Antiplatelet Debate: Con

Jennifer Pickering, BScPhm, ACPR
Hamilton Health Sciences

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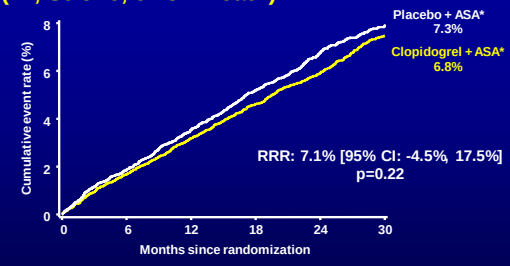
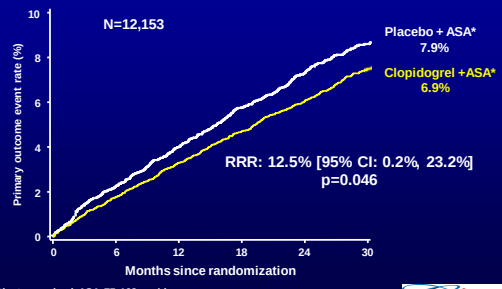
Overall Population: Primary Efficacy Outcome (MI, Stroke, or CV Death)†



†First Occurrence of MI (fatal or non-fatal), stroke (fatal or non-fatal), or cardiovascular death
*All patients received ASA 75-162 mg/day
‡The number of patients followed beyond 30 months decreases rapidly to zero and there are only 21 primary efficacy events that occurred beyond this time (13 clopidogrel and 8 placebo)

Bhatt DL. NEJM 2006;354(16):1706

Patients with Qualifying CV Disease (CAD, CVD or PAD): Primary Efficacy Outcome (MI/Stroke/CV Death)



*All patients received ASA 75-162 mg/day

Bhatt DL. NEJM 2006;354(16):1706

Patients with Qualifying CV Disease (CAD, CVD, PAD): Safety Results

Safety Outcome* - N (%)	Clopidogrel + ASA (n=6062)	Placebo + ASA (n=6091)	RR (95% CI)	p value
GUSTO Severe Bleeding	95 (1.6)	84 (1.4)	1.14 (0.85, 1.52)	0.39
Fatal	19 (0.3)	13 (0.2)	1.47 (0.73, 2.97)	0.28
Primary ICH	19 (0.3)	21 (0.3)	0.91 (0.49, 1.69)	0.76
GUSTO Moderate Bleeding	128 (2.1)	79 (1.3)	1.63 (1.23, 2.15)	<0.001

*Adjudicated outcomes by intention to treat analysis

Bhatt DL. NEJM 2006;354(16):1706

DAPT Outcomes:

Table 2. Stent Thrombosis and Major Adverse Cardiovascular and Cerebrovascular Events.*

Outcome	Continued Thienopyridine (N=5020)	Placebo (N=4941)	Hazard Ratio, Thienopyridine vs. Placebo (95% CI)†	P Value†
	no. of patients (%)			
Stent thrombosis‡	19 (0.4)	65 (1.4)	0.29 (0.17–0.48)	<0.001
Definite	15 (0.3)	58 (1.2)	0.26 (0.14–0.45)	<0.001
Probable	5 (0.1)	7 (0.1)	0.71 (0.22–2.23)	0.55
Major adverse cardiovascular and cerebrovascular events§	211 (4.3)	285 (5.9)	0.71 (0.59–0.85)	<0.001
Death	98 (2.0)	74 (1.5)	1.36 (1.00–1.85)	0.05
Cardiac	45 (0.9)	47 (1.0)	1.00 (0.66–1.52)	0.98
Vascular	5 (0.1)	5 (0.1)	0.98 (0.28–3.39)	0.98
Noncardiovascular	48 (1.0)	22 (0.5)	2.23 (1.32–3.78)	0.002
Myocardial infarction	99 (2.1)	198 (4.1)	0.47 (0.37–0.61)	<0.001
Stroke	37 (0.8)	43 (0.9)	0.80 (0.51–1.25)	0.32
Ischemic	24 (0.5)	34 (0.7)	0.68 (0.40–1.17)	0.16
Hemorrhagic	13 (0.3)	9 (0.2)	1.20 (0.50–2.91)	0.68
Type uncertain	0	1 (<0.1)	—	0.32

Mauri L et al NEJM 2014;37:2155

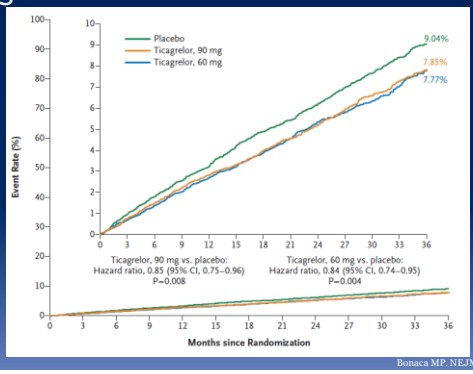
DAPT: Bleeding

Table 3. Bleeding End Point during Month 12 to Month 30.*

Bleeding Complications	Continued Thienopyridine (N=4710)	Placebo (N=4649)	Difference	Two-Sided P Value for Difference
	no. of patients (%)		*percentage points (95% CI)*	
GUSTO severe or moderate†	119 (2.5)	73 (1.6)	1.0 (0.4 to 1.5)	0.001
Severe	38 (0.8)	26 (0.6)	0.2 (–0.1 to 0.6)	0.15
Moderate	81 (1.7)	48 (1.0)	0.7 (0.2 to 1.2)	0.004
BARC type 2, 3, or 5	263 (5.6)	137 (2.9)	2.6 (1.8 to 3.5)	<0.001
Type 2	145 (3.1)	72 (1.5)	1.5 (0.9 to 2.1)	<0.001
Type 3	122 (2.6)	68 (1.5)	1.1 (0.6 to 1.7)	<0.001
Type 5	7 (0.1)	4 (0.1)	0.1 (–0.1 to 0.2)	0.38

Mauri L et al NEJM 2014;37:2155

Pegasus: Death/MI/Stroke



Bonaca MP. NEJM 2015

Table 3. Safety End Points as 3-Year Kaplan–Meier Estimates.*

End Point	Ticagrelor, 90 mg (N=6988)	Ticagrelor, 60 mg (N=6958)	Placebo (N=6996)	Ticagrelor, 90 mg vs. Placebo		Ticagrelor, 60 mg vs. Placebo	
				Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value
	number (percent)						
Bleeding							
TIMI major bleeding	127 (2.60)	115 (2.30)	54 (1.06)	2.69 (1.96–3.70)	<0.001	2.32 (1.68–3.21)	<0.001
TIMI minor bleeding	66 (1.31)	55 (1.18)	18 (0.36)	4.15 (2.47–7.00)	<0.001	3.31 (1.94–5.63)	<0.001
Bleeding requiring transfusion	122 (2.43)	105 (2.09)	37 (0.72)	3.75 (2.59–5.42)	<0.001	3.08 (2.12–4.48)	<0.001
Bleeding leading to study-drug discontinuation	453 (7.81)	354 (6.15)	86 (1.50)	5.79 (4.60–7.29)	<0.001	4.40 (3.48–5.57)	<0.001
Fatal bleeding or nonfatal intracranial hemorrhage	32 (0.63)	33 (0.71)	30 (0.60)	1.22 (0.74–2.01)	0.43	1.20 (0.73–1.97)	0.47
Intracranial hemorrhage	29 (0.56)	28 (0.61)	23 (0.47)	1.44 (0.83–2.49)	0.19	1.33 (0.77–2.31)	0.31
Hemorrhagic stroke	4 (0.07)	8 (0.19)	9 (0.19)	0.51 (0.16–1.64)	0.26	0.97 (0.37–2.51)	0.94
Fatal bleeding	6 (0.11)	11 (0.25)	12 (0.26)	0.58 (0.22–1.54)	0.27	1.00 (0.44–2.27)	1.00
Other adverse event							
Dyspnea	1205 (18.93)	987 (15.84)	383 (6.38)	3.55 (3.16–3.98)	<0.001	2.81 (2.50–3.17)	<0.001
Event leading to study-drug discontinuation	430 (6.50)	297 (4.55)	51 (0.79)	8.89 (6.65–11.88)	<0.001	6.06 (4.50–8.15)	<0.001
Serious adverse event	22 (0.41)	23 (0.45)	9 (0.15)	2.68 (1.24–5.83)	0.01	2.70 (1.25–5.84)	0.01
Renal event	166 (3.30)	173 (3.43)	161 (2.89)	1.17 (0.94–1.46)	0.15	1.17 (0.94–1.45)	0.15
Bradyarrhythmia	107 (2.04)	121 (2.32)	106 (1.98)	1.15 (0.88–1.50)	0.31	1.24 (0.96–1.61)	0.10
Gout	115 (2.28)	101 (1.97)	74 (1.51)	1.77 (1.32–2.37)	<0.001	1.48 (1.10–2.00)	0.01

* TIMI denotes Thrombolysis in Myocardial Infarction.

Bonaca MP. NEJM 2015

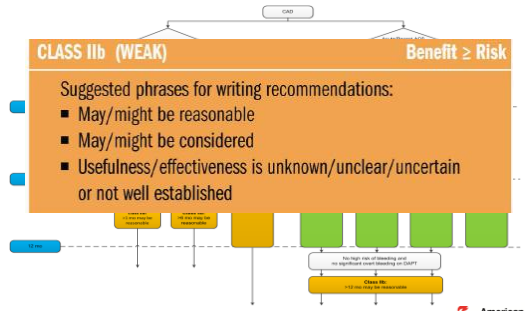
Canadian Cardiovascular Society | Société canadienne de cardiologie

Antiplatelet Therapy for Secondary Prevention in the First Year Following PCI: ACS AND PCI

2. We suggest continuation of a $P2Y_{12}$ inhibitor with ASA beyond 12 months be considered in patients with a high thrombosis risk and a low bleeding risk (Weak Recommendation, Low Quality Evidence)

Canadian Journal of Cardiology 2013 (29):1334-1345

Figure 1. Master Treatment Algorithm for Duration of $P2Y_{12}$ Inhibitor Therapy in Patients With CAD Treated With DAPT



AMERICAN COLLEGE of CARDIOLOGY

American Heart Association. life is why

Circulation 2016;133: epub access on line March 29,2016

Extending DAPT ? -

- After Stent Implantation
  - Decrease in late stent thrombosis and ischemic complications ≈ 1-2%
  - Increase in major bleed ≈ 1%
- Patients with prior MI (PEGASUS)
  - Absolute decrease in ischemic events of ≈1.2%
  - Absolute increase in TIMI major bleeding events ≈ 1.2%
- Potential for confusion between ticagrelor 90 mg and 60 mg indications
- Weak recommendation from published guidelines

Rebuttal

- We knew of this MI subgroup in 2006 and did nothing.
- Weak recommendation in guidelines so caution needed in broad application
- Money better spent on smoking cessation or medication compliance initiatives