Audience Response and Q&A System Instructions

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  • Locate and open the session
  • Tap or click “Polling/Social Q&A” button

• On your phone, tablet or laptop via web browser
  • URL: aha2019.cnf.io
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Polls will appear on your device when speakers activate slides containing ARS questions.
Ticagrelor with Aspirin or Alone in High-Risk Patients after Coronary Intervention for ACS

- Discussant -

Michelle L. O’Donoghue, MD MPH
Senior Investigator, TIMI Study Group
Associate Professor, Harvard Medical School
CV Division, Brigham and Women’s Hospital
Audience Response Question

Q: What is your current practice regarding use of DAPT for patients who are stented in the setting of ACS? (in absence of known need for anticoagulation)

a) **Indefinite** use of both ASA and P2Y12 inhibitor
b) **Indefinite** use of ASA and **discontinue** P2Y12 inhibitor after 12 months
c) **Indefinite** use of ASA and **discontinue** P2Y12 inhibitor after 3-12 months
d) **Discontinue** ASA after 1-3 months in all patients and **continue** ticagrelor or prasugrel alone
e) **Discontinue** ASA after 1-3 months in all patients and **continue** clopidogrel alone
f) **Discontinue** ASA after 1-3 months only in patients at **high bleeding risk** and continue P2Y12i
Poll: Q: What is your current practice regarding use of DAPT for patients who are stented in the setting of ACS? (in absence of known need for anticoagulation)
More Prolonged DAPT Reduces Ischemic Events Post MI

### Event Rate (%)

- **MACE**
  - Aspirin Alone: 6.4%
  - Extended DAPT: 4.4%
  - Relative Risk (RR): 0.70
  - P Value: 0.003

- **CV Death**
  - Aspirin Alone: 2.3%
  - Extended DAPT: 2.6%
  - RR: 0.85
  - P Value: 0.03

- **MI**
  - Aspirin Alone: 3.5%
  - Extended DAPT: 1.7%
  - RR: 0.81
  - P Value: 0.02

- **Stroke**
  - Aspirin Alone: 1.4%
  - Extended DAPT: 1.4%
  - RR: 0.50
  - P Value: 0.02

### Definitions
- **MACE**: CV Death, MI, Stroke
- **Stent Thrombosis** (Def/Prob)

** RR 0.78  
P = 0.001

** RR 0.85  
P = 0.03

** RR 0.70  
P = 0.003

** RR 0.81  
P = 0.02

** RR 0.50  
P = 0.02

More Prolonged DAPT Increases Risk of Bleeding

- **RR 1.73** \( P = 0.004 \)
- **RR 1.03** \( P = NS \)
- **RR 0.92** \( P = NS \)

Aspirin vs Clopidogrel: Evidence to Date

CAPRIE: 19,185 patients with recent stroke, MI or symptomatic PAD

Vascular death, MI or ischemic stroke

Bleeding Complications

<table>
<thead>
<tr>
<th></th>
<th>Clopidogrel alone</th>
<th>ASA alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any GI bleed</td>
<td>1.99%</td>
<td>2.66%</td>
</tr>
<tr>
<td>Severe GI bleed</td>
<td>0.49%</td>
<td>0.71%</td>
</tr>
<tr>
<td>ICH</td>
<td>0.35%</td>
<td>0.49%</td>
</tr>
</tbody>
</table>

RRR 8.7% (95% CI 0.3-16.5)

p = 0.043

CAPRIE Steering Committee. Lancet 1996; 348:1329
TWILIGHT-ACS: Study Design

High-Risk PCI Patients (N=9006)

Enrollment Period
3 Months

Randomization Period
12 Months

Randomization

ACS= 4614

Double-blind

Ticagrelor + Aspirin

Ticagrelor + Placebo

Key Features

• Current analysis restricted to ACS cohort (65% of randomized pts)
• All patients required to have ≥1 high-risk clinical and angiographic feature
• ≥50% had ≥4 high-risk clinical or angiographic features (including 35% DM, 61% w/ multi-vessel dz); STEMI excluded
• Comparable adherence between Rx arms
TWILIGHT-ACS: Primary Results

Placebo vs Aspirin
HR (95%CI): 0.47 (0.36 to 0.61)
p < 0.001

Placebo vs Aspirin
HR (95%CI): 0.97 (0.74 to 1.28)
p = 0.84

Baber et al., AHA Scientific Sessions 2019

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P2Y12 Monotherapy vs DAPT: Evidence to Date

**GLOBAL LEADERS**
- Open label, 18 countries
- 15,968 pts w/ ACS (47%) or stable CAD post DES
- Experimental arm: Ticagrelor monotherapy post M1
- Control arm: Clopi (stable CAD) or ticagrelor (ACS) x12mos + ASA 75-100mg

**SMART-CHOICE**
- Open label, 33 sites in Korea
- 2993 pts w/ ACS (58%) or stable CAD post DES
- Experimental arm: ASA discontinued at M3 then any P2Y12 inhibitor monotherapy
- Control arm: Any P2Y12 inhibitor + ASA

**STOP DAPT-2**
- Open label, 90 sites in Japan
- 3045 pts w/ ACS (38%) or stable CAD post DES
- Experimental arm: Clopidogrel monotherapy post M1
- Control arm: Clopidogrel + ASA

**twilight**
- Double-blind, 11 countries
- 7119 pts w/ NSTEACS (65%) or stable CAD post DES
- Experimental arm: Ticagrelor monotherapy post M3
- Control arm: Ticagrelor + ASA

Safety & Efficacy of Monotherapy with P2Y12 Inhibitor vs DAPT 1-3m post PCI

**Primary Bleeding Outcome**

<table>
<thead>
<tr>
<th>Study</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GLOBAL LEADERS</strong> (n=15968)</td>
<td>0.86 (0.67-1.11)</td>
</tr>
<tr>
<td>(Open-label; 47% ACS; BL-M12)</td>
<td></td>
</tr>
<tr>
<td><strong>SMART CHOICE</strong> (n=2993)</td>
<td>0.58 (0.36-0.92)</td>
</tr>
<tr>
<td>(Open-label; 58% ACS; BL-M12)</td>
<td></td>
</tr>
<tr>
<td><strong>STOP DAPT 2</strong> (n=3045)</td>
<td>0.26 (0.11-0.64)</td>
</tr>
<tr>
<td>(Open-label; 38% ACS; BL-M12)</td>
<td></td>
</tr>
<tr>
<td><strong>TWILIGHT</strong> (n=7199)</td>
<td>0.56 (0.45-0.68)</td>
</tr>
<tr>
<td>(Double-blind; 65% NSTEACS; M3-M15)</td>
<td></td>
</tr>
<tr>
<td><strong>OVERALL</strong> (n=29,125)</td>
<td>0.60 (0.42-0.84)</td>
</tr>
</tbody>
</table>

**MACE**

<table>
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<tr>
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</tr>
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<tbody>
<tr>
<td><strong>GLOBAL LEADERS</strong> (n=15968)</td>
<td>0.83 (0.69-1.00)</td>
</tr>
<tr>
<td><strong>SMART CHOICE</strong> (n=2993)</td>
<td>1.19 (0.76-1.85)</td>
</tr>
<tr>
<td><strong>STOP DAPT 2</strong> (n=3045)</td>
<td>0.79 (0.49-1.29)</td>
</tr>
<tr>
<td><strong>TWILIGHT</strong> (n=7199)</td>
<td>0.99 (0.78-1.25)</td>
</tr>
<tr>
<td><strong>OVERALL</strong> (n=29,125)</td>
<td>0.91 (0.79-1.04)</td>
</tr>
</tbody>
</table>

O’Donoghue ML et al., Unpublished

Safety & Efficacy of Monotherapy with P2Y12 inhibitor vs DAPT 1-3m post ACS

### Primary Bleeding Outcome

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<tr>
<th>Study</th>
<th>HR (95% CI)</th>
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<tr>
<td>GLOBAL LEADERS ACS</td>
<td>0.52 (0.33-0.81)</td>
</tr>
<tr>
<td>SMART CHOICE ACS</td>
<td>0.56 (0.30-1.05)</td>
</tr>
<tr>
<td>TWILIGHT ACS</td>
<td>0.47 (0.36-0.61)</td>
</tr>
<tr>
<td>OVERALL</td>
<td>0.49 (0.40-0.61)</td>
</tr>
</tbody>
</table>

### MACE

<table>
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<tr>
<th>Study</th>
<th>HR (95% CI)</th>
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</thead>
<tbody>
<tr>
<td>GLOBAL LEADERS ACS</td>
<td>0.73 (0.51-1.03)</td>
</tr>
<tr>
<td>SMART CHOICE ACS</td>
<td>1.06 (0.61-1.85)</td>
</tr>
<tr>
<td>TWILIGHT ACS</td>
<td>0.97 (0.73-1.28)</td>
</tr>
<tr>
<td>OVERALL</td>
<td>0.89 (0.73-1.09)</td>
</tr>
</tbody>
</table>

O'Donoghue ML et al., Unpublished

MACE data for STOP DAPT2 in ACS not previously published

Tomiak et al., JAMA Cardiol 2019:epub; Hahn et al., JAMA 2019;321:2428; Watanabe et al., JAMA 2019;321:2414; Mehran et al., NEJM 2019:epub

ScientificSessions.org #AHA19
Remaining Questions

• For patients on monotherapy, which P2Y12 inhibitor is best choice?
  ➢ Should we require genotyping or platelet function testing for patients on clopidogrel monotherapy?

• Could ASA be safely discontinued before 1-3 months?

• Beyond M12, should a P2Y12 inhibitor be continued indefinitely without ASA?

• Even though the study population was high-risk, patient selection always raises questions about universal generalizability.

• Current study excluded STEMI patients, although reasonable representation across prior trials.
Conclusions

• Discontinuation of aspirin markedly reduces bleeding when stopped 1-3 months post PCI and/or ACS for patients initially started on DAPT

• The evidence to date does not indicate that stopping ASA leads to any increase in the risk of MACE

• These findings now extend to patients with ACS, including those with high-risk clinical and angiographic features