
# Anticoagulation Therapy in SELECTeD Cancer Patients at Risk of Recurrence of Venous Thromboembolism

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on behalf of the select-d Collaborative Group

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# Disclosures

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- Helsinn
- Bayer AG
- Leo Pharma

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- Bayer AG

# Study context

- Investigator-initiated academic trial
- Coordinated by the Warwick University Clinical Trials Unit
- Supported by an unrestricted grant from Bayer AG
- Rivaroxaban supplied by Bayer AG
- EudraCT number: 2012-005589-37

# Background

- 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

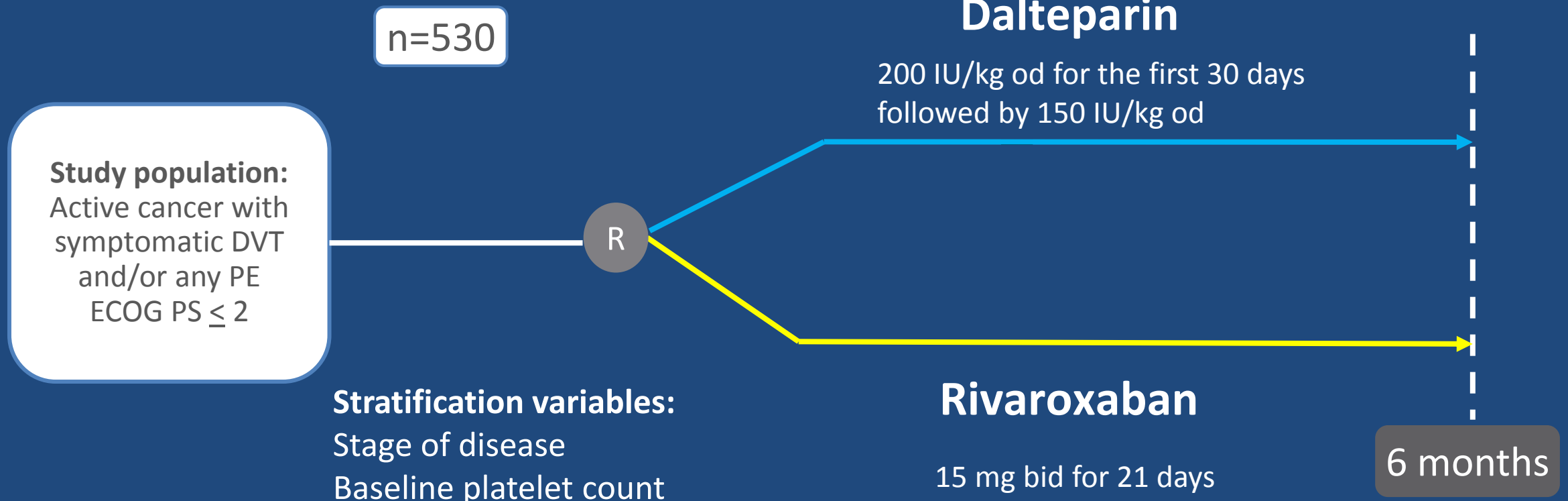
[1]Hutten et al. *Journal of Clinical Oncology* 2000; 18, 3078-3083

# 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

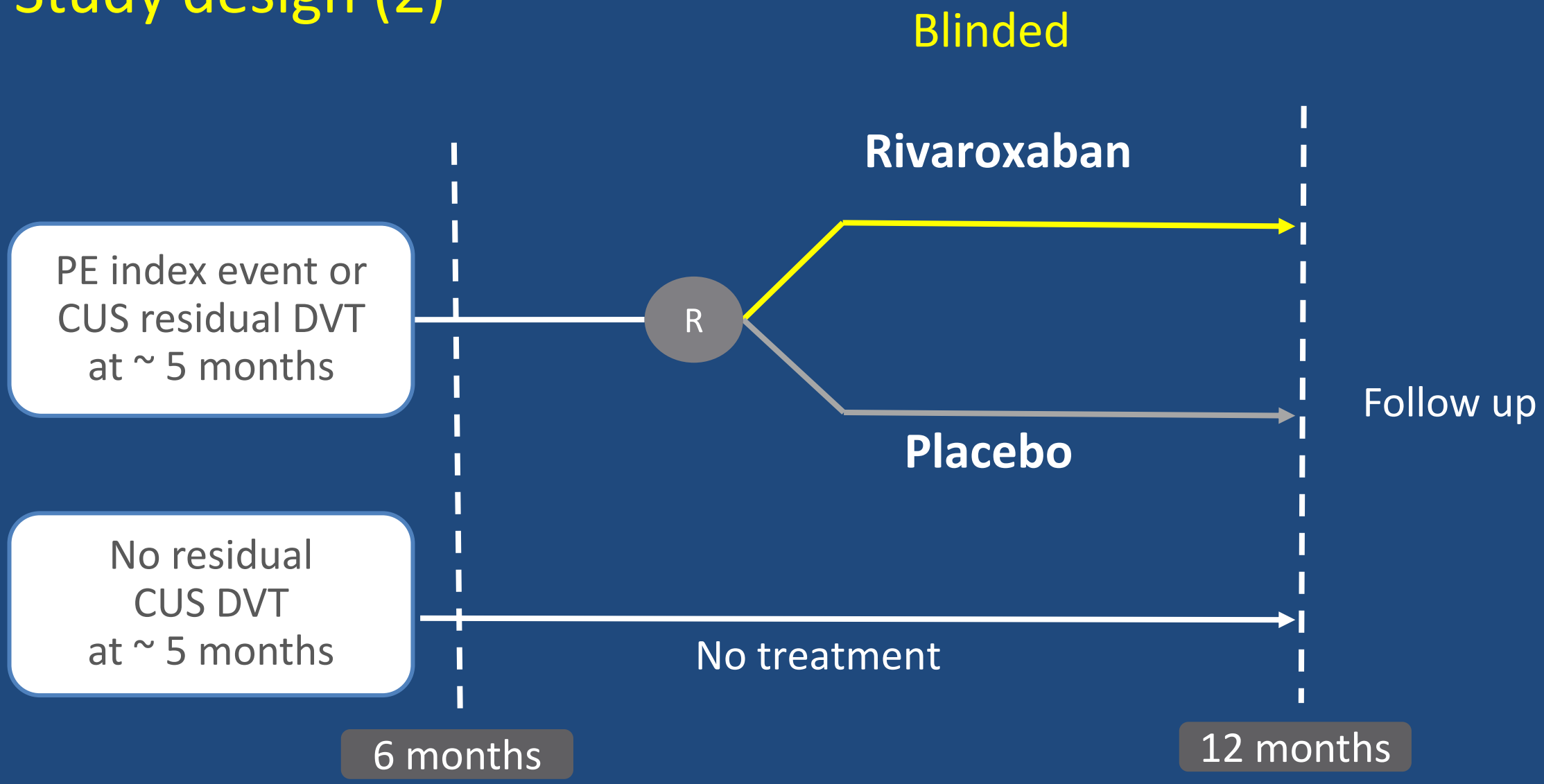
# Study design (1)

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




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

# Study design (2)



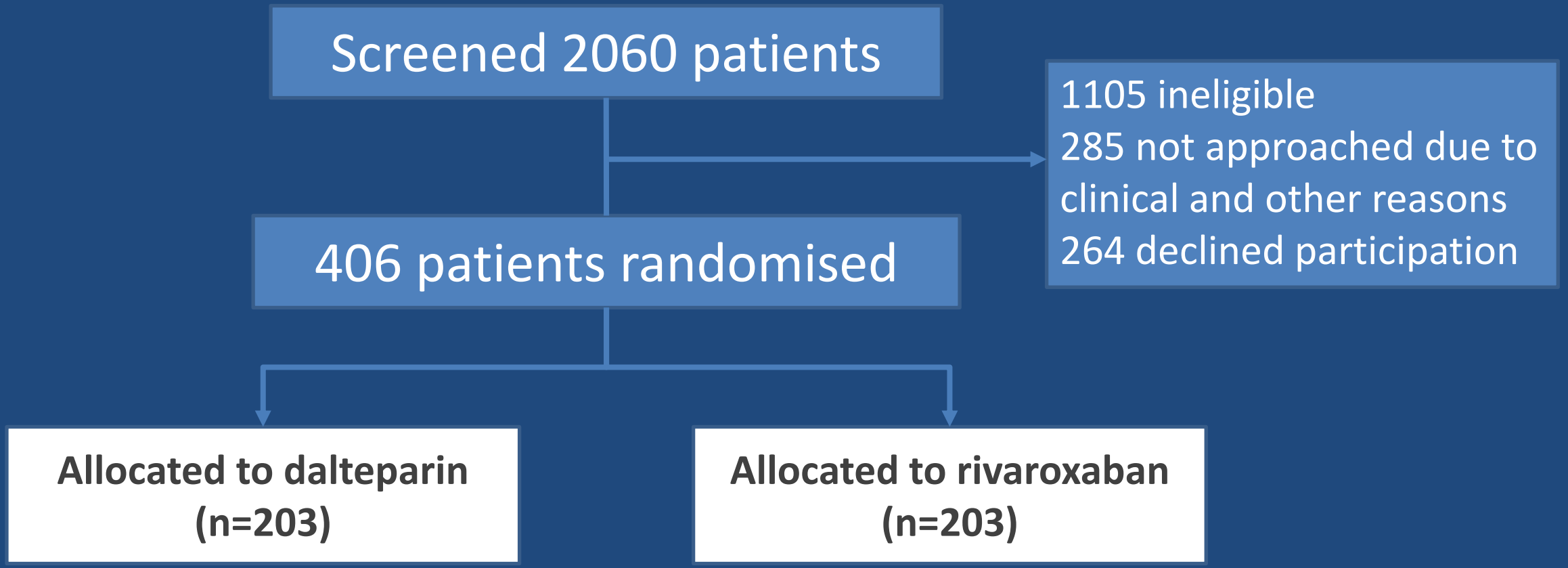
# Statistical considerations

- A sample size of 530 patients would provide:
  - estimates of VTE recurrence rates at 6 months to within +/- 4% assuming a VTE recurrence rate at 6 months of 10%
  - 300 patients for the second randomisation, assuming 70% eligible at 6 months and 80% agreed to participate

# Trial progress

- First patient randomised in October 2013
- Changes to protocol based on DMC recommendations in June 2016
  - The second randomisation was closed to patients randomised into the trial after 31st August 2016 due to low recruitment (n=92)
  - Sample size reduced from 530 to 400 patients (increased the width of the 95% CI for VTE recurrence rate from 8% to 9%)
  - Patients with oesophageal and gastro-oesophageal cancer were excluded due to apparent imbalance in major bleeding rates compared to other tumour types
- Final bleeding adjudication committee, 24th November 2017

# Recruitment




- Recruitment between October 2013 and December 2016 from 58 sites across the UK

# Baseline characteristics

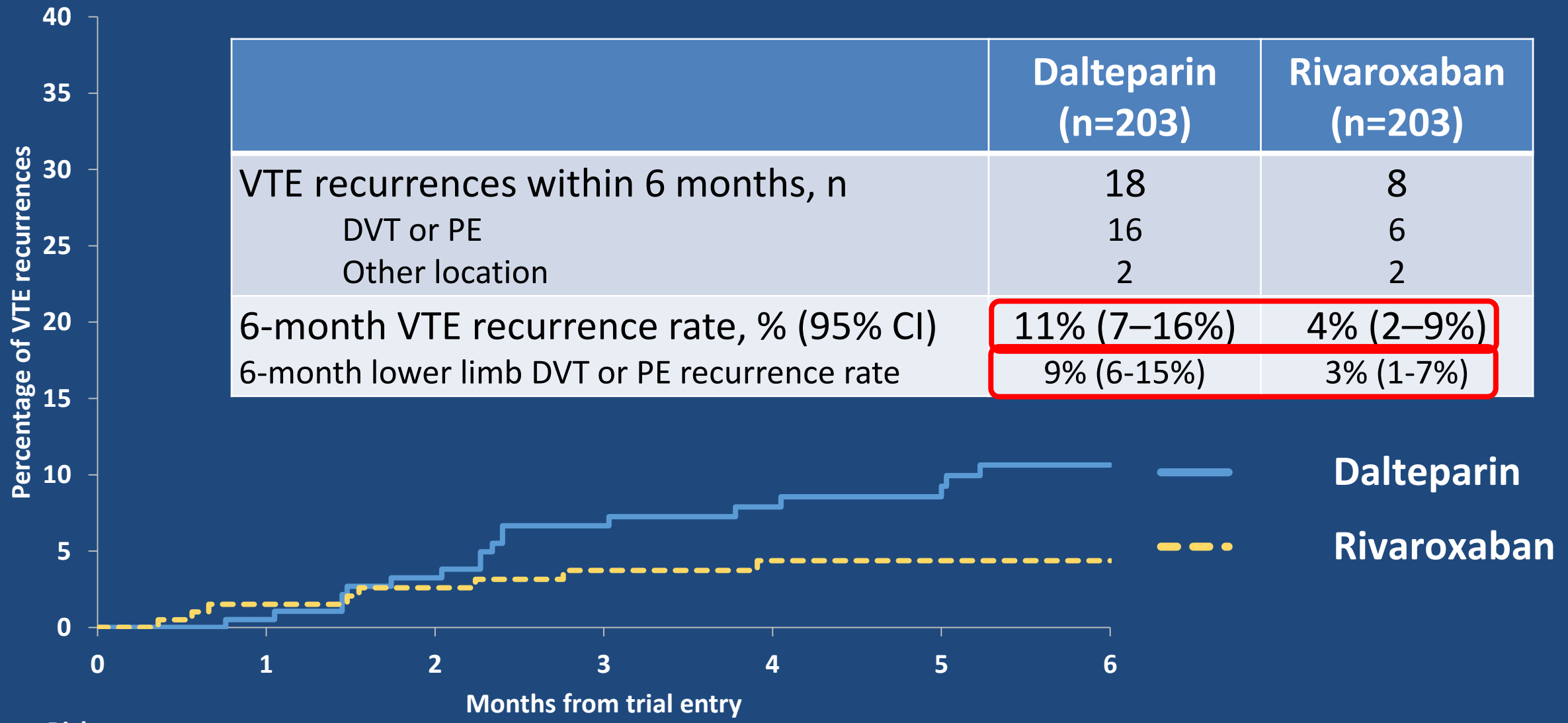
| Factor | Dalteparin % (n=203) | Rivaroxaban % (n=203) |
|---|---|---|
| Age: years, median (range) | 67 (34–87) | 67 (22–87) |
| Gender: male | 48 | 54 |
| Stage of Cancer:<br>- metastatic | 59 | 59 |
| ECOG PS:<br>- 0,1<br>- 2 | 76<br>21 | 72<br>26 |
| Qualifying VTE:<br>- symptomatic VTE<br>- incidental PE | 48<br>52 | 46<br>54 |

# Primary tumour type

| | Dalteparin, % (n = 203) | Rivaroxaban, % (n = 203) |
|---|---|---|
| Colorectal | 23 | 27 |
| Lung | 12 | 11 |
| Breast | 10 | 9 |
| Ovarian | 9 | 5 |
| Pancreatic | 5 | 9 |
| Lymphoma | 6 | 5 |
| Oesophageal/gastro-oesophageal | 9 | 5 |
| Prostate | 3 | 6 |
| Bladder | 2 | 5 |
| Other | 21 | 18 |

# VTE recurrence

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




**Numbers at Risk:**

| | | | | |
|---|---|---|---|---|
| Dalteparin | 203 | 171 | 139 | 115 |
| Rivaroxaban | 203 | 174 | 149 | 134 |

# Bleeding - number of patients (%)

| Category | Dalteparin (n=203) | Rivaroxaban (n=203) |
|---|---|---|
| Major* | 6 (3%) | 11 (5%) |
| Clinically relevant non-major | 6 (3%) | 25 (12%) |
| Total | 12 (6%) | 36 (17%) |

*1 fatal bleeding event in each arm
Most major bleeding events were gastrointestinal bleeding;  no CNS bleeds
Most CRNMBs were gastrointestinal or urological

# Overall survival

| | Dalteparin | Rivaroxaban |
|---|---|---|
| 6-months overall survival, % (95% CI) | 70% (63–76%) | 75% (69–81%) |

- Overall 104 (26%) patients died
- 92 (88%) died from progressive cancer
- 2 (2%) fatal PEs

# Summary

- Overall, 1 in 5 patients who were screened, participated in the study
- In this large randomised pilot study, estimates were established for recurrent VTE and major bleeding rates
- The total burden of recurrent VTE is reported:
  - 5% DVT/PE
  - 1% other venous sites
- The high mortality in the study population and clinician choice indicated that the second randomisation was not feasible

# Main conclusion

- We conclude that in terms of therapeutic decision making, a careful discussion between the patient and the physician should take place concerning the risk of recurrence and the risk of bleeding

# Thank you to all the patients who participated in select-d

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