ΕΛΛΗΝΙΚΗ ΚΑΡΔΙΟΛΟΓΙΚΗ ΕΤΑΙΡΕΙΑ
ΠΑΝΕΛΛΗΝΙΑ ΣΕΜΙΝΑΡΙΑ ΟΜΑΔΩΝ ΕΡΓΑΣΙΑΣ / 2018
Ομάδα Εργασίας Αιμοδυναμικής και Επεμβατικής Καρδιολογίας

Φαρμακολογία στα οξέα στεφανιαία σύνδρομα. Νεώτερα αντιπηκτικά φάρμακα και αντιαιμοπεταλιακή αγωγή στην PCI.

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Θεσσαλονίκη, 9/2/2018
• Disclosures: None
A Clinical Trial Comparing Three Antithrombotic-Drug Regimens after Coronary-Artery Stenting

Table 3. Primary and Secondary Events in the First 30 Days after Stenting.*

<table>
<thead>
<tr>
<th>Event</th>
<th>Aspirin Alone (N=557)</th>
<th>Aspirin and Warfarin (N=550)</th>
<th>Aspirin and Ticlopidine (N=516)</th>
<th>P Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary end point</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>20 (3.6)</td>
<td>16 (2.7)</td>
<td>3 (0.5)</td>
<td>0.001</td>
</tr>
<tr>
<td>Recanalization of target lesion</td>
<td>19 (3.4)</td>
<td>14 (2.5)</td>
<td>3 (0.5)</td>
<td>0.002</td>
</tr>
<tr>
<td>PTCA</td>
<td>3 (0.5)</td>
<td>1 (0.2)</td>
<td>1 (0.2)</td>
<td>0.63</td>
</tr>
<tr>
<td>Angiographically evident thrombus</td>
<td>17 (3.1)</td>
<td>14 (2.5)</td>
<td>3 (0.5)</td>
<td>0.003</td>
</tr>
<tr>
<td>Recurrent myocardial infarction</td>
<td>15 (2.7)</td>
<td>11 (2.1)</td>
<td>3 (0.5)</td>
<td>0.01</td>
</tr>
<tr>
<td>Q-wave</td>
<td>8 (1.4)</td>
<td>8 (1.5)</td>
<td>1 (0.2)</td>
<td>0.04</td>
</tr>
<tr>
<td>Non-Q-wave</td>
<td>7 (1.3)</td>
<td>3 (0.5)</td>
<td>2 (0.4)</td>
<td>0.27</td>
</tr>
<tr>
<td><strong>Other clinical events</strong></td>
<td></td>
<td></td>
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<tr>
<td>Procedure-related myocardial infarction</td>
<td>16 (2.9)</td>
<td>23 (4.2)</td>
<td>23 (4.2)</td>
<td>0.41</td>
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<tr>
<td>Q-wave</td>
<td>4 (0.7)</td>
<td>0</td>
<td>0</td>
<td>0.04</td>
</tr>
<tr>
<td>Non-Q-wave</td>
<td>12 (2.2)</td>
<td>23 (4.2)</td>
<td>23 (4.2)</td>
<td>0.10</td>
</tr>
<tr>
<td>Hemorrhagic complications</td>
<td>10 (1.8)</td>
<td>34 (6.2)</td>
<td>30 (5.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Vascular surgical complications</td>
<td>1 (0.2)</td>
<td>11 (2.0)</td>
<td>11 (2.1)</td>
<td>0.03</td>
</tr>
<tr>
<td>Neutropenia or thrombocytopenia</td>
<td></td>
<td></td>
<td></td>
<td>0.46</td>
</tr>
<tr>
<td>Cebrovascular accident</td>
<td>2 (0.4)</td>
<td>1 (0.2)</td>
<td>0</td>
<td>0.78</td>
</tr>
</tbody>
</table>

*CAVBG denotes coronary-artery bypass grafting, and PTCA percutaneous transluminal coronary angioplasty.
†The P values are for the comparison of the three groups by the chi-square test.

December 3, 1998
DOI: 10.1056/NEJM199812033392303
Antiplatelet Therapy Alone Does Not Provide Adequate Protection from AF-Related Stroke

A randomized trial for DAPT (n=3,335) vs VKA (n=3,371) for prevention of vascular events in patients with AF demonstrated superiority of OAC therapy.

\[
RR = 1.44 \ (95\% \ CI \ 1.18-1.76) \quad p=0.0003
\]

*Composite of stroke, non-CNS embolus, MI and vascular death

The ACTIVE Writing Group. \textit{Lancet} 2006;367:1903–1912
ACC/AHA 2007 Guidelines for management of patients with NSTE-ACS

UA/NSTEMI patient groups at discharge with indication for anticoagulation

Drug-eluting stent group

- ASA*
  - 162–325 mg/day for at least 3–6 months, then 75–162 mg/day indefinitely
  - Clopidogrel#
    - 75 mg/day for at least 1 year
  - Warfarin‡
    - When added to ASA plus clopidogrel an INR of 2.0–2.5 is recommended

Bare-metal stent group

- ASA*
  - 162–325 mg/day for at least 1 month, then 75–162 mg/day indefinitely
  - Clopidogrel#
    - 75 mg/day for at least 1 month and ideally up to 1 year
  - Warfarin‡
    - When added to ASA plus clopidogrel an INR of 2.0–2.5 is recommended

*For ASA allergic patients, use clopidogrel alone (indefinitely), or try desensitization; #for clopidogrel allergic patients, use ticlopidine 250 mg by mouth twice daily; ‡continue ASA indefinitely and warfarin longer term as indicated for specific conditions such as AF

Triple Therapy with a VKA Reduces Thromboembolic Events but Increases Bleeding after PCI in AF Patients

Danish registry data (2000–2009; N=11,480 patients)

Lamberts M et al, Circulation 2012;126:1185–1193
Major bleeding in PCI is associated with an increase in mortality.

Background risk:
- Bleeding
- Shock
- Anaemia
- Transfusion
- Discontinuation of APT
- Ischaemia
- Inflammation
- Stent thrombosis
- Mortality

Compared with patients without bleeding, patients who experience bleeding are more likely to die, not only early (in hospital) but also late (after discharge).

APT, antiplatelet therapy; PCI, percutaneous coronary intervention; Steg et al. Eur Heart J 2011
Reduced bleeding risk and no increase in thrombosis with double vs triple antithrombotic therapy in patients on OACs and undergoing PCI

WOEST study: OAC-treated patients undergoing PCI were randomized to additional clopidogrel (dual therapy) or clopidogrel + ASA (triple therapy)

<table>
<thead>
<tr>
<th>Event</th>
<th>Dual therapy (n=279)</th>
<th>Triple therapy (n=284)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any bleeding</td>
<td>19.4</td>
<td>44.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Major bleeding*</td>
<td>3.2</td>
<td>5.6</td>
<td>0.159</td>
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<tr>
<td>All-cause death</td>
<td>2.5</td>
<td>6.3</td>
<td>0.027</td>
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<tr>
<td>MI</td>
<td>3.2</td>
<td>4.6</td>
<td>0.382</td>
</tr>
<tr>
<td>TVR</td>
<td>7.2</td>
<td>6.7</td>
<td>0.876</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.1</td>
<td>2.8</td>
<td>0.128</td>
</tr>
<tr>
<td>Stent thrombosis</td>
<td>1.4</td>
<td>3.2</td>
<td>0.165</td>
</tr>
</tbody>
</table>

OAC + clopidogrel associated with significant reduction in major bleeding and no increase in thrombotic events vs triple therapy with OAC + clopidogrel + ASA

Bold values indicate statistical significance; *TIMI classification. 573 patients receiving OAC and undergoing PCI in open-label WOEST (What is the Optimal antiplatElet and anticoagulant therapy in patients with oral anticoagulation and coronary StenTing) trial. AF was not a prerequisite; however, 69% of patients in both the double therapy and triple therapy treatment groups were using OACs for AF/atrial flutter; ASA, acetylsalicylic acid; PCI, percutaneous coronary intervention; TVR, target vessel revascularization; TIMI, Thrombolysis in Myocardial Infarction; Dewilde et al. Lancet 2013
**Population:**
patients with paroxysmal, persistent or permanent NVAF undergoing PCI (with stent placement)

**Design:** An open-label, randomized, controlled phase IIIb safety study

- Rivaroxaban 15 mg OD* plus single antiplatelet‡
- Rivaroxaban 2.5 mg BID* plus DAPT§
- Rivaroxaban 15 mg OD* plus low-dose ASA
- VKA (INR 2.0–3.0)¶ plus DAPT§
- VKA plus low-dose ASA

**DAPT duration (1 or 6 months)**

- N=2,124
- Decision for DAPT duration: 1, 6 or 12 months

**End of treatment (12 months)**

- 12 mos: 100%
- 1 mo: 16%
- 6 mos: 35%
- 12 mos: 49%

**12 mos:** 100%

---

*CrCl 30–49 ml/min: 10 mg OD; ‡first dose 72–96 hours after sheath removal; †clopidogrel (75 mg daily)
(alternative use of prasugrel or ticagrelor allowed, but capped at 15%); §ASA (75–100 mg daily) plus clopidogrel (75 mg daily)
(alternative use of prasugrel or ticagrelor allowed, but capped at 15%); ¶first dose 12–72 hours after sheath removal

Both Rivaroxaban Strategies was Associated With Significantly Improved Safety

Rivaroxaban 15 mg OD plus single antiplatelet vs VKA plus DAPT: HR=0.59; (95% CI 0.47–0.76); p<0.001

Rivaroxaban 2.5 mg BID plus DAPT vs VKA plus DAPT: HR=0.63 (95% CI 0.50–0.80); p<0.001
Efficacy was Comparable Between All Three Treatment Strategies*

Rivaroxaban 15 mg OD plus single antiplatelet vs VKA plus DAPT: HR=1.08; (95% CI 0.69–1.68); p=0.750

Rivaroxaban 2.5 mg BID plus DAPT vs VKA plus DAPT: HR=0.93 (95% CI 0.59–1.48); p=0.765

*Trial not powered to definitively demonstrate either superiority or non-inferiority for efficacy endpoints

Prevention of Bleeding in Patients with Atrial Fibrillation Undergoing PCI

C. Michael Gibson, M.D., Roxana Mehran, M.D., Christoph Bode, M.D., Jonathan Halperin, M.D., Freek W. Verheugt, M.D., Peter Wildgoose, Ph.D., Mary Birmingham, Pharm.D., Juliana Ianus, Ph.D., Paul Burton, M.D., Ph.D., Martin van Eickels, M.D., Serge Korjian, M.D., Yazen Daaboul, M.D., Gregory Y.H. Lip, M.D., Marc Cohen, M.D., Steen Husted, M.D., Eric D. Peterson, M.D., M.P.H., and Keith A. Fox, M.B., Ch.B.

This trial has several limitations. First, the secondary analyses showed that the efficacy of each of the two doses of rivaroxaban was similar to that of standard therapy. However, the number of secondary efficacy end points in this study was small, and the trial was not powered to definitively establish either superiority or noninferiority. Using the rate for a major adverse cardiovas-

...standard-therapy group. The overall trial is underpowered, and individual efficacy end points within subgroups are even more underpowered. Even nist plus DAPT for 1, 6, or 12 months. The three groups had similar efficacy rates, although the observed broad confidence intervals diminish the surety of any conclusions regarding efficacy.
**Study Design:** Multicenter, randomized, open-label trial following a PROBE design

*Study drug should be administered 6 hours after sheath removal and no later than ≤120 hrs post-PCI (≤72 hrs is preferable).* PROBE, prospective, randomized, open, blinded end-point; R, randomization; BMS, bare metal stent; DES, drug-eluting stent. ClinicalTrials.gov: NCT02164864; Cannon et al. Clin Cardiol 2016

**Patients with AF undergoing PCI with stenting**

- **Randomization ≤120 hours post-PCI**

- **N=2725**

**Dabigatran 150 mg BID + P2Y12 inhibitor**

- **Dabigatran 110 mg BID + P2Y12 inhibitor**

- **Warfarin (INR 2.0–3.0) + P2Y12 inhibitor + ASA**

6-month minimum treatment duration with visits every 3 months for the first year, then visits and telephone contact alternating every 3 months and a 1-month post-treatment visit

**Mean duration of follow-up: ~14 months**

- **Dabigatran (110 or 150 mg)**

- **P2Y12 inhibitor**

- **Warfarin**

- **P2Y12 inhibitor**

- 1 month of ASA

- 6 months of ASA (DES)
Primary Endpoint: Time to first ISTH major or clinically relevant non-major bleeding event

HR: 0.52 (95% CI: 0.42–0.63)  
Non-inferiority P<0.0001  
P=0.002

HR: 0.72 (95% CI: 0.58–0.88)  
Non-inferiority P<0.0001  
P=0.002

Full analysis set presented. HRs and Wald CIs from Cox proportional-hazard model. For the dabigatran 110 mg vs warfarin comparison, the model is stratified by age, non-elderly vs elderly (<70 or ≥70 in Japan and <80 or ≥80 years old elsewhere). For the dabigatran 150 mg vs warfarin comparison, an unstratified model is used, elderly patients outside the USA are excluded. Non-inferiority P value is one sided (alpha=0.025). Wald two-sided P value from (stratified) Cox
**Time to death or thromboembolic event, or unplanned revascularization**

**HR: 1.04 (95% CI: 0.84–1.29)**

Non-inferiority P = 0.0047

Non-inferiority P value is one sided (alpha=0.025). Results presented are Step 3 of hierarchical testing procedure, testing non-inferiority of dabigatran dual therapy (combined doses) to warfarin triple therapy in death or thromboembolic event and unplanned revascularization.
### Additional individual thromboembolic endpoints

<table>
<thead>
<tr>
<th></th>
<th>Dabigatran n 110 mg dual therapy (n=981) n (%)</th>
<th>Warfarin triple therapy (n=981) n (%)</th>
<th>D110 DT vs warfarin TT</th>
<th>Dabigatran n 150 mg dual therapy (n=763) n (%)</th>
<th>Warfarin triple therapy (n=764) n (%)</th>
<th>D150 DT vs warfarin TT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR (95% CI)</td>
<td>P value</td>
<td></td>
<td>HR (95% CI)</td>
<td>P value</td>
<td></td>
</tr>
<tr>
<td>All-cause death</td>
<td>55 (5.6)</td>
<td>48 (4.9)</td>
<td>1.12 (0.76–1.65)</td>
<td>0.56</td>
<td>30 (3.9)</td>
<td>35 (4.6)</td>
</tr>
<tr>
<td>Stroke</td>
<td>17 (1.7)</td>
<td>13 (1.3)</td>
<td>1.30 (0.63–2.67)</td>
<td>0.48</td>
<td>9 (1.2)</td>
<td>8 (1.0)</td>
</tr>
<tr>
<td>Unplanned revascularization</td>
<td>76 (7.7)</td>
<td>69 (7.0)</td>
<td>1.09 (0.79–1.51)</td>
<td>0.61</td>
<td>51 (6.7)</td>
<td>52 (6.8)</td>
</tr>
<tr>
<td>MI</td>
<td>44 (4.5)</td>
<td>29 (3.0)</td>
<td>1.51 (0.94–2.41)</td>
<td>0.09</td>
<td>26 (3.4)</td>
<td>22 (2.9)</td>
</tr>
<tr>
<td>Stent thrombosis</td>
<td>15 (1.5)</td>
<td>8 (0.8)</td>
<td>1.86 (0.79–4.40)</td>
<td>0.15</td>
<td>7 (0.9)</td>
<td>7 (0.9)</td>
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</tbody>
</table>

Results presented are times to event. Stent thrombosis is time to definite stent thrombosis.
<table>
<thead>
<tr>
<th>Concomitant Therapy, Number of Days Post Randomization</th>
<th>Dabigatran 110 Dual-therapy (n=981)</th>
<th>Dabigatran 150 Dual-therapy (n=763)</th>
<th>Warfarin Triple-therapy (n=981)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antiplatelets</td>
<td></td>
<td></td>
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<tr>
<td>1 day</td>
<td>973 (99.2)</td>
<td>751 (98.4)</td>
<td>967 (98.6)</td>
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<td>30 days</td>
<td>965 (98.4)</td>
<td>747 (97.9)</td>
<td>935 (93.3)</td>
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<tr>
<td>45 days</td>
<td>962 (98.1)</td>
<td>747 (97.9)</td>
<td>926 (94.4)</td>
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<td>90 days</td>
<td>949 (96.7)</td>
<td>744 (97.5)</td>
<td>917 (93.5)</td>
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<td>105 days</td>
<td>947 (96.5)</td>
<td>739 (96.9)</td>
<td>909 (92.7)</td>
</tr>
<tr>
<td>365 days</td>
<td>567 (57.8)</td>
<td>456 (59.8)</td>
<td>553 (56.4)</td>
</tr>
<tr>
<td>430 days</td>
<td>319 (32.5)</td>
<td>237 (31.1)</td>
<td>319 (32.5)</td>
</tr>
<tr>
<td>Acetylsalicylic acid</td>
<td></td>
<td></td>
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<tr>
<td>1 day</td>
<td>112 (11.4)</td>
<td>75 (9.8)</td>
<td>954 (97.2)</td>
</tr>
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<td>30 days</td>
<td>65 (6.6)</td>
<td>49 (6.4)</td>
<td>873 (89.0)</td>
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<tr>
<td>45 days</td>
<td>53 (5.4)</td>
<td>42 (5.5)</td>
<td>793 (80.8)</td>
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<td>90 days</td>
<td>48 (4.9)</td>
<td>35 (4.6)</td>
<td>616 (62.8)</td>
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<tr>
<td>105 days</td>
<td>38 (3.9)</td>
<td>33 (4.3)</td>
<td>281 (28.6)</td>
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<tr>
<td>365 days</td>
<td>45 (4.6)</td>
<td>31 (4.1)</td>
<td>142 (14.5)</td>
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<tr>
<td>430 days</td>
<td>44 (4.5)</td>
<td>31 (4.1)</td>
<td>105 (10.7)</td>
</tr>
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<td>Clopidogrel</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>1 day</td>
<td>848 (86.4)</td>
<td>663 (86.9)</td>
<td>886 (90.3)</td>
</tr>
<tr>
<td>30 days</td>
<td>853 (87.2)</td>
<td>661 (86.6)</td>
<td>856 (87.3)</td>
</tr>
<tr>
<td>45 days</td>
<td>853 (87.2)</td>
<td>663 (86.9)</td>
<td>845 (86.1)</td>
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<tr>
<td>90 days</td>
<td>842 (85.8)</td>
<td>664 (87.0)</td>
<td>835 (85.1)</td>
</tr>
<tr>
<td>105 days</td>
<td>842 (85.8)</td>
<td>661 (86.6)</td>
<td>830 (84.6)</td>
</tr>
<tr>
<td>365 days</td>
<td>496 (50.6)</td>
<td>388 (52.2)</td>
<td>489 (49.5)</td>
</tr>
<tr>
<td>430 days</td>
<td>261 (26.6)</td>
<td>198 (26.0)</td>
<td>262 (26.7)</td>
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<tr>
<td>Ticagrelor</td>
<td></td>
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<tr>
<td>1 day</td>
<td>124 (12.6)</td>
<td>92 (12.1)</td>
<td>77 (7.8)</td>
</tr>
<tr>
<td>30 days</td>
<td>110 (11.2)</td>
<td>86 (11.3)</td>
<td>70 (7.1)</td>
</tr>
<tr>
<td>45 days</td>
<td>104 (10.6)</td>
<td>84 (11.0)</td>
<td>67 (6.8)</td>
</tr>
<tr>
<td>90 days</td>
<td>104 (10.6)</td>
<td>79 (10.4)</td>
<td>64 (6.5)</td>
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<tr>
<td>105 days</td>
<td>103 (10.5)</td>
<td>79 (10.4)</td>
<td>63 (6.4)</td>
</tr>
<tr>
<td>365 days</td>
<td>48 (4.9)</td>
<td>43 (5.6)</td>
<td>31 (3.2)</td>
</tr>
<tr>
<td>430 days</td>
<td>24 (2.4)</td>
<td>19 (2.5)</td>
<td>15 (1.5)</td>
</tr>
</tbody>
</table>
Dual Antithrombotic Therapy with Dabigatran after PCI in Atrial Fibrillation

Christopher P. Cannon, M.D., Deepak L. Bhatt, M.D., M.P.H., Jonas Oldgren, M.D., Ph.D., Gregory Y.H. Lip, M.D., Stephen G. Ellis, M.D., Takeshi Kimura, M.D., Michael Maeng, M.D., Ph.D., Bela Merkely, M.D., Uwe Zeymer, M.D., Savion Gropper, M.D., Ph.D., Matias Nordaby, M.D., Eva Kleine, M.Sc., Ruth Harper, Ph.D., Jenny Manassie, B.Med.Sc., James L. Januzzi, M.D., Jurrien M. ten Berg, M.D., Ph.D., P. Gabriel Steg, M.D., and Stefan H. Hohnloser, M.D., for the RE-DUAL PCI Steering Committee and Investigators*

In the initial protocol, a sample size of 8520 patients had been planned to allow for a coprimary end-point comparison of thromboembolic-event rates in each dual-therapy group versus the triple-therapy group; however, enrollment of this number of patients in a timely fashion was determined to be infeasible. The protocol was amended to specify the current sample size, and the comparison of thromboembolic-event rates in the two dual-therapy groups combined versus the triple-therapy group was changed to a secondary end point.

With respect to the composite efficacy end point, our prespecified criterion for noninferiority was met. This trial, which involved 2725 patients, was not powered to allow for comparisons of individual components of this end point. We thus have to exercise caution in examining the nonsignificant small numerical excesses in some components of this end point. It is impor-

There are limitations to our trial. First, we amended the protocol and enrolled a smaller number of patients than we had originally planned to enroll, and this limits the power of the trial to examine efficacy according to dabigatran dose. For
58 ετών, άρρεν
Πρόσθιο NSTEMI
Algorithm for dual antiplatelet therapy (DAPT) in patients with an indication for oral anticoagulation undergoing percutaneous coronary intervention (PCI)

Patients with an indication for oral anticoagulation undergoing PCI

- Concerns about ischaemic risk prevailing
- Concerns about bleeding risk prevailing

Time from treatment initiation:
- 1 mo.
- 3 mo.
- 6 mo.
- 12 mo.
- Beyond 12 mo.

Diagram:
- A = Aspirin
- C = Clopidogrel
- O = Oral anticoagulation
What are the implications for clinical practice in PCI?
Canadian Cardiovascular Society Guidelines Recommend OAC + single AP after Elective PCI

For patients with AF and recent elective PCI

Age <65 and CHADS$_2$ = 0

ASA plus clopidogrel for 12 months

ASA alone after 12 months

Age ≥65 or CHADS$_2$ ≥ 1

OAC* plus clopidogrel for 12 months

OAC* alone after 12 months

*A NOAC is preferred over warfarin for patients with NVAF

**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>
Strategies to avoid bleeding complications in patients treated with oral anticoagulant

- Assess ischaemic and bleeding risks using validated risk predictors (e.g. CHA$_2$DS$_2$-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 when NOACs are not contra-indicated.

- 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 P2Y$_{12}$ inhibitor of choice.

- Use low-dose (≤100 mg daily) aspirin.

- Routine use of PPIs.
High-risk features of stent-driven recurrent ischaemic events

<table>
<thead>
<tr>
<th>Feature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior stent thrombosis on adequate antiplatelet therapy.</td>
</tr>
<tr>
<td>Stenting of the last remaining patent coronary artery.</td>
</tr>
<tr>
<td>Diffuse multivessel disease especially in diabetic patients.</td>
</tr>
<tr>
<td>Chronic kidney disease (i.e. creatinine clearance &lt;60 mL/min).</td>
</tr>
<tr>
<td>At least three stents implanted.</td>
</tr>
<tr>
<td>At least three lesions treated.</td>
</tr>
<tr>
<td>Bifurcation with two stents implanted.</td>
</tr>
<tr>
<td>Total stent length &gt;60 mm.</td>
</tr>
<tr>
<td>Treatment of a chronic total occlusion.</td>
</tr>
</tbody>
</table>
Unfavourable patient profile for a combination of oral anticoagulant and antiplatelet therapy

- Short life expectancy.
- Ongoing malignancy.
- Poor expected adherence.
- Poor mental status.
- End stage renal failure.
- Advanced age.
- Prior major bleeding/prior haemorrhagic stroke.
- Chronic alcohol abuse.
- Anaemia.
- Clinically significant bleeding on dual antithrombotic therapy.
ΕΥΧΑΡΙΣΤΩ
For patients requiring OAC, new ESC focused update recommends dual or triple therapy after PCI with stent depending on individual patient risk factors.

When a NOAC is used, the **lowest dose effective for stroke prevention in AF** should be applied.

**Dabigatran 110 mg is the only reduced-dose NOAC to be fully tested** for effectiveness in stroke prevention in AF.

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*High ischaemic risk is considered as an acute clinical presentation or anatomical/procedural features, which might increase the risk for MI; †Dabigatran 110 mg BID (Class IIa C), rivaroxaban 15 mg OD (Class IIb B), or apixaban 2.5 mg BID (Class IIa C) according to selected study population in pivotal studies; ASA, acetylsalicylic acid; Valgimigli et al. Eur Heart J 2017*
Guidelines recommend the following in patients with AF after PCI:

<table>
<thead>
<tr>
<th>Time (months)</th>
<th>Elective PCI with stent(^1,2)</th>
<th>Urgent PCI after ACS(^1-3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 months</td>
<td>Triple therapy OAC+A+C</td>
<td>Triple therapy OAC+A+C</td>
</tr>
<tr>
<td>1 month</td>
<td>Dual therapy OAC+A or C</td>
<td>Dual therapy OAC+A or C</td>
</tr>
<tr>
<td>6 months</td>
<td>OAC monotherapy</td>
<td>OAC monotherapy</td>
</tr>
<tr>
<td>12 months</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- High bleeding risk/low atherothrombotic risk: **shorten dual therapy**
- High atherothrombotic risk/low bleeding risk: **lengthen triple therapy**
- High bleeding risk/low atherothrombotic risk: **shorten triple therapy**

In selected patients, dual therapy may be considered instead of triple therapy\(^1\)

European guidelines suggest that NOACs may be used in triple/dual therapy,\(^1-3\) whereas US guidelines recommend a VKA\(^4,5\)

Time to first ISTH major or CRNM bleeding event in relation to ticagrelor or clopidogrel

Dabigatran 110 dual therapy

Dabigatran 150 dual therapy

Patients at risk
Dabigatran 110 dual therapy ticagrelor 132
Dabigatran 110 dual therapy clopidogrel 847
Warfarin triple therapy ticagrelor 91
Warfarin triple therapy clopidogrel 856

Patients at risk
Dabigatran 150 dual therapy ticagrelor 104
Dabigatran 150 dual therapy clopidogrel 650
Warfarin triple therapy ticagrelor 73
Warfarin triple therapy clopidogrel 673

Full analysis set presented. HRs and Wald CIs from Cox proportional-hazard model. For the dabigatran 110 vs warfarin comparison, the model is stratified by age, non-elderly vs elderly (<70 or ≥70 years in Japan and <80 or ≥80 years old elsewhere). For the dabigatran 150 vs warfarin comparison, an unstratified model is used, elderly patients outside the United States are excluded. Non-inferiority P value is one sided (alpha=0.025). Wald two-sided P value from (stratified) Cox proportional-hazard model (alpha=0.05).

CI, confidence interval; CRNM, clinically relevant non-major; HR, hazard ratio; ISTH, International Society on Thrombosis and Haemostasis.
Primary reason for early discontinuation from treatment period

Early discontinuations were highest in the VKA plus DAPT group; discontinuation due to patient decision was significantly higher in this group vs both rivaroxaban groups.

There were no patients lost to follow up.

* \( p = 0.016; \) ** \( p < 0.001 \)

What is new in the 2017 ESC focussed update on DAPT?

Change in recommendations

Before 2017
- Pretreatment with P2Y₁₂ inhibitors when PCI is planned
- Liberal use of PPI to mitigate GI bleeding risk
- Elective surgery requiring discontinuation of the P2Y12 inhibitor after 1 month
- Ticagrelor interruption of 3 days prior elective surgery
- Dual therapy as an alternative to triple therapy when bleeding risk outweighs the ischaemic risk
- Discontinuation of antiplatelet treatment in patients treated with DAC should be considered at 12 months.
- Routine platelet function testing to adjust therapy

2017
- The occurrence of actionable bleeding while on DAPT should prompt reconsideration of type and duration of DAPT regimen.
- The decision for DAPT duration should be dynamic and reassessed during the course of the initially selected DAPT regimen.
- Discontinuation of P2Y₁₂ inhibitor therapy after 6 months when stenting ACS patients with PRECISE-DAPT ≥ 25
- 6-month DAPT regimen in patients with SCAD treated with drug-coated balloon
- Early administration of ticagrelor/ clopidogrel in NSTE-ACS with invasive approach
- Ticagrelor 60 mg b.i.d preferred over other oral P2Y12 inhibitors for DAPT continuation >12 months in post-MI

New/revised concepts

Metallic stent and DAPT duration
Switch between P2Y₁₂ inhibitors
Risk scores to guide DAPT duration
- PRECISE DAPT score
- DAPT score
Specific profiling
- Definition of complex PCI
- Unfavourable profile for DAC and APT
- Gender considerations and special populations
DAPT duration without stenting
- Medical management
- CABG or cardiac surgery
Anticoagulation and DAPT
- Acute and chronic setting
- Dosing regimen

www.escardio.org/guidelines

2017 ESC Focused Update on DAPT in Coronary Artery Disease, developed in collaboration with EACTS (European Heart Journal 2017 - doi:10.1093/eurheartj/ehx419)