I prefer Prasugrel in AMI patients

Mamas A. Mamas
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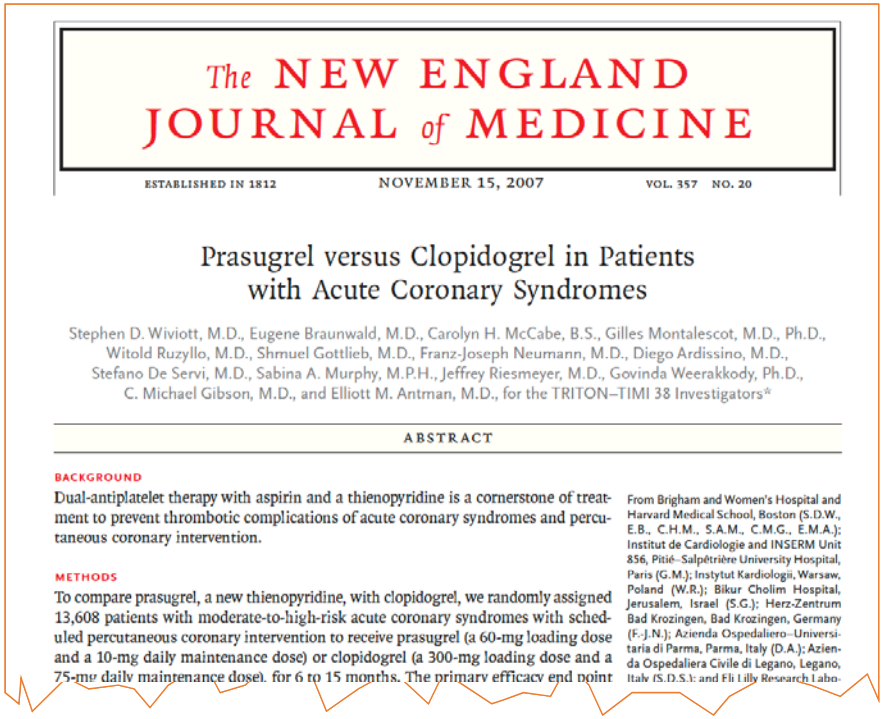
University of Keele
@MMamas1973

Both Prasugrel and Ticagrelor are superior to Clopidogrel; But which do I prefer?

Keele Cardiovascular Research Group



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 15, 2007 VOL. 357 NO. 20

Prasugrel versus Clopidogrel in Patients with Acute Coronary Syndromes

Stephen D. Wiviott, M.D., Eugene Braunwald, M.D., Carolyn H. McCabe, B.S., Gilles Montalescot, M.D., Ph.D., Witold Ruzyllo, M.D., Shmuel Gottlieb, M.D., Franz-Joseph Neumann, M.D., Diego Ardissino, M.D., Stefano De Servi, M.D., Sabina A. Murphy, M.P.H., Jeffrey Riesmeyer, M.D., Govinda Weerakkody, Ph.D., C. Michael Gibson, M.D., and Elliott M. Antman, M.D., for the TRITON–TIMI 38 Investigators*

ABSTRACT

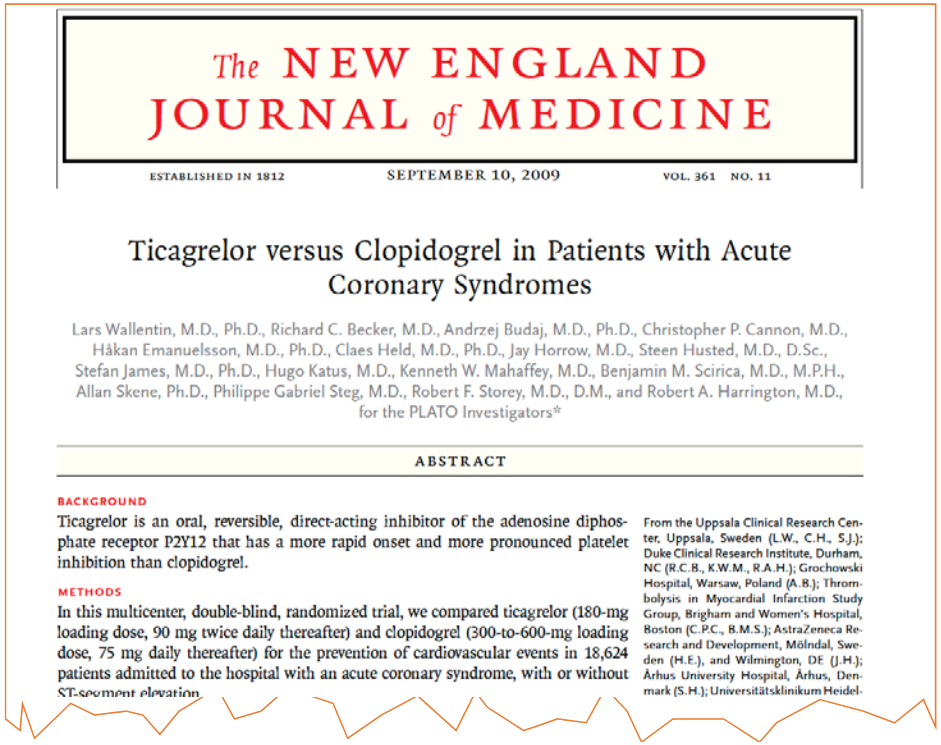
BACKGROUND

Dual-antiplatelet therapy with aspirin and a thienopyridine is a cornerstone of treatment to prevent thrombotic complications of acute coronary syndromes and percutaneous coronary intervention.

METHODS

To compare prasugrel, a new thienopyridine, with clopidogrel, we randomly assigned 13,608 patients with moderate-to-high-risk acute coronary syndromes with scheduled percutaneous coronary intervention to receive prasugrel (a 60-mg loading dose and a 10-mg daily maintenance dose) or clopidogrel (a 300-mg loading dose and a 75-mg daily maintenance dose), for 6 to 15 months. The primary efficacy end point

From Brigham and Women's Hospital and Harvard Medical School, Boston (S.D.W., E.B., C.H.M., S.A.M., C.M.G., E.M.A.); Institut de Cardiologie and INSERM Unit 856, Pitié–Salpêtrière University Hospital, Paris (G.M.); Instytut Kardiologii, Warsaw, Poland (W.R.); Bikur Cholim Hospital, Jerusalem, Israel (S.G.); Herz-Zentrum Bad Krozingen, Bad Krozingen, Germany (F.-J.N.); Azienda Ospedaliero–Universitaria di Parma, Parma, Italy (D.A.); Azienda Ospedaliera Civile di Legano, Legano, Italy (S.D.S.); and Eli Lilly Research Labo-



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 10, 2009 VOL. 361 NO. 11

Ticagrelor versus Clopidogrel in Patients with Acute Coronary Syndromes

Lars Wallentin, M.D., Ph.D., Richard C. Becker, M.D., Andrzej Budaj, M.D., Ph.D., Christopher P. Cannon, M.D., Håkan Emanuelsson, M.D., Ph.D., Claes Held, M.D., Ph.D., Jay Horrow, M.D., Steen Husted, M.D., D.Sc., Stefan James, M.D., Ph.D., Hugo Katus, M.D., Kenneth W. Mahaffey, M.D., Benjamin M. Scirica, M.D., M.P.H., Allan Skene, Ph.D., Philippe Gabriel Steg, M.D., Robert F. Storey, M.D., D.M., and Robert A. Harrington, M.D., for the PLATO Investigators*

ABSTRACT

BACKGROUND

Ticagrelor is an oral, reversible, direct-acting inhibitor of the adenosine diphosphate receptor P2Y12 that has a more rapid onset and more pronounced platelet inhibition than clopidogrel.

METHODS

In this multicenter, double-blind, randomized trial, we compared ticagrelor (180-mg loading dose, 90 mg twice daily thereafter) and clopidogrel (300-to-600-mg loading dose, 75 mg daily thereafter) for the prevention of cardiovascular events in 18,624 patients admitted to the hospital with an acute coronary syndrome, with or without ST-segment elevation.

From the Uppsala Clinical Research Center, Uppsala, Sweden (L.W., C.H., S.J.); Duke Clinical Research Institute, Durham, NC (R.C.B., K.W.M., R.A.H.); Grochowski Hospital, Warsaw, Poland (A.B.); Thrombolysis in Myocardial Infarction Study Group, Brigham and Women's Hospital, Boston (C.P.C., B.M.S.); AstraZeneca Research and Development, Mölndal, Sweden (H.E.), and Wilmington, DE (J.H.); Århus University Hospital, Århus, Denmark (S.H.); Universitätsklinikum Heidel-

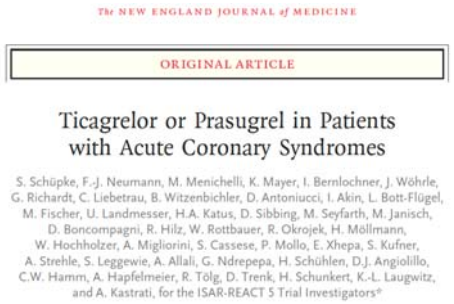
I prefer Prasugrel in AMI patients because:

Keele Cardiovascular Research Group

- Clinical efficacy (Superior RCT and real world comparative data)
- Clinical Safety
- Pharmacological efficacy
- Tolerability by patients

Keele Cardiovascular Research Group

Superior Clinical efficacy (RCT and real world comparative data)



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Trial

- Randomized controlled, multi-centre trial in patients in whom invasive management planned, planned to receive Ticagrelor or Prasugrel

Primary Endpoint

- Composite of death, myocardial infarction or stroke at 12 months

Secondary Endpoints

- BARC 3-5 Bleeding (safety endpoint)
- Individual components of primary endpoint
- Stent thrombosis

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Ticagrelor or Prasugrel in Patients with Acute Coronary Syndromes

S. Schüpke, F.-J. Neumann, M. Menichelli, K. Mayer, I. Bernlochner, J. Wöhrle, G. Richardt, C. Liebetrau, B. Witzenbichler, D. Antoniucci, I. Akin, L. Bott-Flügel, M. Fischer, U. Landmesser, H.A. Katus, D. Sibbing, M. Seyfarth, M. Janisch, D. Boncompagni, R. Hilz, W. Rottbauer, R. Okrojek, H. Möllmann, W. Hochholzer, A. Migliorini, S. Cassese, P. Mollo, E. Xhepa, S. Kufner, A. Strehle, S. Leggewie, A. Allali, G. Ndrepepa, H. Schühlen, D.J. Angiolillo, C.W. Hamm, A. Hapfelmeier, R. Tölg, D. Trenk, H. Schunkert, K.-L. Laugwitz, and A. Kastrati, for the ISAR-REACT 5 Trial Investigators*

Protocol

STEMI

Randomization

Ticagrelor
180 mg loading

Prasugrel
60 mg loading

Angiography + PCI

Ticagrelor
90 mg 1-0-1

Prasugrel
10 mg 1-0-0*

Duration of ADP receptor therapy: 12 months
Concomitant ASA: 75-150 mg/d
In patients with known coronary anatomy
* Prasugrel 5 mg in patients ≥ 75 years of age or weight < 60 kg

Unstable Angina, NSTEMI

Randomization

Ticagrelor
180 mg loading

Prasugrel#
60 mg loading

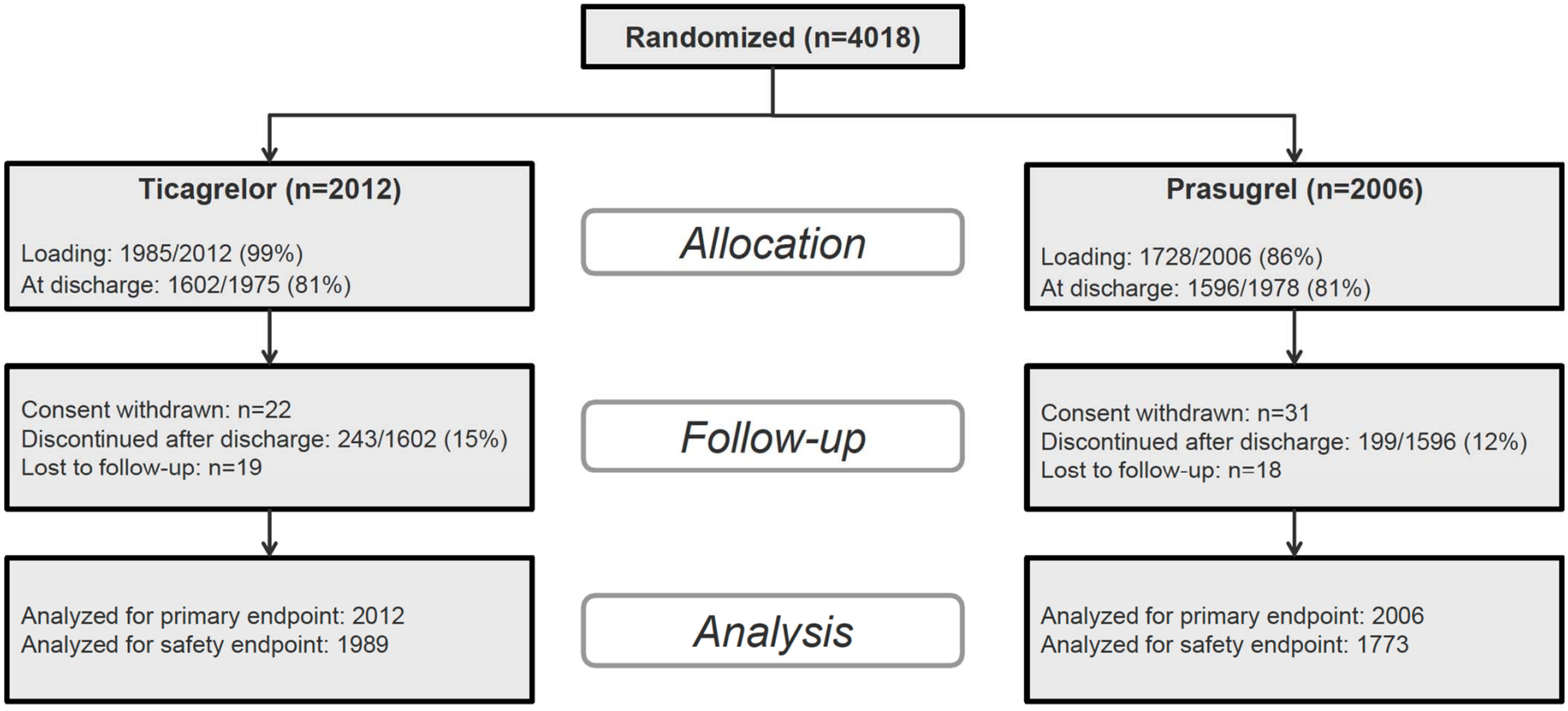
Angiography

Prasugrel
60 mg loading

PCI

Ticagrelor
90 mg 1-0-1

Prasugrel
10 mg 1-0-0*


Randomized (n=4018)
Ticagrelor (n=2012)
Loading: 1985/2012 (99%)
At discharge: 1602/1975 (81%)
Prasugrel (n=2006)
Loading: 1728/2006 (86%)
At discharge: 1596/1978 (81%)
Allocation
Consent withdrawn: n=22
Discontinued after discharge: 243/1602 (15%)
Lost to follow-up: n=19
Consent withdrawn: n=31
Discontinued after discharge: 199/1596 (12%)
Lost to follow-up: n=18
Follow-up
Analyzed for primary endpoint: 2012
Analyzed for safety endpoint: 1989
Analyzed for primary endpoint: 2006
Analyzed for safety endpoint: 1773
Analysis

Primary End point
(Composite of Death, MI, or Stroke)

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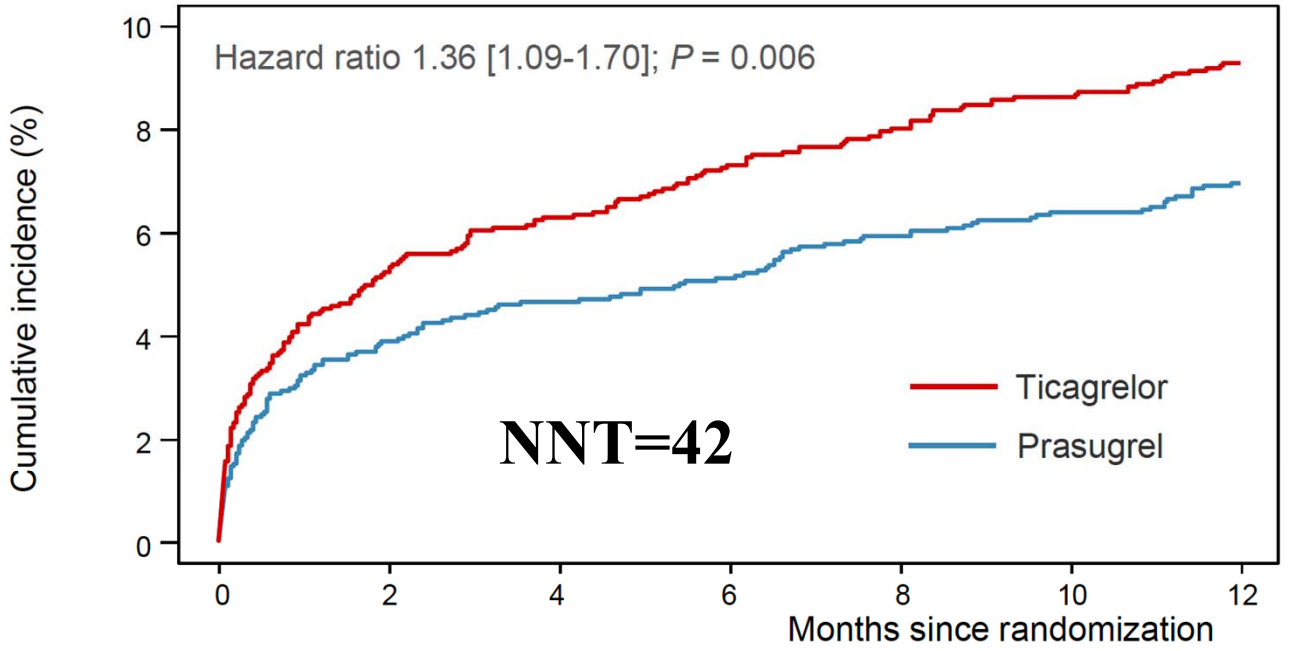

No. at Risk							
Ticagrelor	2012	1877	1857	1835	1815	1801	1772
Prasugrel	2006	1892	1877	1862	1839	1829	1803

BARC Type 3-5 Bleeding

(Safety End point)

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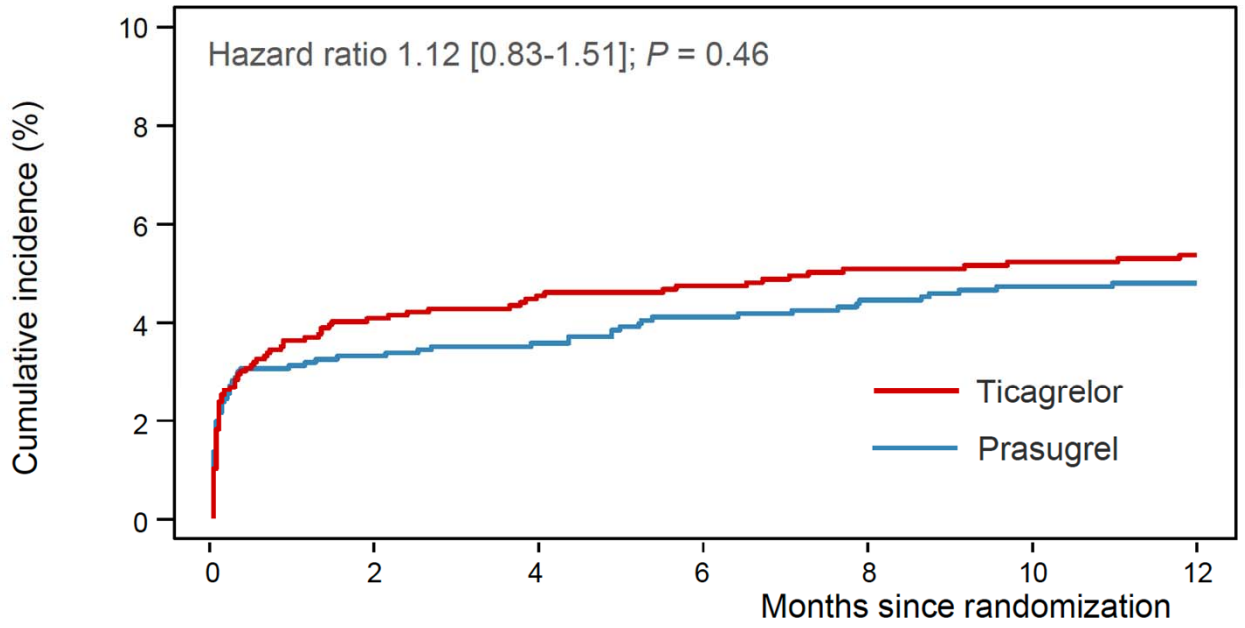

No. at Risk							
Ticagrelor	1989	1441	1399	1356	1319	1296	1266
Prasugrel	1773	1465	1427	1397	1357	1333	1307

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Table 2. Clinical End Points.*

End Point	Ticagrelor Group (N= 2012)	Prasugrel Group (N= 2006)	Hazard Ratio (95% CI)	P Value
Primary end point: death, myocardial infarction, or stroke — no. (%)	184 (9.3)	137 (6.9)	1.36 (1.09–1.70)	0.006
Death — no. (%)				
From any cause	90 (4.5)	73 (3.7)	1.23 (0.91–1.68)	
From cardiovascular cause	63 (3.2)	59 (3.0)		
From noncardiovascular cause	27 (1.4)	14 (0.7)		
Myocardial infarction — no. (%)†	96 (4.8)	60 (3.0)	1.63 (1.18–2.25)	
Type 1 — no.	52	35		
Type 2 — no.	4	3		
Type 4a — no.	19	11		
Type 4b — no.	20	11		
Type 5 — no.	1	0		
STEMI — no.	31	14		
Stroke				
Any — no. (%)	22 (1.1)	19 (1.0)	1.17 (0.63–2.15)	
Ischemic — no.	16	17		
Hemorrhagic — no.	6	2		
Definite or probable stent thrombosis — no. (%)	26 (1.3)	20 (1.0)	1.30 (0.72–2.33)	
Definite stent thrombosis — no. (%)	22 (1.1)	12 (0.6)		
Secondary safety end point: BARC type 3, 4, or 5 bleeding — no./total no. (%)‡	95/1989 (5.4)	80/1773 (4.8)	1.12 (0.83–1.51)	0.46
BARC 3a	47	41		
BARC 3b	32	31		
BARC 3c	4	2		
BARC 4	8	2		
BARC 5a	1	0		
BARC 5b	3	4		

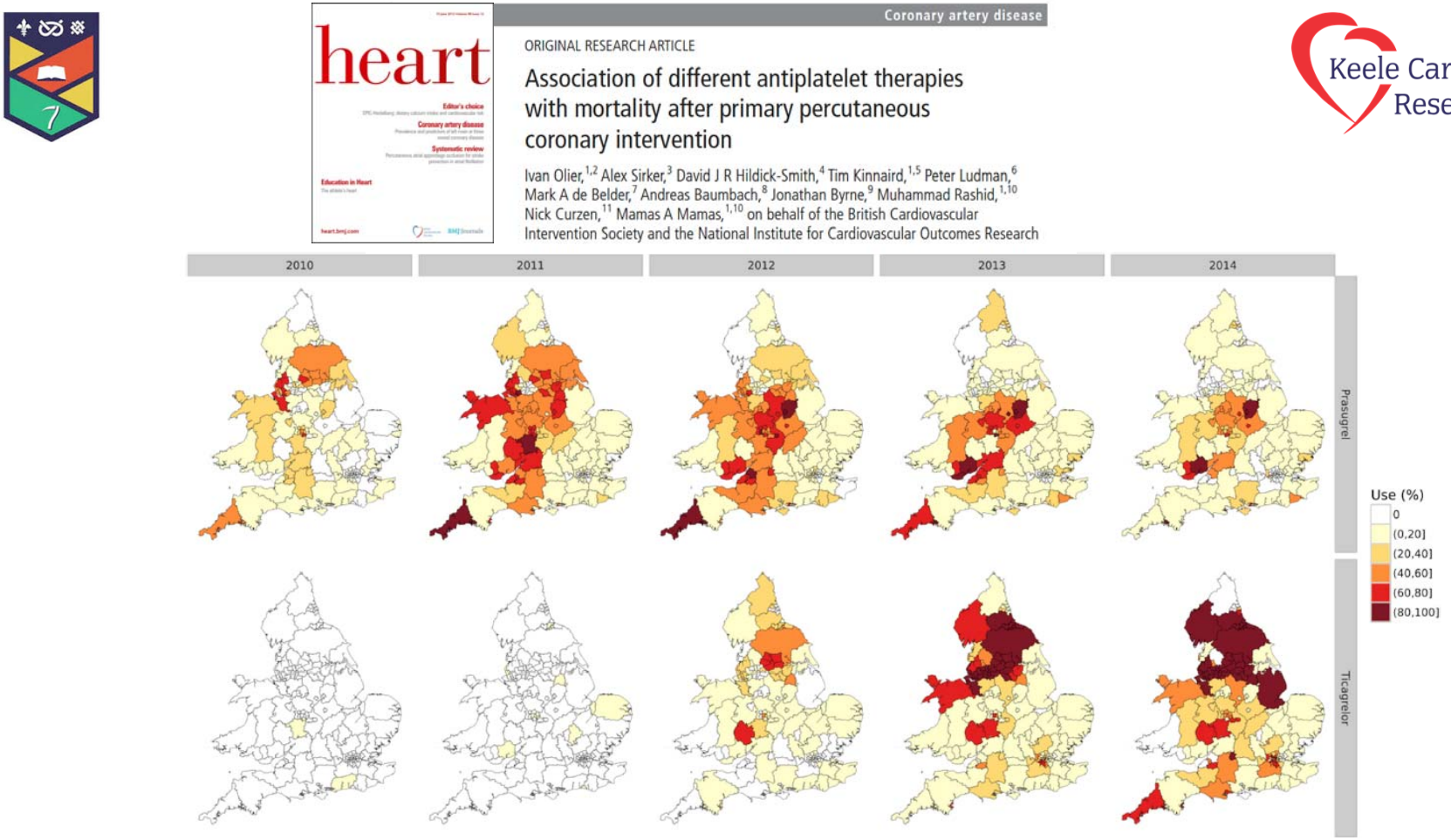

Figure 2 Changes in use of antiplatelet drugs in primary care trusts in England and local health boards in Wales.

Olier et al. Heart 2018; DOI 10.1136/heartjnl-2017-312366

Coronary artery disease

ORIGINAL RESEARCH ARTICLE

Association of different antiplatelet therapies with mortality after primary percutaneous coronary intervention

Ivan Olier,[1,2] Alex Sirker,[3] David J R Hildick-Smith,[4] Tim Kinnaird,[1,5] Peter Ludman,[6] Mark A de Belder,[7] Andreas Baumbach,[8] Jonathan Byrne,[9] Muhammad Rashid,[1,10] Nick Curzen,[11] Mamas A Mamas,[1,10] on behalf of the British Cardiovascular Intervention Society and the National Institute for Cardiovascular Outcomes Research

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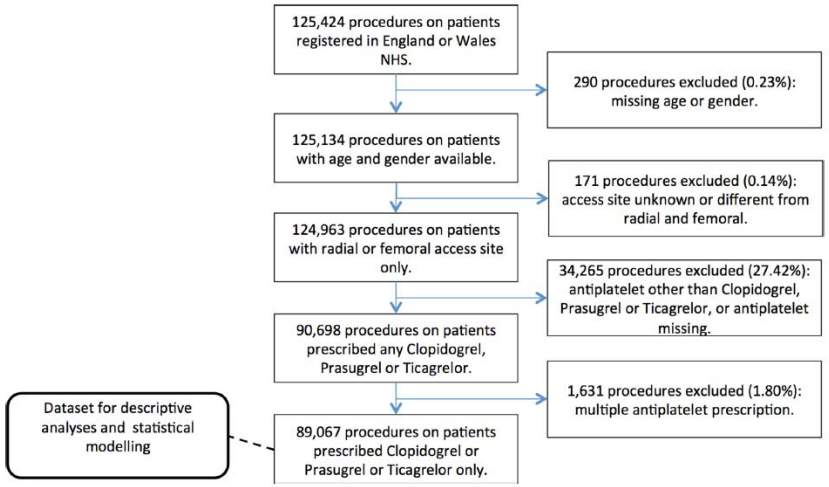
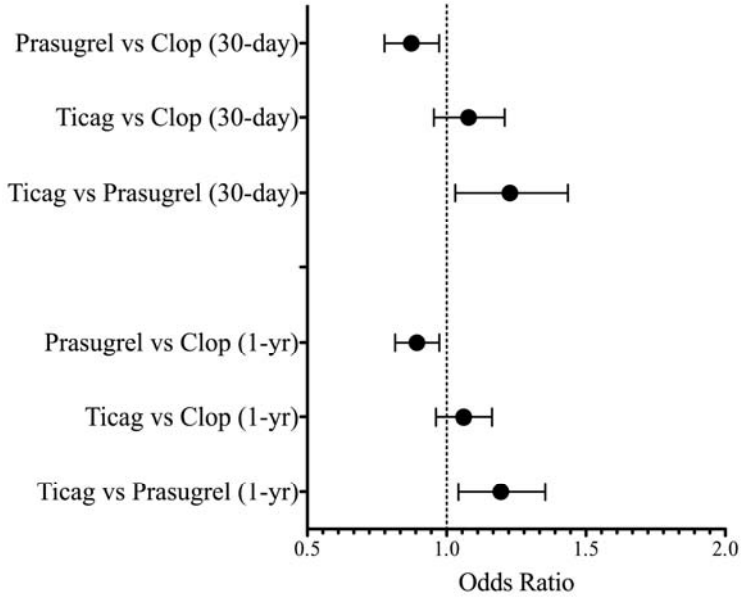


Figure 1 Flow chart for procedure inclusion/exclusion. NHS, National Health Service.



Olier et al. Heart 2018; DOI 10.1136/heartjnl-2017-312366

ORIGINAL RESEARCH ARTICLE

Real-World Data of Prasugrel vs. Ticagrelor in Acute Myocardial Infarction: Results from the RENAMI Registry

Ovidio De Filippo[1] · Martina Cortese[1] · Fabrizio D'Ascenzo[1] · Sergio Raposeiras-Roubin[2] · Emad Abu-Assi[2] · Tim Kinnaird[3] · Albert Ariza-Solé[4] · Sergio Manzano-Fernández[5] · Christian Templin[6] · Lazar Velicki[7,8] · Ioanna Xanthopoulou[9] · Enrico Cerrato[10] · Andrea Rognoni[11] · Giacomo Boccuzzi[12] · Antonio Montefusco[1] · Andrea Montabone[12] · Salma Taha[13] · Alessandro Durante[14] · Sebastiano Gili[6] · Giulia Magnani[6] · Michele Autelli[1] · Alberto Grosso[1] · Pedro Flores Blanco[5] · Alberto Garay[4] · Giorgio Quadri[15] · Ferdinando Varbella[16] · Berenice Caneiro Queija[2] · Rafael Cobas Paz[2] · Maria Cespón Fernández[2] · Isabel Muñoz Pousa[2] · Diego Gallo[15] · Umberto Morbiducci[13] · Alberto Domínguez-Rodríguez[16] · Mariano Valdés[5] · Angel Cequier[4] · Dimitrios Alexopoulos[9] · Andrés Iñiguez-Romo[2] · Mauro Rinaldi[1]

- 4424 ACS patients from 11 centres in 6 European countries

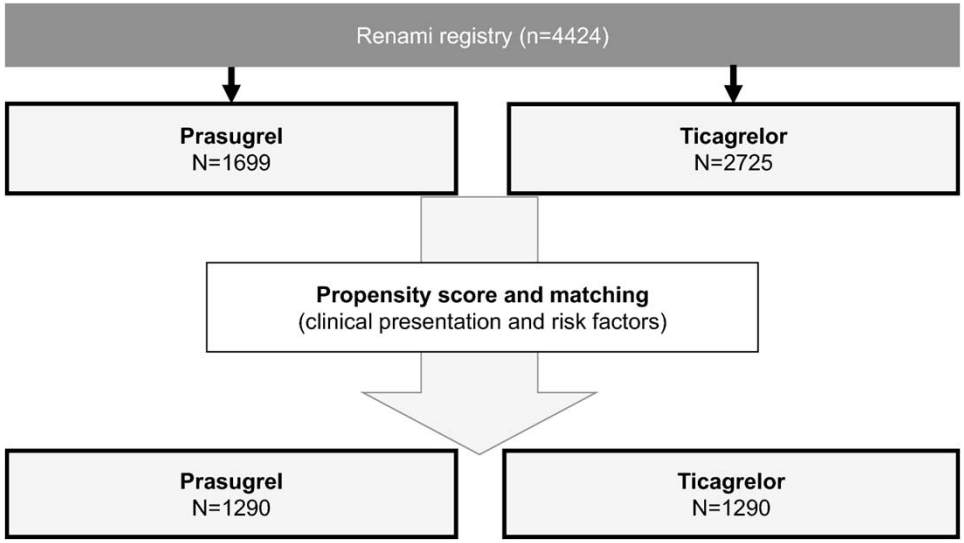


Table 1 Baseline features of patients after propensity score matching

Baseline feature	Prasugrel $n=1290$ (50)	Ticagrelor $n=1290$ (50)	p value
Age > 75, years	72 (5.6)	89 (6.9)	0.166
Female sex	201 (15.6)	209 (16.2)	0.667
Body weight < 60 kg	55 (4.3)	52 (4.0)	0.767
Diabetes mellitus	353 (27.4)	325 (25.2)	0.210
Insulin	44 (3.4)	26 (2.0)	0.029
HTA	666 (51.6)	699 (54.2)	0.193
Dyslipidemia	702 (54.4)	693 (53.7)	0.722
CAD	237 (18.4)	222 (17.2)	0.440
Prior AMI	186 (14.4)	162 (12.6)	0.167
Prior PCI	203 (15.7)	189 (14.7)	0.443
Prior CABG	12 (0.9)	16 (1.2)	0.447
Prior stroke	18 (1.4)	22 (1.7)	0.524
Prior bleeding	30 (2.3)	40 (3.1)	0.226
Malignancy	52 (4.0)	55 (4.3)	0.767
ACS			0.662
STEMI	876 (67.9)	881 (8.3)	
NSTEMI	302 (23.4)	287 (2.2)	
UA	112 (8.7)	122 (9.5)	
Creatinine > 1.5 mg/dl	58 (4.6)	69 (5.3)	0.057
LVEF < 40%	107 (8.3)	125 (9.7)	0.215

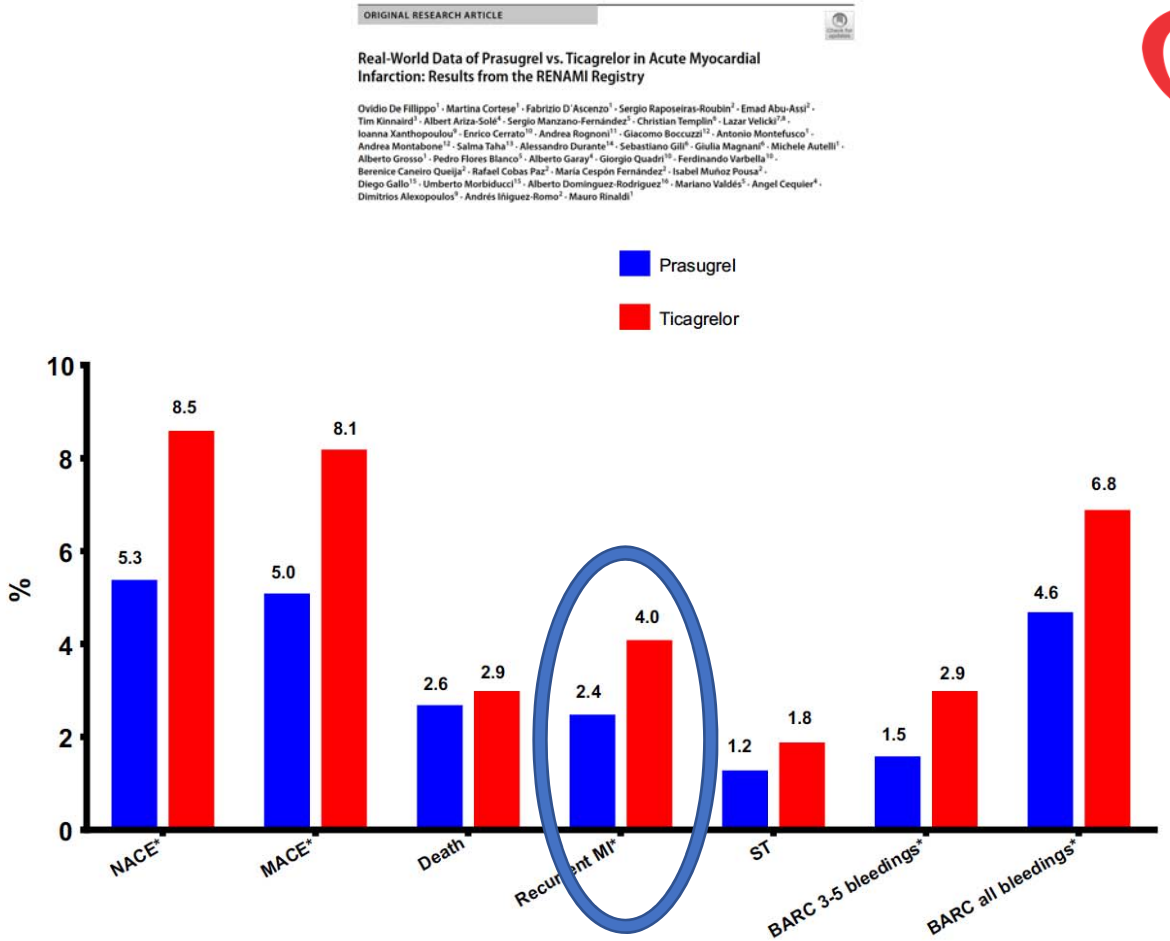


Fig. 2 12-month outcomes after propensity score matching. *BARC* Bleeding Academic Research Consortium, *MACE* major adverse cardiovascular events, *MI* myocardial infarction, *NACE* net adverse clinical events, *ST* stent thrombosis

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Table 3. Thrombolysis in Myocardial Infarction (TIMI) Bleeding End Points in the Overall Cohort at 15 Months.*

End Point	Prasugrel (N=6741)	Clopidogrel (N=6716)	Hazard Ratio for Prasugrel (95% CI)	P Value
	no. of patients (%)			
Non–CABG-related TIMI major bleeding (key safety end point)	146 (2.4)	111 (1.8)	1.32 (1.03–1.68)	0.03
Related to instrumentation	45 (0.7)	38 (0.6)	1.18 (0.77–1.82)	0.45
Spontaneous	92 (1.6)	61 (1.1)	1.51 (1.09–2.08)	0.01
Related to trauma	9 (0.2)	12 (0.2)	0.75 (0.32–1.78)	0.51
Life-threatening†	85 (1.4)	56 (0.9)	1.52 (1.08–2.13)	0.01
Related to instrumentation	28 (0.5)	18 (0.3)	1.55 (0.86–2.81)	0.14
Spontaneous	50 (0.9)	28 (0.5)	1.78 (1.12–2.83)	0.01
Related to trauma	7 (0.1)	10 (0.2)	0.70 (0.27–1.84)	0.47
Fatal‡	21 (0.4)	5 (0.1)	4.19 (1.58–11.11)	0.002
Nonfatal	64 (1.1)	51 (0.9)	1.25 (0.87–1.81)	0.23
Intracranial	19 (0.3)	17 (0.3)	1.12 (0.58–2.15)	0.74
Major or minor TIMI bleeding	303 (5.0)	231 (3.8)	1.31 (1.11–1.56)	0.002
Bleeding requiring transfusion§	244 (4.0)	182 (3.0)	1.34 (1.11–1.63)	<0.001
CABG-related TIMI major bleeding¶	24 (13.4)	6 (3.2)	4.73 (1.90–11.82)	<0.001

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Table 4. Safety of the Study Drugs.*

End Point	Ticagrelor Group	Clopidogrel Group	Hazard or Odds Ratio for Ticagrelor Group (95% CI)†	P Value
Primary safety end points — no./total no. (%)				
Major bleeding, study criteria	961/9235 (11.6)	929/9186 (11.2)	1.04 (0.95–1.13)	0.43
Major bleeding, TIMI criteria‡	657/9235 (7.9)	638/9186 (7.7)	1.03 (0.93–1.15)	0.57
Bleeding requiring red-cell transfusion	818/9235 (8.9)	809/9186 (8.9)	1.00 (0.91–1.11)	0.96
Life-threatening or fatal bleeding, study criteria	491/9235 (5.8)	480/9186 (5.8)	1.03 (0.90–1.16)	0.70
Fatal bleeding	20/9235 (0.3)	23/9186 (0.3)	0.87 (0.48–1.59)	0.66
Nonintracranial fatal bleeding	9/9235 (0.1)	21/9186 (0.3)		0.03
Intracranial bleeding	26/9235 (0.3)	14/9186 (0.2)	1.87 (0.98–3.58)	0.06
Fatal	11/9235 (0.1)	1/9186 (0.01)		0.02
Nonfatal	15/9235 (0.2)	13/9186 (0.2)		0.69
Secondary safety end points — no./total no. (%)				
Non–CABG-related major bleeding, study criteria	362/9235 (4.5)	306/9186 (3.8)	1.19 (1.02–1.38)	0.03
Non–CABG-related major bleeding, TIMI criteria	221/9235 (2.8)	177/9186 (2.2)	1.25 (1.03, 1.53)	0.03
CABG-related major bleeding, study criteria	619/9235 (7.4)	654/9186 (7.9)	0.95 (0.85–1.06)	0.32
CABG-related major bleeding, TIMI criteria	446/9235 (5.3)	476/9186 (5.8)	0.94 (0.82–1.07)	0.32
Major or minor bleeding, study criteria	1339/9235 (16.1)	1215/9186 (14.6)	1.11 (1.03–1.20)	0.008
Major or minor bleeding, TIMI criteria‡	946/9235 (11.4)	906/9186 (10.9)	1.05 (0.96–1.15)	0.33

Clinical Safety

Keele Cardiovascular Research Group

- CABG related bleeding most important / frequent bleeding complications in TRITON / PLATO
- The ability to give Prasugrel **AFTER** angiogram when decision to treat with PCI made, means that increased CABG related bleeding complications with potent P2Y12 minimised

Keele Cardiovascular Research Group

Diagnosis + Transfer to cath lab >2h to <24h

NSTEMI / Troponin +, 4033 patients Clopidogrel-naïve or chronic 75 mg/d

Planned angio/PCI between 2h and 48h

Randomisation

Pras 30 mg | Placebo

Cath lab

Pras 30 mg: Angio → PCI

Placebo: Angio → PCI → Pras 60 mg

30-day Follow-up

PE: CV death, MI, stroke, urgent revasc., GPI bailout @ 7d
SEs: All TIMI major bleeding @ 7d; NetClinBenefit @ 7d

Pras 10(5) for 30d

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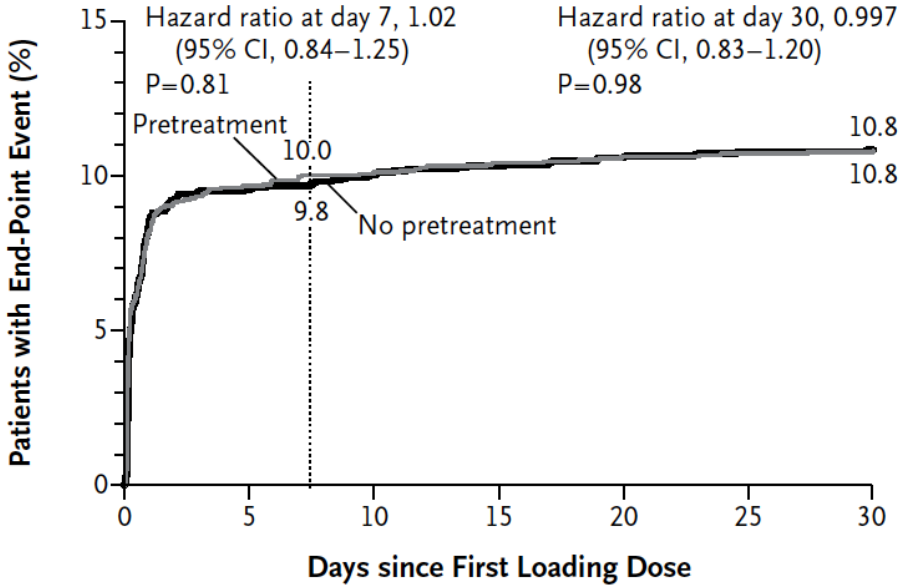
Pretreatment with Prasugrel in Non–ST-Segment Elevation Acute Coronary Syndromes

Gilles Montalescot, M.D., Ph.D., Leonardo Bolognese, M.D., Dariusz Dudek, M.D., Ph.D., Patrick Goldstein, M.D., Christian Hamm, M.D., Jean-Francois Tanguay, M.D., Jurrien M. ten Berg, M.D., Ph.D., Debra L. Miller, R.N., Timothy M. Costigan, Ph.D., Jochen Goedicke, M.D., Johanne Silvain, M.D., Ph.D., Paolo Angioli, M.D., Jacek Legutko, M.D., Ph.D., Margit Niethammer, M.D., Zuzana Motovska, M.D., Ph.D., Joseph A. Jakubowski, Ph.D., Guillaume Cayla, M.D., Ph.D., Luigi Oltrona Visconti, M.D., Eric Vicaut, M.D., Ph.D., and Petr Widimsky, M.D., D.Sc., for the ACCOAST Investigators*

Keele Cardiovascular Research Group

A Primary Efficacy End Point



No. at Risk

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

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

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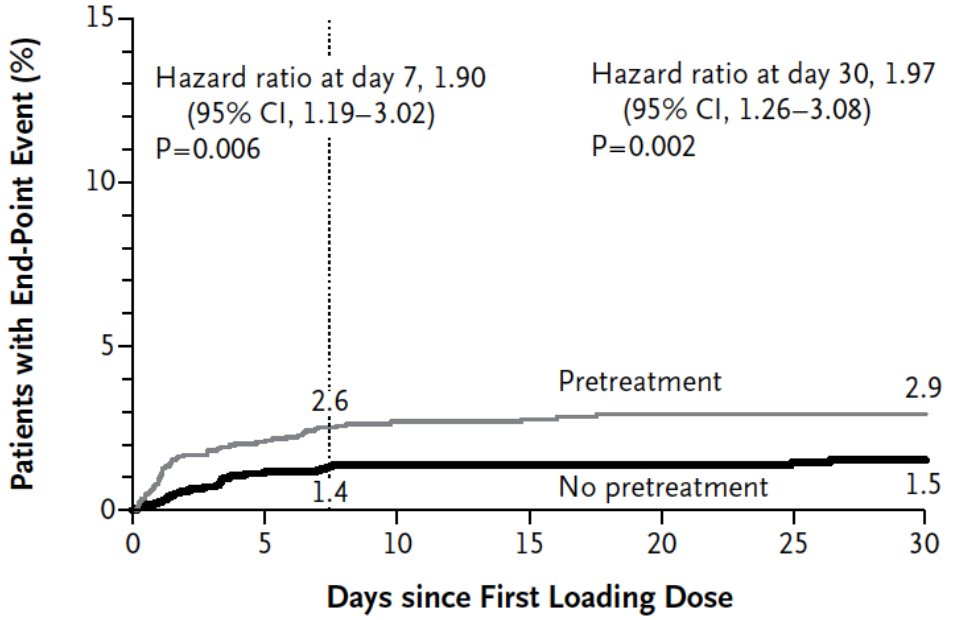

No. at Risk

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

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Comparison of Prasugrel and Ticagrelor Loading Doses in ST-Segment Elevation Myocardial Infarction Patients

RAPID (Rapid Activity of Platelet Inhibitor Drugs) Primary PCI Study

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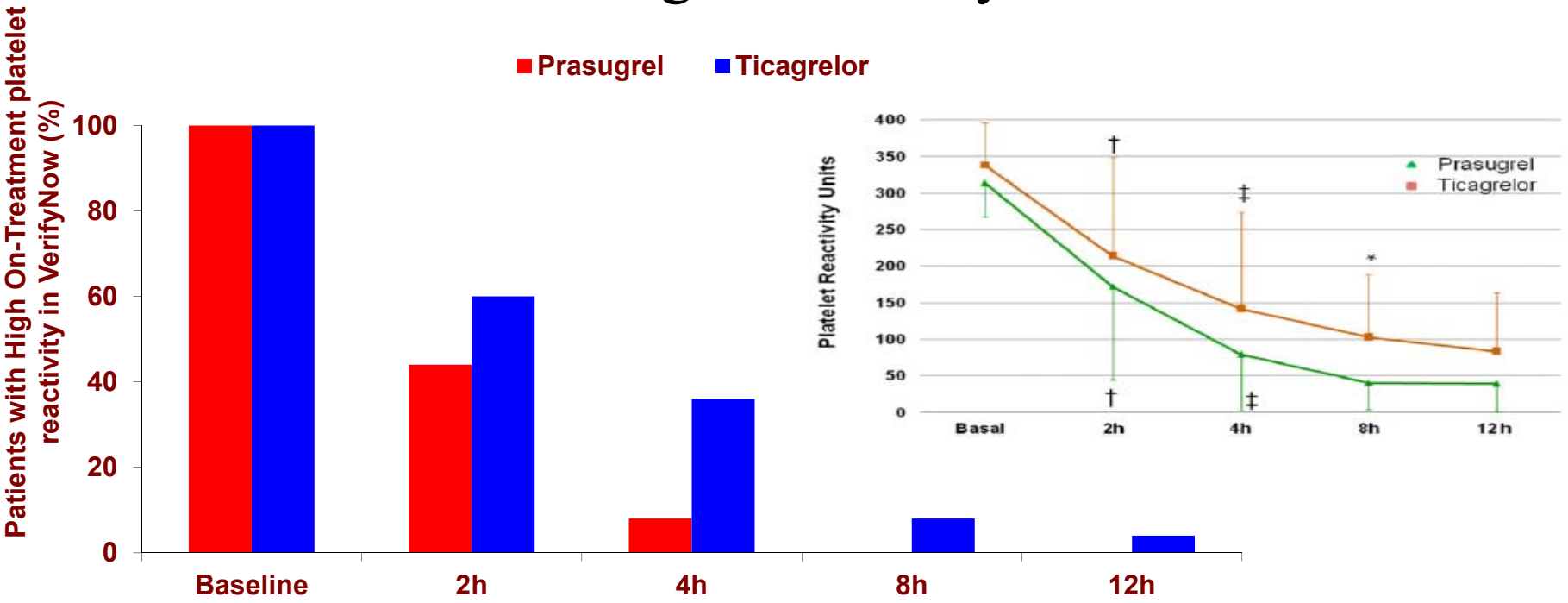
Pharmacological efficacy



Premature Ticagrelor Discontinuation in Secondary Prevention of Atherosclerotic CVD

JACC Review Topic of the Week

Sameer Arora, MD,[a,*] Kamal Shemisa, MD,[b,*] Muthiah Vaduganathan, MD, MPH,[c] Arman Qamar, MD,[c] Ankur Gupta, MD, PhD,[b] Sushil K. Garg, MD,[d] Dharam J. Kumbhani, MD, SM,[b] Helen Mayo, MLS,[e] Houman Khalili, MD,[f] Ambarish Pandey, MD, MSCS,[b] Sandeep R. Das, MD, MPH, MBA[f]

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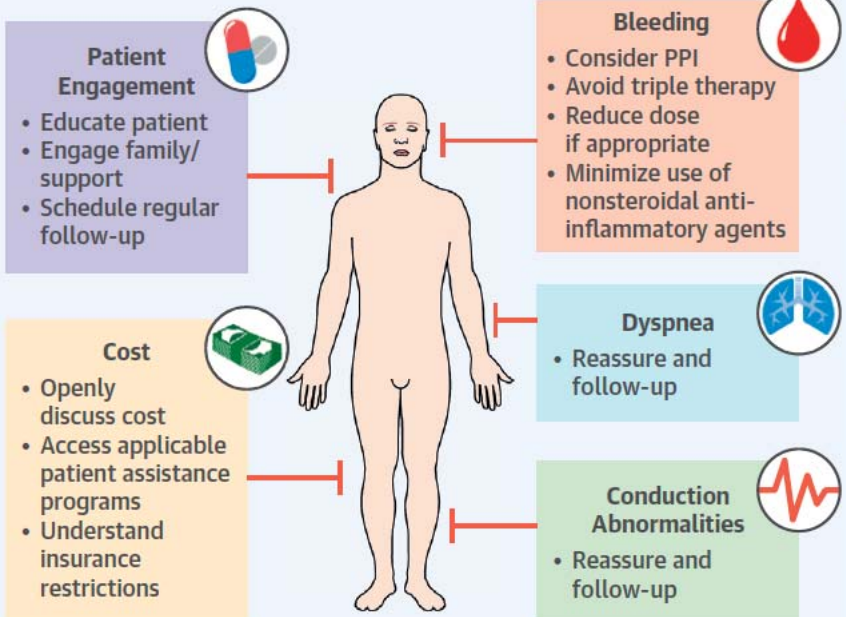
Strategies to Mitigate Adverse Effects



Mechanisms of Adverse Effects

Bleeding

Rapid and more potent $P2Y_{12}$ inhibition

Dyspnea

↑ in plasma adenosine and $P2Y_{12}$ inhibition

Conduction Abnormalities

↑ in plasma adenosine

Risk of Ticagrelor Discontinuation

Study	Ticagrelor Dose	RR (95% CI)
PLATO (2009)	90 mg	1.09 (1.03, 1.15)
PEGASUS-TIMI 54 (2015)	90 mg	1.50 (1.41, 1.58)
PEGASUS-TIMI 54 (2015)	60 mg	1.34 (1.26, 1.42)
SOCRATES (2016)	90 mg	1.19 (1.10, 1.29)
EUCLID (2017)	90 mg	1.16 (1.10, 1.22)
Overall (I^2 = 94.6%; p < 0.001)		1.25 (1.11, 1.39)

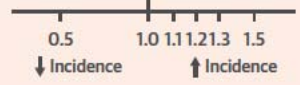


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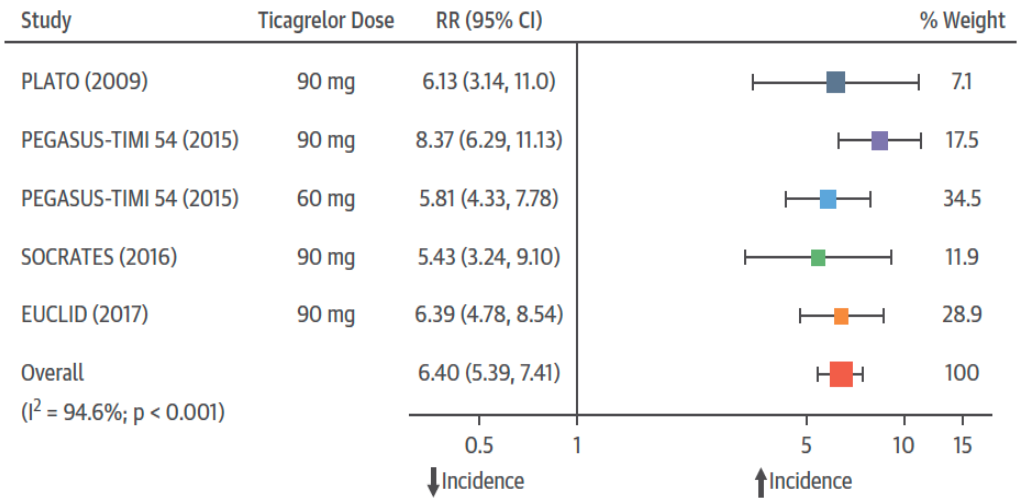
FIGURE 2 Dyspnea-Related Discontinuation Risk for Ticagrelor Versus Comparator



ISAR REACT 5: Greater discontinuation of Ticagrelor (15%) vs Prasugrel (12%) P<0.05, median time to discontinuation 84 days (Ticagralor vs 102 days (Prasugrel)

Summary

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I prefer Prasugrel because:

- Superior to Ticagralor in RCTs and Real world data
- Superior platelet inhibition
- Ability to give Prasugrel after angiogram when decision made to PCI, thereby avoiding increased risk of CABG related bleeds if pt managed surgically
- Better tolerated by patients