PCI IN HIGH BLEEDING RISK PATIENTS

GEORGIA KARABELA

INTERVENTIONAL CARDIOLOGY DEPARTMENT
METROPOLITAN HOSPITAL
NO CONFLICT OF INTEREST
TOPICS

DEFINITION OF HIGH BLEEDING RISK

ASSESSING BLEEDING RISK
- INCIDENCE OF BLEEDING POST-PCI

PERIPROCEDURAL MANAGEMENT OF ANTITHROMBOTIC THERAPY

WHAT TYPE OF STENT

ANTITHROMBOTIC THERAPY POST PCI
DURATION OF AGENT

STABLE vs. ACS
GUIDE LINES

SUMMARY
PATIENTS AT HIGH RISK OF BLEEDING

- Intensity of antithrombotic therapy: DAPT plus an oral anticoagulant
- 5-10% of pts scheduled for PCI are receiving oral anticoagulation

- Age ≥ 75 years
- Prior history of bleeding
- Heart failure
- Peripheral artery disease
- Hypertension
- Abnormal renal or liver function
- Stroke
- Anaemia
- Malignancy
- Chronic steroid use
## INCIDENCE OF BLEEDING POST-PCI

<table>
<thead>
<tr>
<th>Study</th>
<th>Incidence</th>
<th>Timeframe</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADAPT-DES study</td>
<td>8.582 pts</td>
<td>10 months</td>
<td>6.2%</td>
</tr>
<tr>
<td>EDUCATE registry</td>
<td>2.159 pts</td>
<td>6 months</td>
<td>2%</td>
</tr>
<tr>
<td>REGISTRY study</td>
<td>8.137 pts</td>
<td>30 days</td>
<td>4.8%</td>
</tr>
<tr>
<td>Second REGISTRY study</td>
<td>22.798 pts</td>
<td>12 months</td>
<td>2.5%</td>
</tr>
</tbody>
</table>

*JACC Cardiovasc Interv 2015*  
*J Am Coll Cardiol 2015*
## PROGNOSIS OF BLEEDING POST-PCI

<table>
<thead>
<tr>
<th>Study Type</th>
<th>pts</th>
<th>Increased Rate of All-Cause Mortality</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADAPT-DES study</td>
<td>8.582</td>
<td>Increased rate of all-cause mortality</td>
<td>P=0.006</td>
</tr>
<tr>
<td>EDUCATE registry</td>
<td>2.159</td>
<td>Higher risk for death or MI</td>
<td>P=0.001</td>
</tr>
<tr>
<td>REGISTRY study</td>
<td>8.137</td>
<td>Higher risk for death or MI</td>
<td>(HR): 7.16</td>
</tr>
<tr>
<td>Second REGISTRY study</td>
<td>22.798</td>
<td>Higher risk for death or MI</td>
<td>(HR): 3.38</td>
</tr>
</tbody>
</table>

*JACC Cardiovasc Interv 2015*

*J Am Coll Cardiol 2015*
## ASSESSING BLEEDING RISK

<table>
<thead>
<tr>
<th>HAS-BLED Risk Score</th>
<th>OBRI Risk Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension (SBP &gt;160 mmHg)</td>
<td>Age &gt;65 years</td>
</tr>
<tr>
<td>Abnormal renal/ liver function (1 point for each)</td>
<td>History of stroke</td>
</tr>
<tr>
<td>Stroke</td>
<td>History of GIB</td>
</tr>
<tr>
<td>Bleeding</td>
<td>Recent MI, HCT &lt;30%, Cr &gt;1.5 mg/dL, or diabetes mellitus</td>
</tr>
<tr>
<td>Labile INRs (TTR &lt;60%)</td>
<td></td>
</tr>
<tr>
<td>Elderly (age &gt;65 years)</td>
<td></td>
</tr>
<tr>
<td>Drugs (antiplatelet agents / NSAIDs) or excess alcohol (1 point for each)</td>
<td></td>
</tr>
</tbody>
</table>

*Eur Heart J 2010  
Circulation 2010*
### ABC-Bleeding risk calculation:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Option</th>
<th>Accepted range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior Bleeding</td>
<td>Yes/No</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td>Accepted range 44 - 90 (years)</td>
</tr>
<tr>
<td>hs-troponin T (ng/L)</td>
<td></td>
<td>Accepted range 3.3 - 66 (ng/L)</td>
</tr>
<tr>
<td>GDF-15 (ng/L)</td>
<td></td>
<td>Accepted range 450 - 7250 (ng/L)</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td></td>
<td>Accepted range 10.5 - 17.8 (g/dL)</td>
</tr>
</tbody>
</table>

[Calculate estimated risk]
Risk scores validated for dual antiplatelet therapy duration decision-making

<table>
<thead>
<tr>
<th></th>
<th>PRECISE-DAPT score</th>
<th>DAPT score</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Time of use</strong></td>
<td>At the time of coronary stenting</td>
<td>After 12 months of uneventful DAPT</td>
</tr>
<tr>
<td><strong>DAPT duration</strong></td>
<td>Short DAPT (3–6 months) vs. Standard/long DAPT (12–24 months)</td>
<td>Standard DAPT (12 months) vs. Long DAPT (30 months)</td>
</tr>
<tr>
<td>strategies assessed</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Score calculation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HB</td>
<td>≥2 11-5 11 10-5 ≤10</td>
<td>Age</td>
</tr>
<tr>
<td>WBC</td>
<td>≤5 6 10 12 14 16 18 ≥20</td>
<td>65 to &lt;75</td>
</tr>
<tr>
<td>Age</td>
<td>≤60 60 70 80 ≥90</td>
<td>&lt;65</td>
</tr>
<tr>
<td>CrCl</td>
<td>≥1.00 0.80 0.60 0.40 0.20 0</td>
<td>Cigarette smoking</td>
</tr>
<tr>
<td>Prior</td>
<td>No Yes</td>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>Bleeding</td>
<td></td>
<td>MI at presentation</td>
</tr>
<tr>
<td>Score</td>
<td>0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30</td>
<td>Prior PCI or prior MI</td>
</tr>
<tr>
<td>Points</td>
<td></td>
<td>Paclitaxel-eluting stent</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Stent diameter &lt;3 mm</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CHF or LVEF &lt;30%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vein graft stent</td>
</tr>
</tbody>
</table>

**Score range**: 0 to 100 points

**Decision making cut-off suggested**
- Score ≥25 → Short DAPT
- Score <25 → Standard/long DAPT

**Score range**: -2 to 10 points

**Decision making cut-off suggested**
- Score ≥22 → Long DAPT
- Score <2 → Standard DAPT

**Calculator**
- www.precisedaptscore.com
- www.daptstudy.org

[Image and text extracted from European Heart Journal (2017) 0, 1–48]
# Use of risk scores as guidance for the duration of dual antiplatelet therapy

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class (^a)</th>
<th>Level (^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>The use of risk scores designed to evaluate the benefits and risks of different DAPT durations(^c) may be considered.(^{15,18})</td>
<td>IIb</td>
<td>A</td>
</tr>
</tbody>
</table>

**DAPT** = dual antiplatelet therapy.

\(^{a}\) Class of recommendation.

\(^{b}\) Level of evidence.

\(^{c}\) The DAPT and PRECISE-DAPT scores are those currently fulfilling these requirements.
PCI IN HIGH BLEEDING RISK PATIENTS

PERIPROCEDURAL MANAGEMENT OF ANTITHROMBOTIC THERAPY
DUAL ANTIPLATELET THERAPY

Aspirin plus clopidogrel is the preferred combination for patients receiving OAC

For stable patients clopidogrel rather any other P2Y12 receptor blocker (Grade1A)
For patients with ACS clopidogrel rather any other P2Y12 receptor blocker (Grade1C) (600mg load, 75mg daily)
Exceptions include those who are allergic to clopidogrel and those with prior stent thrombosis while taking clopidogrel

Prasugrel was associated with a Greater risk of any Bleeding events with no significant difference in the thrombosis risk

Am Coll Cardiol 2013
TRANSLATE ACS Study
JACC Cardiovasc Interv 2015
ANTICOAGULANT MANAGEMENT

For patients taking warfarin:
Perform an elective PCI at the lower therapeutic INR level
Perform an urgent PCI
If INR <2: full dose heparin
If INR 2-2.5: reduced doses of heparin ACT: 200-225
If INR >2.5: reduced dose of heparin even further

For patients taking NOAC:
We stop the last dose about 24 hours before (Grade 2B)
In patients with renal insufficiency we give the last dose 36 to 48 hours before the procedure particularly with dabigatran

No need for bridging with LMWH (Exceptions include those with very high thrombotic risk)

Europace†2015
N Engl J Med 2013
PERIPROCEDURAL MANAGEMENT

The use of IIbIIIa inh. should be minimized

**Radial access** rather than the femoral artery decreases the risk of periprocedural bleeding

- If a transradial approach is not an option, careful management of femoral artery hemostasis including the use of a closure device

*JAMA 2014, 312:1981*
WHAT TYPE OF STENT

Some experts have suggested the earlier endothelialization seen with BMS compared with DES might lead to a relatively decreased risk of stent Thrombosis.

There is no high quality evidence that demonstrates that the use of BMS is superior to second generation DES in this setting.
The Zotarolimus-eluting Endeavor sprint stent in Uncertain DES candidates (ZEUS)

M. Valgimigli, MD, PhD
Erasmus MC, Rotterdam
The Netherlands

JACC Cardiovasc Interv 2016
N Engl J Med 2015, 373
Study Design

Urgent or emergent coronary stenting in pts fulfilling ≥1 of the below:

**High Bleeding Risk**
- Need for OACs
- Previous Relevant Bleeding
- Age > 80 y/o
- Bleeding diathesis
- Known Anemia (Hb<10 gr/dl)
- Need for CCS or NSAID

**High Thrombotic Risk**
- Intolerance to ASA
- Intolerance to any P2Y<sub>12</sub>
- Planned surgery w/in 1 year
- Cancer-life expectancy >1 Y
- Pro-thrombotic diathesis

**Low Restenosis Risk**
- Planned stent ≥3.0 mm, apart from LMCA and SVG intervention or for ISR lesions

Rx: 1:1, Sx: inclusion criteria

1,606 pts, 20 sites in *Italy, Switzerland, Portugal* and Hungary from June 2011 to September 2012

Endeavor Sprint Zotarolimus-eluting Stent

Primary Endpoint: Death, Myocardial Infarction or Target Vessel Revascularization at 12 months

Thin-strut Bare Metal Stent

*Am Heart J. 2013 Nov;166(5):831-8*
ZEUS trial
Major Adverse Cardiovascular events
primary endpoint

HR: 0.76 (0.61-0.95), P=0.011

2 pts, one in each group, were lost to follow-up after hospital discharge
ZEUS trial
Definite or Probable Stent Thrombosis

No. at Risk
BMS  804  763  739  723  712  701  692  685
E-ZES 802  767  758  741  733  721  713  708

HR: 0.48 (0.27-0.88), P=0.019
ZEUS trial
Bleeding events in the two groups

BARC scale

P=N.S. for all comparisons
Biolimus-Coated vs. Bare-Metal Coronary Stents in High Bleeding Risk Patients

Philip Urban, Alexandre Abizaid, Ian T. Meredith, Stuart J. Pocock, Didier Carrié, Christoph Naber, John Gregson, Samantha Greene, Hans Peter Stoll and Marie-Claude Morice for the LEADERS FREE Investigators
LEADERS FREE Trial Design

Prospective, double-blind randomized (1:1) trial
2466 High bleeding risk (HBR) PCI patients

- Primary safety endpoint:
  Composite of cardiac death, MI, definite / probable stent thrombosis
  at 1 year (non-inferiority then superiority)

- Primary efficacy endpoint:
  Clinically-driven TLR at 1 year (superiority)

DAPT mandated for 1 month only, followed by long-term SAPT

N Engl J Med 2015, 373
LEADERS FREE Trial Design
Primary Safety Endpoint (Cardiac Death, MI, ST)

Number at Risk

<table>
<thead>
<tr>
<th></th>
<th>DCS</th>
<th>BMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1221</td>
<td>1146</td>
<td>1105</td>
</tr>
<tr>
<td>1081</td>
<td>1066</td>
<td>1037</td>
</tr>
<tr>
<td>1045</td>
<td>1000</td>
<td></td>
</tr>
</tbody>
</table>

390 days chosen for assessing primary EP to capture potential events driven by the 360 day FU contact
**LEADERS FREE Trial Design**

**Primary Efficacy Endpoint (Clinically-Driven TLR)**

<table>
<thead>
<tr>
<th>Days</th>
<th>Cumulative Percentage with Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>90</td>
<td>9.8%</td>
</tr>
<tr>
<td>180</td>
<td>12%</td>
</tr>
<tr>
<td>270</td>
<td>390 days</td>
</tr>
<tr>
<td></td>
<td>P for superiority &lt; 0.001</td>
</tr>
</tbody>
</table>

**Number at Risk**

<table>
<thead>
<tr>
<th></th>
<th>DCS</th>
<th>BMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>1221</td>
<td>1211</td>
</tr>
<tr>
<td>90</td>
<td>1167</td>
<td>1131</td>
</tr>
<tr>
<td>180</td>
<td>1130</td>
<td>1072</td>
</tr>
<tr>
<td>270</td>
<td>1098</td>
<td>1034</td>
</tr>
<tr>
<td>390</td>
<td>1053</td>
<td>984</td>
</tr>
</tbody>
</table>

390 days chosen for assessing primary EP to capture potential events driven by the 360 day FU contact.
SENIOR: A Randomized Trial of a Bioabsorbable Polymer-Based Metallic DES vs a BMS With Short DAPT in Patients With Coronary Artery Disease Older Than 75 Years

Lancet 2018,391
THE SENIOR TRIAL DESIGN

Prospective, single-blind randomized (1:1) trial
1200 Patients ≥ 75 years old (stable synd. or ACS)

596 pts bioabsorbable polymer (synergy) DES

VS.

604 pts BMS

DAPT mandated for 1 month for stable and 6 months for ACS

• Primary endpoint:
  MACCE: Composite of cardiac death, MI, IDTLR or stroke

• Secondary endpoint:
  Bleeding, Thrombosis

Lancet 2018,391
THE SENIOR TRIAL

Primary endpoint:
MACCE: Composite of cardiac death, MI, IDTLR or stroke

Secondary outcomes for BP-DES vs. BMS:
BARC 2-5 bleeding: 4.5% vs. 5.0%, p = 0.68
Stent thrombosis: 0.5% vs. 1.4%, p = 0.13
ANTITHROMBOTIC THERAPY POST PCI

Duration of triple therapy
Stable and ACS

woest
Pionner
Isar triple
The WOEST Trial: First randomised trial comparing two regimens with and without aspirin in patients on oral anticoagulant therapy undergoing coronary stenting

Willem Dewilde, Tom Oirbans, Freek Verheugt, Johannes Kelder, Bart De Smet, Jean-Paul Herrman, Tom Adriaenssens, Mathias Vrolix, Antonius Heestermans, Marije Vis, Saman Rasoul, Kaioum Sheikjoesoef, Tom Vandendriessche, Carlos Van Mieghem, Kristoff Cornelis, Jeroen Vos, Guus Brueren, Nicolien Breet and Jurriën ten Berg

The WOEST Trial= What is the Optimal antiplatelet and anticoagulant therapy in patients with oral anticoagulation and coronary Stenting (clinicaltrials.gov NCT00769938)
573 patients underwent 1:1 randomization.

284 were assigned to Double therapy group:
- No PCI (n=3)
- Withdrawn informed consent (n=2)*
- Lost to follow up (n=1)
- Did not meet inclusion criteria (n=1)

289 were assigned to Triple therapy group:
- No PCI (n=1)
- Withdrawn informed consent (n=2)*
- Lost to follow up (n=1)
- Did not meet inclusion criteria (n=2)

279 patients were included in Intention to treat analysis

284 patients were included in Intention to treat analysis

* withdrawn informed consent; in double group 2 patients and triple group 1 patient were included in intention to treat analysis until the day of withdrawal.
MI=any myocardial infarction; TVR= target vessel revascularisation (PCI + CABG); ST= stent thrombosis
An Open-label, Randomized, Controlled, Multicenter Study Exploring Two Treatment Strategies of Rivaroxaban and a Dose-Adjusted Oral Vitamin K Antagonist Treatment Strategy in Subjects With Atrial Fibrillation Who Undergo Percutaneous Coronary Intervention PIONEER AF-PCI

Gibson et al. AHA 2016
Patients With Atrial Fibrillation Undergoing Coronary Stent Placement: PIONEER AF-PCI

- 2100 patients with NVAF
- Coronary stenting
- No prior stroke/TIA, GI bleeding, Hb<10, CrCl<30

Primary endpoint: TIMI major + minor + bleeding requiring medical attention
Secondary endpoint: CV death, MI, and stroke (Ischemic, Hemorrhagic, or Uncertain Origin)

- Rivaroxaban 15 mg qd*
  Clopidogrel 75 mg qd†

- Rivaroxaban 2.5 mg bid
  Clopidogrel 75 mg qd†
  Aspirin 75-100 mg qd‡

- Rivaroxaban 15 mg QD
  Aspirin 75-100 mg qd

- VKA (target INR 2.0-3.0)
  Clopidogrel 75 mg qd†
  Aspirin 75-100 mg qd

- VKA (target INR 2.0-3.0)
  Aspirin 75-100 mg qd

*Rivaroxaban dosed at 10 mg once daily in patients with CrCl of 30 to <50 mL/min.
†Alternative P2Y₁₂ inhibitors: 10 mg once-daily prasugrel or 90 mg twice-daily ticagrelor.
‡Low-dose aspirin (75-100 mg/d). ∆ Open label VKA

Gibson et al. AHA 2016
Kaplan-Meier Estimates of First Occurrence of Clinically Significant Bleeding Events

Treatment-emergent period: period starting after the first study drug administration following randomization and ending 2 days after stop of study drug. Clinically significant bleeding is the composite of TIMI major, TIMI minor, and BRMA.

Hazard ratios as compared to the VKA group are based on the (stratified, only for Overall, 2.5 mg BID/15 mg QD comparing VKA) Cox proportional hazards model. Log-Rank P-values as compared to VKA group are based on the (stratified, only for Overall, 2.5 mg BID/15 mg QD comparing VKA) two-sided log rank test.

Gibson et al. AHA 2016
Kaplan-Meier Estimates of First Occurrence of CV Death, MI or Stroke

Cardiovascular Death, Myocardial Infarction, or Stroke (%)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>0</th>
<th>30</th>
<th>60</th>
<th>90</th>
<th>180</th>
<th>270</th>
<th>360</th>
</tr>
</thead>
<tbody>
<tr>
<td>Riva + P2Y&lt;sub&gt;12&lt;/sub&gt;</td>
<td>694</td>
<td>648</td>
<td>633</td>
<td>621</td>
<td>590</td>
<td>562</td>
<td>430</td>
</tr>
<tr>
<td>Riva + DAPT</td>
<td>704</td>
<td>662</td>
<td>640</td>
<td>628</td>
<td>596</td>
<td>570</td>
<td>457</td>
</tr>
<tr>
<td>VKA + DAPT</td>
<td>695</td>
<td>635</td>
<td>607</td>
<td>579</td>
<td>543</td>
<td>514</td>
<td>408</td>
</tr>
</tbody>
</table>

Riva + P2Y<sub>12</sub> v. VKA + DAPT
HR=1.08 (95% CI: 0.69-1.68)
p=0.750

Riva + DAPT v. VKA + DAPT
HR=0.93 (95% CI: 0.59-1.48)
p=0.765

Treatment-emergent period: period starting after the first study drug administration following randomization and ending 2 days after stop of study drug.

Composite of adverse CV events is composite of CV death, MI, and stroke.

Hazard ratios as compared to VKA group are based on the (stratified, only for the Overall, 2.5 mg BID/15 mg QD comparing VKA) Cox proportional hazards model.

Log-Rank P-values as compared to the VKA group are based on the (stratified, only for Overall, 2.5 mg BID/115 mg QD comparing VKA) two-sided log rank test.

6 Subjects were excluded from all efficacy analyses because of violations in Good Clinical Practice guidelines.

Gibson et al. AHA 2016
In pts with AF undergoing PCI with placement of stents, the administration of either low-dose rivaroxaban plus a P2Y<sub>12</sub> inhibitor for 12 months or very-low-dose rivaroxaban plus DAPT for 1, 6, or 12 months was associated with a lower rate of clinically significant bleeding than was standard therapy with a vitamin K antagonist plus DAPT for 1, 6, or 12 months.

Gibson et al. AHA 2016
**ISAR-TRIPLE**

**Trial design:** Patients with an indication for oral anticoagulation (OAC) and undergoing DES PCI were randomized to either 6 weeks or 6 months of triple therapy (aspirin + clopidogrel + OAC initially, aspirin + OAC indefinitely). Patients were followed for 9 months.

**Results**

- Primary endpoint: Composite of death, MI, stent thrombosis, stroke, TIMI major bleeding at 9 months for 6 weeks vs. 6 months of triple therapy: 9.8% vs. 8.8%, HR 1.14, 95% CI 0.68-1.91, p = 0.63
- Cardiac death, MI, stent thrombosis, ischemic stroke: 4.0% vs. 4.3%, p = 0.87; TIMI major bleeding: 5.3% vs. 4.0%, p = 0.44
- Stent thrombosis: 0.7% vs. 0%

**Conclusions**

- 6-week duration of triple therapy is not superior to a 6-month duration of triple therapy in patients undergoing DES PCI, who also had an indication for OAC use
- Trial was underpowered to assess smaller bleeding differences

*J Am Coll Cardiol. 2015*
ISAR-TRIPLE TRIAL

To evaluate clinical outcomes of a therapy duration of

6 weeks clopidogrel

versus

6 months clopidogrel

after DES implantation in patients receiving concomitantly aspirin and oral anticoagulation
ISAR-TRIPLE TRIAL
Secondary endpoint

Cardiac death, myocardial infarction, stent thrombosis or ischemic stroke

HR 0.93 (0.43 - 2.05), p=0.87

TIMI major bleeding

HR 1.35 (0.64 - 2.84), p=0.44

J Am Coll Cardiol. 2015
Algorithm for dual antiplatelet therapy (DAPT) in patients treated with percutaneous coronary intervention

Percutaneous Coronary Intervention

Treatment indication
- Stable Coronary Artery Disease
  - DES/BMS or DCB
    - High Bleeding Risk
      - No
        - 6 mo. DAPT
          - Class I A'
      - Yes
        - 1 mo. DAPT
          - Class IIb C
- Acute Coronary Syndrome
  - DES/BMS or DCB
    - BRS
    - High Bleeding Risk
      - No
        - 6 mo. DAPT
          - Class IIa B
      - Yes
## Dual antiplatelet therapy duration in patients with indication for oral anticoagulation

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>It is recommended to administer periprocedurally aspirin and clopidogrel in patients undergoing coronary stent implantation.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>In patients treated with coronary stent implantation, triple therapy with aspirin, clopidogrel and OAC should be considered for 1 month, irrespective of the type of stent used.</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>Triple therapy with aspirin, clopidogrel and OAC for longer than 1 month and up to 6 months should be considered in patients with high ischaemic risk due to ACS or other anatomical/procedural characteristics, which outweigh the bleeding risk.</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>Dual therapy with clopidogrel 75 mg/day and OAC should be considered as an alternative to 1-month triple antithrombotic therapy in patients in whom the bleeding risk outweighs the ischaemic risk.</td>
<td>IIa</td>
<td>A</td>
</tr>
</tbody>
</table>
Dual antiplatelet therapy duration in patients with indication for oral anticoagulation (continued)

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discontinuation of antiplatelet treatment in patients treated with OAC should be considered at 12 months.</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>In patients with an indication for VKA in combination with aspirin and/or clopidogrel, the dose intensity of VKA should be carefully regulated with a target INR in the lower part of the recommended target range and a time in the therapeutic range &gt;65–70%.</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>When a NOAC is used in combination with aspirin and/or clopidogrel, the lowest approved dose effective for stroke prevention tested in AFib trials should be considered.</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>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.</td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td>The use of ticagrelor or prasugrel is not recommended as part of triple antithrombotic therapy with aspirin and OAC.</td>
<td>III</td>
<td>C</td>
</tr>
</tbody>
</table>
Management need to be individualized based on careful consideration of patient characteristics as well as patient preferences.