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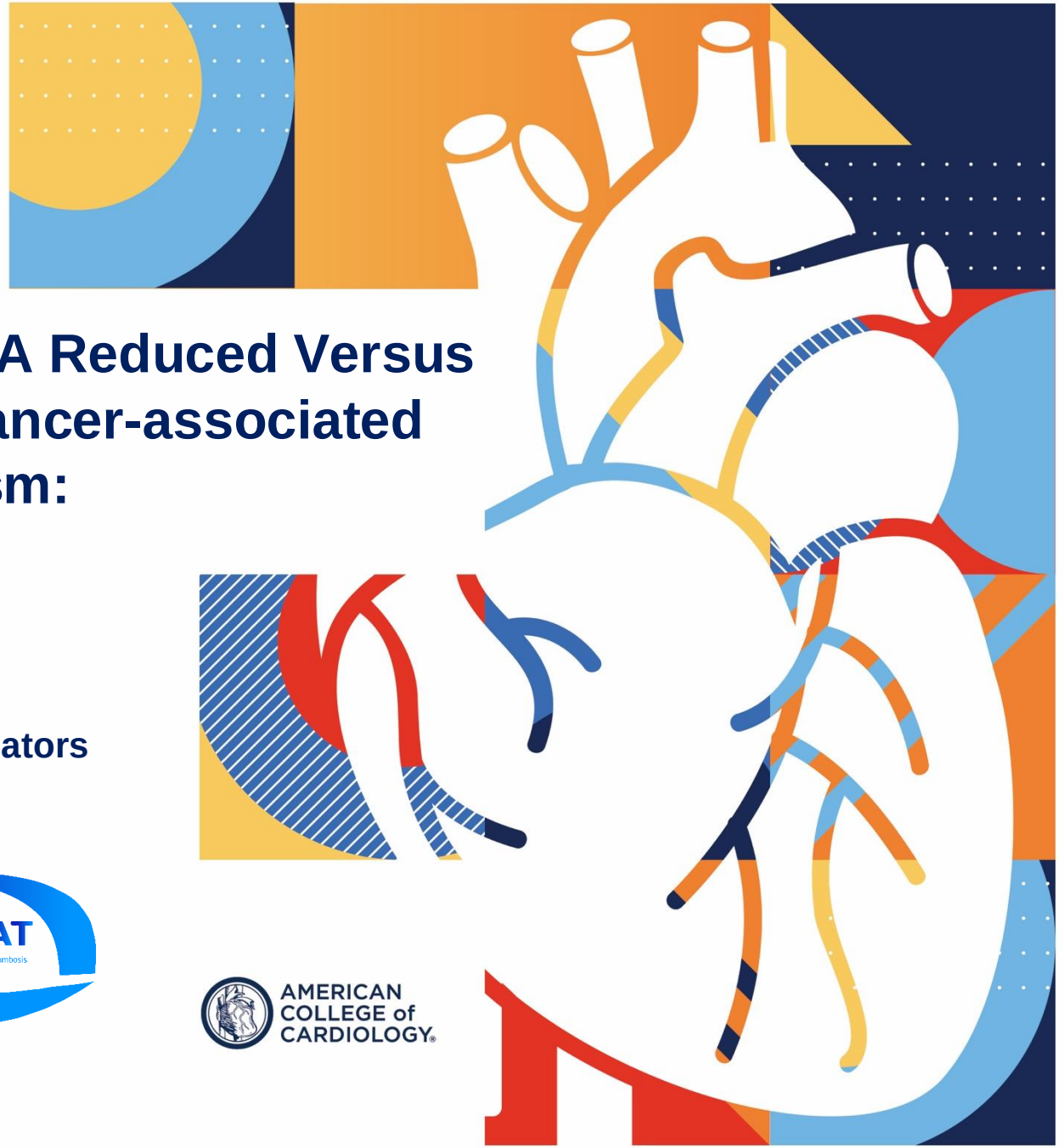

Extended Anticoagulant Treatment With A Reduced Versus Full Dose Apixaban In Patients With Cancer-associated Venous Thromboembolism:

The API-CAT Study

Isabelle Mahé, M.D., Ph.D.,
on behalf of the Steering Committee and the API-CAT Investigators

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Investigator Sponsored Study
Responsibility and Management : AP-HP, France
Funding : BMS-Pfizer Alliance

API-CAT
Apixaban Cancer Associated Thrombosis

AMERICAN COLLEGE of CARDIOLOGY

ASSISTANCE PUBLIQUE HÔPITAUX DE PARIS

Background

- The life expectancy of patients with cancer-associated thrombosis is improving
- The risk of recurrent VTE declines over time, whereas the risk of bleeding remains substantial
- International guidelines suggest continuing anticoagulant therapy for as long as the cancer remains active or cancer treatment is ongoing

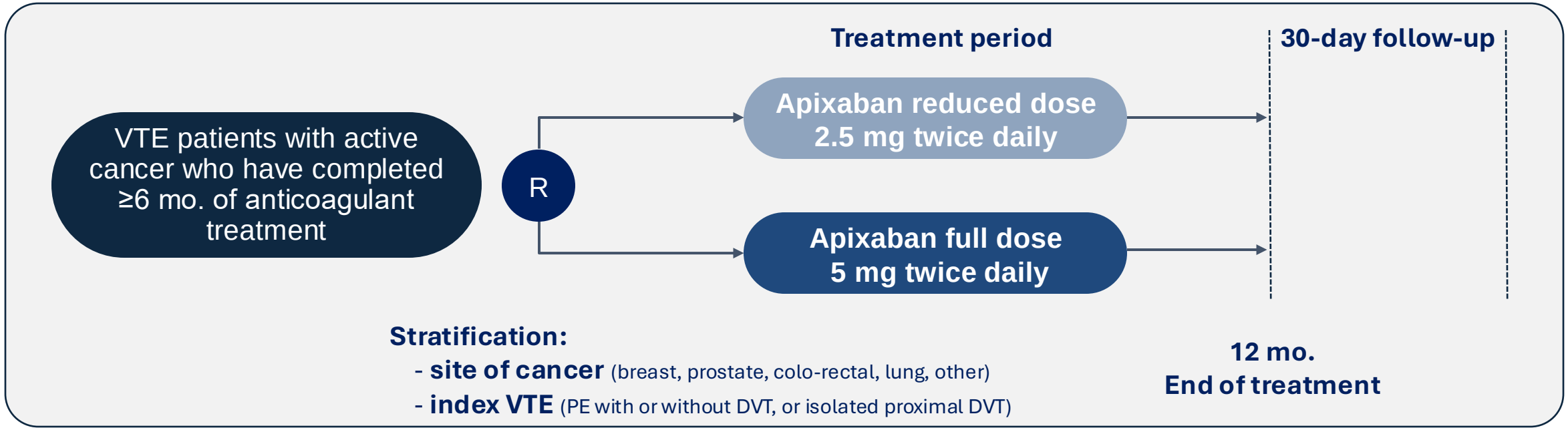
Hypothesis

The use of a reduced dose of anticoagulant could be as effective as, and safer than, a full dose for extended VTE treatment

Design: randomized double-blind study

To determine, in a hierarchical test procedure, whether a low-dose of apixaban (2.5 mg bid) is

- **non-inferior** to a full dose of apixaban (5 mg bid) for **prevention of recurrent VTE**
- **superior** to a full dose of apixaban (5 mg bid) for **clinically relevant bleeding**



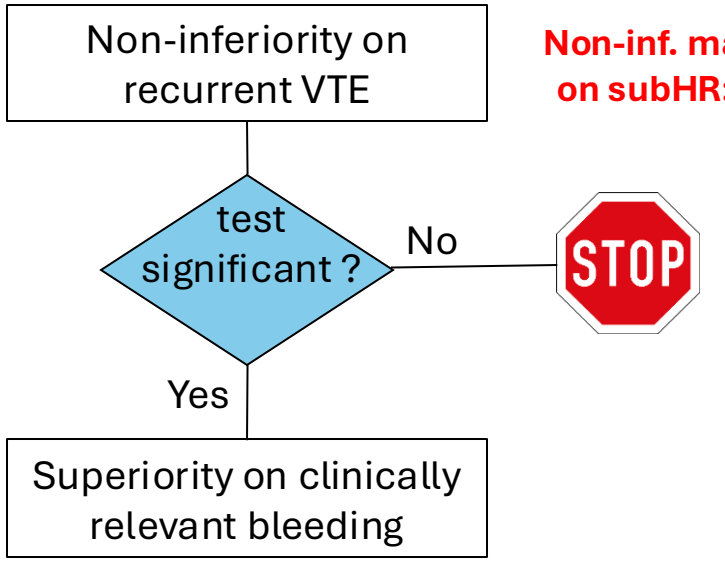
Mahé I, et al. Thromb Haemost 2022, 122 : 646-656

Methods

Outcomes within 12 months

- **Primary outcome: adjudicated recurrent VTE, composite of**
  - recurrent symptomatic VTE
  - incidental VTE
  - VTE-related death
- **Key secondary outcome: adjudicated clinically relevant bleeding, composite of**
  - major bleeding
  - clinically relevant non-major bleeding

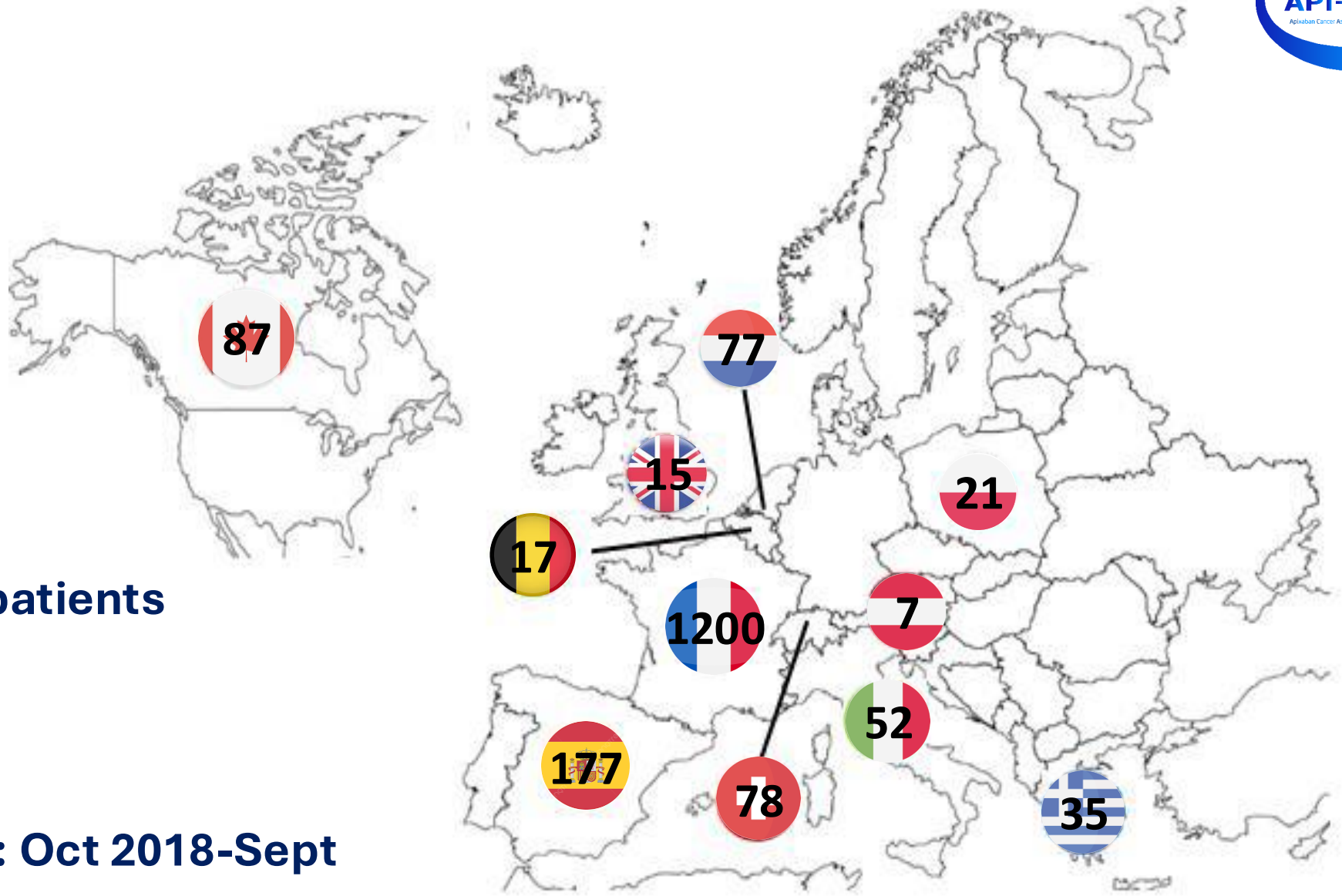
Hierarchical procedure



Statistical analysis

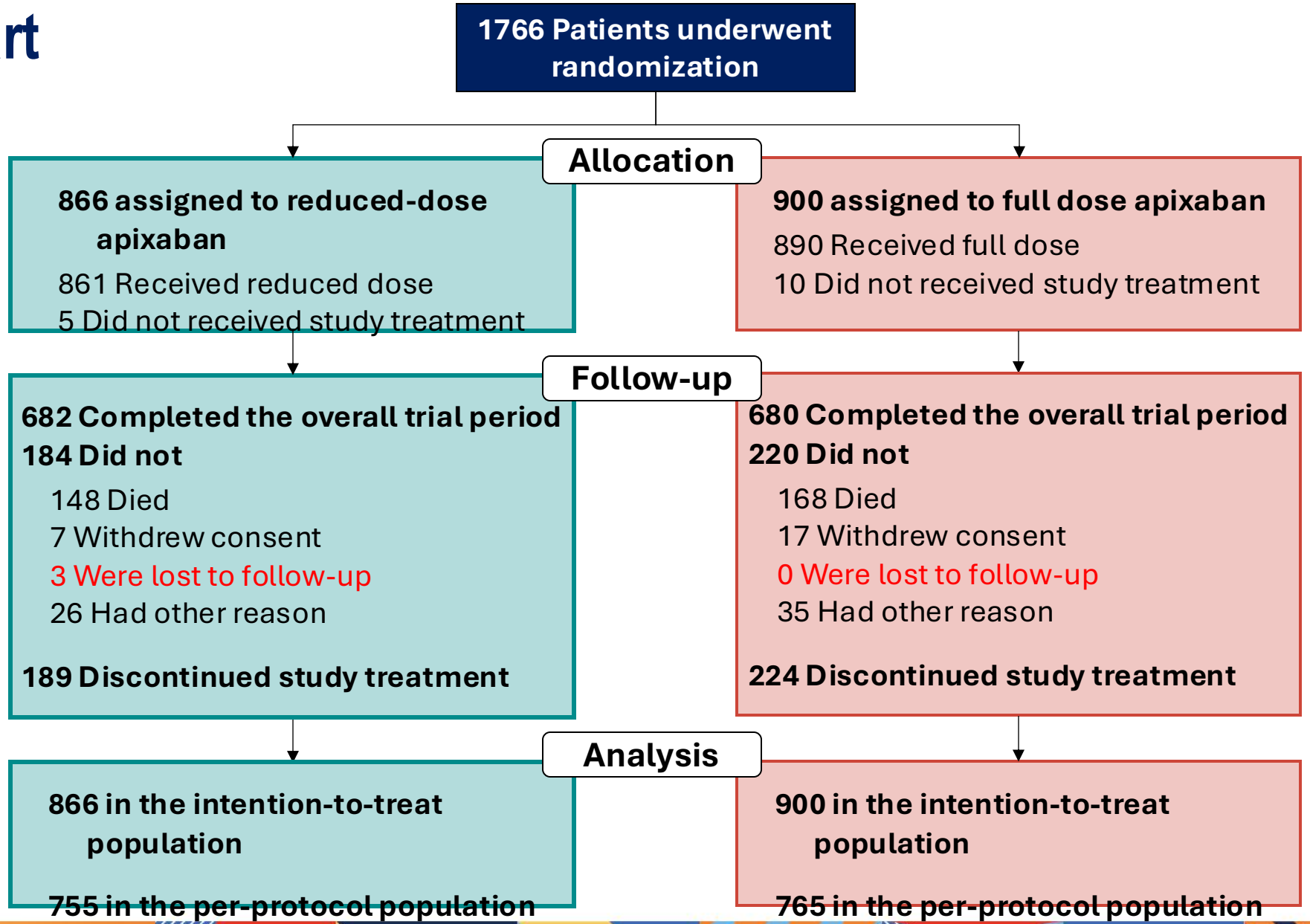
- Sample size 1722 patients to conclude for both primary and key secondary outcomes
- Time-to-event analysis: Fine and Gray model for competing risk of death (SubHR and 95% CI)
- Intention-to treat and per-protocol populations

Enrollment



- 1766 randomized patients
- 121 centers
- 11 countries
- Enrollment period: Oct 2018-Sept 2023

Flow chart



Patient characteristics

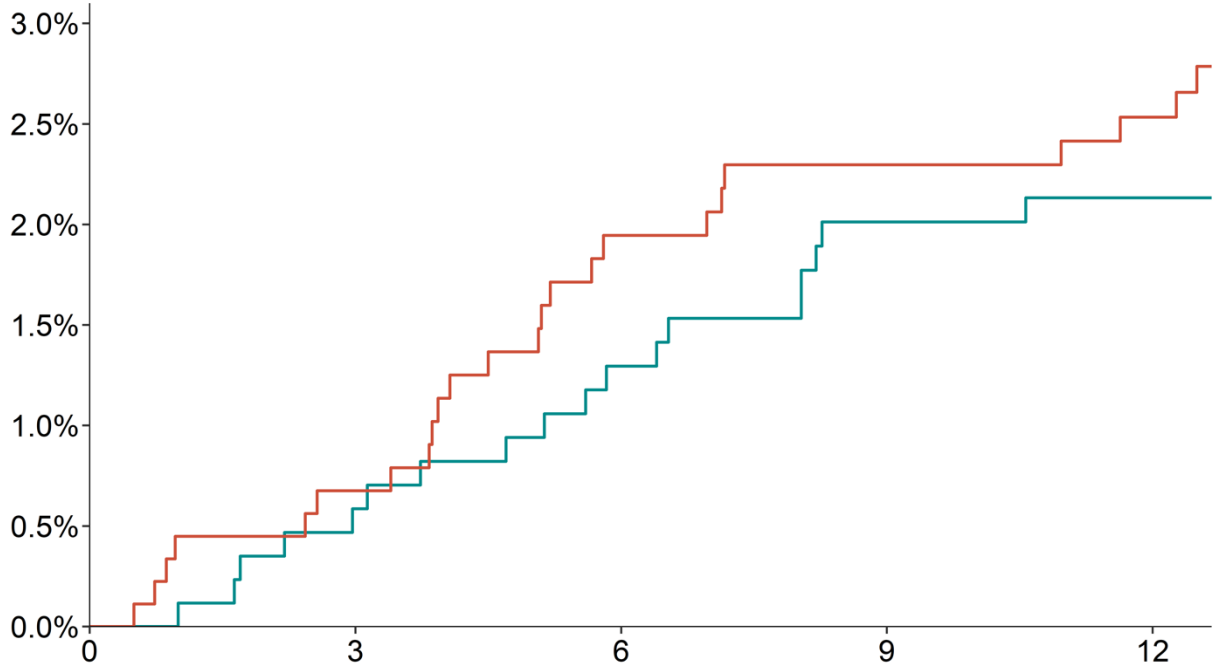
	Overall (N = 1766)
Mean age	67.4 yrs ± 11.2
Male	43.4 %
History of VTE	18.5 %
Creatinine clearance <50 ml/min	13.7 %
Index VTE (randomization strata)	
PE ± proximal DVT	75.5 %
Proximal DVT only	24.5 %

	Overall (N = 1766)
Site of cancer (randomization strata)	
Breast	22.7 %
Colorectal	15.3 %
Lung	11.3 %
Prostate	9.3 %
Others	41.4 %
Metastatic cancer	65.8 %
ECOG 2	7.4 %

Median time since index event	8.0 mo.
Median duration of the study drug	11.8 mo.

Results: primary efficacy outcome *(Composite of recurrent symptomatic VTE or incidental VTE)*

	Apixaban Reduced dose (N=866)	Apixaban Full dose (N=900)	Subhazard Ratio (95% CI)	p-value
Recurrent VTE — no. (%)	18 (2.1)	24 (2.8)	0.76 (0.41 to 1.41)	0.001 for non-inferiority



Percentages are the cumulative incidence

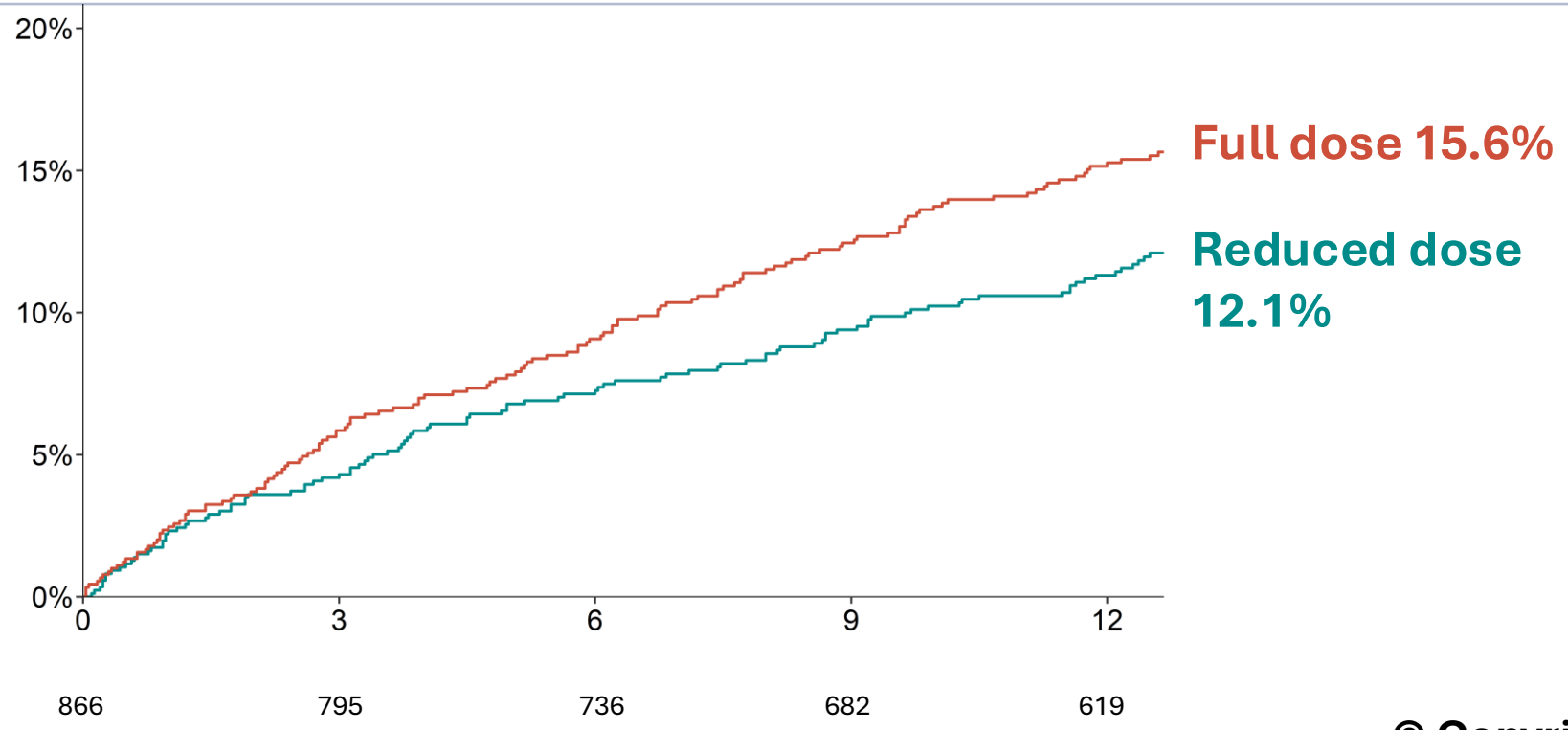
Results: primary efficacy outcome

	Apixaban Reduced dose (N=866)	Apixaban Full dose (N=900)	Subhazard Ratio (95% CI)	p-value
Recurrent VTE — no. (%)	**18 (2.1)**	**24 (2.8)**	**0.76 (0.41 to 1.41)**	**0.001 for non-inferiority**
Recurrent symptomatic VTE	**17 (2.0)**	**18 (2.1)**		
Lower limb DVT	8	6		
PE	9	10		
Upper limb DVT	1	3		
CVC-related thrombosis	1	2		
Recurrent Incidental VTE	**1 (0.1)**	**6 (0.7)**		

Percentages are the cumulative incidence

Results: key secondary safety outcome (composite of MB or CRNMB)

	Apixaban Reduced dose (N=866)	Apixaban Full dose (N=900)	Subhazard Ratio (95% CI)	p-value
Clinically relevant bleeding —no. (%)	102 (12.1)	136 (15.6)	0.75 (0.58 to 0.97)	0.03 for superiority



Percentages are the cumulative incidence

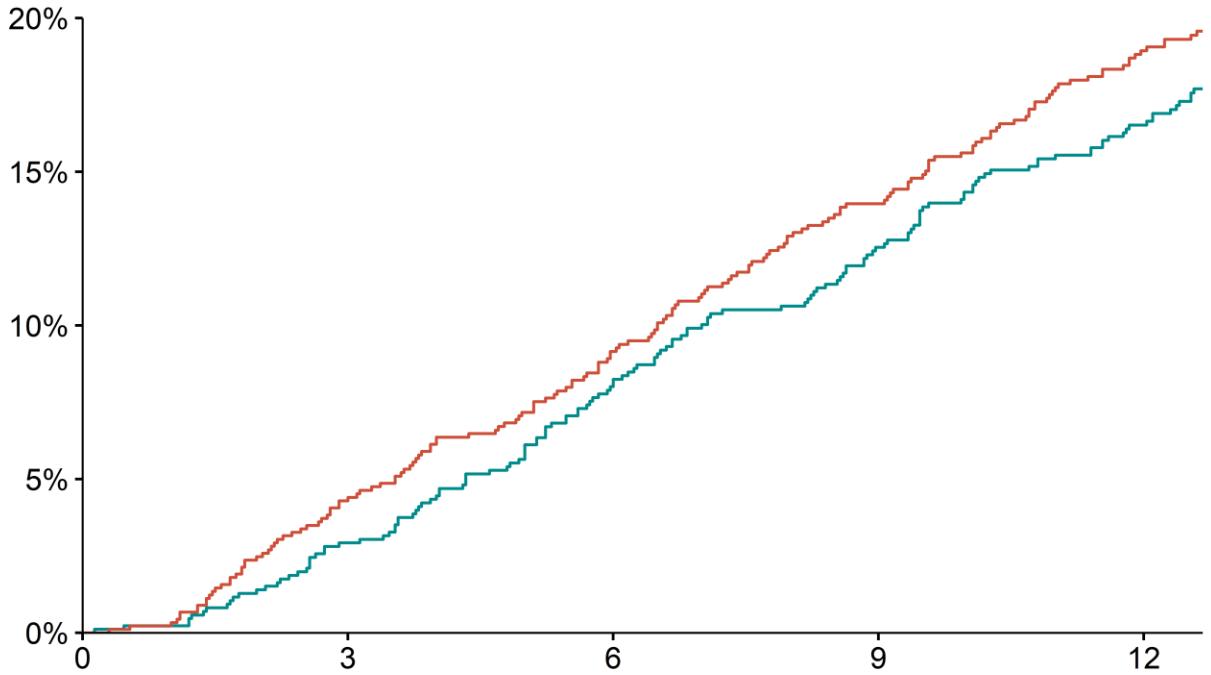
Results: key secondary safety outcome (composite of MB or CRNMB)

	Apixaban Reduced dose (N=866)	Apixaban Full dose (N=900)	Subhazard Ratio (95% CI)	p-value
Clinically relevant bleeding — no. (%)	**102 (12.1)**	**136 (15.6)**	**0.75 (0.58 to 0.97)**	**0.03 for superiority**
Major bleeding	**24 (2.9)**	**37 (4.3)**	**0.66 (0.40 to 1.10)**	
Fatal	2	2		
Major gastrointestinal bleeding	12	25		
Upper	6	13		
Lower	7	13		
CRNMB	**84 (10.0)**	**107 (12.3)**	**0.79 (0.59 to 1.05)**	

Percentages are the cumulative incidence

Results: all-cause death

	Apixaban Reduced dose (N=866)	Apixaban Full dose (N=900)	Hazard Ratio (95% CI)	p-value
All-cause death — no. (%)	148 (17.7)	168 (19.6)	0.96 (0.86 to 1.06)	0.42



Percentages are the cumulative incidence

Conclusion

In patients with active cancer who have completed at least 6 months of anticoagulant treatment

- Extended anticoagulant therapy with reduced-dose apixaban was non-inferior to full-dose apixaban **to prevent recurrent venous thromboembolism**
- The reduced dose resulted in a lower incidence of clinically relevant bleeding

Our results indicate that these patients may be eligible to receive a reduced dose of apixaban for extended treatment

Investigators

France – Abraham P, Accassat S, Alexandra J-F, Alexandre J, Alexandre J, Aouate D, Aquilanti S, Armengol G, Arpin D, Artifoni M, Assaad S, Assaf E, Auberger B, Ayllon J, Barnier A, Barthier S, Baudout D, Baumgaertner I, Bazan F, Beguinot M, Benainous R, Benhamou Y, Benmammar K.E, Benmaziane Teillet A, Bensaoula O, Bertoletti L, Beuzeboc P, Bigou Y, Blaise S, Blouet A, Bogaert A, Bonhomme S, Bouallagui I, Bouattour M, Boulon C, Boustany R, Boutruche B, Brain E, Brebion N, Brehon M, Bressollette L, Breuil N, Brezault C, Brisot D, Brocard F, Buchmuller A, Burgy M, Burnod A, Cajfinger F, Candia A, Candia A, Carcaud C, Carinato H, Charasson M, Chastaingt L, Chelghoum M, Chidiac J, Cojocarasu O, Conforti R, Connault J, Constans J, Coriat R, Cornand D, Coudene A, Couturaud F, Daoud H, David J, De La Fouchardiere C, de Magalhaes E, De Saint Martin L, Debourdeau P Deiana L, Delrue M, Demolombe S, Dermine S, Dieras V, Djennaoui S, Dourthe L-M, Doutrelon C, Dronne W, Dublanchet N, Dupas S, Durant C, Durieu I, Eche Gass A, Edeline J, Elalamy I, Elias A, Elias M, Emmerich J, Escande A, Espitia O, Falchero L, Falvo N, Fard D, Farès Y, Ferec M, Ferrari E, Fonsegrive C, Frechier L Fuerea A-C, Gatineau M, Gautier G, Gavoille L, Gerotziafas G, Gerotziafas G, Gestin S, Giauffret F, Gobert C, Gourdier A-S, Grange C, Guillaumat J, Guillemin A, Gut-Gobert C, Happe F, Henni S, Herreman C, Hourmant B, Huguet R, Imbert B, Jagu A, Jandot M, Joly C, Joly M, Journeau L, Kaddour M, Kalbacher E, Kempf E, Kriegel I, Kubina J-M, L'Heveder C, Labbaoui M, Lacroix P, Lacut K, Laguerre B, Lam Y.H, Lammens J, Lamuraglia M, Lanéelle D, Le Brun C-E, Le Gloan S, Le Jeune S, Le Mao R, Le Moigne E, le Roy G, Le Seve JD, Lebel A, Leblanc C, Ledan F, Lefeuvre C, Lega J-C, Leroyer C, Lhorte P, Lim P, Lo S Lopez-Sublet M, Mahé G, Mahé I, Mandon C, Marchal T, Marques N, Masmoudi S, Massiani M.A, Mauger C, Mayeur D, Mechenin M, Meneveau N, Menez C, Meyer G, Meyer P, Michon-Pasturel U, Miranda S, Misbahi R, Monange B, Moriceau G, Morin A, N'guyen T, Nepveu O, Odier L, Pan-Petesch B, Pante V, Papageorgiou L, Papageorgiou L, Pastre J, Pernod G, Peyrachon B, Pinsolle J, Plaisance L.A, Planquette B, Poénou G, Poénou G, Poggi J.N, Pottier C, Poureau P-G, Provencal J, Quéré I, Ramondou P, Raymond E, Reynaud Q, Robin S, Roemer-Becuwe C, Roth G, Roudot H, Saldana Gallo C, Salta S, Sanchez O, Santy Modeliar S, Sarlon Bertoli G, Sartre B, Savary X, Schmidt J, Scotté F, Seinturier C, Semenou D, Sevestre M-A, Simon D, Sinzogan-Eyoum C, Slama B, Soudet S, Spaeth D, Spano J.P, Staudacher L, Stoclin A, Sverdlin R, Tazi Y, Tequi V, Thenault-Lebredonchel M-H, Thierry-Vuillemin A, Toledano E, Tossen G, Tournigand C, Trager S, Trensz P, Trichet C, Tromeur C, Ulusakarya A, Valmar C, Vauleon E, Versini E, Zelek L, Zenati N.

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Study Drug : Fabreguettes JR, Franquet L, Alloux C

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Extended Reduced-Dose Apixaban for Cancer-Associated Venous Thromboembolism

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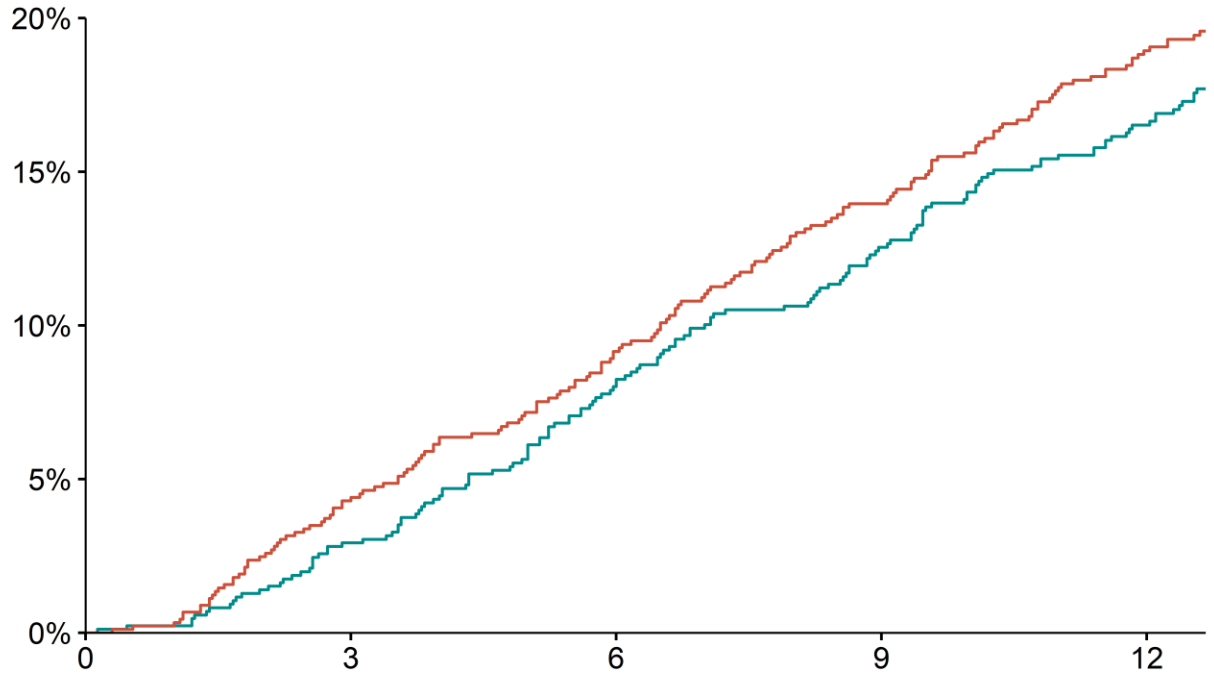
Results: major bleeding

	Apixaban Reduced dose (N=866)	Apixaban Full dose (N=900)	Hazard Ratio (95% CI)
Major bleeding — no. (%)	24 (2.9)	37 (4.3)	0.66 (0.40 to 1.10)



Percentages are the cumulative incidence

Subgroup analysis (ITT population)