McMaster University

Population Health Research Institute
HEALTH THROUGH KNOWLEDGE

Scientific Sessions

OUTCOMES IN THE OCEANIC-STROKE RANDOMIZED, PLACEBO-CONTROLLED TRIAL OF FXIA INHIBITION WITH ASUNDEXIAN IN PARTICIPANTS WITH NON-CARDIOEMBOLIC STROKE OR TRANSIENT ISCHEMIC ATTACK BY NON-LABORATORY FRAMINGHAM RISK SCORE CATEGORY

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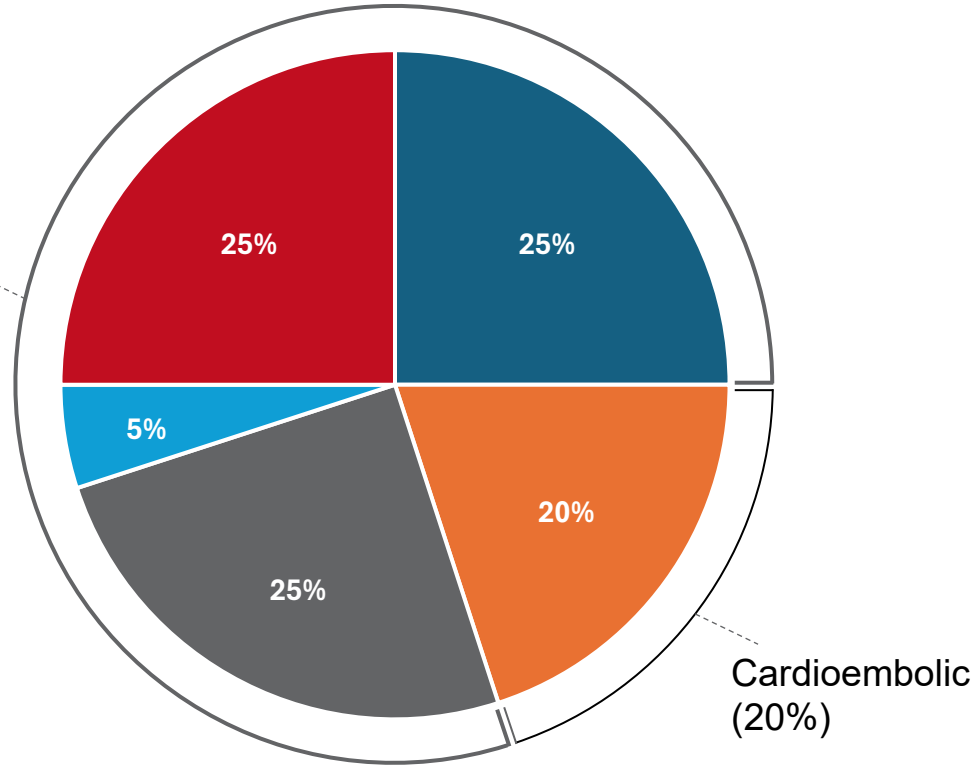
American Heart Association.

#ScientificSessions26

DISCLOSURES

M.S. declares consulting for Bayer, Regeneron, Novartis, Anthos, Sirius, ADARx; research funding for the current study from Bayer paid to his institution; research funding for AXIOMATIC-SSP from BMS and Janssen; serving on an endpoint review committee for AtriCure.

ISCHEMIC STROKE SUBTYPES

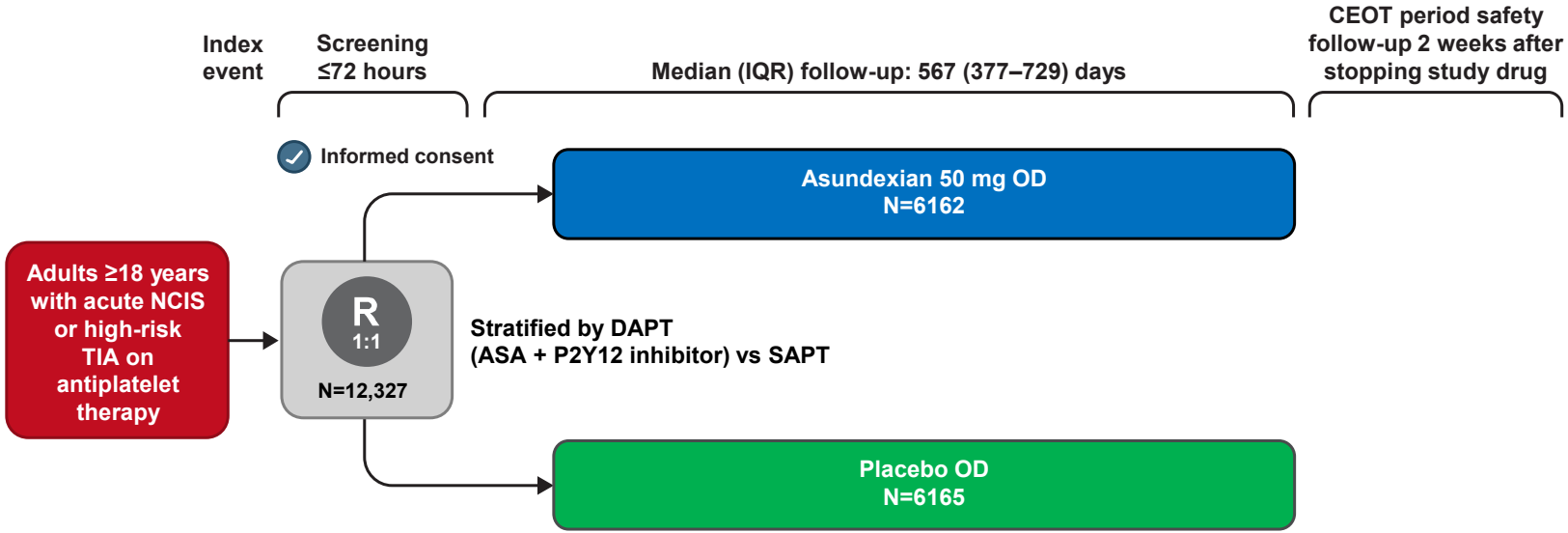


NCIS TOAST Subtypes

- Large-artery atherosclerosis
- Lacunar
- Other/rare
- Cryptogenic (ESUS)

NCIS, non-cardioembolic ischemic stroke; TOAST, Trial of Org 10172 in Acute Stroke Treatment; ESUS, embolic stroke of undetermined source.
Hart RG, et al. *Lancet Neurol*. 2014;13:429–438.

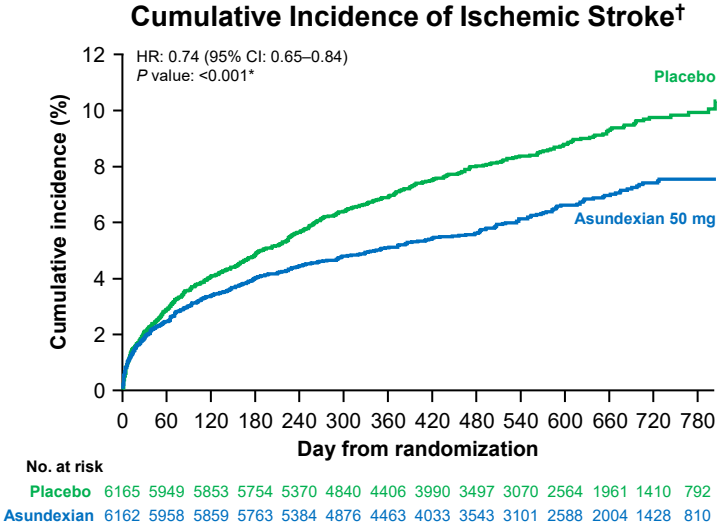
OCEANIC-STROKE OVERVIEW

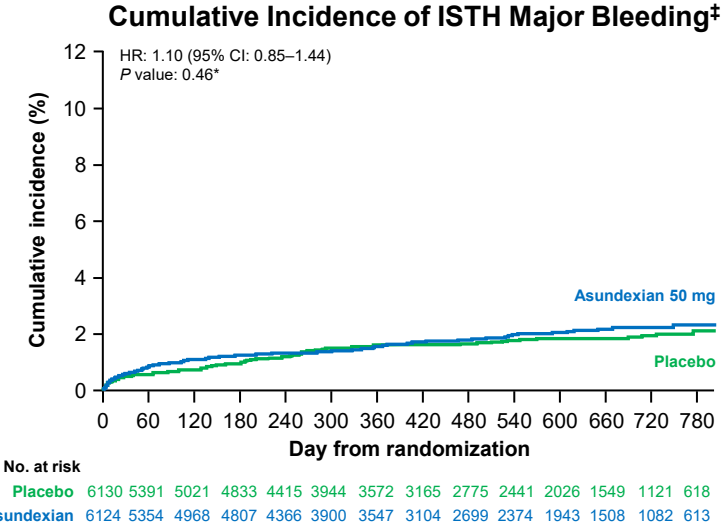


ASA, acetylsalicylic acid; CEOT, common end of treatment; DAPT, dual antiplatelet therapy; IQR, interquartile range; NCIS, non-cardioembolic ischemic stroke; OD, once daily; P2Y12, purinergic receptor Y12; R, randomization; SAPT, single antiplatelet therapy; TIA, transient ischemic attack.

1. Sharma M, et al. *Eur Stroke J*. 2026;11(1):aakaf017; 2. Sharma M, et al. *N Engl J Med*. 2026;394(15):1467-1479.

OCEANIC-STROKE PRIMARY EFFICACY AND SAFETY ENDPOINTS





**P* value is obtained from stratified log-rank test (stratified by baseline intention of DAPT). csHR and 95% CI are provided here.
†ARR at 1 year was 1.9%, with a NNT of 54; and at 2 years ARR was 2.2%, with an NNT of 46. Cumulative incidence curves are estimated by Aalen–Johansen method. Plot truncated at Day 820; based on the full analysis set.
‡Cumulative incidence curves are estimated by Aalen–Johansen method, truncated at Day 820.

ARR, absolute risk reduction; CI, confidence interval; csHR, cause-specific hazard ratio; DAPT, dual antiplatelet therapy; HR, hazard ratio; ISTH, International Society on Thrombosis and Haemostasis; NNT, needed to treat.
Sharma M, et al. *N Engl J Med*. 2026;394(15):1467–1479.

OBJECTIVE AND METHODS

Baseline vascular risk may affect both efficacy and safety of antithrombotics[1]

Objectives

- To describe the baseline characteristics of participants by non-laboratory Framingham Risk Score (FRS) and determine the effect of asundexian according to baseline risk factors

Methods

- Exploratory post-hoc analysis
- Participants were classified into non-laboratory FRS categories using baseline data
- Non-laboratory FRS:
  - Age, sex, BMI, SBP, antihypertensive use, current smoking, diabetes
  - 10-year CVD risk: low (5 to <10%); intermediate (10–19%); high (≥20%)[2]
- Cox proportional hazard models constructed for the primary and secondary efficacy and safety outcomes and net clinical benefit outcomes and estimates tested for interaction with FRS score

BMI, body mass index; CVD, cardiovascular disease; FRS, Framingham Risk Score; SBP, systolic blood pressure.

1. Daghlas I, et al. *Stroke*. 2024;55:385–391. 2. de Menezes-Júnior, LAA. *Sci Rep*. 2025;15:42757. 3. Dehghan, A. et al. *Journal of translational medicine* 2023; 21: 687.

BASELINE CHARACTERISTICS BY NON-LABORATORY FRS CATEGORY

	Low Risk (N=570)	Intermediate Risk (N=1871)	High Risk (N=9823)
Age (years), mean (SD)	50.9 (10.4)	62.0 (10.9)	69.6 (9.5)
Female sex, no. (%)	297 (52.1)	935 (50.0)	2856 (29.1)
BMI (kg/m^2), mean (SD)	26.1 (4.9)	26.5 (4.9)	27.3 (4.9)
BMI categories, no. (%)			
<25 kg/m^2	256 (44.9)	835 (44.6)	3375 (34.4)
25 to <30 kg/m^2	227 (39.8)	655 (35.0)	3990 (40.6)
≥30 kg/m^2	87 (15.3)	381 (20.4)	2458 (25.0)
SBP (mmHg), mean (SD)	121.9 (13.8)	128.9 (15.8)	144.5 (17.9)
Anti-hypertensive use	210 (36.8)	1258 (67.2)	8803 (89.6)
Current smoking	84 (14.7)	303 (16.2)	2905 (29.6)
Diabetes	23 (4.0)	197 (10.5)	4003 (40.8)

Non-laboratory-based FRS includes age, sex, BMI, SBP, antihypertensive use, current smoking, diabetes. N=63 of randomized patients with incomplete FRS: missing smoking status (n=3), SBP (n=2), BMI (n=52), and age out of score range (n=9).
BMI, body mass index; FRS, Framingham Risk Score; SBP, systolic blood pressure; SD, standard deviation.

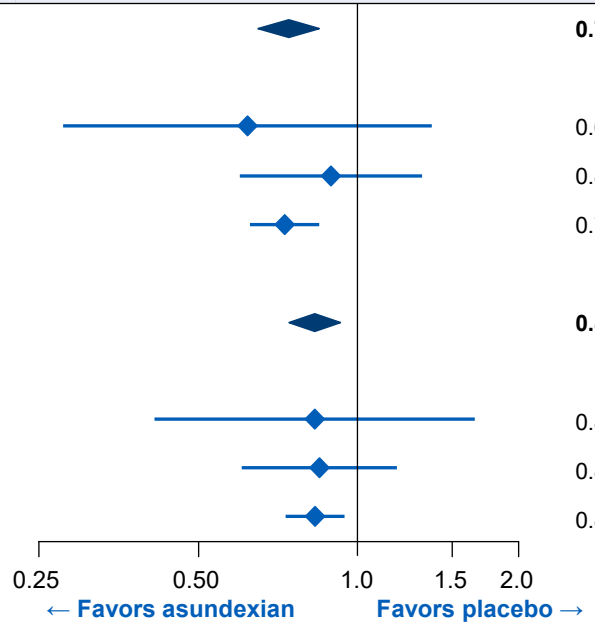
BASELINE CHARACTERISTICS BY NON-LABORATORY FRS CATEGORY (CONT'D)

	Low Risk (N=570)	Intermediate Risk (N=1871)	High Risk (N=9823)
Index event, no. (%)			
Ischemic stroke	563 (98.8)	1814 (97.0)	9239 (94.1)
High-risk TIA	7 (1.2)	57 (3.0)	582 (5.9)
TOAST classification of index stroke, no. (%)			
Large-artery atherosclerosis	175 (31.1)	653 (36.0)	4141 (44.8)
Small-vessel occlusion (lacune)	88 (15.6)	419 (23.1)	2122 (23.0)
Stroke of other determined etiology	47 (8.3)	60 (3.3)	240 (2.6)
Stroke of undetermined etiology	242 (43.0)	658 (36.3)	2574 (27.9)
Cardioembolism	11 (2.0)	24 (1.3)	161 (1.7)
Planned dual antiplatelet therapy with ASA and a P2Y12 inhibitor at randomization (stratification factor), no. (%)	315 (55.3)	1094 (58.5)	6256 (63.7)

Non-laboratory-based FRS includes age, sex, BMI, SBP, antihypertensive use, current smoking, diabetes. N=63 of randomized patients with incomplete FRS: missing smoking status (n=3), SBP (n=2), BMI (n=52), and age out of score range (n=9).
ASA, acetylsalicylic acid; BMI, body mass index; FRS, Framingham Risk Score; P2Y12, purinergic receptor Y12; SBP, systolic blood pressure; TIA, transient ischemic attack; TOAST, Trial of Org 10172 in Acute Stroke Treatment.

EFFICACY OUTCOMES

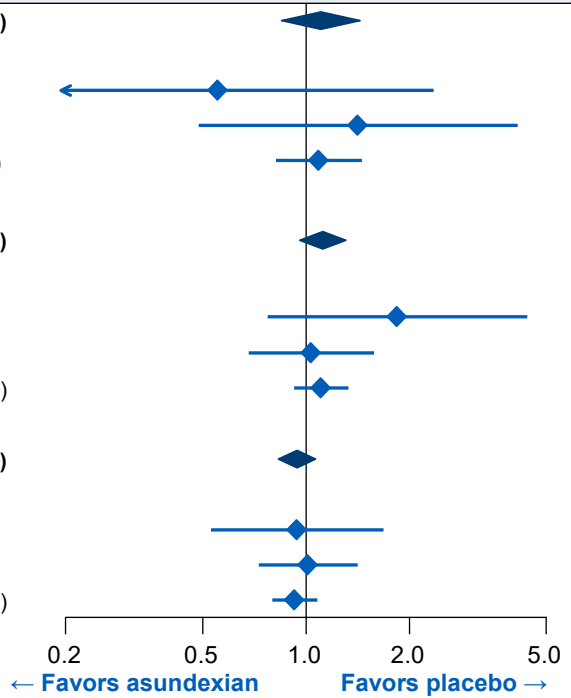
	Asundexian n/N (%)	Placebo n/N (%)	HR (95% CI)	*P* interaction
Ischemic stroke	**384/6162 (6.2%)**	**518/6165 (8.4%)**	**0.74 (0.65–0.84)**	
FRS				0.58
Low risk	10/284 (3.5%)	16/286 (5.6%)	0.62 (0.28–1.36)	
Intermediate risk	47/916 (5.1%)	56/955 (5.9%)	0.89 (0.60–1.31)	
High risk	327/4939 (6.6%)	443/4884 (9.1%)	0.73 (0.63–0.84)	
CV death, MI, or stroke	**568/6162 (9.2%)**	**685/6165 (11.1%)**	**0.83 (0.74–0.92)**	
FRS				0.99
Low risk	15/284 (5.3%)	18/286 (6.3%)	0.83 (0.42–1.64)	
Intermediate risk	64/916 (7.0%)	80/955 (8.4%)	0.84 (0.61–1.17)	
High risk	489/4939 (9.9%)	581/4884 (11.9%)	0.83 (0.73–0.93)	



Exploratory efficacy analysis using intent-to-treat population. Non-laboratory-based FRS includes age, sex, BMI, SBP, antihypertensive use, current smoking, diabetes. Patients with incomplete risk scores (n=63) are excluded. Analyses were performed using a stratified Cox PH model (stratified by baseline intention of DAPT). BMI, body mass index; CI, confidence interval; CV, cardiovascular; DAPT, dual antiplatelet therapy; DM, diabetes mellitus; FRS, Framingham Risk Score; HR, hazard ratio; MI, myocardial infarction; PH, proportional hazards; SBP, systolic blood pressure.

SAFETY OUTCOMES

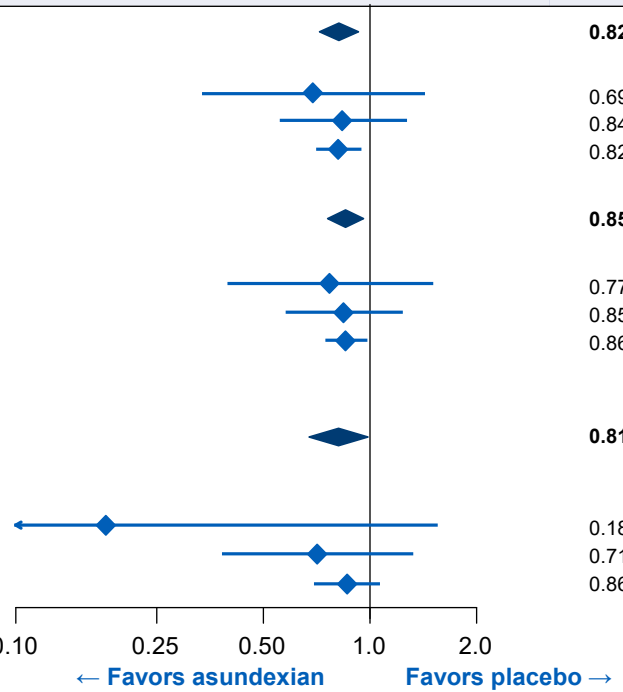
	Asundexian n/N (%)	Placebo n/N (%)	HR (95% CI)	*P* interaction
ISTH major bleeding	**117/6124 (1.9%)**	**107/6130 (1.7%)**	**1.10 (0.85–1.44)**	
FRS				0.60
Low risk	3/282 (1.1%)	5/283 (1.8%)	0.55 (0.13–2.33)	
Intermediate risk	8/911 (0.9%)	6/951 (0.6%)	1.42 (0.49–4.08)	
High risk	105/4909 (2.1%)	96/4858 (2.0%)	1.09 (0.83–1.44)	
ISTH major or CRNM bleeding	**339/6124 (5.5%)**	**307/6130 (5.0%)**	**1.12 (0.96–1.30)**	
FRS				0.47
Low risk	15/282 (5.3%)	8/283 (2.8%)	1.84 (0.78–4.36)	
Intermediate risk	45/911 (4.9%)	47/951 (4.9%)	1.04 (0.69–1.56)	
High risk	278/4909 (5.7%)	251/4858 (5.2%)	1.11 (0.93–1.31)	
Minor bleeding	**479/6124 (7.8%)**	**512/6130 (8.4%)**	**0.94 (0.83–1.07)**	
FRS				0.87
Low risk	24/282 (8.5%)	24/283 (8.5%)	0.94 (0.53–1.66)	
Intermediate risk	73/911 (8.0%)	77/951 (8.1%)	1.01 (0.74–1.40)	
High risk	380/4909 (7.7%)	407/4858 (8.4%)	0.93 (0.81–1.07)	



Exploratory safety analysis while patients were on treatment. Non-laboratory-based FRS includes age, sex, BMI, SBP, antihypertensive use, current smoking, diabetes. Patients with incomplete risk scores (n=63) were excluded. Analyses were performed using stratified Cox PH model (stratified by baseline intention of DAPT). BMI, body mass index; CI, confidence interval; CRNM, clinically relevant nonmajor; DAPT, dual antiplatelet therapy; DM, diabetes mellitus; FRS, Framingham Risk Score; HR, hazard ratio; ISTH, International Society on Thrombosis and Haemostasis; PH, proportional hazards; SBP, systolic blood pressure.

NET CLINICAL BENEFIT OUTCOMES

	Asundexian n/N (%)	Placebo n/N (%)	HR (95% CI)	*P* interaction
Ischemic stroke or ISTH major bleeding	**430/6124 (7.0%)**	**529/6130 (8.6%)**	**0.82 (0.72–0.93)**	
FRS				0.92
Low risk	13/282 (4.6%)	18/283 (6.4%)	0.69 (0.34–1.42)	
Intermediate risk	42/911 (4.6%)	54/951 (5.7%)	0.84 (0.56–1.26)	
High risk	374/4909 (7.6%)	454/4858 (9.3%)	0.82 (0.71–0.94)	
CV death, stroke, MI or ISTH major bleeding	**518/6124 (8.5%)**	**611/6130 (10.0%)**	**0.85 (0.76–0.96)**	
FRS				0.97
Low risk	16/282 (5.7%)	20/283 (7.1%)	0.77 (0.40–1.49)	
Intermediate risk	50/911 (5.5%)	64/951 (6.7%)	0.85 (0.58–1.22)	
High risk	451/4909 (9.2%)	521/4858 (10.7%)	0.86 (0.76–0.97)	
All-cause mortality, disabling stroke, fatal bleeding or symptomatic intracranial bleeding	**189/6124 (3.1%)**	**234/6130 (3.8%)**	**0.81 (0.67–0.99)**	
FRS				0.28
Low risk	1/282 (0.4%)	5/283 (1.8%)	0.18 (0.02–1.54)	
Intermediate risk	17/911 (1.9%)	26/951 (2.7%)	0.71 (0.39–1.31)	
High risk	171/4909 (3.5%)	198/4858 (4.1%)	0.86 (0.70–1.06)	



Exploratory safety analysis while patients were on treatment. Non-laboratory-based FRS includes age, sex, BMI, SBP, antihypertensive use, current smoking, diabetes. Patients with incomplete risk scores (n=63) are excluded. Analyses were performed using a stratified Cox PH model (stratified by baseline intention of DAPT). BMI, body mass index; CI, confidence interval; CV, cardiovascular; DAPT, dual antiplatelet therapy; DM, diabetes mellitus; FRS, Framingham Risk Score; HR, hazard ratio; ISTH, International Society on Thrombosis and Haemostasis; MI, myocardial infarction; PH, proportional hazards; SBP, systolic blood pressure.

CONCLUSIONS

In patients with recent NCIS or high-risk TIA, asundexian reduced ischemic stroke with similar bleeding versus placebo across all FRS risk categories

- There was no significant interaction between treatment and FRS risk categories for efficacy and safety outcomes
- There was no evidence that the effect of asundexian differs by baseline vascular risk

Limitations

- Most participants were in the high-risk FRS category
- The proportion of participants categorized as low risk was limited and estimates in this group should be interpreted with caution

FRS, Framingham Risk Score; NCIS, non-cardioembolic ischemic stroke; TIA, transient ischemic attack.

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Thank you!

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