New Strategies and New Data- Beyond Guidelines

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Conflict of Interest Statement

- Research Support: Bayer, Boehringer Ingelheim, BMS, Leo
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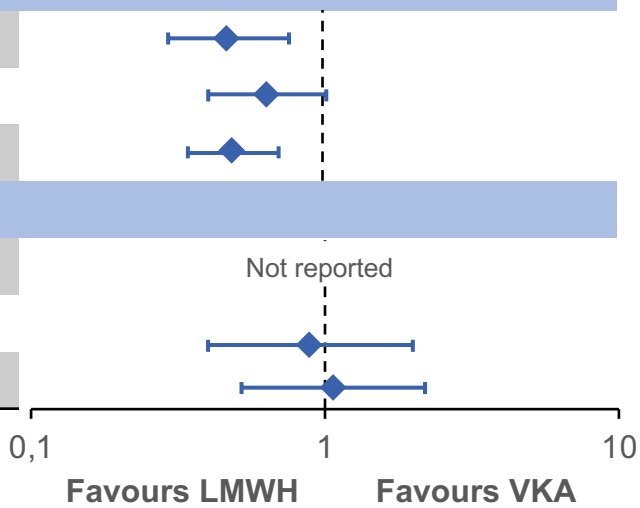
- Scientific Advisory Board: Pfizer, BMS, Leo, Bayer

Data-streams that Underpin the Emerging Practice of Using DOACs in CAT

- Data behind the LMWH related guidelines
- Randomised studies
  - SELECTeD (Rivaroxaban)
  - HOKUSAI (Edoxaban)
- Early guidance (ISTH 2018)
- ‘Beyond Guidelines’ practice and data
  - Patient views
  - DOAC Vs VKA registration programmes
    - CAT subgroup analyses
  - ‘Real World’ data
    - Insight on how clinicians interpret data
    - Insight on how to adapt the data to practice

LMWH in Cancer Associated Thrombosis Treatment: Efficacy and Safety Observed in the CLOT and CATCH Trial

	LMWH monotherapy		LMWH overlapping with VKA		HR (95% CI)
	n/N	(%)	n/N	(%)	
Recurrent VTE					
CLOT study*[1]	27/336	8.0	53/336	15.8	
CATCH study#[2]	31/449	6.9	45/451	10.0	
Meta-analysis‡[3]	**42/591**	**7.1**	**82/571**	**14.4**	
Major bleeding					
CLOT study*[1]	19/338	5.6	12/335	3.6	Not reported
CATCH study#[2]	12/449	2.9	11/451	2.4	
Meta-analysis§[3]	**37/556**	**6.7**	**32/536**	**6.0**	

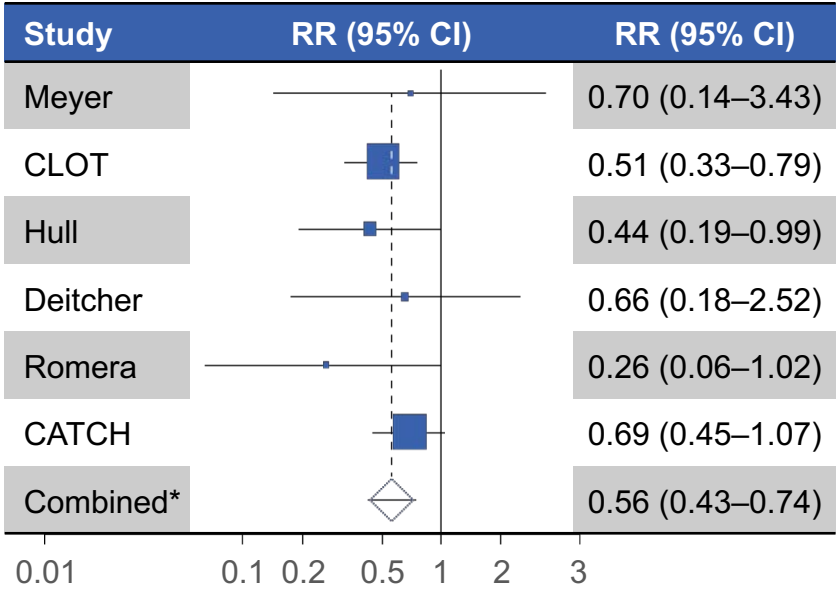


*Dalteparin versus VKA; in the VKA arm the estimated time in therapeutic range was 46% (30% below and 24% above); #tinzaparin versus warfarin; in the warfarin arm the time in therapeutic range was 47% (26% below and 27% above); ‡meta-analysis included four other small studies in addition to the CLOT study; §meta-analysis included three other small studies in addition to the CLOT study

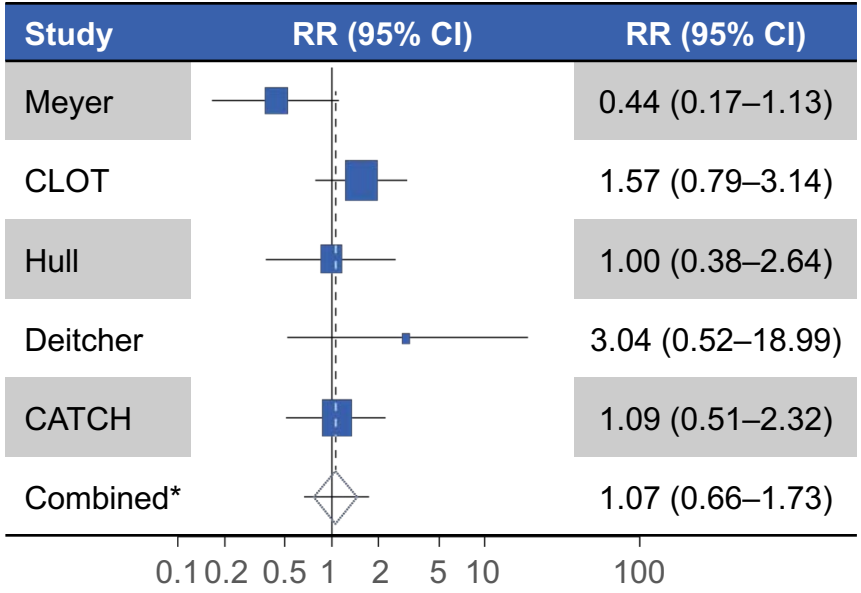
1. Lee AYY *et al*, *New Engl J Med* 2003;349:146–153; 2. Lee AYY *et al, JAMA* 2015;314:677–686; 3. Akl EA *et al*, *Cochrane Database Rev* 2014;7:CD006650

Efficacy and Safety of LMWH versus VKA in the Treatment of Cancer Associated Thrombosis

Recurrent VTE



Major bleeding events



LMWH is associated with a significant reduction in the risk of recurrent VTE without a significant increase in major bleeding episodes vs VKA

*Random effects model

Carrier M, Prandoni P, *Expert Rev Hematol* 2017;10:15–22

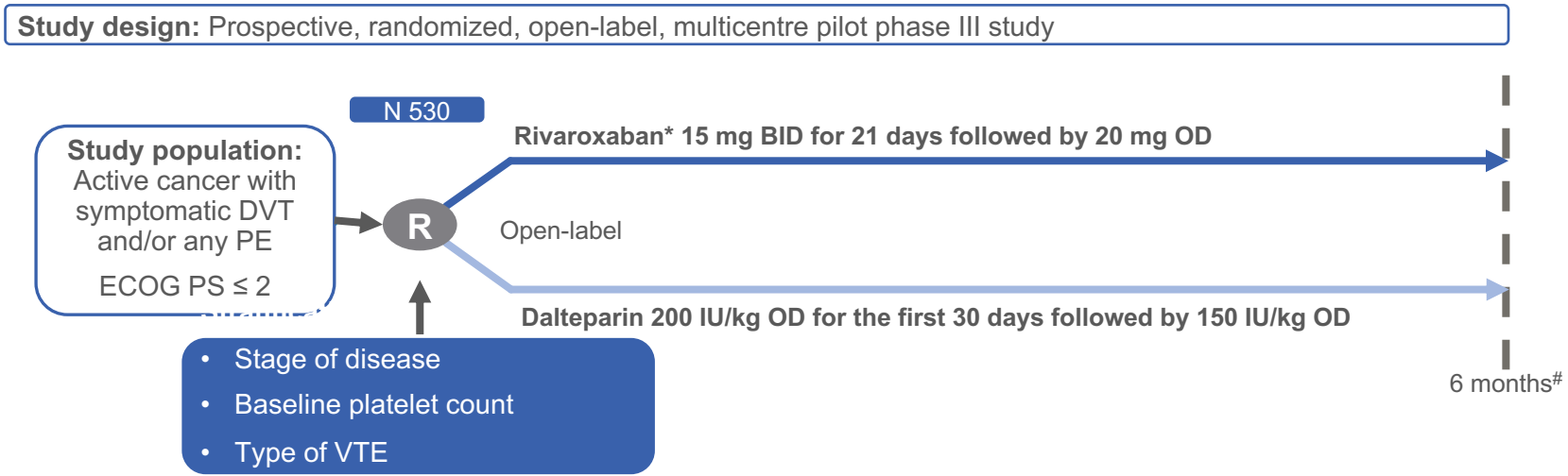
Guideline Recommendations for Treatment of CAT

Society	Recommendations
ESMO 2011[1]	◆ LMWH recommended for long-term (6 months) anticoagulant therapy ◆ Recommendations for duration of therapy depend on the type of cancer, stage of disease and cancer treatment
ESC 2014[2]	◆ LMWH should be considered for the first 3–6 months ◆ LMWH or VKAs should be considered for extended anticoagulation beyond the first 3–6 months
ASCO 2015[3,4]*	◆ LMWH recommended over UFH for the first 5–10 days ◆ LMWH preferred over VKAs for the first 6 months of treatment. VKAs are an acceptable alternative if LMWH is not available ◆ For extended anticoagulation (beyond 6 months) LMWH or VKAs may be considered for selected patients# with active cancer ◆ **Use of NOACs is not currently recommended for patients with cancer and VTE owing to limited data**
ACCP 2016[5]	◆ LMWH preferred over VKA or NOAC therapy ◆ **There is no preference between VKA, dabigatran, rivaroxaban, apixaban or edoxaban** ◆ Extended therapy (>3 months) *recommended* over 3 months of therapy for patients who do not have a high bleeding risk (*suggested* if bleeding risk is high)

*Updated ASCO guidelines were published in 2015; reassessment of available new data did not prompt any changes from the 2013 recommendations[5]; #such as those with metastatic disease or receiving chemotherapy

1. Mandala M *et al*, *Ann Oncol* 2011;22:vi85–vi92; 2. Konstantinides S *et al*, *Eur Heart J* 2014;35:3033–3069; 3. Lyman GH *et al*, *J Clin Oncol* 2013;17:2189–2204; 4. Lyman GH *et al*, *J Clin Oncol* 2015;33:654–656; 5. Kearon C *et al*, *Chest* 2016: doi:10.1016/j.chest.2015.11.026

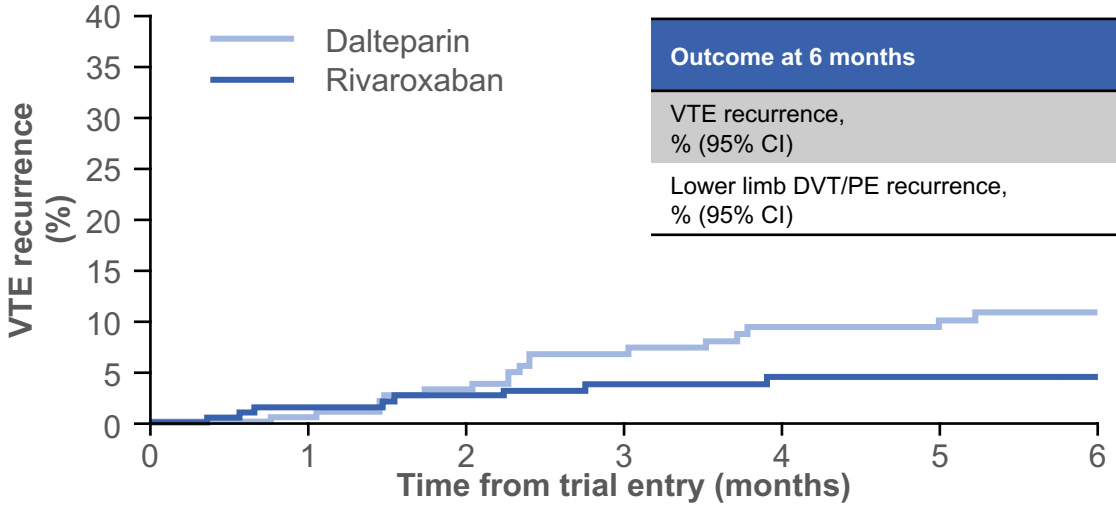
select-d: Phase III Pilot Study Comparing Rivaroxaban versus Dalteparin for the Treatment of Cancer Associated Thrombosis



*For patients with CrCl 30–49 ml/min dosing recommendations as in rivaroxaban SmPC; #The second randomization phase for extended treatment of VTE from 6 to 12 months for patients with PE as an index event or patients with Residual DVT at 5 month assessment was closed due to low recruitment. Sample size reduced from 530 to 400 patients for main trial comparison (95% CI for VTE recurrence +/-4.5%)

Young A *et al*, *Thromb Res* 2016;140:S172–S173; EudraCT number: 2012-005589-37; Bach M *et al*, *Thromb Haemost* 2016;116:S24–S32; Data on File

select-d Primary Outcome: Lower Incidence of VTE Recurrence Events with Rivaroxaban Versus Dalteparin

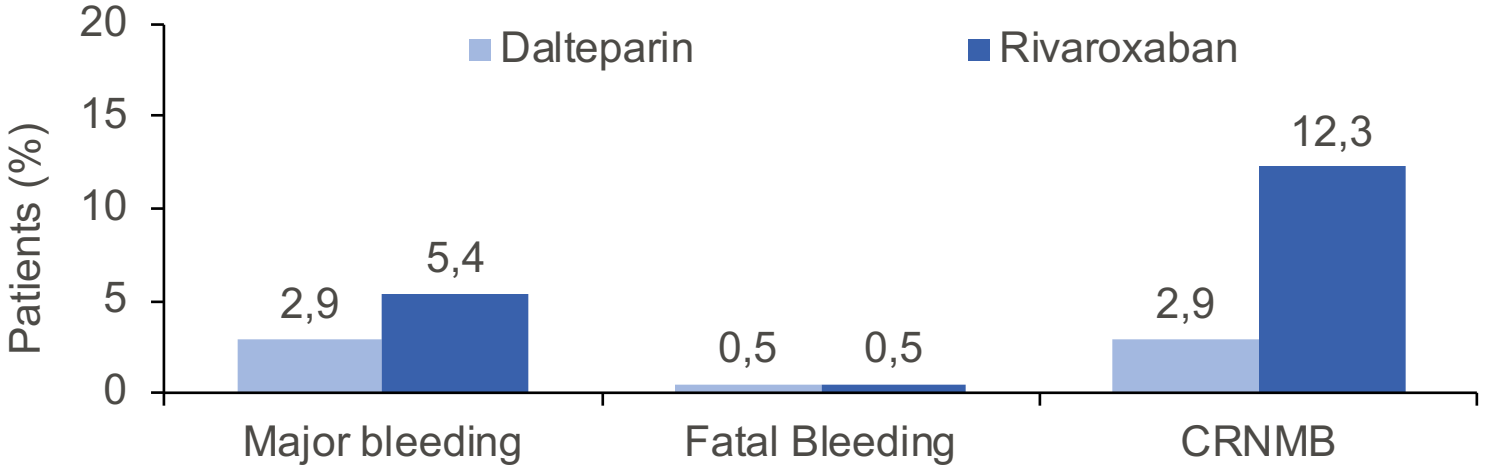


Outcome at 6 months	Rivaroxaban (n=203)	Dalteparin (n=203)
VTE recurrence, % (95% CI)	4 (2–9)	11 (7–16)
Lower limb DVT/PE recurrence, % (95% CI)	3 (1-7)	9 (6-15)

Number at risk				
Dalteparin	203	171	139	115
Rivaroxaban	203	174	149	134

Young A *et al*, ASH 2017: Abstract 625; Available at: http://www.clinicaltrialresults.org/

select-d Secondary Outcome: Incidence of Major, Fatal and Clinically Relevant Non-Major Bleedings



Most Major Bleeding events were Gastrointestinal Bleeds*. No Central Nervous System Bleeding was observed in rivaroxaban and dalteparin groups.

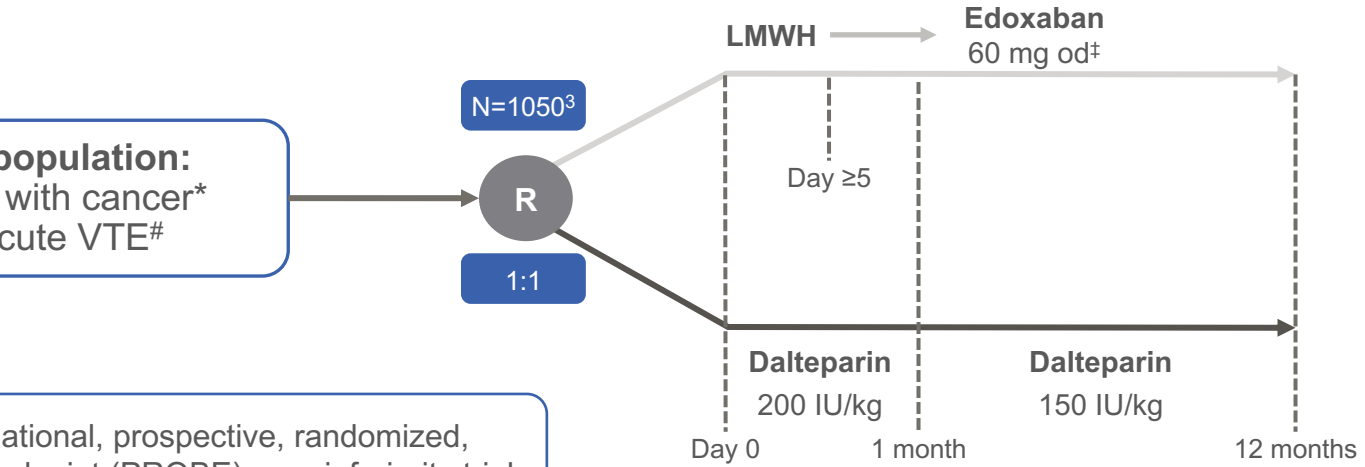
* All bleedings events were adjudicated .Overall survival at 6 months was 70%(63-76%) in the rivaroxaban group and 75%(69-81%) in the dalteparin group.

Young A *et al*, ASH 2017: Abstract 625; Available at: http://www.clinicaltrialresults.org/

Hokusai-VTE-Cancer: Study Design

Rationale: To assess the efficacy and safety of edoxaban (after ≥5 days of LMWH) versus dalteparin for the treatment of VTE in patients with cancer*[1–3]

Study population:
Patients with cancer*
and acute VTE#

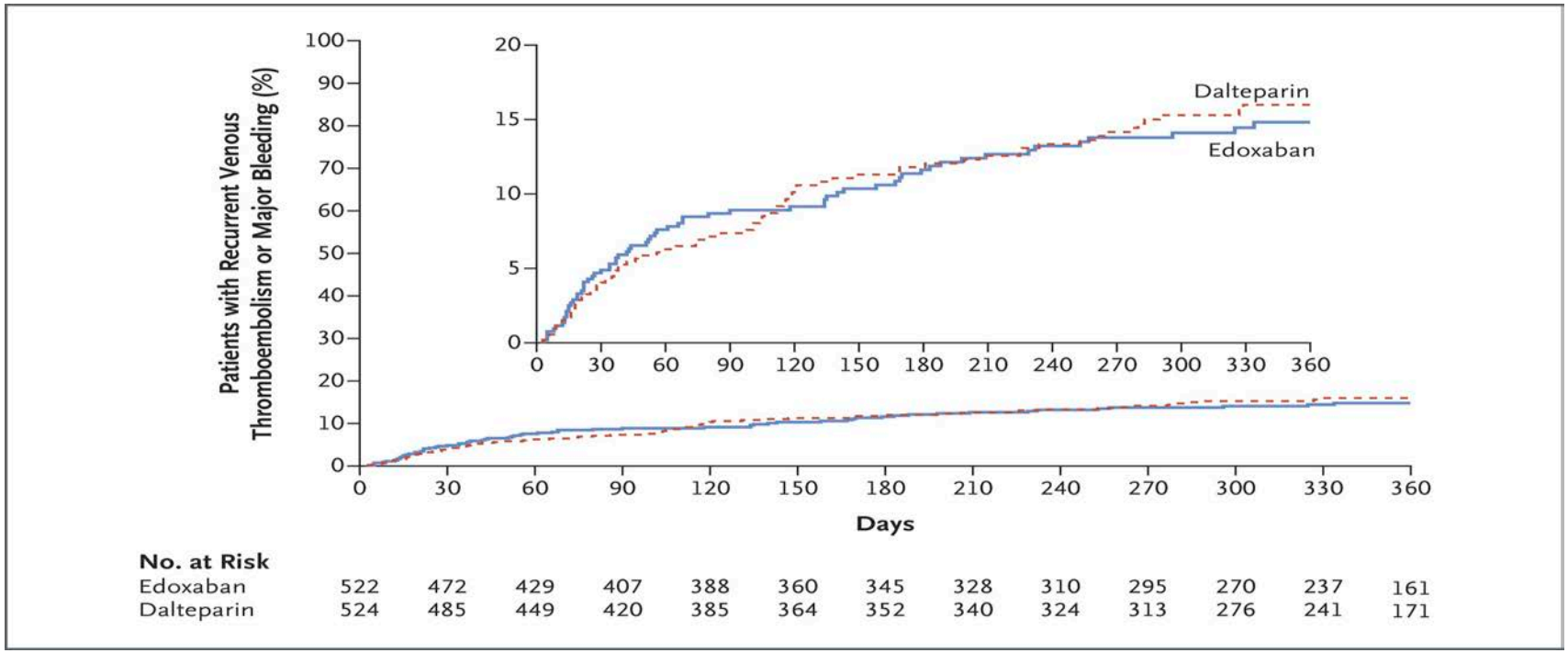


Short design: Multinational, prospective, randomized, open-label, blinded endpoint (PROBE), non-inferiority trial

*Cancer must be other than basal-cell or squamous cell carcinoma of the skin, be active or diagnosed within 2 years prior to randomization and objectively confirmed. Active cancer was defined as any of the following: diagnosis of cancer within the past 6 months; recurrent, regionally advanced or metastatic disease; currently receiving treatment or having received any treatment for cancer during the 6 months prior to randomization; or a haematological malignancy not in complete remission; #symptomatic or incidental VTE; ‡dose adjustment to 30 mg od in patients with a body weight ≤60 kg or CrCl 30–50ml/min, or concomitant use of P-glycoprotein inhibitors

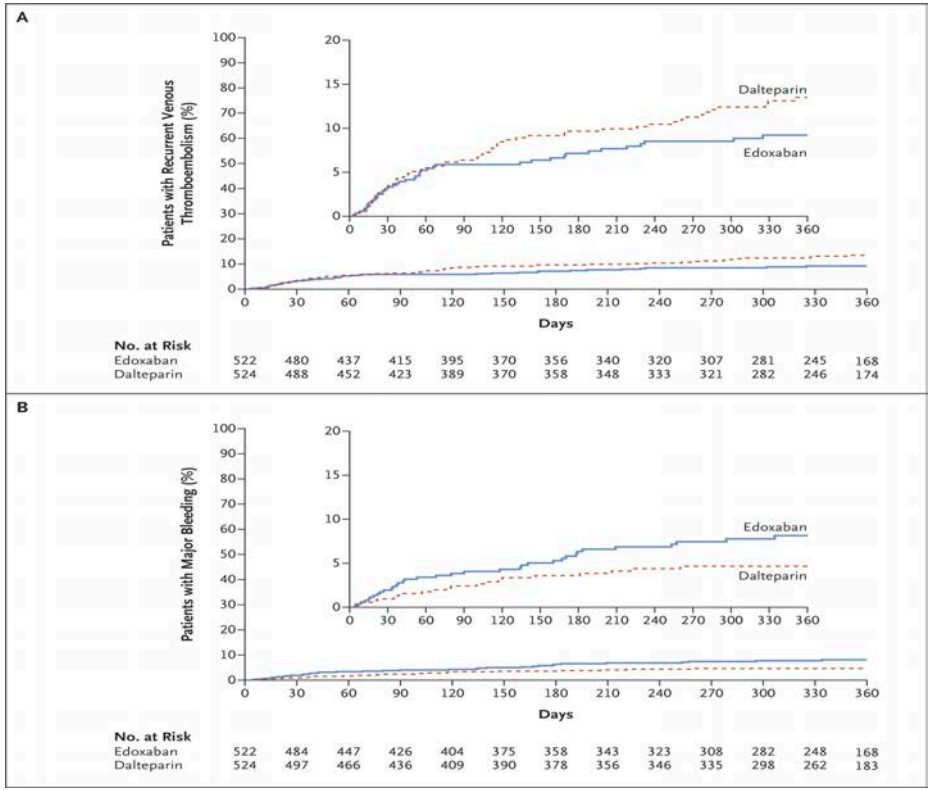
1. Daiichi Sankyo, Inc. https://clinicaltrials.gov/ct2/show/NCT02073682; 2. van Es *et al*, *Thromb Haemostat* 2015;114;1268–1276; 3. Raskob GE *et al*, ASH 2017: Abstract LBA-6

Hokusai-VTE-Cancer **Composite Primary Outcome** – First Recurrent VTE or Major Bleeding Event



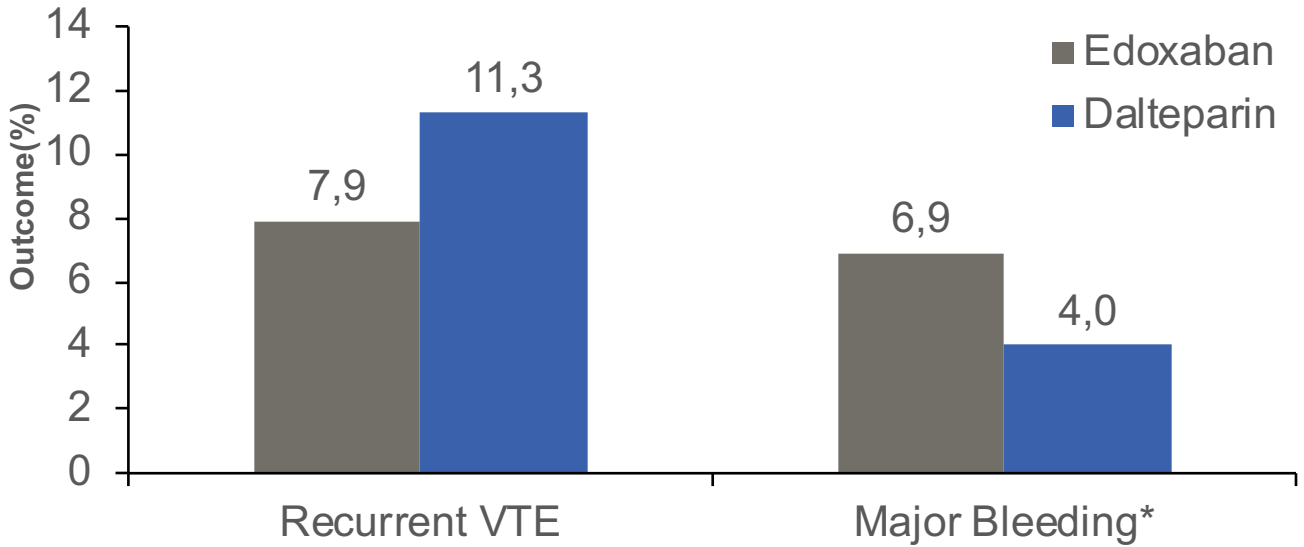
Raskob GE et al. N Engl J Med 2018;378:615-624

Hokusai VTE Cancer
Recurrent VTE and Major Bleeding – 12 Months



Raskob GE et al. N Engl J Med 2018;378:615-624

Hokusai VTE Cancer
Recurrent VTE and Major Bleeding – 12 Months



***GI bleeding in patients with GI cancers; #p=0.09; ‡p=0.04**

Raskob G *et al*, *N Engl J Med* 2018;378:615–624

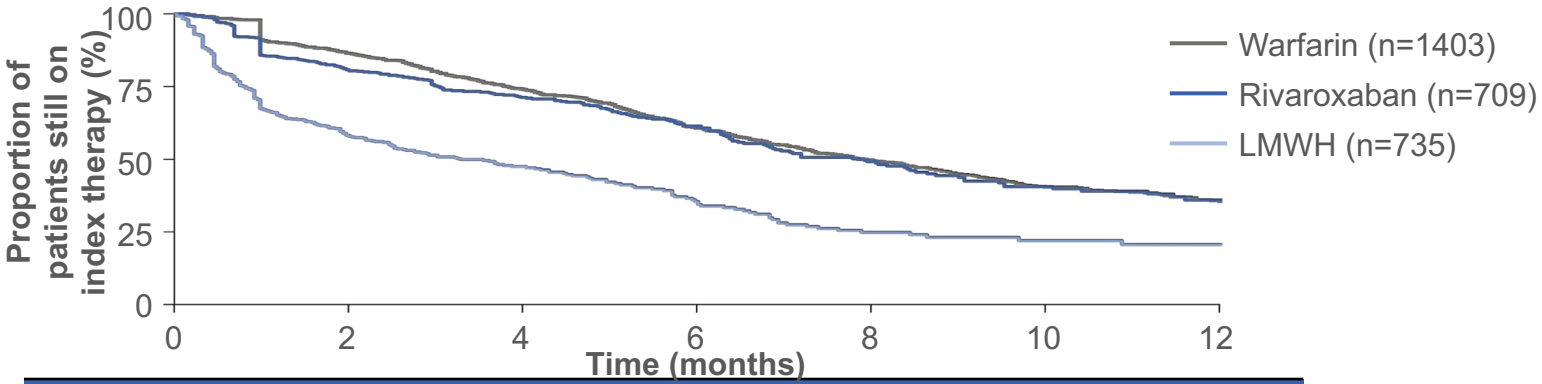
Guidance from the SCC of the ISTH for Treatment of CAT

Society	Recommendations
ISTH 2018[1]	◆ The use of specific NOACs is suggested in CAT patients with low risk of bleeding and no drug-drug interaction with current systemic therapy ◆ Rivaroxaban and Edoxaban are highlighted as the only NOACs with RCT evidence vs LMWH in CAT patients and a class effect of the NOACs should not be readily assumed ◆ LMWHs are an acceptable alternative ◆ **Treatment decisions should include *shared decision making with an informed patient*** ◆ The use of LMHW is suggested in CAT patients with high risk of bleeding (**gastrointestinal cancers; at high risk of bleeding from genitourinary tract; gastrointestinal mucosal abnormalities**) ◆ Rivaroxaban and Edoxaban can be considered as an alternative in the absence of drug-drug interactions with current systemic therapy and after ***shared decision making with an informed patient***

*1.Khorana, A. *et al*, *Journal of Thrombosis and Haemostasis, 16: 1–4*

What Else Do we Know that Governs Use?

Higher Persistence on Index Therapy in Cancer Patients Using Rivaroxaban or Warfarin versus LMWH



Cohort	Median treatment duration	Kaplan–Meier rates	
		6 months	12 months
LMWH	3.3	37%	21%
Warfarin	7.9	61%	35%
Rivaroxaban	7.9	61%	36%

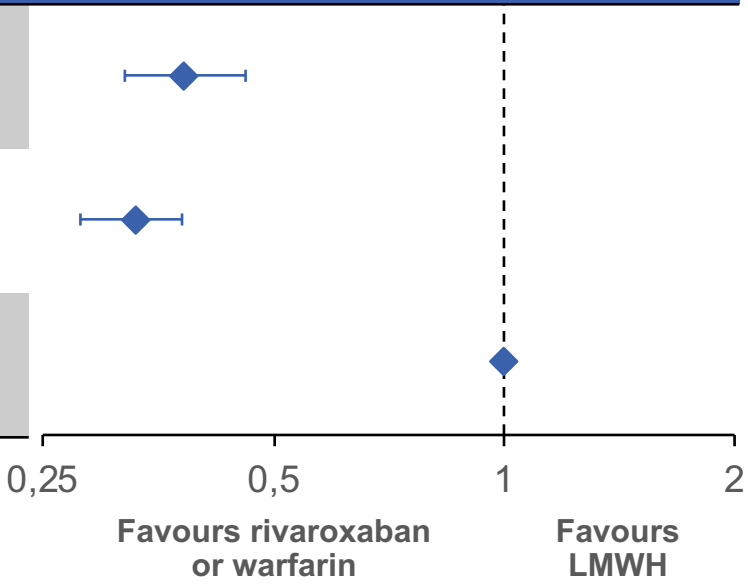
*Discontinuation was defined as a gap of no more than 60 days between the end of the days of supply of a dispensing and the start date of he next dispensing of the index therapy, if any

Khorana AA *et al*, *Res Pract Thromb Haemost* 2017;1:14–22

Higher Risk of Discontinuation of Index Therapy on LMWH versus Rivaroxaban or Warfarin

Risk of discontinuation with rivaroxaban or warfarin versus LMWH

Drug	HR	95% CI
Rivaroxaban	0.38	0.32–0.46
Warfarin	0.33	0.28–0.38
LMWH	N/A	N/A



Khorana AA *et al*, *Res Pract Thromb Haemost* 2017;1:14–22

Patient Perspectives on LMWH Vs DOACs

- Most patients experienced unwanted effects as result of injections, but these were acceptable in context o a cancer patient.
- Tablet w but only if as effective.

SHARED DECISION MAKING
ISTH 2018

Obviously you're covered in bruise so you don't look great, but I'm now covered in scars and colostomy bags and that sort of things, it seems a very small price to pay. It becomes a bit relative really. - P21

uld serve the would tablet, but…if s are an advantage then it's worth putting up with the discomfort. - P11

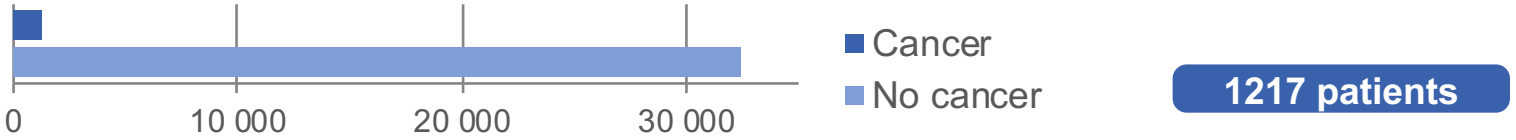
Hutchinson, A., Rees, S., Maraveyas, A., Young, A. Date, K., and Johnson, M. 'Patient and carer experience of oral and injected anticoagulation for cancer-associated thrombosis: select-D qualitative sub study'. Palliative Medicine in Press

Can We Individualise CAT Treatment ?

‘Extracted’ Data from Registration Trials

NOAC Phase III VTE Trials: Inclusion of Patients with Cancer

Phase III NOAC trials including more than 30,000 patients



Drug	Trial name	Patients with cancer	
		n/N	%
Rivaroxaban[1]	EINSTEIN DVT	207/3449	6.0
	EINSTEIN PE	223/4832	4.6
	EINSTEIN EXT	54/1196	4.5
Dabigatran[2]	RE-COVER	121/2539	4.8
	RE-COVER II	100/2589	3.9
	RE-MEDY	119/2586	4.2
	RE-SONATE	N/A	N/A
Apixaban[1]	AMPLIFY	143/5395	2.7
	AMPLIFY-EXT	42/2482	1.7
Edoxaban[1]	Hokusai-VTE	208/8240	2.5

1. Wharin C *et al*, *Blood Rev* 2014;28:1–4; 2. Vedovati M *et al*, *Chest* 2015;147:475–483

Efficacy and Safety of NOACs and LMWH versus VKA in the Treatment of Cancer Associated Thrombosis

Recurrent VTE

NOAC studies

	No. patients with event/ no. of patients		Relative risk (95% CI)	Weight	Relative risk (95% CI)
	NOAC	VKA			
EINSTEIN	6/232	8/198		25.3%	0.64 (0.23–1.81)
Hokusai-VTE	4/109	7/99		19.1%	0.52 (0.16–1.72)
RE-COVER	10/173	12/162		41.6%	0.78 (0.35–1.76)
AMPLIFY	3/81	5/78		14%	0.58 (0.14–2.34)
Pooled, random-effects model	**23/595**	**32/537**		**100%**	**0.66 (0.39–1.11)**

0.1 1.0 10.0 vs VKA

Lower risk with NOAC Higher risk with NOAC

LMWH studies

	No. patients with event/ no. of patients		Relative risk (95% CI)	Weight	Relative risk (95% CI)
	LMWH	VKA			
Meyer	2/71	3/75		3.8%	0.7 (0.12–4.09)
Lee	27/336	53/336		68.6%	0.51 (0.33–0.79)
Hull	6/100	10/100		12.9%	0.6 (0.23–1.59)
Deitcher	4/61	3/30		5.2%	0.66 (0.16–2.74)
Romera	2/36	7/33		9.5%	0.26 (0.06–1.17)
Pooled, random-effects model	**41/604**	**76/574**		**100%**	**0.52 (0.36–0.74)**

0.1 1.0 10.0 vs VKA

Lower risk with LMWH Higher risk with LMWH

Major bleeding

NOAC studies

	No. patients with event/ no. of patients		Relative risk (95% CI)	Weight	Relative risk (95% CI)
	NOAC	VKA			
EINSTEIN	6/232	8/196		34.6%	0.63 (0.22–1.79)
Hokusai-VTE	5/109	3/99		19%	1.51 (0.37–6.17)
RE-COVER	6/159	7/152		32.9%	0.82 (0.28–2.38)
AMPLIFY	2/87	4/80		13.5%	0.46 (0.09–2.44)
Pooled, random-effects model	**19/587**	**22/527**		**100%**	**0.78 (0.42–1.44)**

0.1 1.0 10.0 vs VKA

Lower risk with NOAC Higher risk with NOAC

LMWH studies

	No. patients with event/ no. of patients		Relative risk (95% CI)	Weight	Relative risk (95% CI)
	LMWH	VKA			
Meyer	5/71	12/75		22.3%	0.4 (0.13–1.19)
Lee	19/338	12/335		49.2%	1.6 (0.77–3.36)
Hull	7/100	7/100		22.8%	1 (0.34–2.96)
Deitcher	6/67	1/34		5.8%	3.25 (0.37–28.12)
Pooled, random-effects model	**37/576**	**32/544**		**100%**	**1.06 (0.5–2.23)**

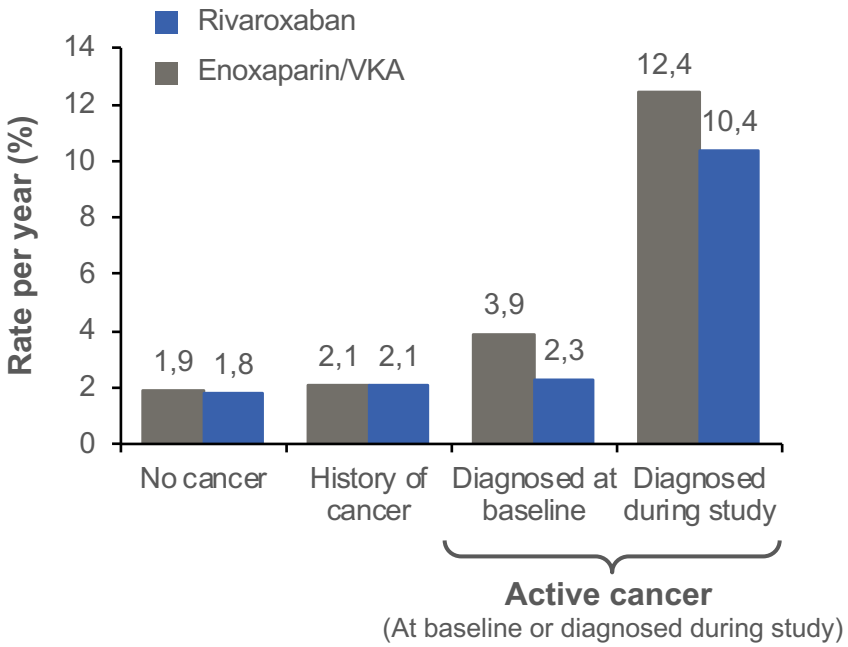
0.1 1.0 10.0 vs VKA

Lower risk with LMWH Higher risk with LMWH

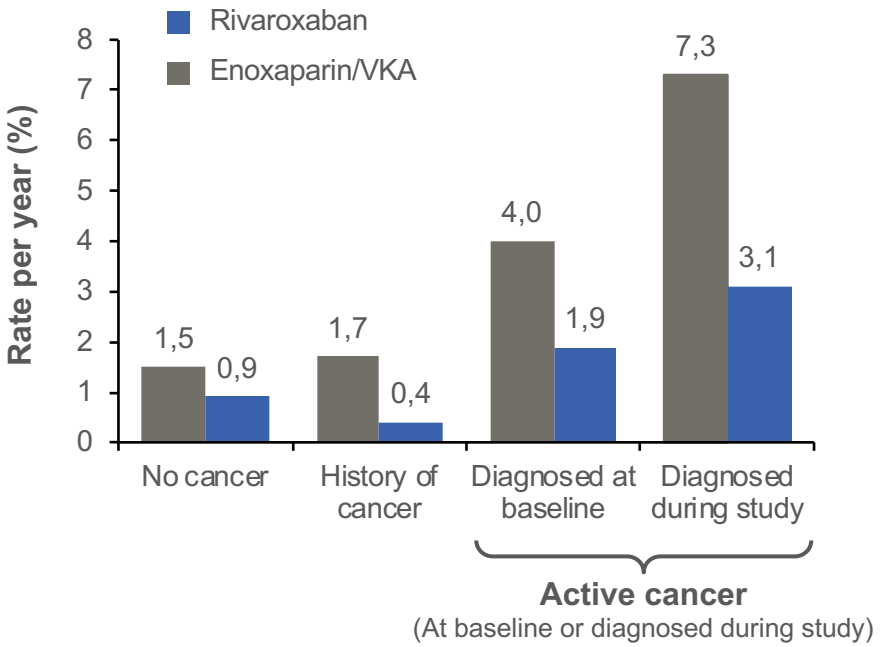
Carrier M *et al*, *Thromb Res* 2014;134:1214–1219

EINSTEIN DVT/PE: Outcomes by Cancer Status

Recurrent VTE (ITT population)

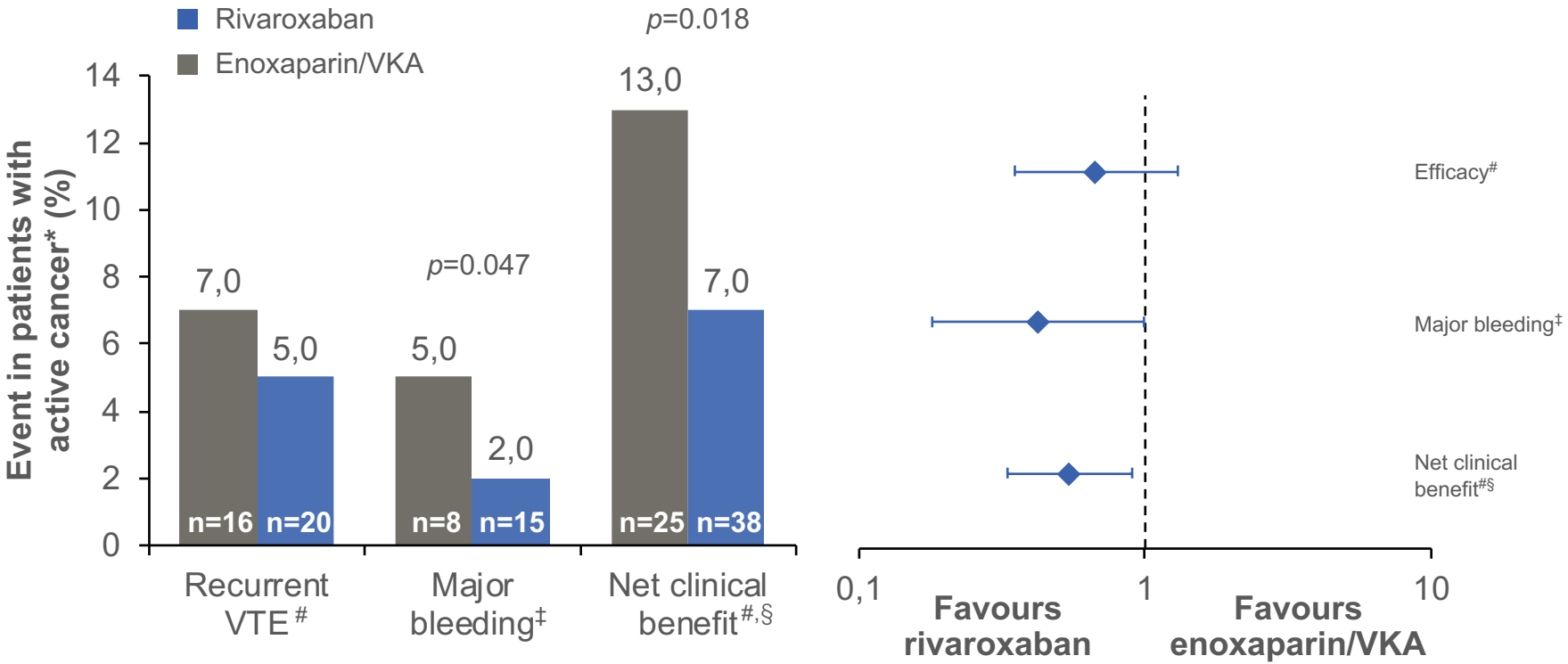


Major bleeding (safety population)



Prins MH *et al*, *Lancet Haematol* 2014;1:e37–e46

EINSTEIN PE/DVT: Effective Treatment in Patients with Active Cancer, with Significant Reduction in Major Bleeding



*At baseline or during the study period; #ITT population: N=8281; patients with active cancer, n=655;
‡safety population: N=8246; patients with active cancer, n=651; §composite of recurrent VTE and major bleeding

1. Prins MH *et al*, *Lancet Haematol* 2014;1:e37–e46

Can we Individualise CAT Treatment ?

Data from ‘Real World’ Use

Rivaroxaban Effectiveness and Safety in VTE Patients with Active Cancer in Real-World Studies

Study	Type	Treatment arm	n	Treatment duration, months, median	Recurrent VTE %	Major bleeding %	Mortality %
XALIA[1]*	Prospective, observational study	Rivaroxaban*	146	5.0	3.4	1.4	4.8
		Early switchers#	30	6.5	3.3	0.0	0.0
		Standard anticoagulation‡	141	7.1	4.3	5.0	4.3
		LMWH	223	5.5	4.5	3.6	24.7
Mayo[2]	Prospective registry	Rivaroxaban	135	7.3§	2.8	2.2	30
		LMWH	121	5.8§	1.7	5.8	41
		(*p*-value)	–	NR	(0.45)	(0.20)	**(0.047)**
MSK[3]	Prospective cohort study	Rivaroxaban	200	NR	4.4	2.2	17.6

*Treated with rivaroxaban alone or who received heparin or fondaparinux for 48 hours before switching to rivaroxaban; #treated with rivaroxaban who received heparin/fondaparinux for >48 hours–14 days and/or a VKA for 1–14 days before changing to rivaroxaban; ‡initial treatment with unfractionated heparin, LMWH or fondaparinux, usually overlapping with and followed by a VKA; §average follow-up

1. Ageno W *et al*, *TH Open* 2017;1:e33–e42; 2. McBane RD *et al*, ACC 2016: Abstract 1243M-05; 3. Mantha S *et al*, *J Thromb Thrombolysis* 2017;43:166–171

Real World Data: MSKCC Experience

Quality assessment initiative

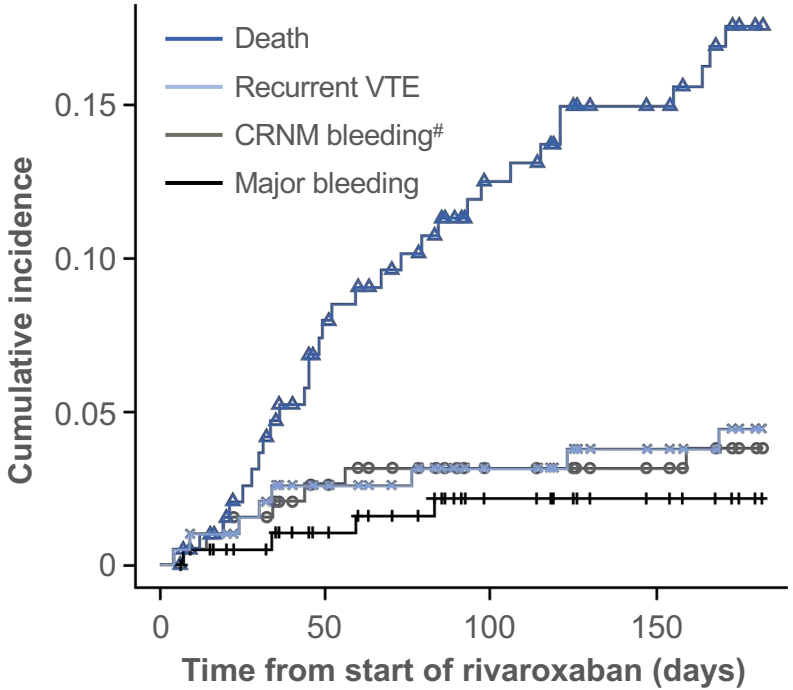
- 200 patients with active cancer and CAT treated with rivaroxaban
  - Intended to receive ≥6 months of therapy
- Several exclusions:
  - CrCl <30 ml/min
  - Liver function tests >3× ULN
  - Expected malabsorption at stomach or small bowel
  - Active GU or GI lesions
  - Untreated primary CNS neoplasm
  - A body weight <50 or >150 kg
  - Any antiplatelet agent other than ASA 81 mg daily and any significant drug interaction
- Empirically dose-reduced: patients ≥75 years old received rivaroxaban 10 mg bid for 3 weeks followed by 15 mg od

ASA, acetylsalicylic acid; CAT, cancer-associated thrombosis; CNS, central nervous system; CrCl, creatinine clearance; GI, gastrointestinal; GU, gastrouritary; MSKCC, Memorial Sloan Kettering Cancer Center; ULN, upper limit of normal

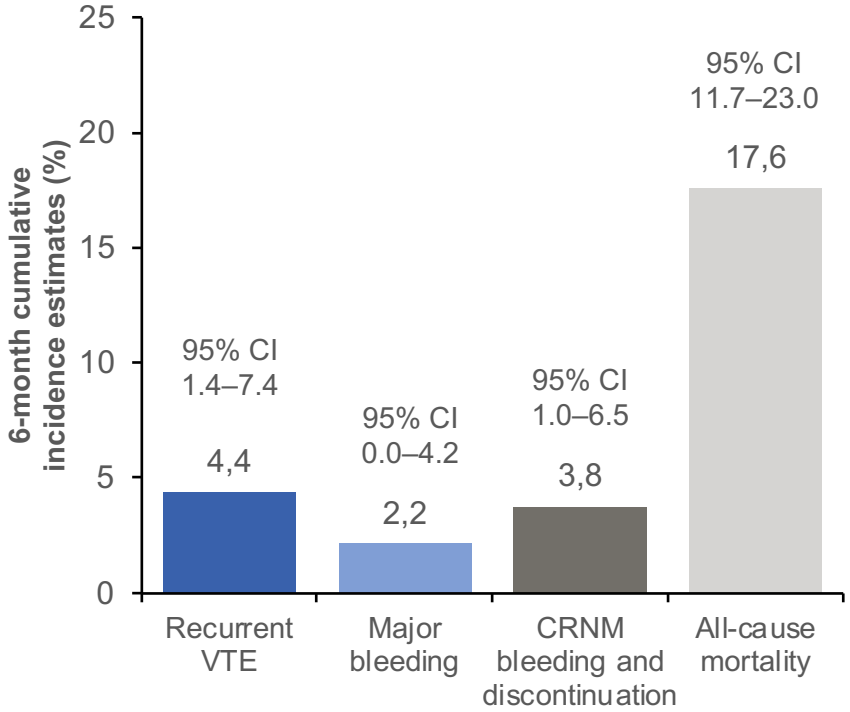
Mantha S *et al, J Thromb Thrombolysis* 2017;43:166–171

Memorial Sloan Kettering Cancer: Outcome Rates in Patients with Cancer Similar to the EINSTEIN Trials[1,2]

Cumulative incidence for competing risks[1]



6-month cumulative incidence estimates[1]



Planned duration of at least 6 months (53% of patients were observed for the full 6 months). *Leading to discontinuation of rivaroxaban

1. Mantha S *et al*, *J Thromb Thrombolysis* 2017;43:166–171; 2. Prins MH *et al*, *Lancet Haematol* 2014;1:e37-e46

Patient Checklist – LMWH or DOAC or both?

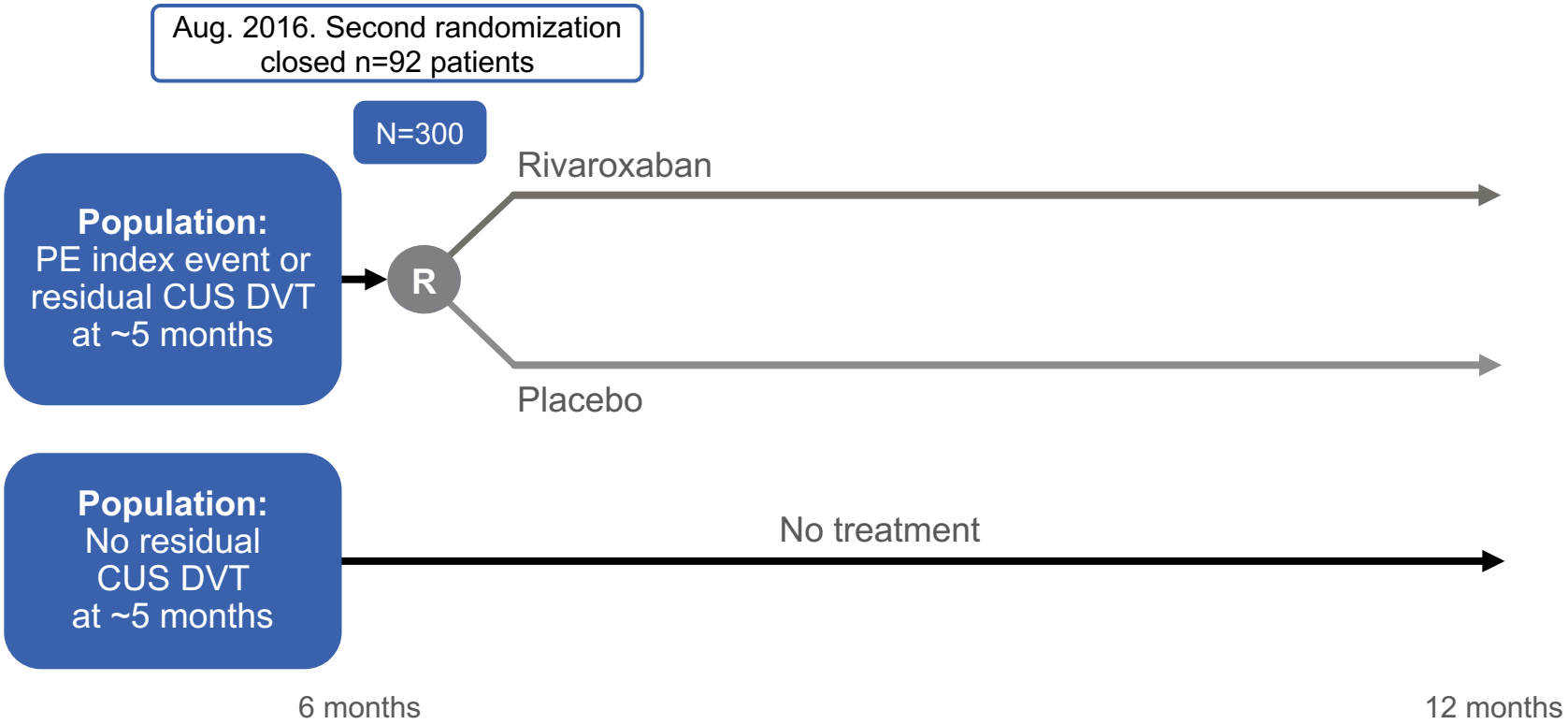
- Patient Preference
- Cancer (lesion) in situ?
- Chemotherapy and other Concomitant Medications
- Renal Function
- Comorbidities
- Cancer Type
- Nausea and Vomiting*
- ? Weight
- ?

*Reiss H, Ay C; Bauersachs R et al. *The Oncologist* 2018; 23:1–18.

How long?

Both Studies –SELECTeD and HOKUSAI VTE Cancer tried to produce Data in this setting

SELECTeD: Study Design (2)



Young A *et al*, ASH 2017: Abstract 625; Available at: http://www.clinicaltrialresults.org/; select-d protocol. https://warwick.ac.uk/fac/med/research/ctu/trials/cancer/select-d/select-d_protocol_v2.0_09-apr-2013.pdf [accessed 21 Mar 2018]

Treatment and 2° Prevention of VTE in Cancer

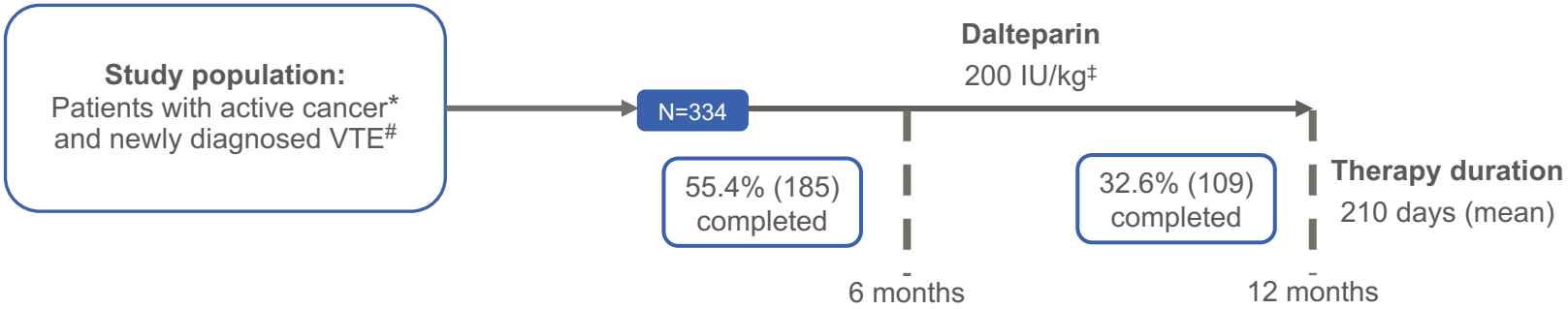
- ASCO: Extende anticoagulation with LMWH or VKA may be considered beyond 6/12 for patient tatic disease or patients who are receiving chemotherapy
  - Length of secondar
    - LONGHE A NCT01164046 (6 m)
    - ALICAT ISRCTN ulant (+6 m)– Funde NIHR

Failed to Recruit
Downscaled to a Registry

Failed Feasibility –Trial Closed without achieving endpoint--

DALTECAN: Study Design and Completion Rates

Rationale: To assess the safety of dalteparin between >6–12 months for cancer-associated VTE



Study design: Prospective, multicentre, open-label, single-arm, long-term study

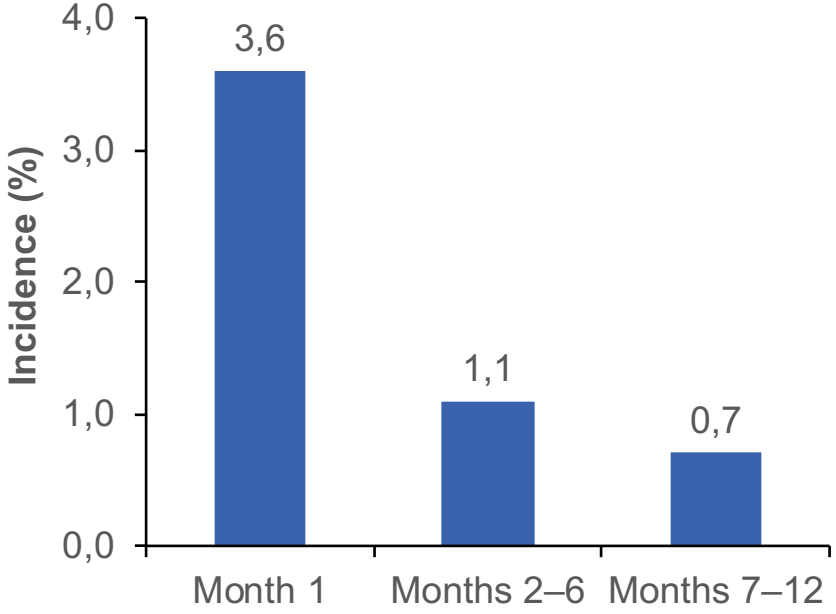
Primary endpoint: Major bleeding rate (months 7–12)
Other endpoints: Major bleeding rate (months 1, 2–6) and recurrent VTE rate (months 1, 2–6, 7–12)

*Diagnosis (excluding basal cell or squamous cell carcinoma of the skin) within 6 months before enrolment, having received cancer therapy within the previous 6 months, or having documented recurrent or metastatic cancer; #symptomatic proximal DVT of the lower extremity, PE or both; ‡ Initial dose of 200IU/kg/day with a maximum dose of 18000IU for the first month. During months 2–12, pre-filled syringes according to the patients weight were supplied: 7500IU for body weight ≤56kg, 10000IU for body weight 57–68kg, 12500IU for 69–82kg, 15000IR for 83–98kg and 18000IU for >99kg

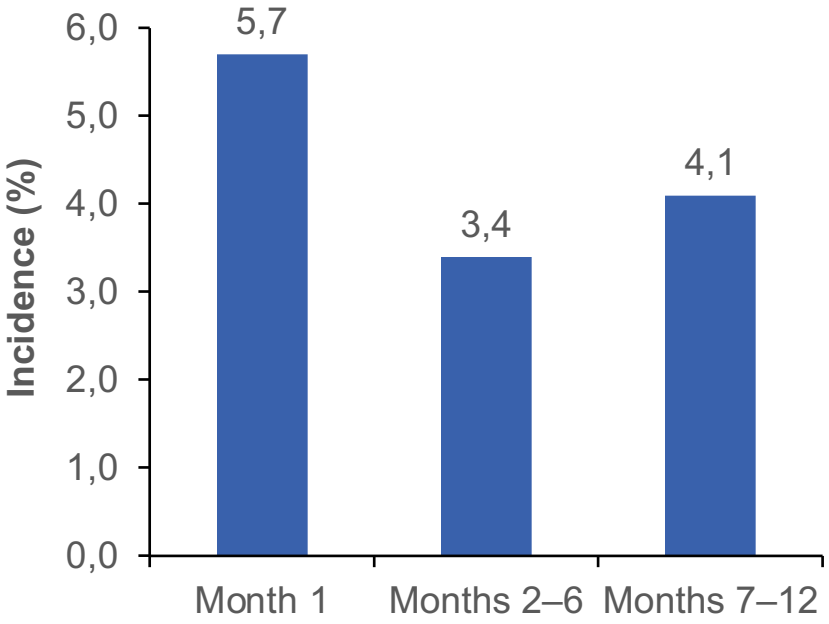
Francis CW *et al*, *Thrombosis and Haemostasis* 2015;13;1028–1035

DALTECAN: Efficacy and Safety of LMHW in the Extended Treatment of Cancer Associated Thrombosis

Major bleeding events



Recurrent VTE



Francis CW *et al*, *J Thromb Haemost* 2015;13:1028–1035

Rivaroxaban Ongoing Trials in Cancer Associated Thrombosis

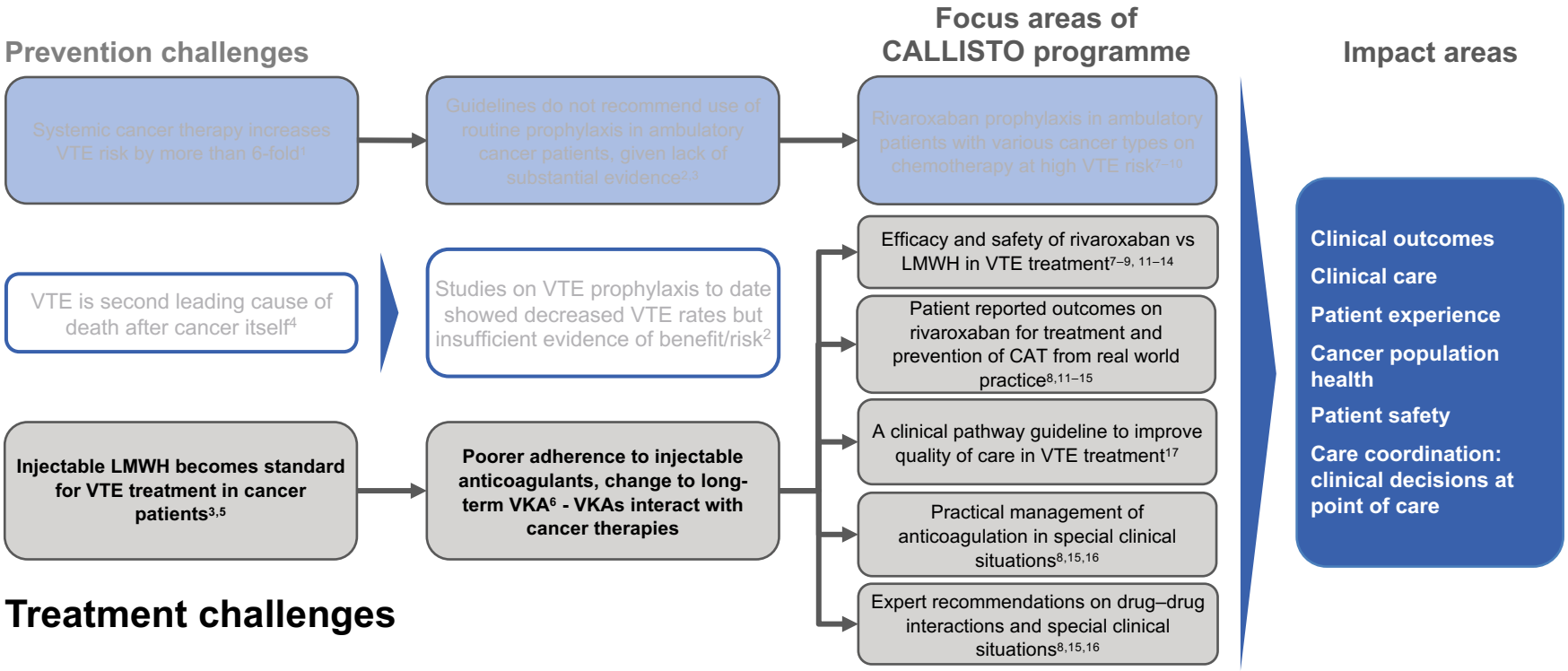
The CALLISTO Program

The CALLISTO Programme

Cancer Associated thrombosis – expLoring soLutions for patIentS through Treatment and prevention with rivarOxaban

Novel "umbrella" programme that addresses multiple clinically relevant questions in cancer-associated thrombosis via multiple studies, expert recommendations and a survey, the combination of which will result in improved quality of care in oncology

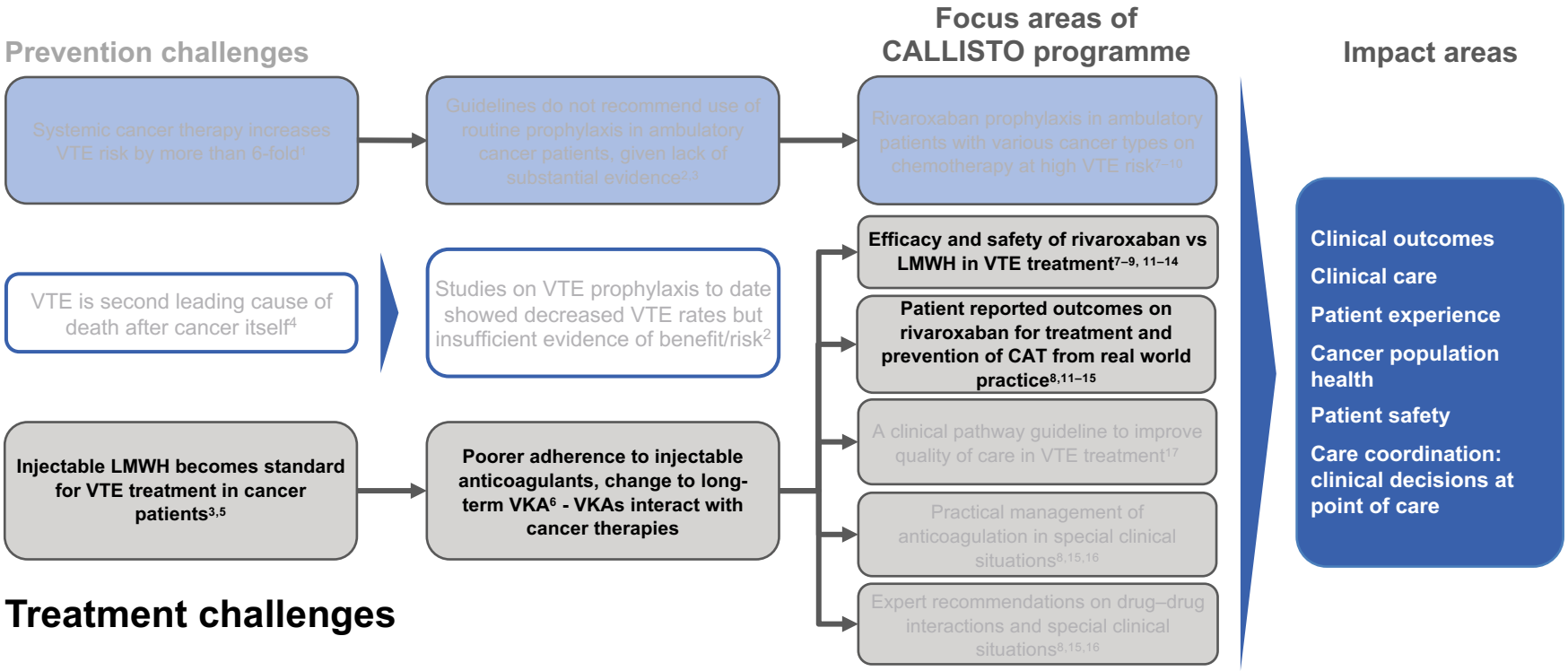
CALLISTO Aims to Address the Unmet Medical Needs in CAT



1. Heit JA *et al*, *Arch Intern Med* 2000;160:809–815; 2. Di Nisio M *et al*, *Cochrane Database Rev* 2014;CD008500; 3. Lyman GH *et al*, *J Clin Oncol* 2013;17:2189–2204;
4. Khorana AA *et al*, *J Thromb Haemost* 2007;5:632–634; *5. Lyman GH et al*, *J Clin Oncol* 2007;25:5490–5505; 6. Khorona A *et al*, *Thromb Res* 2016;145:51–53;
7. Janssen Research & Development, LLC. https://clinicaltrials.gov/ct2/show/NCT02555878; 8. Bach M *et al*, *Thromb Haemost* 2016;116:S24–S32;
9. Khorana AA *et al*, *Thromb Haemost.* 2017: doi:10.1160/TH17-03-0171; 10. Fadoi Foundation, Italy. https://clinicaltrials.gov/ct2/show/NCT03055026; 11. EudraCT: 2012-005589-3;
12. Young A *et al*, *Thromb Res* 2016;140:S172–S173; 13. AIO-Studien-gGmbH. www.clinicaltrials.gov/ct2/show/NCT02583191; 14. Riess H *et al. Dtsch med Wochenschr* 2015;140:S22–S23;
15. Bayer. https://clinicaltrials.gov/ct2/show/NCT02742623; 16. http://frontline2.tri-london.ac.uk/; 17. Mantha S *et al*, *J Thromb Thrombolyis* 2016: doi:10.1007/s11239-016-1429-1

CALLISTO

CALLISTO Aims to Address the Unmet Medical Needs in CAT



1. Heit JA *et al*, *Arch Intern Med* 2000;160:809–815; 2. Di Nisio M *et al*, *Cochrane Database Rev* 2014;CD008500; 3. Lyman GH *et al*, *J Clin Oncol* 2013;17:2189–2204;
4. Khorana AA *et al*, *J Thromb Haemost* 2007;5:632–634; *5. Lyman GH et al*, *J Clin Oncol* 2007;25:5490–5505*;* 6. Khorona A *et al*, *Thromb Res* 2016;145:51–53;
7. Janssen Research & Development, LLC. https://clinicaltrials.gov/ct2/show/NCT02555878; 8. Bach M *et al*, *Thromb Haemost* 2016;116:S24–S32;
9. Khorana AA *et al*, *Thromb Haemost.* 2017: doi:10.1160/TH17-03-0171; 10. Fadoi Foundation, Italy. https://clinicaltrials.gov/ct2/show/NCT03055026; 11. EudraCT: 2012-005589-3;
12. Young A *et al*, *Thromb Res* 2016;140:S172–S173; 13. AIO-Studien-gGmbH. www.clinicaltrials.gov/ct2/show/NCT02583191; 14. Riess H *et al. Dtsch med Wochenschr* 2015;140:S22–S23;
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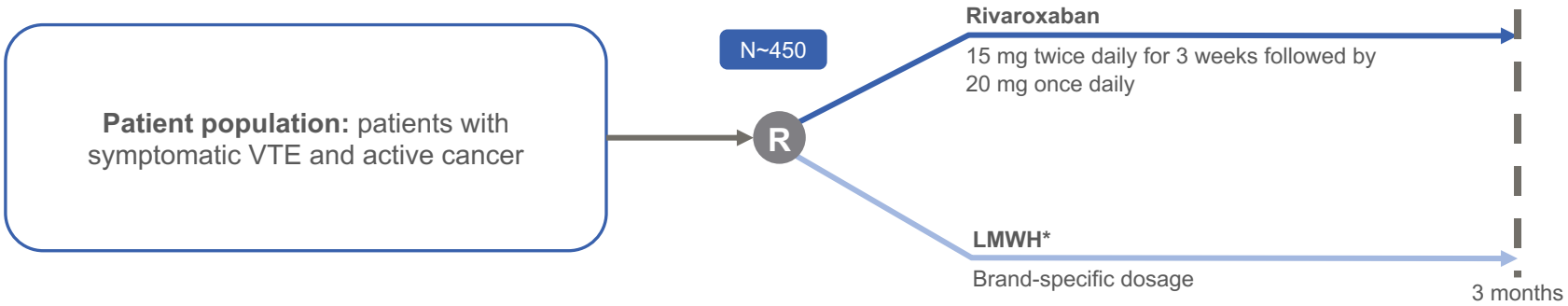
CALLISTO

CONKO 011: Study Design

Rationale: Patient-reported treatment satisfaction measured by the Anti-Clot Treatment Scale with rivaroxaban versus standard of care[1,2]



Short design: Prospective, multicentre, randomized, open-label phase III study

Indication: VTE treatment in patients with cancer

FPFV: Q1-16

LPLV: TBD

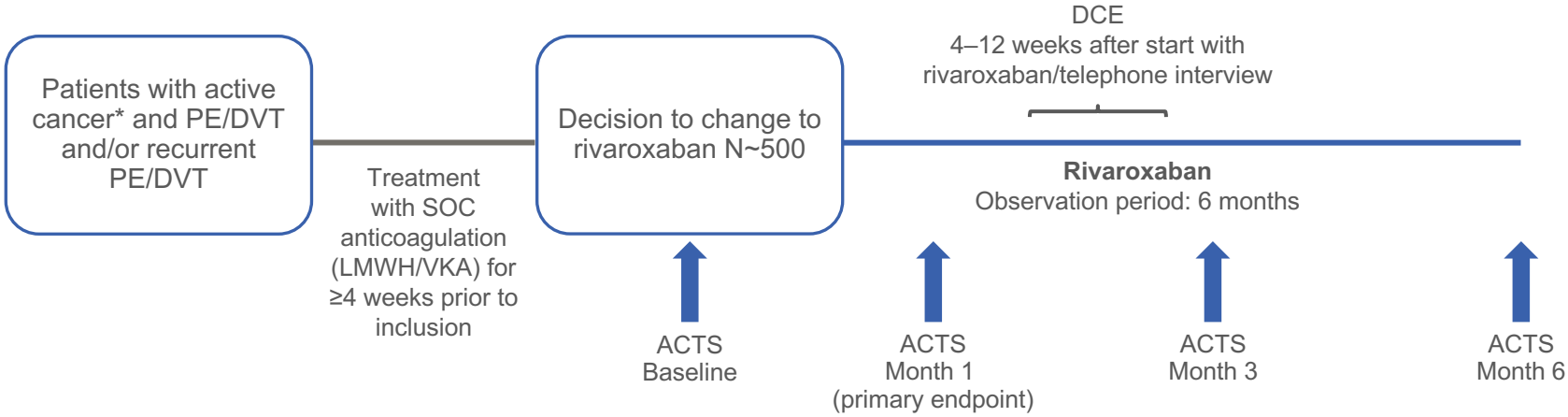
*Standard as used in participating site

1. Riess H *et al*, *Dtsch med Wochenschr* 2015;140:S22–S23; 2. AIO-Studien-gGmbH. https://clinicaltrials.gov/ct2/show/NCT02583191

CONKO-011 AIO-SUP-0115/ass

COSIMO: Study Design

Rationale: To assess patient-reported treatment satisfaction with regard to the ACTS burden score for the use of rivaroxaban for treatment of VTE and/or prevention of recurrent VTE in patients with active cancer changing to this therapy[1,2]



Short design: International, prospective, non-interventional cohort study

Indication: VTE treatment and/or prevention of recurrent VTE in patients with active cancer

FPFV: Q4-16
LPLV: Q3-18

*Diagnosis or treatment of cancer in the previous <6 months, or recurrent or metastatic cancer other than fully treated basal cell or squamous cell carcinoma of the skin

Bayer. https://clinicaltrials.gov/ct2/show/NCT02742623;

COSIMO

Conclusions

- There are now 2 RCTs of DOACs in CAT treatment (Rivaroxaban & Edoxaban)
- Patients and physicians have options but treatment decisions need care and need to be shared with informed patients
  - ISTH guidance 2018 already produced
  - More guidelines are expected to materialize soon
- Real world data are useful as they reflect selection 'bias' that however seems to optimize treatments with patient safety at the centre e.g. avoidance of
  - Active GI lesions
  - Multiple concurrent medications
  - Poor end organ function (Liver, Kidney)
- We still have questions over optimal length of treatment
- [1]CALLISTO is a novel 'umbrella' programme that involves multiple parallel clinical trials, that build on the recent advent of Rivaroxaban.

1. Bach M *et al*, *Thromb Haemost* 2016;116:S24–S32


Thank you
anthony.maraveyas@hey.nhs.uk