ESMO PRECEPTORSHIP PROGRAMME
SUPPORTIVE AND PALLIATIVE CARE
Multidisciplinary management, standards of care, therapeutic targets and future perspectives

Lugano, Switzerland
1-2 February 2019

CHAIR: Karin Jordan, Germany
CO-CHAIR: Florian Strasser, Switzerland

SPEAKERS:
Matti Aapro, Switzerland
Jann Arends, Germany
Maria Die-Trill, Spain
Manuela Eicher, Switzerland
Berit Jordan, Germany
Florian Scotté, France
Jayne Wood, United Kingdom
Prevention and management of thromboembolism including the new role of Novel Oral Anticoagulants (NOACs) in cancer patients
PREVENTION and MANAGEMENT of THROMBOEMBOLISM

Is there a role for Direct Oral Anticoagulants (DOACs)?

Matti Aapro MD
Cancer Center, Genolier, Switzerland
Member ESMO Supportive Care Faculty
Study Group leader and Past-President of MASCC
(Multinational Association for Supportive Care in Cancer)
Honorary President of AFSOS
(French-speaking Association for Supportive Care)
And Advisor to JASCC
(Japanese Association for Supportive Care)
DISCLOSURE OF INTEREST

Dr. Matti Aapro

Consultant to
Accord, Amgen, BMS, Celgene, Clinigen, Eisai, Genomic Health, GSK, Helsinn, Hospira, JnJ, Merck, Merck Serono, Novartis, Pfizer, Pierre Fabre, Roche, Sandoz, Tesaro, Teva, Vifor

and has received honoraria for lectures at symposia of
Accord, Amgen, Bayer Schering, Biocon, Boehringer, Cephalon, Chugai, Eisai, DrReed, Genomic Health, Glenmark, GSK, Helsinn, Hospira, Ipsen, JnJ, OrthoBiotech, Kirin Kyowa, Merck, Merck Serono, Novartis, Pfizer, Pierre Fabre, Roche, Sandoz, Sanofi, Tesaro, Taiho, Teva, Vifor
DO NOT REINVENT THE WHEEL
(but an update is needed)

Palliative and supportive care

Management of Venous Thromboembolism (VTE) in Cancer Patients: ESMO Clinical Practice Guidelines

Authors: M. Mandalà, A. Falanga and F. Roila

Antithrombotic therapy for prophylaxis and treatment of venous thromboembolism in patients with cancer: review of the literature on current practice and emerging options

Cihan Ay,1 Pieter Willem Kamphuisen,2 Giancarlo Agnelli3

ABSTRACT
The treatment of cancer-associated venous thromboembolism (VTE) is difficult because cancer patients with VTE on anticoagulation are at an increased risk of bleeding compared with patients without VTE. This review summarises the evidence supporting the current standard of care and emerging treatment options. In difficult-to-treat subpopulations, where clinical data are often lacking, this review also provides the best clinical practice strategies based on the available data. The use of therapeutic doses of parenteral anticoagulants in patients with cancer-associated VTE for at least 3 to 6 months is supported by the current clinical data. After embolism (PE), is 1 to 2 per 1000 person-years among the general population.1 However, the incidence of VTE is up to 5.5-fold higher in patients with cancer versus patients without cancer.2-5 Overall, cancer accounts for an estimated 18% of the total number of VTE cases, and VTE is a leading cause of death among patients with cancer.2-5 The survival rates are also lower, prognosis worse and healthcare costs higher in cancer patients with VTE compared with those without.6-11 Vitamin K antagonists (VKAs) with initial
Prevention and Management of Thrombosis

Annie Young
Warwick Medical School, UK

ESMO Preceptorship, Lugano, 17th April 2018
Disclosures

Honoraria from:

MSD
Helsinn
Bayer
Leo Pharma

Educational grant from:

Bayer
Epidemiology
Cancer Associated Thrombosis (CAT)

150+ years on......

• Common Condition  *Bidirectional Relationship*

• *2\(^{nd}\) most common and preventable cause of death in outpatients with cancer*

• Cancer patients 4-7 fold increased risk of VTE in comparison to general population

• Incidence of VTE: High and rising, highest in first few months after cancer diagnosis

• 20-30% of all first VTEs are CAT (Trousseau’s syndrome)

Timp et al. 2013 *Blood* 122 (10): 1712-1723
Walker et al. 2013 *Eur J Cancer* 49 (6): 1404-1413
Current Guidelines ‘Risk Assessment’

• Based on consensus, the Panel recommends that patients with cancer be assessed for VTE risk at time of chemotherapy initiation and periodically thereafter.................

• In the outpatient setting, risk assessment can be conducted using a validated risk assessment tool (e.g. ..................)

Lyman GH et al. 2013 J Clin Oncol. 31: 2189-2204
Current Guidelines ‘Risk Assessment’

• Based on consensus, the Panel recommends that patients with cancer be assessed for VTE risk at time of chemotherapy initiation and periodically thereafter.................

• In the outpatient setting, risk assessment can be conducted using a validated risk assessment tool (e.g. Khorana)

Lyman GH et al. 2013 *J Clin Oncol.* 31: 2189-2204
## Khorana Risk Assessment?

<table>
<thead>
<tr>
<th>Patient characteristic (site of cancer)</th>
<th>Risk score*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very high risk (stomach, pancreas)</td>
<td>2</td>
</tr>
<tr>
<td>High risk (lung, lymphoma, gynaecological, bladder, testicular)</td>
<td>1</td>
</tr>
<tr>
<td>Prechemotherapy platelet count $350 \times 10^9/\text{l}$ or more</td>
<td>1</td>
</tr>
<tr>
<td>Haemoglobin level less than 110 g/l or use of red cell growth factors</td>
<td>1</td>
</tr>
<tr>
<td>Prechemotherapy leucocyte count more than $11 \times 10^9/\text{l}$</td>
<td>1</td>
</tr>
<tr>
<td>BMI 35 kg/m$^2$ or more</td>
<td>1</td>
</tr>
</tbody>
</table>

Thromboprophylaxis
The Hospitalised Patient
## Anticoagulant Prophylaxis to Prevent Objectively Diagnosed VTE

### High-risk hospitalized medical patients

<table>
<thead>
<tr>
<th>Study</th>
<th>Rate of VTE with anticoagulant vs placebo</th>
<th>ARR</th>
<th>RRR</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MEDENOX¹</td>
<td>Placebo 14.9% vs Placebo 5.5% Enoxaparin 40 mg</td>
<td>9.4%</td>
<td>63%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PREVENT²</td>
<td>Placebo 5.0% vs Placebo 2.8% Dalteparin 5000 units</td>
<td>2.2%</td>
<td>45%</td>
<td>0.0015</td>
</tr>
<tr>
<td>ARTEMIS³</td>
<td>Placebo 10.5% vs Placebo 5.6% Fondaparinux 2.5 mg</td>
<td>4.9%</td>
<td>47%</td>
<td>–</td>
</tr>
<tr>
<td>EXCLAIM⁴</td>
<td>Placebo 4.0% vs Placebo 2.5% Enoxaparin 40 mg</td>
<td>-1.53%</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

MEDENOX Subanalysis: VTE Prophylaxis Also Decreases the Rate of VTE Events in Cancer Patients

CHF, chronic heart failure; CRF, chronic respiratory failure between day 1 and day 14
Attempted Approach 1: Treat Cancer as a ‘Generic’ Diagnosis

SAVE-ONCO study

- Patients (N=3212) with solid tumours receiving chemotherapy randomized (1:1) to semuloparin 20 mg od or placebo for duration of chemotherapy course
- 59% risk reduction in PE rate (OR=0.41; 95% CI 0.19–0.85)

<table>
<thead>
<tr>
<th></th>
<th>Semuloparin % (n/N)</th>
<th>Placebo % (n/N)</th>
<th>HR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall VTE</td>
<td>1.2 (20/1608)</td>
<td>3.4 (55/1604)</td>
<td>0.36 (0.21–0.60)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Attempted Approach 2: Study a ‘High-Risk’ Cancer

Kaplan–Meier plot of the incidence of VTE ≤2 years of diagnosis of five different types of cancer with (A) metastatic-stage and (B) regional-stage disease at the time of diagnosis

Chew HK et al, Arch Intern Med 2006;166:458–464
Attempted Approach 2: The FRAGEM Study in Pancreatic Ca

Cumulative probability of VTE occurrence

POTENTIAL SUBSTITUTION OF LMWH BY DOACs

NB: « warfarins » ARE inferior to LMWH in CANCER patients….
Direct Oral Anticoagulants (DOACs):
Potential Disadvantages of the Oral Route

◆ Oral route may not be ideal in cancer patients (vomiting, obstruction, nausea, anorexia, enteric neuropathy, etc.)\(^1\)
◆ Limited experience in patients with liver and renal impairment\(^2\)
◆ Reducing the dose (i.e. for occurrence of thrombocytopenia) more challenging than with LMWHs\(^1\)
◆ Interactions with anticancer and supportive drugs have not been systematically assessed

Apixaban for Prevention of VTE in Patients with Metastatic Cancer Receiving Chemotherapy

- Advanced or metastatic cancer patients undergoing first-line or second-line chemotherapy
- Double-blind, randomized phase 2 pilot study in 125 patients
  - Apixaban 5 mg, 10 mg or 20 mg od or placebo od for 12 weeks
  - Treatment began within 4 weeks of the start of chemotherapy

<table>
<thead>
<tr>
<th>N (%), 95% CI</th>
<th>Apixaban 5 mg od (n=32)</th>
<th>Apixaban 10 mg od (n=29)</th>
<th>Apixaban 20 mg od (n=32)</th>
<th>Placebo od (n=29)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major bleeding</td>
<td>0 (0), (0.0–11)</td>
<td>0 (0), (0.0–12)</td>
<td>2 (6.3), (0.8–21)</td>
<td>1 (3.4), (0.1–18)</td>
</tr>
<tr>
<td>CRNM bleeding</td>
<td>1 (3.1), (0.1–16)</td>
<td>1 (3.4), (0.1–18)</td>
<td>2 (6.3), (0.8–21)</td>
<td>0 (0.0), (0.0–12)</td>
</tr>
<tr>
<td><strong>Secondary outcome</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VTE</td>
<td>0 (0.0), (0.0–11)</td>
<td>0 (0.0), (0.0–12)</td>
<td>0 (0.0), (0.0–11)</td>
<td>3 (10.3), (2.2–27)</td>
</tr>
</tbody>
</table>

No fatal bleeding events reported
CASSINI: Study Design

**Rationale:** Assess the efficacy and safety of rivaroxaban versus placebo for VTE prophylaxis in ambulatory cancer patients initiating systemic cancer therapy and at high risk of VTE\(^1,2\)

**Population:** Patients with various cancer types initiating systemic chemotherapy at high risk of VTE\(^*\)

- **Rivaroxaban** 10 mg od\(^\dagger\)
  - 180±3 days treatment period with follow-up visits every 8 weeks (±7 days)
- **Placebo**

**Short design:** Multinational, multicentre, randomized, double-blind, placebo-controlled phase IIIb superiority study

**Indication:** VTE prevention in patients with cancer

**FPFV:** Q4-15
**LPLV:** Q3-18

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LBA-1 Rivaroxaban Thromboprophylaxis in High-Risk Ambulatory Cancer Patients Receiving Systemic Therapy: Results of a Randomized Clinical Trial (CASSINI)

Program: General Sessions
Session: Late-Breaking Abstracts Session
Hematology Disease Topics & Pathways:
Therapies, Clinically relevant

Tuesday, December 4, 2018, 7:30 AM-9:15 AM
Hall AB (San Diego Convention Center)

Alok A. Khorana¹, Gerald A. Soff², Ajay K. Kakkar³, Saroj Vadhan–Raj⁴, Hanno Riess⁵, Ted Wun⁶, Michael B. Streiff, MD ⁷, David A. Garcia, MD⁸, Howard A. Liebman⁹, Chandra Belani¹⁰, Eileen M. O’Reilly¹¹, Jai N Patel¹², Habte A. Yimer¹³, Peter Wildgoose¹⁴, Paul Burton¹⁴, Ujjwala Vijapurkar¹⁵, Simrati Kaul¹⁴, John Eikelboom¹⁶, Robert D. McBane, MD¹⁷, Kenneth A. Bauer, MD¹⁸, Nicole M. Kuderer¹⁹ and Gary H. Lyman¹⁹
A. Primary Events up to Day 180, All Randomized Patients

- **Cumulative Event Rate (%)**
  - **Placebo**
  - **Rivaroxaban**

- **Relative Days from Randomization**
  - 0
  - 56
  - 112
  - 180
  - 210

- **Number at risk**
  - Placebo: 421
  - Rivaroxaban: 420

- **Cumulative Event Rate (%)**
  - Placebo: 369
  - Rivaroxaban: 367

- **p-value (Log rank test)**: 0.101
- **HR (95% CI)**: 0.66 (0.40, 1.09)

B. Primary Endpoint Events During Treatment, All Randomized Patients

- **Cumulative Event Rate (%)**
  - **Placebo**
  - **Rivaroxaban**

- **Relative Days from Randomization**
  - 0
  - 56
  - 112
  - 180
  - 210

- **Number at risk**
  - Placebo: 421
  - Rivaroxaban: 420

- **Cumulative Event Rate (%)**
  - Placebo: 336
  - Rivaroxaban: 338

- **p-value (Log rank test)**: 0.007
- **HR (95% CI)**: 0.40 (0.20, 0.80)

C. Composite of Primary Endpoint Events and All-Cause Mortality up to Day 180, All Randomized Patients

- **Cumulative Event Rate (%)**
  - **Placebo**
  - **Rivaroxaban**

- **Relative Days from Randomization**
  - 0
  - 56
  - 112
  - 180
  - 210

- **Number at risk**
  - Placebo: 421
  - Rivaroxaban: 420

- **Cumulative Event Rate (%)**
  - Placebo: 374
  - Rivaroxaban: 377

- **p-value (Log rank test)**: 0.030
- **HR (95% CI)**: 0.75 (0.57, 0.97)

- **Number at risk**
  - Placebo: 421
  - Rivaroxaban: 420

- **Cumulative Event Rate (%)**
  - Placebo: 312
  - Rivaroxaban: 327

- **p-value (Log rank test)**: 0.030
- **HR (95% CI)**: 0.75 (0.57, 0.97)

- **Number at risk**
  - Placebo: 421
  - Rivaroxaban: 420

- **Cumulative Event Rate (%)**
  - Placebo: 188
  - Rivaroxaban: 211

- **p-value (Log rank test)**: 0.030
- **HR (95% CI)**: 0.75 (0.57, 0.97)
Thromboprophylaxis Conclusions

• Thromboprophylaxis should be practised in acutely ill cancer patients

• Guidelines do not recommend use of routine thromboprophylaxis in ambulatory cancer patients other than in high-risk patients (e.g. pancreatic cancer) \(^2\)–\(^6\)

• Individualisation is recommended – Khorana score should be considered

• Risk adaptive models may identify ambulatory cancer patients who would most benefit from thromboprophylaxis need testing

• Evidence for DOACs in this setting is lacking but more studies are underway

• Care needs to be taken in the study designs to cater for the right patients
Prophylaxis of Venous Thromboembolism in Cancer Patients

Prevention ‘YES’:  
- Patients with multiple myeloma and therapy with angiogenesis inhibitors/dexamethasone 
- Patients with major surgery, prior to surgery and 7-10 days thereafter 
- Extended prophylaxis up to 4 weeks after major abdominal or pelvic surgery for patients with other risk factors

Prevention ‘NO’:  
- No routine thromboprophylaxis for outpatients - ?high risk

Lyman GH et al., J Clin Oncol 2015, 33:654-6
Background – Treatment of VTE in cancer patients

- VTE in cancer is a major challenge
- Cancer patients are at increased risk of recurrent VTE and major bleeding on anticoagulant therapy\(^1\)
- LMWH is the recommended standard for treatment and prevention of recurrent VTE in cancer patients
- Direct oral anticoagulants (DOACs) are recommended for the management of patients with VTE *without* cancer
- Limited data for DOACs in patients with cancer-associated thrombosis

\(^1\)Hutten et al. *Journal of Clinical Oncology* 2000; 18, 3078-3083
Treatment of Venous Thromboembolism in Cancer

- LMWH\textsuperscript{1}
- ‘CLOT’ and CATCH LMWH vs WARFARIN Studies\textsuperscript{2,3}
- UFH – if renal impairment
- Fondaparinux – for patients with HIT
- EINSTEIN rivaroxaban Substudy\textsuperscript{4}

1. Akl EA et al. 2011 Cochrane Reviews 15 CD006650
2. Lee AY et al. NEJM 2003 349: 146-153
DOACs vs LMWH

Main research objectives

• To assess VTE recurrence in cancer patients with a first VTE, treated with rivaroxaban or dalteparin
• To assess rates of major and clinically relevant non-major bleeding
• To assess extended anticoagulation treatment beyond 6 months in selected patients
**Study design**

Prospective, randomised, open-label, multicentre pilot phase III trial

**Study population:**
Active cancer with symptomatic DVT and/or any PE
ECOG PS ≤ 2

**Stratification variables:**
• Stage of disease
• Baseline platelet count
• Type of VTE
• Risk of clotting by tumour type

**Dalteparin**
200 IU/kg od for the first 30 days followed by 150 IU/kg od

**Rivaroxaban**
15 mg bid for 21 days followed by 20 mg od

n=530

6 months
## VTE recurrence

**Dalteparin** (n=203) | **Rivaroxaban** (n=203)
---|---
VTE recurrences within 6 months, n  
DVT or PE  
Other location | 18  
16  
2 | 8  
6  
2
6-month VTE recurrence rate, % (95% CI)  
6-month lower limb DVT or PE recurrence rate | 11% (7–16%)  
9% (6-15%) | 4% (2–9%)  
3% (1-7%)
**Hazard ratio (95% CI)** | 0.43 (0.19-0.99)

### Numbers at Risk:

<table>
<thead>
<tr>
<th></th>
<th>Dalteparin</th>
<th>Rivaroxaban</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dalteparin</td>
<td>203</td>
<td>203</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>203</td>
<td>203</td>
</tr>
</tbody>
</table>

### Months from trial entry

- **Dalteparin**
- **Rivaroxaban**

![Graph showing VTE recurrence rates over time](image-url)
## Major bleeds

<table>
<thead>
<tr>
<th>Months from trial entry</th>
<th>Dalteparin (n=203)</th>
<th>Rivaroxaban (n=203)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
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<tr>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Numbers at Risk:

- Dalteparin: 203
- Rivaroxaban: 203

### Major bleed*, n

- Dalteparin: 6
- Rivaroxaban: 11

### 6 month major bleed rate, % (95% CI)

- Dalteparin: 4% (2-8%)
- Rivaroxaban: 6% (3-11%)

### Hazard ratio major bleeds (95% CI)

- Dalteparin: 1.83 (0.68-4.96)

### Graph

- Solid line: Dalteparin
- Dashed line: Rivaroxaban

*1 fatal bleed in each arm; 2. Mostly GI bleeds
Clinically relevant non-major bleeds

<table>
<thead>
<tr>
<th>Clinically relevant non-major bleed</th>
<th>Dalteparin (n=203)</th>
<th>Rivaroxaban (n=203)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 month CRNMB rate, % (95% CI)</td>
<td>4% (2-9%)</td>
<td>13% (9-19%)</td>
</tr>
<tr>
<td>Hazard ratio for CRNMB (95% CI)</td>
<td>3.76 (1.63-8.69)</td>
<td></td>
</tr>
</tbody>
</table>

• Overall, 1 in 5 patients who were screened, participated in the study
• Recurrent VTE was significantly reduced in favour of rivaroxaban: HR 0.43 (0.19-0.99)
• No difference in major bleeding: HR 1.83 (0.68-4.96)
• CRNMB was significantly greater in the rivaroxaban arm: HR 3.76 (1.63-8.69)
• The high mortality and clinician choice made the second randomisation non-feasible
## 2 DOAC “Cancer” Trials

<table>
<thead>
<tr>
<th></th>
<th><strong>Hokusai-VTE-Cancer</strong>(^1)</th>
<th><strong>select-d</strong>(^2-4)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Design</strong></td>
<td>Non-inferiority</td>
<td>Randomized pilot</td>
</tr>
<tr>
<td><strong>Patients</strong></td>
<td>Active cancer</td>
<td>Active cancer</td>
</tr>
<tr>
<td><strong>Rx</strong></td>
<td>◆ LMWH 5 days edoxaban po od</td>
<td>◆ Rivaroxaban po od</td>
</tr>
<tr>
<td></td>
<td>◆ Dalteparin s.c. od</td>
<td>◆ Dalteparin s.c. od</td>
</tr>
<tr>
<td></td>
<td>◆ 6 months and up to 12 months</td>
<td>◆ 6 months and second randomization</td>
</tr>
<tr>
<td><strong>Outcome</strong></td>
<td>Composite of recurrent VTE or major bleeding</td>
<td>Primary: recurrent VTE</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Secondary: major bleeding and CRNM bleeding</td>
</tr>
<tr>
<td><strong>Sample size</strong></td>
<td>1050</td>
<td>406</td>
</tr>
<tr>
<td><strong>Results</strong></td>
<td>• Recurrent VTE: 3.4% in favour of edoxaban</td>
<td>• Recurrent VTE: 7.0% in favour of rivaroxaban</td>
</tr>
<tr>
<td></td>
<td>• Major bleeding: 2.9% in favour of dalteparin</td>
<td>• Major bleeding: 2.0% in favour of dalteparin</td>
</tr>
</tbody>
</table>


1. /;
Xarelto is an anticoagulant medicine (a medicine that prevents blood clotting) used in adults:

- to prevent venous thromboembolism (VTE, the formation of blood clots in the veins) in patients who are undergoing surgery to replace a hip or knee;
- to prevent stroke (caused by a blood clot in the brain) and systemic embolism (a blood clot in another organ) in patients with non-valvular atrial fibrillation (irregular rapid contractions of the upper chambers of the heart);
- to treat deep vein thrombosis (DVT, a blood clot in a deep vein, usually in the leg) and pulmonary embolism (a clot in a blood vessel supplying the lungs), and to prevent DVT and pulmonary embolism from re-occurring.
- to prevent atherothrombotic events (problems caused by blood clots and hardening of the arteries) after an acute coronary syndrome. Acute coronary syndrome is a group of conditions that includes unstable angina (a severe type of chest pain) and heart attack. Xarelto is used together with antiplatelet medicines, which prevent the formation of blood clots.

Xarelto contains the active substance rivaroxaban.
4.1 Therapeutic indications

Prevention of venous thromboembolic events (VTE) in adult patients who have undergone elective hip or knee replacement surgery.

Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation (NVAF), with one or more risk factors, such as prior stroke or transient ischaemic attack (TIA); age $\geq 75$ years; hypertension; diabetes mellitus; symptomatic heart failure (NYHA Class $\geq$ II).

Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults (see section 4.4 for haemodynamically unstable PE patients).
Lixiana is an anticoagulant medicine (a medicine that prevents blood clotting) used in adults:

....to prevent stroke (caused by blood clots in the brain) and systemic embolism (blood clots in other organs) in patients with non-valvular atrial fibrillation (irregular rapid contractions of the upper chambers of the heart). It is used in patients who have one or more risk factors, such as having had a previous stroke, high blood pressure, diabetes, heart failure or being 75 years old or over;

...to treat deep-vein thrombosis (DVT, a blood clot in a deep vein, usually in the leg) and pulmonary embolism (a clot in a blood vessel supplying the lungs), and to prevent DVT and pulmonary embolism from re-occurring.

Lixiana contains the active substance edoxaban.
Pradaxa (dabigatran) is used for the following:

...to prevent the formation of blood clots in the veins in adults who have had an operation to replace a hip or knee;

...to prevent stroke and the formation of clots in adults who have an abnormal heart beat called ‘non-valvular atrial fibrillation’ and are considered to be at risk of stroke;

...to treat deep vein thrombosis (DVT, a blood clot in a deep vein, usually in the leg) and pulmonary embolism (PE, a clot in a blood vessel supplying the lungs), and to prevent these conditions from reoccurring in adults.

The medicine can only be obtained with a prescription.
EMA HAS NOT APPROVED BETRIXABAN
WHAT IS YOUR CONCERN ABOUT USE OF DOACs?
WHAT IS YOUR CONCERN ABOUT USE OF DOACs?

FDA Clears First Reversal Agent for Rivaroxaban, Apixaban ...
https://www.dicardiology.com/.../fda-clears-first-reversal-agent-riv... ▼ Traduire cette page
7 mai 2018 - The U.S. Food and Drug Administration (FDA) has approved Portola Pharmaceuticals' Andexxa, the first antidote indicated for patients treated ...

CHMP Extends Review Period for Portola Pharmaceuticals' Ondexxya ...
https://globenewswire.com/.../CHMP-Extends-Review-Period-for-P... ▼ Traduire cette page
11 déc. 2018 - The CHMP informed Portola yesterday that it will provide a list of outstanding ... The Company's two FDA-approved medicines are Andexxa® ...
ANYTHING ELSE ON DOAC action reversal?
Praxbind is a medicine used to neutralise the effects of dabigatran (the active substance of Pradaxa), a medicine that treats and prevents blood clots. Praxbind is used to rapidly stop the anticlotting effect of dabigatran, before emergency surgery or in case of life-threatening bleeding.

Praxbind contains the active substance idarucizumab.
WHAT IS YOUR CONCERN ABOUT USE OF DOACs?
Duration of Treatment

- Risk of thrombosis vs risk of bleeding
- + status of malignancy, type of treatment, QoL and patient preference
- Guidelines state “to consider 12 months anticoagulation” in the treatment of symptomatic VTE in patients who have advanced or metastatic cancer (ASCO); (ESMO); (ACCP).
- UK Studies – ALICAT¹ and

State of the Art: Guidance on Prevention and Treatment of CAT

Guidance Statements on:

- appropriate workup to search for occult ca
- thromboprophylaxis – risk-stratified
- treatment duration – for at least 6 months
- sub-segmental *incidental PE* – case by case basis
- treatment strategies – recurrence and IVC filters

“scientia potestas est”