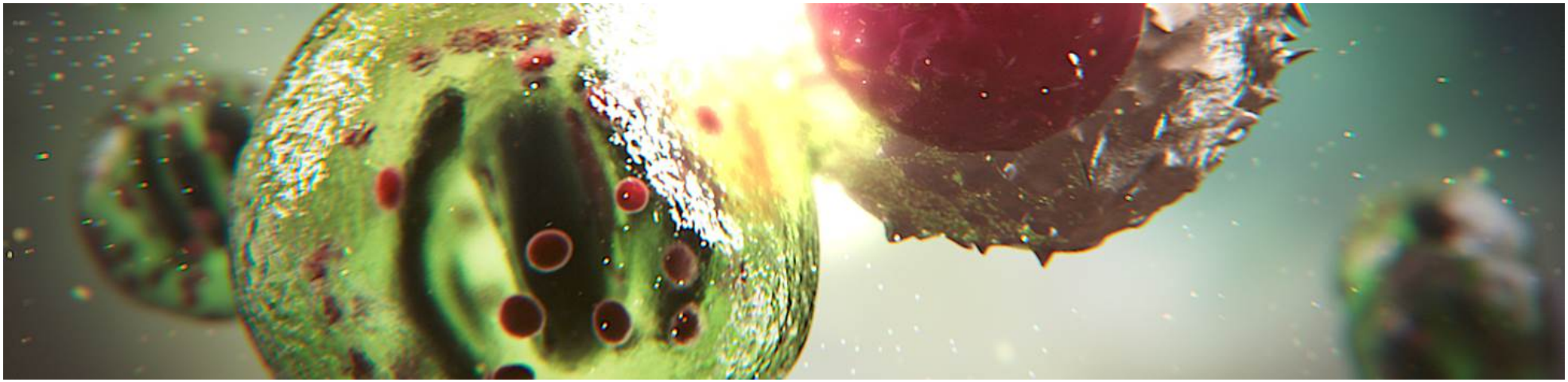
Investor science conference call: American College of Cardiology 2015

San Diego, California, USA

16 March 2015



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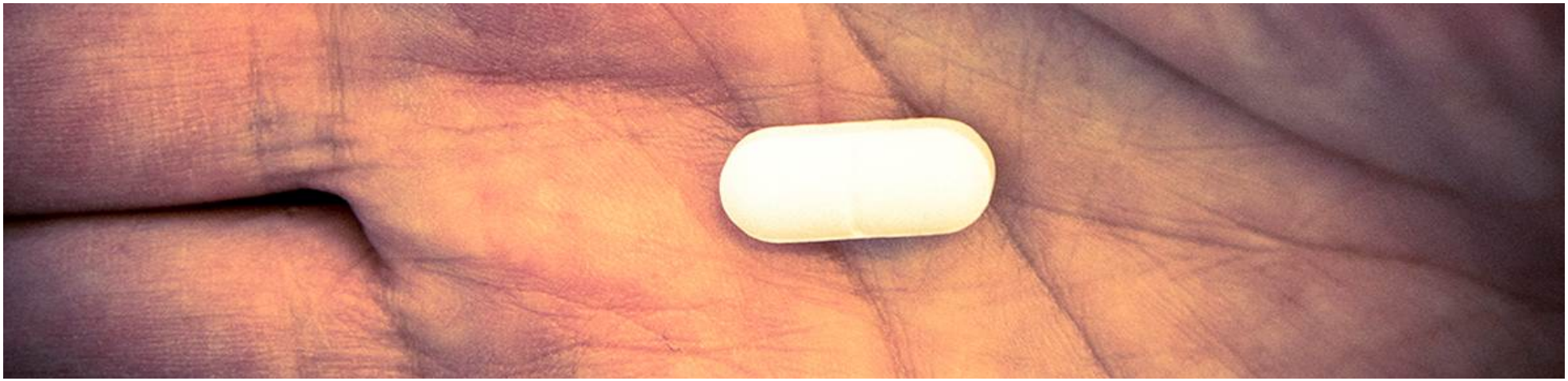
This presentation contains certain forward-looking statements with respect to the operations, performance and financial condition of the Group. Although we believe our expectations are based on reasonable assumptions, any forward-looking statements, by their very nature, involve risks and uncertainties and may be influenced by factors that could cause actual outcomes and results to be materially different from those predicted.

The forward-looking statements reflect knowledge and information available at the date of preparation of this presentation and AstraZeneca undertakes no obligation to update these forward-looking statements. We identify the forward-looking statements by using the words 'anticipates', 'believes', 'expects', 'intends' and similar expressions in such statements. Important factors that could cause actual results to differ materially from those contained in forward-looking statements, certain of which are beyond our control, include, among other things: the loss or expiration of patents, marketing exclusivity or trade marks, or the risk of failure to obtain patent protection; the risk of substantial adverse litigation/government investigation claims and insufficient insurance coverage; exchange rate fluctuations; the risk that R&D will not yield new products that achieve commercial success; the risk that strategic alliances and acquisitions will be unsuccessful; the impact of competition, price controls and price reductions; taxation risks; the risk of substantial product liability claims; the impact of any failure by third parties to supply materials or services; the risk of failure to manage a crisis; the risk of delay to new product launches; the difficulties of obtaining and maintaining regulatory approvals for products; the risk of failure to observe ongoing regulatory oversight; the risk that new products do not perform as we expect; the risk of environmental liabilities; the risks associated with conducting business in emerging markets; the risk of reputational damage; the risk of product counterfeiting; the risk of failure to successfully implement planned cost reduction measures through productivity initiatives and restructuring programmes; the risk that regulatory approval processes for biosimilars could have an adverse effect on future commercial prospects; and the impact of increasing implementation and enforcement of more stringent anti-bribery and anti-corruption legislation.

Nothing in this presentation should be construed as a profit forecast.

Introduction

Thomas Kudsk Larsen, Head of Investor Relations



Welcome, agenda & introduction

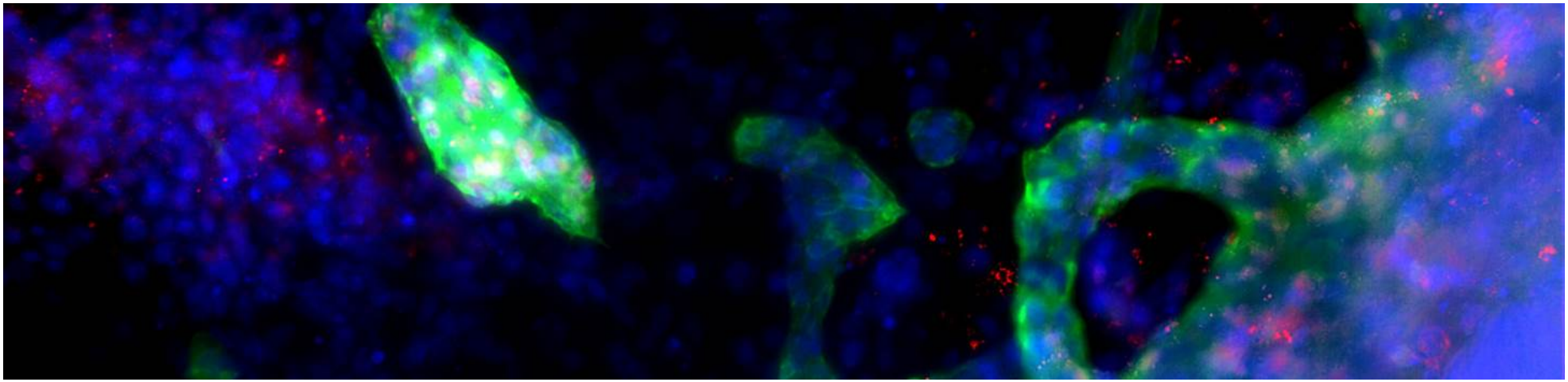
- Welcome
- PEGASUS-TIMI 54 trial
- *BRILINTA*® / *BRILIQUE*™ clinical & business status
- Q&A

Estimated duration up to one hour

PEGASUS-TIMI 54 trial

Dr. Marc Sabatine, PEGASUS TIMI-54 Primary Investigator

Brigham and Women's Hospital, Massachusetts, USA



Prevention of Cardiovascular Events in Patients With Prior Heart Attack Using Ticagrelor Compared to Placebo on a Background of Aspirin

Marc S. Sabatine, MD, MPH
on behalf of the PEGASUS-TIMI 54
Executive & Steering Committees and Investigators

NCT00526474

Background

- Current guidelines recommend adding a $P2Y_{12}$ receptor antagonist to aspirin only for the first year after an acute coronary syndrome (ACS)
- However, several lines of evidence suggest more prolonged therapy may be beneficial in Pts w/ prior MI
  - Landmark analyses from 1-year ACS trials of $P2Y_{12}$ antag
  - Post-hoc MI subgroup analysis from CHARISMA
- Ticagrelor is a potent, reversibly-binding, direct-acting $P2Y_{12}$ antagonist with established efficacy for the first year after an ACS

Hypothesis

The addition of ticagrelor to standard therapy (including low-dose aspirin) would reduce the incidence of major adverse cardiovascular events during long-term follow-up in patients with a history of MI

Trial Organization

TIMI Study Group

Eugene Braunwald (Chair)
Marc P. Bonaca (Co-PI)
S Morin & P Fish (Operations)
Marc S. Sabatine (PI)
Stephen D. Wiviott (CEC Chair)
SA Murphy & Kelly Im (Statistics)

Executive Cmte

Eugene Braunwald (Chair)
Deepak L. Bhatt
Ph. Gabriel Steg
Marc S. Sabatine
Marc Cohen
Robert Storey

Sponsor: AstraZeneca

Peter Held
Per Johanson
Barbro Boberg
Eva Jensen
Ann Maxe Ahlbom
Olof Bengtsson

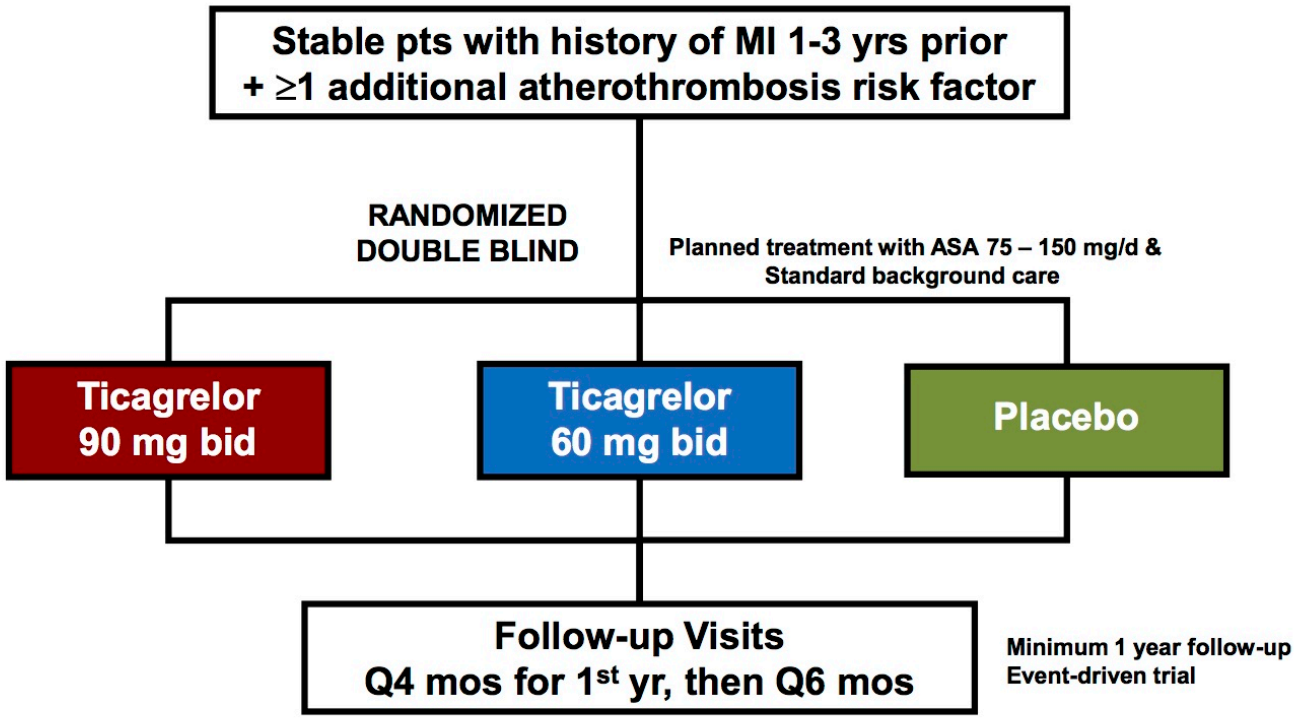
Independent Data Monitoring Cmte

Jeffrey L. Anderson (Chair)
Freek W.A.Verheugt
David L. DeMets
Terje R. Pedersen
Harvey D. White

Steering Committee

Argentina
R. Diaz/E Paolasso
Australia
P Aylward
Belgium
F Van der Werf
Brazil
J Nicolau
Bulgaria
A Goudev
Canada
P Theroux
Chile
R Corbalan
China
D Hu
Colombia
D Isaza
Czech Republic
J Spinar
France
G Montalescot/PG Steg
Germany
C Hamm
Hungary
R Kiss
Italy
D Ardissino
Japan
S Goto
Netherlands
T Oude Ophuis
Norway
F Kontny
Peru
F Medina
Philippines
MT Abola
Poland
A Budaj
Romania
D Dimulescu
Russia
M Ruda
S. Africa
A Dalby
S. Korea
K Seung
Slovakia
G Kamensky
Spain
J Lopez-Sendon
Sweden
M Dellborg
Turkey
S Guneri
UK
R Storey
Ukraine
A Parkhomenko
USA
Bonaca/Bhatt/Cohen

Trial Design



Bonaca MP et al. *Am Heart J* 2014;167:437-44

Key Inclusion & Exclusion Criteria

KEY INCLUSION

- Age ≥50 years
- At least 1 of the following:
  - Age ≥65 years
  - Diabetes requiring medication
  - 2nd prior MI (>1 year ago)
  - Multivessel CAD
  - CrCl <60 mL/min
- Tolerating ASA and able to be dosed at 75-150 mg/d

KEY EXCLUSION

- Planned use of $P2Y_{12}$ antagonist, dipyridamole, cilostazol, or anticoag
- Bleeding disorder
- History of ischemic stroke, ICH, CNS tumor or vascular abnormality
- Recent GI bleed or major surgery
- At risk for bradycardia
- Dialysis or severe liver disease

Bonaca MP et al. *Am Heart J* 2014;167:437-44

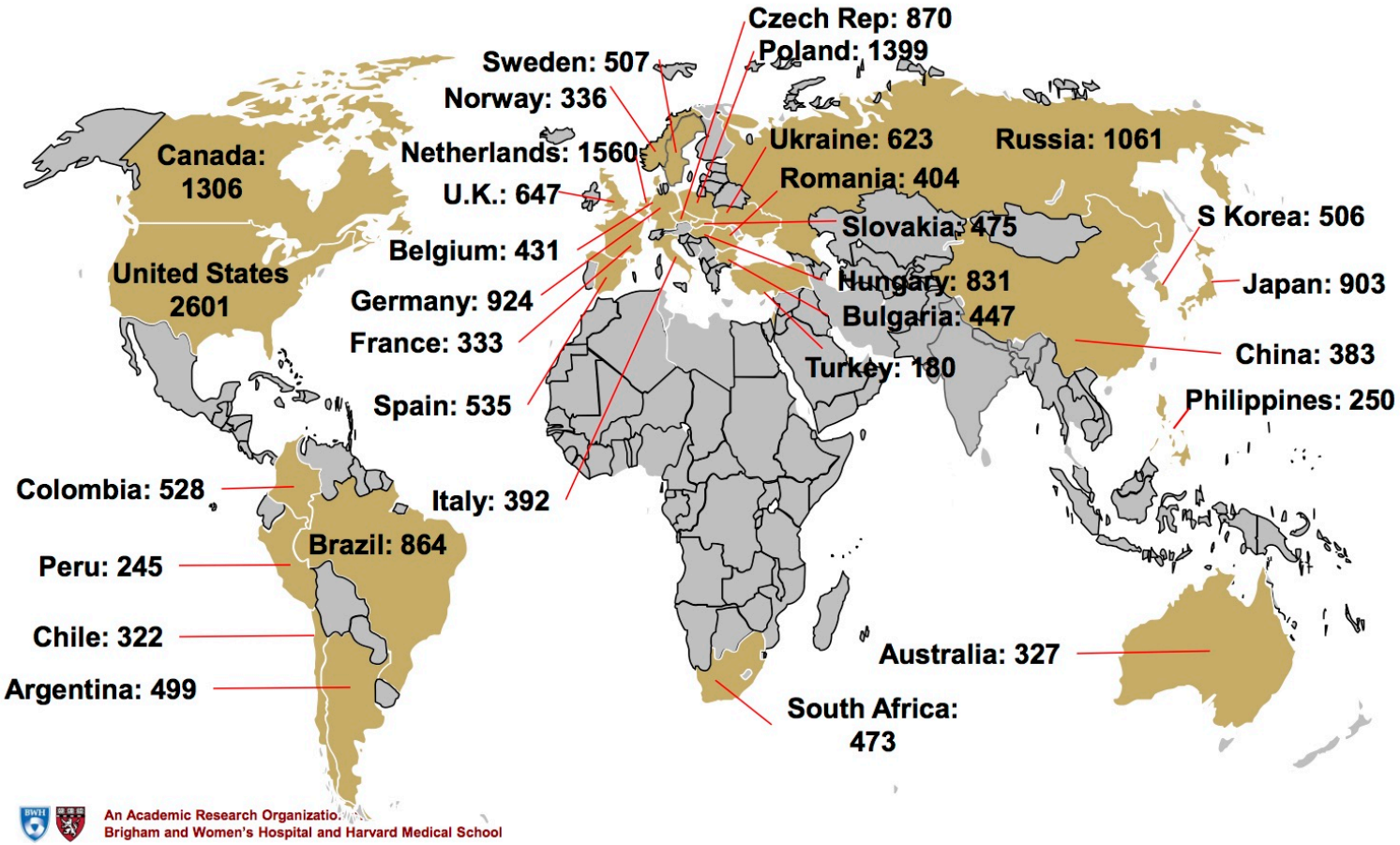
Endpoints

- **Efficacy: hierarchical testing**
  - Primary: cardiovascular (CV) death, MI, or stroke
  - Secondary: CV death; all-cause mortality
  - Prespecified exploratory: substituting coronary for CV death; other individual coronary and cerebrovascular ischemic outcomes; pooling ticagrelor doses
- **Safety**
  - Primary: TIMI Major Bleeding
  - Other: intracranial hemorrhage (ICH), fatal bleeding
  - AEs/SAEs
- **TIMI Clinical Events Committee (CEC)**
  - Adjudicated all efficacy endpoints & bleeding events
  - Members unaware of treatment assignments

Bonaca MP et al. *Am Heart J* 2014;167:437-44

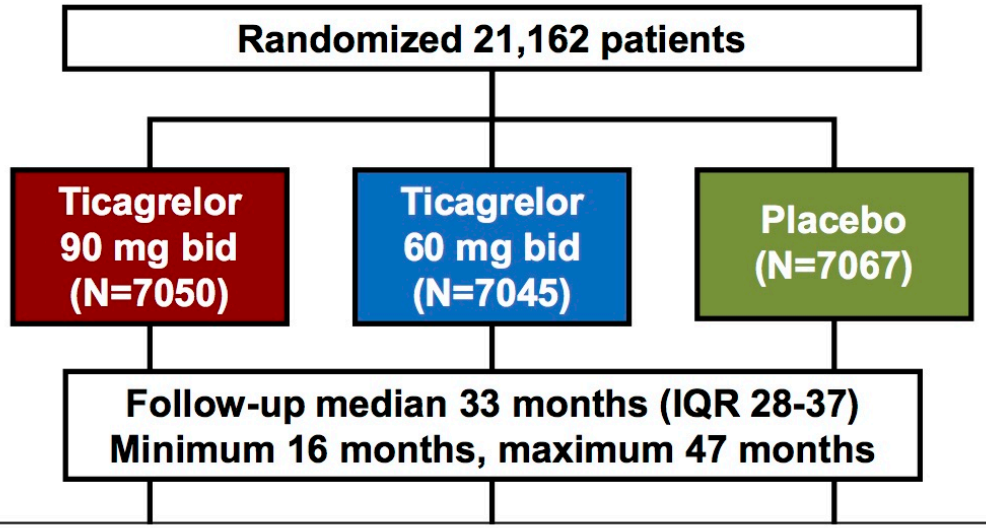
Global Enrollment

21,162 patients randomized at 1161 sites in 31 countries between 10/2010 – 5/2013



An Academic Research Organization
Brigham and Women's Hospital and Harvard Medical School

Follow-Up



Premature perm. drug discontinuation	12%/yr	11%/yr	8%/yr
Withdrew consent	0.7% total	0.7% total	0.7% total
Lost to follow-up	3 patients	6 patients	1 patient

Ascertainment for primary endpoint was complete for 99% of potential patient-years of follow up

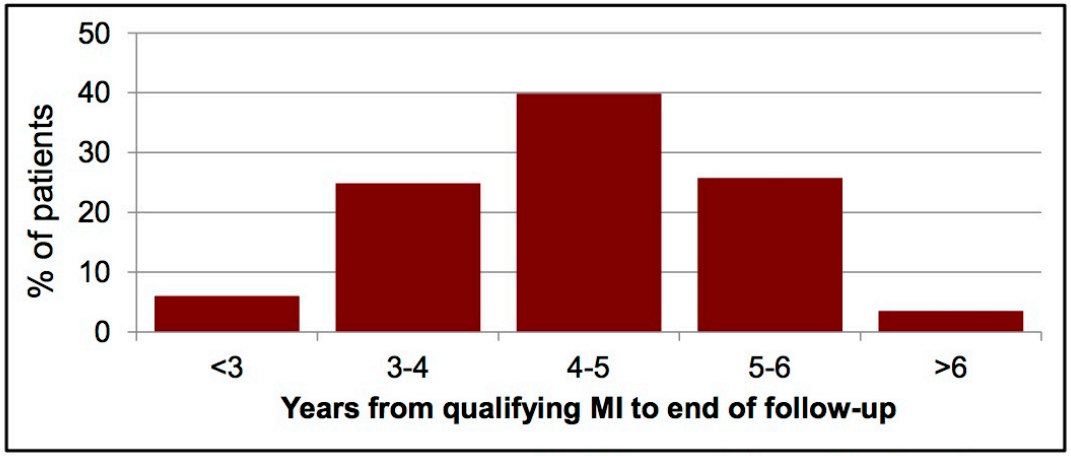
Baseline Characteristics

Characteristic	Value
Age – yr, mean (SD)	65 (8)
Female	24
Hypertension	78
Hypercholesterolemia	77
Current smoker	17
Diabetes mellitus	32
Estimated GFR <60 mL/min/1.73m^2	23
History of PCI	83
Multivessel coronary disease	59
History of more than 1 prior MI	17

No difference between treatment arms.
Values for categorical variables are %.

Baseline Characteristics

Characteristic	Value
Qualifying Event	
Years from MI – median (IQR)	1.7 (1.2 – 2.3)
History of STEMI	53
History of NSTEMI	41
MI type unknown	6



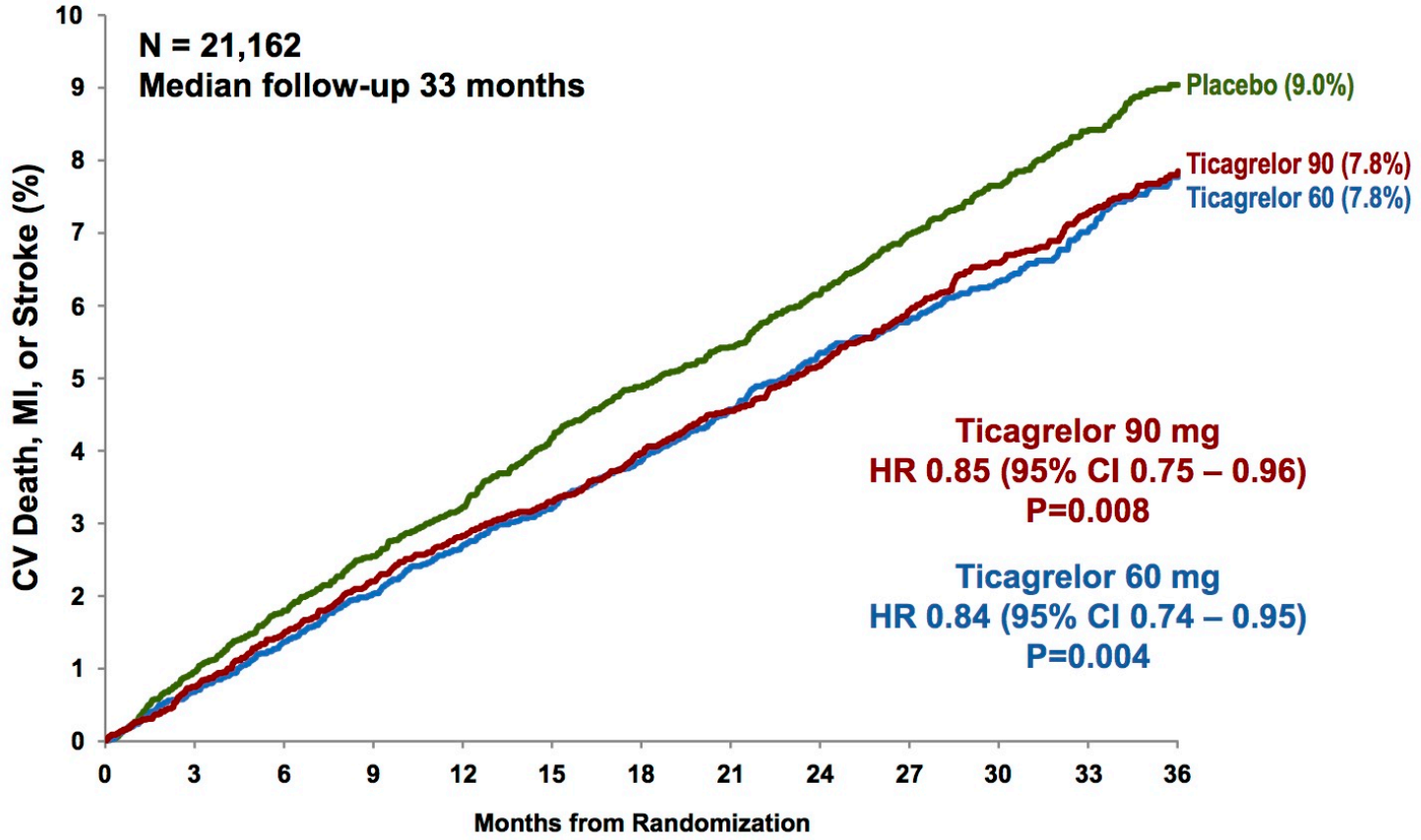
No difference between treatment arms.
Values for categorical variables are %.

Baseline Characteristics

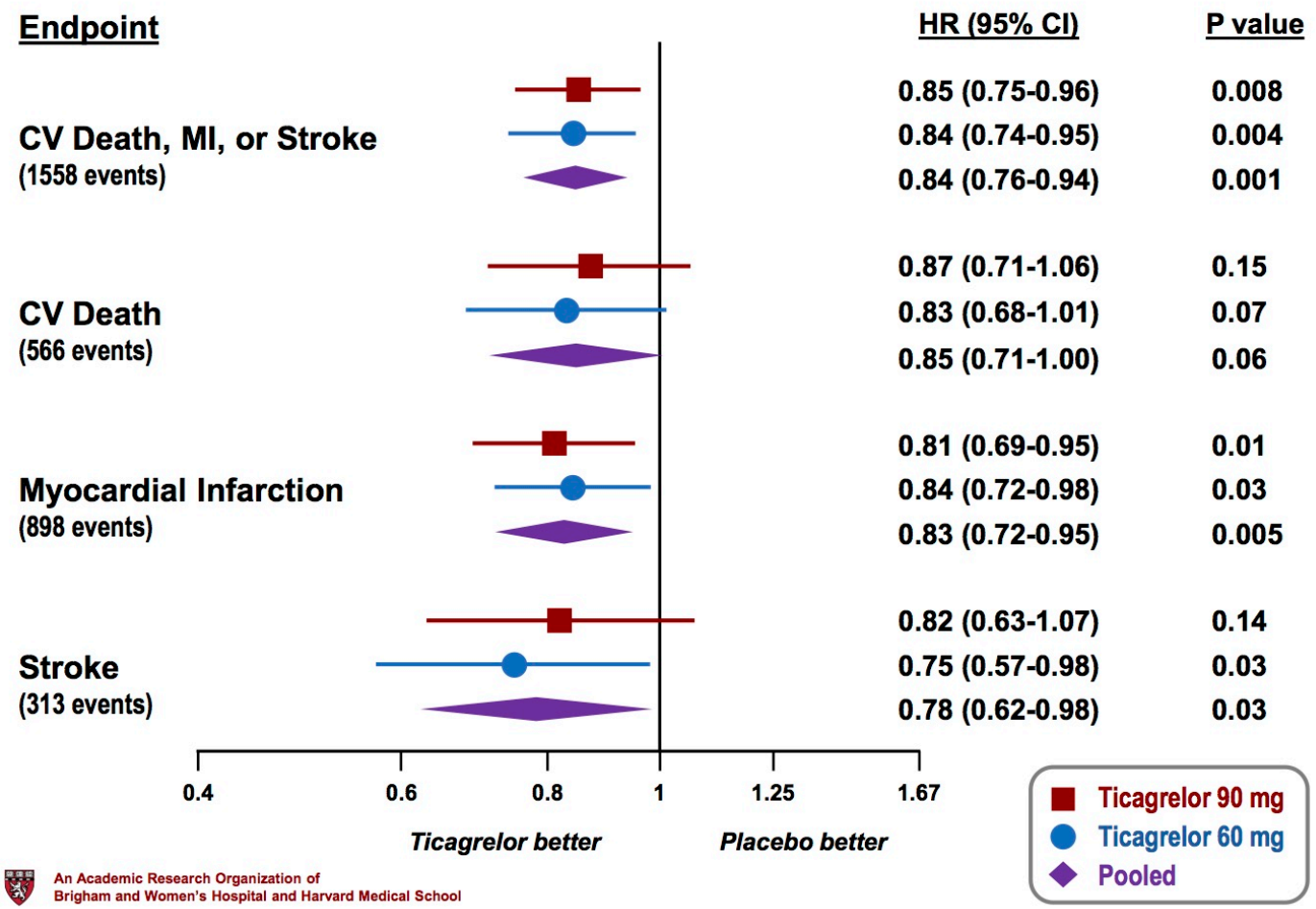
Characteristic	Value
Qualifying Event	
Years from MI – median (IQR)	1.7 (1.2 – 2.3)
History of STEMI	53
History of NSTEMI	41
MI type unknown	6
Medications at enrollment	
Aspirin (any dose)	99.9
Dose 75-100 mg/d	97.3
Statin	93
Beta-blocker	82
ACEI or ARB	80

No difference between treatment arms.
Values for categorical variables are %.

Primary Endpoint



Components of Primary Endpoint



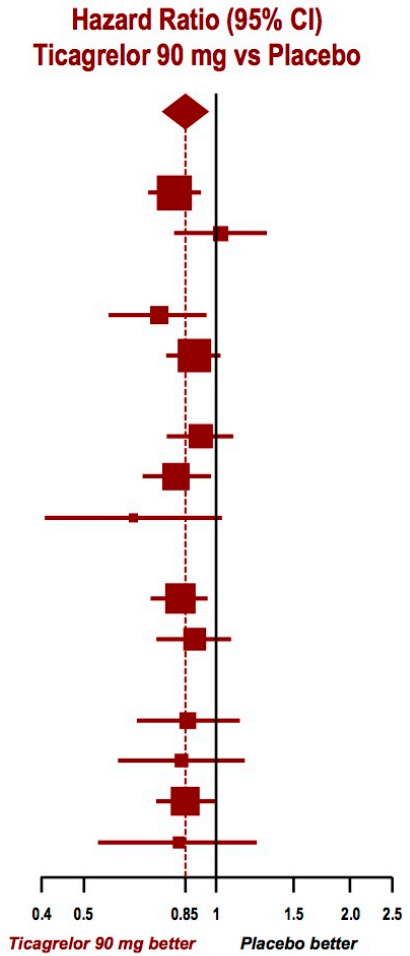
Other Efficacy Outcomes

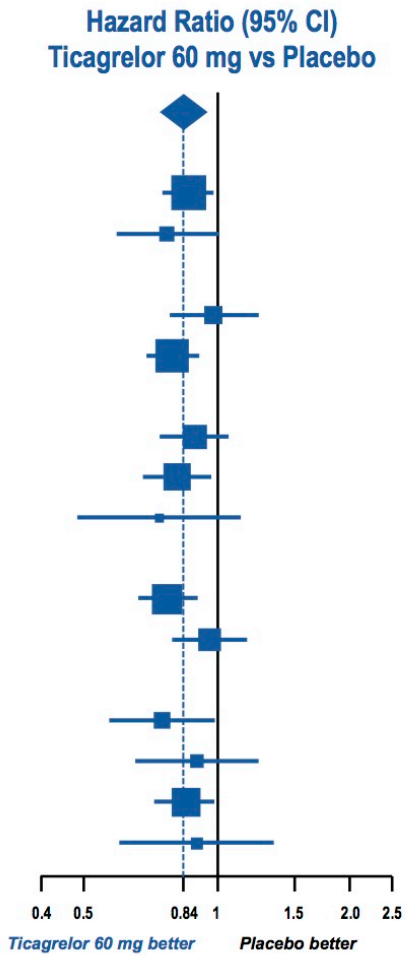
Outcome	Ticagrelor 90 mg bid (N=7050)	Ticagrelor 60 mg bid (N=7045)	Placebo (N=7067)	Ticagrelor 90 vs Placebo p-value	Ticagrelor 60 vs Placebo p-value
	3-yr KM rate (%)				
Coronary Death, MI, or Stroke	7.0	7.1	8.3	HR 0.82 P=0.002	HR 0.83 P=0.003
Coronary Death or MI	5.6	5.8	6.7	HR 0.81 P=0.004	HR 0.84 P=0.01
Coronary Death	1.5	1.7	2.1	HR 0.73 P=0.02	HR 0.80 P=0.09
Death from any cause	5.2	4.7	5.2	HR 1.00 P=0.99	HR 0.89 P=0.14

Efficacy for 1° EP in Subgroups

Subgroup	Pts
All Patients	21,162
Age at Randomization	
Age < 75	18,079
Age ≥ 75	3,083
Sex	
Female	5,060
Male	16,102
Qualifying MI	
NSTEMI	8,583
STEMI	11,329
Unknown	1,223
Time from Qualifying MI	
< 2 years	12,980
≥ 2 years	8,155
Region	
North America	3,907
South America	2,458
Europe	12,428
Asia	2,369

All P values for heterogeneity >0.05





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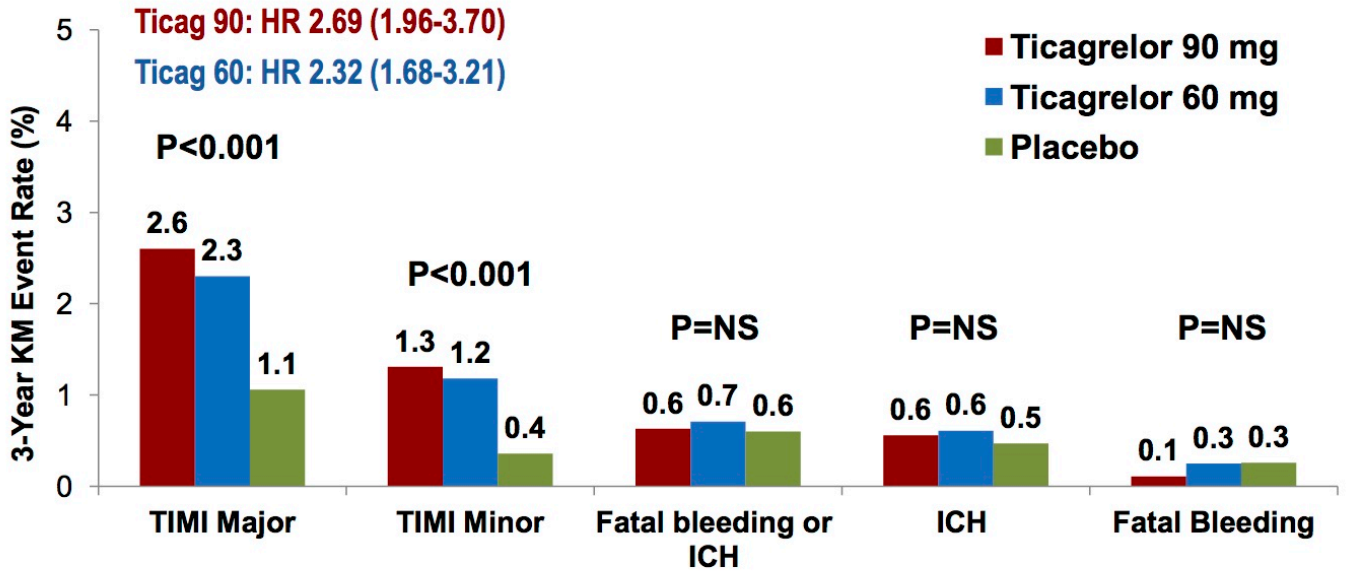
Bleeding


Ticag 90: HR 2.69 (1.96-3.70)
Ticag 60: HR 2.32 (1.68-3.21)
Ticagrelor 90 mg
Ticagrelor 60 mg
Placebo
3-Year KM Event Rate (%)
0
1
2
3
4
5
P<0.001
2.6
2.3
1.1
P<0.001
1.3
1.2
0.4
P=NS
0.6
0.7
0.6
P=NS
0.6
0.6
0.5
P=NS
0.1
0.3
0.3
TIMI Major
TIMI Minor
Fatal bleeding or ICH
ICH
Fatal Bleeding

Other Adverse Events

Adverse Event	Ticagrelor 90 mg bid (N=6988)	Ticagrelor 60 mg bid (N=6958)	Placebo (N=6996)	Ticagrelor 90 vs Placebo p-value	Ticagrelor 60 vs Placebo p-value
	3-yr KM rate (%)				
Dyspnea AE	18.9	15.8	6.4	P<0.001	P<0.001
Leading to study drug d/c	6.5	4.6	0.8	P<0.001	P<0.001
Severe	1.2	0.6	0.2	P<0.001	P<0.001
Bradyarrhythmia	2.0	2.3	2.0	P=0.31	P=0.10
Gout	2.3	2.0	1.5	P<0.001	P=0.01

Summary

- Adding ticagrelor to low-dose aspirin in stable patients with a history of MI reduced the risk of CV death, MI or stroke
- The benefit of ticagrelor was consistent
  - For both fatal & non-fatal components of primary endpoint
  - Over the duration of treatment
  - Among major clinical subgroups
- Ticagrelor increased the risk of TIMI major bleeding, but not fatal bleeding or ICH
- The two doses of ticagrelor had similar overall efficacy, but bleeding and other side effects tended to be less frequent with 60 mg bid dose

Conclusion

Long-term dual antiplatelet therapy with low-dose aspirin and ticagrelor should be considered in appropriate patients with a myocardial infarction.

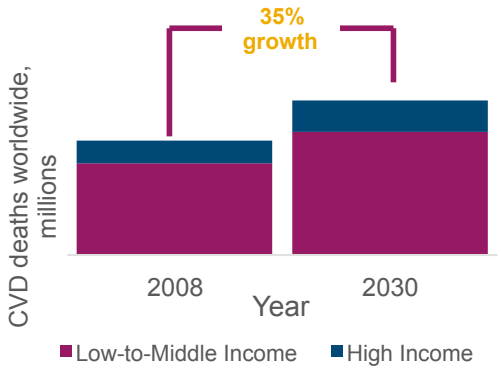
BRILINTA® / *BRILIQUE*™
Clinical & business status

Tom Keith-Roach, *BRILINTA*® Task Force leader

Global #1 cause of death[1,2], >17m per year[1]

Cardiovascular disease (CVD) worldwide

17.3 million to 23.3 million



~70%

of total global CVD deaths are due to ischaemic heart disease and cerebrovascular disease[3]

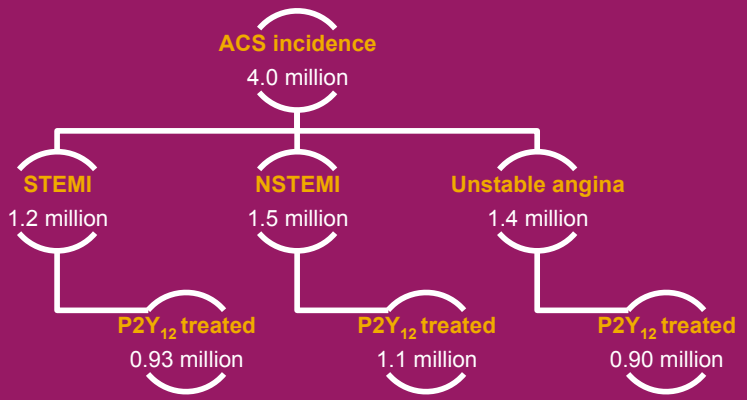
Source, Notes: 1. Global status report on non-communicable diseases 2010. Geneva, World Health Organization, 2011. 2. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PLoS Med, 2006, 3(11):e442. 3. World Heart Federation website, based on World Health Organization causes of death 2008 summary tables

BRILINTA® / BRILIQUE™
Indicated for the treatment of ACS

Indication

- Indicated to reduce the rate of thrombotic CVD events in patients with ACS
- Shown to reduce the rate of a combined end point of CVD death, MI, or stroke compared to clopidogrel

PLATO[1] study, epidemiology

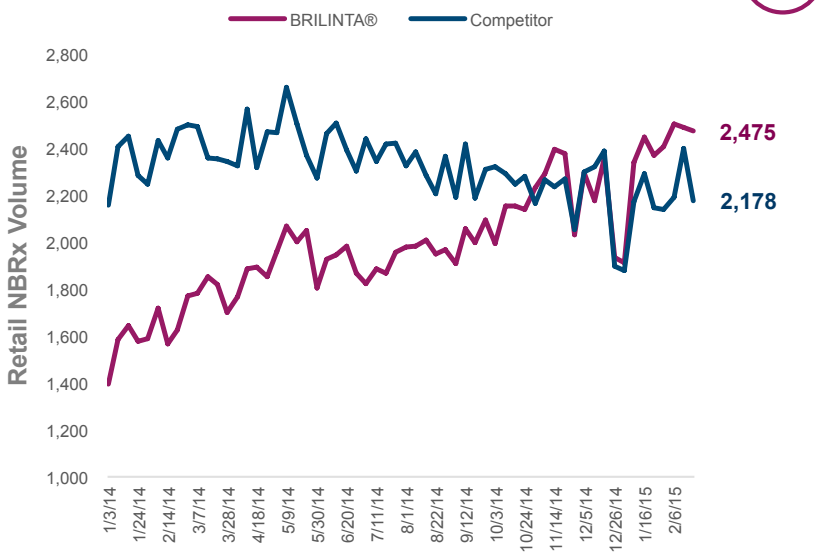


Definitions: ACS – Acute Coronary Syndrome; MI – Myocardial Infarction; STEMI – ST Segment Elevation Myocardial Infarction; NSTEMI – Non-ST Segment Elevation myocardial Infarction; and ASA – Aspirin. **Notes:** 1. Markets include Australia, China, EU5, Japan, Russia and United States only. **Source:** Kantar Health (2010), GRACE registry (2007), National Health & Wellness Survey (2013), medical literature, internal data

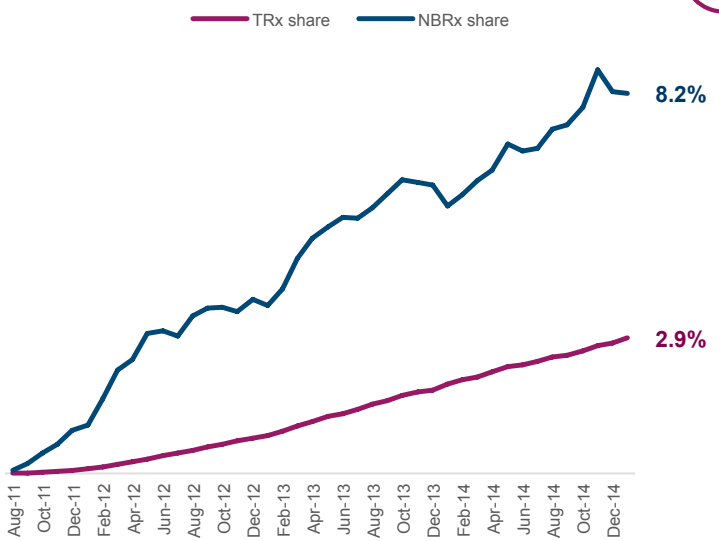
US performance

Momentum has led to branded NBRx leadership

Branded oral anti-platelet (OAP) retail new-to-brand prescription (NBRx) share[1]



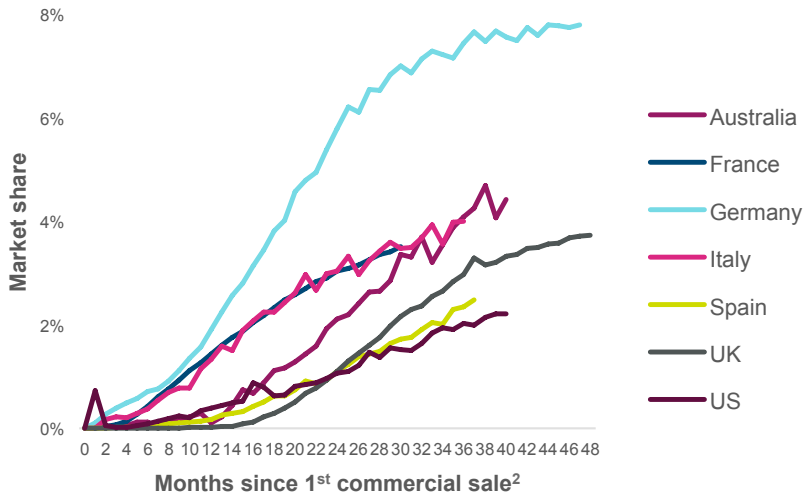
Monthly brand total prescriptions (TRx) and NBRx share, OAP class[2]



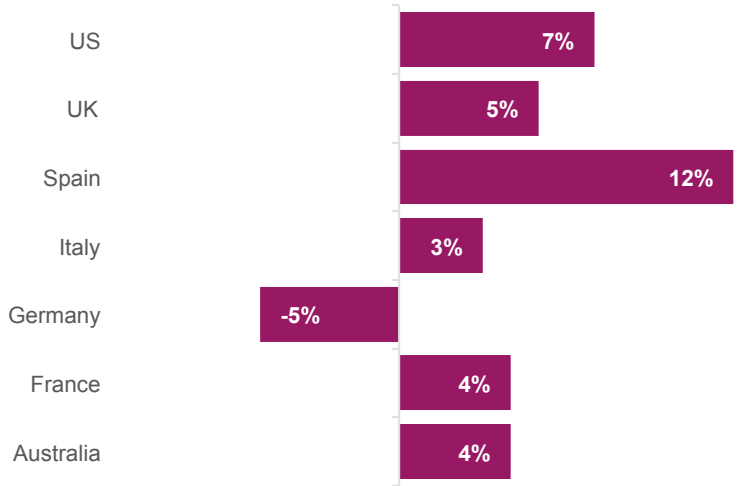
Source, Notes: 1. IMS Health NPA through w/e February 20, 2015. 2. IMS Health NPA, Monthly data through January 2015.

Global performance
Positive momentum continues through FY 2014

OAP share, volume: Retail + hospital[1]



Monthly brand share, OAP class[3]

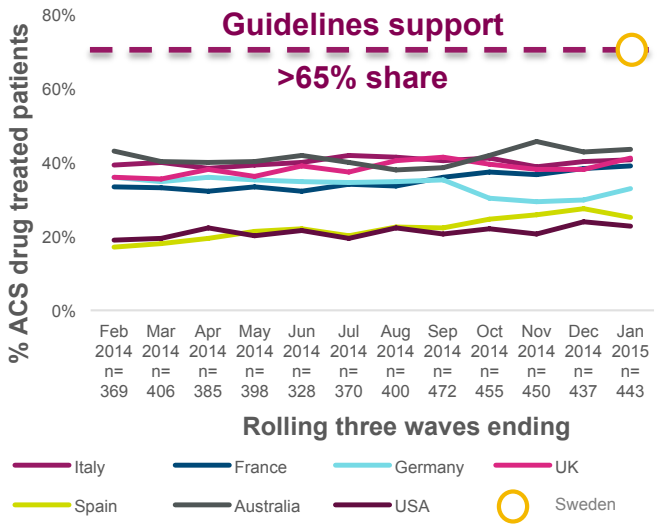


Source, Notes: 1. IMS MIDAS. Spain retail only. 2. Month 1 = month of 1st external sales data for product (does not reflect commercial launch timing). 3. IMS Hospital Discharge Tracker, AstraZeneca commissioned report.

Significant future opportunities

International guidelines support *BRILINTA® / BRILIQUE™* for >65% patients treated for 12 months

ACS discharge share[1]



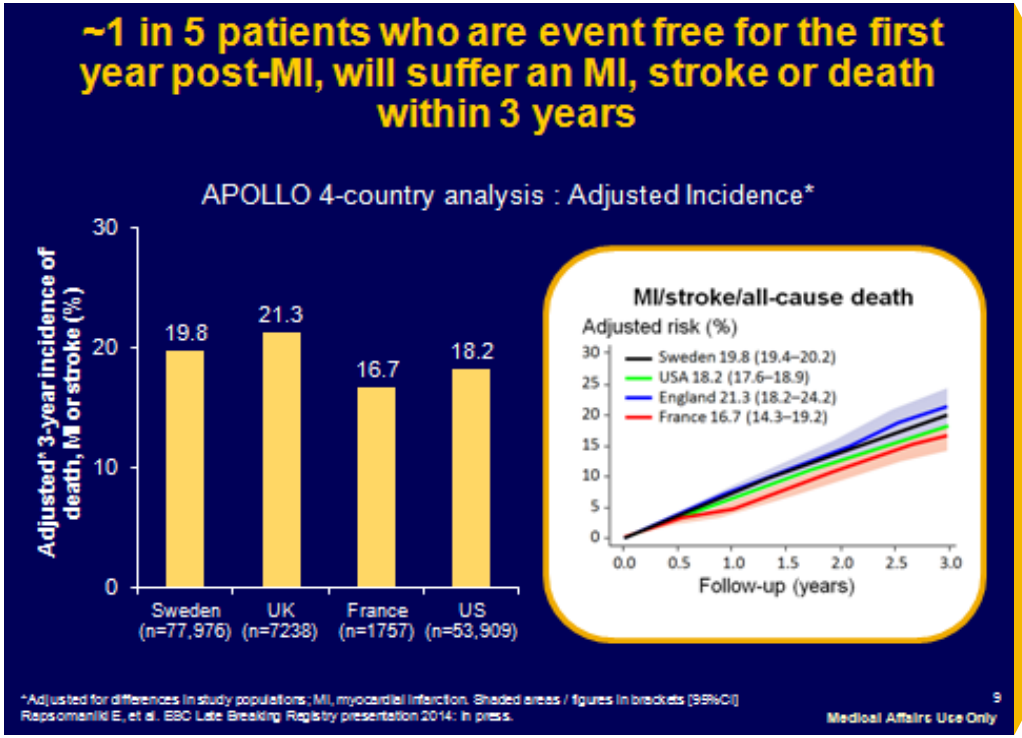
Patients reaching 12 months[2]

Country	% patients at 12 months
Italy	67%
Australia	51%
United Kingdom	50%
France	41%
Spain	34%
Germany	30%
United States	21%

Source: 1. IMS Hospital discharge tracker, AstraZeneca commissioned. 2. AstraZeneca.

Beyond 12 months
Patients remain at a significant risk

APOLLO; late-breaking registry presentation at the 2014 European Society of Cardiology



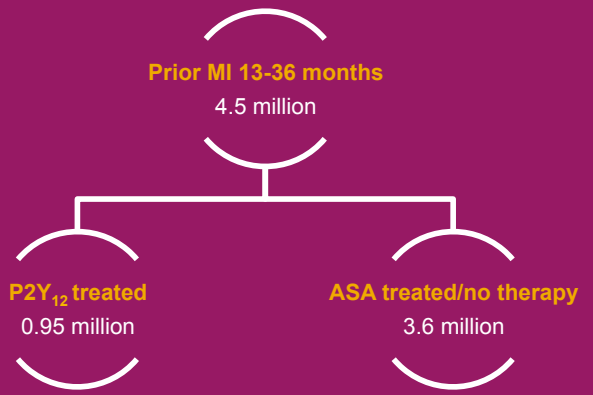
Patients who are event free in first year after their index event will suffer a **MI, stroke or death in the subsequent three years**

PEGASUS-TIMI 54 study of BRILINTA® / *BRILIQUE*™ meets primary endpoint in both 60mg and 90mg doses

PEGASUS-TIMI 54 study

- Investigated 60mg and 90mg ticagrelor vs. placebo in patients (low-dose aspirin) aged 50 and older with a history of heart attack and one additional CVD risk factor[1]
- Designed to better understand the management of patients more than 12 months after their heart attack, who remain at high risk for major thrombotic events

PEGASUS-TIMI 54 study, epidemiology[2]



Definitions: ACS – Acute Coronary Syndrome; MI – myocardial Infarction; STEMI – ST Segment Elevation myocardial Infarction; NSTEMI – Non-ST Segment Elevation myocardial Infarction; and ASA – Aspirin **Notes:** 1. Bonaca MP, Bhatt DL, Braunwald E, et al. Design and rationale for the Prevention of Cardiovascular Events in Patients With Prior Heart Attack Using Ticagrelor Compared to Placebo on a Background of Aspirin–Thrombolysis in Myocardial Infarction 54 PEGASUS-TIMI 54) trial. Am Heart J. 2014;167:437-44. 2. Markets include Australia, China, EU5, Japan, Russia and United States only. **Source:** Kantar Health (2010), GRACE Registry (2007), National Health & Wellness Survey (2013), medical literature, internal data

Outstanding collaboration with TIMI Study Group

Publication, regulatory, prepare to launch

Study metrics

- 21,000 patients in 31 countries
- >210,000 patient visits
- <0.1% patients lost to follow-up

Publication, regulatory

- FDA and EMA submissions complete
- Parallel presentation and publication ACC/ NEJM[1]

Towards launch

- Regulatory submission
- Pre-launch planning
- Disease and risk education

1 The New England Journal of Medicine

PARTHENON programme

Four regulatory submissions expected in three years

	Patients enrolled	Comparator	OAP access	Billion Days of Therapy	2015	2016	2017	2018
PLATO *Acute Coronary Syndrome*	18,624	clopidogrel	20%	1.3%	Launched			
PEGASUS *Prior MI*	21,162	placebo	20%	1.4%	Data	Expected launch		
SOCRATES *Stroke/TIA*	9,600	ASA	31%	2.3%		Data	Expected launch	
EUCLID *Peripheral Arterial Disease*	13,500	clopidogrel	69%	5.3%			Data	Expected launch
THEMIS *Diabetes*	17,000	placebo	84%	6.8%			Data	Exp. launch

- Increase in access to OAP market volume: >4.2x
- Increase in access to billion Days of Therapy: >5.5x

2015 priorities: Execution and launch

1. **Guideline implementation in ACS**
2. **Launch *BRILINTA®* / *BRILIQUE™* into post MI**
3. **Build the franchise – three world-class business units in coronary, stroke and PAD[1]**

1 Peripheral Arterial Disease

Summary

- Worldwide 2014 sales for *BRILINTA®* / *BRILIQUE™* were $476m up 70%[1]
- Strong brand momentum in the United States continues
- PEGASUS-TIMI 54 met its primary endpoint in both 60mg and 90mg doses
- Upcoming SOCRATES study in stroke: From indication to franchise

1 At constant exchange rates

Questions & Answers

Participants

- **Dr. Marc Sabatine**, PEGASUS-TIMI 54 Primary Investigator (P.I.)
- **Tom Keith-Roach**, *BRILINTA®* / *BRILIQUE™* Task Force leader
- **Elisabeth Björk**, Head of Global Medicines Development for Cardiovascular and Metabolic Disease
- **Marc Ditmarsch**, *BRILINTA®* / *BRILIQUE™* Clinical Development Lead
- **Tomas Andersson**, *BRILINTA®* / *BRILIQUE™* Medical Science Director

Please press *1 on your phone to indicate that you wish to ask a question