Update on Dual Antiplatelet Therapy

Salma Chbib
B.Pharm., Pharm.D., BCCCP

Al Shorouk Hospital – Cleopatra Hospitals Group

2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS

The Task Force for dual antiplatelet therapy in coronary artery disease of the European Society of Cardiology (ESC) and of the European Association for Cardio-Thoracic Surgery (EACTS)
Dual Anti-platelet
What are our choices?

Thienopyridine
- Clopidogrel
- Prasugrel

Cyclopentyl-triazolopyrimidine
Non-thienopyridine derivative
- Ticagrelor

Irreversible
P2Y12 receptor inhibition

Reversible
P2Y12 receptor inhibition
**Clopidogrel**

**Onset**
2 hours after loading dose

**Doses**
Loading: 75 / 300 / 600 mg
Maintenance: 75 mg Every 24Hr

**CrCl < 15 mL/min**
No dose adjustment; use with caution

**Hepatic Impairment**
Child A – C: ✔

**Ticagrelor**

**Onset**
30 minutes after loading dose

**Doses**
Loading: 180 mg
Maintenance: 90 mg Every 12Hr

**CrCl < 15 mL/min**
Not recommended

**Child C:** ✗

---

**Clopidogrel**

**Contraindications**
Previous intracranial hemorrhage

**Withdrawal before surgery**
5 days

**Price per 7 days of treatment**
Plavix: 51.25 L.E./week

**Ticagrelor**

**Contraindications**

**Withdrawal before surgery**
3 days

**Price per 7 days of treatment**
Brilique: 86.5 L.E./week
Switching?
When is it recommended

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>In patients with ACS who were previously exposed to clopidogrel, switching from clopidogrel to ticagrelor is recommended early after hospital admission at a loading dose of 180 mg irrespective of timing and loading dose of clopidogrel, unless contra-indications to ticagrelor exist.</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Additional switching between oral P2Y_{12} inhibitors may be considered in cases of side effects/drug intolerance according to the proposed algorithms.</td>
<td>IIb</td>
<td>C</td>
</tr>
</tbody>
</table>

How to switch
How to switch in acute setting

LD after 24 hours last Ticagrelor
LD irrespective of prior Clopidogrel
Measures to minimize bleeding while on DAPT

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>In patients treated with DAPT, a daily aspirin dose of 75–100 mg is recommended.</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>A PPI in combination with DAPT is recommended.</td>
<td>I</td>
<td>B</td>
</tr>
</tbody>
</table>
What are the indications of DAPT

- STEMI treated with fibrinolytic
- ACS undergoing CABG
- ACS for medical treatment
- Stable CAD treated with PCI
- Stable CAD for medical treatment
- Stable CAD undergoing PCI
- Stable CAD undergoing CABG

Bleeding risk scores; What are they good for?
DAPT vs. Precise DAPT

- Tailoring the **duration**
  - $\uparrow$ ischemic protection / $\downarrow$ bleeding risk

---

### Table: PRECISE-DAPT score vs. DAPT score

<table>
<thead>
<tr>
<th>Time of use</th>
<th>Score calculation</th>
<th>Score range</th>
<th>Decision making cut-off suggested</th>
<th>Calculator</th>
</tr>
</thead>
<tbody>
<tr>
<td>At the time of coronary stenting</td>
<td></td>
<td>0 to 100 points</td>
<td>Score $\geq 5$ → Short DAPT</td>
<td><a href="http://www.precisedaptscore.com">www.precisedaptscore.com</a></td>
</tr>
<tr>
<td>After 12 months of uneventful DAPT</td>
<td></td>
<td>$-2$ to $10$ points</td>
<td>Score $&lt; 2$ → Standard DAPT</td>
<td><a href="http://www.daptstudy.org">www.daptstudy.org</a></td>
</tr>
</tbody>
</table>

---

**Recommendations**

The use of risk scores designed to evaluate the benefits and risks of different DAPT durations may be considered.
Irrespective of stent type ↓
1 – 6 months depending on bleeding risk

Duration of DAPT → Stable CAD patients treated with PCI

Clopidogrel ↓

Duration of DAPT → ACS patients

Default length of therapy: 1 year

Medical therapy
CABG
PCI

Six-month therapy in high bleeding risk patients
No bleeding complication at 1 year → DAPT > 1 yr
No bleeding complication at 1 year & high ischemic risk, defined as:

≥ 50 years of age, and one or more of the following features:

1. Age ≥ 65 years, 2. Diabetes mellitus requiring medication, 3. a second prior spontaneous myocardial infarction, 4. multivessel coronary artery disease or 5. chronic renal dysfunction CrCL< 60 mL/min

Ticagrelor 60mg Q12hrs up to 36 mo

Duration of DAPT

After lytic therapy

Evidence is in support of: 1 month of treatment

However

Invasive management afterwards / benefit of DAPT irrespective of whether revascularization takes place

It is reasonable to prolong DAPT further in these patient depending on the bleeding risk
Duration of DAPT

In patients requiring OAC

**Clopidogrel**

Duration up to 6 months in patients with high ischemic risk

1 month of triple therapy

Clopidogrel + OAC can be used from the beginning for patients with high bleeding risk

---

**Letter**

**Clinical characteristic**

**Points awarded**

<table>
<thead>
<tr>
<th>Letter</th>
<th>Clinical characteristic</th>
<th>Points awarded</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>Hypertension</td>
<td>1</td>
</tr>
<tr>
<td>A</td>
<td>Abnormal renal and liver function (1 point each)</td>
<td>1 or 2</td>
</tr>
<tr>
<td>S</td>
<td>Stroke</td>
<td>1</td>
</tr>
<tr>
<td>B</td>
<td>Bleeding</td>
<td>1</td>
</tr>
<tr>
<td>L</td>
<td>Labile INRs</td>
<td>1</td>
</tr>
<tr>
<td>E</td>
<td>Elderly (e.g. age &gt; 65 years)</td>
<td>1</td>
</tr>
<tr>
<td>D</td>
<td>Drugs or alcohol (1 point each)</td>
<td>1 or 2</td>
</tr>
</tbody>
</table>

Maximum 9 points

---

Duration of DAPT

In patients requiring OAC

**Strategies to avoid bleeding complications in patients treated with oral Anticoagulants**

- Assess ischaemic and bleeding risks using validated risk predictors (e.g. CHA2DS2-VASC, ABC, HAS-BLED) with a focus on modifiable risk factors.
- Keep triple therapy duration as short as possible; dual therapy after PCI (oral anticoagulant and clopidogrel) to be considered instead of triple therapy.
- Consider the use of NOACs instead of VKA.
- Consider a target INR in the lower part of the recommended target range and maximize time in therapeutic range (i.e. > 65–70%) when VKA is used.
- Consider the lower NOAC regimen tested in approval studies and apply other NOAC regimens based on drug-specific criteria for drug accumulation.
- Clopidogrel is the P2Y12 inhibitor of choice.
- Use low-dose (≤ 100 mg daily) aspirin.
- Routine use of PPIs.
Duration of DAPT

In patients requiring OAC

**Strategies to avoid bleeding complications in patients treated with oral anticoagulants**

Consider the lower NOAC regimen tested in approval studies and apply other NOAC regimens based on drug-specific criteria for drug accumulation.3

- Apixaban 5 mg b.i.d. or apixaban 2.5 mg b.i.d. if at least two of the following: age ≥80 years, body weight ≤60 kg or serum creatinine level ≥1.5 mg/dL (133 μmol/L); dabigatran 110 mg b.i.d.; edoxaban 60 mg q.d. or edoxaban 30 mg q.d. if any of the following: creatinine clearance (CrCl) of 30–50 mL/min, body weight ≤60 kg, concomitant use of verapamil or quinidine or dronedarone; rivaroxaban 20 mg q.d. or rivaroxaban 15 mg q.d. if CrCl 30–49 mL/min.

When rivaroxaban is used in combination with aspirin and/or clopidogrel, rivaroxaban 15 mg q.d. may be used instead of rivaroxaban 20 mg q.d.**

Except for dabigatran, the benefit of lower doses of NOAC, such as rivaroxaban 15 mg OD, in stroke prevention is uncertain

---

**Duration of DAPT**

In patients requiring OAC

**After 1 year**

**OAC alone**

In stabilized event-free patients; OAC + aspirin may not be more protective but associated with excess bleeding

**SAPT + OAC**

1. Patients at very high risk of coronary events
2. Patients with mechanical prosthesis and atherosclerotic disease.
References


European Society of Cardiology (2017) focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS

European Society of Cardiology (2017) Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation

Lexicomp®, Ticagrelor Monograph.

Lexicomp®, Clopidogrel Monograph.

Thank you