(313-L01) Rolling the Dice with Triple Therapy

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Disclosure

- The program chair and presenters for this continuing education activity have reported no relevant financial relationships.
Antithrombotic therapy for ACS

- Aspirin
- Clopidogrel
- Prasugrel
- Ticagrelor
- Vorapaxar
- Cilostazol
- Combination therapy – Dual Antiplatelet Therapy (DAPT)
- Oral Anticoagulation (OAC)
  - “Triple Therapy”
    - DAPT + OAC
    - Triple antiplatelet therapy
DAPT: How did it get here?
CURE study

NSTEMI presenting within 24 hours of symptom onset
(n = 12562)

Clopidogrel 300mg load then 75mg daily + aspirin 75-325 mg daily for 3-12 months
(n=6259)

Placebo + aspirin 75-325 mg daily
(n= 6303)

Primary endpoint: CV death + stroke + MI
Mean follow-up: 9 months

## CURE: Efficacy results

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Clopidogrel</th>
<th>Placebo</th>
<th>RRR</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CV death/MI/Stroke (primary endpoint)</td>
<td>9.3%</td>
<td>11.8%</td>
<td>20%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>MI</td>
<td>5.2%</td>
<td>6.7%</td>
<td>23%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.2%</td>
<td>1.4%</td>
<td>14%</td>
<td>NS</td>
</tr>
<tr>
<td>CV Death</td>
<td>5.1%</td>
<td>5.5%</td>
<td>7%</td>
<td>NS</td>
</tr>
</tbody>
</table>

Number needed to treat to prevent one primary endpoint event = 40 patients for 9 months

## CURE: Safety results

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Clopidogrel</th>
<th>Placebo</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major bleeding</td>
<td>3.7%</td>
<td>2.7%</td>
<td>0.001</td>
</tr>
<tr>
<td>Life-threatening bleeding</td>
<td>2.2%</td>
<td>1.8%</td>
<td>NS</td>
</tr>
<tr>
<td>Non life-threatening bleeding</td>
<td>1.5%</td>
<td>0.9%</td>
<td>0.002</td>
</tr>
<tr>
<td>Minor bleeding</td>
<td>5.1%</td>
<td>2.4%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Transfusion of ≥ 2 units blood</td>
<td>2.8%</td>
<td>2.2%</td>
<td>0.02</td>
</tr>
<tr>
<td>Total bleeding complications</td>
<td>8.5%</td>
<td>5%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Number needed to harm = 100**

Major bleeding episodes were defined as substantially disabling bleeding, intraocular bleeding leading to the loss of vision, or bleeding necessitating the transfusion of at least 2 units of blood.

Minor bleeding: other hemorrhages that led to interruption of study medication.
## CURE: Life-threatening bleeding

<table>
<thead>
<tr>
<th>Event</th>
<th>Clopidogrel</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Life-threatening</td>
<td>2.2%</td>
<td>1.8%</td>
</tr>
<tr>
<td>Fatal bleeding</td>
<td>0.2%</td>
<td>0.2%</td>
</tr>
<tr>
<td>Hemoglobin drop &gt; 5 g/dL</td>
<td>0.9%</td>
<td>0.9%</td>
</tr>
<tr>
<td>Hypotension requiring inotropes</td>
<td>0.5%</td>
<td>0.5%</td>
</tr>
<tr>
<td>Hemorrhagic stroke</td>
<td>0.1%</td>
<td>0.1%</td>
</tr>
<tr>
<td>Surgery required</td>
<td>0.7%</td>
<td>0.7%</td>
</tr>
<tr>
<td>Received &gt; 4 units of blood</td>
<td>1.2%</td>
<td>1.0%</td>
</tr>
</tbody>
</table>
CURE: Conclusions

- Clopidogrel use associated with a 20% RRR in the primary endpoint:
  - Driven by reduction in MI
- Major bleeding increased by 38%
  - No difference in life-threatening bleeding
  - Minor and total bleeding were significantly increased

Complications of Stents

- Stent thrombosis
  - This is a complication of ALL stents
  - Is the most feared complication
  - Is the timing of thrombosis different?

- What are the concerns with stent thrombosis?

- Can the risk be modified or minimized?

Stent Thrombosis: Why are we concerned?

- Present as MI
  - Usually STEMI

- Always requires emergent PCI for management
- 30-day mortality: 10 – 25 %
- Recurrence: 20% will have a second episode within 2 years

P2Y$_{12}$ inhibitor therapy should be **given for 1 year** to patients with STEMI treated with coronary stents during primary PCI using the following maintenance doses:

- Clopidogrel 75 mg daily; or
- Prasugrel 10 mg daily; or
- Ticagrelor 90 mg twice a day

Continuation of a P2Y$_{12}$ inhibitor **beyond 1 year** may be considered in patients undergoing DES placement.

Duration of DAPT per NSTEMI Guideline

P2Y$_{12}$ inhibitor therapy should be given for at least 1 year to post PCI patients treated with coronary stents using the following maintenance doses:

- Clopidogrel 75 mg daily; or
- Prasugrel 10 mg daily; or
- Ticagrelor 90 mg twice a day

P2Y$_{12}$ inhibitor therapy should be given for up to 1 year in patients who do not receive coronary stents using the maintenance doses:

- Clopidogrel 75 mg daily; or
- Ticagrelor 90 mg twice a day

Continuation of a P2Y$_{12}$ inhibitor beyond 1 year may be considered in patients undergoing stent implantation

Amsterdam E, et al. J Am Coll Cardiol. 2014;64:e139-228
P2Y$_{12}$ inhibitor therapy should be **given for at least 1 year** to post PCI patients treated with coronary stents for ACS, using the following maintenance doses:

- Clopidogrel 75 mg daily; or
- Prasugrel 10 mg daily; or
- Ticagrelor 90 mg twice a day

Continuation of DAPT beyond 12 months may be considered in patients undergoing DES placement.

Clopidogrel should be given to patients receiving drug-eluting stents for a non-ACS indication for at least 12 months if the patients are not at high risk of bleeding; or in patients receiving bare metal stents for a non-ACS indication for a minimum of 1 month, but ideally for 12 months:

- If the patient received a bare metal stent and is at increased risk of bleeding, then clopidogrel should be given for a minimum of 2 weeks.
Dual antiplatelet therapy (DAPT) Study

- Objectives:
  - In patients with DES: whether DAPT beyond 12 months is associated with:
    - reduction in stent thrombosis and/or
    - major adverse cardiovascular and cerebrovascular events (MACCE)
      - Defined as a composite of: Death, MI, stroke
  - To determine the impact of prolonged DAPT on moderate or severe bleeding

DAPT Study Design

12 Month observational period: Open label ASA + wallen (n: 25,682)

THIENOPYRIDINE + ASPIRIN (n: 5020)

PLACEBO + ASPIRIN (n: 4941)

3-Month observational period: On ASA, off Thienopyridine

Time in months after index stent procedure

Thienopyridine: Clopidogrel (65%), Prasugrel (35%) of patients enrolled

Results: MACCE Endpoint

Primary Analysis Period

- 12-30 Months: HR 0.71 (0.59-0.85)
- 4.3% vs. 5.9%
- P<0.001

Cumulative Incidence of Death, Myocardial Infarction or Stroke

Months After Enrollment

<table>
<thead>
<tr>
<th># At Risk</th>
<th>Treatment Ends</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thienopyridine</td>
<td>5020</td>
</tr>
<tr>
<td>Placebo</td>
<td>4941</td>
</tr>
</tbody>
</table>

Results: Stent Thrombosis

Results: Myocardial Infarction

55% of these events were NOT RELATED to stent thrombosis

Primary Analysis Period

12-30 Months:
HR 0.47 (0.37-0.61)
2.1% vs. 4.1%
P<0.001

DAPT: Safety results

![Graph showing safety results for Thienopyridine and Placebo.

- Moderate or severe bleeding: Thienopyridine 2.5%, Placebo 1.6%, p=0.001
- Moderate bleeding: Thienopyridine 1.7%, Placebo 1.0%, p=0.004
- Severe bleeding: Thienopyridine 0.8%, Placebo 0.6%, p=0.15]
DAPT Score: New risk tool to help?

- **Objective:**
  - To develop a decision tool to identify whether a patient is more or less likely to benefit from prolonged DAPT beyond 1 year
  - Account for risks of recurrent ischemia and bleeding simultaneously

- **Derived from patients in DAPT trial**
  - Those that tolerated DAPT for at least one year
  - Important to review DAPT trial exclusion criteria
    - These patients would not apply to the risk scoring system

Yeh RW. JAMA 2016;315:1735-1749.
# DAPT Score

<table>
<thead>
<tr>
<th>Variable</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient Characteristics</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Age:</strong></td>
<td></td>
</tr>
<tr>
<td>≥ 75 years-old</td>
<td>- 2</td>
</tr>
<tr>
<td>65 – 74</td>
<td>- 1</td>
</tr>
<tr>
<td>≤ 64</td>
<td>0</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1</td>
</tr>
<tr>
<td>Current cigarette smoker</td>
<td>1</td>
</tr>
<tr>
<td>Prior PCI or prior MI</td>
<td>1</td>
</tr>
<tr>
<td>CHF or LVEF &lt; 30%</td>
<td>2</td>
</tr>
<tr>
<td><strong>Index Procedure Characteristic</strong></td>
<td></td>
</tr>
<tr>
<td>MI at presentation</td>
<td>1</td>
</tr>
<tr>
<td>Vein graft PCI</td>
<td>2</td>
</tr>
<tr>
<td>Stent Diameter &lt; 3 mm</td>
<td>1</td>
</tr>
<tr>
<td><strong>TOTAL SCORE</strong></td>
<td>-2 – 10 points</td>
</tr>
</tbody>
</table>

Yeh RW. JAMA 2016;315:1735-1749.
DAPT Score

- DAPT score may help identify patients where:
  - Ischemic benefits outweigh the risks of bleeding
  - Bleeding outweighs risk of ischemic events

Yeh RW. JAMA 2016;315:1735-1749.
Aspirin and Warfarin in ACS
# Aspirin and Warfarin in ACS

<table>
<thead>
<tr>
<th>Study</th>
<th>Subjects, n</th>
<th>ASA alone</th>
<th>Warfarin alone</th>
<th>ASA + Warfarin</th>
<th>HR (95%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHAMP†</td>
<td>5059</td>
<td>31.4</td>
<td>30.9</td>
<td>1.01</td>
<td>(0.9-1.14)</td>
<td>NS</td>
</tr>
<tr>
<td>ASPECT-2†</td>
<td>993</td>
<td>9</td>
<td>5</td>
<td>5</td>
<td>0.52</td>
<td>(0.28-0.98)</td>
</tr>
<tr>
<td>APRICOT-2*</td>
<td>274</td>
<td>34</td>
<td>14</td>
<td></td>
<td></td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>WARIS-II†</td>
<td>3630</td>
<td>20</td>
<td>16.7</td>
<td>15</td>
<td>0.71</td>
<td>(0.6-0.83)</td>
</tr>
</tbody>
</table>

†= death, MI, or stroke; *= Death, reinfarction, revascularization

When complications arise...

- ACS-associated complications
  - Atrial fibrillation
  - Prosthetic Heart Valves
  - Left ventricular thrombus
  - VTE
ACTIVE Trials

Adults in AF or 2 AF episodes in last 6 months

Active A
- Aspirin
- Aspirin + Clopidogrel

Active W
- Aspirin + Clopidogrel
- VKA

1° Outcome: Composite of stroke, non-CNS systemic embolism, MI, CV death
2° Outcome: Stroke; individual outcomes of composite, bleeding, net clinical benefit

Connolly SJ, et al. NEJM 2009; 360: 2066-78
## ACTIVE-A

<table>
<thead>
<tr>
<th></th>
<th>Clopidogrel/ASA n (%/yr)</th>
<th>ASA n (%/yr)</th>
<th>RR (95%)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ischemic Outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary Outcome</td>
<td>832 (6.8)</td>
<td>924 (7.6)</td>
<td>0.89 (0.81-0.98)</td>
<td>0.01</td>
</tr>
<tr>
<td>Stroke</td>
<td>296 (2.4)</td>
<td>408 (3.3)</td>
<td>0.72 (0.62-0.83)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MI</td>
<td>90 (0.7)</td>
<td>115 (0.9)</td>
<td>0.78 (0.59-1.03)</td>
<td>0.08</td>
</tr>
<tr>
<td>Non-CNS embolism</td>
<td>54 (0.4)</td>
<td>56 (0.4)</td>
<td>0.96 (0.66-1.4)</td>
<td>0.84</td>
</tr>
<tr>
<td>Death</td>
<td>825 (6.4)</td>
<td>841 (6.6)</td>
<td>0.98 (0.89-1.08)</td>
<td>0.69</td>
</tr>
<tr>
<td><strong>Bleeding</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major</td>
<td>251 (2)</td>
<td>162 (1.3)</td>
<td>1.57 (1.29-1.92)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Minor</td>
<td>408 (3.5)</td>
<td>175 (1.4)</td>
<td>2.24 (2.03-2.89)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Any Bleeding</td>
<td>1014 (9.7)</td>
<td>651 (5.7)</td>
<td>1.68 (1.52-1.85)</td>
<td>0.001</td>
</tr>
<tr>
<td>Net Clinical Benefit</td>
<td>968</td>
<td>996</td>
<td>0.97 (0.89-1.06)</td>
<td>0.54</td>
</tr>
</tbody>
</table>

Connolly SJ, et al. NEJM 2009; 360: 2066-78
<table>
<thead>
<tr>
<th></th>
<th>Clopidogrel/ASA n (%/yr)</th>
<th>ASA n (%/yr)</th>
<th>RR (95%)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ischemic events</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary Outcome</td>
<td>234 (5.6)</td>
<td>165 (3.93)</td>
<td>1.44 (1.18-1.76)</td>
<td>0.0003</td>
</tr>
<tr>
<td>Stroke</td>
<td>100 (2.39)</td>
<td>59 (1.4)</td>
<td>1.72 (1.24-2.37)</td>
<td>0.001</td>
</tr>
<tr>
<td>MI</td>
<td>36 (0.86)</td>
<td>23 (0.55)</td>
<td>1.58 (0.94-2.67)</td>
<td>0.09</td>
</tr>
<tr>
<td>Non-CNS embolism</td>
<td>18 (0.43)</td>
<td>4 (0.1)</td>
<td>4.66 (1.58-13.8)</td>
<td>0.005</td>
</tr>
<tr>
<td>Death</td>
<td>159 (3.8)</td>
<td>158 (3.76)</td>
<td>0.93 (0.45-1.94)</td>
<td>0.85</td>
</tr>
<tr>
<td><strong>Bleeding Events</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major</td>
<td>101 (2.42)</td>
<td>93 (2.21)</td>
<td>1.10 (0.83-1.45)</td>
<td>0.53</td>
</tr>
<tr>
<td>Minor</td>
<td>568 (13.58)</td>
<td>481 (11.45)</td>
<td>1.23 (1.09-139)</td>
<td>0.0009</td>
</tr>
<tr>
<td>Any Bleeding</td>
<td>644 (15.40)</td>
<td>555 (13.21)</td>
<td>1.21 (1.08-1.35)</td>
<td>0.001</td>
</tr>
<tr>
<td>Net clinical benefit</td>
<td>316 (7.56)</td>
<td>229 (5.45)</td>
<td>1.41 (1.19-1.67)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Thrombosis

- No data for treating active thrombosis (LVT or VTE) with antiplatelet therapy alone
Triple Therapy

- Triple therapy is defined as dual-antiplatelet therapy (DAPT) with concomitant oral anticoagulation.
Guidelines
“In patients undergoing PCI, bare-metal stents may be considered to minimized the required duration of DAPT. Anticoagulation may be interrupted at the time of the procedure to reduce the risk of bleeding at the site of peripheral arterial puncture. (Level Of Evidence: C)”

“Following coronary revascularization (percutaneous or surgical) in patients with AF and a CHA2DS2-VASc score of ≥2, it may be reasonable to use Clopidogrel concurrently with oral anticoagulants but without aspirin. (Level Of Evidence: B)”
2015 EHS Guidelines for Management of ACS in Patients Presenting Without Persistent STEMI

For those patients being treated with triple therapy:

- Assess ischemic/bleeding risk with validated risk predictors (CHA$_2$DS$_2$-VASc, HAS-BLED)
- Keep TT duration as short as possible
- Consider warfarin target INR 2.0 – 2.5
- Clopidogrel is the P2Y$_{12}$ inhibitor of choice
- Use low-dose (≤ 100mg daily) Aspirin
- Use concomitant PPI therapy if history of GI bleed or at increased risk of GI bleed

Case 1

AJ is a 68 year-old man with a history of recent NSTE-ACS which was treated with a drug-eluting stent to his LAD who presented to his primary care physicians office complaining of progressively worsening shortness of breath over the past week. An ECG obtained in the office reveals atrial fibrillation and AJ is referred to the hospital for further management. While in the hospital, the team decides to manage AJ with rate control.
Case 1

- Past Medical History:
  - Hypertension
  - Diabetes
  - CAD
    - s/p MI 3 months ago
  - Osteoarthritis
  - Allergic rhinitis

- Social History:
  - Current smoker – 1 pack/day

- Current Medications:
  - Aspirin 81 mg daily
  - Prasugrel 10 mg daily
  - Atorvastatin 80 mg daily
  - Lisinopril 10 mg daily
  - Amlodipine 5 mg daily
  - Metformin 1000 mg BID
  - Sitagliptin 100 mg daily
  - Loratadine 10 mg daily
Case # 2

BW is an 75 year-old woman with a history of aortic stenosis (AS), who was admitted to the hospital for consideration of valve replacement secondary to repeated heart failure admissions due to AS. She was in the hospital for management of volume overload with intravenous loop diuretics for 5 days.

- The surgery team is consulted and agrees that she is a candidate for surgical aortic valve replacement
- BW receives a mechanical aortic valve, and is now out of the ICU and on the step-down floor
Case # 2

- **Past Medical History**
  - Hypertension
  - Aortic Stenosis
  - CAD
  - Taxus DES placed in her left circumflex artery 15 months ago
  - Osteoporosis
  - GERD

- **Medications:**
  - Aspirin 81 mg daily
  - Atorvastatin 40 mg daily
  - Vitamin D 2000 units daily
  - Calcium 500 mg TID
  - Pantoprazole 40 mg daily
  - Clopidogrel 75 mg daily (currently holding)
  - Warfarin dosed to target INR 2-3

Surgical team pages you for recommendations:  Clopidogrel
Making the case for triple therapy
APPRAISE-2

ACS presenting with within last 7 days and 2 additional risk factors:
- Age >65
- Diabetes
- MI in last 5 yrs
- Cerebrovascular disease
- Peripheral vascular disease
- Heart failure
- CrCl <60 ml/min
- No revascularization

Apixaban 5mg BID + Standard Therapy*

Placebo+ Standard Therapy*

Primary Outcome: Composite of cardiovascular death, MI, or CVA.
Primary Safety Outcome: TIMI-major bleeding

APPRAISE-2

- No significant difference in the primary outcome:

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Apixaban N=3705</th>
<th>Placebo N=3687</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CV death, MI, ischemic stroke</td>
<td>7.5</td>
<td>7.9</td>
<td>0.509</td>
</tr>
<tr>
<td>CV death, MI, ischemic stroke, UA</td>
<td>9.5</td>
<td>10</td>
<td>0.430</td>
</tr>
<tr>
<td>Death</td>
<td>4.2</td>
<td>3.9</td>
<td>0.514</td>
</tr>
<tr>
<td>CV death</td>
<td>2.8</td>
<td>2.9</td>
<td>0.754</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>4.9</td>
<td>5.3</td>
<td>0.509</td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td>0.6</td>
<td>0.9</td>
<td>0.145</td>
</tr>
<tr>
<td>Unstable angina</td>
<td>2.3</td>
<td>2.4</td>
<td>0.670</td>
</tr>
<tr>
<td>Definite stent thrombosis</td>
<td>0.9</td>
<td>1.3</td>
<td>0.150</td>
</tr>
</tbody>
</table>

# Appraise 2: Major Bleeding

<table>
<thead>
<tr>
<th></th>
<th>Apixaban N=3705</th>
<th>Placebo N=3687</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIMI major</td>
<td>1.3</td>
<td>0.5</td>
<td>0.001</td>
</tr>
<tr>
<td>TIMI major or minor</td>
<td>2.2</td>
<td>0.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ISTH major</td>
<td>2.7</td>
<td>1.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ISTH major or clinically relevant non-major</td>
<td>3.2</td>
<td>1.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GUSTO severe</td>
<td>1.0</td>
<td>0.3</td>
<td>0.001</td>
</tr>
<tr>
<td>Intracranial</td>
<td>0.3</td>
<td>0.1</td>
<td>0.030</td>
</tr>
</tbody>
</table>
Appraise 2: Conclusions

- The addition of apixaban to contemporary antiplatelet therapy increases major bleeding
  - No significant reduction in ischemic events
- Adding an anticoagulant to currently recommended anti-platelet treatment post-ACS should be used cautiously
  - only in patients with clear indications for both an anticoagulant and antiplatelet therapy.
- Further research is needed to explore different antithrombotic combinations and doses that might have a different risk-benefit ratio
ATLAS-ACS 2 – TIMI 51

Stabilized patients with ACS within last 7 days
- If <55 yo, must also have DM or prior MI

Rivaroxaban 2.5mg BID
Rivaroxaban 5mg BID
Placebo

Primary Outcome:
Composite of cardiovascular death, MI, or CVA

Primary Safety Outcome:
Non-CABG TIMI-major bleeding

Months After Randomization

**PRIMARY EFFICACY ENDPOINT:**

Rivaroxaban (both doses)

HR 0.84 (0.74-0.96)
ARR 1.7%
NNT = 59

Estimated Cumulative Rate (%)

Placebo

Rivaroxaban (both doses)

Primary Endpoint: 2.5 mg BID Dose

- CV Death/MI/Stroke: P=0.007
- CV Death: P=0.005
- All cause Death: P=0.004

## ATLAS-ACS 2

<table>
<thead>
<tr>
<th>Event</th>
<th>2.5 mg BID (N=5114)</th>
<th>5 mg BID (N=5115)</th>
<th>Combined (N=10,229)</th>
<th>Placebo (N=5113)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIMI major bleeding not associated with CABG</td>
<td>65 (1.8)</td>
<td>82 (2.4)</td>
<td>147 (2.1)</td>
<td>19 (0.6)</td>
</tr>
<tr>
<td>TIMI minor bleeding</td>
<td>32 (0.9)</td>
<td>49 (1.6)</td>
<td>81 (1.3)</td>
<td>20 (0.5)</td>
</tr>
<tr>
<td>TIMI bleeding requiring medical attention</td>
<td>492 (12.9)</td>
<td>637 (16.2)</td>
<td>1129 (145)</td>
<td>282 (7.5)</td>
</tr>
<tr>
<td>Intracranial hemorrhage</td>
<td>14 (0.4)</td>
<td>18 (0.7)</td>
<td>32 (0.6)</td>
<td>5 (0.2)</td>
</tr>
<tr>
<td>Fatal bleeding</td>
<td>6 (0.1)</td>
<td>15 (0.4)</td>
<td>21 (0.3)</td>
<td>9 (0.2)</td>
</tr>
</tbody>
</table>

ATLAS-ACS 2: Conclusions

- The primary efficacy endpoint of CV death, MI and stroke was reduced when added to standard therapy for both rivaroxaban.
- CV and all cause death were reduced in the rivaroxaban 2.5 mg BID group.
  - When 2.5 mg PO BID of rivaroxaban was added to ASA + thienopyridine, cardiovascular death was reduced by 38% and all cause death by 36%.
- These doses are not currently FDA approved.
- Does the dose/intensity of anticoagulation need to be lower with DOACs when combined with DAPT.
Danish National Patient Registry

- 2 separate cohort studies using data from the national EMR
  - Patients admitted with first-time MI (2000-2005)
  - Admissions with atrial fibrillation as primary or secondary diagnosis (1997-2006)

- Included subjects >30 yo who received prescriptions for aspirin, clopidogrel, warfarin, or any combination of the three

- 1° Outcome: Bleeding events per patient-year
  - AF study also looked at stroke incidence

## Danish National Patient Registry

<table>
<thead>
<tr>
<th></th>
<th>Patients treated for AF</th>
<th>Patients treated for MI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Incidence (% per person-yr)</td>
<td>Unadjusted risk ratio (95% CI)</td>
</tr>
<tr>
<td>ASA alone</td>
<td>3.7</td>
<td>0.96 (0.95 – 0.96)</td>
</tr>
<tr>
<td>Clopidogrel Alone</td>
<td>5.6</td>
<td>1.45 (1.22 – 1.66)</td>
</tr>
<tr>
<td>VKA alone</td>
<td>3.9</td>
<td>Reference</td>
</tr>
<tr>
<td>ASA/Clopidogrel</td>
<td>7.4</td>
<td>1.91 (1.59 – 2.21)</td>
</tr>
<tr>
<td>ASA/VKA</td>
<td>6.9</td>
<td>1.75 (1.71 – 1.79)</td>
</tr>
<tr>
<td>Clopidogrel/VKA</td>
<td>13.9</td>
<td>3.57 (2.88 – 4.22)</td>
</tr>
<tr>
<td>Triple Therapy</td>
<td>15.7</td>
<td>4.03 (3.22 – 4.78)</td>
</tr>
</tbody>
</table>

Danish National Patient Registry

Hazard Ratios (HRs) for the risk of Non-fatal (n=9758) and fatal (n=3537) ischemic strokes by group

- Warfarin Monotherapy
- Aspirin Monotherapy
- Clopidogrel Monotherapy
- Aspirin + Clopidogrel
- Warfarin + Aspirin
- Warfarin + Clopidogrel
- Triple Therapy
Age 18-80 years old with an indication for PCI and a clear need for ≥ one year oral anticoagulation

- Warfarin, Clopidogrel, ASA
- Warfarin and Clopidogrel

WOEST

- **Primary Endpoint:**
  - Bleeding rates (TIMI, GUSTO, BARC)

- **Secondary Endpoint:**
  - Composite of death, MI, stroke, target vessel revascularization, and stent thrombosis
  - Each item individually

Primary Endpoint:
Total number of TIMI bleeding events

![Graph showing cumulative incidence of bleeding over time for triple and double therapy groups.](graph.png)

- **Triple therapy group**: 44.9%
- **Double therapy group**: 19.5%

\[ \text{p}<0.001 \]
\[ \text{HR}=0.36 \quad 95\%\text{CI}[0.26-0.50] \]

Primary Endpoint:
Bleeding events TIMI classification

Double therapy group
Triple therapy group

<table>
<thead>
<tr>
<th>TIMI Level</th>
<th>Double Therapy</th>
<th>Triple Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimal</td>
<td>6.5</td>
<td>16.7</td>
</tr>
<tr>
<td>TIMI Minor</td>
<td>11.2</td>
<td>27.2</td>
</tr>
<tr>
<td>TIMI Major</td>
<td>3.3</td>
<td>5.8</td>
</tr>
<tr>
<td>Any TIMI bleeding</td>
<td>19.5</td>
<td>44.9</td>
</tr>
</tbody>
</table>

p<0.001  p<0.001  p=0.159  p<0.001
WOEST: Secondary Endpoint

- Death: 2.6% (Double therapy group) vs. 6.4% (Triple therapy group)
- MI: 3.3% (Double therapy group) vs. 4.7% (Triple therapy group)
- TVR: 7.3% (Double therapy group) vs. 6.8% (Triple therapy group)
- Stroke: 1.1% (Double therapy group) vs. 2.9% (Triple therapy group)
- ST: 1.5% (Double therapy group) vs. 3.2% (Triple therapy group)
WOEST: Conclusions

- First randomized trial to address the optimal antiplatelet therapy in patients on OAC undergoing coronary stenting
  - OAC plus clopidogrel causes less bleeding than triple antithrombotic therapy
  - Secondary endpoint was met: with double therapy there is no excess of thrombotic/thromboembolic events
  - Less all-cause mortality with double therapy

- The study was powered to show superiority on the primary bleeding endpoint, but not to show non-inferiority on the secondary endpoint
RE-LY Trial

- Use of antiplatelet therapy at any point during trial was 38.4%
  - Aspirin alone = 32%
  - Clopidogrel alone = 1.9%
  - DAPT = 4.5%

Hazard ratios for stroke and systemic embolism, major bleeding and other outcomes for patients with and without concomitant antiplatelet therapy.

RE-LY Trial

Event rate (%/year)

Major Bleed
- Warfarin, No Antiplatelet: 2.8
- Warfarin with SAPT: 6.3
- Warfarin with DAPT: 5.5
- Dabigatran 150, No Antiplatelet: 4.6
- Dabigatran 150 with SAPT: 3.5
- Dabigatran 150 with DAPT: 5.4
- Dabigatran 110, No Antiplatelet: 2.2
- Dabigatran 110 with SAPT: 2.2
- Dabigatran 110 with DAPT: 3.8

Minor Bleed
- Warfarin, No Antiplatelet: 2.6
- Warfarin with SAPT: 14.4
- Warfarin with DAPT: 19.0
- Dabigatran 150, No Antiplatelet: 4.3
- Dabigatran 150 with SAPT: 13.4
- Dabigatran 150 with DAPT: 16.8
- Dabigatran 110, No Antiplatelet: 3.8
- Dabigatran 110 with SAPT: 11.7
- Dabigatran 110 with DAPT: 15.5

Extracranial Bleed
- Warfarin, No Antiplatelet: 2.2
- Warfarin with SAPT: 11.7
- Warfarin with DAPT: 15.5
- Dabigatran 150, No Antiplatelet: 3.7
- Dabigatran 150 with SAPT: 15.7
- Dabigatran 150 with DAPT: 20.9
- Dabigatran 110, No Antiplatelet: 2.4
- Dabigatran 110 with SAPT: 2.6
- Dabigatran 110 with DAPT: 2.8

Intracranial Bleed
- Warfarin, No Antiplatelet: 0.5
- Warfarin with SAPT: 0.7
- Warfarin with DAPT: 0.7
- Dabigatran 150, No Antiplatelet: 0.7
- Dabigatran 150 with SAPT: 0.4
- Dabigatran 150 with DAPT: 0.4
- Dabigatran 110, No Antiplatelet: 0.2
- Dabigatran 110 with SAPT: 0.2
- Dabigatran 110 with DAPT: 0.2

WAR-STENT Registry

- Prospective, multicenter, observational study of patients already on warfarin who are undergoing PCI with stenting
  - Evaluations performed for both the index hospitalization and 12-month follow-up
  - Comparison groups: TT, DT, and DAPT

- Outcomes:
  - Incidence of MACE (CV death, MI, revascularization, stroke, VTE)
  - TIMI major and minor bleeding
WAR-STENT Registry

Low thromboembolic risk
- CHADS$_2$ <2
- Bioprosthetic heart valve
- Remote VTE history
- Dilated cardiomyopathy
- LV aneurysm

Non-low thromboembolic risk
- CHADS$_2$ ≥2
- Mechanical heart valve
- Prior cardiogenic embolism
- Intracardiac thrombus
- VTE in last 6 months

WAR-STENT Registry

In hospital:

<table>
<thead>
<tr>
<th></th>
<th>Overall (n= 411)</th>
<th>Low Thromboembolic Risk (n=31)</th>
<th>Non-Low Thromboembolic Risk (n=380)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major adverse cardiovascular events</td>
<td>11 (2.7%)</td>
<td>0</td>
<td>11 (2.9%)</td>
<td>0.71</td>
</tr>
<tr>
<td>Death</td>
<td>7 (1.7%)</td>
<td>0</td>
<td>7 (1.8%)</td>
<td>0.44</td>
</tr>
<tr>
<td>Non-fatal MI</td>
<td>1 (0.2%)</td>
<td>0</td>
<td>1 (0.2%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Stroke</td>
<td>3 (0.7%)</td>
<td>0</td>
<td>3 (0.8%)</td>
<td>1.00</td>
</tr>
<tr>
<td>DVT/PE</td>
<td>0</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>9 (2.1%)</td>
<td>0</td>
<td>9 (2.3%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Minor bleeding</td>
<td>20 (4.8%)</td>
<td>3 (9.6%)</td>
<td>17 (4.4%)</td>
<td>0.18</td>
</tr>
</tbody>
</table>

All access-site bleeding occurred inpatients undergoing PCI via the femoral approach

WAR-STENT Registry

- At 12-month follow-up
  - NS difference in MACE, both composite and individually
  - Bleeding:
    - Total bleeding events: no difference across groups
    - MAJOR bleeds: no difference across groups
    - MINOR bleeds: significantly more for the TT group

AFCAS Registry

- Prospective, multicenter, observational study of patients with atrial fibrillation who are undergoing PCI with stenting
  - Follow-up performed at months 1, 3, 6, and 12

- Outcomes:
  - MACCE (mortality, MI, revascularization, ST, CVA/TIA)
  - Bleeding (per BARC criteria)
  - Total adverse events (MACCE plus bleeding)

AFCAS Registry

- At baseline, triple therapy was more often prescribed if:
  - Permanent atrial fibrillation at baseline
  - ACS was the indication for PCI
  - Those with a prior history of venous thromboembolism
  - Multiple stents were placed

## AFCAS Registry

<table>
<thead>
<tr>
<th></th>
<th>TT, n=679</th>
<th>DAPT, n=162</th>
<th>VKA/C, n=73</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total MACCE, n (%)</td>
<td>147 (22)</td>
<td>33 (20)</td>
<td>13 (18)</td>
<td>0.72</td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td>14 (2)</td>
<td>7 (4)</td>
<td>1 (1)</td>
<td>0.2</td>
</tr>
<tr>
<td>Peripheral embolism</td>
<td>6 (1)</td>
<td>1 (0.6)</td>
<td>0</td>
<td>0.69</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>43 (6)</td>
<td>4 (3)</td>
<td>4 (6)</td>
<td>0.16</td>
</tr>
<tr>
<td>Revascularization</td>
<td>54 (8)</td>
<td>10 (6)</td>
<td>7 (10)</td>
<td>0.62</td>
</tr>
<tr>
<td>Definite/Probable stent thrombosis</td>
<td>9 (1)</td>
<td>3 (2)</td>
<td>2 (3)</td>
<td>0.6</td>
</tr>
<tr>
<td>All cause mortality, n (%)</td>
<td>75 (11)</td>
<td>18 (11)</td>
<td>5 (7)</td>
<td>0.54</td>
</tr>
</tbody>
</table>

Abbreviations: DAPT, dual antiplatelet therapy; MACCE, major adverse cardiac/cerebrovascular events; TIA, transient ischemic attack; TT, triple therapy; VKA, vitamin K antagonist; VKA/C, vitamin K antagonist plus clopidogrel.
### AFCAS Registry

<table>
<thead>
<tr>
<th></th>
<th>TT, n=679</th>
<th>DAPT, n=162</th>
<th>VKA/C, n=73</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total bleedings, n (%)</td>
<td>119 (18)</td>
<td>33 (20)</td>
<td>12 (16)</td>
<td>0.66</td>
</tr>
<tr>
<td>Minor (BARC 2)</td>
<td>51 (8)</td>
<td>13 (8)</td>
<td>7 (10)</td>
<td>0.81</td>
</tr>
<tr>
<td>Major, n (%)</td>
<td>69 (10)</td>
<td>20 (12)</td>
<td>5 (7)</td>
<td>0.43</td>
</tr>
<tr>
<td>BARC 3a</td>
<td>31 (5)</td>
<td>6 (4)</td>
<td>4 (6)</td>
<td>0.82</td>
</tr>
<tr>
<td>BARC 3b</td>
<td>20 (3)</td>
<td>12 (8)</td>
<td>0</td>
<td>0.005</td>
</tr>
<tr>
<td>BARC 3c</td>
<td>7 (1)</td>
<td>2 (1)</td>
<td>1 (1)</td>
<td>0.95</td>
</tr>
<tr>
<td>BARC 5</td>
<td>10 (2)</td>
<td>0</td>
<td>0</td>
<td>0.17</td>
</tr>
<tr>
<td>Total events, n (%) (MACCE + bleeding)</td>
<td>219 (40)</td>
<td>56 (40)</td>
<td>21 (34)</td>
<td>0.67</td>
</tr>
</tbody>
</table>

Abbreviations: BARC, Bleeding Academic Research Consortium; DAPT, dual antiplatelet therapy; MACCE, major adverse cardiac/cerebrovascular events; TIA, transient ischemic attack; TT, triple therapy; VKA, vitamin K antagonist; VKA/C, vitamin K antagonist plus clopidogrel.

ISAR TRIPLE

Adults who require oral anticoagulation with ACS/Angina receiving new DES

VKA & ASA for all

Clopidogrel 75mg daily for 6 weeks

Clopidogrel 75mg daily for 6 months

Fiedler, et al. JACC, 2015; 65(16): 1619-29
ISAR TRIPLE

- Primary Endpoint: composite of death, MI, definite ST, stroke, and TIMI-major bleed
- Secondary Endpoints:
  - Composite of ischemic events
  - Composite of bleeding events
  - Each event individually

Fiedler, et al. JACC, 2015; 65(16): 1619-29
ISAR-Triple: Results

Death, myocardial infarction, stent thrombosis, stroke or TIMI major bleeding

HR 1.14 (95%, CI 0.68 – 1.91), p=0.63

Fiedler, et al. JACC, 2015; 65(16): 1619-29
### ISAR-Triple: Results

<table>
<thead>
<tr>
<th></th>
<th>6-week group (n=307)</th>
<th>6-month group (n=307)</th>
<th>Hazard Ratio (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>4%</td>
<td>5.2%</td>
<td>0.75 (0.35 – 1.59)</td>
<td>0.45</td>
</tr>
<tr>
<td>Cardiac Death</td>
<td>1.7%</td>
<td>3%</td>
<td>0.56 (0.19 – 1.66)</td>
<td>0.29</td>
</tr>
<tr>
<td>MI</td>
<td>2%</td>
<td>0</td>
<td>-</td>
<td>0.03</td>
</tr>
<tr>
<td>Definite stent thrombosis</td>
<td>0.7%</td>
<td>0</td>
<td>-</td>
<td>0.50</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.3%</td>
<td>2%</td>
<td>0.67 (0.14 – 2.78)</td>
<td>0.75</td>
</tr>
</tbody>
</table>
| Ischemic stroke          | 1%                   | 1.3%                  | 0.75 (0.11 – 4.40)    | 0.99    

Fiedler, et al. JACC, 2015; 65(16): 1619-29
ISAR-Triple: Major Bleeding (BARC)

HR 0.94 (0.73 - 1.21), p=0.63

Cumulative Incidence (%)

Months After Randomization

Fiedler, et al. JACC, 2015; 65(16): 1619-29
PIioneer AF-PCI: A Study Exploring Two Strategies of Rivaroxaban and One of Oral VKA in Patients with AF who undergo PCI

Adults with history of AF who have undergone PCI with stent placement

Stratified by intended duration of DAPT

1° Outcome: TIMI clinically significant bleeding
2° Outcome: time to bleeds, MACE, composite of bleed/MACE events

Questions still remain...

- How long do we keep triple therapy?
- When de-escalating, which OAP do we keep?
- What about P2Y\textsubscript{12}-inhibitors other than Clopidogrel?
- What about the other DOACs?
- What is the long-term risk of thromboembolic complications?
On the horizon...
WOEST-2 Registry

- Prospective, multicenter, non-interventional cohort study involving patients with AF and/or prosthetic heart valves undergoing coronary revascularization
  - Chronic therapy with any oral anticoagulation
  - Receiving any P2Y$_{12}$-inhibitor concomitantly

- Outcomes:
  - Composite of non-fatal MI or stroke, systemic embolism, and cardiovascular death
  - Bleeding episodes requiring hospitalization or change in antithrombotic therapy

https://clinicaltrials.gov/ct2/show/NCT02635230
REDUAL-PCI: Evaluation of Dual Therapy With Dabigatran vs. Triple Therapy With Warfarin in Patients With AF That Undergo a PCI With Stenting

Adults >18 yo with non-valvular atrial fibrillation being treated for ACS/angina with PCI-S (DES or BMS)

Dabigatran 110mg BID plus Clopidogrel or Ticagrelor

Dabigatran 150mg BID plus Clopidogrel or Ticagrelor

Warfarin (INR 2.0-3.0) plus Aspirin plus Clopidogrel or Ticagrelor

1° Outcome: time to first ISTH major bleed or clinically relevant non-major bleed
2° Outcomes: death, non-CV death, CV death, MI, CVA, SE, ST, composites

https://clinicaltrials.gov/ct2/show/NCT02164864
GEMINI-ACS 1: Safety of Rivaroxaban vs ASA in addition to either Clopidogrel or Ticagrelor therapy in participants with ACS

Adult with ACS event ≤48 hrs
(<55 yo must also have DM or prior-MI)

- Rivaroxaban plus Clopidogrel or Ticagrelor
- Aspirin plus Clopidogrel or Ticagrelor

1° Outcome: TIMI clinically significant bleeding events

RT-AF: Rivaroxaban in Patients With Atrial Fibrillation and Coronary Artery Disease Undergoing PCI

- Age 18-80 yo with indication for long-term anticoagulation and severe coronary lesion undergoing PCI
- Rivaroxaban 2.5-5 mg BID
  - Ticagrelor 90 mg BID
- Warfarin (INR 1.8 – 2.5)
  - Aspirin 100 mg daily
  - Clopidogrel 75mg daily

1° Outcome: Major or clinically relevant bleeding (ISTH)
2° Outcome: Composite of death/MI/ST/Ischemic stroke

AUGUSTUS Trial: Apixaban vs VKA in Patients With AF and ACS or PCI

Adults with AF on oral anticoagulation with stent placement \( \leq 2 \) weeks with planned P2Y\(_{12}\) use for at least 6 months

**6 months P2Y\(_{12}\) inhibitor for all**

1° Outcome: ISTH major or clinically non-major bleeding events by group

2° Outcomes: Bleeding, MACE, re-hospitalizations

[Link to ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/NCT02415400)
APPROACH-ACS-AF: Apixaban vs Phenprocoumon in Patients with ACS and AF

Adult patients with ACS post-PCI requiring oral anticoagulation for AF/Aflutter (CHADS_2 VASc ≥2)

Apixaban 5mg/d plus Clopidogrel 75mg/d for 6 months

Phenprocoumon (INR 2.0 – 3.0), Aspirin, and Clopidogrel

HAS-BLED <3: Triple therapy for 6 months

HAS-BLED 3: Triple therapy for one month, then Phenprocoumon & Clopidogrel alone

1° Outcome: BARC type ≥2 bleeding

2° Outcome: composite of death, MI, ST, CVA/SE; all individually

https://clinicaltrials.gov/ct2/show/NCT02789917
EDOX-APT Trial: Edoxaban in Patients with Coronary Artery Disease on Dual Antiplatelet Therapy with Aspirin and Clopidogrel

Adults with angiographically documented CAD who have completed at least 30 days DAPT

1° Outcome: Clot strength +/- Edoxaban, TEG high-dose edoxaban vs DAPT
2° Outcome: Clot strength +/- Aspirin, TEG high-dose edoxaban + DAPT vs high-dose edoxaban + clopidogrel

https://www.clinicaltrials.gov/ct2/show/NCT02567461
Case 1

- AJ is a 68 year-old man with a history of recent NSTE-ACS which was treated with a drug-eluting stent to his LAD who presented to his primary care physicians office complaining of progressively worsening shortness of breath over the past week. An ECG obtained in the office reveals atrial fibrillation and AJ is referred to the hospital for further management. While in the hospital, the team decides to manage AJ with rate control.
Case 1

- **Past Medical History:**
  - Hypertension
  - Diabetes
  - CAD
    - s/p MI 3 months ago
  - Osteoarthritis
  - Allergic rhinitis

- **Social History:**
  - Current smoker – 1 pack/day

- **Current Medications:**
  - Aspirin 81 mg daily
  - Prasugrel 10 mg daily
  - Atorvastatin 80 mg daily
  - Lisinopril 10 mg daily
  - Amlodipine 5 mg daily
  - Metformin 1000 mg BID
  - Sitagliptin 100 mg daily
  - Loratadine 10 mg daily
Case 1: Question # 1

Which of the following would you recommend to reduce the risk of stroke in AJ?

a) Continue DAPT
b) Discontinue prasugrel
c) Add warfarin
d) Add a DOAC
Case 1: Question # 2

AJ chooses to be placed on anticoagulation therapy. Which of the following would you suggest at this time?

- a) Discontinue aspirin, add warfarin
- b) Switch prasugrel to clopidogrel, add warfarin
- c) Continue aspirin, prasugrel, add warfarin
- d) Continue aspirin, prasugrel, add DOAC
- e) Switch prasugrel to clopidogrel, add DOAC
Case # 2

- BW is an 75 year-old woman with a history of aortic stenosis (AS), who was admitted to the hospital for consideration of valve replacement secondary to repeated heart failure admissions due to AS. She was in the hospital for management of volume overload with intravenous loop diuretics for 5 days.
  - The surgery team is consulted and agrees that she is a candidate for surgical aortic valve replacement
  - BW receives a mechanical aortic valve, and is now out of the ICU and on the step-down floor
Case # 2

Past Medical History
- Hypertension
- Aortic Stenosis
- CAD
- Taxus DES placed in her left circumflex artery 15 months ago
- Osteoporosis
- GERD

Medications:
- Aspirin 81 mg daily
- Atorvastatin 40 mg daily
- Vitamin D 2000 units daily
- Calcium 500 mg TID
- Pantoprazole 40 mg daily
- Clopidogrel 75 mg daily (currently holding)
- Warfarin dosed to target INR 2-3

Surgical team pages you for recommendations: Clopidogrel
How would you manage BW’s antithrombotic therapy?

a) Continue triple therapy (aspirin, clopidogrel, warfarin)
b) Discontinue clopidogrel
c) Change warfarin to DOAC (aspirin, clopidogrel, DOAC)
d) Discontinue aspirin
Key Takeaways

- **Key Takeaway #1**
  - Triple therapy with DAPT + OAC increases bleeding, but is often unavoidable in clinical practice

- **Key Takeaway #2**
  - DAPT is recommended in patients with recent ACS and stent placement, and OAC alone does not provide protection

- **Key Takeaway #3**
  - OAC is superior to DAPT in stroke prevention in AF

- **Key Takeaway #4**
  - Dual therapy options with either single antiplatelet therapy plus OAC (either warfarin or DAOC) have potential, but ongoing clinical trial data will clarify the risks and benefits of this strategy compared with triple therapy
Questions?