

Anticoagulation updates

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Financial Disclosure

I have no financial disclosures to declare

Educational need

We make decisions about anticoagulation choice and duration for anticoagulation use

We manage patients who are on DOAC and antiplatelet therapy

We are consulted on patients with new intracranial bleed in patients who are on DOAC

There is new literature around FXI/XIa inhibitors

Objectives

To learn appropriate choice and duration of antithrombotic use both in the therapeutic and prophylactic areas

To discuss the need for continuation of antiplatelet in patient who get started on a DOAC

To apply evidence in decisions around resumption of anticoagulation in patients who are presenting with an intracranial hemorrhage.

To review the existing literature around FXI/XIa inhibitors

Poll Everywhere

[Pollev.com/ukhm](https://pollev.com/ukhm)

Text UKHM to 22333

Case 1

A 58 year old woman presents to the ED with newly acute unprovoked DVT. Which anticoagulant would you prescribe?

- A. LMWH
- B. Apixaban
- C. Edoxaban
- D. Rivaroxaban

COBRRA Trial

RCT, blinded endpoint adjudication

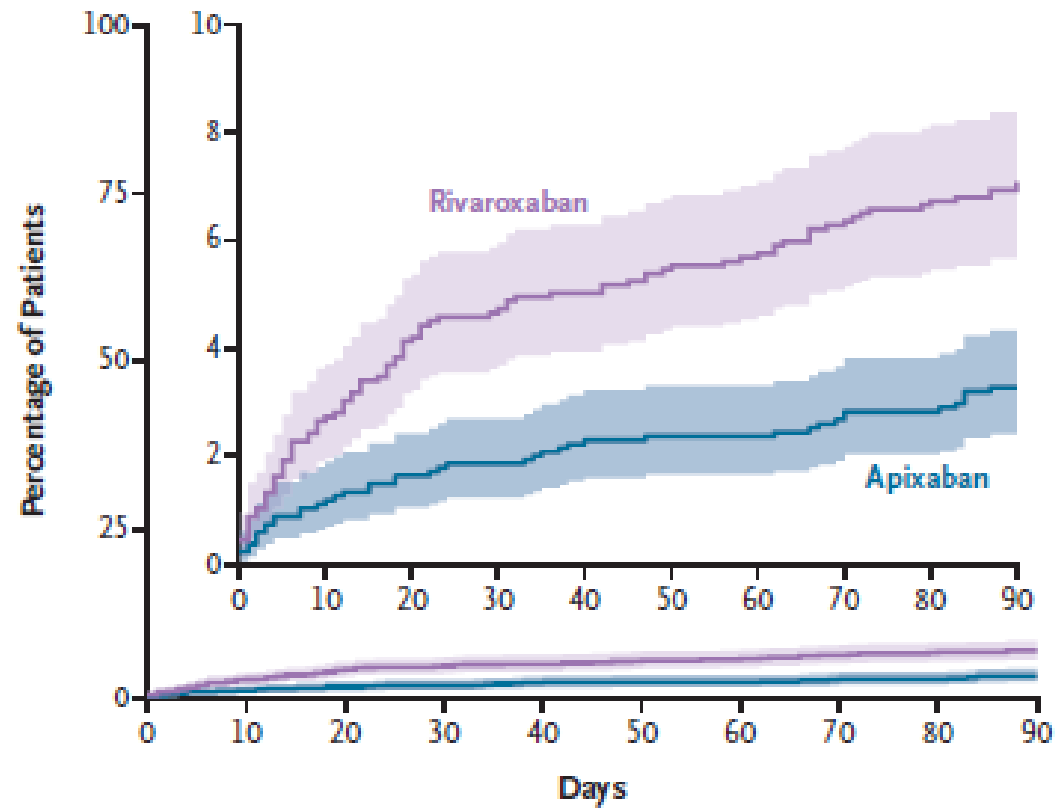
2,760 patients, 32 centers

Randomized:

- Apixaban
- Rivaroxaban

Primary Outcome: Clinically relevant bleeding, major bleeding + clinically relevant nonmajor bleeding

COBRRA Trial



Conclusion

In patients with acute DVT or PE, apixaban should be considered the preferred DOAC when bleeding risk matters

Case 2

72-year-old woman is admitted with an acute pulmonary embolism after a 10-day hospitalization for severe pneumonia. Her medical history is notable for obesity (BMI 36 kg/m²) and rheumatoid arthritis. She has no history of bleeding, and normal renal function. You start her on apixaban. What would be your recommendation for duration on anticoagulation?

- A. Apixaban full dose for 3 months
- B. Apixaban full dose for 6 months
- C. Apixaban full dose for 3 months and then 1/2 dose for 3 months
- D. Apixaban full dose for 3 months and then aspirin for another 3 months

Hi-PRO Trial

RCT, double blinded 600 patients, single center

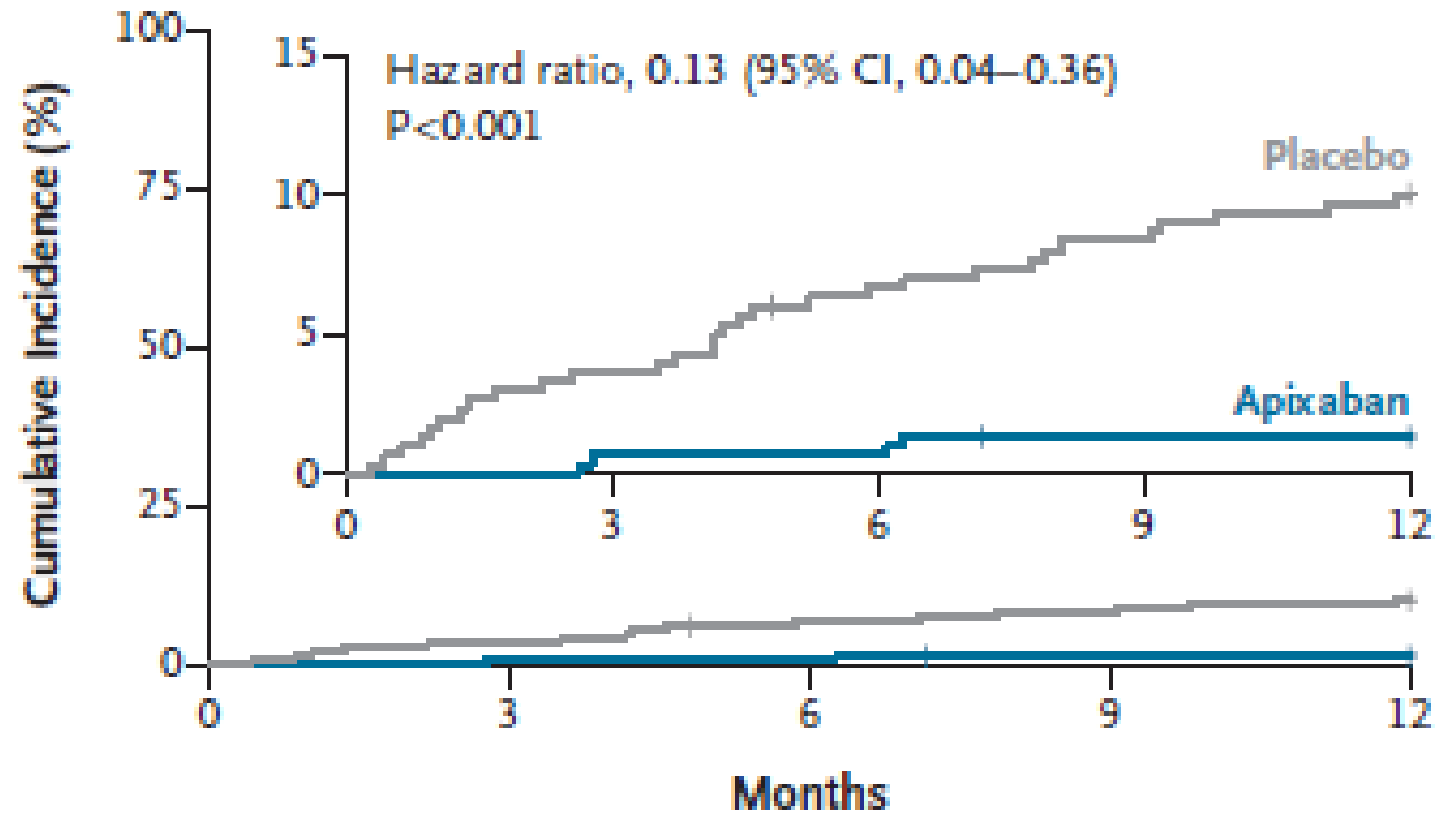
Randomized:

- Apixaban
- Placebo

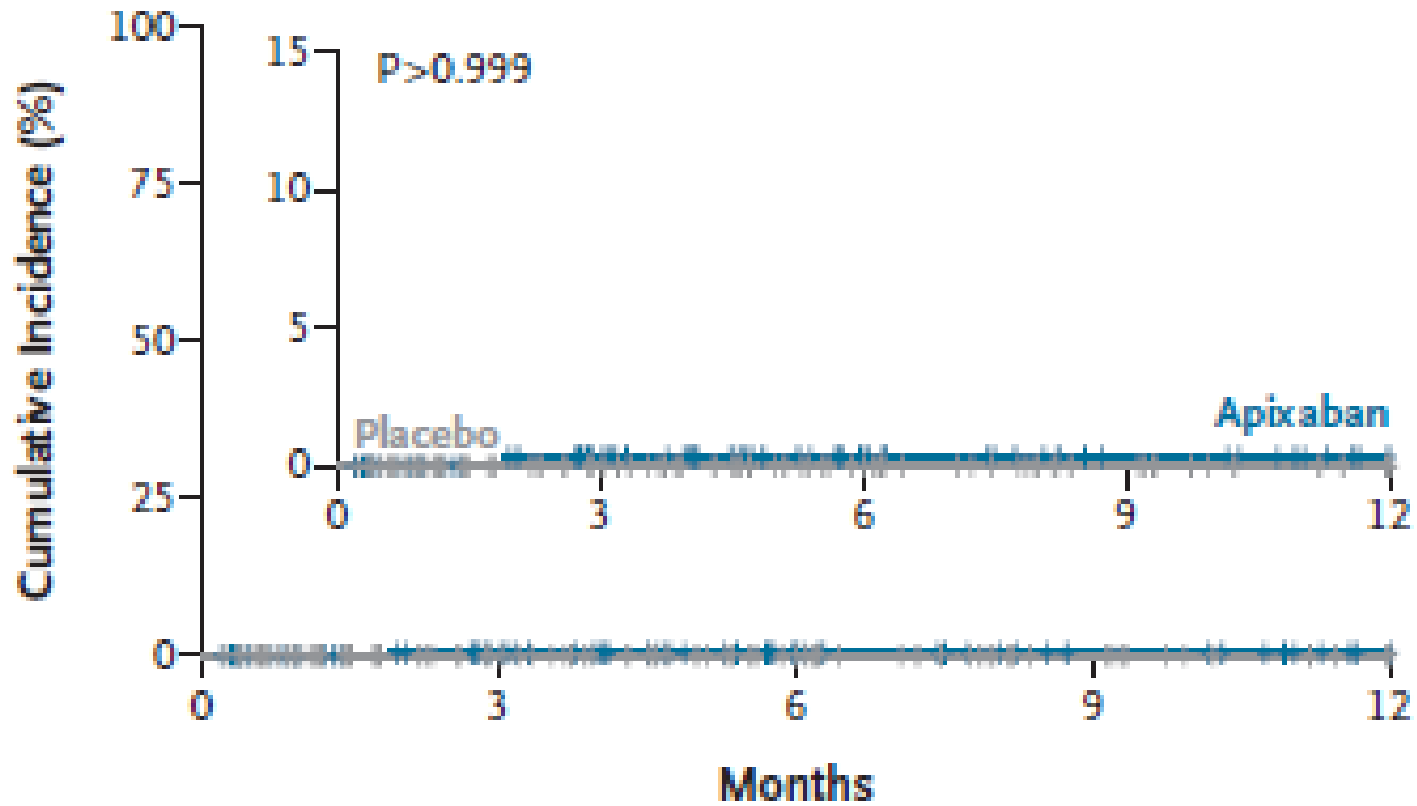
Primary Efficacy: Symptomatic recurrent VTE

Primary safety: Major bleeding (ISTH definition)

Symptomatic recurrent VTE



Major bleeding



Conclusion

Among patients with provoked VTE and enduring risk factors, extending anticoagulation evidence supports the use of extended anticoagulation

Case 3

A 72-year-old man with chronic coronary syndrome underwent PCI with drug-eluting stent placement 3 years ago. He presents with newly diagnosed atrial fibrillation and is being started on apixaban for stroke prevention. He has diabetes and prior MI but no recent ACS, PCI, or stent thrombosis. Will you continue him on aspirin?

A. Yes

B. No

AQUATIC Trial

RCT, double blinded 872 patients, 51 centers

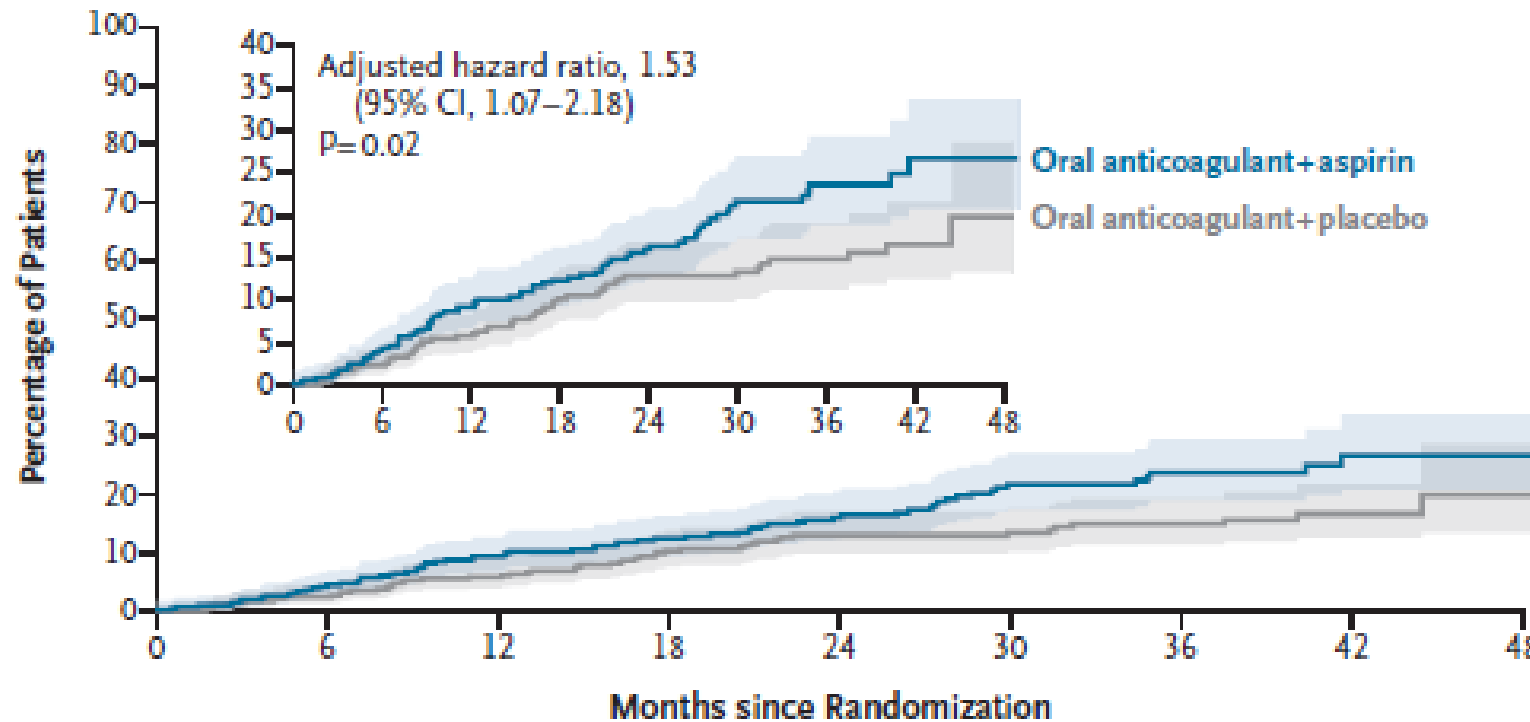
Randomized:

- Aspirin
- Placebo

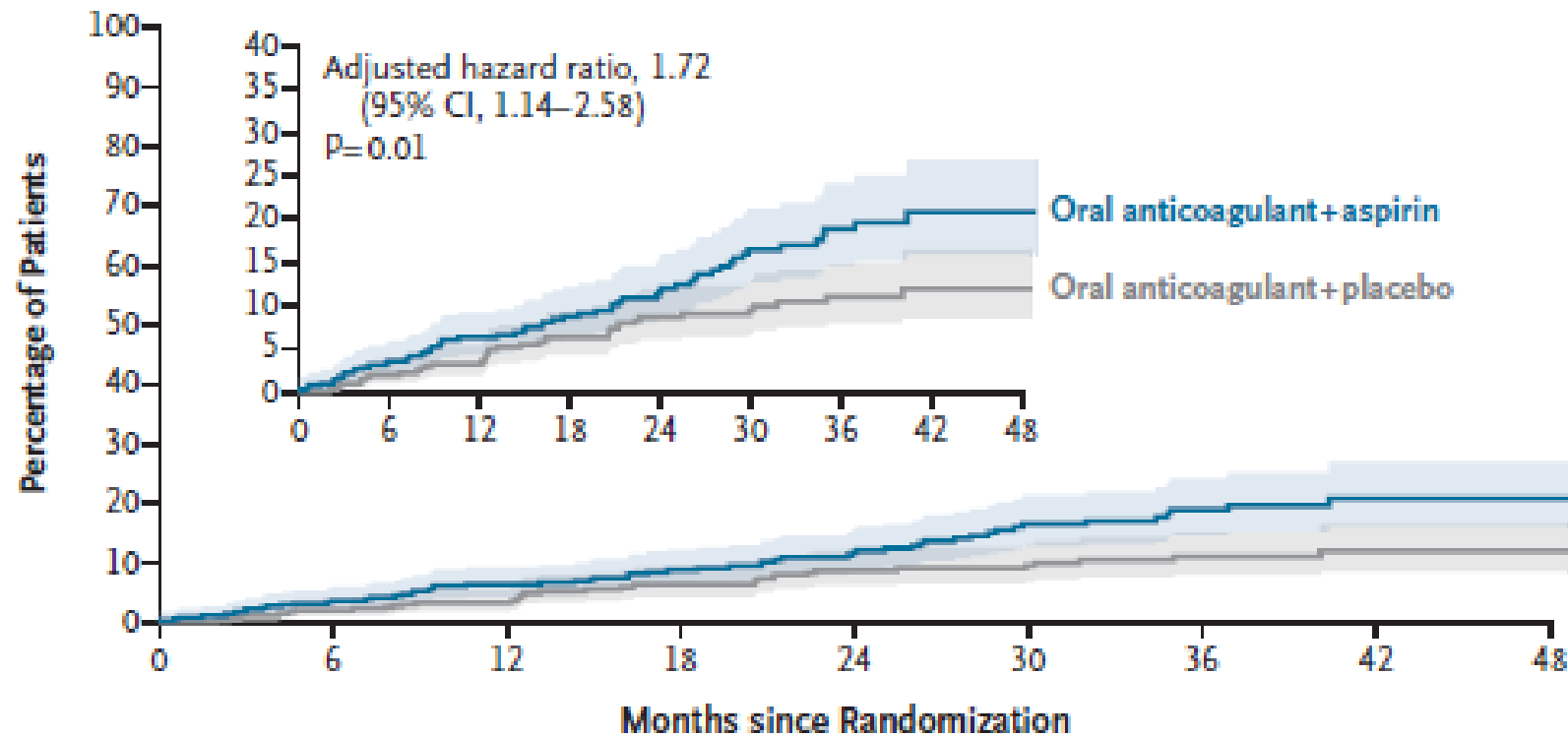
Primary Efficacy: Composite of CV death, MI, stroke, systemic embolism, coronary revascularization, acute limb ischemia

Primary safety: Major bleeding (ISTH definition)

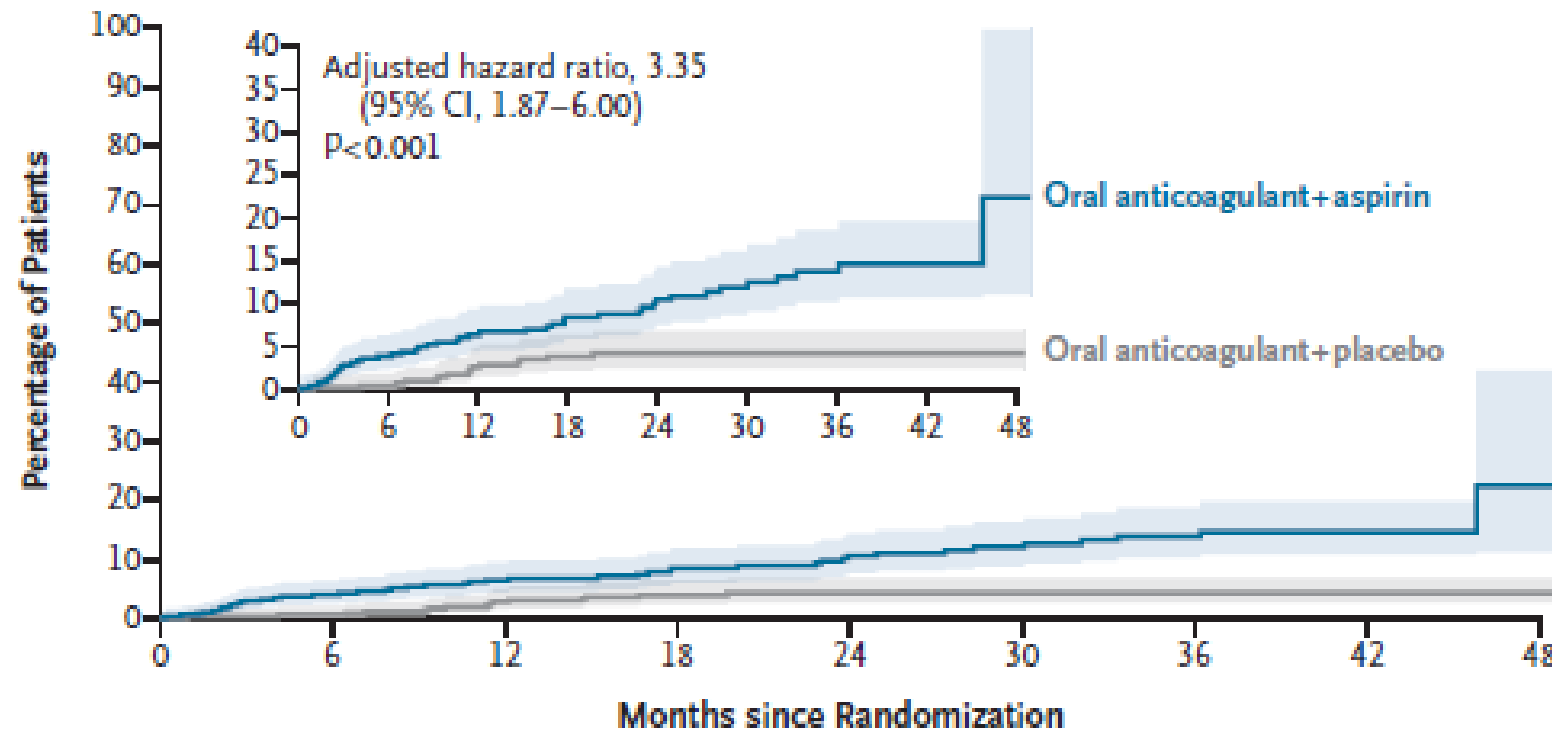
Primary efficacy



Death



Major bleeding



Conclusion

In patients with chronic coronary syndrome, prior PCI, and an indication for long-term oral anticoagulation, continuation of aspirin was not beneficial.

Case 4

A 76-year-old patient with chronic coronary syndrome underwent PCI with drug-eluting stent placement 3 years ago. The patient has atrial fibrillation and is taking apixaban for long-term stroke prevention. The patient has had no recurrent ischemic events or stent thrombosis since PCI. Would you continue her clopidogrel on discharge?

A. Yes

B. No

ADAPT-AF-DES Trial

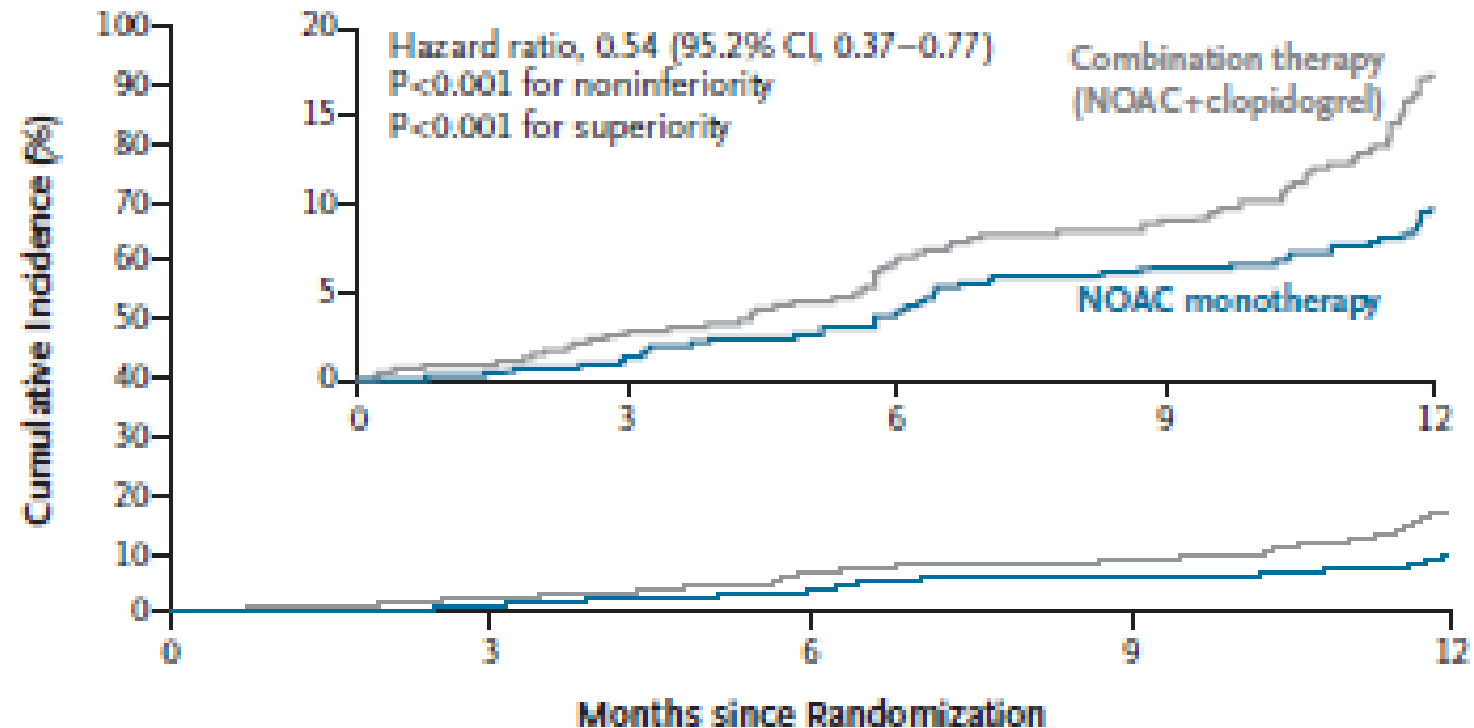
RCT, open-labeled, 960 patients, 32 centers

Randomized:

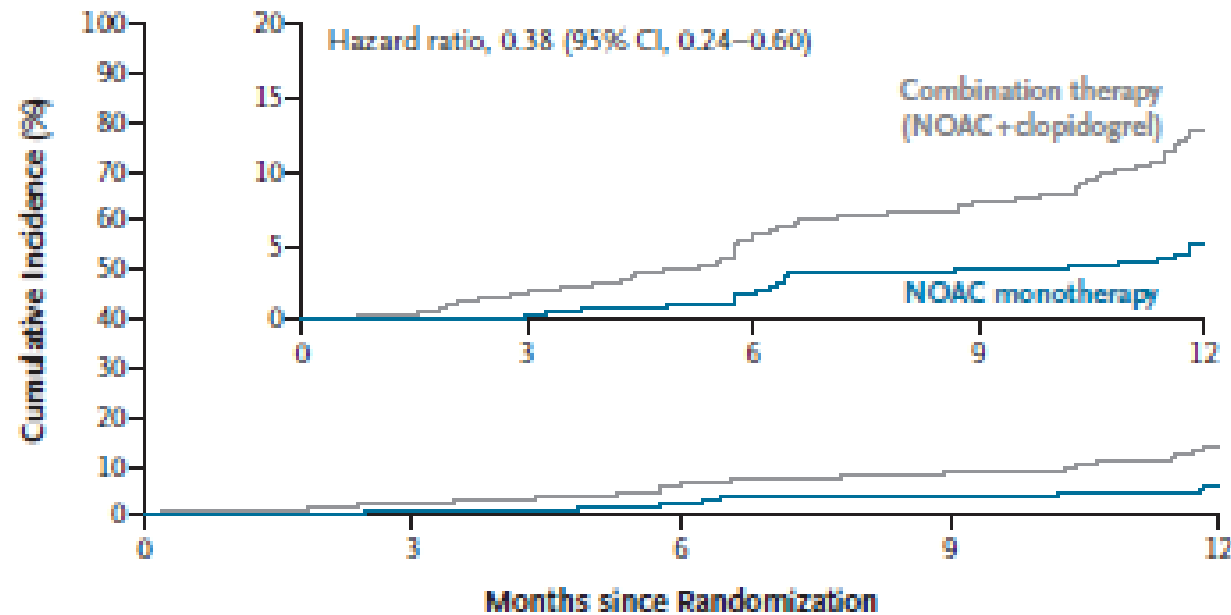
- DOAC monotherapy
- DOAC + clopidogrel

Primary end point: Net adverse clinical events

Net Adverse Clinical events



Major/clinically relevant nonmajor bleeding



Conclusion

In patients with atrial fibrillation more than 1 year after drug-eluting stent implantation, DOAC monotherapy has improved net clinical outcomes compared with continued DOAC plus clopidogrel.

Case 5

A 76-year-old woman with atrial fibrillation on apixaban 5 mg twice daily is admitted for an elective total hip arthroplasty under spinal anesthesia. Orthopedic surgery asks for recommendations regarding perioperative anticoagulation management. Which of the following is the most appropriate recommendation?

- A. Continue apixaban through surgery
- B. Hold apixaban for 2 days before surgery without heparin bridging
- C. Hold apixaban for 3 days before surgery without heparin bridging
- D. Hold apixaban for 3 days before surgery and bridge with LMWH

PAUSE-2 Pilot Trial

Randomized pilot trial, open-label, 159 patients, 32 centers

Randomized:

- PAUSE Strategy
- ARSA Strategy

Primary end point: Perioperative residual DOAC level

PAUSE management

DOAC	CrCl (mmol/L)	DOAC interruption (no DOAC on shaded days)						DOAC resumption ^a (no DOAC on shaded days)			
		Day -5	-4	-3	-2	-1		Day+1	+2	+3	+4
Apixaban	<i>All</i>						Preop blood sample, no DOAC day of surgery				
Dabigatran	<i>CrCl ≥50</i>										
	<i>CrCl <50</i>										
Edoxaban	<i>All</i>										
Rivaroxaban	<i>All</i>										

ASRA management

DOAC	CrCl (mmol/L)	DOAC interruption (no DOAC on shaded days)					Preop blood sample, no DOAC day of surgery	DOAC resumption ^a (no DOAC on shaded days)			
		Day -5	-4	-3	-2	-1		Day+1	+2	+3	+4
Apixaban	All			Heparin bridging if high risk for thrombosis							
Dabigatran	CrCl >80										
	CrCl 50-80										
	CrCl 30-49										
Edoxaban	All										
Rivaroxaban	All										

PAUSE-2 Pilot Trial

Outcome	ASRA	PAUSE
Median residual DOAC level	19 ng/ml	20 ng/ml
DOAC level <30 ng/ml	95.6%	94.4%
DOAC level 30-50 ng/ml	1.4%	2.8%
DOAC level >50 ng/ml	2.9%	2.8%

Conclusion

Shorter DOAC interruption (PAUSE) performed similarly to longer interruption (ASRA) before high-risk surgery.

Case 6

A 79-year-old patient with atrial fibrillation experienced a spontaneous intracerebral hemorrhage (ICH) 2 months ago and has recovered with a modified Rankin Scale score of 3. You are considering long-term stroke prevention. Which of these statements is correct?

- A. DOACs reduced ischemic stroke without increasing recurrent ICH
- B. DOACs reduced ischemic stroke but increased recurrent ICH
- C. DOACs increased ischemic stroke and recurrent ICH
- D. DOACs had no significant effect on either ischemic stroke or recurrent ICH

PRESTIGE-AF Trial

RCT, open-label, 319 patients, 75 hospitals

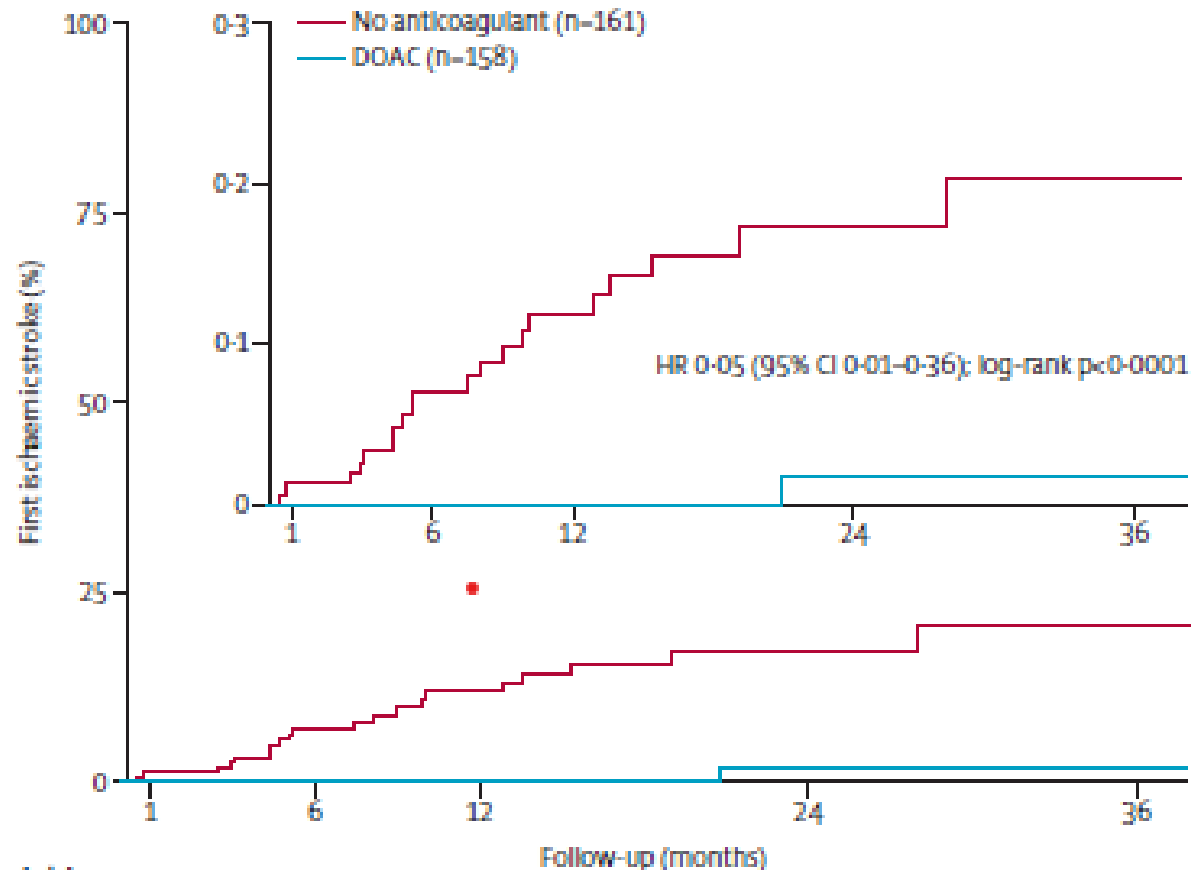
Randomized:

- DOAC
- No anticoagulation

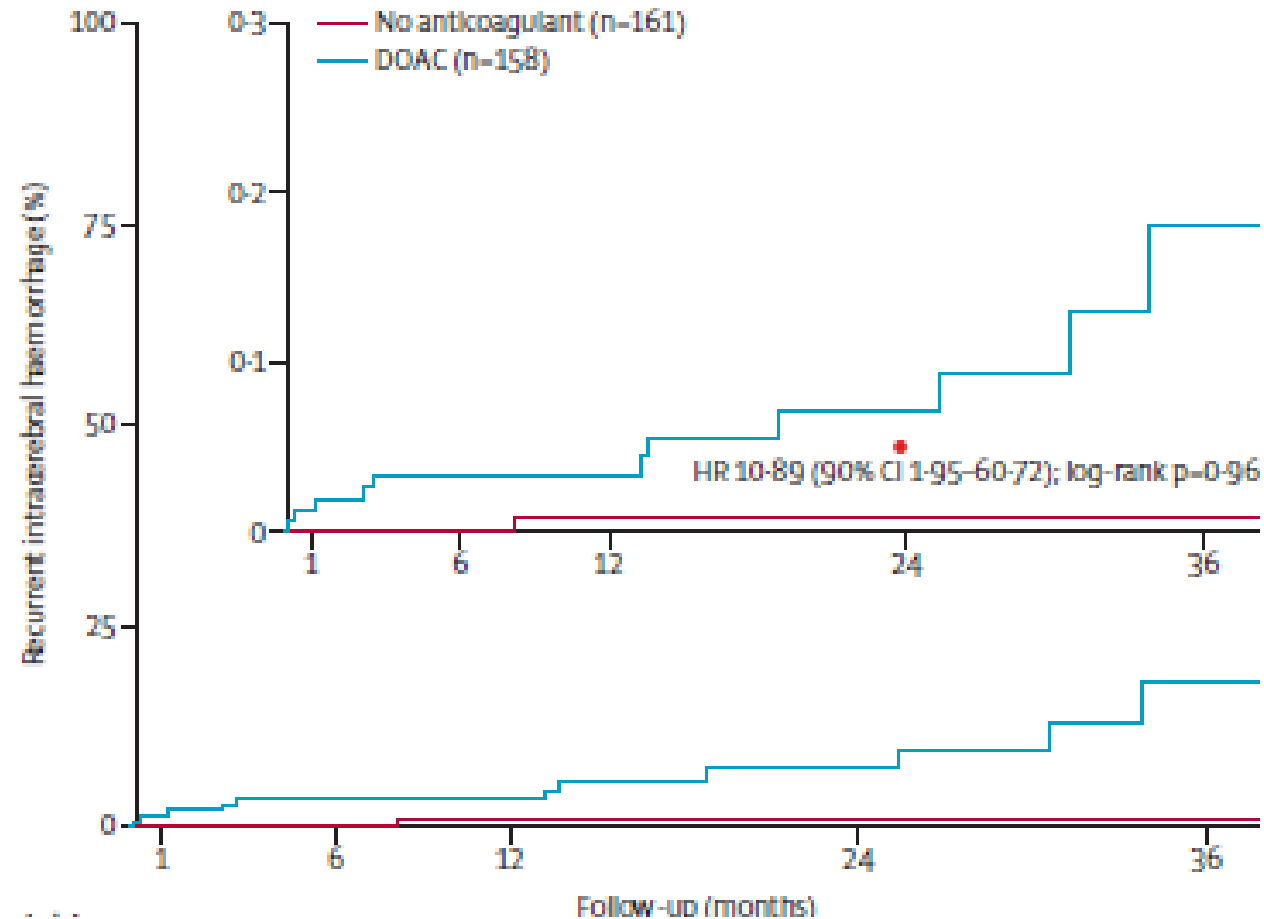
Co-primary endpoints:

- First ischemic stroke
- First recurrent intracerebral hemorrhage

First ischemic stroke



Recurrent ICH



Conclusion

In survivors of intracerebral hemorrhage with atrial fibrillation, DOAC therapy substantially reduces ischemic stroke risk but increases recurrent intracerebral hemorrhage risk.

Case 7

A 78-year-old man on apixaban presents with a large spontaneous intracerebral hemorrhage. He is obtunded and requires urgent reversal of anticoagulation. Which of the following would you pick?

- A. Vitamin K
- B. 4-Factor Prothrombin Complex Concentrate
- C. Idarucizumab
- D. Andexanet alfa

Antidotes for Anticoagulation Reversal

Review available and emerging reversal agents

Design: Narrative review

Key Questions

- Which antidotes provide effective reversal?
- What are the safety concerns?
- Where are the remaining evidence gaps?

Antidotes for Anticoagulation Reversal

Anticoagulant	Preferred Reversal Strategy
UFH	Protamine
Warfarin	4F-PCC + Vitamin K
Dabigatran	Idarucizumab
Apixaban/Rivaroxaban	4F-PCC

Andexanet Alfa

Produces rapid reduction in anti-Xa activity (~92%).

Better hemostatic efficacy than usual care/PCC

- 67.0% vs 53.1% effective hemostasis

Increased thrombotic events usual care/PCC

- 10.3% vs 5.6%

No mortality benefit demonstrated

Antidotes for Anticoagulation Reversal

Andexanet Alfa:

- Withdrawn from U.S. market in December 2025 because of FDA safety concerns
- Better surrogate hemostasis
- Does not necessarily translate into improved survival

Conclusion

4F-PCC is the pragmatic approach for life-threatening apixaban and rivaroxaban-associated bleeding while safer, better-studied Xa reversal strategies are sought

Case 8

A 78-year-old patient is admitted with pneumonia and reduced mobility. What would you choose for VTE prophylaxis?

- A. Unfractionated heparin (UFH)
- B. Direct oral anticoagulants (DOACs)
- C. Low-molecular-weight heparin (LMWH)
- D. None of the above

Thromboprophylaxis in Medical Inpatients

Systematic review and network meta-analysis

22 RCTs, 43,840 patients

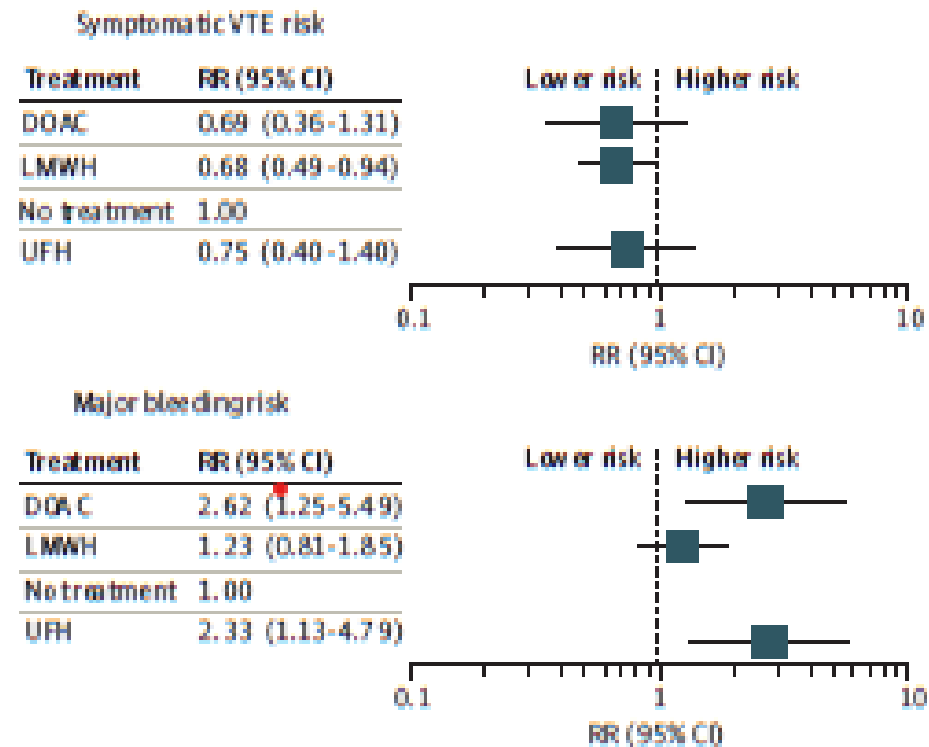
Randomized:

- LMWH, UFH, DOACs
- No treatment/placebo

Primary Outcome:

- Symptomatic DVT, Symptomatic VTE, PE

Thromboprophylaxis in Medical Inpatients



Conclusion

LMWH appears to provide the best balance of VTE prevention and bleeding risk for appropriately selected acutely ill medical inpatients.

OCEANIC-AF Trial

Phase RCT, double blinded, 14,810 patients, 1,035 centers

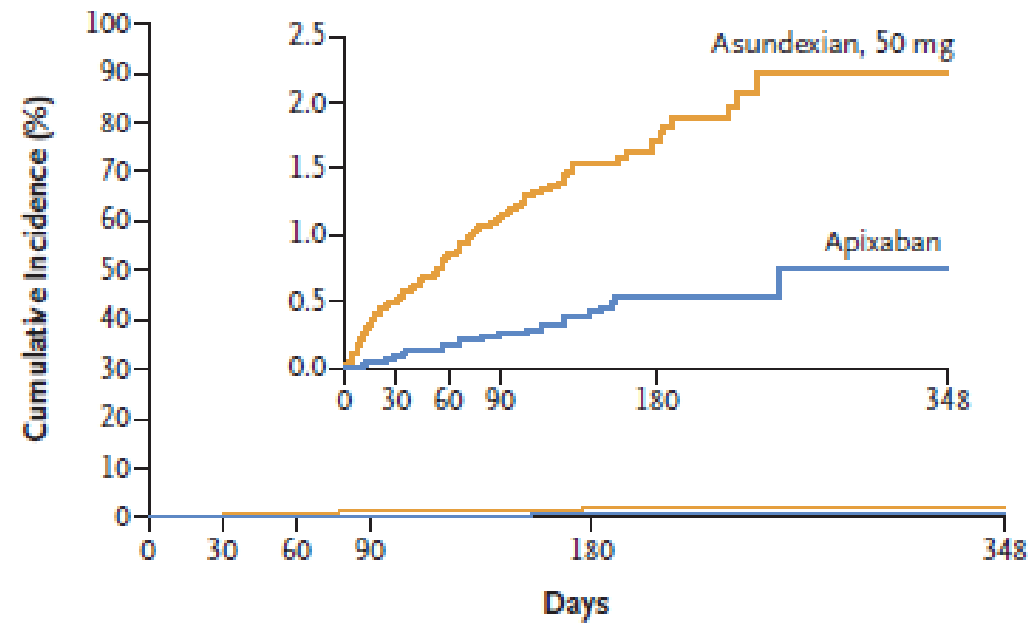
Randomized:

- Asundexian (Factor Xla inhibitor)
- Apixaban

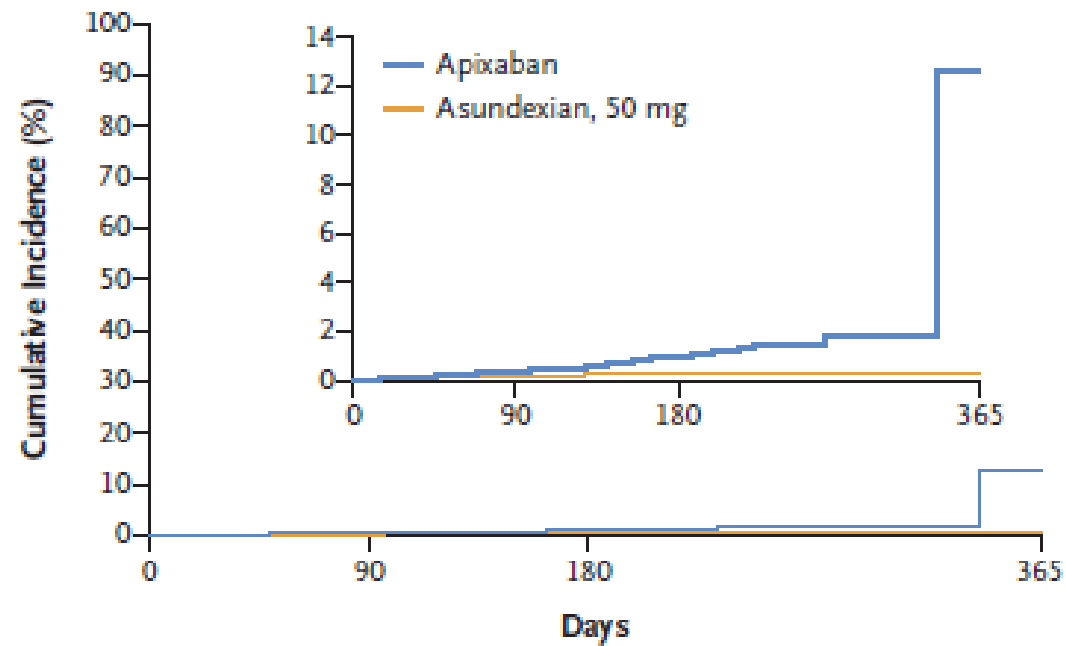
Primary Efficacy: Stroke or systemic embolism

Primary safety: ISTH major bleeding

Stroke or Systemic Embolism



Major bleeding



Conclusion

Factor Xla inhibition with asundexian was not an effective substitute for apixaban in atrial fibrillation.

OCEANIC-STROKE Trial

Phase 3, RCT, double blinded, 12,327 patients, 702 centers

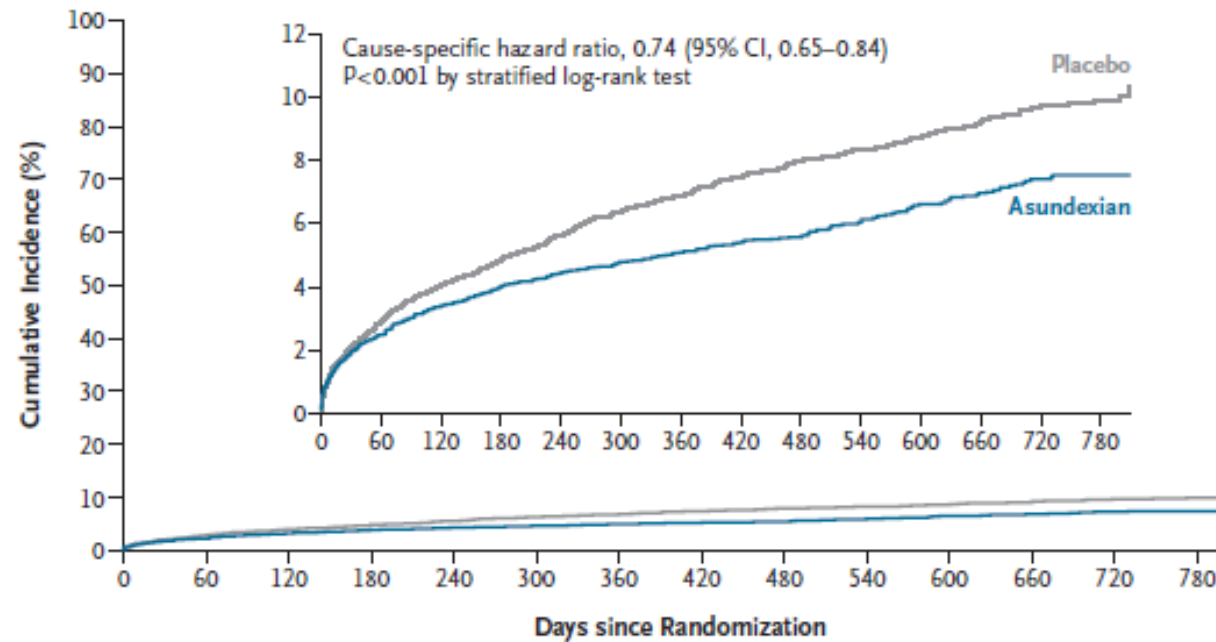
Randomized:

- Asundexian (Factor Xla inhibitor)
- Placebo

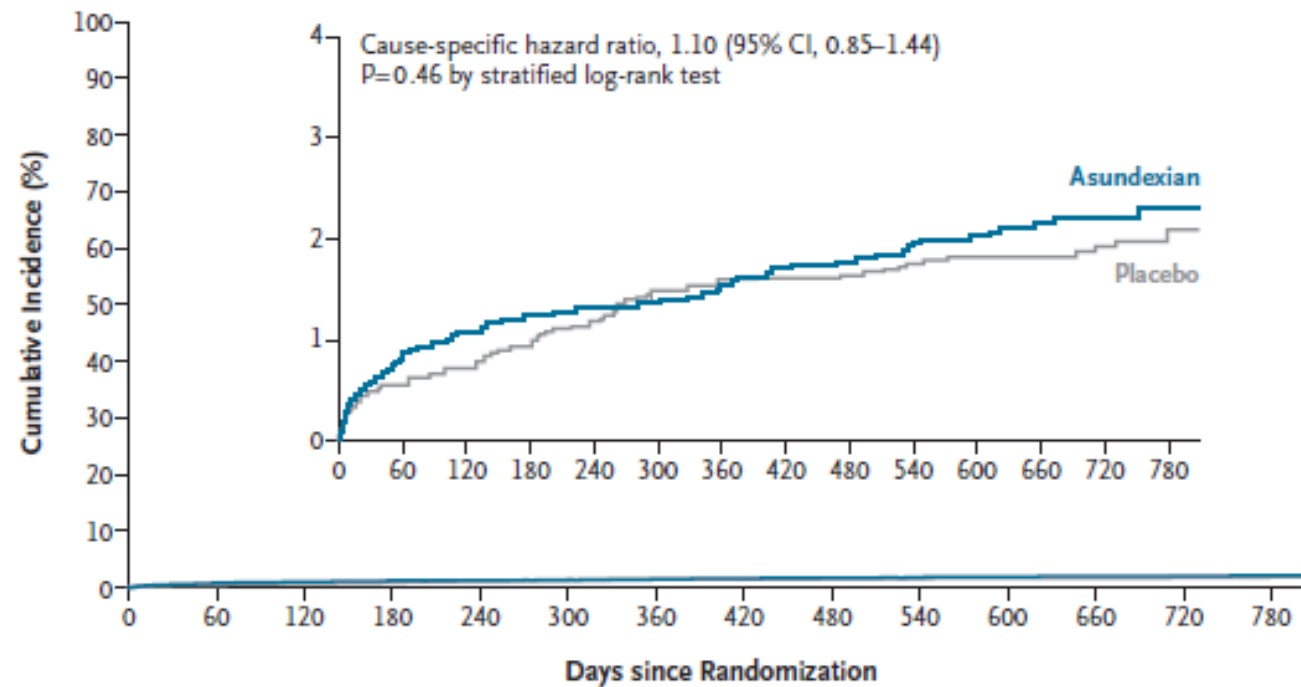
Primary Efficacy: Ischemic stroke

Primary safety: Major bleeding (ISTH definition)

Ischemic Stroke



Major Bleeding



Conclusion

Asundexian (Factor Xla inhibitor) appears to be a promising adjunct to antiplatelet therapy for secondary stroke prevention without increasing major bleeding

Take home points

Apixaban is preferred for acute VTE

Consider low-dose apixaban for extended VTE prevention

Stop aspirin and clopidogrel when long-term anticoagulation alone is sufficient

Hold DOACs before high-risk surgery, no bridging

Restarting anticoagulation after ICH requires individualized decisions

Use 4-factor PCC for reversal of Xa inhibitor

LMWH remains first-line for inpatient VTE prophylaxis

Factor XI/XIa inhibitors are promising but not yet practice-changing