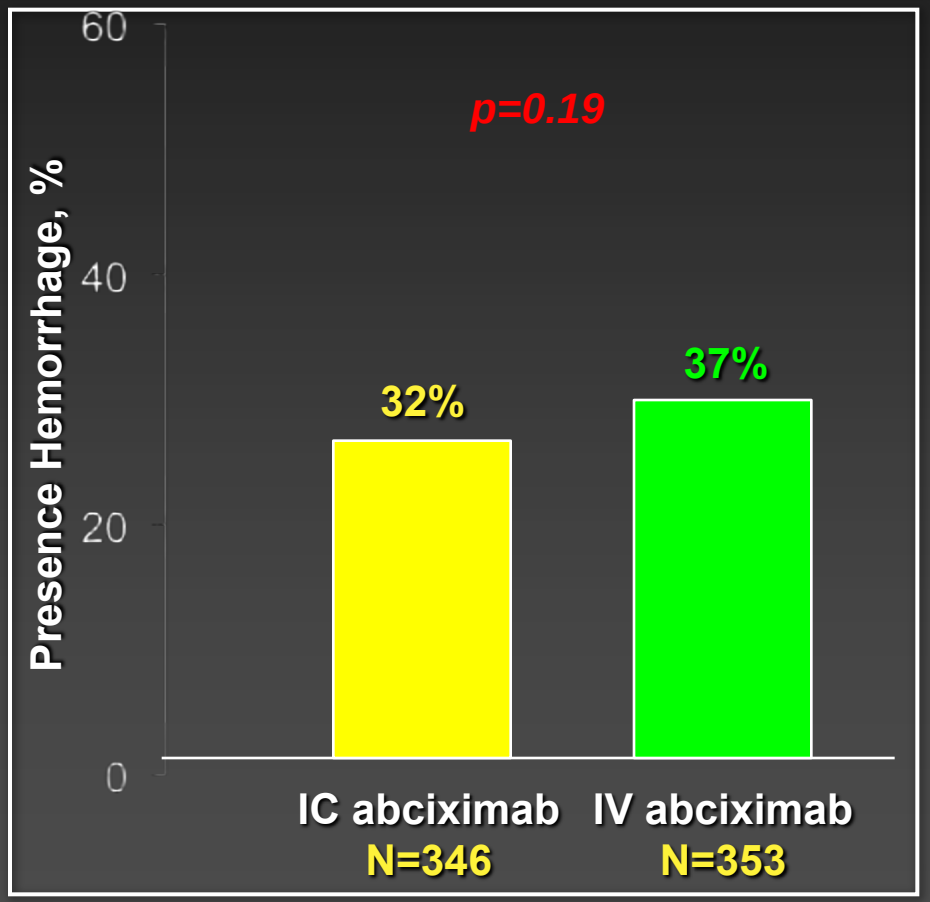


Reperfusion Injury

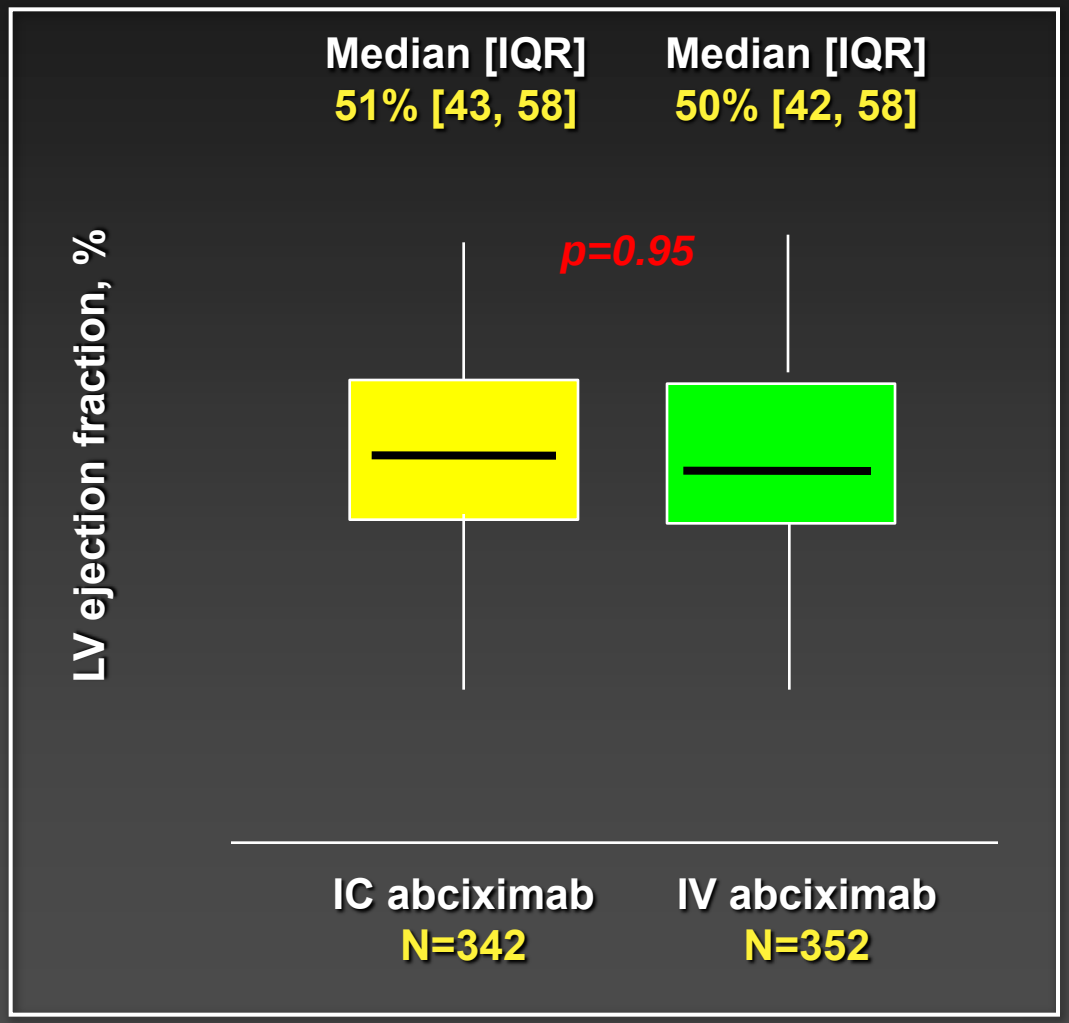
Microvascular obstruction



Hemorrhage

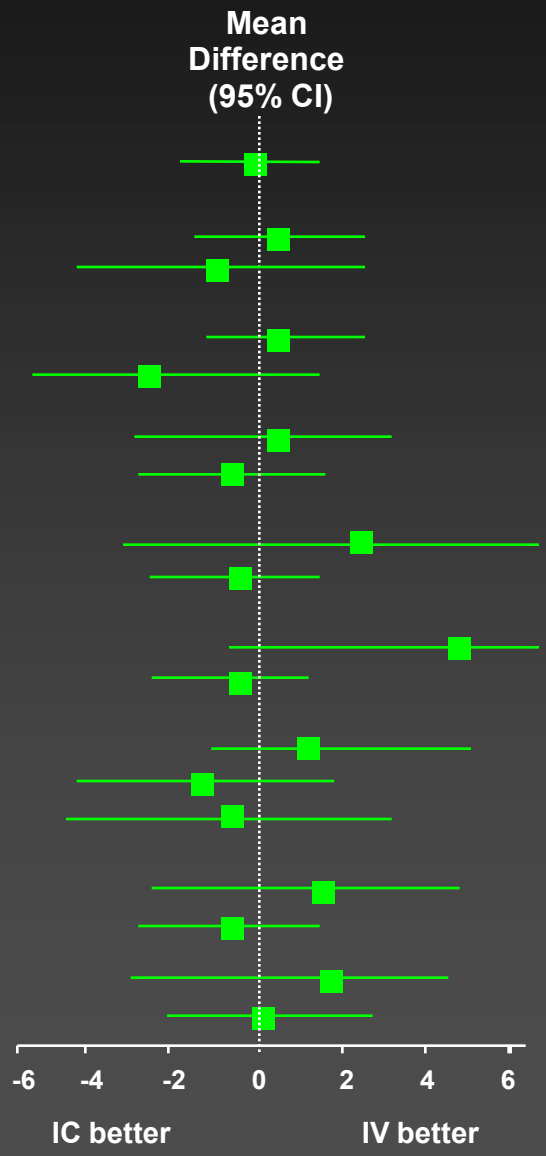


CMR – LV Ejection Fraction



Infarct Size - Subgroups

Baseline variable	N	Infarct size (%LV) IC abciximab	Infarct size (%LV) IV abciximab	Mean Difference (95% CI)	p-value for interaction
All Patients	774	18 (13)	18 (13)	-0.2 (-2.9;1.5)	0.52
Male sex	586	18 (13)	18 (12)	0.1 (-2.0;2.1)	0.49
Female sex	188	18 (12)	19 (12)	-1.4 (-4.9;2.1)	
Age < 75 years	656	18 (13)	18 (12)	0.2 (-1.7;2.1)	0.46
Age ≥ 75 years	118	18 (12)	21 (12)	-3.1 (-7.6;1.3)	0.11
Anterior MI	353	21 (14)	21 (14)	0.1 (-2.8;3.0)	0.79
Non-anterior MI	388	15 (10)	15 (10)	-0.7 (-2.7;1.3)	0.42
Killip-class II to IV	91	28 (16)	25 (13)	3.0 (-3.1;9.0)	0.50
Killip-class I	683	16 (11)	17 (12)	-0.9 (-2.8; 0.8)	0.71
TIMI flow post PCI 0 to II	89	24 (14)	19 (9)	4.4 (-0.5;9.3)	0.96
TIMI-flow post PCI III	685	17 (12)	18 (13)	-0.9 (-2,8;1.0)	0.50
Symptom onset-randomization < 3 h	334	17 (13)	15 (12)	2.0 (-0.7;4.6)	0.85
Symptom onset-randomization 3-6 h	296	19 (13)	20 (13)	-1.6 (-4.5;1.3)	0.37
Symptom onset-randomization > 6h	136	18 (12)	20 (12)	-1.2 (-5.3;2.8)	0.60
Thrombectomy	187	20 (12)	19 (13)	1.4 (-2.2;5.0)	0.47
No thrombectomy	587	17 (13)	18 (12)	-0.8 (-2.9;1.2)	0.78
Prasugrel	173	18 (13)	17 (11)	0.6 (-3.0;4.3)	0.84
No prasugrel	419	19 (13)	19 (13)	0.2 (-2.2;2.7)	0.89



Clinical Outcome 12 Months – CMR Substudy

	IC	IV	OR	95% CI	P
Death/Reinfarction/new CHF					
n/total n (%)	24/390 (6.2)	29/399 (7.3)	0.84	0.48-1.46	0.53
Death					
Overall n/total n (%)	13/390 (3.3)	8/399 (2.0)	1.69	0.69-4.11	0.25
Cardiac	10	6			
Non-cardiac	3	2			
Reinfarction					
n/total n (%)	9/390 (2.3)	12/399 (3.0)	0.76	0.32-1.83	0.54
New CHF					
n/total n (%)	8/390 (2.1)	16/399 (4.0)	0.50	0.21-1.19	0.11

CMR and Outcome

Characteristic		MACE	No MACE	p
Infarct size (%LV)	Median (IQR) Mean (SD) n	24 (18 - 31) 24 (14) 50	16 (8 - 24) 18 (12) 718	<0.001
Myocardial salvage index	Median (IQR) Mean (SD) n	37 (23 - 55) 43 (26) 44	52 (33 - 69) 53 (26) 644	0.01
Late MO present n (%)		28 / 50 (56%)	350 / 718 (49%)	0.32
Late MO (%LV)	Median (IQR) n	0.6 (0 - 2.7) 50	0 (0 - 1.6) 718	0.09
Hemorrhage present n (%)		19 / 48 (40%)	228 / 660 (35%)	0.66
Hemorrhage (%LV)	Median (IQR) n	0 (0 – 2.1) 47	0 (0 - 1.3) 645	0.36
LV ejection fraction (%)	Median (IQR) Mean (SD) n	40 (33 - 47) 42 (14) 53	51 (44 - 58) 51 (10) 736	<0.001

Summary + Conclusions

- This largest multicenter CMR study in STEMI patients to date demonstrates that IC as compared to IV abciximab did not result in a difference in myocardial damage and/or reperfusion injury.

- The results of the AIDA STEMI CMR substudy therefore confirm the lack of difference in the combined endpoint of death, reinfarction or congestive heart failure of the AIDA STEMI trial.

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