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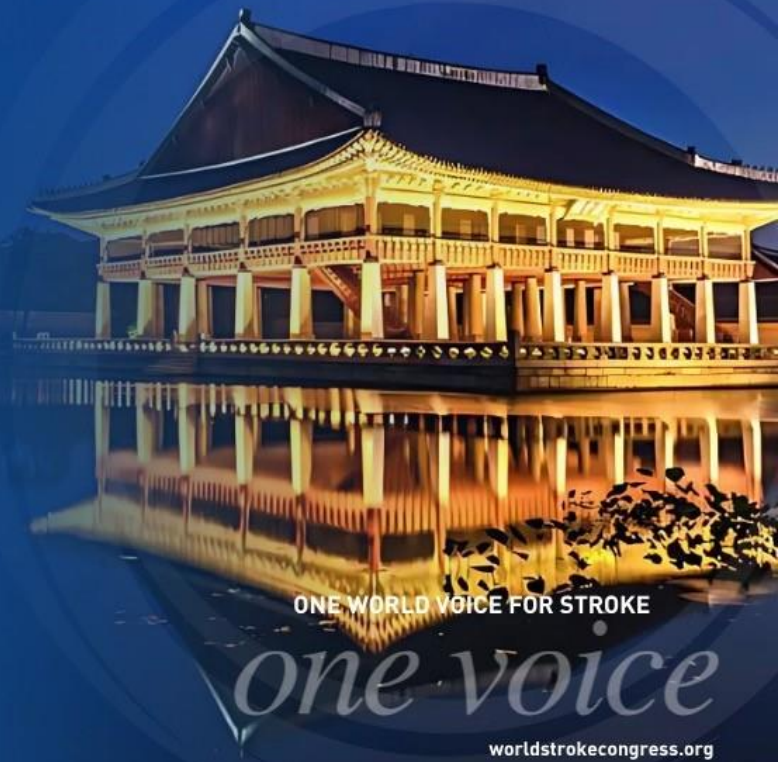
Korean Stroke Society

Effect of factor XIa inhibitor asundexian on ischemic stroke recurrence according to baseline infarct pattern: MRI substudy of OCEANIC-STROKE trial

Raed A. Joundi,[1] Ashkan Shoamanesh, Qiang Dong, Teriyuki Hirano, Pablo Amaya, Charlotte Cordonnier, Scott E. Kasner, Jeffrey L. Saver, Georgios Tsivgoulis, Bruce C.V. Campbell, Martin Kovar, Robert Mikulik, Gisele Sampaio Silva, José M. Ferro, Daniel Bereczki, Agnieszka Slowik, Robin Lemmens, Jaime Masjuan, Michael Knoflach, Roland Veltkamp, Thompson Robinson, Peter Turcani, Gian Marco De Marchis, I-Hui Lee, Serefnur Ozturk, Ivan Staikov, Andrea Zini, Andrew M. Demchuk, P.N. Sylaja, Fan Kee Hoo, Saule T. Turespekova, Karleen Schulze, Lizhen Xu, Angela Wang, Jodi Miller, Pablo Colorado, Lars Keller, Eva Muehlhofer, Eric Smith, Mukul Sharma

1. Presenting author: Department of Medicine, Population Health Research Institute, McMaster University, Hamilton, Ontario, Canada



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Disclosure

- This study was funded by Bayer AG.
- Asundexian is not yet approved for use in secondary stroke prevention
- RAJ disclosures honoraria/expenses, consulting/advisory board activities, and research funding from Bayer AG

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OCEANIC-STROKE primary efficacy and safety endpoints

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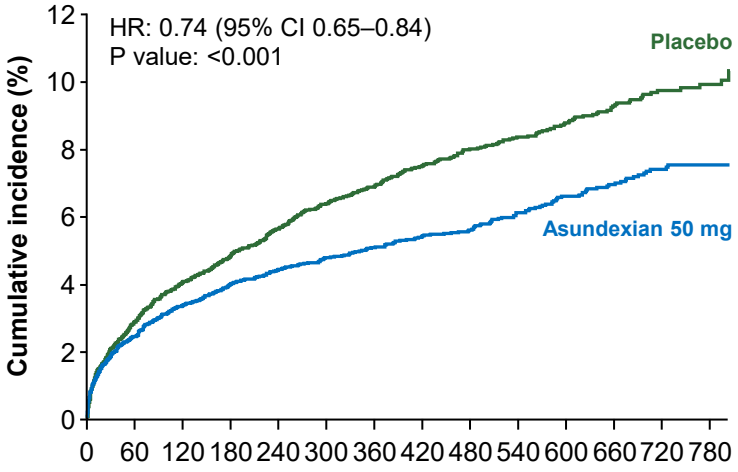
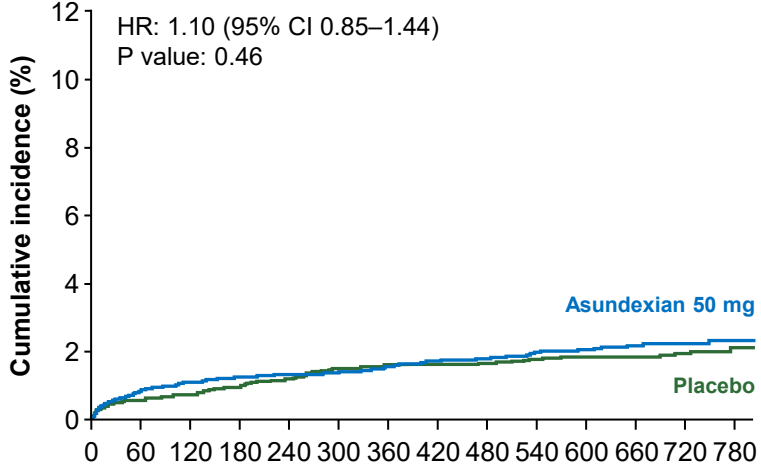
- Asundexian 50 mg daily with antiplatelet therapy reduced ischemic stroke (csHR: 0.74; 95% CI 0.65–0.84), without increasing ISTH major bleeding compared with antiplatelet therapy alone

Cumulative incidence of ischemic stroke



No. at risk														
Placebo	6165	5949	5853	5754	5370	4840	4406	3990	3497	3070	2564	1961	1410	792
Asundexian 50 mg	6162	5958	5859	5763	5384	4876	4463	4033	3543	3101	2588	2004	1428	810

Cumulative incidence of ISTH major bleeding

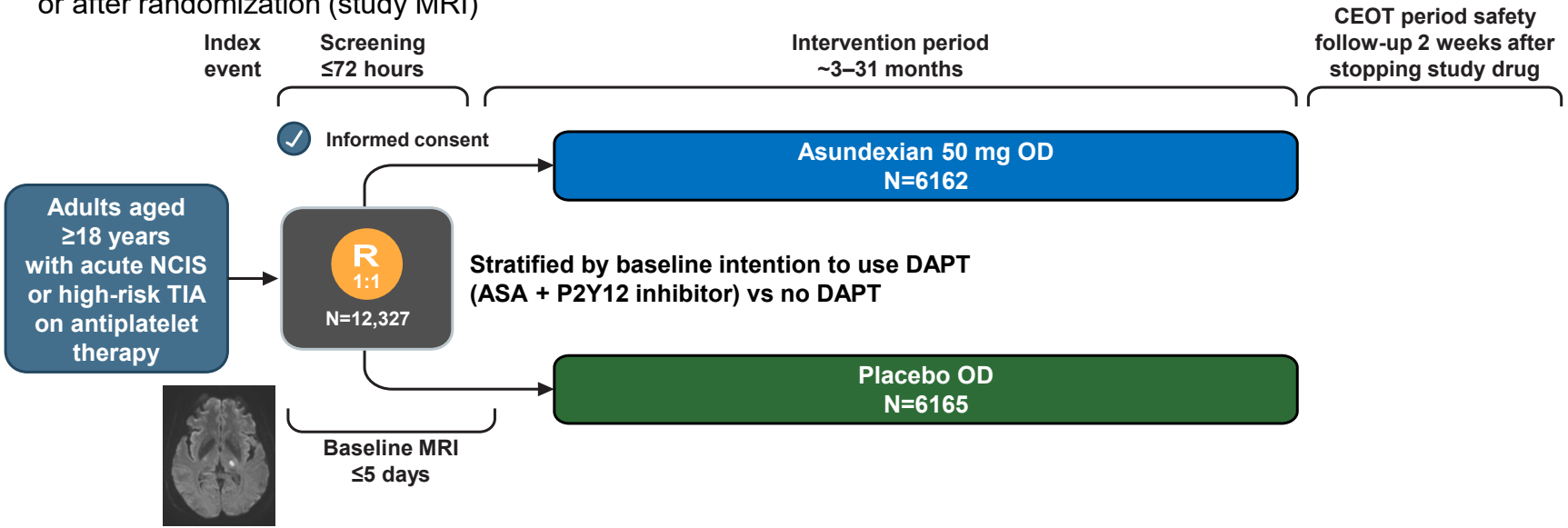


No. at risk														
Placebo	6130	5391	5021	4833	4415	3944	3572	3165	2775	2441	2026	1549	1121	618
Asundexian 50 mg	6124	5354	4968	4807	4366	3900	3547	3104	2699	2374	1943	1508	1082	613

From *The New England Journal of Medicine*, Sharma M, et al., Asundexian for Secondary Stroke Prevention, Vol. 394, pp. 1467–1479. Copyright © 2026 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.
CI, confidence interval; csHR, cause-specific hazard ratio; HR, hazard ratio; ISTH, International Society on Thrombosis and Haemostasis. Sharma M, et al. *N Engl J Med.* 2026;394(15):1467–1479.

OCEANIC-STROKE: Study design

- Index event was NCIS and no contraindications for MRI
- Baseline MRI within 5 days of symptoms, either before randomization (as clinically initiated MRI) or after randomization (study MRI)



ASA, acetylsalicylic acid; CEOT, common end of treatment; DAPT, dual antiplatelet therapy; MRI, magnetic resonance imaging; 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. *Eur Stroke J.* 2026;11(1):aakaf017.

Background and objective of MRI sub-study

- Infarct pattern on MRI is associated with risk of stroke recurrence and bleeding
  - Multiple DWI+ infarcts or cortical → higher rate of recurrence[1]
  - Small subcortical infarct → marker of intracranial bleeding risk[2]

- Pre-specified objectives:
  1. Evaluate the distribution of MRI infarct patterns in OCEANIC-STROKE, including proportion of single small subcortical infarct
  2. Evaluate ischemic stroke recurrence and ISTH major bleeding according to baseline MRI infarct pattern
  3. Explore whether the treatment effect of asundexian differed across infarct patterns

DWI, diffusion-weighted imaging; MRI, magnetic resonance imaging.

1. Wen HM, et al. *Neurology*. 2004;63(7):1317–1319. 2. Tanaka K, et al. *Ann Neurol*. 2024;95(4):774–787.

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Methods: MRI substudy

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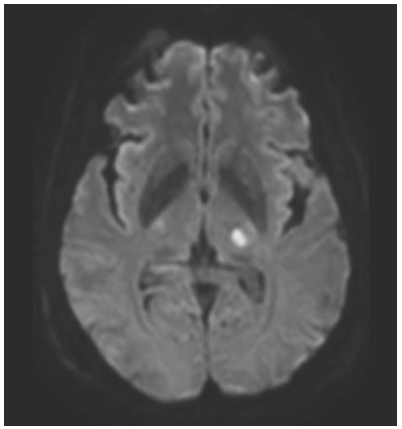
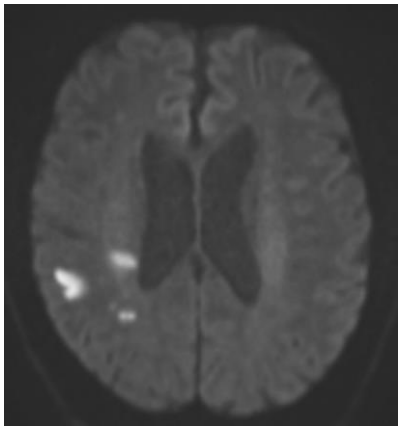
- Standardized MRI protocol: FLAIR, DWI, ADC, and SWI / GRE obtained within 5 days of index event. All sites provided phantom scans for qualification
- MRI scans centrally adjudicated for presence of DWI+ lesions, location, and size, and categorized as:
  - Single small (<15 mm) subcortical infarct
  - Multiple infarcts
  - One or more large (>15 mm) infarcts
  - One or more cortical infarcts

Potential embolic topography



Single, small subcortical



Multiple, large, or cortical†

†Patient can be in multiple categories.
ADC, apparent diffusion coefficient; DWI, diffusion-weighted imaging; DWI+, diffusion-weighted imaging–positive; FLAIR, fluid-attenuated inversion recovery; GRE, gradient-echo; MRI, magnetic resonance imaging; SWI, susceptibility-weighted imaging.

Methods: MRI substudy

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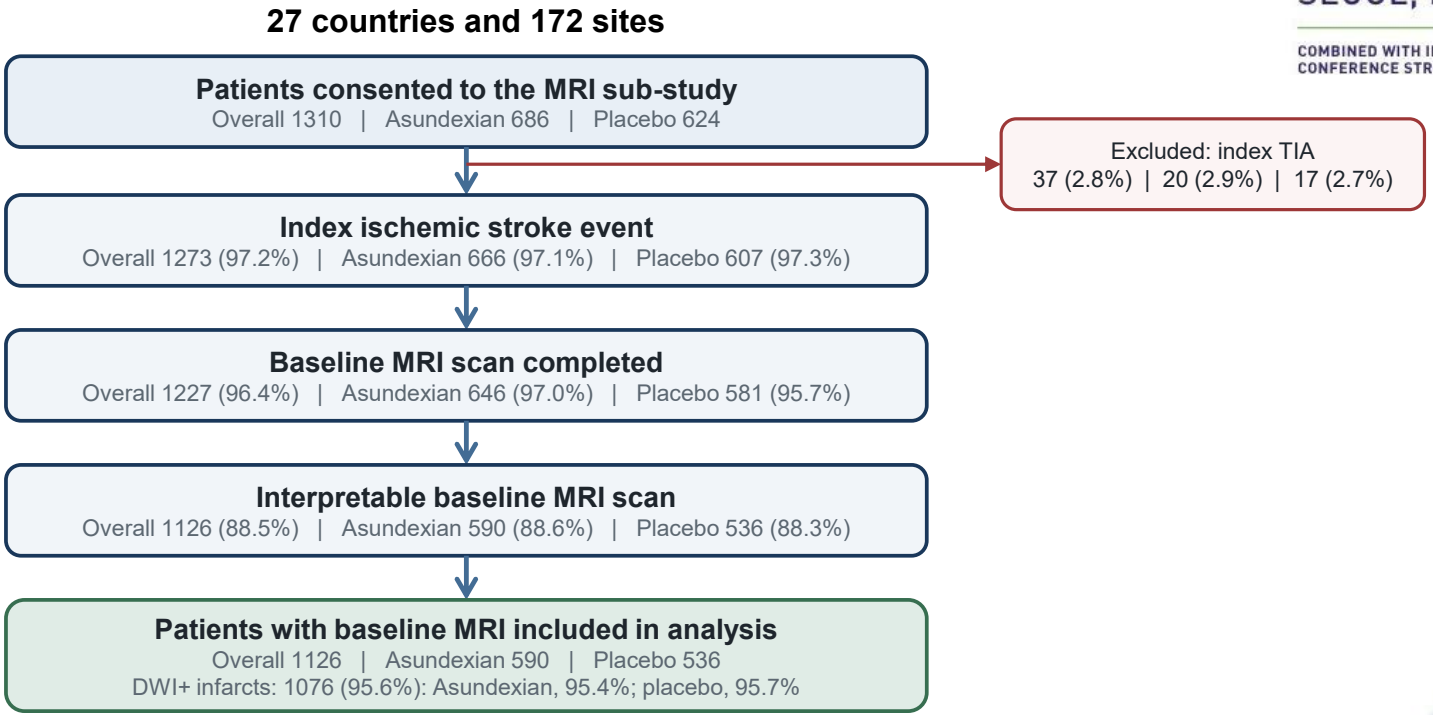
- We described the proportions of each MRI infarct pattern
- We calculated rates of ischemic stroke recurrence by baseline MRI infarct pattern
- We used Cox proportional hazards models to calculate csHR stratified by baseline DAPT use for asundexian versus placebo on:
  - recurrent ischemic stroke
  - ISTH major bleeding

  } By baseline infarct pattern

csHR, cause-specific hazard ratio; DAPT, dual antiplatelet therapy; MRI, magnetic resonance imaging.

MRI sub-study participant flow



DWI+, diffusion-weighted imaging positive; MRI, magnetic resonance imaging; TIA, transient ischemic attack.

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Baseline characteristics of MRI substudy participants by treatment arms

Characteristic	Asundexian 50 mg N=590	Placebo N=536
Age, mean (SD), years	67.7 (10.2)	67.0 (10.5)
Female sex, n (%)	194 (32.9)	160 (29.9)
Medical history, n (%)		
Current or former tobacco use	276 (46.8)	293 (54.7)
Hypertension	460 (78.0)	419 (78.2)
Diabetes	202 (34.2)	185 (34.5)
Previous stroke or TIA	112 (19.0)	113 (21.1)
Coronary artery disease	92 (15.6)	77 (14.4)
TOAST classification, n (%)		
Large-artery atherosclerosis	248 (42.0)	229 (42.7)
Small-vessel occlusion (lacune)	122 (20.7)	117 (21.8)
Other determined etiology	13 (2.2)	16 (3.0)
Undetermined etiology	197 (33.4)	160 (29.9)
Cardioembolism	10 (1.7)	14 (2.6)
NIHSS at randomization, median (IQR)	2.0 (1.0–4.0)	2.0 (1.0–4.0)
Intravenous thrombolysis only, n (%)	123 (20.8)	115 (21.5)
Endovascular therapy ± IV thrombolysis, n (%)	32 (5.4)	43 (8.0)
Planned DAPT, n (%)	352 (59.7)	311 (58.0)
Time from index event to baseline MRI, mean (SD), hours	58.2 (39.9)	56.5 (34.3)

DAPT, dual antiplatelet therapy; IQR, interquartile range; IV, intravenous; MRI, magnetic resonance imaging; NIHSS, National Institutes of Health Stroke Scale; SD, standard deviation; TIA, transient ischemic attack; TOAST, Trial of Org 10172 in Acute Stroke Treatment.

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Baseline hemorrhagic transformation and white matter hyperintensity severity by treatment (DWI+ population)

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Hemorrhagic transformation of any DWI+ infarcts (highest class observed), n (%)	Asundexian 50 mg N=563	Placebo N=513
None	404 (71.8)	375 (73.1)
Yes	159 (28.2)	138 (26.9)
HI1	94 (16.7)	77 (15.0)
HI2	62 (11.0)	60 (11.7)
PH1	3 (0.5)	1 (0.2)
PH2	0 (0.0)	0 (0.0)
Fazekas score: Peri-ventricular		
0: Absent	67 (11.9)	78 (15.2)
1: Caps or pencil-thin lining	261 (46.4)	238 (46.4)
2: Smooth halo	174 (30.9)	145 (28.3)
3: Irregular periventricular signal extending into deep white matter	61 (10.8)	52 (10.1)
Deep white matter Fazekas score		
0: Absent	39 (6.9)	61 (11.9)
1: Punctuate foci	269 (47.8)	244 (47.6)
2: Beginning confluence	189 (33.6)	157 (30.6)
3: Large confluent areas	66 (11.7)	51 (9.9)

DWI+, diffusion-weighted imaging–positive; HI, hemorrhagic infarction; PH, parenchymal hematoma.

Baseline microbleed severity by treatment

Microbleeds	Asundexian 50 mg N=590	Placebo N=536
No	361 (61.2)	316 (59.0)
Yes	229 (38.8)	220 (41.0)
Microbleed count		
Mean (SD)	4.5 (10.1)	5.5 (11.2)
Median (IQR)	2 (1–4)	2 (1–4)
Median (min, max)	2 (1–127)	2 (1–108)
Microbleed severity		
1–2 CMBs	143 (62.4)	135 (61.4)
3–10 CMBs	66 (28.8)	63 (28.6)
>10 CMBs	20 (8.7)	22 (10.0)
Chronic intraparenchymal macrobleeds (>10 mm) present (excluding hemorrhagic transformation of infarcts)	15 (2.5)	11 (2.1)

CMB, cerebral microbleed; IQR, interquartile range.

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Prevalence of baseline MRI lesion types was comparable between treatment arms (DWI+ population)†

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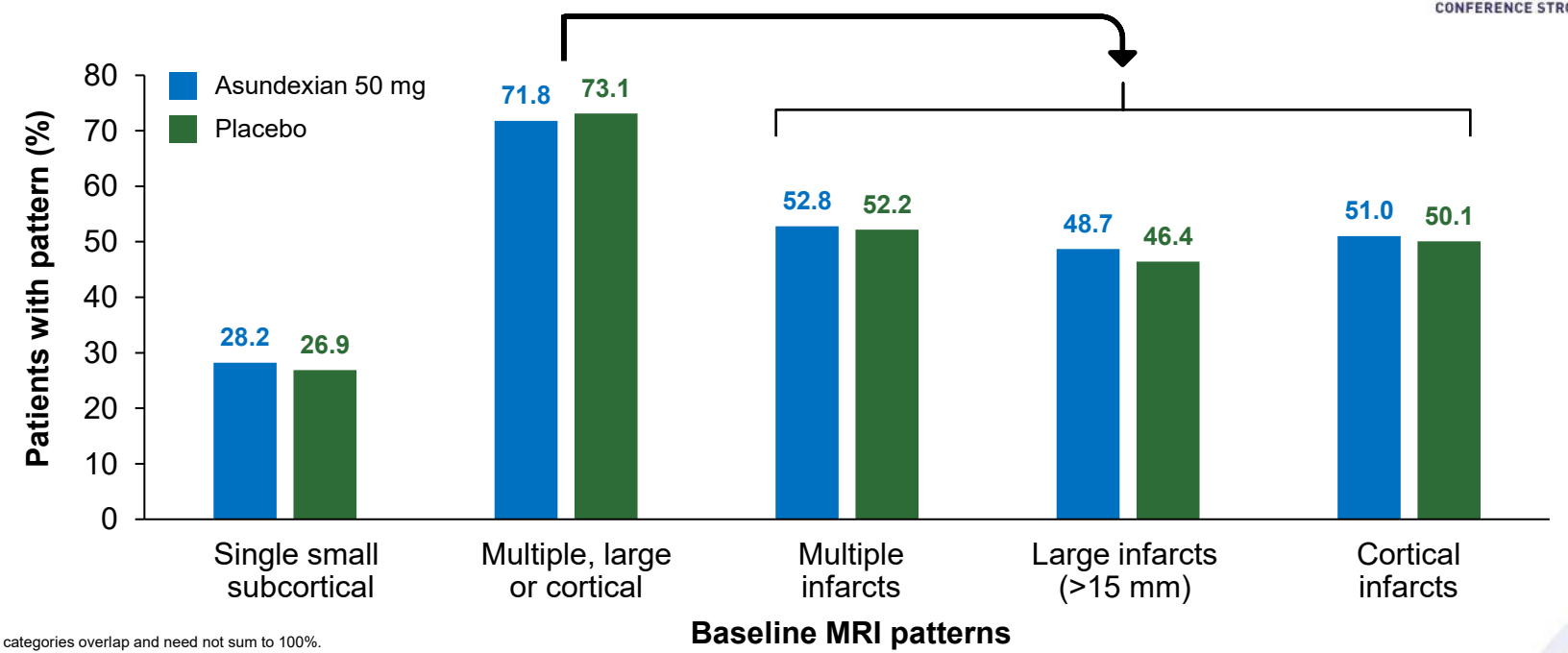

†Lesion categories overlap and need not sum to 100%.
DWI+, diffusion-weighted imaging–positive; MRI, magnetic resonance imaging.

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Efficacy endpoints: ischemic stroke and all stroke

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Variable, n (%)	Overall with baseline scan	Asundexian 50 mg	Placebo	csHR (95% CI)
Ischemic stroke				
All MRI sub-study population*	111/1126 (9.9)	47/590 (8.0)	64/536 (11.9)	0.66 (0.45–0.96)
DWI+ population	108/1076 (10.0)	46/563 (8.2)	62/513 (12.1)	0.67 (0.46–0.98)
All stroke† (ischemic and hemorrhagic stroke)				
All MRI sub-study	115/1126 (10.2)	49/590 (8.3)	66/536 (12.3)	0.66 (0.46–0.96)
DWI+ population	112/1076 (10.4)	48/563 (8.5)	64/513 (12.5)	0.67 (0.46–0.98)

*Median follow-up 1.7 years, IQR 1.04-2.07

†There were two hemorrhagic strokes in each arm

CI, confidence interval; csHR, cause-specific hazard ratio; DWI+, diffusion-weighted imaging–positive; MRI, magnetic resonance imaging.

Occurrence of ischemic stroke by treatment, stratified by baseline infarct pattern (DWI+ population)

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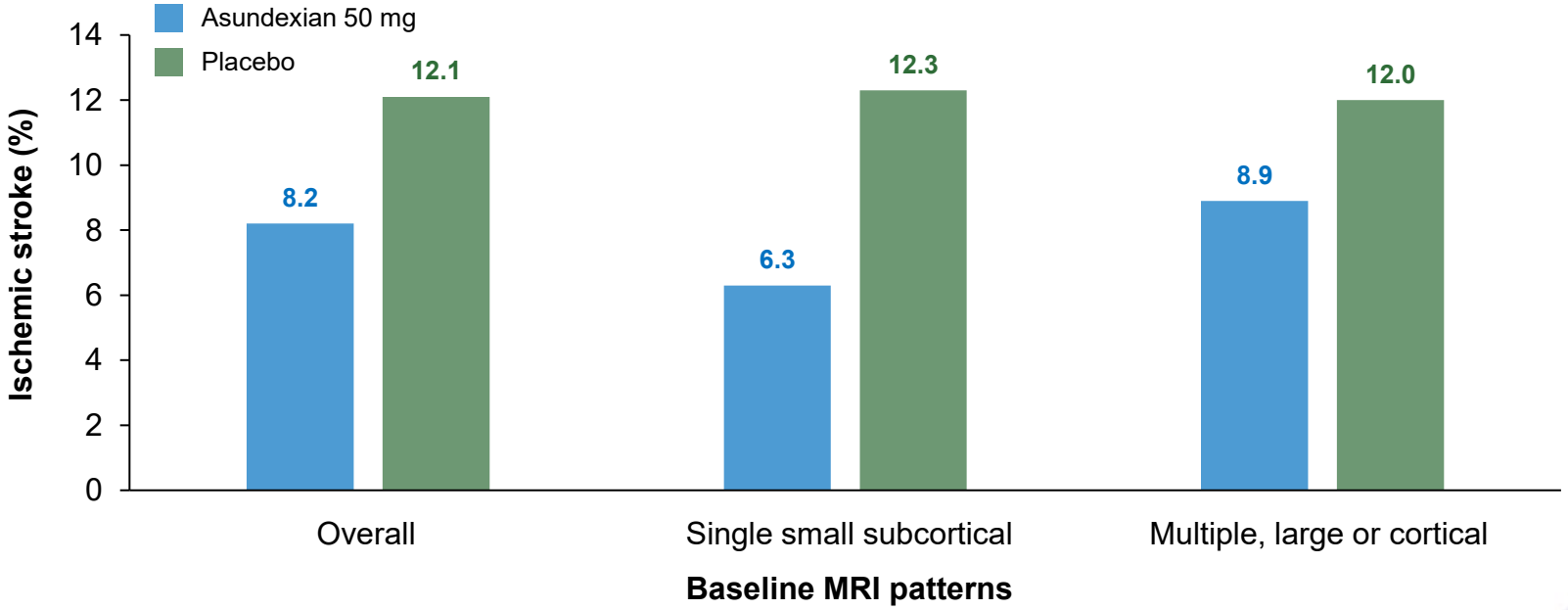

Occurrence of ischemic stroke by treatment, stratified by baseline infarct pattern (DWI+ population)

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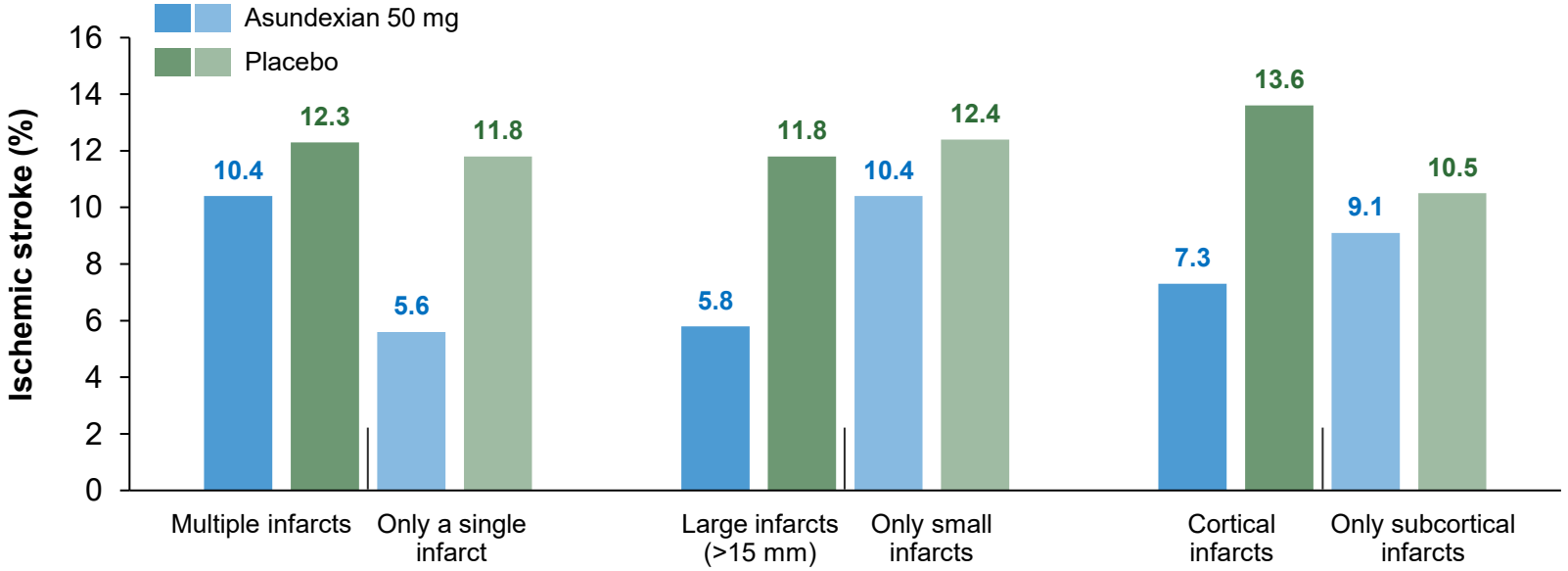

DWI+, diffusion-weighted imaging–positive; MRI, magnetic resonance imaging.

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Efficacy: Ischemic stroke

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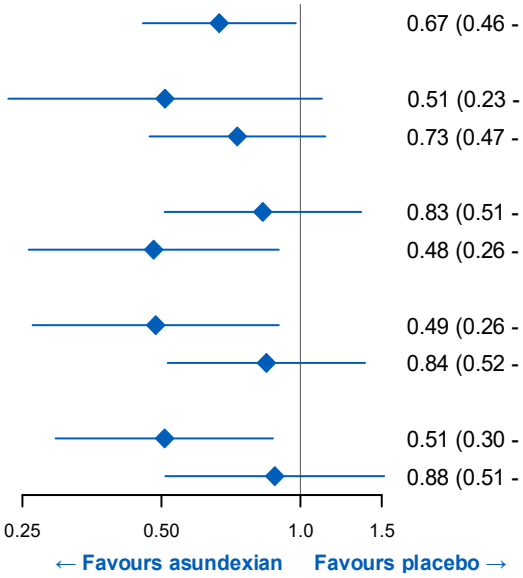
There was no heterogeneity of treatment effect of asundexian on ischemic stroke according to baseline infarct pattern

	Asundexian n/N(%)	Placebo n/N(%)	HR (95% CI)	P interaction
DWI+ population	46/563 (8.2%)	62/513 (12.1%)	0.67 (0.46 - 0.98)	
Single small subcortical DWI+ infarct	10/159 (6.3%)	17/138 (12.3%)	0.51 (0.23 - 1.11)	0.43
Multiple, large or cortical infarcts	36/404 (8.9%)	45/375 (12.0%)	0.73 (0.47 - 1.13)	
Multiple infarcts	31/297 (10.4%)	33/268 (12.3%)	0.83 (0.51 - 1.35)	0.17
Only single infarct	15/266 (5.6%)	29/245 (11.8%)	0.48 (0.26 - 0.90)	
One or more large infarcts	16/274 (5.8%)	28/238 (11.8%)	0.49 (0.26 - 0.90)	0.17
Only small infarcts	30/289 (10.4%)	34/275 (12.4%)	0.84 (0.52 - 1.38)	
One or more cortical infarcts	21/287 (7.3%)	35/257 (13.6%)	0.51 (0.30 - 0.87)	0.16
Only subcortical infarcts	25/276 (9.1%)	27/256 (10.5%)	0.88 (0.51 - 1.52)	



CI, confidence interval; csHR, cause-specific hazard ratio; DWI+, diffusion-weighted imaging–positive; HR, hazard ratio; MRI, magnetic resonance imaging.

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The efficacy across MRI infarct patterns is consistent with the results of the TOAST clinical subtypes in the main OCEANIC trial

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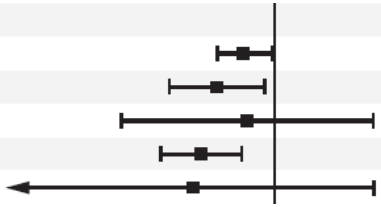
Subgroup	Asundexian	Placebo	Cause-Specific Hazard Ratio (95% CI)
	no. of events/total no. of patients (%)		
Stroke subtype			
Large-artery atherosclerosis	203/2512 (8.1)	247/2484 (9.9)	0.82 (0.68–0.98)
Small-vessel occlusion	59/1290 (4.6)	90/1349 (6.7)	0.68 (0.49–0.94)
Stroke of other determined cause	9/161 (5.6)	13/188 (6.9)	0.84 (0.36–1.96)
Stroke of undetermined cause	83/1786 (4.6)	127/1710 (7.4)	0.61 (0.46–0.81)
Cardioembolism	4/89 (4.5)	8/107 (7.5)	0.58 (0.17–1.95)

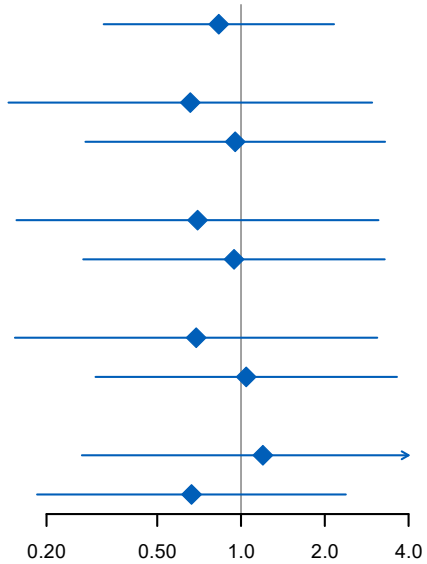


MRI, magnetic resonance imaging; TOAST, Trial of Org 10172 in Acute Stroke Treatment.
Sharma M, et al. *N Engl J Med*. 2026;394(15):1467–1479.

Safety: ISTH major bleeding

There was no heterogenicity of treatment effect of asundexian on ISTH major bleeding according to baseline infarct pattern

	Asundexian n/N(%)	Placebo n/N(%)	HR (95% CI)	P interaction
DWI+ population	8/563 (1.4%)	9/511 (1.8%)†	0.83 (0.32 - 2.16)	
Single small subcortical DWI + infarct	3/159 (1.9%)	4/138 (2.9%)	0.66 (0.15 - 2.96)	0.71
Multiple, large or cortical infarcts	5/404 (1.2%)	5/373 (1.3%)	0.95 (0.28 - 3.29)	
Multiple infarcts	3/297 (1.0%)	4/267 (1.5%)	0.70 (0.16 - 3.12)	0.77
Only single infarct	5/266 (1.9%)	5/244 (2.0%)	0.94 (0.27 - 3.28)	
One or more large infarcts	3/274 (1.1%)	4/236 (1.7%)	0.69 (0.15 - 3.09)	0.74
Only small infarcts	5/289 (1.7%)	5/275 (1.8%)	1.04 (0.30 - 3.63)	
One or more cortical infarcts	4/287 (1.4%)	3/255 (1.2%)	1.20 (0.27 - 5.36)	0.55
Only subcortical infarcts	4/276 (1.4%)	6/256 (2.3%)	0.66 (0.19 - 2.38)	



CI, confidence interval; csHR, cause-specific hazard ratio; DWI+, diffusion-weighted imaging–positive; HR, hazard ratio; ISTH, International Society on Thrombosis and Haemostasis. MRI, magnetic resonance imaging.

Three symptomatic intracranial hemorrhages in each arm

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Conclusion

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- Baseline infarct patterns in the MRI sub-study included all expected patterns, including single small subcortical strokes

- The treatment effect of asundexian was directionally consistent across baseline MRI infarct patterns, with no evidence of treatment-effect heterogeneity
  - The MRI results are consistent with, and reinforce, results of the TOAST subgroup analysis demonstrating effect of asundexian across clinical categories

- There was no increase in ISTH major bleeding across MRI infarct patterns and only two hemorrhagic stroke occurrences in each arm, despite high prevalence of hemorrhagic transformation (~30%) and microbleeds (~40%)

ISTH, International Society on Thrombosis and Haemostasis; MRI, magnetic resonance imaging; TOAST, Trial of Org 10172 in Acute Stroke Treatment.

Acknowledgments

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- This study was funded Bayer AG. Asundexian is not yet approved for use.
- Editorial support was provided by Prime Group of Companies (Knutsford, UK), funded by Bayer AG

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