DOACs: The practical side

Terry Dowling
Principal Pharmacist (Haemostasis & Thrombosis) – Guy’s & St. Thomas’ NHS FT
Practice Pharmacist / Trainee ACP – Rushbottom Lane Surgery, Benfleet
Associate Tutor (NMP) – University of East Anglia
Overview

- Focus on stroke prevention in AF
- Getting the dose right
- Case study: back to basics
- Case study: uncertainties
Warm up

1. Mrs RD: 81 years old, AF. PMH: HF, smoker, HTN, COPD
   Creatinine 140, Wt 85kg, CrCl = 30-37ml/min;
   Treating with apixaban:
   a) 5mg BD or
   b) 2.5mg BD

2. Mr GF: 73 years old, new PE. PMH: CKD4, T2DM, HTN
   Cr 190, Wt 65kg, CrCl=28ml/min; Rx rivaroxaban
   15mg BD for 3 weeks then:
   a) 20mg OD or
   b) 15mg OD
Warm up

3. Miss AD, 76yo, PAF treated with amiodarone.  
   PMH: HTN, T2DM, diverticulosis. Cr 97, Wt 66kg,  
   CrCl=48ml/min. Treating with dabigatran:  
   a) 150mg BD or  
   b) 110mg BD or  
   c) 75mg BD

   Cr 83, Wt 93kg, CrCl=85-99ml/min, switch to apixaban:  
   a) 5mg BD or  
   b) 2.5mg BD
DOAC dosing

- More drugs
- More indications
- More criteria for dose reduction
- More errors?!

- In our quest for more accessible, convenient oral anticoagulation, “we are now faced with […] a tyranny of choice” ¹

# Dosing in NVAF

<table>
<thead>
<tr>
<th></th>
<th>Dabigatran (^1)</th>
<th>Apixaban (^2)</th>
<th>Edoxaban (^3)</th>
<th>Rivaroxaban (^4)</th>
</tr>
</thead>
<tbody>
<tr>
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<td>150mg BD</td>
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| **Criteria for dose reduction** | 1. Age ≥80  
2. On verapamil  
3. Consider ↓dose:  
• Reflux/gastritis  
• Age 75-80  
• CrCl 30-50ml/min  
• “Bleed risk”  
Or  
| ≥2 of:  
• Age ≥80  
• Body wt ≤60kg  
• Cr ≥133μmol/L  | ≥1 of:  
• CrCl 15-50ml/min  
• Body wt ≤60kg  
• On ciclosporin, dronedarone, erythromycin, ketoconazole  | CrCl 15-49ml/min |

| **CI / NR** | CrCl <30ml/min | ————————————– CrCl <15ml/min ————————————– |

1. Dabigatran SmPC. Available at [www.medicines.org.uk](http://www.medicines.org.uk);  
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<tr>
<td>Acute</td>
<td>LMWH ≥ 5/7</td>
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<tr>
<td>&gt; 6 months</td>
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<tr>
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| > 6 months | No change | 2.5mg BD | No change | 10mg OD or 20mg OD |
| Caution | CrCl 15-29ml/min | | CrCl 15-29ml/min |
| CI / NR | CrCl <30ml/min | | | CrCl <15ml/min |

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Is the licensed dose the right dose?

• Danish registry – reduced dose DOAC vs standard VKA

• Stroke & systemic embolism
  • NS increase with apixaban (HR 1.19; 95%CI 0.95–1.49)
  • NS decrease with rivaroxaban/dabigatran (HR 0.92 / 0.93)

• Unable to confirm off/on-label dose reduction

• Significant selection bias
  • E.g. overall mean age=73: lowest mean age = warfarin (71), highest mean age = apixaban (83)
  • Higher CHADS-VASc & HAS-BLED scores and renal disease codes predicted apixaban use

Is the licensed dose the right dose?

• ORBIT II AF prospective registry (US)
  - 5,738 patients: 1 in 8 on wrong dose
  - **3.4% overdosed** = ↑ risk all-cause mortality: HR 1.91 (95% CI 1.02–3.60)
  - **9.4% underdosed** = ↑ risk of CV hospitalisation: HR 1.26 (95% CI 1.07–1.50) with no benefits seen in major bleeding (rates similar)

• Predictors of “off-label” dosing
  - High stroke (CHA2DS2-VASc) & bleed (ORBIT) risk
  - Moderate renal impairment (CrCl = 30-50ml/min)

Is the licensed dose the right dose?

• Yao et al (US insurance database):
  – 14,865 patients: ?renal indication for DOAC dose reduction

  – **Overdose** (4%) = ↑ risk of major bleeding (HR 2.19; 95% CI 1.07–4.46) + similar stroke risk

  – **Underdose** (12%) = ↑ stroke risk with apixaban (HR 4.87; 95% CI 1.3–18.26) + similar bleeding rate
    • No statistical difference for dabigatran/rivaroxaban

  – 50% of apixaban underdosing in age > 80 years old

A potential problem…

Single centre study in the US\textsuperscript{1}:

\begin{itemize}
\item 13.3\% patients on reduced dose DOAC
\item Overall, only 43.3\% met criteria for dose reduction
  \begin{itemize}
  \item 54.7\% on rivaroxaban
  \item 32.2\% on dabigatran
  \item 10.7\% on apixaban
  \end{itemize}
\end{itemize}

\textsuperscript{1} Barra M et al. \textit{Am J Med} 2016;129:1198-1204
A potential problem…

• Apixaban 2.5mg bd

  – 4.7% of all apixaban patients in ARISTOTLE\(^1\)

  – 24% to 55% of all apixaban prescriptions in England\(^2\)
    • (includes all indications!)

1 Granger CB et al. NEJM 2011;365:981-992
2 Data from Openprescribing.net Feb-18 (consistent from Jan-17 to Feb-18) accessed 08MAY2018
Case One – Back to Basics
Case 1 - Opportunity calls

- Mrs EE – 93yo
- Warfarin for stroke prevention in AF
- PMH: T2DM, stroke, hyperthyroidism
- DH:
  - AM: metformin, carbimazole
  - PM: citalopram, warfarin

- \( \text{CH} \text{A}_\text{2D} \text{S}_\text{2-VA} \text{S}_\text{c} = \ldots \)
  a) 4      b) 5      c) 6

- \( \text{HA}\text{S- BL} \text{E} \text{D} = \ldots \)
  a) 1      b) 2      c) 3
## Stroke risk

<table>
<thead>
<tr>
<th>CHA2DS2-VASc components</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart failure / LVSD</td>
<td>1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1</td>
</tr>
<tr>
<td><strong>Aged ≥75 years</strong></td>
<td>2</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1</td>
</tr>
<tr>
<td>Stroke/TIA/TE</td>
<td>2</td>
</tr>
<tr>
<td>Vascular disease (prior ACS, PAD, IHD)</td>
<td>1</td>
</tr>
<tr>
<td>Aged 65–74 years</td>
<td>1</td>
</tr>
<tr>
<td><strong>Sex category (i.e. female)</strong></td>
<td>1</td>
</tr>
<tr>
<td>Maximum score</td>
<td>9</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total score</th>
<th>Adj. stroke rate (%/year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>1.3</td>
</tr>
<tr>
<td>2</td>
<td>2.2</td>
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<tr>
<td>3</td>
<td>3.2</td>
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<tr>
<td>4</td>
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<tr>
<td>5</td>
<td>6.7</td>
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<tr>
<td>6</td>
<td>9.8</td>
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<tr>
<td>7</td>
<td>9.6</td>
</tr>
<tr>
<td>8</td>
<td>6.7</td>
</tr>
<tr>
<td>9</td>
<td>15.2</td>
</tr>
</tbody>
</table>

Camm et al. Eur Heart J 2010;31:2369–2429
### Bleeding risk on OAC

<table>
<thead>
<tr>
<th>Letter</th>
<th>Clinical characteristic</th>
<th>Score</th>
<th>Total score</th>
<th>Major bleeds /100 PY</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>Hypertension</td>
<td>1</td>
<td></td>
<td>1.13</td>
</tr>
<tr>
<td>A</td>
<td>Abnormal renal / liver function (1 each)</td>
<td>1 or 2</td>
<td></td>
<td>1.02</td>
</tr>
<tr>
<td>S</td>
<td>Stroke</td>
<td>1</td>
<td></td>
<td>1.88</td>
</tr>
<tr>
<td>B</td>
<td>Bleeding</td>
<td>1</td>
<td></td>
<td>3.74</td>
</tr>
<tr>
<td>L</td>
<td>Labile INRs</td>
<td>1</td>
<td></td>
<td>8.70</td>
</tr>
<tr>
<td>E</td>
<td>Elderly (e.g. age &gt;65 years)</td>
<td>1</td>
<td></td>
<td>12.50</td>
</tr>
<tr>
<td>D</td>
<td>Drugs or alcohol (1 point each)</td>
<td>1 or 2</td>
<td></td>
<td>ND</td>
</tr>
</tbody>
</table>

**Maximum score**: 9

Validated in DOACs with similar intervention threshold of 2%/yr

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Case 1 – But she’s fine on warfarin...

- Requires DN for INR phlebotomy (wheelchair bound)
  - Poor veins

- Unstable INRs – over last 6 months:
  - 3 failed samples (poor veins)
  - Six INRs >3 (four >5), nine INRs <2
  - Admission for INR >10 (Sept 2015)
  - Retest every 7-14 days
  - TTR = 37%

- Daughter refills dosette box weekly to include warfarin
Q: What is a good TTR, who should be switched?

• Reduction in major bleeding significantly higher for DOACs vs VKA when TTR<66% (vs TTR>66%)

• Efficacy benefits heterogeneous: unable to compare

• Not identified TTR where warfarin > DOAC (efficacy or safety)

TTR Correlates with Stroke

Stroke survival in 37,907 AF patients – UK General Practice Research Database (27,458 warfarin users and 10,449 not treated with an antithrombotic)\(^1\)

AF: atrial fibrillation; TTR: time in therapeutic range.

Adapted from Gallagher et al. 2011\(^1\).

Case 1 – Making the change

- Cr 71, CrCl = 47.3ml/min
- 68.5kg

1. Which drug?
2. Which dose?
3. Does it matter?
4. How to decide?
### So how do I decide?

<table>
<thead>
<tr>
<th>Choosing the oral anticoagulant drug to fit the patient profile</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent stroke, systemic embolic event, or transient ischaemic attack despite good anticoagulation control (TTR &gt;70%)</td>
<td>Dabigatran 150 mg BID</td>
</tr>
<tr>
<td>Moderate-to-severe renal impairment (CrCl 15–49 mL/min)</td>
<td>Apixaban 5 mg BID*, rivaroxaban 15 mg once daily, dabigatran (if CrCl 30–49 mL/min)†, or edoxaban 30 mg once daily‡</td>
</tr>
<tr>
<td>High risk of gastrointestinal bleeding</td>
<td>Apixaban 5 mg BID* or dabigatran 110 mg BID§</td>
</tr>
<tr>
<td>Gastrointestinal symptoms or dyspepsia</td>
<td>Apixaban 5 mg BID*, rivaroxaban 20 mg once daily¶, or edoxaban 60 mg once daily</td>
</tr>
<tr>
<td>High risk of bleeding (HAS-BLED ≥3)</td>
<td>Dabigatran 110 mg BID§, apixaban 5 mg BID*, or edoxaban 60 mg once daily</td>
</tr>
<tr>
<td>Once daily dosing or preference to have a lower pill burden</td>
<td>VKA, rivaroxaban 20 mg once daily¶, or edoxaban 60 mg once daily</td>
</tr>
<tr>
<td>Asian patients (consider drugs with reduced risk of intracranial haemorrhage and major bleeding in Asian subgroups)</td>
<td>Apixaban 5 mg BID*, dabigatran†, or edoxaban 60 mg once daily</td>
</tr>
<tr>
<td>Less likely to do well on VKA with good TTR (SAME-TTR, score ≥2)</td>
<td>VKA with additional education and more regular follow-up, dabigatran†, rivaroxaban 20 mg once daily¶, apixaban 5 mg BID*, or edoxaban 60 mg once daily</td>
</tr>
</tbody>
</table>

Reviews & Prescribing Decision Aids

- Savelieva I, Camm AJ. *Clin Cardiol* 2014;37(1):32-47
- Millar CM, Laffan MA. *Clinical Medicine* 2017;17(3):233-244

- **EHRA Practical Guide 3ed:**

- Keele University decision support tool
  [https://www.anticoagulation-dst.co.uk/](https://www.anticoagulation-dst.co.uk/)
<table>
<thead>
<tr>
<th>Measure</th>
<th>Pooled DOAC Events/Total</th>
<th>Pooled Warfarin Events/Total</th>
<th>Risk Ratio</th>
<th>95% CIs</th>
<th>p</th>
<th>Outcome</th>
</tr>
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<tbody>
<tr>
<td><strong>Efficacy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischaemic Stroke</td>
<td>665/29292</td>
<td>724/29221</td>
<td>0.92</td>
<td>0.83-1.02</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>Hemorrhagic stroke</td>
<td>130/29292</td>
<td>263/29221</td>
<td>0.49</td>
<td>0.38-0.64</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>413/29292</td>
<td>432/29221</td>
<td>0.97</td>
<td>0.78-1.20</td>
<td>0.97</td>
<td></td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>2022/29292</td>
<td>2245/29221</td>
<td>0.90</td>
<td>0.851-0.95</td>
<td>0.0003</td>
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<tr>
<td><strong>Safety</strong></td>
<td></td>
<td></td>
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<tr>
<td>Intracranial hemorrhage</td>
<td>204/29287</td>
<td>425/29211</td>
<td>0.48</td>
<td>0.39-0.59</td>
<td>&lt;0.0001</td>
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<tr>
<td>Gastrointestinal bleeding</td>
<td>751/29287</td>
<td>591/29211</td>
<td>1.25</td>
<td>1.01-1.55</td>
<td>0.043</td>
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<tr>
<td>• On ciclosporin,</td>
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<tr>
<td>dronedarone, erythromycin,</td>
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<tr>
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**CI / NR**

| CrCl < 30ml/min            |                   |                |                |                   |

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1. Dabigatran SmPC. Available at [www.medicines.org.uk](http://www.medicines.org.uk);
2. Apixaban SmPC. Available at [www.medicines.org.uk](http://www.medicines.org.uk);
3. Edoxaban SmPC. Available at [www.medicines.org.uk](http://www.medicines.org.uk);
Estimating Renal Function\textsuperscript{1,2}

- Use Cockcroft – Gault equation as per pivotal studies
  - Avoid MDRD / CKD-EPI based eGFR
- What weight?
  - Actual weight used in trials
  - Extremes of weight & age poorly represented
  - Avoid IBW – risk of underdose
  - Consider adjusted body weight in extreme of weight

\textsuperscript{1} http://www.lambethccg.nhs.uk/news-and-publications/meeting-papers/south-east-london-area-prescribing-committee/Documents/Cardiovascular\%20Disease\%20Guidelines/Creatinine\%20clearance\%20guidance\%20July\%202017.pdf

\textsuperscript{2} https://www.sps.nhs.uk/articles/what-factors-need-to-be-considered-when-dosing-patients-with-renal-impairment-2/
Switching – complicated?

- SmPCs: (AF) switch from VKA when...

<table>
<thead>
<tr>
<th></th>
<th>Apixaban</th>
<th>Dabigatran</th>
<th>Edoxaban</th>
<th>Rivaroxaban</th>
</tr>
</thead>
<tbody>
<tr>
<td>INR threshold</td>
<td>&lt; 2.0</td>
<td>&lt; 2.0</td>
<td>≤ 2.5</td>
<td>≤ 3.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(≤ 2.5 in VTE)</td>
</tr>
</tbody>
</table>

- Simplified approach in non-high risk maintenance VKA* patients, e.g.

<table>
<thead>
<tr>
<th>INR</th>
<th>Instruction</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 2.0</td>
<td>Start immediately</td>
</tr>
<tr>
<td>2.0 to 2.9</td>
<td>Start following day</td>
</tr>
<tr>
<td>3.0 to 3.5</td>
<td>Start in 2 days</td>
</tr>
<tr>
<td>&gt; 3.5</td>
<td>Recheck INR 2-3 days</td>
</tr>
</tbody>
</table>

*Not phenprocoumon!
Case 1 – Outcome

• No frequent venepuncture required
  – ↓ burden on district nurse service
  – ↓ pain from difficult phlebotomy

• Dosette from pharmacy
  – Remove daughter’s commitment to weekly refill
Case Two - Uncertainties
Case 2 - Uncertainties

- Mr RG: 62yo male, truck driver, PAF, HTN, T2DM
- Switched from warfarin to rivaroxaban 20mg once daily

### Assessments

<table>
<thead>
<tr>
<th></th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHA₂DS₂-VASc</td>
<td>2</td>
</tr>
<tr>
<td>HAS-BLED</td>
<td>0</td>
</tr>
<tr>
<td>Wt</td>
<td>143kg</td>
</tr>
<tr>
<td>Height</td>
<td>180cm</td>
</tr>
<tr>
<td>BMI</td>
<td>44.1kg/m²</td>
</tr>
<tr>
<td>Cr</td>
<td>100μmol/L</td>
</tr>
<tr>
<td>CrCl (adj)</td>
<td>98ml/min</td>
</tr>
<tr>
<td>Hb</td>
<td>146g/L</td>
</tr>
<tr>
<td>ALT</td>
<td>26</td>
</tr>
</tbody>
</table>

### Medication

- Atorvastatin
- Metoprolol
- Metformin
- Candesartan
- Omeprazole
- Amlodipine
- Humulin I
- Beconase nasal
Can we use a DOAC?

ISTH SSC¹

- Avoid DOACs if BMI >40 or Wt >120kg
  - Available evidence suggests peaks may be reduced & clearance may be increased; risk of underdosing
- If using DOACs in above, check drug-specific plasma peak & trough
  - by anti-Xa (a/r/e) or dTT (d), or mass spec (any).
  - If out of range, change to VKA rather than dose adjust

What do we know?

Phase II/III data:

- Clear associated between weight/BSA & Vd
- Effect on plasma levels is modest
  - <25% reduction in plasma concentrations
- SPCs: “No dose adjustment necessary”

1 De Caterina R, Lip GY. Clin Res Cardiol 2017;106(8):565-572
Pivotal Studies

• No exclusions based on weight / BMI
• > 15% subjects >100kg

• Efficacy & safety endpoints consistent in patients >100kg
  – Also shown in meta-analysis¹

• Limitations: sparsity of outcome data beyond:
  – Weight >120kg
  – BMI >40kg/m²

Kinetic studies

Specifically recruiting >120kg:

- **Apixaban**: 30% and 20% reduction in Cmax & AUC \(^1\)
  - Weight: mean 137kg SD +/- 18.3kg
- **Rivaroxaban**: No change in Cmax \(^2\)
  - Weight: Mean 132kg SD +/- 10kg

Local data (2017) – No troughs below expected range \(^3\)

- 30 patients (26 SPAF)
  - rivaroxaban (19) & apixaban (11)
  - Weight: mean 137kg SD +/- 22kg

\(^1\) Upreti VV et al. *Br J Clin Pharmacol* 2013;76:908-916
\(^3\) Mahir Z et al. unpublished data
“Real World Data”

Dresden registry (prospective) – AF

• 9.8% patients with BMI >35kg/m²
  – Highest BMI 57.2kg/m²

• No dose adjustments

• Cardiovascular outcomes, major bleeding and all-cause mortality consistent with general study population

• Beware the BMI paradox!

1 Titti L et al. *Int J Cardiol* 2018;262:85-91
Case 2 – more complications

Back to Mr RG…
• Continue rivaroxaban 20mg od (with main meal!)
• Assess trough plasma level

But 2 months later…
• Chest pain – calls 999
• ECG in ambulance: STEMI
• Transferred for PPCI
What do we know?

- DAPT is indicated post ACS & PCI
  - Superior to aspirin alone\(^1\)
  - Optimal duration varies

- DAPT is inferior to OAC for stroke prevention in AF\(^2\)

- Triple therapy significantly increases bleeding risk
  - VKA + aspirin + clopidogrel = >3 fold ↑ in non-fatal+fatal bleeding\(^3\)

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1 Roffi M et al. *Eur Heart J* 2016;37:267-315
3 Hansen ML et al. *Arch Int Med* 2010;170:1433-1441
Prospective studies

- WOEST
- PIONEER AF-PCI
- RE-DUAL PCI

- Single versus double antiplatelet
  - In combination with OAC
- Primary endpoint is “safety” only (bleeding)
  - Underpowered for “efficacy” (MACE, stent thrombosis etc)
WOEST

• OAC = VKA
• 65% RRR in all bleeding
  – 19.4% and 44.4% respectively
  – High rates driven by minor bleeds
  – TIMI major 3% and 6% respectively (n.s.)
• Composite efficacy endpoint
  – Death, MI, revascularisation, stroke, stent thrombosis
  – HR 0.6 (95%CI 0.38-0.94)
  – Underpowered
• Non-standard OAC: INR target 2.0

PIONEER AF-PCI

• Triple therapy: VKA (2-3) + DAPT
  – 1, 3 or 12 months DAPT: 50% = 12mo

• Rivaroxaban
  – 15mg od (2/3 AF dose) + P2Y₁₂
  – 2.5mg bd (ACS dose) + DAPT

• 40% RRR bleeding with rivaroxaban arms
  – Composite TIMI major + clinically significant bleeding

• 12% STEMI
  – Bleeding: Riva15 = 14.6%, Triple therapy = 36%

• P2Y₁₂ choice: 5% ticagrelor, <2% prasugrel
RE-DUAL PCI

- Triple therapy: VKA (2-3) + DAPT
  - 1 month BMS, 3 months DES
- Dabigatran + P2Y\textsubscript{12}
  - 150mg bd – 30% RRR bleeding
  - 110mg bd – 50% RRR bleeding
- Bleeding: ISTH Major bleed + CRNM bleed
- P2Y\textsubscript{12} choice: 12% ticagrelor
- Non-inferiority for composite secondary endpoint
  - MI, Stroke, SSE, death, unplanned revascularisation
  - Combined analysis of both dabigatran arms vs warfarin
Summary

• Non-guideline INR targets
  – WOEST INR target 2.0 (1.5 to 2.5)
  – PIONEER / RE-DUAL target 2.5 (2.0 to 3.0)
  – ECS: 2.25 (2-2.5) \(^1\)

• Not powered for efficacy
  – But no signal for loss of efficacy

• Rivaroxaban doses not proven in SPAF
  – Both dabigatran doses effective for SPAF

• Clear reduction in clinically significant bleeding

• All the evidence is for clopidogrel as P2Y\(_{12}\) inh of choice
  – Registry data: increased bleeding with ticagrelor / prasugrel – avoid\(^1\)

\(^1\) Steffel J et al. Eur Heart J 2018;39:1330-1393
Guidelines

• Constantly evolving
  – New antithrombotic strategies
  – New generation DES with shorter DAPT requirements

• Significantly reduced duration of triple therapy

• Practical advice
  – PPI throughout combined antithrombotic therapy (COGENT\textsuperscript{1})
  – \textbf{Specify plan \& duration prior to discharge}\textsuperscript{2}

2 Steffel J et al. \textit{Eur Heart J} 2018;39:1330-1393
Factors to shorten combination therapy
- (Uncorrectable) high bleeding risk
- Low atherothrombotic risk (by REACH or SYNTAX score if elective; GRACE ≥140 if ACS)

Factors to lengthen combination therapy
- First-generation DES
- High atherothrombotic risk (scores as above; stenting of the left main, proximal LAD, proximal bifurcation; recurrent MIs; stent thrombosis etc.) and low bleeding risk

Steffel J et al. Eur Heart J 2018;39:1330-1393
Coming soon…

<table>
<thead>
<tr>
<th></th>
<th>AUGUSTUS</th>
<th>ENTRUST-AF-PCI</th>
<th>RT-AF</th>
<th>WOEST 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Design</td>
<td>RCT</td>
<td>RCT</td>
<td>RCT</td>
<td>Prospective cohort registry</td>
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<tr>
<td>Primary endpoint</td>
<td>Safety</td>
<td>Safety</td>
<td>Safety</td>
<td>Efficacy &amp; safety</td>
</tr>
</tbody>
</table>
Post 12 months

- Combination antithrombotics increased MB but no benefit on stroke or mortality
  - Post hoc analyses of pivotal DOAC studies in AF

- Retrospective cohort study\(^1\):
  - VKA + single antiplatelet in stable CAD (>12 months event free)
  - No reduction in MI or TE events
  - 50% increase in major bleeding

- Still a caveat in guidance for *exceptionally high risk* patients for recurrent MI / stent thrombosis

\(^1\) Lamberts M et al. *Circulation* 2014;129:1577-1585
What’s the message?

- Right drug
- **Right Dose!!!**
  - Use Cockcroft-Gault CrCl calculation
- We are still exploring at the edge of the normal distribution (watch this space)
- Always have a plan for concomitant antiplatelets
Thank you for listening

London SCN AF Toolkit
http://www.londonscn.nhs.uk/publication/atrial-fibrillation-toolkit-for-london/

London SCN Excellence in anticoagulant care

terry.dowling@gstt.nhs.uk
www.c4ht.com
@MrT_Dowling