World Stroke Organization

17TH WORLD STROKE CONGRESS

2025 OCTOBER 22—24 BARCELONA, SPAIN

ONE WORLD VOICE FOR STROKE

FACTOR XIA (FXIA) INHIBITION WITH ASUNDEXIAN AFTER ACUTE NON-CARDIOEMBOLIC STROKE OR HIGH-RISK TRANSIENT ISCHEMIC ATTACK (TIA): METHODS AND BASELINE DATA FOR THE OCEANIC-STROKE TRIAL

M. Sharma, R. Joundi, Q. Dong, T. Hirano, S. Kasner, J. Saver, J. Masjuan, A. Demchuk, C. Cordonnier, D. Bereczki, G. Tsivgoulis, R. Veltkamp, I. Staikov, H-J. Bae, B. Campbell, A. Zini, I-H. Lee, S. Ameriso, M. Kovar, R. Mikulik, R. Lemmens, J. Ferro, T. Robinson, H. Christensen, S. Ozturk, R. Leker, P. Turcani, A. Slowik, P. Amaya, F.K. Hoo, G.M. De Marchis, M. Knoflach, P.N. Sylaja, J. Putaala, J.M. Coutinho, H. B. van der Worp, E. Miglane, V. Matijosaitis, A.G. Lindgren, G. Sampaio Silva, E. Sandset, S. Turuspekova, E. Muehlhofer, A. Shoamanesh for the OCEANIC-STROKE Steering Committee and Investigators

worldstrokecongress.org

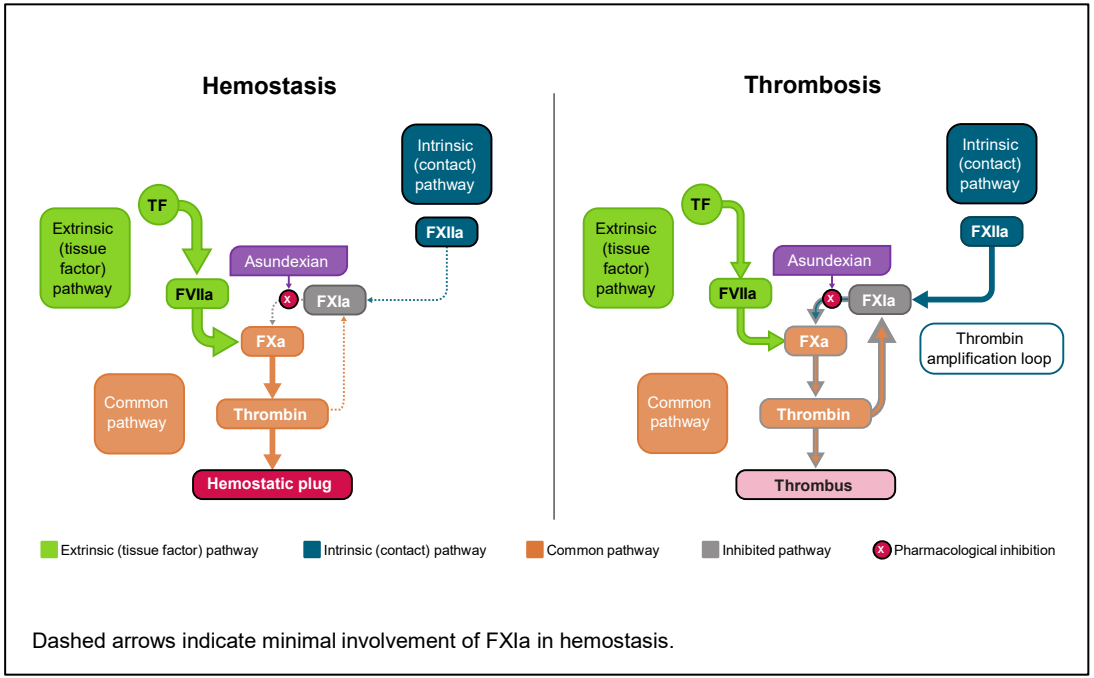
Faculty Disclosure

	No, nothing to disclose
x	Yes, please specify:

Company Name	Honoraria/ Expenses	Consulting/ Advisory Board	Funded Research	Royalties/ Patent	Stock Options	Ownership/ Equity Position	Employee	Other (please specify)
Bayer		x	x					
Regeneron		x						
Anthos		x						
Bristol Myers Squibb			x					
Janssen			x					

Background

- Genetic FXI deficiency is associated with a reduced risk of ischemic stroke without increased risk of ICH[1–3]
- FXI is activated to FXIa by thrombin through a feedback loop
- FXI has a minor role in hemostasis but may increase pathologic thrombosis
- Potential to uncouple hemostasis from thrombosis makes FXIa an attractive therapeutic target



Dashed arrows indicate minimal involvement of FXIa in hemostasis.

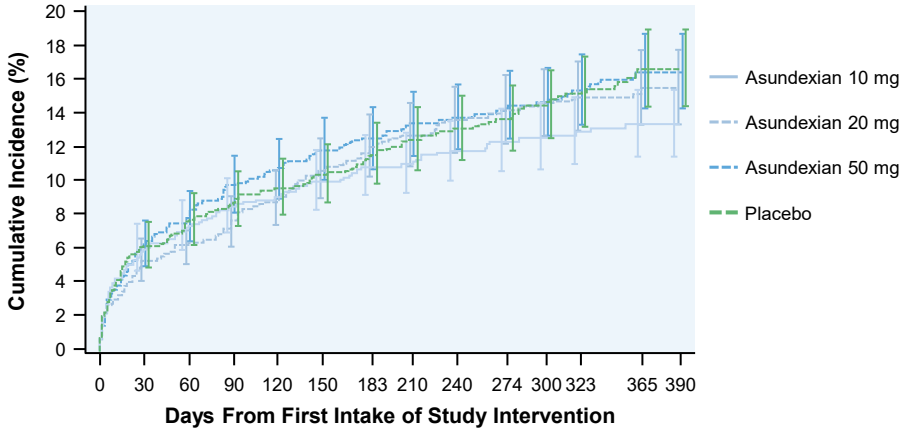
FVIIa, activated Factor VII; FXa, activated Factor X; FXI, Factor XI; FXIa, activated Factor XI; FXIIa, activated Factor XII; ICH, intracerebral hemorrhage; TF, tissue factor.

1. Gill D, et al. *Stroke*. 2018;49(11):2761-3. 2. Salomon O, et al. *Blood*. 2008;111(8):4113-7. 3. Georgi B, et al. *Stroke*. 2019;50(11):3004-12.

Asundexian

- Direct oral inhibitor of FXIa[1,2]
  - Mainly fecal excretion
  - Once daily dosing
- Decreases arterial and venous thrombi in animal models with no effect on bleeding time – alone or with DAPT
- Phase II studies > 4000 participants showed[3–6]
  - > 90% inhibition of FXIa at peak and trough
  - No significant increase in major bleeding over placebo with or without antiplatelets
- Less major bleeding than apixaban

Aalen-Johansen Plot for All Bleeding in Phase II Trials of Asundexian



Number of subjects at risk

840	712	681	658	628	612	598	559	503	444	377	332	207	2
843	734	698	678	641	621	595	550	488	423	362	327	209	1
845	718	675	642	622	607	595	532	482	429	367	325	212	1
851	723	684	664	635	622	601	531	479	426	358	316	199	1

At-risk subject counts were calculated as at start of timepoint.

Eikelboom JW, et al. *J Am Coll Cardiol*. 2024;83(6):669-78

DAPT, dual antiplatelet therapy; FXIa, activated Factor XI.

1. Heitmeier S, et al. *J Thromb Haemost.* 2022;20(6):1400-11; 2. Piel I, et al. *Eur J Drug Metab Pharmacokinet.* 2023;48(4):411-25;
3. Rao SV, et al. *Circulation.* 2022;146(16):1196-206; 4. Piccini JP, et al. *Lancet.* 2022;399(10333):1383-90;
5. Shoamanesh A, et al. *Lancet.* 2022;400(10357):997-1007; 6. Eikelboom JW, et al. *J Am Coll Cardiol.* 2024;83(6):669-78.

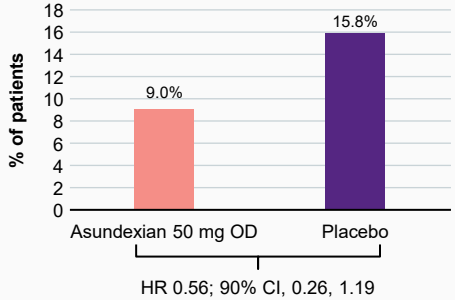
PACIFIC-STROKE: Efficacy Outcomes

Secondary and exploratory efficacy outcomes

Outcome (overall population)	Asundexian 50 mg OD (n=447)	Placebo (n=456)	Asundexian 50 mg OD vs. placebo
	Patients, n (%)	Patients, n (%)	HR (90% CI)
Symptomatic ischemic stroke	22 (4.9)	28 (6.1)	**0.80 (0.50, 1.27)**
Recurrent ischemic stroke or TIA	24 (5.4)	38 (8.3)	**0.64 (0.41, 0.98)**

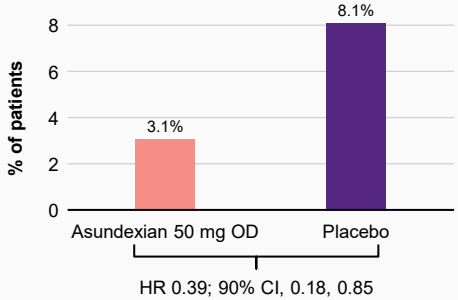
Recurrent stroke and TIA in exploratory post hoc subgroup analysis

A. Patients with large artery stroke (TOAST, n=320)



Positive trend shown for reduction in ischemic stroke with asundexian 50 mg OD

B. Patients with any extra-/intracranial atherosclerosis (vascular imaging, n=791)



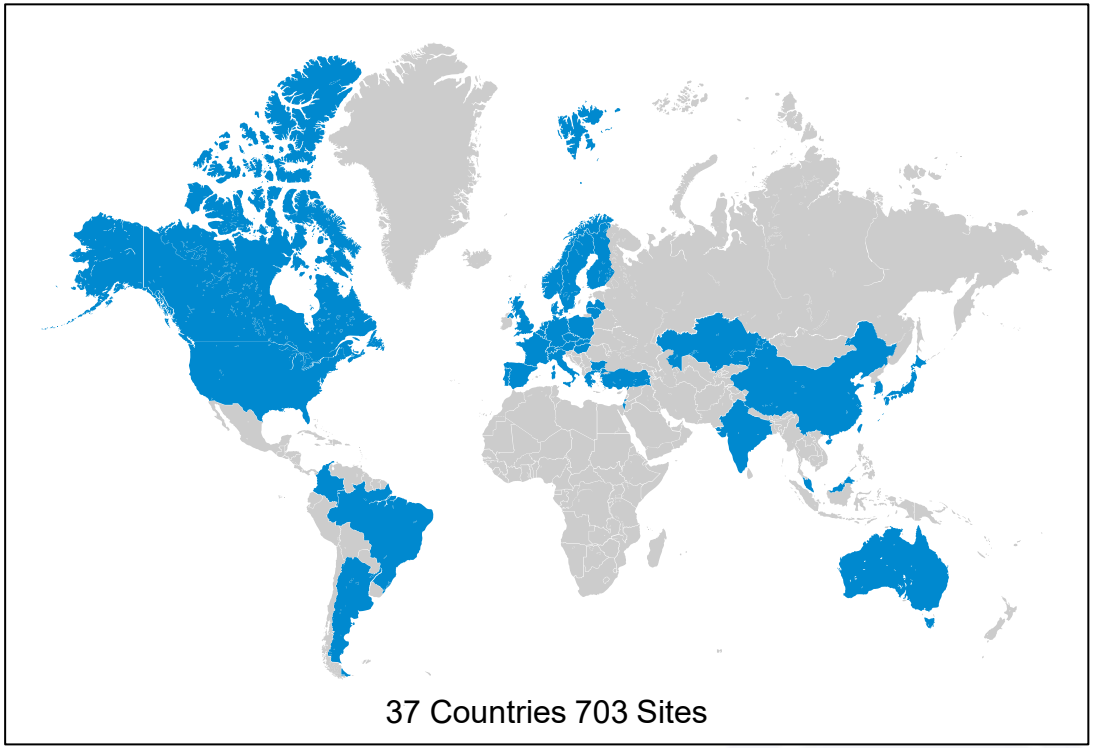
Patients with atherosclerosis had fewer recurrent strokes and TIAs with asundexian 50 mg OD

CI, confidence interval; HR, hazard ratio; OD, once daily; TIA, transient ischemic attack; TOAST, Trial of ORG 10172 in Acute Stroke Treatment.

Shoamanesh A, et al. *Lancet.* 2022;400(10357):997-1007.

OCEANIC-STROKE

- OCEANIC-STROKE is a placebo-controlled, double-blinded, event-driven, Phase III, randomized trial
- Comparing oral asundexian 50 mg OD and placebo in participants with acute non-cardioembolic ischemic stroke or high-risk TIA treated with antiplatelets



OD, once daily; TIA, transient ischemic attack.

OCEANIC-STROKE: Key Endpoints

Endpoints (time to first occurrence)	
Primary efficacy	**Primary safety**
Ischemic stroke	ISTH major bleeding
Secondary efficacy	**Secondary safety**
• All strokes (ischemic and hemorrhagic) • Composite of CV death, MI or stroke • Composite of all-cause mortality, MI or stroke • Ischemic stroke in the first 90 days • Disabling stroke (mRS ≥3 at 90 days) • All-cause mortality • TIA	• Composite of ISTH major or CRNM bleeding • ISTH clinically relevant non-major bleeding • Symptomatic intracranial hemorrhage • Hemorrhagic stroke • Fatal bleeding • Minor bleeding

CRNM, clinically relevant non-major; CV, cardiovascular; ISTH, International Society on Thrombosis and Haemostasis; MI, myocardial infarction; mRS, modified Rankin score; TIA, transient ischemic attack.

Key Inclusion and Exclusion Criteria

Key inclusion:

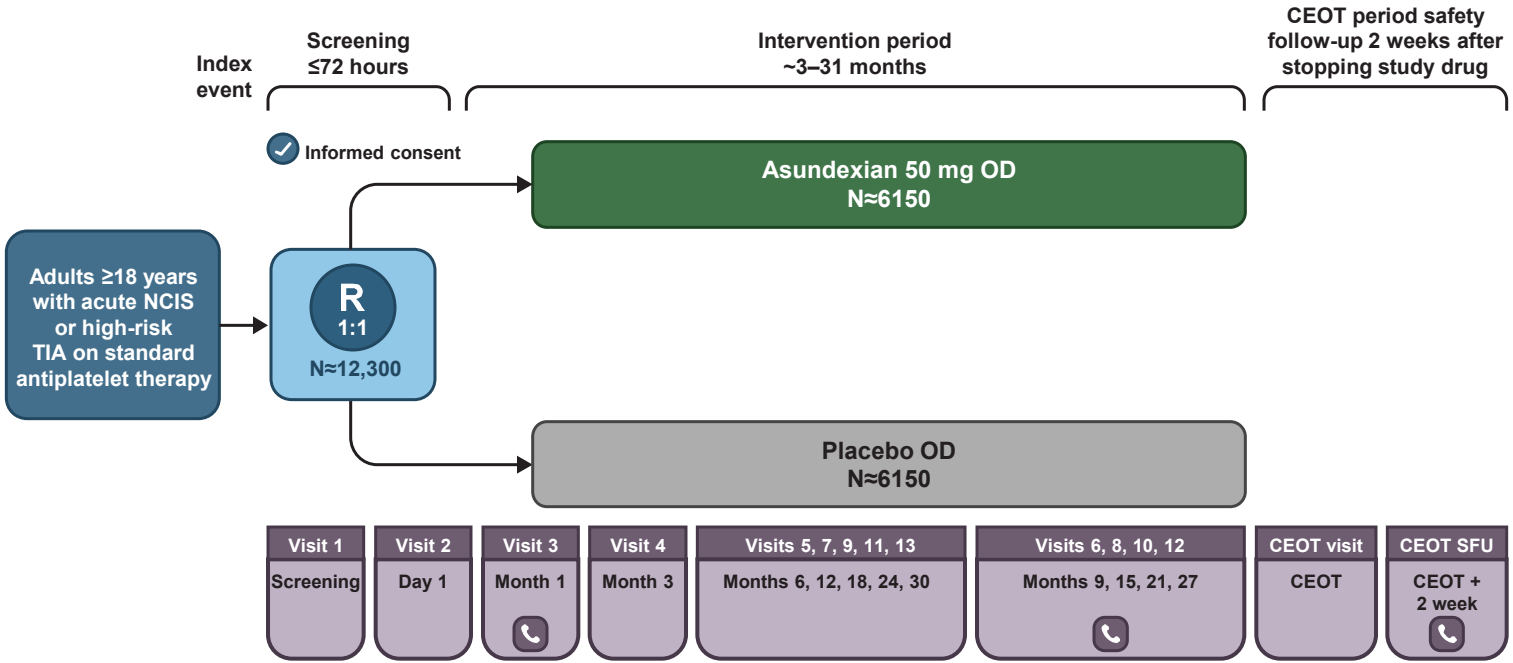
- Participants aged ≥18 years, within 72 hours of symptom onset:
  - Non-cardioembolic ischemic stroke (NIHSS ≤ 15) **or** high-risk TIA (ABCD^2 6 or 7)
  - History of atherosclerosis **or** evidence of plaque on imaging **or** non-lacunar stroke on imaging
  - Plan for antiplatelet therapy, single or dual

Key exclusion:

- History of AF or other cardioembolic source requiring anticoagulation
- Ischemic stroke within 7 days of index event
- Strokes following procedures (TAVI, CABG) or other specific cause (e.g. vasculitis)
- End-stage renal disease requiring dialysis
- Active non-trivial bleeding (e.g. PH1 or PH2); asymptomatic HT and CMB permitted
- History of non-traumatic ICH; significant GI bleeding within 6 months

ABCD^2, age, blood pressure, clinical features, duration of symptoms, and diabetes; AF, atrial fibrillation; CABG, coronary artery bypass grafting; CMB, cerebral microbleed; GI, gastrointenstinal; HT, hemorrhagic transformation; ICH, intracerebral hemorrhage; NIHSS, National Institutes of Health Stroke Scale; TAVI, transcatheter aortic valve implantation; TIA, transient ischemic attack.

OCEANIC-STROKE: Study Design



- phone visit

- If applicable, visits will continue after Month 30 in the same way as before until CEOT visit.
- Day 1 is the day of randomization.

CEOT, common end of treatment; NCIS, non-cardioembolic ischemic stroke; OD, once daily; R, randomization; SFU, safety follow-up; TIA, transient ischemic attack.

Participant Demographics (as of 06/05/25)

Characteristics	Participants
Randomized, N	12,327
Age, years, mean (SD)	67.6 (10.8)
Female sex, n (%)	4111 (33.3)
Previous history of stroke or TIA, n (%)	2633 (21.4)
Coronary artery disease, n (%)	1945 (15.8)
Hypertension, n (%)	9780 (79.3)
Diabetes mellitus, n (%)	4238 (34.4)
Current smoker, n (%)	3309 (26.8)

SD, standard deviation; TIA, transient ischemic attack.

Participant Characteristics (as of 06/05/25)

World Stroke Organization
17TH WORLD STROKE CONGRESS
2025 OCTOBER 22—24 BARCELONA, SPAIN

Geographic region	Participants
Western Europe*, n (%)	4844 (39.3)
Asia, n (%)	3528 (28.6)
Eastern Europe, n (%)	1823 (14.8)
North America, n (%)	1565 (12.7)
South America, n (%)	567 (4.6)
Race	**Participants**
White, n (%)	8185 (66.4)
Black, n (%)	283 (2.3)
Asian, n (%)	3450 (28.0)
Other, n (%)	409 (3.3)

*Includes Australia and Israel.

Index Event Characteristics (as of 06/05/25)

Characteristics	Participants
Index event, n (%)	
Ischemic stroke	11,676 (94.7)
TIA	649 (5.3)
TOAST Subtype of index event, n (%)*	
Large-artery atherosclerosis	5028 (43.1)
Stroke of undetermined etiology	3504 (30.0)
Small-vessel occlusion	2591 (22.2)
Stroke of other etiology	358 (3.1)
Cardioembolic	193 (1.7)
Data missing	2 (0.0)
NIHSS at presentation*	
Median (min, max)	3 (0, 39)
Median (IQR)	3 (2, 6)
NIHSS at randomization*	
Median (min, max)	2 (0, 26)
Median (IQR)	2 (1, 4)

*Only applies to ischemic stroke.
IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale; TIA, transient ischemic attack.

Index Event Treatment (as of 06/05/25)

Treatment	Participants
Intravenous thrombolysis and/or endovascular therapy, n (%)	3199 (27.4)
Intravenous thrombolysis only	2312 (19.8)
Endovascular therapy only	371 (3.2)
Intravenous thrombolysis and endovascular therapy	516 (4.4)
Planned antiplatelet therapy at randomization, n (%)	
Dual antiplatelet therapy (ASA and a P2Y12 inhibitor)	7714 (62.6)
Single antiplatelet therapy	4613 (37.4)

ASA, acetylsalicylic acid (aspirin)

Summary

- Large Phase II dataset used to design the OCEANIC-STROKE trial
- 12,327 participants randomized between January 2023 and February 2025
  - Pragmatic design and unmet need
- Demographics & stroke subtypes generalizable to global stroke population
  - Range of stroke subtypes including small-vessel occlusion
  - NIHSS up to 15
- Well treated stroke & TIA population:
  - Dual antiplatelets planned as standard initial treatment in 63%
  - 27.4% of index ischemic stroke had thrombolysis and/or mechanical thrombectomy
- OCEANIC-STROKE will be the first completed superiority trial of a FXIa inhibitor for prevention of recurrent ischemic stroke

FXIa, activated Factor XI; NIHSS, National Institutes of Health Stroke Scale; TIA, transient ischemic attack.

Acknowledgements

- This study was sponsored by Bayer AG
- Editorial support was provided by Scion (a division of Prime, London, UK), funded by Bayer AG
- We thank the Steering Committee and independent Data Monitoring Committee members, the study operations teams, the investigators, the study site coordinators, and especially the patients and their families, who made this study possible

Steering Committee

Mike Sharma (Chair), Ashkan Shoamanesh (Co-Chair), Pierre Amarenco, Pablo Amaya, Sebastian Francisco Ameriso, Hee-Joon Bae, Daniel Bereczki, Bruce Campbell, Hanne Christensen, Charlotte Cordonnier, Jonathan Coutinho, Gian Marco De Marchis, Andrew Demchuk, Qiang Dong, John Eikelboom, Jose Ferro, Teruyuki Hirano, Fan Kee Hoo, Scott Kasner, Michael Knoflach, Martin Kovar, I-Hui Lee, Ronen Leker, Robin Lemmens, Arne Lindgren, Jaime Masjuan, Vaidas Matijosaitis, Evija Miglane, Robert Mikulik, Eva Muehlhofer, Hardi Mundl, Serefnur Ozturk, Jukka Putaala, Tom Robinson, Gisele Sampaio Silva, Else Sandset, Jeff Saver, Kevin Sheth, Agnieszka Slowik, Ivan Staikov, PN Sylaja, Cristina Tiu, Georgios Tsivgoulis, Peter Turcani, Saule Turuspekova, H. Bart van der Worp, Roland Veltkamp, Andrea Zini

Independent Data Monitoring Committee

Jonathan Halperin, Steven Greenberg, Thomas Cook, Saskia Middeldorp, Marta Rubiera del Fuego

Please scan the QR code to access a copy of this presentation with supplementary information