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International Stroke Conference

QUALIFYING ISCHEMIC STROKE SUBTYPES AND RESPONSE TO ASUNDEXIAN: PRESPECIFIED SECONDARY ANALYSIS OF THE OCEANIC-STROKE TRIAL

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American Stroke Association.
A division of the American Heart Association.

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DISCLOSURES

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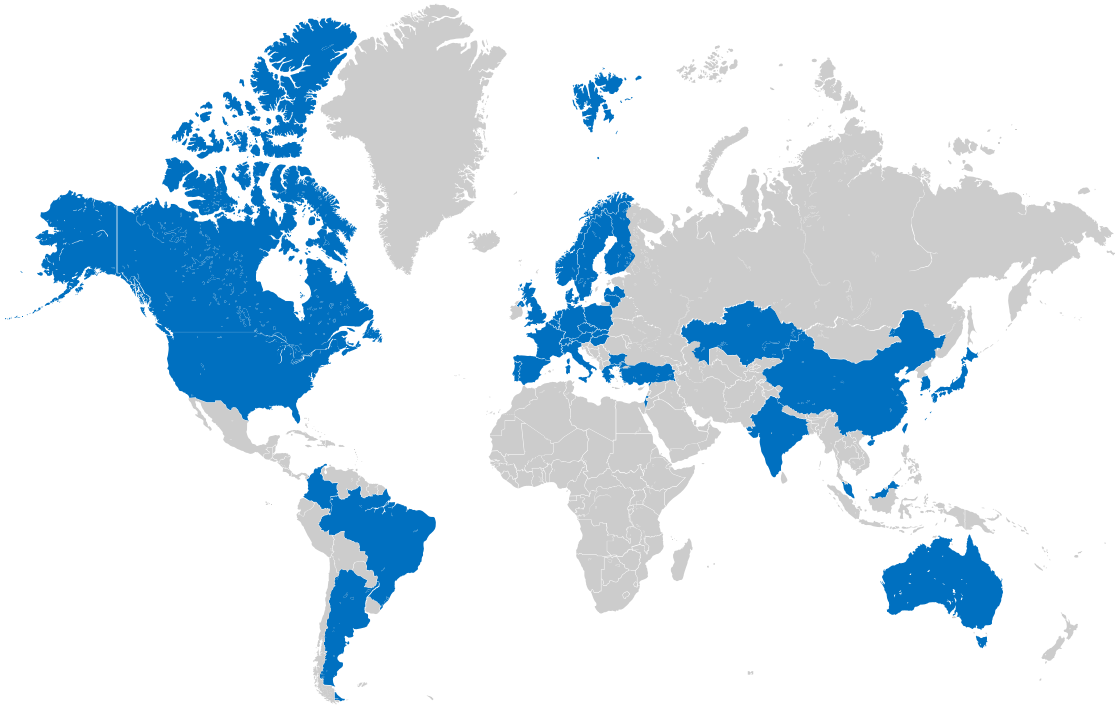
OCEANIC-STROKE

Design

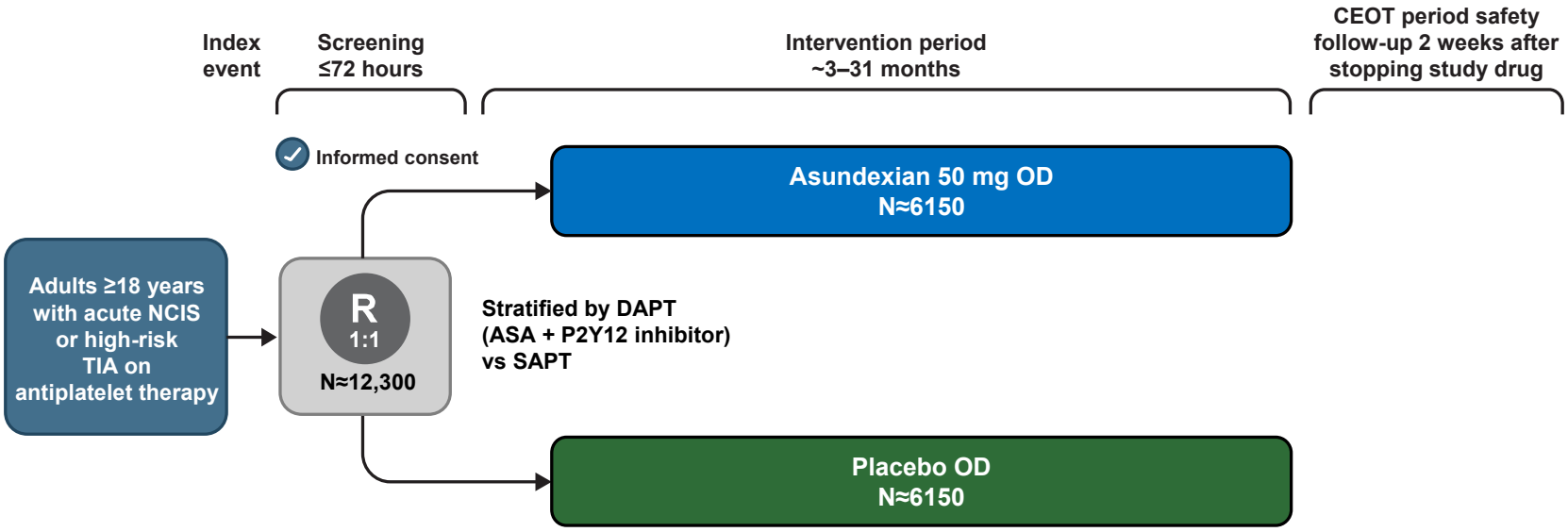
- OCEANIC-STROKE
  - Placebo-controlled
  - Double-blinded
  - Event-driven Phase 3 RCT
- Comparing asundexian 50 mg once daily with placebo
- Patients with non-cardioembolic stroke or high-risk TIA



37 Countries/Regions 702 Sites

RCT, randomized controlled trial; TIA, transient ischemic attack.

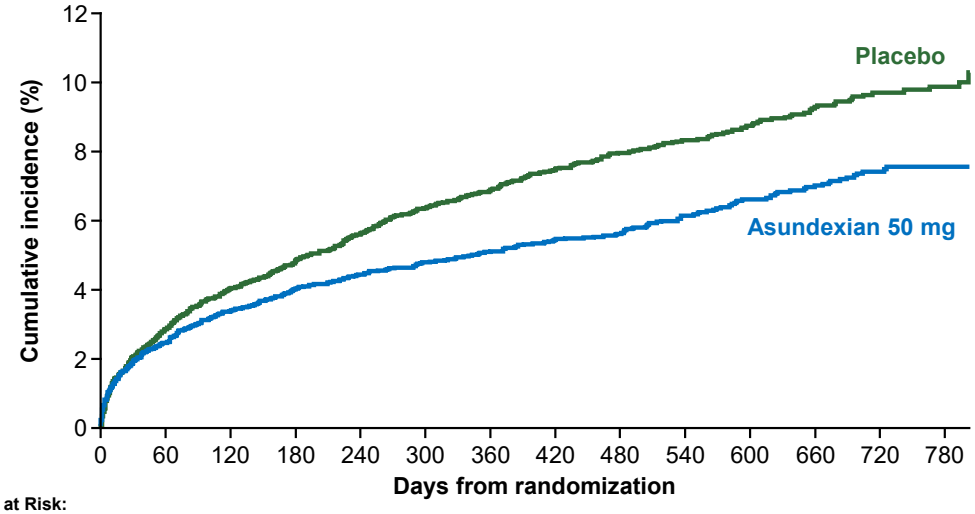
OCEANIC-STROKE: STUDY DESIGN



ASA, aspirin; CEOT, common end of treatment; DAPT, dual antiplatelet therapy; NCIS, non-cardioembolic ischemic stroke; OD, once daily; P2Y12, purinergic receptor Y12; R, randomization; SAPT, single antiplatelet therapy; TIA transient ischemic attack.
Sharma M, et al. *European Stroke Journal.* 2026;11(1):aakaf017.

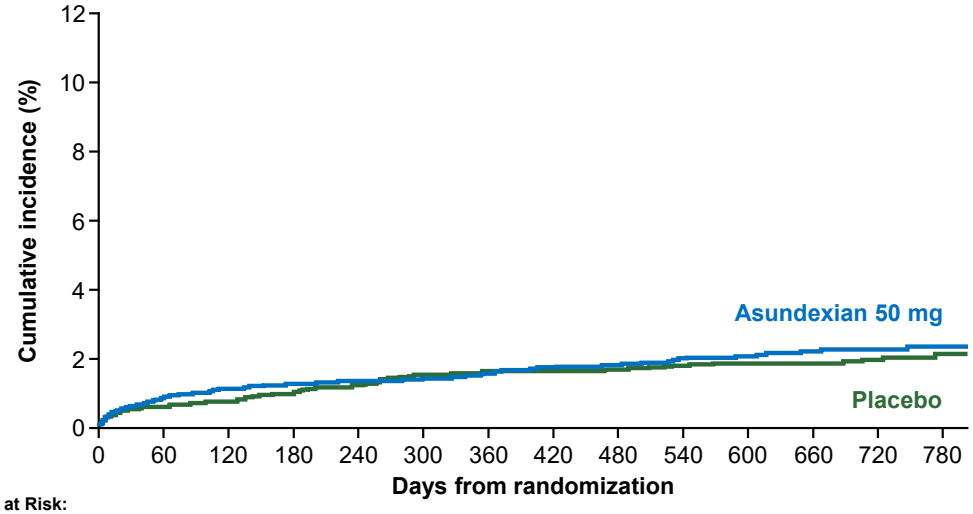
OCEANIC-STROKE: PRIMARY EFFICACY AND SAFETY OUTCOMES

Ischemic stroke: HR 0.74 (95% CI 0.65–0.84), p<0.001



No. at Risk:														
Placebo	6165	5949	5853	5754	5370	4840	4406	3990	3497	3070	2564	1961	1410	792
Asundexian	6162	5958	5859	5763	5384	4876	4463	4033	3543	3101	2588	2004	1428	810

Major bleeding: HR 1.10 (95% CI 0.85–1.44), p=0.46



No. at Risk:														
Placebo	6130	5391	5021	4833	4415	3944	3572	3165	2775	2441	2026	1549	1121	618
Asundexian	6124	5354	4968	4807	4366	3900	3547	3104	2699	2374	1943	1508	1082	613

*P value is obtained from stratified log-rank test (stratified by baseline intention of DAPT). Cause-specific HR and 95% CI are provided here.
Cumulative incidence curves are estimated by Aalen–Johansen method, truncated at Day 820.
CI, confidence interval; DAPT, dual antiplatelet therapy; HR, hazard ratio.

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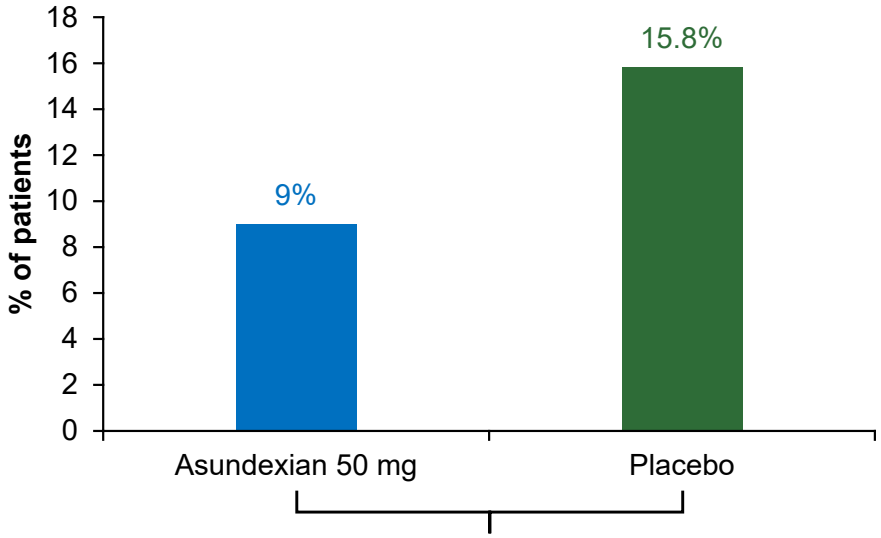
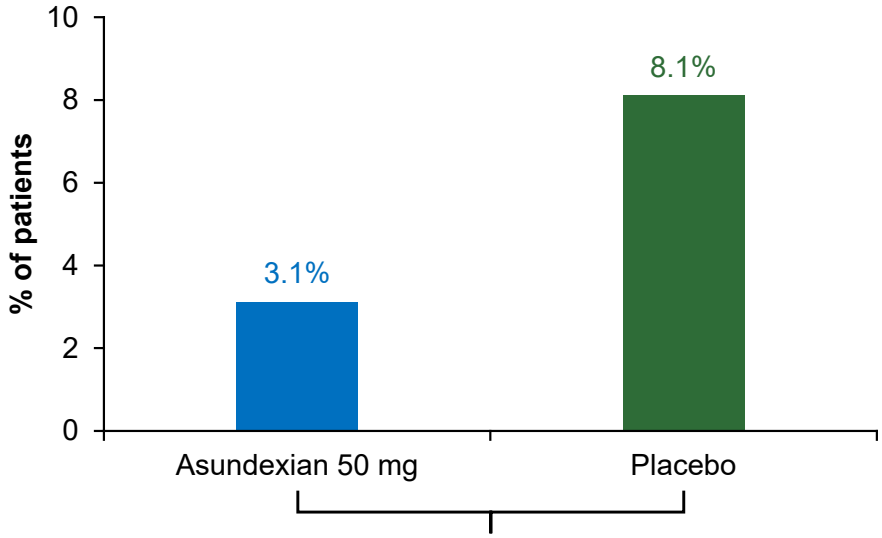
PACIFIC-STROKE: SUGGESTION OF GREATER EFFICACY IN DISTINCT STROKE SUBTYPES

Patients with large artery stroke (TOAST, N=320)



HR 0.56, 90% CI 0.26–1.19

Patients with any extra-/intracranial atherosclerosis (vascular imaging, N=791)



HR 0.39, 90% CI 0.18–0.85

Patients with atherosclerosis had fewer recurrent strokes and TIA with asundexian 50 mg

CI, confidence interval; HR, hazard ratio; TIA, transient ischemic attack; TOAST, Trial of Org 10172 in Acute Stroke Treatment.
Shoamanesh et al. *Lancet*. 2022;400(10357):997–1007.

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PRESPECIFIED SECONDARY ANALYSIS OF PATIENTS WITH QUALIFYING NON-CARDIOEMBOLIC ISCHEMIC STROKE

- According to qualifying non-cardioembolic ischemic stroke subtype (TOAST Criteria)[1]
  - **Large artery atherosclerosis**
  - **Small-vessel occlusion***
  - **Stroke of undetermined etiology**
    - Including sensitivity analysis confined to patients with embolic stroke of undetermined source (ESUS)

*Patients with small-vessel occlusion were required to have a clinical history or vascular imaging evidence of atherosclerosis for eligibility.
TOAST, Trial of Org 10172 in Acute Stroke Treatment.
1. Adams et al. *Stroke*. 1993;24(1);35–41.

OCEANIC-STROKE SUBTYPE OF QUALIFYING NON-CARDIOEMBOLIC ISCHEMIC STROKE

Characteristics	Asundexian 50 mg	Placebo
Index event, n (%)		
Ischemic stroke	5839 (94.8)	5838 (94.7)
High-risk TIA	323 (5.2)	325 (5.3)
TOAST subtype of index event,† n (%)		
Large-artery atherosclerosis	2512 (43.0)	2484 (42.5)
Stroke of undetermined etiology	1786 (30.6)	1710 (29.3)
Small-vessel occlusion	1290 (22.1)	1349 (23.1)
Stroke of other etiology	161 (2.8)	188 (3.2)
Cardioembolic	89 (1.5)	107 (1.8)

†Stroke index event only.
TIA, transient ischemic attack; TOAST, Trial of Org 10172 in Acute Stroke Treatment.

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BASELINE DEMOGRAPHICS ACCORDING TO QUALIFYING ISCHEMIC STROKES SUBTYPE

	Total (N=11,131)	Large-artery atherosclerosis (N=4996)	Small-vessel occlusion (N=2639)	Stroke of undetermined etiology (N=3496)
Age, mean (SD)	67.5 (10.8)	68.1 (10.4)	66.1 (10.5)	67.6 (11.5)
Female sex, n (%)	3688 (33.1)	1545 (30.9)	842 (31.9)	1301 (37.2)
Race, n (%)	11,131	4996	2639	3496
White	7265 (65.3)	3114 (62.3)	1388 (52.6)	2763 (79.0)
Black	242 (2.2)	102 (2.0)	46 (1.7)	94 (2.7)
Asian	3274 (29.4)	1641 (32.8)	1152 (43.7)	481 (13.8)

SD, standard deviation.

PAST MEDICAL HISTORY ACCORDING TO QUALIFYING ISCHEMIC STROKES SUBTYPE

	Total (N=11,131)	Large-artery atherosclerosis (N=4996)	Small-vessel occlusion (N=2639)	Stroke of undetermined etiology (N=3496)
Medical history, n (%)				
Current/former tobacco use	5984 (53.8)	2800 (56.0)	1384 (52.4)	1800 (51.5)
Hypertension	8829 (79.3)	4059 (81.2)	2191 (83.0)	2579 (73.8)
Diabetes	3738 (33.6)	1831 (36.6)	939 (35.6)	968 (27.7)
Previous stroke or TIA	2359 (21.2)	1128 (22.6)	616 (23.3)	615 (17.6)
Coronary artery disease	1747 (15.7)	829 (16.6)	360 (13.6)	558 (16.0)
Peripheral artery disease	429 (3.9)	226 (4.5)	99 (3.8)	104 (3.0)

TIA, transient ischemic attack.

BASELINE STROKE SEVERITY AND MANAGEMENT ACCORDING TO QUALIFYING ISCHEMIC STROKE SUBTYPE

	Total (N=11,131)	Large-artery atherosclerosis (N=4996)	Small-vessel occlusion (N=2639)	Stroke of undetermined etiology (N=3496)
NIHSS score of index event at presentation				
Median (IQR)	3.0 (2.0, 6.0)	4.0 (2.0, 6.0)	3.0 (2.0, 5.0)	3.0 (2.0, 6.0)
≤3	5234 (52.7)	2022 (48.1)	1278 (58.2)	1703 (55.5)
4–7	3231 (32.5)	1439 (34.2)	780 (35.5)	867 (28.2)
≥8	1464 (14.7)	743 (17.7)	138 (6.3)	501 (16.3)
Intravenous thrombolysis and/or endovascular therapy,† n (%)				
Intravenous thrombolysis or endovascular therapy	3030 (27.2)	2611 (28.7)	442 (16.7)	1154 (33.0)
Planned antiplatelet therapy at randomization, n (%)				
Single antiplatelet therapy	4192 (37.7)	1620 (32.4)	1010 (38.3)	1562 (44.7)
Dual (ASA and a P2Y12 inhibitor)	6939 (62.3)	3376 (67.6)	1629 (61.7)	1934 (55.3)

†Stroke index event only.
ASA, aspirin; IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale; P2Y12, purinergic receptor Y12.

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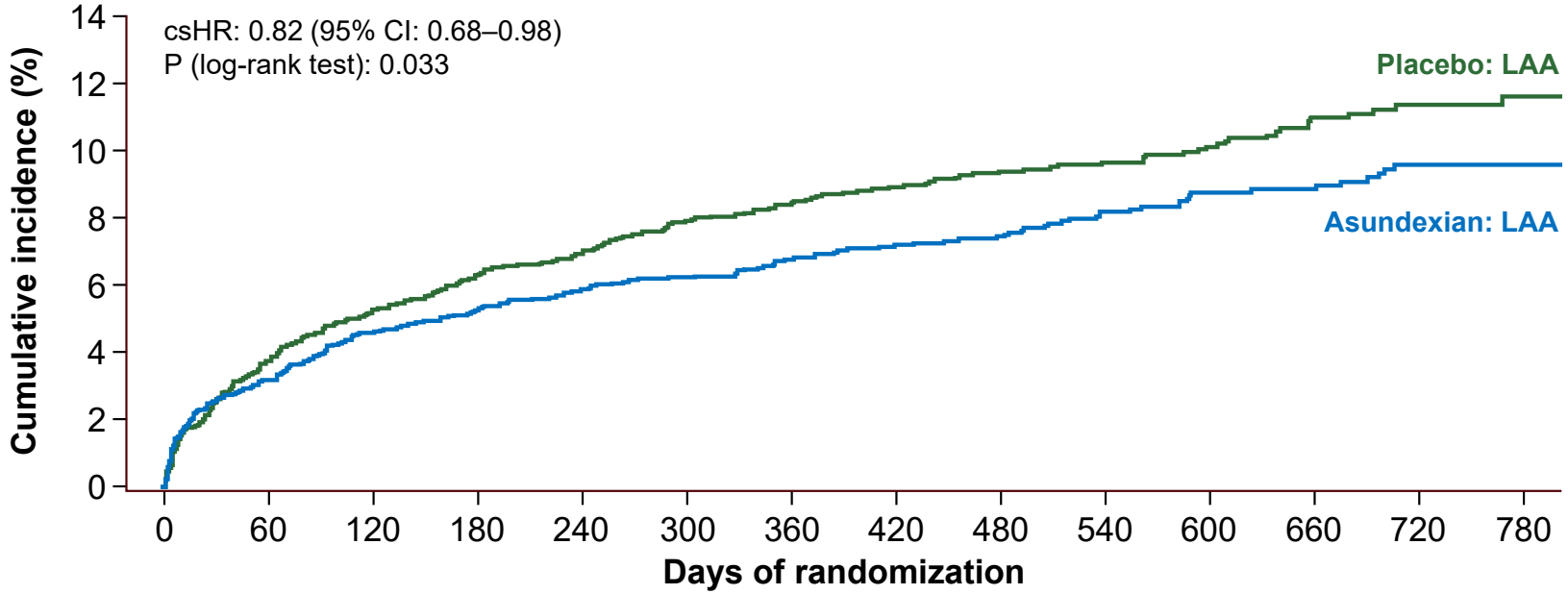
NO TREATMENT INTERACTION FOR EFFICACY OUTCOMES ACROSS ISCHEMIC STROKE SUBTYPES

Efficacy endpoints	Large-artery atherosclerosis			Small-vessel occlusion			Stroke of undetermined etiology			Inter. P-value
	Asundexian n (%) (N=2512)	Placebo n (%) (N=2484)	Asundexian vs Placebo HR (95% CI)†	Asundexian n (%) (N=1290)	Placebo n (%) (N=1349)	Asundexian vs Placebo HR (95% CI)†	Asundexian n (%) (N=1786)	Placebo n (%) (N=1710)	Asundexian vs Placebo HR (95% CI)†	
Primary efficacy endpoint (ischemic stroke)§	203 (8.08)	247 (9.94)	0.82 (0.68–0.98)	59 (4.57)	90 (6.67)	0.68 (0.49–0.94)	83 (4.65)	127 (7.43)	0.61 (0.46–0.81)	0.21
All strokes (ischemic and hemorrhagic)	211 (8.40)	257 (10.3)	0.82 (0.68–0.98)	65 (5.04)	99 (7.34)	0.68 (0.50–0.93)	87 (4.87)	132 (7.72)	0.62 (0.47–0.81)	0.21
Disabling or a fatal stroke*	72 (2.87)	86 (3.46)	0.83 (0.61–1.14)	19 (1.47)	25 (1.85)	0.80 (0.44–1.46)	26 (1.46)	51 (2.98)	0.48 (0.30–0.77)	0.15

†Cause-specific hazard ratios are estimated from stratified cox proportional hazards model (stratified by baseline intention of T). §Ischemic stroke here includes undetermined stroke. *Stroke of any type during the trial associated with a mRS of ≥3 at 90 days after the recurrent stroke or an increase of 1 point if the last available mRS before the recurrent stroke event was ≥3.
CI, confidence interval; HR, hazard ratio; mRS, modified Rankin Scale.

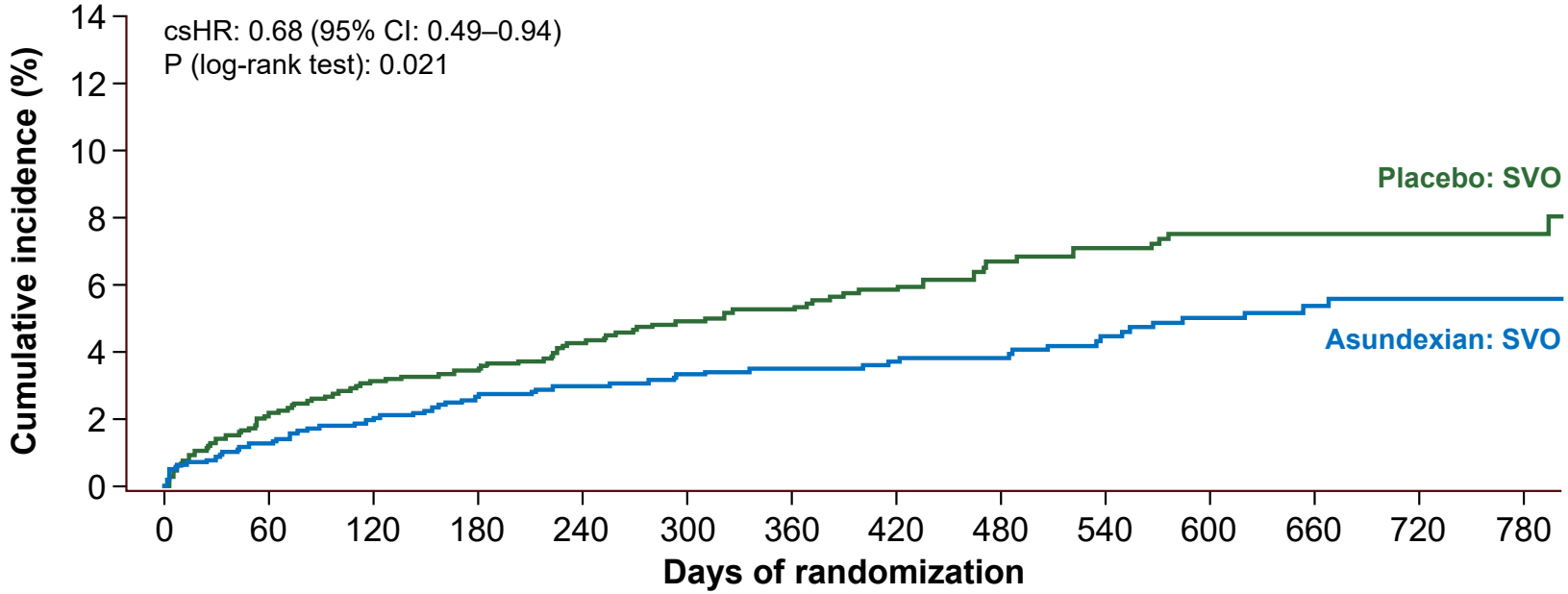
CUMULATIVE INCIDENCE OF THE PRIMARY EFFICACY ENDPOINT OF ISCHEMIC STROKE IN THE LARGE-ARTERY ATHEROSCLEROSIS SUBGROUP



No. at Risk														
Placebo: LAA	2484	2373	2327	2279	2152	1942	1778	1621	1413	1243	1035	797	574	313
Asundexian: LAA	2512	2406	2349	2310	2161	1954	1783	1598	1402	1215	1016	796	584	329

Cumulative incidence curves (Aalen-Johansen) are truncated at Day 820.
CI, confidence interval; csHR, cause-specific hazard ratio; LAA, large-artery atherosclerosis.

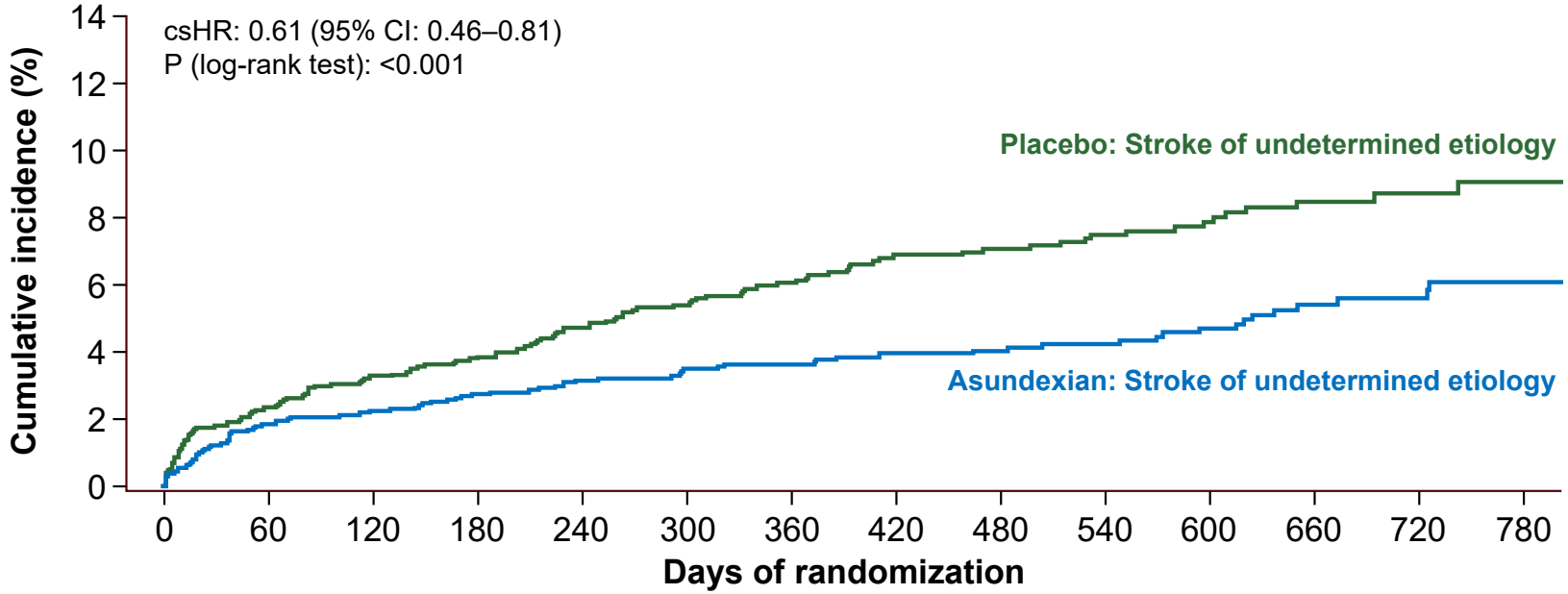
CUMULATIVE INCIDENCE OF THE PRIMARY EFFICACY ENDPOINT OF ISCHEMIC STROKE IN THE SMALL-VESSEL OCCLUSION SUBGROUP



No. at Risk														
Placebo: SVO	1349	1311	1295	1286	1208	1104	992	901	798	706	613	474	351	200
Asundexian: SVO	1290	1266	1250	1231	1167	1065	974	896	785	705	617	467	319	164

Cumulative incidence curves (Aalen-Johansen) are truncated at Day 820.
CI, confidence interval; csHR, cause-specific hazard ratio, SVO: small-vessel occlusion.

CUMULATIVE INCIDENCE OF THE PRIMARY EFFICACY ENDPOINT OF ISCHEMIC STROKE IN THE STROKE OF UNDETERMINED ETIOLOGY SUBGROUP



No. at Risk														
Placebo: SUE	1710	1661	1638	1611	1472	1297	1169	1038	907	789	636	476	332	190
Asundexian: SUE	1786	1737	1719	1690	1562	1407	1290	1156	1018	894	714	547	385	225

Cumulative incidence curves (Aalen-Johansen) are truncated at Day 820.
CI, confidence interval; csHR, cause-specific hazard ratio, SUE, stroke of undetermined etiology.

NO TREATMENT INTERACTION FOR SAFETY OUTCOMES ACROSS ISCHEMIC STROKE SUBTYPES

Safety endpoints	Large-artery atherosclerosis			Small-vessel occlusion			Stroke of undetermined etiology			Inter. P-value
	Asundexian n (%) (N=2496)	Placebo n (%) (N=2468)	Asundexian vs Placebo HR (95% CI)†	Asundexian n (%) (N=1280)	Placebo n (%) (N=1342)	Asundexian vs Placebo HR (95% CI)†	Asundexian n (%) N=1777	Placebo n (%) N=1705	Asundexian vs Placebo HR (95% CI)†	
Primary safety endpoint: ISTH major bleeding	53 (2.1)	44 (1.8)	1.20 (0.80–1.79)	23 (1.8)	30 (2.2)	0.82 (0.48–1.42)	29 (1.6)	25 (1.5)	1.11 (0.65–1.90)	0.52
Symptomatic intracranial hemorrhage (including intracerebral hemorrhage)	14 (0.6)	12 (0.5)	1.17 (0.54–2.54)	13 (1.0)	12 (0.9)	1.19 (0.54–2.60)	9 (0.5)	9 (0.5)	0.95 (0.38–2.40)	0.93
Hemorrhagic stroke	4 (0.2)	5 (0.2)	0.80 (0.21–2.98)	6 (0.5)	8 (0.6)	0.82 (0.28–2.37)	2 (0.1)	5 (0.3)	0.38 (0.07–1.98)	0.72

†Cause-specific hazard ratios are estimated from stratified cox proportional hazards model (stratified by baseline intention of T).
CI, confidence interval; HR, hazard ratio; ISTH, International Society on Thrombosis and Haemostasis.

CONSISTENT RESULTS IN PATIENTS WITH EMBOLIC STROKE OF UNDETERMINED SOURCE

Endpoints	ESUS			No ESUS			Inter. P-value
	Asundexian n (%)	Placebo n (%)	Asundexian vs Placebo HR (95% CI)†	Asundexian n (%)	Placebo n (%)	Asundexian vs Placebo HR (95% CI)†	
Primary efficacy endpoint (ischemic stroke)§	N=924 42 (4.5)	N=920 76 (8.3)	– 0.53 (0.37–0.78)	N=4914 316 (6.4)	N=4918 409 (8.3)	– 0.77 (0.67–0.89)	0.07
ISTH major bleeding	N=923 16 (1.7)	N=918 14 (1.5)	– 1.11 (0.54–2.27)	N=4878 90 (1.8)	N=4885 89 (1.8)	– 1.02 (0.76–1.37)	0.80

§Ischemic stroke here includes undetermined stroke.
†Cause-specific hazard ratios are estimated from stratified cox proportional hazards model (stratified by baseline intention of DAPT).
CI, confidence interval; DAPT, dual antiplatelet therapy; ESUS, embolic stroke of undetermined source; HR, hazard ratio; ISTH, International Society on Thrombosis and Haemostasis.

CONCLUSION

- OCEANIC-STROKE enrolled a large representative sample of non-cardioembolic ischemic stroke subtypes.
- Asundexian reduced ischemic and disabling stroke, without increasing ISTH major bleeding or intracranial hemorrhage across all qualifying ischemic stroke subtypes.
- These findings were consistent in patients with qualifying ESUS.
- Asundexian provides a novel efficacious and safe secondary stroke prevention treatment for patients with non-cardioembolic ischemic stroke, irrespective of underlying etiology.

ESUS, embolic stroke of undetermined source; ISTH, International Society on Thrombosis and Haemostasis.

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Steering Committee

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