DAPT in CAD, Acute & Chronic CAD, antiplatelet therapy non-responders

Annual Ohio ACC Conference
October 14, 2017
Ernest L. Mazzaferri Jr, MD, FACC, FSCAI

Improving People's Lives Through Innovations in Personalized Health Care
Disclosures

- No financial disclosures related to this talk
AGENDA:

- DAPT in CAD

- Background
- DAPT in Stable Ischemic Heart Disease (SIHD)
- DAPT in Acute Coronary Syndromes (ACS)

- Update on antiplatelet therapy non-responders
Dual Antiplatelet Therapy (DAPT): Why do we care?

- Fundamental trade-off between decreasing ischemic risk and increasing bleeding risk
- Bleeding Complications (GI, procedures/surgeries), cost, convenience
  - Major bleeding ↑ mortality at 3 years
- Stent Thrombosis
  - 1st gen DES ↑ stent thrombosis
  - stent thrombosis equals STEMI
  - Up to 25% mortality
- ACC/AHA and European Society of Cardiology: 2011-2014:
  - DAPT for a minimum of one year with Drug Eluting Stents
- Most contemporary studies of DAPT have compared:
  - Shorter (3 to 6 months) vs 12 months of DAPT
  - Longer (18 to 48 months) vs 12 months of DAPT
### Clinical and Procedural Factors Associated with Risk

<table>
<thead>
<tr>
<th>Increased Ischemic Risk/Risk of Stent Thrombosis</th>
<th>Increased Bleeding Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>(may favor longer-duration DAPT)</td>
<td>(may favor shorter-duration DAPT)</td>
</tr>
</tbody>
</table>

**Increased ischemic risk**
- Advanced age
- ACS presentation
- Multiple prior MIs
- Extensive CAD
- Diabetes mellitus
- CKD

**Increased risk of stent thrombosis**
- ACS presentation
- Diabetes mellitus
- Left ventricular ejection fraction <40%
- First-generation drug-eluting stent
- Stent undersizing
- Stent underdeployment
- Small stent diameter
- Greater stent length
- Bifurcation stents
- In-stent restenosis

**Increased bleeding risk**
- History of prior bleeding
- Oral anticoagulant therapy
- Female sex
- Advanced age
- Low body weight
- CKD
- Diabetes mellitus
- Anemia
- Chronic steroid or NSAID Rx

---

**Stent Thrombosis**

(25%+ mortality)
2nd Generation DES (Resolute/Promus/Xience/Synergy)

- 11 studies of patients treated with stents assessing shorter and longer duration of DAPT
- 2nd generation DES have better outcomes

- Newer generation DES (Resolute/Promus/Xience/Synergy)
  - Thinner metallic struts, -limus
  - Improved biocompatibility and lower polymer mass
  - Biodegradable polymers
  - Polymer free surfaces,
  - Proven efficacy and safety over early DES

<table>
<thead>
<tr>
<th><strong>P2Y&lt;sub&gt;12&lt;/sub&gt; Inhibitors</strong></th>
<th>Clopidogrel (Plavix&lt;sup&gt;®&lt;/sup&gt;)</th>
<th>Prasugrel (Effient&lt;sup&gt;®&lt;/sup&gt;)</th>
<th>Ticagrelor (Brilinta&lt;sup&gt;®&lt;/sup&gt;)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Loading Dose</strong></td>
<td>300-600mg 75 mg</td>
<td>60mg 10mg</td>
<td>180mg 90mg bid</td>
</tr>
<tr>
<td><strong>Maintenance</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Route</strong></td>
<td>Oral</td>
<td>Oral</td>
<td>Oral</td>
</tr>
<tr>
<td><strong>Prodrug</strong></td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td><strong>Hepatic</strong></td>
<td>2C19, 1A2</td>
<td>3A, 2B6</td>
<td>3A4/5</td>
</tr>
<tr>
<td>Metabolism</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Mortality Benefit</strong></td>
<td>Baseline</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Max Platelet</strong></td>
<td>35</td>
<td>79</td>
<td>88</td>
</tr>
<tr>
<td>Inhibition (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Time to 50%</strong></td>
<td>120-240</td>
<td>60</td>
<td>30</td>
</tr>
<tr>
<td>platelet</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>inhibition (min)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Phase III trials</strong></td>
<td>CURE/CREDO</td>
<td>TRITON TIMI-38</td>
<td>PLATO</td>
</tr>
<tr>
<td><strong>Absolute</strong></td>
<td>Allergy</td>
<td>Allergy</td>
<td>Allergy</td>
</tr>
<tr>
<td><strong>Contraindications</strong></td>
<td></td>
<td>h/o TIA/Stroke</td>
<td>h/o ICH</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines


Developed in Collaboration With the American Association for Thoracic Surgery, American Society of Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Anesthesiologists, and Society of Thoracic Surgeons.

Endorsed by Preventive Cardiovascular Nurses Association and Society for Vascular Surgery

Focused Update Writing Group*

Glenn N. Levine, MD, FACC, FAHA, Chair
Eric R. Bates, MD, FACC, FAHA, FSCAI
John A. Bittl, MD, FACC
Ralph G. Brindis, MD, MPH, MACC, FAHA
Stephan D. Fihn, MD, MPH
Lee A. Fleisher, MD, FACC, FAHA
Christopher B. Granger, MD, FACC, FAHA
Richard A. Lange, MD, MBA, FACC
Michael J. Mack, MD, FACC*
Laura Mauri, MD, MSc, FACC, FAHA, FSCAI
Roxana Mehran, MD, FACC, FAHA, FSCAI*
Deborah Mukherjee, MD, FACC, FAHA, FSCAI
L. Kristin Newby, MD, MHS, FACC, FAHA*

Patrick T. O’Gara, MD, FACC, FAHA
Marc S. Sabatine, MD, MPH, FACC, FAHA*
Peter K. Smith, MD, FACC
Sidney C. Smith, Jr., MD, FACC, FAHA

*Focused Update writing group members are required to recuse themselves from voting on sections to which their specific relationships with industry may apply; see Appendix I for detailed information.

This document was approved by the American College of Cardiology Board of Trustees and the American Heart Association Science Advisory and Coordinating Committee in February 2016, and the American Heart Association Executive Committee in March 2016.

2016 Guideline Update: 3 Critical Questions:

1. In patients treated with newer (non-first) generation DES for (1) SIHD or (2) ACS, compared with 12 months of DAPT, **is 3-6 months of DAPT as effective** in preventing stent thrombosis, preventing MACE and/or reducing bleeding complications?

2. In patients treated with newer (non-first) generation DES, compared with 12 months of DAPT, **does >12 (18-48) months of DAPT result in differences** in mortality rate, decreased MACE, decreased stent thrombosis, and/or increased bleeding?

3. In post-MI (NSTEMI or STEMI) patients who are clinically stable and >12 months past their event, **does continued DAPT**, compared with aspirin monotherapy, result in differences in mortality rate, decreased nonfatal MI, decreased MACE, and/or increased bleeding?
Is 3-6 months of DAPT enough post PCI with DES*?

<table>
<thead>
<tr>
<th>Short Term</th>
<th>Length</th>
<th>Stents</th>
</tr>
</thead>
<tbody>
<tr>
<td>RESET</td>
<td>3 vs 12 mos</td>
<td>3M arm only Endeavor (zotarolimus ES) 12M R-ZES (42%), EES (30%), SES (28%)</td>
</tr>
<tr>
<td>OPTIMIZE</td>
<td>3 vs 12 mos</td>
<td>100% E-ZES</td>
</tr>
<tr>
<td>EXCELLENT</td>
<td>6 vs 12 mos</td>
<td>EES vs SES</td>
</tr>
<tr>
<td>ISAR-SAFE</td>
<td>6 vs 12 mos</td>
<td>Any DES</td>
</tr>
<tr>
<td>SECURITY</td>
<td>6 vs 12 mos</td>
<td>R-ZES 42%, BES 25%, EES 20%</td>
</tr>
<tr>
<td>PRODIGY</td>
<td>6 vs 24 mos</td>
<td>BMS 25%, EES 25%, PES 25%, ZES 25%</td>
</tr>
<tr>
<td>ITALIC</td>
<td>6 vs 24 mos</td>
<td>Xience EES</td>
</tr>
</tbody>
</table>

*The trials primarily enrolled low-risk (non-ACS) patients, with only a small proportion having had a recent MI. The main endpoints of these noninferiority trials were composite ischemic events (or net composite events) and stent thrombosis.
Short term DAPT: Randomized trials

No differences observed in PEP’s

<table>
<thead>
<tr>
<th>Trial</th>
<th>Short DAPT</th>
<th>Longer DAPT</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RESET</td>
<td>3 v 12 mo</td>
<td>n=2117</td>
<td>p=0.84</td>
</tr>
<tr>
<td>OPTIMIZE</td>
<td>3 v 12 mo</td>
<td>n=3119</td>
<td>p=0.84</td>
</tr>
<tr>
<td>EXCELLENT</td>
<td>6 v 12 mo</td>
<td>n=1443</td>
<td>p=0.60</td>
</tr>
<tr>
<td>ISAR-SAFE</td>
<td>6 v 12 mo</td>
<td>n=4005</td>
<td>p=non-inf &lt; 0.001</td>
</tr>
<tr>
<td>SECURITY</td>
<td>6 v 12 mo</td>
<td>n=1399</td>
<td>p=0.47</td>
</tr>
<tr>
<td>PRODIGY</td>
<td>6 v 24 mo</td>
<td>n=1970</td>
<td>p=0.91</td>
</tr>
<tr>
<td>ITALIC</td>
<td>6 v 24 mo</td>
<td>n=1850</td>
<td>p=0.85</td>
</tr>
</tbody>
</table>

*included 1st generation DES
*included BMS
Short term DAPT: Randomized trials

No Difference in Stent Thrombosis

Definite or probable

*included 1st generation DES
*included BMS
Short term DAPT: Randomized trials

Major bleeding rates

<table>
<thead>
<tr>
<th>Trial</th>
<th>Short DAPT</th>
<th>Longer DAPT</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RESET</td>
<td>3 v 12 mo n=2117</td>
<td>3 v 12 mo n=3119</td>
<td>p=0.16</td>
</tr>
<tr>
<td>OPTIMIZE</td>
<td>6 v 12 mo n=1443</td>
<td>6 v 12 mo n=4005</td>
<td>p=0.41</td>
</tr>
<tr>
<td>EXCELLENT</td>
<td>6 v 12 mo n=1399</td>
<td>6 v 12 mo n=1970</td>
<td>p=0.42</td>
</tr>
<tr>
<td>ISAR-SAFE</td>
<td>6 v 24 mo n=1850</td>
<td>6 v 12 mo n=1970</td>
<td>p=0.74</td>
</tr>
<tr>
<td>SECURITY</td>
<td>6 v 24 mo n=1970</td>
<td>6 v 24 mo n=1850</td>
<td>p=0.46</td>
</tr>
<tr>
<td>PRODIGY</td>
<td>6 v 24 mo n=1970</td>
<td>6 v 24 mo n=1850</td>
<td>p=0.04</td>
</tr>
</tbody>
</table>

*included 1st generation DES
*included BMS
Is > 12 months of DAPT better post PCI with DES *?

<table>
<thead>
<tr>
<th>Short Term</th>
<th>Length</th>
<th>Stents</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRODIGY</td>
<td>6 vs 24 mos</td>
<td>BMS 25%, EES 25%, PES 25%, ZES 25%</td>
</tr>
<tr>
<td>ITALIC</td>
<td>6 vs 24 mos</td>
<td>Xience EES</td>
</tr>
<tr>
<td>DES-LATE</td>
<td>12 vs 24 mos</td>
<td>SES (57%), PES (24%), ZES (19%)</td>
</tr>
<tr>
<td>DAPT</td>
<td>12 vs 30 mos</td>
<td>EES (48%), PES (27%), E-ZES (13%), SES (11%)</td>
</tr>
<tr>
<td>ARTIC</td>
<td>12 vs 18-30 mos</td>
<td>1st gen DES (40%), 2nd gen DES (60%)</td>
</tr>
</tbody>
</table>

*The trials primarily enrolled low-risk (non-ACS) patients, with only a small proportion having had a recent MI. The main endpoints of these noninferiority trials were composite ischemic events (or net composite events) and stent thrombosis.

Long term DAPT: Randomized trials

One trial with lower MACE

<table>
<thead>
<tr>
<th>Trial</th>
<th>Duration 1</th>
<th>Duration 2</th>
<th>n 1</th>
<th>n 2</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRODIGY**</td>
<td>6 v 24 mo</td>
<td>6 v 24 mo</td>
<td>1970</td>
<td>1850</td>
<td>0.91</td>
</tr>
<tr>
<td>ITALIC</td>
<td>6 v 24 mo</td>
<td>12 v 18-30 mo</td>
<td>1259</td>
<td></td>
<td>0.58</td>
</tr>
<tr>
<td>ARCTIC*</td>
<td>12 v 24 mo</td>
<td>12 v 24 mo</td>
<td>2701</td>
<td></td>
<td>0.17</td>
</tr>
<tr>
<td>DES-LATE*</td>
<td>12 v 30 mo</td>
<td>12 v 30 mo</td>
<td>9961</td>
<td></td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*included 1st generation DES
*included BMS
Long term DAPT: Randomized trials
Longer DAPT associated with more bleeding

**Included 1st generation DES
*Included BMS**
Enrolled: Subjects treated with DES or BMS (excluded if on OAC or life expectancy < 3 years) (40% ACS)
Randomized: Free from MI, stroke, repeat revascularization, moderate or severe bleeding, adherent to DAPT

Index Stent Procedure
0-12 Mos: All pt’s Open-Label DAPT
12 mos: 1:1 Randomization
12-30 mos: Blinded treatment
Follow-up
30 mos: PEP
33 mos

DES Subjects 22,866
9,961 (44%)
5,020 Thienopyridine + ASA
4,941 Placebo + ASA
9,499 (95.4%)
9,390 (94.3%)

5,261 events in 1st year
7,644 eligible: 5,808 withdrew, 1,741 missed window

Primary Safety Endpoint
(Moderate or Severe Bleeding)

Cumulative Incidence (%)

- Moderate or Severe: p = 0.001
- Moderate: p = 0.004
- Severe: p = 0.15
- BARC 2: p < 0.001
- BARC 3: p < 0.001
- BARC 5: p = 0.38

Thienopyridine + ASA
Placebo + ASA

Co-Primary Effectiveness End Points & Components

- Definite ST
- Probable ST
- MACCE
- Death
- MI
- Isch. stroke
- Hem. stroke

Cumulative Incidence (%)

- Thienopyridine + ASA
- Placebo + ASA

- $p < 0.001$
- $p = 0.052$
- $p = 0.16$
- $p = 0.68$

DAPT Study Results Summary

- The rates of ST and MACCE at 12-30 months were significantly reduced with continued (30M) DAPT vs. placebo (12M DAPT) \(^1,2\) ~ 40% patients had 1\(^{\text{st}}\) generation DES

- However, continued DAPT was associated with an increase in bleeding events \(^1,2\)

- 56% not randomized (23% of Patients excluded from analysis due to interruption in 1\(^{\text{st}}\) 12 months, 33% withdrew or missed window)

- These results call for physicians to determine individualized DAPT duration based on risk profile \(^4\)

---

3 Kereiakes DJ, et al. Comparison of ischemic and bleeding events after drug-eluting stents or bare metal stents in subjects receiving dual antiplatelet therapy: results from the randomized Dual Antiplatelet Therapy (DAPT) Study. AHA 2014.
Studies relevant to DAPT > 1 yr after ACS

- CHARISMA Post Hoc Analysis:
  - CAD or multiple RF for CAD assigned to ASA alone or ASA + Plavix x 28 months (no decrease ischemic events but increase bleeding)
  - Substudy of patients with prior MI
    - 1.7% absolute decrease in composite endpoint of CV death/MI/Stroke with DAPT
    - No benefit in those with CAD without MI

- PEGASUS TIMI-54
  - 1 to 3 years after MI with additional high-risk features to either DAPT (with ticagrelor 60 mg or 90 mg twice daily) or continued aspirin monotherapy
    - >80% patients had PCI
    - After a mean of 33 months of therapy, DAPT, when compared with aspirin monotherapy, resulted in a 1.2% to 1.3% absolute reduction in the primary composite endpoint of cardiovascular death, MI, or stroke and a 1.2% to 1.5% absolute increase in major bleeding
### DAPT Score

- **Total Score Range** -2 to 10
  - **Lower score** quartiles associated with higher rates of moderate or severe bleeding (p =0.006)
  - **Higher score** quartiles associated with higher rates of MI/ST (p<0.001)

#### Variable | Points
--- | ---
Age ≥75 y | -2
Age 65 to <75 y | -1
Age <65 y | 0
Current cigarette smoker | 1
Diabetes mellitus | 1
MI at presentation | 1
Prior PCI or prior MI | 1
Stent diameter <3 mm | 1
Paclitaxel-eluting stent | 1
CHF or LVEF <30% | 2
Saphenous vein graft PCI | 2


- <2 favors shorter **DAPT**
- ≥2 favorable benefit/risk ratio for **prolonged DAPT**
2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines


Developed in Collaboration With the American Association for Thoracic Surgery, American Society of Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Anesthesiologists, and Society of Thoracic Surgeons
After PCI, aspirin should be continued indefinitely*.

PCI, lifelong single antiplatelet therapy (SAPT) is recommended, usually ASA**

Generally agreed upon exceptions:
1) Intracranial or spinal surgery
2) Posterior chamber of eye surgery
3) TURP
### DAPT in ACS

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>B-R</td>
<td>In patients with STEMI or NSTEMI, treated with <strong>BMS or DES</strong> implantation, P2Y₁₂ inhibitor therapy should be given for at least 12 months.</td>
</tr>
<tr>
<td>I</td>
<td>B-NR</td>
<td>In patients treated with DAPT, the recommended daily dose of <strong>aspirin is 81 mg</strong> (range, 75 mg to 100 mg).</td>
</tr>
<tr>
<td>IIa</td>
<td>B-R</td>
<td>In patients STEMI or NSTEMI after coronary stent implantation, it is reasonable to <strong>use ticagrelor in preference to clopidogrel</strong> for maintenance P2Y₁₂ inhibitor therapy.</td>
</tr>
<tr>
<td>IIa</td>
<td>B-R</td>
<td>In patients STEMI or NSTEMI after coronary stent implantation who are not at high risk for bleeding complications and who <strong>do not have a history of stroke or TIA</strong>, it is reasonable to choose <strong>prasugrel over clopidogrel</strong> for maintenance P2Y₁₂ inhibitor therapy.</td>
</tr>
<tr>
<td>COR</td>
<td>LOE</td>
<td>Recommendations</td>
</tr>
<tr>
<td>-----</td>
<td>-----</td>
<td>-----------------</td>
</tr>
<tr>
<td>IIb</td>
<td>A</td>
<td>In patients with STEMI or NSTEMI treated with <strong>coronary stent implantation</strong> who have tolerated DAPT without a bleeding complication and who are <strong>not at high bleeding risk</strong> continuation of <strong>DAPT for longer than 12 months</strong> may be reasonable. (e.g., prior bleeding on DAPT, coagulopathy, oral anticoagulant use)</td>
</tr>
<tr>
<td>IIb</td>
<td>C-LD</td>
<td>In patients with STEMI or NSTEMI after <strong>DES</strong> implantation who develop <strong>a high risk of bleeding</strong>, or <strong>develop significant overt bleeding</strong>, <strong>discontinuation of P2Y\textsubscript{12} inhibitor therapy after 6 months</strong> may be reasonable. (e.g., treatment with oral anticoagulant therapy, major intracranial surgery)</td>
</tr>
<tr>
<td>III: Harm</td>
<td>B-R</td>
<td><strong>Prasugrel should not be administered</strong> to patients with a prior history of stroke or TIA.</td>
</tr>
</tbody>
</table>

**SR** indicates systematic review.
**DAPT in Stable Ischemic Heart Disease (SIHD)**

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>A</td>
<td>In patients with SIHD, after <strong>BMS</strong> implantation, <strong>clopidogrel</strong> should be given for a minimum of <strong>1 month</strong> (NB – <strong>NO</strong> ticagrelor nor prasugrel)</td>
</tr>
<tr>
<td>I</td>
<td>B-R</td>
<td>SR In patients with SIHD after <strong>DES</strong> implantation, therapy with <strong>clopidogrel</strong> should be given for <strong>at least 6 months</strong> (NB – <strong>NO</strong> ticagrelor nor prasugrel)</td>
</tr>
<tr>
<td>I</td>
<td>B-NR</td>
<td>In patients treated with DAPT, the recommended daily dose of aspirin is <strong>81 mg</strong> (range, 75 mg to 100 mg).</td>
</tr>
</tbody>
</table>

SR indicates systematic review.

Levine et al. 2016 ACC/AHA Guideline DAPT with CAD; *Circulation.* 2016;133
## DAPT in SIHD

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIb</td>
<td>A</td>
<td>In patients with SIHD after <strong>BMS or DES</strong> implantation who have tolerated DAPT without a bleeding complication and who are <strong>not at high bleeding risk</strong> continuation of <strong>clopidogrel for longer than 1 month</strong> in patients treated with BMS or longer than 6 months in patients treated with DES may be reasonable. (e.g., prior bleeding on DAPT, coagulopathy, oral anticoagulant use)</td>
</tr>
<tr>
<td>IIb</td>
<td>C-LD</td>
<td>In patients with SIHD treated with DAPT after <strong>DES</strong> implantation who develop a <strong>high risk of bleeding</strong> or develop significant overt bleeding, <strong>discontinuation of clopidogrel therapy after 3 months</strong> may be reasonable. (e.g., treatment with oral anticoagulant therapy), are at high risk of severe bleeding complication (e.g., major intracranial surgery)</td>
</tr>
</tbody>
</table>

SR indicates systematic review.

Levine et al. 2016 ACC/AHA Guideline DAPT with CAD; *Circulation.* 2016;133
What about triple therapy?

- Assess ischemic and bleeding risks using validated risk predictors (e.g., CHA2DS2-VASc, HAS-BLED)
- Keep triple therapy duration as short as possible; dual therapy only (oral anticoagulant and clopidogrel) may be considered in select patients
- Consider a target INR of 2.0–2.5 when warfarin is used
- Clopidogrel is the P2Y12 inhibitor of choice
- Use low-dose (≤100 mg daily) aspirin
- PPIs should be used in patients with a history of gastrointestinal bleeding and are reasonable to use in patients with increased risk of gastrointestinal
Antiplatelet therapy non-responders

- Adverse cardiovascular events on DAPT believed 2/2 variable pharmacodynamic efficacy of P2Y12 or ASA
- Patients with "high on-treatment platelet reactivity" (HPR) have been labeled as being nonresponsive, hyporesponsive, or resistant
  - observational studies have demonstrated a link between HPR and recurrent ischemic events in stented patients
- The totality of evidence to support prospective evaluation of personalized antiplatelet therapy based on platelet function is neither consistent nor complete
  - ACC/AHA and ESC Guidelines do not recommend platelet reactivity testing on a routine basis at this time
- Clinically, treatment failure is best defined as the occurrence of a thrombotic event/ischemic event during DAPT
  - Non-compliance
  - Inadequate response to the antiplatelet therapy
  - Mechanical issue with stent
- Clinical judgement needed for adjustment of DAPT

Circulation. 2012 Mar;125(10):1276-87
Summary – DAPT in CAD

- Fundamental trade-off between decreasing ischemic risk and increasing bleeding risk
  - Complex decision making process

- ACS with DES
  - P2Y12 for at least one year (including BMS), ticagrelor/prasugrel preferred
  - Discontinuation of P2Y12 at 6 months may be reasonable
  - Continuation of P2Y12 beyond 30 months may be reasonable
  - DAPT calculator not in guidelines (but validated clinically)

- SIHD with DES
  - P2Y12 for at least six months preferred (clopidogrel)

- Lifelong SAPT (usually ASA 81mg) is recommended for all pt’s with stents unless:
  - Brain/SC surgery, Posterior eye chamber, TURP
  - Some debate in patients on systemic anticoagulation

- Personalized antiplatelet therapy based on platelet function is neither consistent nor complete and not routinely recommended