Faculty Disclosures

Speaker Panel

● Boehringer Ingelheim
● Bristol-Myers Squibb/Sanofi Aventis
● Daiichi Sankyo/Eli Lilly
Outline

- Review pathophysiology of clot formation
- Overview of antiplatelet therapies
- Discuss platelet function variability
The Platelet

- Small, anucleate blood cell
- Primary function is to maintain hemostasis
- 1.5 trillion circulating throughout body, with life span of approximately 10 days
- Adheres to breaches in vessel endothelium
- Secretes clotting factors, vasoconstrictors, and growth factors upon activation
Role of the Platelet in Non-ST-Elevation Acute Coronary Syndromes

Plaque fissure/rupture → Platelet adhesion → Platelet activation → Platelet aggregation → Thrombotic occlusion

Intervene here → ...before occlusion occurs

White HD. *Am J Cardiol.* 1997; 80(4A):2B-10B.
Steps in platelet plug formation: Adhesion
Steps in platelet plug formation: Activation
Steps in platelet plug formation: Aggregation
Platelet shape change and aggregation
• GP IIb-IIIa inhibitors displace fibrinogen in existing thrombi to disaggregate thrombus and prevent further platelet cross-linking and thrombosis

• GP IIb-IIIa inhibitors prevent platelet activation by blocking GP IIb-IIIa (outside-in signaling)

Thrombin Receptors

Prothrombin

Heparin & enoxaparin reduce indirectly and partially block one pathway to platelet activation

Thrombin

Bivalirudin inactivates some thrombin molecules, indirectly and partially blocking one pathway to platelet activation

Thromboxane A₂

Aspirin only blocks one pathway to platelet activation

Platelet Activating Factor

Fibrinogen

GP IIb-IIIa

Thrombin Receptors

Sheer Forces

Collagen

Serotonin

Fibrinogen (GP IIb-IIIa)

Plasmin

Epinephrine

ADP (P₂Y₁₂)

ADP (P₂Y₁₁)

Thienopyridines (ie, clopidogrel) only block one pathway to platelet activation

High-dose heparin stimulates PAF which activates platelets

• GP IIb-IIIa inhibitors prevent further platelet activation by preventing fibrinogen-induced platelet activation

White HD. *Am J Cardiol* 1997; 80:2B-10B.
Phillips DR, Scarborough RM. *Am J Cardiol* 1997; 80(4A):11B-20B.
Currently Available Antiplatelet Therapies

**Oral**
- Aspirin
- Dipyridamole
- Thienopyridines: P2Y<sub>12</sub> inhibitor of platelet function
  - Clopidogrel (Plavix)
  - Ticlopidine (Ticlid)
  - Prasugrel (Effient)
- Cilostazol
- Ticagrelor (Brilinta) – Pending FDA Approval

**Intravenous**
- Glycoprotein (GP) IIb/IIIa inhibitor of platelet function
  - ReoPro (abciximab)
  - Integrilin (eptifibatide)
  - Aggrastat (tirofiban)
Target Directed Therapy
Antiplatelet Agents

- ticagrelor
- prasugrel
- clopidogrel
- ticlopidine

ADP = adenosine diphosphate, TXA2 = thromboxane A2, COX = cyclooxygenase.

Aspirin

- The simplest drug available in cardiology
  - Old and oral, once a day
- One of the most efficacious
- The cheapest available
- Therefore:
  - The most cost-effective
Aspirin in Acute MI: ISIS-2

Placebo alone: 568/4300 (13.2%)

Aspirin alone: 461/4295 (10.7%)

Streptokinase alone: 448/4300 (10.4%)

Streptokinase plus aspirin: 343/4292 (8.0%)

Cumulative Number of Vascular Deaths

Days From Randomization
Dose-Dependence and Aspirin Efficacy

<table>
<thead>
<tr>
<th>Aspirin Dose</th>
<th># Trials</th>
<th>OR* (%)</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>500–1500 mg</td>
<td>34</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>160–325 mg</td>
<td>19</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>75–150 mg</td>
<td>12</td>
<td>32</td>
<td></td>
</tr>
<tr>
<td>&lt;75 mg</td>
<td>3</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Any aspirin</td>
<td>65</td>
<td>23</td>
<td></td>
</tr>
</tbody>
</table>

Rationale for Newer Antiplatelet Therapies

- Despite treatment with aspirin and heparin, the incidence of MI and CV death during hospitalization remains high at 6-8%.
- Long term, the incidence of these events remains high at 6-8% per year.
- Majority of patients who enter the hospital for acute coronary syndrome (ACS) are already on aspirin therapy.

Clopidogrel (Plavix)

- Requires 2 step metabolism via cytochrome P450

- Platelet aggregation inhibition
  - 75 mg - 3 to 5 days
  - 300 mg - 4 to 6 hours
  - 600 mg – 1 to 2 hours

- Potential resistance mechanisms

- Variability in individual response

- Lower potency - anti-platelet effect (~40%)
Clopidogrel Metabolism

Clopidogrel

Hepatic metabolism and hydrolysis

PRODRUG CONVERSION

Active agent forms disulfide bridge with cysteine of P2Y12 receptor

P2Y12 receptor

Platelet

Irreversible binding

Active metabolite

Portal circulation
Efficacy of Clopidogrel vs Aspirin
MI, Ischemic Stroke, or Vascular Death (n=19,185)


**Event Rate per Year**

- **Aspirin:** 5.83%
- **Clopidogrel:** 5.32%

Over 5 years of follow-up, there was an 8.7% relative risk reduction in clopidogrel compared to aspirin. *P* = .045

* ITT analysis
The primary outcome occurred in 9.3% of patients in the clopidogrel + ASA group and 11.4% in the placebo + ASA group.
CHARISMA - MI/Stroke/CV Death

CAD, CVD or PAD (N=12,153)

RRR: 12.5% [95% CI: 0.2%, 23.2%]

p=0.046

Placebo + ASA*

7.9%

Clopidogrel + ASA*

6.9%

Primary outcome event rate (%)

0 2 4 6 8 10

0 6 12 18 24 30

Months since randomization

Multiple Risk Factor (N=3,284)

RRR: -20% [95% CI: -58.8%, 9.3%]

p=0.20

Clopidogrel + ASA*

6.6%

Placebo + ASA*

5.5%

Primary outcome event rate (%)

0 2 4 6 8 10

0 6 12 18 24 30

Months since randomization

## Clopidogrel Across Spectrum of CAD

<table>
<thead>
<tr>
<th>Acute STEMI</th>
<th>UA/NSTEMI</th>
<th>PCI</th>
<th>Long-term 2° (1°) prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLARITY*</td>
<td>CURE†</td>
<td>Credo†</td>
<td>CAPRIE§ [Lancet 1996]</td>
</tr>
<tr>
<td>COMMIT† (CCS-2)</td>
<td></td>
<td></td>
<td>CHARISMA†</td>
</tr>
</tbody>
</table>

### 98,809 Patients Enrolled in Randomized Clinical Trials

<table>
<thead>
<tr>
<th>STEMI</th>
<th>UA/NSTEMI</th>
<th>PCI</th>
<th>MI/Stroke/PAD</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 Days + Benefit</td>
<td>1 Year + Benefit</td>
<td>1 Year + Benefit</td>
<td>1-3 Years + Benefit</td>
</tr>
</tbody>
</table>

*Clopidogrel vs. placebo. †Clopidogrel + ASA. §Clopidogrel vs. ASA.

Aggrenox

- Combination capsule
- Dipyridamole 200mg depot pellets + low dose aspirin 25mg
- Inhibits the uptake of adenosine into cells
  - RBC’s, plts, endothelial cells
- Increases the local concentration of adenosine
- Adenosine is a potent inhibitor of platelet aggregation similar to prostacyclin (Pgl2)
European/Australasian Stroke Prevention in Reversible Ischaemia Trial (ESPRIT)

- 4500 pts with average f/u of 3.5 years

![Graph showing cumulative event rate over time comparing ASA and ASA + DP groups for primary outcome event and ischaemic events.](image-url)
PRoFESS - The world's largest trial in prevention of recurrent stroke

- 20,332 pts enrolled with average f/u of 2.5 years
- Comparison of Aggrenox to Clopidogrel in Secondary CVA Prevention
PRoFESS Trial – Time until recurrent stroke

• No clinical difference between Aggrenox or Plavix

Is aspirin, Plavix and Aggrenox enough for everyone?

Do we have a need for newer agents?
Clopidogrel Response Variability (300 vs. 600 mg): Importance of Dose (n = 190)

Resistance = 28% (300 mg)
Resistance = 8% (600 mg)

(Gurbel PA et al. J Am Coll Cardiol. 2005;45:1392)
Possible Causes/Mechanisms of Response Variability

- **Genetic**
  - Receptors: polymorphisms to P2Y12 receptor; H2 haplotype
  - Enzymes: P450 (2B6, 2C9, 2C19, 3A4, 3A5), COX-1, COX-2, Thromboxane A2 synthetase

- **Pharmacokinetic/Bioavailability**
  - Non-compliance/Premature discontinuation
  - Underdosing
  - Poor absorption
  - Possible drug-drug interactions

- **Pharmacodynamic**
  - Incomplete suppression of thromboxane A2 generation (ASA)
  - Accelerated plt turnover, with introduction of newly formed plts
  - Stress-induced COX-2 in plts (ASA)
  - Increased plt sensitivity to ADP and collagen

- **Environment/concomitant disease**
  - Diabetes mellitus
  - CAD and CKD
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- **Environment/concomitant disease**
  - Diabetes mellitus
  - CAD and CKD
Long-term Use of Clopidogrel After Stenting Is Associated With Decreased Mortality

- Retrospective study which included patients with ACS receiving either a DES or BMS and discharged from a Veterans Health Administration hospital from 2003 to 2004.
- Clopidogrel use was assessed by pharmacy-dispensing data.
- In multivariable analysis, discontinuation of clopidogrel remained significantly associated with higher mortality risk (HR, 2.40; 95% CI, 1.61-3.58).

**Graph:**
- Cumulative Mortality Rate vs. Follow-up Time (d)
- Yellow line: Off clopidogrel
- Red line: On clopidogrel
- N=1,455

Unadjusted cumulative all-cause mortality rates between patients discontinuing and continuing clopidogrel.

BMS = bare metal stent.
Factors Influencing DES Thrombosis

9-Month Cumulative Stent Thrombosis

Patients (%)

<table>
<thead>
<tr>
<th>Factor</th>
<th>Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>2.5</td>
</tr>
<tr>
<td>Unprotect. left main artery</td>
<td>3.3</td>
</tr>
<tr>
<td>Bifurcation 2 stents</td>
<td>3.9</td>
</tr>
<tr>
<td>Renal failure</td>
<td>6.2</td>
</tr>
<tr>
<td>Prior brachytherapy</td>
<td>8.7</td>
</tr>
<tr>
<td>Premature antiplatelet therapy withdrawal</td>
<td>29</td>
</tr>
</tbody>
</table>

DES=drug-eluting stent.
Allergy Issues

- ASA and clopidogrel allergy is very important in DES implantation decisions
- ASA desensitization is possible
  - NOT for anaphylaxis
- Clopidogrel desensitization reported
- CCU setting for desensitization attempts
- Ticlopidine, cilostazol, prasugrel, other alternative options
Prasugrel (Effient)

- Thienopyridine
- Hydrolysis by intestinal carboxylesterases
- Oxidation by intestinal and hepatic CYP-450
- Increased potency > 80% inhibition
Active Metabolite Formation: Clopidogrel and Prasugrel

Clopidogrel

85% Inactive Metabolites

Oxidation (Cytochrome P450)

CYPs:
1A2
2C19
2B6

Active Metabolite

Prasugrel

Hydrolysis (Esterases)

CYPs:
3A
2B6
2C9
2C19

Active Metabolite

CYPs:
3A
2B6
2C9
2C19

Oxidation (Cytochrome P450)
IPA: Prasugrel and Clopidogrel Loading Dose

The relationship between IPA and clinical activity has not been established.

2. Effient Full Prescribing Information.
   Please see Important Safety Information, including Boxed Warning, and Full Prescribing Information provided.
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*
TRial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition With Prasugrel (TRITON)-TIMI 38

ACS (UA/NSTEMI or STEMI) and Planned PCI, N=13,608

Aspirin

Randomized Double-blind

Aspirin

Prasugrel
60-mg loading dose/
10-mg maintenance dose

Clopidogrel
300-mg loading dose/
75-mg maintenance dose

Median duration of follow up = 14.5 months

- Primary efficacy endpoint:
  - Composite CV death, nonfatal MI, or nonfatal stroke
- Safety endpoints:
  - Non–CABG-related: TIMI major bleeding, including life-threatening bleeding, and TIMI major or minor bleeding

Balance of Efficacy and Safety

CV Death / MI / Stroke
- Prasugrel: HR 1.32 (1.03-1.68), P=0.03
- Clopidogrel: HR 0.81 (0.73-0.90), P=0.0004

TIMI Major NonCABG Bleeds
- Prasugrel: NNT = 46
- Clopidogrel: NNH = 167

1.38 events
1.35 events

35 events
35 events
Stent Thrombosis
(ARC Definite + Probable)

Any Stent at Index PCI
N= 12,844

Clopidogrel
2.4
(142)

Prasugrel
1.1
(68)

HR 0.48
P <0.0001
NNT= 77
Net Clinical Benefit
Death, MI, Stroke,
Major Bleed (non CABG)

ITT = 13,608

Clopidogrel
13.9
HR 0.87
P = 0.004

Prasugrel
12.2

Events per 1000 pts

All Cause Mortality
Clop 3.2%
Pras 3.0%
P = 0.64
The “Greater Inhibition is Better” Hypothesis In Dual Antiplatelet Therapy

C. Michael Gibson, M.D. 2008
Prasugrel (Effient) – FDA Approved 7/09
Box Warnings

- Active pathological bleeding
- History of TIA or stroke
- Urgent need for surgery, including CABG
- Over age 75, unless high risk (DM or STEMI)
- Under 60 kg – consider 5mg dose
Ticagrelor (Brilinta): an oral reversible P2Y$_{12}$ antagonist

Ticagrelor is a cyclo-pentyl-triazolo-pyrimidine (CPTP)

- **Direct acting**
  - Not a prodrug; does not require metabolic activation
  - Rapid onset of inhibitory effect on the P2Y$_{12}$ receptor
  - Greater inhibition of platelet aggregation than clopidogrel

- **Reversibly bound**
  - Degree of inhibition reflects plasma concentration
  - Faster offset of effect than clopidogrel
  - Functional recovery of all circulating platelets
The NEW ENGLAND JOURNAL of MEDICINE

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*
PLATO study design

NSTE-ACS (moderate-to-high risk) STEMI (if primary PCI)
Clopidogrel-treated or -naive;
randomised within 24 hours of index event
(N=18,624)

Clopidogrel
If pre-treated, no additional loading dose;
if naive, standard 300 mg loading dose,
then 75 mg qd maintenance;
(additional 300 mg allowed pre PCI)

Ticagrelor
180 mg loading dose, then
90 mg bid maintenance;
(additional 90 mg pre-PCI)

6–12-month exposure

Primary endpoint: CV death + MI + Stroke
Primary safety endpoint: Total major bleeding

PCI = percutaneous coronary intervention; ASA = acetylsalicylic acid;
CV = cardiovascular; TIA = transient ischaemic attack
K-M estimate of time to first primary efficacy event (composite of CV death, MI or stroke)

<table>
<thead>
<tr>
<th>No. at risk</th>
<th>Ticagrelor</th>
<th>Clopidogrel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days after randomisation</td>
<td>9,333</td>
<td>9,291</td>
</tr>
<tr>
<td>60</td>
<td>8,628</td>
<td>8,521</td>
</tr>
<tr>
<td>120</td>
<td>8,460</td>
<td>8,362</td>
</tr>
<tr>
<td>180</td>
<td>8,219</td>
<td>8,124</td>
</tr>
<tr>
<td>240</td>
<td>6,743</td>
<td>6,743</td>
</tr>
<tr>
<td>300</td>
<td>5,161</td>
<td>5,096</td>
</tr>
<tr>
<td>360</td>
<td>4,147</td>
<td>4,047</td>
</tr>
</tbody>
</table>

HR 0.84 (95% CI 0.77–0.92), p=0.0003

K-M = Kaplan-Meier; HR = hazard ratio; CI = confidence interval
Time to major bleeding – primary safety event

No. at risk

<table>
<thead>
<tr>
<th></th>
<th>Ticagrelor</th>
<th>Clopidogrel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days from first IP dose</td>
<td>9,235</td>
<td>9,186</td>
</tr>
<tr>
<td>0</td>
<td>9,235</td>
<td>9,186</td>
</tr>
<tr>
<td>60</td>
<td>7,246</td>
<td>7,305</td>
</tr>
<tr>
<td>120</td>
<td>6,826</td>
<td>6,930</td>
</tr>
<tr>
<td>180</td>
<td>6,545</td>
<td>6,670</td>
</tr>
<tr>
<td>240</td>
<td>5,129</td>
<td>5,209</td>
</tr>
<tr>
<td>300</td>
<td>3,783</td>
<td>3,841</td>
</tr>
<tr>
<td>360</td>
<td>3,433</td>
<td>3,479</td>
</tr>
</tbody>
</table>

HR 1.04 (95% CI 0.95–1.13), p=0.434
Public statements on possible interaction between clopidogrel and proton pump inhibitors

- “PPIs might interfere with the effectiveness of clopidogrel”
- “Clopidogrel less effective when given with these medicines”
- “Concomitant use of a PPI with clopidogrel is not recommended unless considered essential”
**Thienopyridines: Formation of Active Metabolite**

**Pro-drugs**

- **Clopidogrel**
  - **85% Inactive Metabolites**
  - Oxidation (Cytochrome P450)

- **Prasugrel**
  - Hydrolysis (Esterases)

**CYPs:**
- 1A2
- 2C19
- 2B6

**Active Metabolite**

- Proton pump inhibitors

**CYPs:**
- 3A
- 2B6
- 2C9

**Active Metabolite**
Risk of CV Events for Patients Taking Clopidogrel in Combination with a PPI


Adjusted OR 1.25 (95% CI 1.11-1.41)
Degree of CYP2C19 Inhibition

- Weak or no inhibition of CYP2C19
- Strong CYP2C19 inhibitor

- Pantoprazole
- Rabeprazole
- Esomeprazole
- Omeprazole
- Lansoprazole
COGENT Trial

- Only randomized trial to compare proton pump inhibitor (PPI) omeprazole with placebo in pts taking clopidogrel

- Determine if any CV interaction between clopidogrel and PPI

- Determine if PPI vs placebo decreases important GI events
No significant difference seen

PPI group did significantly better

Possible Causes/Mechanisms of Response Variability

- **Genetic**
  - Receptors: polymorphisms to P2Y12 receptor; H2 haplotype
  - Enzymes: P450 (2B6, 2C9, 2C19, 3A4, 3A5), COX-1, COX-2, Thromboxane A2 synthetase

- **Pharmacokinetic/Bioavailability**
  - Non-compliance/Premature discontinuation
  - Underdosing
  - Poor absorption
  - Possible drug-drug interactions

- **Pharmacodynamic**
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  - Stress-induced COX-2 in plts (ASA)
  - Increased plt sensitivity to ADP and collagen

- **Environment/concomitant disease**
  - Diabetes mellitus
  - CAD
CYP2C19 Reduced-function Allele Carrier Status and Clinical Outcomes in Clopidogrel-treated Patients

A Subanalysis From the TRITON-TIMI 38 Trial

CV Death, Nonfatal MI, or Nonfatal Stroke (%)

Number at Risk
Carriers* 395 364 360 348 306 270 181
Non-carriers 1064 1009 999 980 870 755 542

HR 1.53
P=0.01

*Represents a mixture of intermediate and poor metabolizers.

Please see Important Safety Information, including Boxed Warning, and Full Prescribing Information provided.
CYP2C19 Reduced-function Allele Carrier Status and Clinical Outcomes in Prasugrel-treated Patients

A Subanalysis From the TRITON-TIMI 38 Trial

CV Death, Nonfatal MI, or Nonfatal Stroke (%)

0 30 90 180 270 360 450

Days After Randomization

Non-carriers

Carriers

HR 0.89
P=0.27

Number at Risk
Non-carriers 1048 991 982 951 849 750 541
Carriers* 407 383 376 364 320 276 188

*Represents a mixture of intermediate and poor metabolizers.
Please see Important Safety Information, including Boxed Warning, and Full Prescribing Information provided.
WARNING: DIMINISHED EFFECTIVENESS IN POOR METABOLIZERS

See full prescribing information for complete boxed warning.

Effectiveness of Plavix depends on activation to an active metabolite by the cytochrome P450 (CYP) system, principally CYP2C19.

Poor metabolizers treated with Plavix at recommended doses exhibit higher cardiovascular event rates following acute coronary syndrome (ACS) or percutaneous coronary intervention (PCI) than patients with normal CYP2C19 function.

Tests are available to identify a patient's CYP2C19 genotype and can be used as an aid in determining therapeutic strategy.

Consider alternative treatment or treatment strategies in patients identified as CYP2C19 poor metabolizers.
Platelet Function Testing

- **Platelet Aggregation**
  - Light transmittance aggregometry (LTA)
  - Impedence platelet aggregation

- **Flow Cytometry**
  - Gp IIb/IIIa receptor activation
  - P-selectin expression
  - Leukocyte-platelet aggregates
  - Vasodilator-associated stimulated phosphoprotein (VASP)

- **Point-of-Care**
  - Ultegra rapid platelet function analyzer (VerifyNow)
  - Thromboeastograph (TEG)
  - Plateletworks
  - Cone and plate(let) analyzer (IMPACT)
Platelet Function Testing
Successful PCI with DES without major complication or GPIIb/IIIa use

VerifyNow P2Y12 Assay 12-24 hours post-PCI

PRU ≥ 230?

Yes

Non-Responder

No

Responder

Random Selection

N = 583

“Tailored Therapy” clopidogrel 600mg*, then clopidogrel 150-mg/day

“Standard Therapy” placebo loading dose, then clopidogrel 75mg +placebo/day

“Standard Therapy” placebo loading dose clopidogrel 75mg +placebo/day

N = 1100

N = 1100

A

B

Clinical Follow-up And Platelet Function Assessment at 30 days, 6M

Primary Endpoint: 6 month CV Death, Non-Fatal MI, ARC definite/prob ST

Safety Endpoint: GUSTO Moderate or Severe Bleeding

Price MJ et al, Am Heart J 2009

*Total first day dose
Primary Endpoint: CV Death, MI, Stent Thrombosis

Observed event rates are listed; P value by log rank test.
Secondary Comparison: High vs. Not High Reactivity
Treated with Clopidogrel 75-mg daily

Observed event rates are listed. P value by log-rank test.
Platelet Function Testing

- No “gold standard” for platelet function testing

- No data to support platelet function guided therapy

- Ongoing trials to evaluate tailored therapy for decreased responders

- More data is required before widespread use of assays
Summary - Take Home Points

- Aspirin is safe and effective for all CV pts
- Aggrenox benefit seen mainly in stroke pts
- Safety of clopidogrel has been confirmed in a broad range of pts with stable and unstable CAD
- Compared with clopidogrel, prasugrel and ticagrelor provide a significant reduction in ischemic events in ACS pts, and marked reductions in stent thrombosis (both BMS and DES)
Summary - Take Home Points

- *Prasugrel use Limitations:*
  - Continued risk of major bleeding over time may outweigh the risk of thrombotic events in some pts
- *Clopidogrel works great in most patients*
- *Ticagrelor will likely be approved for use soon*
- *Genetic and platelet function testing are available and trial results are pending*
- *Cost-savings of generic Plavix will likely lead to insurance companies supporting these technologies*
Off the Mark

by Mark Parisi

www.offthemark.com

Atlantic Features Syndicate, Inc., Mark Parisi

Mark.Parisi@aol.com

Chunky Style

BLOOD

WITH

EXTRA

PLATELETS!