Updates in management of Acute Coronary Syndromes

Antithrombotic treatments

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Rome Cardiology Forum 2014

UP-DATES
(Clinical and for every day practice)

- Is testing for clopidogrel resistance useful?
- Safer approach to Cardiac and no-cardiac surgery after PCI?
- How to manage DAPT + OAC also at the light of NOAs?
- Length of DAPT?
- Novel data on prasugrel and ticagrelor?

Recommendations for oral antiplatelet agents (2)

Recommendations	Class	Level
Clopidogrel (300 mg loading dose, 75 mg daily dose) is recommended for patients who cannot receive ticagrelor or prasugrel.	I	A
A 600 mg loading dose of clopidogrel (or a supplementary 300 mg dose at PCI following an initial 300 mg loading dose) is recommended for patients scheduled for an invasive strategy when ticagrelor or prasugrel is not an option.	I	B
A higher maintenance dose of clopidogrel 150 mg daily should be considered for the first 7 days in patients managed with PCI and without increased risk of bleeding.	IIa	B
Increasing the maintenance dose of clopidogrel based on platelet function testing is not advised as routine, but may be considered in selected cases.	IIb	B
Genotyping and/or platelet function testing may be considered in selected cases when clopidogrel is used.	IIb	B
In patients pre-treated with $P2Y_{12}$ inhibitors who need to undergo non-emergent major surgery (including CABG), postponing surgery at least for 5 days after cessation of ticagrelor or clopidogrel, and 7 days for prasugrel, if clinically feasible and unless the patient is at high risk of ischaemic events should be considered.	IIa	C
Ticagrelor or clopidogrel should be considered to be (re-)started after CABG surgery as soon as considered safe.	IIa	B
The combination of aspirin with an NSAID (selective COX-2 inhibitors and non-selective NSAID) is not recommended.	III	C

European Heart Journal (2011) 32:2999–3054
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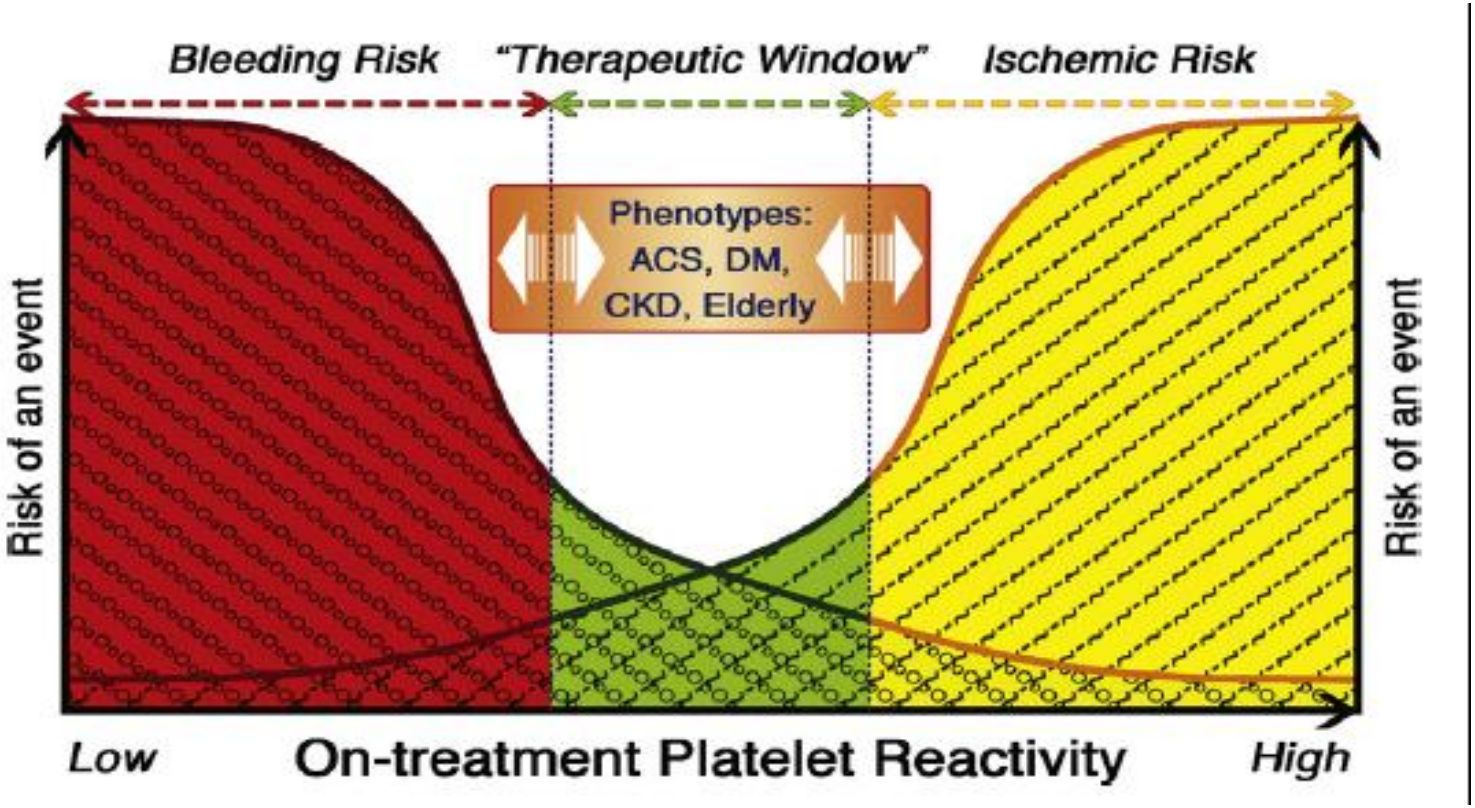
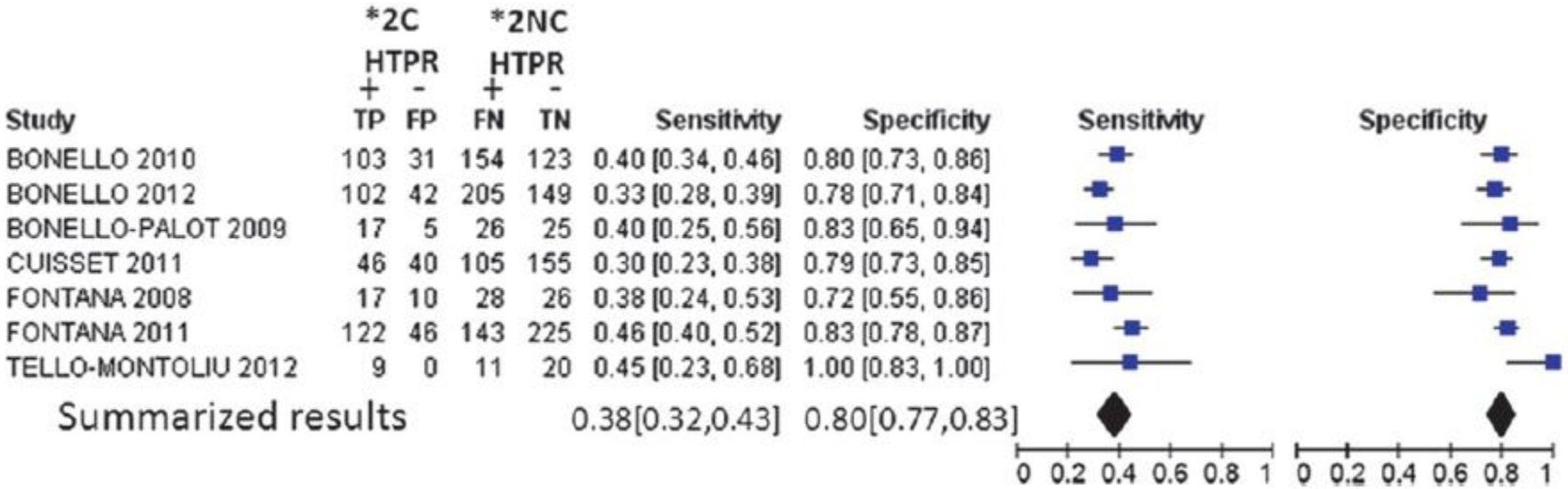


Angiolillo JACC 2013

Genothype testing

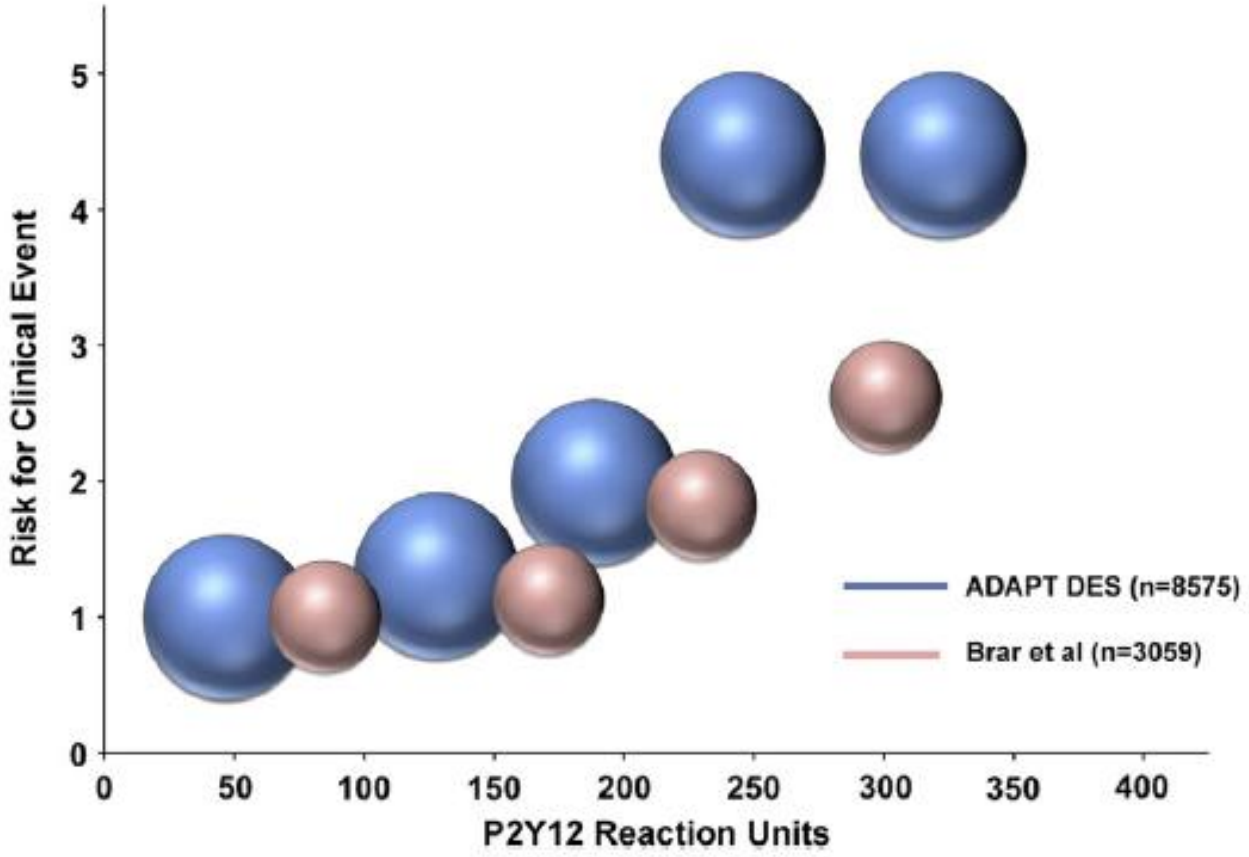


Study	*2C HTPR + TP	*2C HTPR - FP	*2NC HTPR + FN	*2NC HTPR - TN	Sensitivity	Specificity
BONELLO 2010	103	31	154	123	0.40 [0.34, 0.46]	0.80 [0.73, 0.86]
BONELLO 2012	102	42	205	149	0.33 [0.28, 0.39]	0.78 [0.71, 0.84]
BONELLO-PALOT 2009	17	5	26	25	0.40 [0.25, 0.56]	0.83 [0.65, 0.94]
CUISSET 2011	46	40	105	155	0.30 [0.23, 0.38]	0.79 [0.73, 0.85]
FONTANA 2008	17	10	28	26	0.38 [0.24, 0.53]	0.72 [0.55, 0.86]
FONTANA 2011	122	46	143	225	0.46 [0.40, 0.52]	0.83 [0.78, 0.87]
TELLO-MONTOLIU 2012	9	0	11	20	0.45 [0.23, 0.68]	1.00 [0.83, 1.00]
Summarized results					0.38[0.32,0.43]	0.80[0.77,0.83]

data on the association between CYP2C19 genotypes and HTPR.[10,13–18] As shown in the Figure, the summarized sensitivity[19] of the CYP2C19*2 genotype for predicting HTPR was 37.6% (95% CI: 32.2 to 43.3%), yielding a summarized negative predictive value of only 52.3% (95% CI: 44.7% to 59.7%) and a negative likelihood ratio of only 0.77 (95% CI: 0.68 to 0.86). Thus, CYP2C19 genotyping would contribute little to excluding the risk of HTPR or MACE. Routine

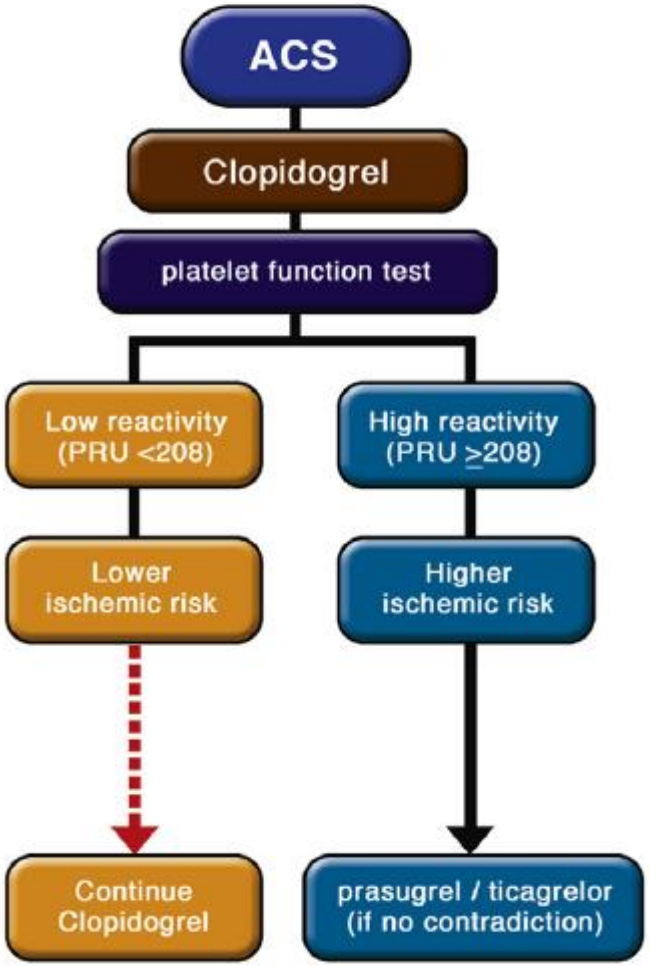
Fontana JAHA 2013

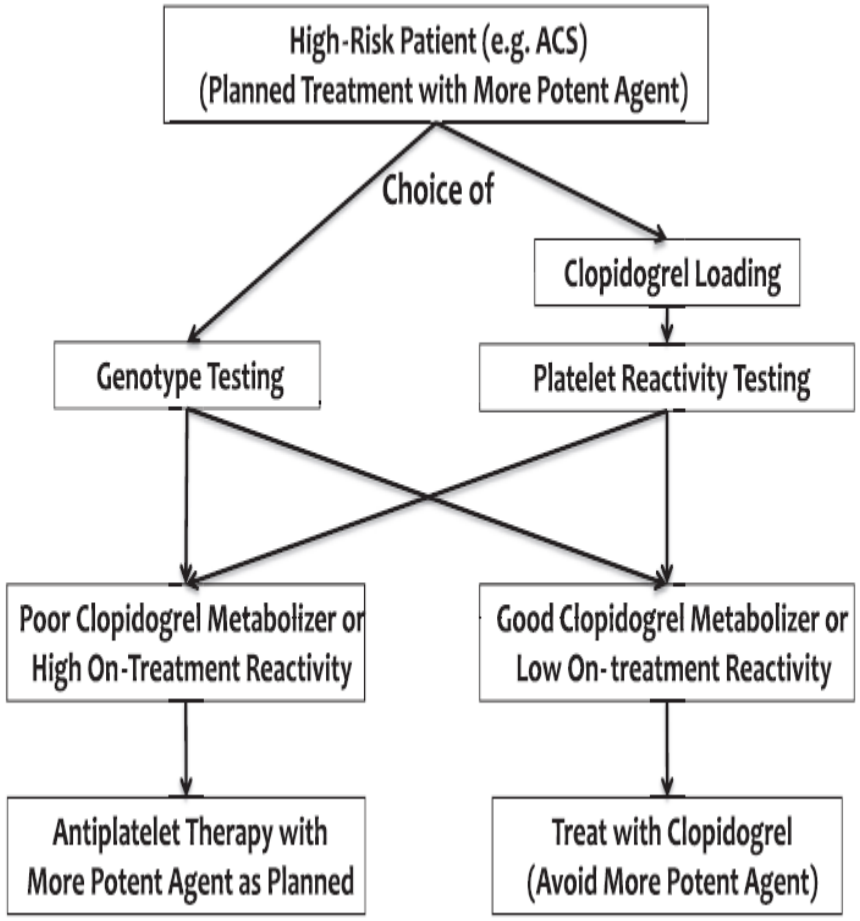
Increased risk of CV events according to PRU



Angiolillo JACC 2013

Possible Algorhytms





Angiolillo JACC 2013

Kirkane JACC 2013

DAPT and Cardiac and no-cardiac surgery

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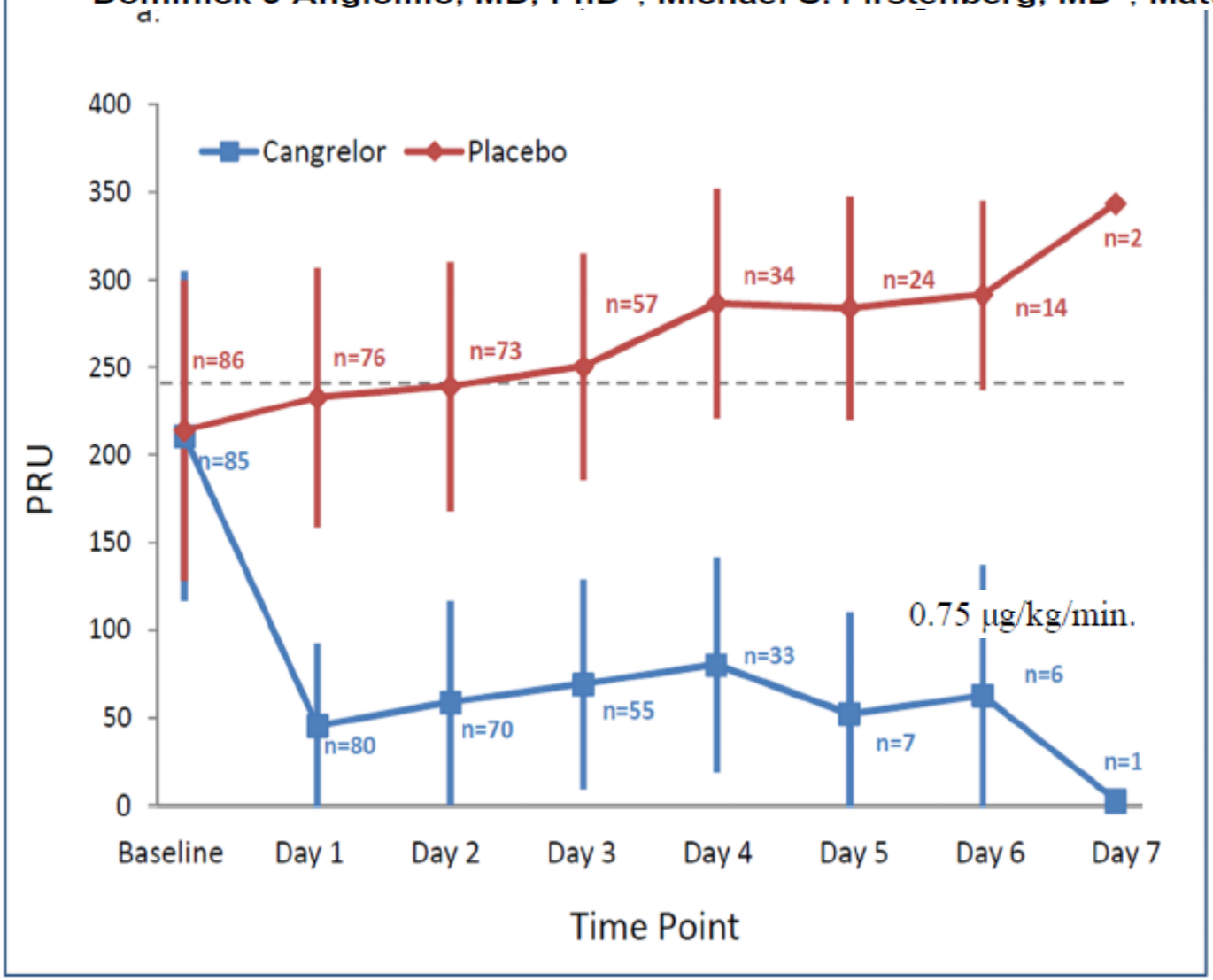
JAMA. 2012 January 18; 307(3): 265–274. doi:10.1001/jama.2011.2002.

Bridging Anti-Platelet Therapy With the Intravenous Agent Cangrelor In Patients Undergoing Cardiac Surgery

Dominick J Angiolillo, MD, PhD[1], Michael S. Firstenberg, MD[2], Matthew J. Price, MD[3],



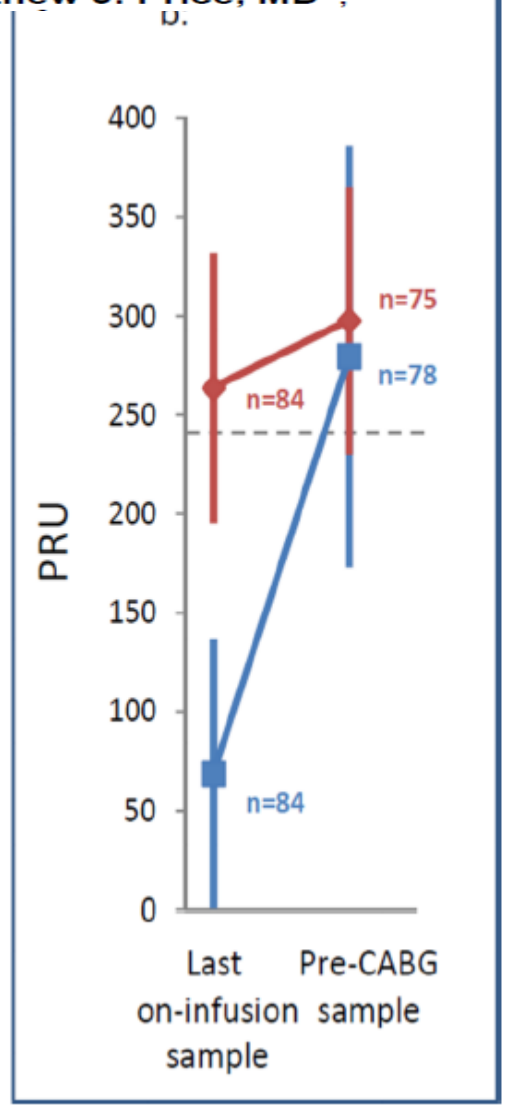


Table 3

CABG-related and pre-operative bleeding events in the Safety Population

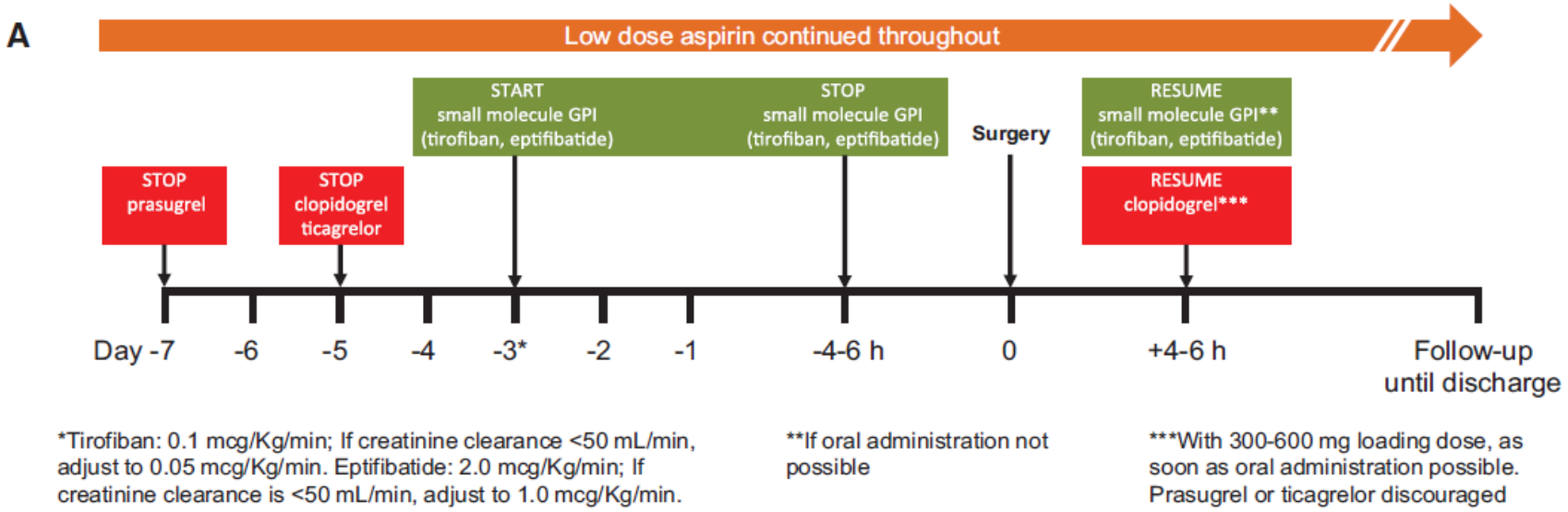
	Cangrelor (N= 106)	Placebo (N= 101)	Relative Risk (95% CI)	p-value
Excessive CABG-related bleeding (primary safety endpoint) (during the CABG procedure through hospital discharge)				
Protocol-defined, No. (%)	12/ 102(11.8)	10/ 96(10.4)	1.1(0.5,2.5)	0.763
surgical re-exploration	2/ 102(2.0)	2/ 96(2.1)	0.9(0.1,6.5)	0.951
24 hour chest tube output of >1.5 liters	8/ 102(7.8)	5/ 96(5.2)	1.5(0.5,4.4)	0.457
incidence of PRBC transfusions > 4 units	6/ 102(5.9)	8/ 96(8.3)	0.7(0.3,2.0)	0.503
BARC-defined, No. (%)	10/ 102(9.8)	10/ 96(10.4)	0.9 (0.4,2.2)	0.886
fatal bleeding	0/ 102(0.0)	0/ 96(0.0)	NA	NA
Perioperative intracranial bleeding within 48 hours	0/ 102(0.0)	0/ 96(0.0)	NA	NA
reoperation following closure of sternotomy for the purpose of controlling bleeding	2/ 102(2.0)	2/ 96(2.1)	0.9(0.1,6.5)	0.951
transfusion of ≥ 5 units of whole blood or PRBC within a 48 hour period	7/ 102(6.9)	8/ 96(8.3)	0.8(0.3,2.2)	0.696
chest tube output ≥ 2 L within a 24 hour period	3/ 102(2.9)	4/ 96(4.2)	0.7(0.2,3.1)	0.642
Pre-operative related bleeding (from randomization until surgical incision)				
ACUITY, No. (%)				
Major	3/ 106(2.8)	1/ 101(1.0)	2.9(0.3,27.0)	0.358
Minor	19/ 106(17.9)	10/ 101(9.9)	1.8(0.9,3.7)	0.101
GUSTO, No. (%)				
Severe/Life threatening	0/ 106(0.0)	0/ 101(0.0)	NA	NA
Moderate	2/ 106(1.9)	1/ 101(1.0)	1.9(0.2,20.7)	0.596
Mild	19/ 106(17.9)	10/ 101(9.9)	1.8(0.9,3.7)	0.101
TIMI, No. (%)				
Major	1/ 106(0.9)	0/ 101(0.0)	NA	NA
Minor	1/ 106(0.9)	0/ 101(0.0)	NA	NA

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association®

Management of Antiplatelet Therapy in Patients With Coronary Artery Disease Requiring Cardiac and Noncardiac Surgery

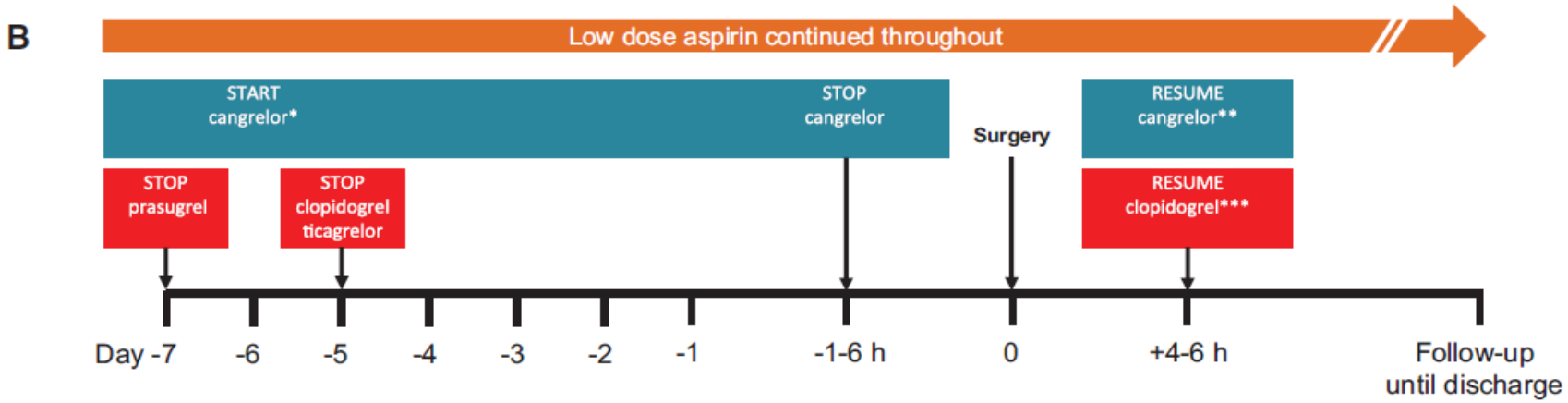
Davide Capodanno and Dominick J. Angiolillo



*Tirofiban: 0.1 mcg/Kg/min; If creatinine clearance <50 mL/min, adjust to 0.05 mcg/Kg/min. Eptifibatide: 2.0 mcg/Kg/min; If creatinine clearance is <50 mL/min, adjust to 1.0 mcg/Kg/min.

**If oral administration not possible

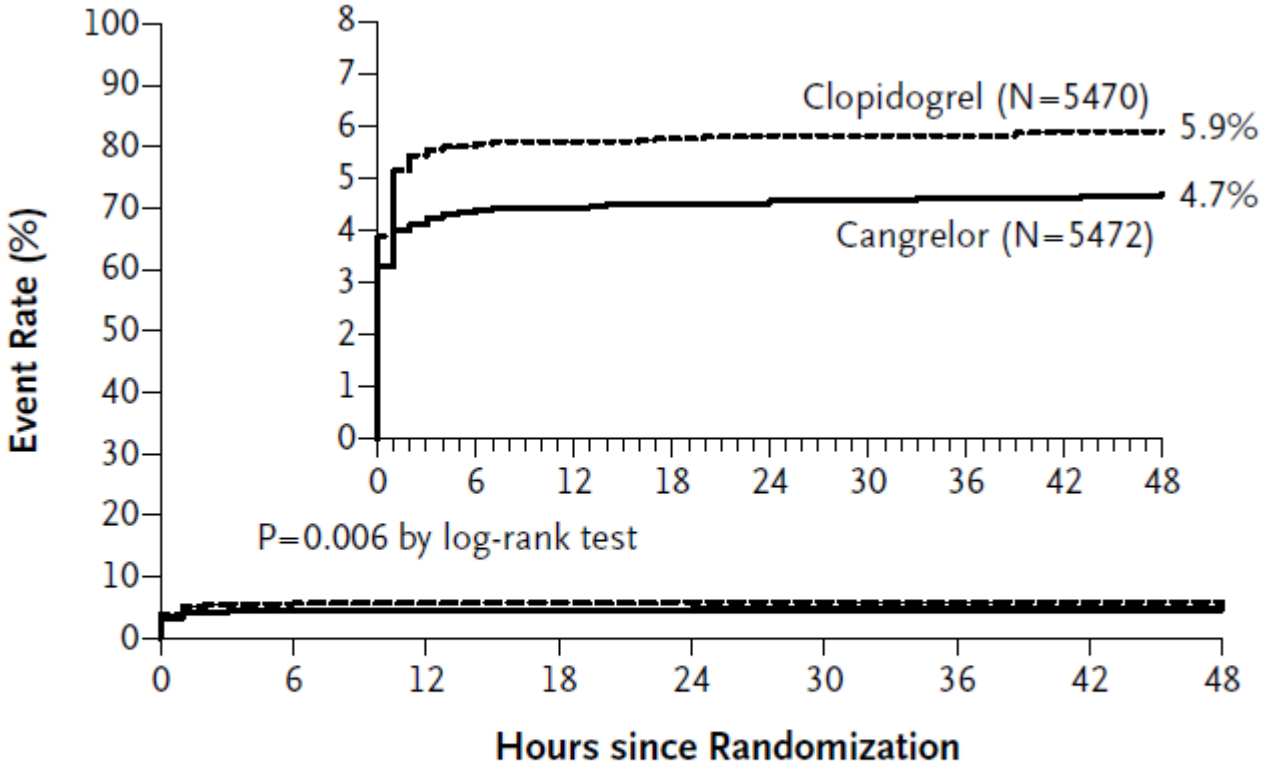
***With 300-600 mg loading dose, as soon as oral administration possible. Prasugrel or ticagrelor discouraged



ORIGINAL ARTICLE

Effect of Platelet Inhibition with Cangrelor during PCI on Ischemic Events

Deepak L. Bhatt, M.D., M.P.H., Gregg W. Stone, M.D.,

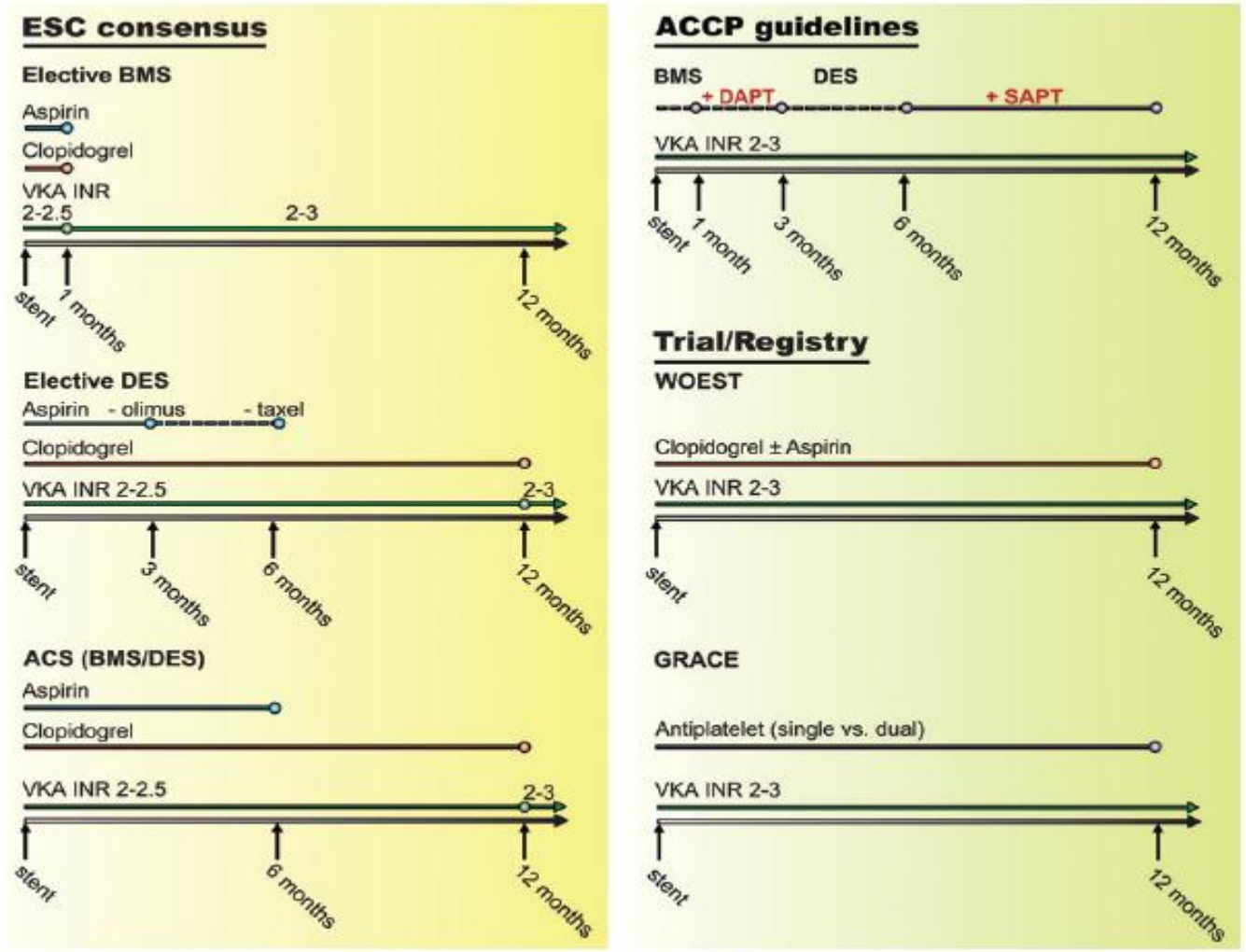


No. at Risk

Cangrelor	5472	5233	5229	5225	5223	5221	5220	5217	5213
Clopidogrel	5470	5162	5159	5155	5152	5151	5151	5147	5147

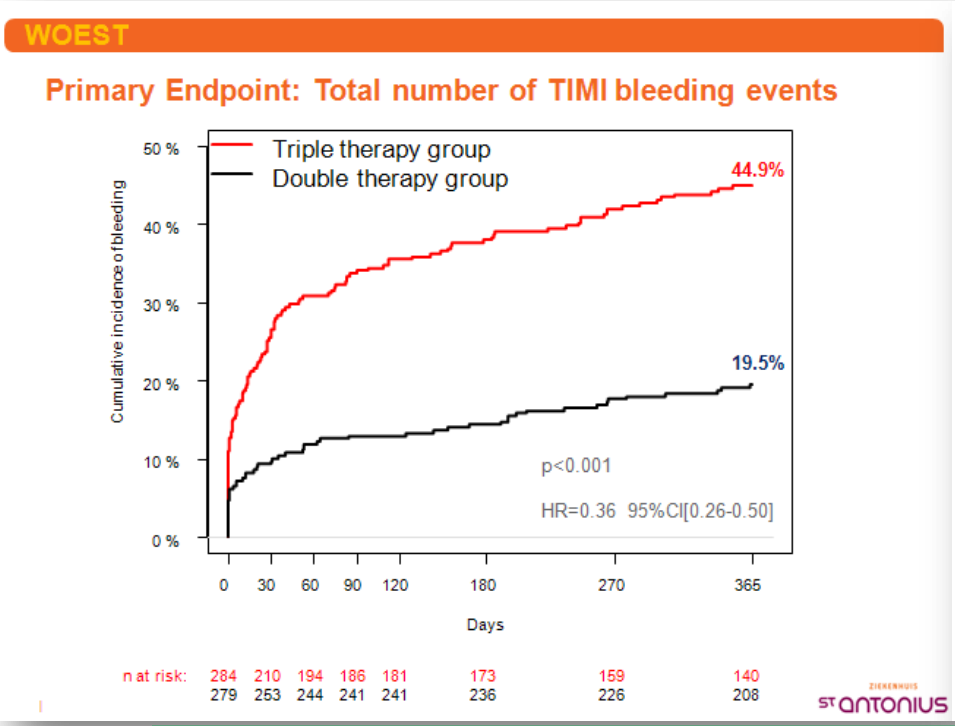
Triple antithrombotic therapy in cardiac patients: more questions than answers

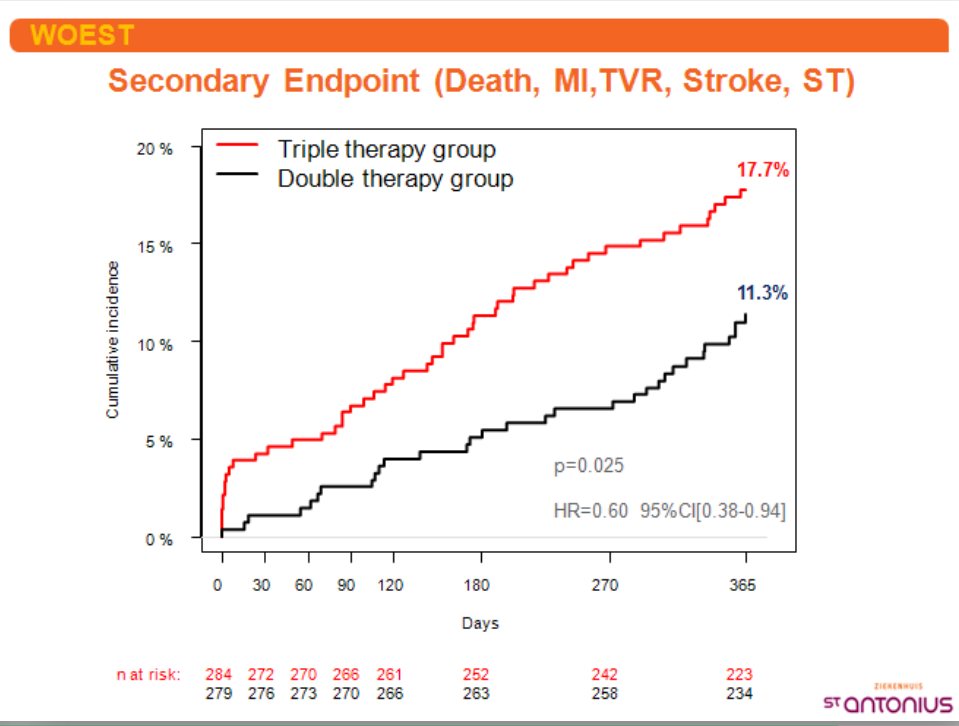
Martin Moser*, Christoph B. Olivier, and Christoph Bode



EHJ 2014

The WOEST Trial: First randomised trial comparing two regimens with and without aspirin in patients on oral anticoagulant therapy undergoing coronary stenting





Paradigm Shift in Interventional Pharmacology: Is it time to drop aspirin?

Oral Anticoagulants in ACS

What about factor IIa antagonists?

~~Ximelagatran~~ (ESTEEM)

~~Dabigatran~~ (stopped phase 2 REDEEM)

What about factor Xa antagonists?

~~Darexaban~~ (RUBY-1)

Rivaroxaban (ATLAS ACS 2)

~~Apixaban~~ (APPRAISE 2)

Not Studied in ACS

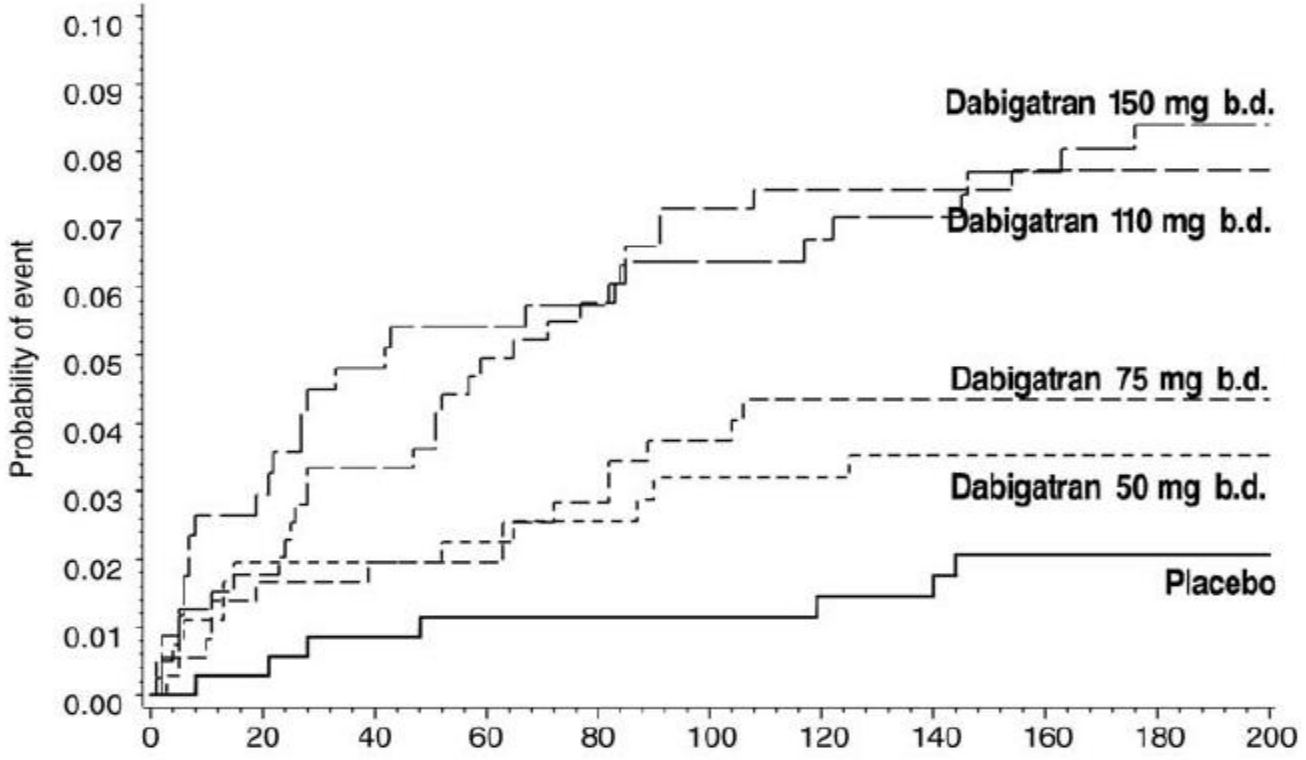
Edoxaban (only Afib, phase III ongoing)

Betrixaban (only Afib, phase II completed)

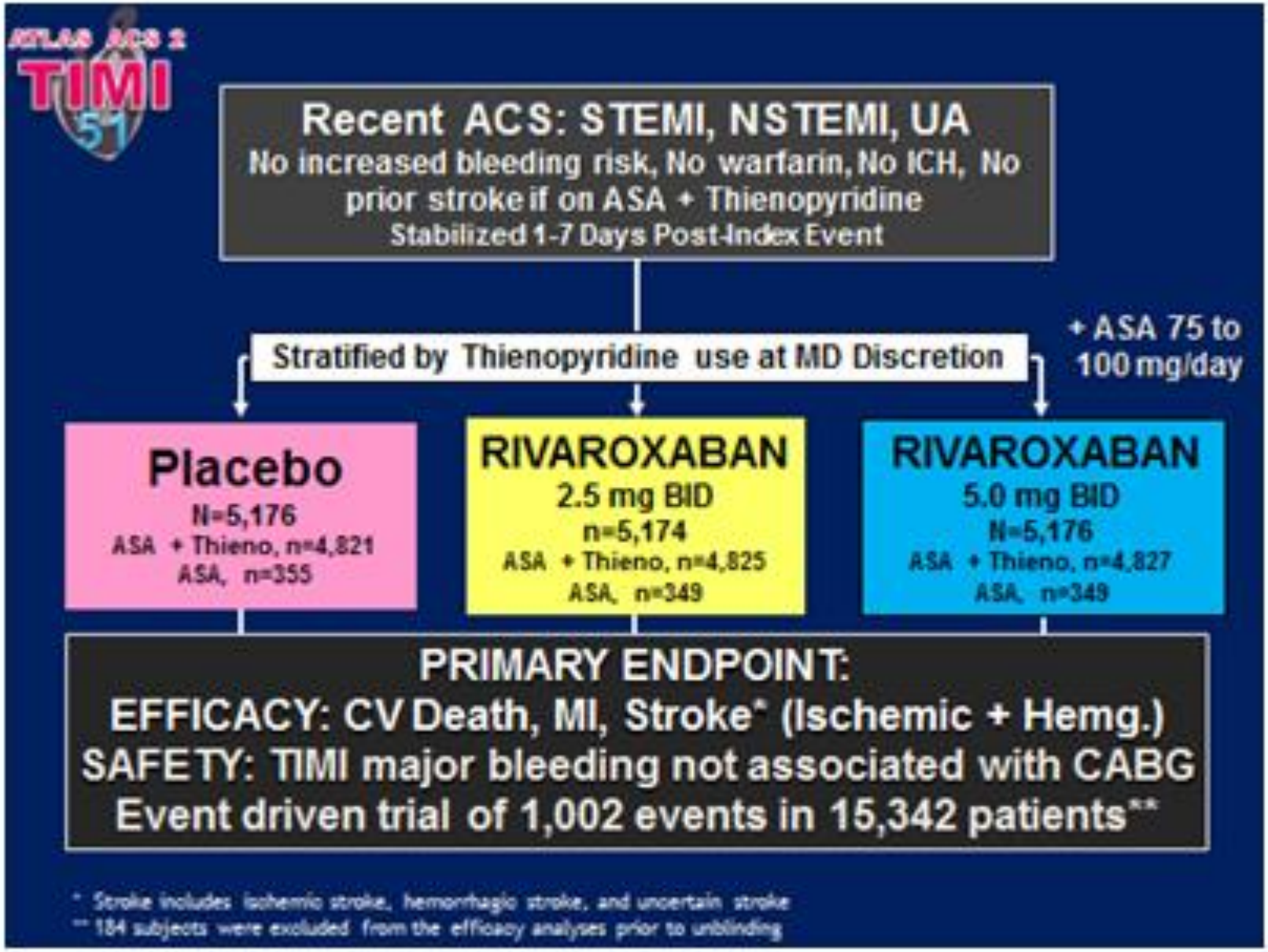
Dabigatran vs. placebo in patients with acute coronary syndromes on dual antiplatelet therapy: a randomized, double-blind, phase II trial

Jonas Oldgren[1*], Andrzej Budaj[2], Christopher B. Granger[3], Yasser Khder[4], Juliet Roberts[5], Agneta Siegbahn[1,6], Jan G.P. Tijssen[7], Frans Van de Werf[8], and Lars Wallentin[1], for the RE-DEEM Investigators

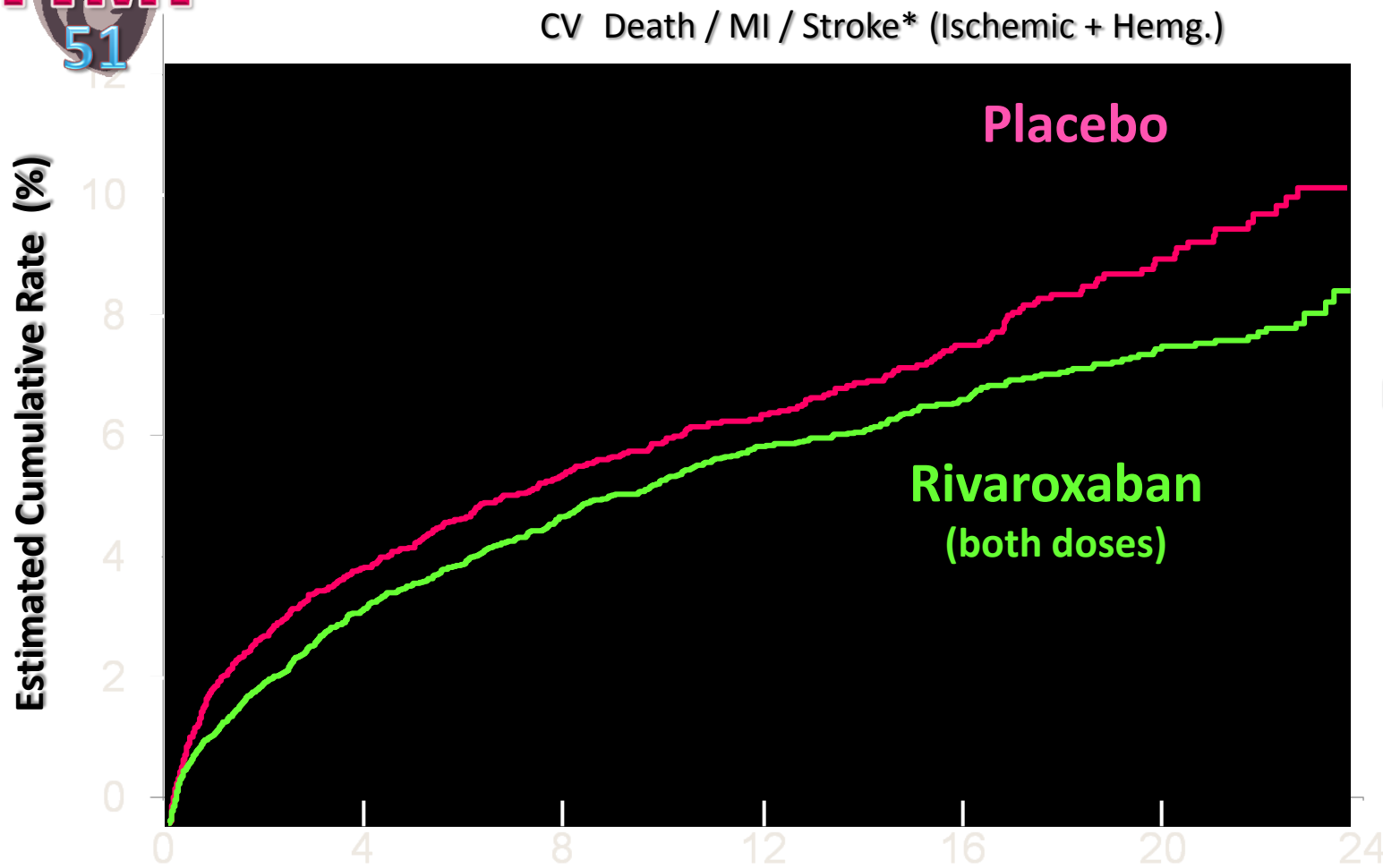
EHJ 2011



No. at risk											
Placebo	371	351	341	338	330	326	322	319	314	246	0
DE 50 mg b.i.d	369	339	330	322	314	305	300	296	290	239	0
DE 75 mg b.i.d	368	348	338	334	327	320	316	313	309	251	0
DE 110 mg b.i.d	406	380	362	352	344	336	330	324	319	261	0
DE 150 mg b.i.d	347	318	305	301	295	287	285	282	278	200	0


ATLAS ACS 2
TIMI
51
Recent ACS: STEMI, NSTEMI, UA
No increased bleeding risk, No warfarin, No ICH, No prior stroke if on ASA + Thienopyridine
Stabilized 1-7 Days Post-Index Event
Stratified by Thienopyridine use at MD Discretion
+ ASA 75 to 100 mg/day
Placebo
N=5,176
ASA + Thieno, n=4,821
ASA, n=355
RIVAROXABAN
2.5 mg BID
n=5,174
ASA + Thieno, n=4,825
ASA, n=349
RIVAROXABAN
5.0 mg BID
N=5,176
ASA + Thieno, n=4,827
ASA, n=349
PRIMARY ENDPOINT:
EFFICACY: CV Death, MI, Stroke* (Ischemic + Hemg.)
SAFETY: TIMI major bleeding not associated with CABG
Event driven trial of 1,002 events in 15,342 patients**
* Stroke includes ischemic stroke, hemorrhagic stroke, and uncertain stroke
** 184 subjects were excluded from the efficacy analyses prior to unblinding

PRIMARY EFFICACY ENDPOINT:



2 Yr KM Estimate

10.7%

8.9%

HR 0.84 (0.74-0.96)
ARR 1.7%

mITT p = 0.008
ITT p = 0.002

NNT = 59

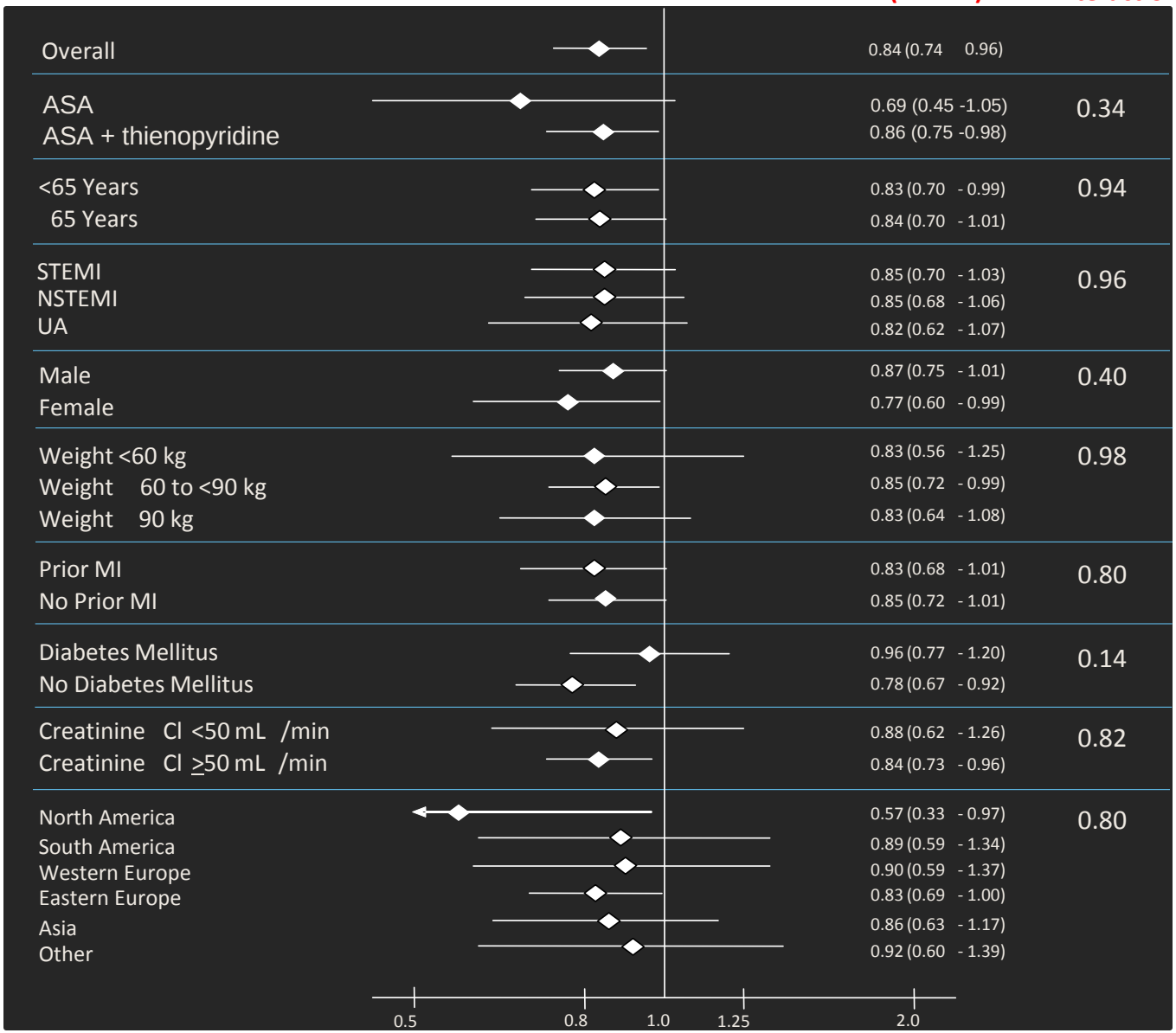
No. at Risk

Placebo	5113	4307	3470	2664	1831	1079	421
Rivaroxaban	10229	8502	6753	5137	3554	2084	831

*: First occurrence of cardiovascular death, MI, stroke (ischemic, hemorrhagic, and uncertain) as adjudicated by the CEC across thienopyridine use strata
Two year Kaplan-Meier estimates, HR and 95% confidence interval estimates from Cox model stratified by thienopyridine use are provided per mITT approach; Stratified log-rank p-values are provided for both mITT and ITT approaches; ARR=Absolute Relative Reduction; NNT=Number needed to treat; Rivaroxaban=Pooled Rivaroxaban 2.5 mg BID and 5 mg BID.

ATLAS ACS 2 TIMI 51

PRIMARY EFFICACY SUBGROUP RESULTS (mITT)



Safety Endpoints

	Placebo	Rivaroxaban 2.5 mg BID	Rivaroxaban 5 mg BID
Non-CABG TIMI Major	0.6%	1.8% (P<0.001)	2.4% (P<0.001)
ICH	0.2%	0.4% (P=0.04)	0.7% (P=0.005)
Fatal	0.2%	0.1% (P=NS)	0.4% (P=NS)
Fatal ICH	0.1%	0.1% (P=NS)	0.2% (P=NS)

2-yr KM event rates

Mega JL, Braunwald E, Wiviott SD, Bassand JP, Bhatt DL, Bode C, Burton P, Cohen M, Cook-Bruns N, Fox KA, Goto S, Murphy SA, Plotnikov AN, Schneider D, Sun X, Verheugt FW, Gibson CM, *NEJM* 2012

However…

Table 2 Missing Data in Contemporary ACS Trials*

Trial Name (Ref. #)	Study Agent	Enrolled, n	Median Follow-Up	Incomplete Follow-Up†	Withdrawal of Consent	Vital Status Unknown‡
ATLAS ACS 2-TIMI 51 (7)	Rivaroxaban	15,526	484 days	2402 (15.5)	1,294 (8.3)	1,117 (7.2)
APPRAISE-2 (9)	Apixaban	7,392	241 days	131 (1.8)	81 (1.1)	Not reported
TRACER (10)	Vorapaxar	12,944	502 days	761 (5.9)	Not reported	249 (1.9)
PLATO (20)	Ticagrelor	18,624	277 days	562 (3.0)	545 (2.9)	2 (0.01%)
TRITON (21)	Prasugrel	13,619	14.5 months	804 (5.9)	665 (4.9)	16 (0.12)

Krantz JACC 2013

Triple therapy with NOAS

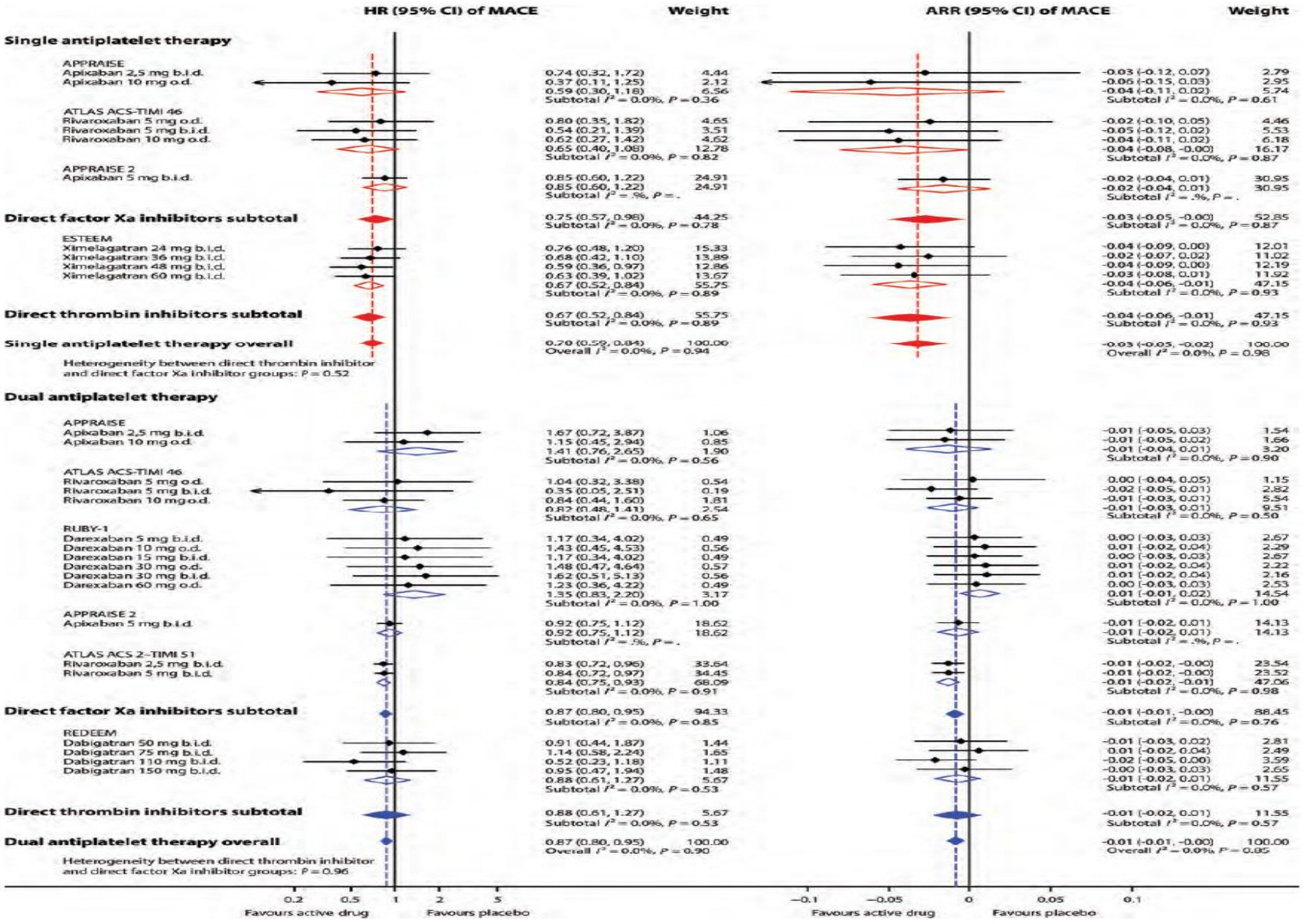
European Heart Journal (2013) 34, 1670–1680
doi:10.1093/eurheartj/eht049

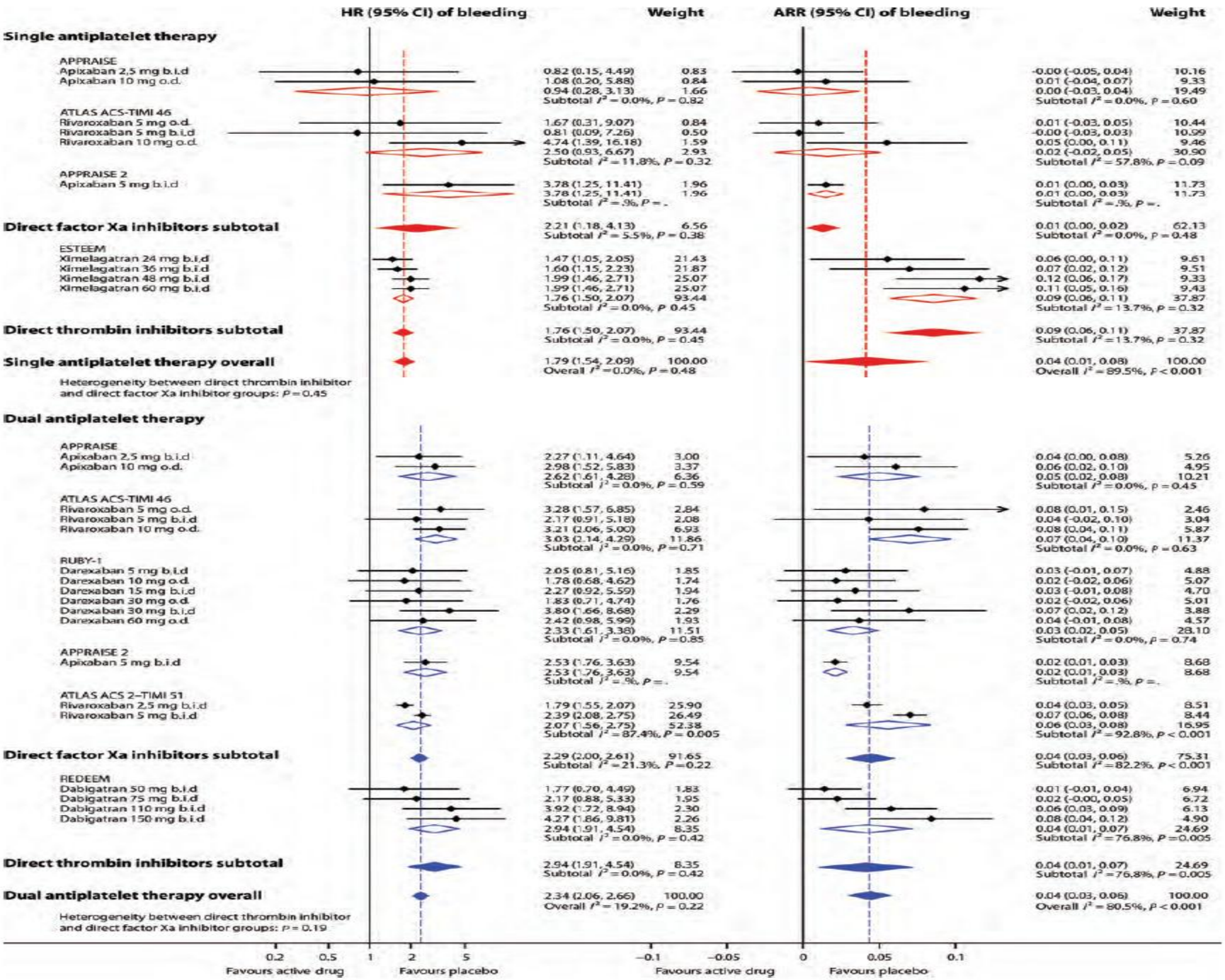
New oral anticoagulants in addition to single or dual antiplatelet therapy after an acute coronary syndrome: a systematic review and meta-analysis

Jonas Oldgren[1,2*], Lars Wallentin[1,2], John H. Alexander[3], Stefan James[1,2], Birgitta Jönelid[1], Gabriel Steg[4,5,6], and Johan Sundström[1,2]

Study	No. of study patients	No. of patients[a] in meta-analysis	Duration	Age[c]	Per cent women	Study treatment	Antiplatelet drugs		Bleeding events used in the present study
							Single (%)	Dual (%)	
ESTEEM[11]	1900	1883	6 months	68	32	Ximelagatran 24, 36, 48, or 60 mg b.i.d., or placebo	100	–	ISTH major and clinically relevant non-major bleeds
APPRAISE-1[12]	1715	1210[b]	6 months	61	24	Apixaban 2.5 mg b.i.d., 10 mg o.d., or placebo	24	76	ISTH major and clinically relevant non-major bleeds
ATLAS ACS-TIMI46[13]	3462	1997[b]	6 months	57	23	Rivaroxaban 5 mg o.d., 5 mg b.i.d., 10 mg o.d., or placebo	25	75	TIMI clinically significant bleeding (TIMI major bleeding, TIMI minor bleeding, or bleeding requiring medical attention)
REDEEM[14]	1878	1861	6 months	62	24	Dabigatran 50, 75, 110. or 150 mg b.i.d. or placebo	2	98	ISTH major and clinically relevant non-major bleeds
RUBY-1[15]	1279	1258	6 months	57	20	Darexaban 5, 15 or 30 mg b.i.d., 10, 30 or 60 mg o.d., or placebo	5	95	ISTH major and clinically relevant non-major bleeds
APPRAISE-2[16]	7392	7315	8 months	67	32	Apixaban 5 mg (or 2.5 mg[d]) b.i.d., or placebo	19	81	TIMI major bleeds; ISTH major and clinically relevant non-major bleeds
ATLAS ACS2-TIMI51[17]	15 526	15 342	13 months	62	25	Rivaroxaban 2.5 or 5 mg b.i.d., or placebo	7	93	TIMI major (non-CABG related) bleeds, TIMI bleeding requiring medical attention

European Heart Journal (2013) **34**, 1670–1680
doi:10.1093/eurheartj/eht049




HR (95% CI) of bleeding
Weight
ARR (95% CI) of bleeding
Weight
Single antiplatelet therapy
APPRAISE
Apixaban 2,5 mg b.i.d
0.82 (0.15, 4.49) 0.83
Apixaban 10 mg o.d.
1.08 (0.20, 5.88) 0.84
0.94 (0.28, 3.13) 1.66
Subtotal I² = 0.0%, P = 0.82
-0.00 (-0.05, 0.04) 10.16
0.01 (-0.04, 0.07) 9.33
0.00 (-0.03, 0.04) 19.49
Subtotal I² = 0.0%, P = 0.60
ATLAS ACS-TIMI 46
Rivaroxaban 5 mg o.d.
1.67 (0.31, 9.07) 0.84
Rivaroxaban 5 mg b.i.d
0.81 (0.09, 7.26) 0.50
Rivaroxaban 10 mg o.d.
4.74 (1.39, 16.18) 1.59
2.50 (0.93, 6.67) 2.93
Subtotal I² = 11.8%, P = 0.32
0.01 (-0.03, 0.05) 10.44
-0.00 (-0.03, 0.03) 10.99
0.05 (0.00, 0.11) 9.46
0.02 (-0.02, 0.05) 30.90
Subtotal I² = 57.8%, P = 0.09
APPRAISE 2
Apixaban 5 mg b.i.d
3.78 (1.25, 11.41) 1.96
3.78 (1.25, 11.41) 1.96
Subtotal I² = .%, P = .
0.01 (0.00, 0.03) 11.73
0.01 (0.00, 0.03) 11.73
Subtotal I² = .%, P = .
Direct factor Xa inhibitors subtotal
2.21 (1.18, 4.13) 6.56
Subtotal I² = 5.5%, P = 0.38
0.01 (0.00, 0.02) 62.13
Subtotal I² = 0.0%, P = 0.48
ESTEEM
Ximelagatran 24 mg b.i.d
1.47 (1.05, 2.05) 21.43
Ximelagatran 36 mg b.i.d
1.60 (1.15, 2.23) 21.87
Ximelagatran 48 mg b.i.d
1.99 (1.46, 2.71) 25.07
Ximelagatran 60 mg b.i.d
1.99 (1.46, 2.71) 25.07
1.76 (1.50, 2.07) 93.44
Subtotal I² = 0.0%, P 0.45
0.06 (0.00, 0.11) 9.61
0.07 (0.02, 0.12) 9.51
0.12 (0.06, 0.17) 9.33
0.11 (0.05, 0.16) 9.43
0.09 (0.06, 0.11) 37.87
Subtotal I² = 13.7%, P = 0.32
Direct thrombin inhibitors subtotal
1.76 (1.50, 2.07) 93.44
Subtotal I² = 0.0%, P = 0.45
0.09 (0.06, 0.11) 37.87
Subtotal I² = 13.7%, P = 0.32
Single antiplatelet therapy overall
1.79 (1.54, 2.09) 100.00
Overall I² = 0.0%, P = 0.48
0.04 (0.01, 0.08) 100.00
Overall I² = 89.5%, P < 0.001
Heterogeneity between direct thrombin inhibitor and direct factor Xa inhibitor groups: P = 0.45
Dual antiplatelet therapy
APPRAISE
Apixaban 2,5 mg b.i.d
2.27 (1.11, 4.64) 3.00
Apixaban 10 mg o.d.
2.98 (1.52, 5.83) 3.37
2.62 (1.61, 4.28) 6.36
Subtotal I² = 0.0%, P = 0.59
0.04 (0.00, 0.08) 5.26
0.06 (0.02, 0.10) 4.95
0.05 (0.02, 0.08) 10.21
Subtotal I² = 0.0%, P = 0.45
ATLAS ACS-TIMI 46
Rivaroxaban 5 mg o.d.
3.28 (1.57, 6.85) 2.84
Rivaroxaban 5 mg b.i.d
2.17 (0.91, 5.18) 2.08
Rivaroxaban 10 mg o.d.
3.21 (2.06, 5.00) 6.93
3.03 (2.14, 4.29) 11.86
Subtotal I² = 0.0%, P = 0.71
0.08 (0.01, 0.15) 2.46
0.04 (-0.02, 0.10) 3.04
0.08 (0.04, 0.11) 5.87
0.07 (0.04, 0.10) 11.37
Subtotal I² = 0.0%, P = 0.63
RUBY-1
Darexaban 5 mg b.i.d
2.05 (0.81, 5.16) 1.85
Darexaban 10 mg o.d.
1.78 (0.68, 4.62) 1.74
Darexaban 15 mg b.i.d
2.27 (0.92, 5.59) 1.94
Darexaban 30 mg o.d.
1.83 (0.71, 4.74) 1.76
Darexaban 30 mg b.i.d
3.80 (1.66, 8.68) 2.29
Darexaban 60 mg o.d.
2.42 (0.98, 5.99) 1.93
2.33 (1.61, 3.38) 11.51
Subtotal I² = 0.0%, P = 0.85
0.03 (-0.01, 0.07) 4.88
0.02 (-0.02, 0.06) 5.07
0.03 (-0.01, 0.08) 4.70
0.02 (-0.02, 0.06) 5.01
0.07 (0.02, 0.12) 3.88
0.04 (-0.01, 0.08) 4.57
0.03 (0.02, 0.05) 28.10
Subtotal I² = 0.0%, P = 0.74
APPRAISE 2
Apixaban 5 mg b.i.d
2.53 (1.76, 3.63) 9.54
2.53 (1.76, 3.63) 9.54
Subtotal I² = .%, P = .
0.02 (0.01, 0.03) 8.68
0.02 (0.01, 0.03) 8.68
Subtotal I² = .%, P = .
ATLAS ACS 2–TIMI 51
Rivaroxaban 2,5 mg b.i.d
1.79 (1.55, 2.07) 25.90
Rivaroxaban 5 mg b.i.d
2.39 (2.08, 2.75) 26.49
2.07 (1.56, 2.75) 52.38
Subtotal I² = 87.4%, P = 0.005
0.04 (0.03, 0.05) 8.51
0.07 (0.06, 0.08) 8.44
0.06 (0.03, 0.08) 16.95
Subtotal I² = 92.8%, P < 0.001
Direct factor Xa inhibitors subtotal
2.29 (2.00, 2.61) 91.65
Subtotal I² = 21.3%, P = 0.22
0.04 (0.03, 0.06) 75.31
Subtotal I² = 82.2%, P < 0.001
REDEEM
Dabigatran 50 mg b.i.d
1.77 (0.70, 4.49) 1.83
Dabigatran 75 mg b.i.d
2.17 (0.88, 5.33) 1.95
Dabigatran 110 mg b.i.d
3.92 (1.72, 8.94) 2.30
Dabigatran 150 mg b.i.d
4.27 (1.86, 9.81) 2.26
2.94 (1.91, 4.54) 8.35
Subtotal I² = 0.0%, P = 0.42
0.01 (-0.01, 0.04) 6.94
0.02 (-0.00, 0.05) 6.72
0.06 (0.03, 0.09) 6.13
0.08 (0.04, 0.12) 4.90
0.04 (0.01, 0.07) 24.69
Subtotal I² = 76.8%, P = 0.005
Direct thrombin inhibitors subtotal
2.94 (1.91, 4.54) 8.35
Subtotal I² = 0.0%, P = 0.42
0.04 (0.01, 0.07) 24.69
Subtotal I² = 76.8%, P = 0.005
Dual antiplatelet therapy overall
2.34 (2.06, 2.66) 100.00
Overall I² = 19.2%, P = 0.22
0.04 (0.03, 0.06) 100.00
Overall I² = 80.5%, P < 0.001
Heterogeneity between direct thrombin inhibitor and direct factor Xa inhibitor groups: P = 0.19
0.2
0.5
1
2
5
Favours active drug
Favours placebo
−0.1
−0.05
0
0.05
0.1
Favours active drug
Favours placebo

New studies

Toward a paradigm shift?

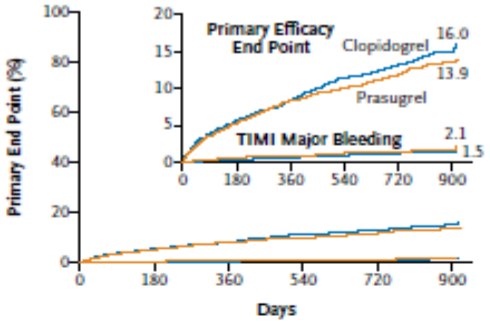
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Prasugrel versus Clopidogrel for Acute Coronary Syndromes without Revascularization

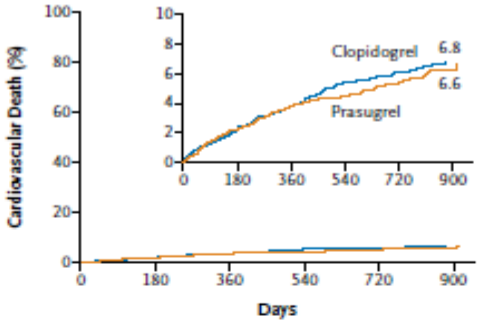
Matthew T. Roe, M.D., M.H.S., Paul W. Armstrong, M.D., Keith A.A. Fox, M.B., Ch.B.,

A Primary End Point



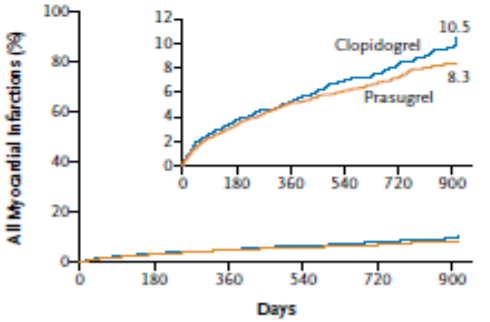
No. at Risk, Primary Efficacy End Point						
Prasugrel	3620	3248	2359	1611	953	389
Clopidogrel	3623	3244	2390	1596	946	399
No. at Risk, Major Bleeding						
Prasugrel	3590	3072	2244	1499	885	427
Clopidogrel	3590	3116	2303	1552	925	425

B Death from Cardiovascular Causes



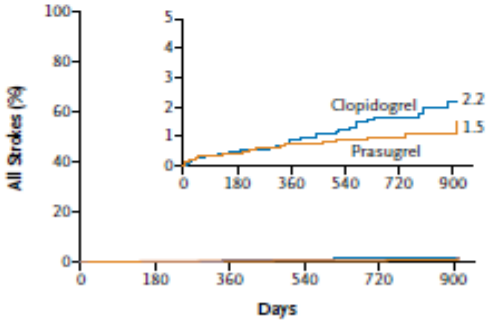
No. at Risk						
Prasugrel	3620	3350	2481	1719	1029	429
Clopidogrel	3623	3361	2504	1703	1024	428

C All Myocardial Infarctions



No. at Risk						
Prasugrel	3620	3257	2369	1620	959	392
Clopidogrel	3623	3255	2404	1611	955	402

D All Strokes



No. at Risk						
Prasugrel	3620	3338	2467	1706	1020	422
Clopidogrel	3623	3346	2486	1684	1012	424

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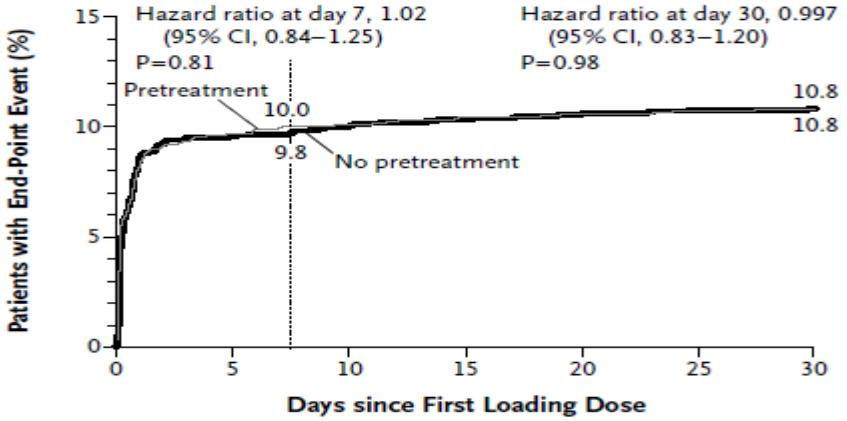
Pretreatment with Prasugrel in Non–ST-Segment Elevation Acute Coronary Syndromes

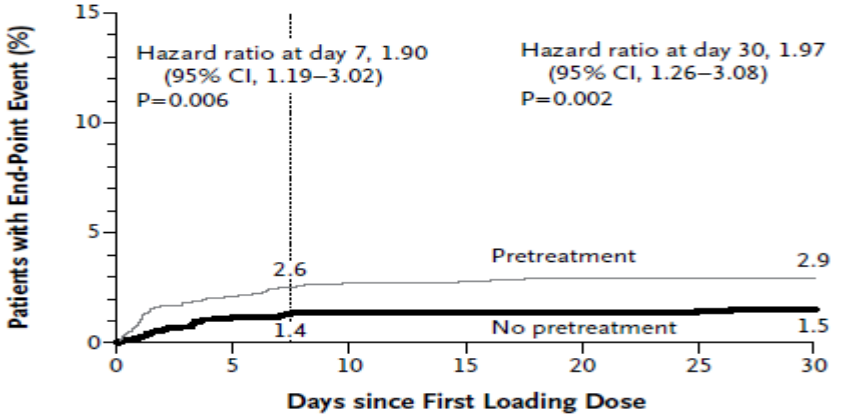
Gilles Montalescot, M.D., Ph.D., Leonardo Bolognese, M.D., Dariusz Dudek, M.D., Ph.D., Patrick Goldstein, M.D.,



No. at Risk

No pretreatment	1996	1788	1775	1769	1762	1752	1621
Pretreatment	2037	1821	1809	1802	1797	1791	1616

B **All TIMI Major Bleeding**



No. at Risk

No pretreatment	1996	1947	1328	1297	1288	1284	1263
Pretreatment	2037	1972	1339	1310	1299	1297	1280

Conclusions

- In the last two years some important issues on anti-thrombotic treatment have been elucidated
- However, at the same time, some long lasting certainties have been “jeopardized” and several paradigm shift are on the move (length of treatment, pre-treatment, use of GPI and s.c. anticoagulants).
- The field is in evolution, more novelties and , perhaps, surprises are to be expected
- For the moment, follow guidelines, but with an eye to new developments..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