WHICH NOAC TO USE FOR VTE

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Declarations

• Previous speaker fees from BMS-Pfizer Alliance
• No other declarations/ conflicts of interest

• I am not a haematologist so don’t ask me about the clotting cascade!
Why Me?

- 7 day Ambulatory Care Service
- DVT 288/year confirmed, 1159 suspected
- PE 129 confirmed, 670 suspected
- Community DVT pathways
- NOACs on our DVT pathway since Jan 2013
- Now our most used anticoagulant
Aims

- Overview
- Current Guidelines
- Look at NOAC trial data
- Practical take home points
- Safe service
Quiz

1. Lixiana is the trade name for which NOAC?
2. Which NOACs need bridging with LMWH?
3. Which is a factor IIa inhibitor?
4. Below what Creatinine Clearance are NOAC contraindicated?
5. Can NOACs be used in cancer related VTE?
6. Which NOAC has an evidenced based dose reduction for treatment after 6/12?
7. Which NOAC can’t go in a docette box?
8. Which NOACs have a reversal agent?
Why is VTE so important?

- **DVT** is common, (1 per 1,000 people/year)
- Complications include PE, PTS

- **PE** incidence 86 per 100,000
- Complications include death, CTEPH
  - Fatal PE is under diagnosed because of non specificity of symptoms
  - About 10% of hospital deaths were attributed to PE in the UK

- VTE causes an estimated 60,000 deaths each year in the UK
- Significant economic burden
  - Annual cost to NHS approx £640m/year

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**2010, estimated number of deaths in the UK per year**

- **VTE**: 56,167
- Traffic accidents: 2,243
- MRSA: 485
- HIV: 267

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Treatment of VTE

- Balance of thrombotic risk vs bleeding risk
- VKA reduces recurrence risk by 80-90%  
  - 1-2%/ year whilst on treatment
- Risk of VTE death  
  - PE 15%  
  - DVT 2%
- Risk of major bleeding  
  - 3%/ year on VKA  
  - Increase to 50% with age/comorbidities  
  - Annual incidence of fatal bleed approx 0.5%/year
- Trend towards lifelong anticoagulation
Risk Factors for Recurrence

- Patient features, nature of index event, risk factors
- Provokation
  - Unprovoked VTE
    - 5 year recurrence risk 20-30%
    - 11% at 1 year
    - 20% at 2 years
    - 30% at 5 years
    - 10%/ year
  - Provoked VTE
    - <3%/ year
- Index event
  - Recurrence risk higher with 1st unprovoked DVT vs PE
    - But PE more likely to recur as PE
  - Lowest risk after isolated distal clot vs proximal
Risk Factors for Recurrence

• Patient factors
  • Increasing age
  • Male sex
    • Men 1st unprovoked VTE 2 x higher risk recurrence
    • Women, oestrogen provoked VTE lowest risk recurrence
  • Thrombophilias
    • Greatest risk with antithrombin deficiency
  • Raised d-dimers 1 month after stopping anticoagulants
Higher recurrence rates in unprovoked VTE

Data from patients with non-active cancer

Adapted from Martinez et al. Thromb Haem 2014; 112. ePub ahead of print.
What treatment options do we have
## VTE treatment: parenteral anticoagulants

<table>
<thead>
<tr>
<th>Unfractionated heparin (UFH)¹</th>
<th>LMWHs²,³</th>
<th>Fondaparinux⁶</th>
</tr>
</thead>
<tbody>
<tr>
<td>◀ Inhibits further clot formation/propagation and permits the patient’s fibrinolytic system (plasmin) to lyse clot</td>
<td>◀ Injectable, SC</td>
<td>◀ Synthetic and selective inhibitor of activated Factor X (Xa)</td>
</tr>
<tr>
<td>◀ Usually given as IV bolus followed by continuous IV infusion</td>
<td>◀ Compared to UFH, LMWHs have greater bioavailability, a more predictable dose response, and a longer half-life</td>
<td>◀ Injectable, SC</td>
</tr>
<tr>
<td>◀ Anticoagulation level monitored by APTR ratio</td>
<td>◀ Enoxaparin (e.g. of LMWH) dosing is OD and weight-based⁴</td>
<td>◀ Longer half-life vs LMWHs (17 hours vs 4 hours)⁵,⁷</td>
</tr>
<tr>
<td>◀ Heparin-induced thrombocytopenia (HIT) and osteoporosis are the most important non-haemorrhagic side effects</td>
<td>◀ Generally, no need for monitoring (anti-Factor Xa assay if needed)</td>
<td>◀ Dosing is OD and based on patient’s weight: &lt;50 kg, 50–100 kg, or &gt;100 kg</td>
</tr>
<tr>
<td></td>
<td>◀ HIT occurs 8 to 10 times less frequently than with UFH⁵</td>
<td>◀ Does not affect routine coagulation tests</td>
</tr>
<tr>
<td></td>
<td></td>
<td>◀ Predominantly dependent on renal clearance</td>
</tr>
<tr>
<td></td>
<td></td>
<td>◀ There are rare spontaneous reports of HIT in patients treated with fondaparinux</td>
</tr>
</tbody>
</table>
# Oral Anticoagulants

<table>
<thead>
<tr>
<th></th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>VKA</strong></td>
<td>◀ Mainstay of therapy since 1960(^1)</td>
<td>◀ Slow onset/offset requires bridging(^1)</td>
</tr>
<tr>
<td></td>
<td>◀ Can be used in severe renal impairment(^2)</td>
<td>◀ Numerous interactions (drugs and food)(^1)</td>
</tr>
<tr>
<td></td>
<td>◀ Anticoagulation can be reversed(^2)</td>
<td>◀ Narrow therapeutic window(^1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>◀ Inter-individual variability in dose response(^1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>◀ Need for INR monitoring(^{1,2})</td>
</tr>
<tr>
<td><strong>NOACs</strong></td>
<td>◀ Predictable pharmacological profiles(^1)</td>
<td>◀ No readily available monitoring for special circumstances (e.g. major bleeding, urgent procedure)</td>
</tr>
<tr>
<td></td>
<td>◀ No major interactions (food or drugs)(^1)</td>
<td>◀ No reversal agent for most (NB dabigatran)</td>
</tr>
<tr>
<td></td>
<td>◀ Do not require routine level monitoring(^1)</td>
<td>◀ No long term data</td>
</tr>
<tr>
<td></td>
<td>◀ ACCP update recommending preferential use over VKA(^3)</td>
<td></td>
</tr>
</tbody>
</table>
Current Guidance

- NICE CG144 – 2012
- SIGN Guideline 122 – 2010
- ESC PE 2014
- NICE TAG for NOAC
# NICE technology appraisal guidance on NOACs in VTE

## Apixaban
- Recommended as an option for treating and for preventing recurrent deep vein thrombosis and pulmonary embolism in adults
- Recommended as an option for the prevention of venous thromboembolism in adults after elective hip or knee replacement surgery

## Rivaroxaban
- Recommended as an option for treating deep vein thrombosis and preventing recurrent deep vein thrombosis and pulmonary embolism after a diagnosis of acute deep vein thrombosis in adults
- Recommended as an option for the prevention of venous thromboembolism in adults having elective total hip replacement surgery or elective total knee replacement surgery

## Dabigatran
- Recommended as an option for the primary prevention of venous thromboembolic events in adults who have undergone elective total hip replacement surgery or elective total knee replacement surgery
- Recommended as an option for treating and for preventing recurrent deep vein thrombosis and pulmonary embolism in adults

## Edoxaban
- Recommended as an option for treating and for preventing recurrent deep vein thrombosis and pulmonary embolism in adults
For VTE and no cancer, as long-term anticoagulant therapy, we suggest dabigatran (Grade 2B), rivaroxaban (Grade 2B), apixaban (Grade 2B), or edoxaban (Grade 2B) over vitamin K antagonist (VKA) therapy, and suggest VKA therapy over low-molecular-weight heparin (LMWH; Grade 2C).

For patients with cancer long-term anticoagulation with LMWH over VKA therapy, and NOAC
VTE Treatment Phases

- **Acute**: To 10 days
- **Longterm**: 3-6 months
- **Extended**: >3-6 months

**Chest 2016 guidelines prevention**
- Automatically discontinuing anticoagulation after a fixed period is discouraged
- Indefinite use of anticoagulation with VKA’s, is discouraged
- Indefinite use of anticoagulation with aspirin discouraged
Navigating the evidence in VTE: NOAC clinical trials
<table>
<thead>
<tr>
<th>NOAC</th>
<th>Trial</th>
<th>Number of patients</th>
<th>Design</th>
<th>Parenteral required before NOAC?</th>
<th>NOAC dosing</th>
<th>Comparator</th>
<th>Treatment length (months)</th>
<th>Follow-up period</th>
<th>Key inclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apixaban</td>
<td>AMPLIFY¹</td>
<td>5,395 DVT: 3,532 PE: 1,896</td>
<td>Double-blind</td>
<td>No</td>
<td>Apixaban 10 mg twice daily for 7d, then 5 mg twice daily</td>
<td>Enoxaparin bridge to warfarin</td>
<td>6</td>
<td>30 days after study completion</td>
<td>DVT/PE requiring treatment for ≥ 6 months</td>
</tr>
<tr>
<td>Dabigatran</td>
<td>RE-COVER²</td>
<td>2,539 DVT:1,749 PE: 786</td>
<td>Double-blind</td>
<td>Required for at least 5 days</td>
<td>Dabigatran 150 mg twice daily</td>
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<td>RE-COVER II³</td>
<td>2,568 DVT: 1,750 PE: 816</td>
<td>Double-blind</td>
<td>Required for at least 5 days</td>
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<td>EINSTEIN-DVT⁴</td>
<td>DVT: 3,449</td>
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<td>No</td>
<td>Rivaroxaban 15 mg twice daily for 21d, then 20 mg once daily</td>
<td>Enoxaparin bridge to VKA</td>
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<td>EINSTEIN-PE⁵</td>
<td>PE: 4,832</td>
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<td>Hokusai-VTE⁶</td>
<td>8,240 DVT: 4,921 PE: 3,319</td>
<td>Double-blind</td>
<td>No</td>
<td>Enoxaparin or UFHafe ≥ 5 days</td>
<td>Enoxaparin bridge to warfarin</td>
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<td>For duration of treatment</td>
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## Practical take homes

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<td></td>
<td></td>
<td></td>
<td></td>
<td>PE with or without DVT</td>
<td></td>
</tr>
</tbody>
</table>
# NOAC extension trial designs for prevention of recurrent VTE

<table>
<thead>
<tr>
<th>Study drug</th>
<th>Trial</th>
<th>Number of patients</th>
<th>Treatment before randomisation</th>
<th>Study drug dosing</th>
<th>Comparator</th>
<th>Treatment length (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apixaban</td>
<td>AMPLIFY-EXT²</td>
<td>2,482</td>
<td>6–12 months of standard therapy or apixaban</td>
<td>Apixaban 2.5 mg or 5 mg twice daily*</td>
<td>Placebo</td>
<td>12</td>
</tr>
<tr>
<td>Dabigatran</td>
<td>RE-SONATE³</td>
<td>1,343</td>
<td>6–18 months of VKA or dabigatran</td>
<td>Dabigatran 150 mg twice daily</td>
<td>Placebo</td>
<td>6</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>EINSTEIN-EXT³</td>
<td>1,196</td>
<td>6 or 12 months of VKA or rivaroxaban</td>
<td>Rivaroxaban 20 mg once daily</td>
<td>Placebo</td>
<td>6 or 12</td>
</tr>
<tr>
<td>Edoxaban†</td>
<td>HOKUSAI-VTE⁴</td>
<td>8,240</td>
<td>No preceding anticoagulation</td>
<td>Edoxaban 60 mg once daily⁶</td>
<td>Warfarin</td>
<td>3 to 12</td>
</tr>
<tr>
<td>Dabigatran‡</td>
<td>RE-MEDY²</td>
<td>2,856</td>
<td>3–12 months of VKA or dabigatran</td>
<td>Dabigatran 150 mg twice daily</td>
<td>Warfarin INR 2.0–3.0</td>
<td>6–36</td>
</tr>
</tbody>
</table>
Other supporting Evidence

- Network meta-analysis
  - Confirms equivalence in terms of efficacy
  - Apixaban sig reduced risk of major and CRNM bleeding vs others
  - Dabigatran lower major/ CRNM bleeding vs rivar/edox
  - Rivaroxaban sig higher CRNM bleeding than dabig/ edox

- Real world data
  - Dresden NOAC registry
    - rivaroxaban CR bleeds may be less frequent and outcome at least no worse than VKA bleeds

- Chest 2016 – Direct comparison of Dabigatran, Rivaroxaban, and Apixaban for Effectiveness and Safety in Nonvalvular AF
  - Apixaban associated with lower bleeding risk and Rivaroxaban with a elevated bleeding risk
Summary of NOAC data

Efficacy

• **Initial Treatment of VTE**
  • NOACs comparable to warfarin in reducing recurrent VTE or VTE-related deaths
  • NOACs were comparable to or superior in reducing the risk of major bleeding compared to warfarin
  • No head to head studies between NOACs
  • Apixaban and rivaroxaban can be initiated without initial LMWH (unlike dabigatran and edoxaban)

• **Prevention of recurrent VTE**
  • NOAC vs placebo, significantly reduced risk of recurrent VTE or VTE-related death
  • Apixaban only NOAC with dose reduction after 6 months

Safety

• NOACS associated with less major/ CRNM bleeding vs VKA
• Apixaban demonstrated comparable major bleeding rates vs placebo for the prevention of recurrent VTE

Each study has its own limitations such as differing patient populations, designs and outcomes.
NOACs in cancer related VTE

- In original trials for NOACs approx. 1000/27000 had cancer
- Remote cancers not on chemo
- Efficacy prevention VTE and major bleeding trend towards favour (over warfarin), not statistically significant

- Hokusai-VTE cancer trial – dalteparin vs edoxaban

- ACCP - For VTE and cancer, we suggest LMWH over VKA (Grade 2B), dabigatran (Grade 2C), rivaroxaban (Grade 2C), apixaban (Grade 2C), or edoxaban (Grade 2C).
So how do we choose in everyday life

Suitable for NOAC

Discuss options

Yes

No

LMWH

Warfarin

Informed patient choice
Who shouldn’t have a NOAC

- Renal disease and creatinine clearance <30ml/min (15ml/min)
- Liver disease and coagulopathy
- Alcohol/ drug misuse
- Cancer
- Drugs
- Anti-platelet therapy (ESC guidance)
- Poor medication compliance
- Thrombolytic agents used
- Pregnancy or pregnancy risk
- Need for a reversal agent
## Important Drug Reactions

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dabigatran</th>
<th>Apixaban</th>
<th>Edoxaban</th>
<th>Rivaroxaban</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atorvastatin</td>
<td>P-gp/CYP3A4</td>
<td>+18%</td>
<td>no effect</td>
<td>no effect</td>
</tr>
<tr>
<td>Digoxin</td>
<td>P-gp</td>
<td>no effect</td>
<td>no effect</td>
<td>no effect</td>
</tr>
<tr>
<td>Verapamil</td>
<td>P-gp/wk CYP3A4</td>
<td>+12–180%</td>
<td>+ 53% (slow release)</td>
<td></td>
</tr>
<tr>
<td>Diltiazem</td>
<td>P-gp/wk CYP3A4</td>
<td>no effect</td>
<td>+40%</td>
<td></td>
</tr>
<tr>
<td>Quinidine</td>
<td>P-gp</td>
<td>+50%</td>
<td>+80%</td>
<td>+50%</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>P-gp</td>
<td>+12–60%</td>
<td>no effect</td>
<td></td>
</tr>
<tr>
<td>Dronedarone</td>
<td>P-gp/CYP3A4</td>
<td>+70–100%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ketoconazole; Itraconazole; Voriconazole;Posaconazole;</td>
<td>P-gp and BCRP/ CYP3A4</td>
<td>+140–150%</td>
<td>+100%</td>
<td>up to +160%</td>
</tr>
</tbody>
</table>

Red – contraindicated; orange – reduce dose; yellow – consider dose reduction if another yellow factor present; hatching – no data available; recommendation made from pharmacokinetic considerations

www.escardio.org/EHRA
<table>
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<tr>
<th>Interaction</th>
<th>Interaction</th>
<th>Dabigatran</th>
<th>Apixaban</th>
<th>Edoxaban</th>
<th>Rivaroxaban</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluconazole</td>
<td>CYP3A4</td>
<td>no data</td>
<td>no data</td>
<td>no data</td>
<td>+42%</td>
</tr>
<tr>
<td>Cyclosporin; tacrolimus</td>
<td>P-gp</td>
<td>no data</td>
<td>no data</td>
<td>no data</td>
<td>+50%</td>
</tr>
<tr>
<td>Clarithromycin; erythromycin</td>
<td>P-gp/ CYP3A4</td>
<td>+15–20%</td>
<td>no data</td>
<td>no data</td>
<td>+30–54%</td>
</tr>
<tr>
<td>HIV protease inhibitors</td>
<td>P-gp and BCRP/ CYP3A4</td>
<td>no data</td>
<td>strong increase</td>
<td>no data</td>
<td>up to +153%</td>
</tr>
<tr>
<td>Rifampicin; St John’s wort; carbamezepine; phenytoin; phenobarbital</td>
<td>P-gp and BCRP/ CYP3A4/CYP2J2</td>
<td>-66%</td>
<td>-54%</td>
<td>-35%</td>
<td>up to -50%</td>
</tr>
<tr>
<td>Antacids</td>
<td>GI absorption</td>
<td>-12-30%</td>
<td>no data</td>
<td>no effect</td>
<td>no effect</td>
</tr>
</tbody>
</table>

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www.escardio.org/EHRA
WHICH NOAC?
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<tr>
<th>Characteristic</th>
<th>Choice</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate renal imp (creat</td>
<td>Apixaban</td>
<td>Less renal clearance than dabigatran</td>
</tr>
<tr>
<td>clearance 30-50 ml/min)</td>
<td>Rivaroxaban</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Edoxaban</td>
<td></td>
</tr>
<tr>
<td>Creat clearance 15-30 ml/min</td>
<td>Apixaban</td>
<td>With caution (Dose reduced edoxaban)</td>
</tr>
<tr>
<td>Upper GI symptoms/ bleed</td>
<td>Apixaban</td>
<td>10% dyspepsia with dabigatran</td>
</tr>
<tr>
<td></td>
<td></td>
<td>More GI bleeding with riva/dabig/edox than warfarin</td>
</tr>
<tr>
<td>Wants OD dosing</td>
<td>Rivaroxaban</td>
<td>Other dosed BD</td>
</tr>
<tr>
<td></td>
<td>Edoxaban</td>
<td></td>
</tr>
<tr>
<td>No LMWH</td>
<td>Apixaban</td>
<td>Dabig/ edoxaban require LMWH</td>
</tr>
<tr>
<td></td>
<td>Rivaroxaban</td>
<td></td>
</tr>
<tr>
<td>Significant CAD</td>
<td>Apixaban</td>
<td>Small MI signal with dabigatran</td>
</tr>
<tr>
<td></td>
<td>Rivaroxaban</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Edoxaban</td>
<td></td>
</tr>
<tr>
<td>Reversal agent</td>
<td>Dabigatran</td>
<td>Idaracizumab</td>
</tr>
</tbody>
</table>
What about Reversal

Dabigatran
- Idaracizumab (Praxbind)

Factor Xa inhibitors
- Andexanet alfa

• Coming soon......
Management of bleeding (including head injury)

STOP DABIGATRAN
(half life 13 hours with normal renal function)

- Do Coagulation screen (APTT, TT)¹
  - Do FBC and renal function (e GFR) and LFTs
  - Ensure time last dose dabigatran documented

- APTT / TT² normal – dabigatran levels – low / absent
- APTT normal with prolonged TT – dabigatran levels low

- APTT and TT prolonged

Dabigatran anticoagulant effect maybe present (consider oral charcoal if dabigatran ingestion <2 hours)

- MILD BLEED
  - Mechanical compression
  - Minor surgical intervention
  - Fluid replacement (excreted renaly)
  - Tranexamic acid oral 25mg/kg / IV 10mg/kg

- MAJOR BLEED
  - Maintain BP and Urine Output

- LIMB/LIFE-THREATENING BLEED
  - Administer Idarucizumab

- Continues to bleed

- Optimise tissue oxygenation
- Control Haemorrhage
  - mechanical compression
  - surgical/radiological intervention
- Tranexamic Acid 1g IV
- Red cell transfusion (aim Hb>70g/L)
- Platelet transfusion (aim platelets >20 x10⁵ /μL or if CNS bleed aim >100 x 10⁵)
- Identify bleeding source e.g. surgery, endoscopy, interventional radiology.

¹If reversal is necessary, administer Idarucizumab. Contact Consultant Haematologist prior to administration
STOP Rivaroxaban (half-life 7-9 hrs) or Apixaban (half-life 12 hours) or Edoxaban (half-life 10-14 hours)

- Do Coag screen to include APTT ratio / prothrombin time (PT)
- Do FBC, eGFR and LFTs
- Ensure time of last dose documented

APTT ratio and PT normal – no rivaroxaban/apixaban anticoagulant effect present. Treat as bleed in non anticoagulated patient.

APTT ratio and PT prolonged – NOAC anticoagulant effect may be present. Consider oral charcoal if ingestion <2 hours ago.

MINOR BLEED
- Mechanical compression
- Minor surgical intervention
- Fluid replacement

MAJOR BLEED (including life threatening)
- Maintain BP and Urine Output
- Optimise tissue oxygenation
- Control Haemorrhage
  - mechanical compression
  - surgical/radiological intervention
  - Tranexamic Acid 1g IV
  - Red cell transfusion (aim Hb >70g/L)
  - Platelet transfusion (aim platelets >50 x10⁹/L or if CNS bleed aim >100 x 10⁹/L)
  - Identify bleeding source e.g. surgery, endoscopy, interventional radiology
  - Prothrombin Complex Concentrate (PCC) – Beriplex – can be considered. Contact Consultant Haematologist for advice as there is limited data on its use.
Starting NOAC

- Creatinine Clearance documented
- Pregnancy test/contraception
- Counselling/FU counselling
- Compliance/Missed doses
- Communication about dose reductions
- Alert cards
- Patient information leaflets
A PATIENT’S GUIDE TO DEEP VEIN THROMBOSIS TREATMENT
Making your service safe

- Educate your staff
- Educate your patients
- Counselling
- Correct dose prescribing
- Overlabelling
- Communication to primary care

- Follow up
- Trust guidelines
- Audit service
Quiz

1. Lixiana is the trade name for which NOAC?
2. Which NOACs need bridging with LMWH?
3. Which is a factor IIa inhibitor?
4. Below what Creatinine Clearance are NOAC contraindicated?
5. Can NOACs be used in cancer related VTE?
6. Which NOAC has an evidenced based dose reduction for treatment after 6/12?
7. Which NOAC can’t go in a docette box?
8. Which NOACs have a reversal agent?
Summary

• NOAC use is increasing for VTE treatment
• Shift in national and international guidelines towards NOAC use
• Safe compared to warfarin, if not better
• Remain some unanswered questions: cancer, pregnancy, DAPT
THANK YOU

Any Questions?
References

- http://journal.publications.chestnet.org/article.aspx?articleid=2479255&resultClick=3
- https://www.escardio.org/Guidelines/Clinical-Practice-Guidelines/Acute-Pulmonary-Embolism-Diagnosis-and-Management-of
- Kieron C et al. 1999 A Comparison of 3 months vs extended anticoagulation for a 1st VTE. NEJM
- Douketis et al. 2003 Clinical Impact of bleeding in pts taking oral ac therapy for VTE. Ann Int Med
- Lee et al. 2003. LMWH vs coumarin for prevention of recurrent VTE in patients with cancer. NEJM
- https://www.nice.org.uk/Guidance/cg144
- NICE technology appraisal guidance (TA287). Rivaroxaban for treating pulmonary embolism and preventing recurrent venous thromboembolism. June 2013;
- NICE technology appraisal guidance (TA57). Rivaroxaban for the prevention of venous thromboembolism after total hip or total knee replacement in adults. April 2009;
- NICE technology appraisal guidance (TA327). Dabigatran etexilate for the treatment and secondary prevention of deep vein thrombosis and/or pulmonary embolism. December 2014
- NICE technology appraisal guidance (TA354). Edoxaban for treating and for preventing deep vein thrombosis and pulmonary embolism. August 2015.
- SIGN Guideline 122 Prevention and management of venous thromboembolism