Intracranial Haemorrhage in Patients With Non-Cardioembolic Ischaemic Stroke or High-Risk TIA: Insights from the OCEANIC-STROKE Randomised Trial of Asundexian for Secondary Stroke Prevention

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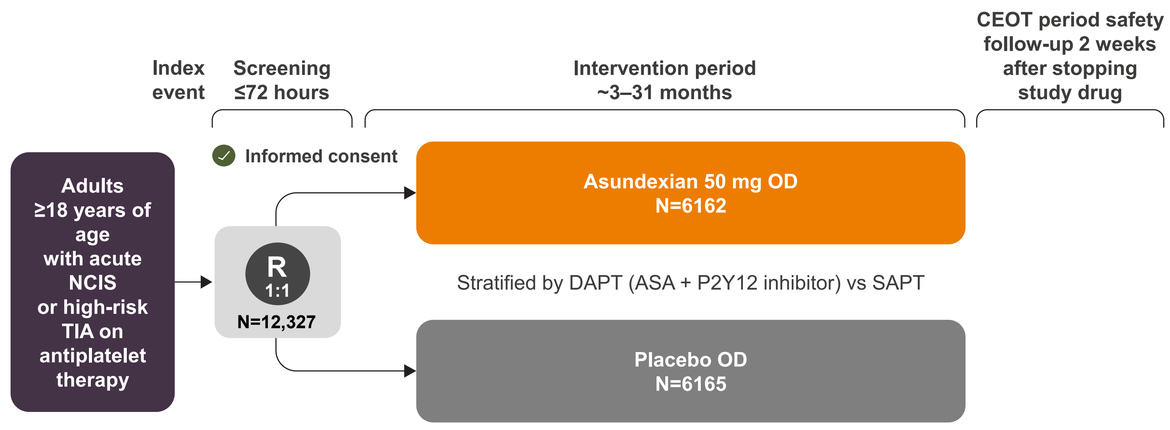
Background and Aims

- In OCEANIC-STROKE, asundexian 50 mg once daily reduced ischaemic stroke (IS) (cause-specific hazard ratio [csHR] 0.74; 95% confidence interval [CI]: 0.65, 0.84) without increasing intracranial haemorrhage (ICrH) compared with placebo.[1] We examined rates, outcomes, and predictors of ICrH and haemorrhagic stroke (HS).

Design

- We randomised 12,327 participants within 72 hours of acute non-cardioembolic IS or high-risk transient ischaemic attack (TIA) to asundexian or placebo (**Figure 1**). This analysis includes 12,254 participants who received ≥1 dose of assigned treatment. Incident ICrH was adjudicated by blinded adjudicators. ICrH outcome was assessed using the 90-day modified Rankin Scale (mRS); disabling ICrH or HS was defined as mRS ≥3 or an increase of ≥1 point if baseline mRS ≥3. Site investigators determined whether ICrH or HS was the cause of death.

Figure 1. Trial schema



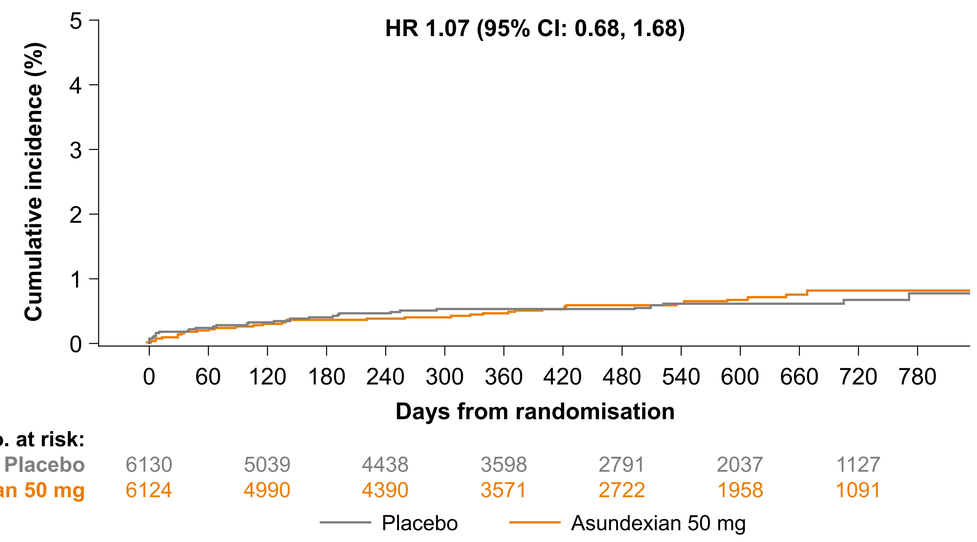
ASA, acetylsalicylic acid; CEOT, common end of treatment; DAPT, dual antiplatelet therapy; NCIS, non-cardioembolic ischaemic stroke; OD, once daily; P2Y12, purinergic receptor Y12; R, randomisation; SAPT, single antiplatelet therapy; TIA, transient ischaemic attack.

Results

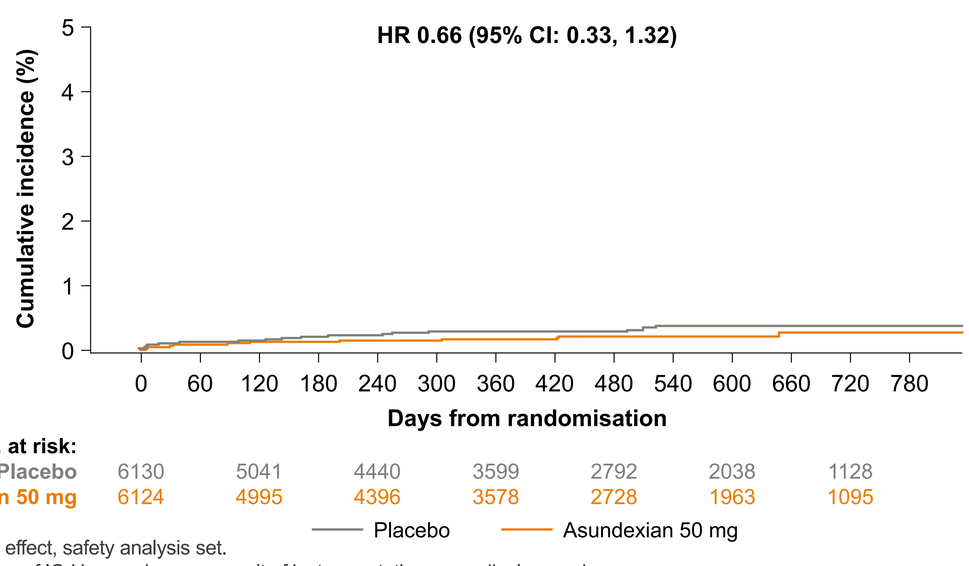
- With 1.2 years median time on treatment, 74 ICrH occurred, including 33 HS. Annualised rates of ICrH were 0.5% for both asundexian and placebo (csHR 1.07; 95% CI: 0.68, 1.68), and, for HS, were 0.2% vs 0.3% (HR 0.66; 95% CI: 0.33, 1.32), respectively (**Figure 2**). Annualised rates of disabling ICrH were 0.3% for both (HR 0.87; 95% CI: 0.46, 1.63) and were 0.2% vs 0.1% (HR 2.23; 95% CI: 0.78, 6.42) for fatal ICrH. Corresponding rates for disabling (0.1% vs 0.2%; HR 0.68; 95% CI: 0.30, 1.50) and fatal HS (0.1% vs 0.1%; HR 1.42; 95% CI: 0.45, 4.46) were low and comparable between groups.

Figure 2. Cumulative incidence of intracranial haemorrhage **(A)** and haemorrhagic stroke **(B)**

(A)



(B)

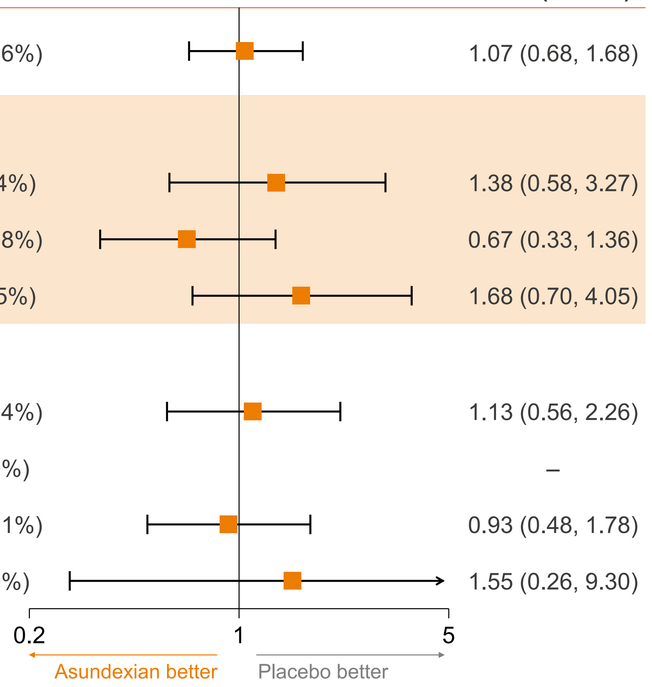


On-treatment + days effect, safety analysis set.
Data excludes 3 cases of ICrH occurring as a result of instrumentation or medical procedures.
CI, confidence interval; HR, hazard ratio; ICrH, intracranial haemorrhage.

- Older age (HR per year 1.04; 95% CI 1.02, 1.06) and Asian race (vs White race; HR 2.29; 95% CI 1.37, 3.84) independently predicted ICrH. There was no heterogeneity in the treatment effect of asundexian on the outcomes of ICrH or HS in subgroup analyses of these variables (**Figures 3 and 4**).

Figure 3. Exploratory subgroup analyses of predictors of intracranial haemorrhage

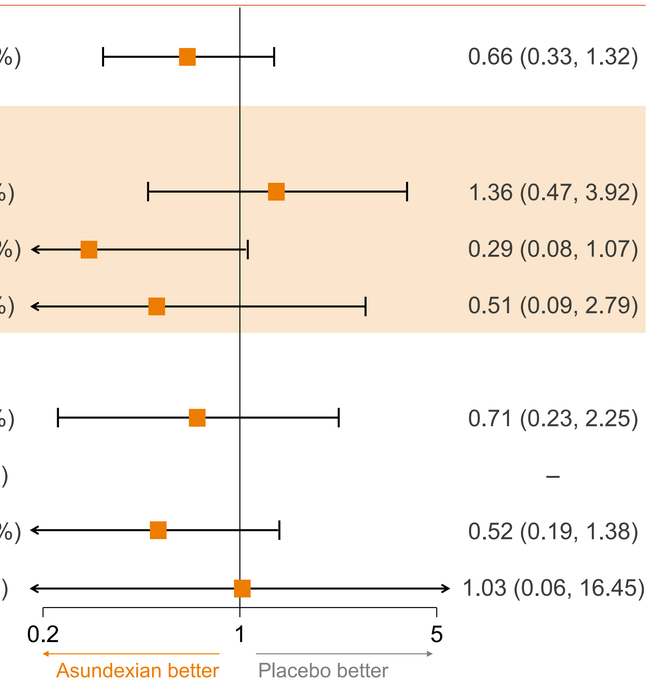
Group	Asundexian	Placebo	HR	csHR (95% CI)
Overall intracranial haemorrhage	38/6124 (0.6%)	36/6130 (0.6%)		1.07 (0.68, 1.68)
Age				
<65 years	12/2297 (0.5%)	9/2292 (0.4%)		1.38 (0.58, 3.27)
65–75 years	13/2302 (0.6%)	19/2308 (0.8%)		0.67 (0.33, 1.36)
>75 years	13/1525 (0.9%)	8/1530 (0.5%)		1.68 (0.70, 4.05)
Race				
White	17/4080 (0.4%)	15/4059 (0.4%)		1.13 (0.56, 2.26)
Black	1/143 (0.7%)	0/137 (0.0%)		–
Asian	17/1708 (1.0%)	19/1730 (1.1%)		0.93 (0.48, 1.78)
Other	3/193 (1.6%)	2/204 (1.0%)		1.55 (0.26, 9.30)



CI, confidence interval; csHR, cause-specific hazard ratio.

Figure 4. Exploratory subgroup analyses of predictors of haemorrhagic stroke

Group	Asundexian	Placebo	HR	csHR (95% CI)
Overall haemorrhagic stroke	13/6124 (0.2%)	20/6130 (0.3%)		0.66 (0.33, 1.32)
Age				
<65 years	8/2297 (0.3%)	6/2292 (0.3%)		1.36 (0.47, 3.92)
65–75 years	3/2302 (0.1%)	10/2308 (0.4%)		0.29 (0.08, 1.07)
>75 years	2/1525 (0.1%)	4/1530 (0.3%)		0.51 (0.09, 2.79)
Race				
White	5/4080 (0.1%)	7/4059 (0.2%)		0.71 (0.23, 2.25)
Black	1/143 (0.7%)	0/137 (0.0%)		–
Asian	6/1708 (0.4%)	12/1730 (0.7%)		0.52 (0.19, 1.38)
Other	1/193 (0.5%)	1/204 (0.5%)		1.03 (0.06, 16.45)



CI, confidence interval; csHR, cause-specific hazard ratio.

Conclusions

- ICrH and HS were infrequent, with similar severity and outcomes between asundexian and placebo. Asundexian is a novel stroke prevention strategy that reduces IS without apparent increases in incident, disabling or fatal ICrH, including HS.

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Reference

1. Sharma M, et al. *N Engl J Med*. 2026;394:1467–1479.

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