MORTALITY AND VASCULAR EVENTS ASSOCIATED WITH INITIAL AND RECURRENT NON-CARDIOEMBOLIC ISCHAEMIC STROKE IN REAL-WORLD SETTINGS IN JAPAN: OBSERVATIONS FROM ASTRIS

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Introduction

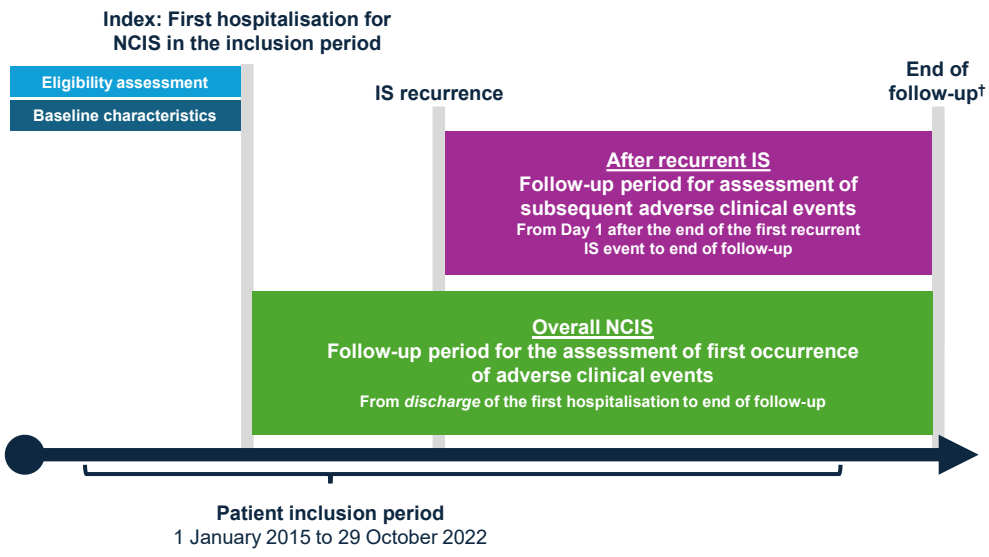
- Worldwide, latest figures show around 94 million prevalent stroke survivors and 12 million incident strokes per annum, with ischaemic stroke (IS) accounting for around two-thirds of the latter.[1]
- Recurrent stroke is common in people who survive an initial stroke, with an estimated 1-year cumulative incidence of 6.8% (95% confidence interval [CI] 5.6−8.0) and 10-year cumulative incidence of 18.0% (95% CI 16.2−19.8).[2]
- In Japan, stroke is one of the most common causes of death,[3] with overall stroke incidence higher in rural than urban communities;[4] however, the rate of recurrent IS and other clinically relevant events is not fully established among patients with non-cardioembolic IS (NCIS) in contemporary clinical settings in Japan.
- Overall, ASTRIS Japan aims to estimate the incidence rate of adverse clinical events among Japanese patients newly diagnosed and hospitalised with acute NCIS or transient ischaemic attack (TIA).
- This subanalysis aims to describe such adverse clinical events and subsequent event rates among patients included in ASTRIS Japan who experienced a first recurrent IS event.

Methods

Study design

- ASTRIS Japan is a non-interventional, retrospective cohort study using a Japanese nationwide electronic medical record (EMR) database maintained by Real-World Data, Co. Ltd, including data from >200 hospitals.
- Included patients were aged ≥18 years with a first hospitalisation for NCIS between 1 January 2015 and 29 October 2022; they were followed from the date of discharge until the earliest of death, end of observability, or end of study period (29 October 2023).
  - Patients with prior occurrence of IS or TIA were excluded.
- The subcohort experiencing a first recurrent IS during follow-up was identified and followed from Day 1 after the end of this event (**Figure 1**).

Figure 1. Design of the ASTRIS Japan study



†Patients were followed until the earliest occurrence of death, end of observability, or end of study period.
All event rates were censored upon the earliest occurrence of IS or death, end of data collection period (29 October 2023), or end of study period. Follow-up time does not consider IS recurrence as a censoring criterion.
IS, ischaemic stroke; NCIS, non-cardioembolic ischaemic stroke.

Statistical analysis

- Descriptive analyses were conducted using summary statistics for continuous and categorical data.

Results

Participants

- A total of 17,869 patients hospitalised for IS were included in the analysis (**Table 1**).
  - Mean age was 74.6 years (standard deviation 12.3) and 44.1% were female.
  - Median (quartile 1, quartile 3) duration of index hospitalization was 17 (10, 32) days.
- For index IS event management: 12,193 (72.3%) received antiplatelet therapy with 61.6% on single therapy, 24.2% on dual therapy, and 1.1% on triple therapy (**Table 1**).

Conclusions

- The rate of adverse clinical events was high after a first NCIS event and substantially higher following a first recurrent IS.
- These findings highlight the need for effective secondary stroke prevention strategies.
- Limitations of this study include:
  - The population was identified based on EMR data and hospital claims without chart review
  - Data are limited by the lack of ability to track IS recurrence prior to hospital discharge
  - Outpatient deaths were only recorded if they were reported in the EMR, so the all-cause mortality rate may be underestimated
  - Associations found in observational studies cannot be directly considered as having a causal relationship.

Table 1. Clinical characteristics and index event management

	All IS (index event) (N=17,869)
Age, years	
Mean (SD)	74.6 (12.3)
Median (Q1, Q3)	77 (68, 84)
Female sex, n (%)	7888 (44.1)
Smoker, n (%)	4509 (25.2)
Japan coma scale at admission, n (%)	
0 – alert	9354 (52.3)
I – awake without stimuli	4514 (25.3)
II – arousable with some stimuli	653 (3.7)
III – unarousable by any forceful stimuli	350 (2.0)
Missing	2998 (16.8)
Comorbidities, n (%)	
Hypertension	12,193 (68.2)
Chronic kidney disease	5571 (31.2)
Diabetes	4935 (27.6)
Coronary artery disease	3995 (22.4)
Heart failure	3649 (20.4)
Cancer	3506 (19.6)
Dementia	2510 (14.0)
Dysphagia	2211 (12.4)
Anaemia	2103 (11.8)
Carotid stenosis or previous carotid revascularisation	1226 (6.9)
Myocardial infarction	753 (4.2)
Peripheral artery disease	466 (2.6)
Premedication, n (%)	
Antihypertensives	6107 (34.2)
Lipid-lowering drugs	3534 (19.8)
Statins	3153 (17.6)
Anti-diabetic medications	2462 (13.8)
Index event management,† n (%)	
Argatroban	3365 (18.8)
Ozagrel	3325 (18.6)
Heparin/low molecular weight heparin	6015 (33.7)
Antiplatelet therapy within 2 days of admission	8512 (47.6)
Edaravone	5372 (30.1)
Osmotherapy	545 (3.0)
Mechanical thrombectomy	153 (0.9)
Intra-artery revascularisation	216 (1.2)
Recombinant tissue-type plasminogen activator	436 (2.4)
Rehabilitation therapy	9464 (53.0)
Antithrombotic medication,† n (%)	
Any antiplatelet therapy	12,193 (72.3)
Single antiplatelet therapy	11,012 (61.6)
Aspirin	5902 (33.0)
Clopidogrel	3687 (20.6)
Prasugrel	40 (0.2)
Cilostazol	2026 (11.3)
Dual antiplatelet therapy	4319 (24.2)
Aspirin + clopidogrel	3054 (17.1)
Aspirin + prasugrel	186 (1.0)
Aspirin + cilostazol	774 (4.3)
Clopidogrel + cilostazol	477 (2.7)
Prasugrel + cilostazol	10 (0.1)
Triple antiplatelet therapy	193 (1.1)
Aspirin + clopidogrel + cilostazol	187 (1.0)
Aspirin + prasugrel + cilostazol	6 (0)
Apixaban	270 (1.5)
Dabigatran	19 (0.1)
Edoxaban	434 (2.4)
Rivaroxaban	144 (0.8)
Warfarin	534 (3.0)

†Assessed during the index hospitalisation.
Q, quartile; SD, standard deviation.

Mortality and clinical events

- Relative to patients with initial NCIS, higher rates of adverse clinical events were observed in the subcohort with a first recurrent IS (n=3081; **Table 2**).
- The respective rates (events per 1000 person-years [95% CI]) of recurrent IS in patients with initial NCIS and the subcohort with a first recurrent IS during follow-up were 107.2 (103.5−110.8) and 199.9 (186.6−213.1).
- The respective median (quartile 1, quartile 3) times to death for patients with an initial IS and first recurrent IS were 366 (100.5, 914.0) and 255 (72.3, 563.8) days.

Table 2. Mortality and clinical events across follow-up in patients with NCIS†

	All IS (index event) (N=17,869)	First recurrent IS during follow-up period (n=3081)
Follow-up time, days		
Mean (SD)	754.0 (765.4)	693.8 (664.6)
Median (Q1, Q3)	517 (64.0, 1241.5)	504 (120.0, 1091.5)
All stroke		
Patients with event‡, n (%)	3470 (19.4)	916 (29.7)
Incidence rate§ per 1000 P-Y (95% CI) – overall follow-up	113.7 (109.9–117.5)	210.6 (196.9–224.2)
IS		
Patients with event‡, n (%)	3292 (18.4)	877 (28.5)
Incidence rate§ per 1000 P-Y (95% CI) – overall follow-up	107.2 (103.5–110.8)	199.9 (186.6–213.1)
Haemorrhagic stroke		
Patients with event‡, n (%)	304 (1.7)	68 (2.2)
Incidence rate§ per 1000 P-Y (95% CI) – overall follow-up	10.0 (8.8–11.1)	15.6 (11.9–19.4)
Cardiac event – MI/unstable angina pectoris		
Patients with event‡, n (%)	654 (3.7)	164 (5.3)
Incidence rate§ per 1000 P-Y (95% CI) – overall follow-up	22.2 (20.5–23.9)	39.6 (33.5–45.6)
Newly diagnosed atrial fibrillation		
Patients with event‡, n (%)	669 (3.7)	216 (7.0)
Incidence rate§ per 1000 P-Y (95% CI) – overall follow-up	22.4 (20.7–24.1)	52.7 (45.7–59.8)
Major bleeding‖		
Patients with event‡, n (%)	1764 (9.9)	403 (13.1)
Incidence rate§ per 1000 P-Y (95% CI) – overall follow-up	60.3 (57.5–63.1)	96.5 (87.1–105.9)
All-cause death¶		
Patients with event‡, n (%)	1049 (5.9)	234 (7.6)
Incidence rate§ per 1000 P-Y (95% CI) – overall follow-up	34.2 (32.1–36.2)	53.3 (46.5–60.2)

†An index stroke event was defined as NCIS if the patient had no history of atrial fibrillation prior to, or within 15 days from, hospitalisation for IS and had not received oral anticoagulant therapy within 90 days before hospitalisation for IS unless they had a record of either deep vein thrombosis/pulmonary embolism or hip/knee surgery.
‡Number of patients with an event across the total follow-up period, starting from the day after discharge until death, end of observability, or end of data-collection period (29 October 2023).
§Incidence rates reflect the first event occurring during follow-up and not necessarily the first ever event in the patient's medical history. Follow-up time was censored upon the earliest of event occurrence, death, end of observability, end of the assessment period (365 days after discharge – applicable only for up to 12-month estimates), or end of data collection period (29 October 2023).
‖Major bleeding was defined by the Cunningham algorithm as any electronic medical record, disease claim information, or discharge summary data with at least one diagnosis code within a hospital admission with a definite/main flag.
¶All-cause death reflects inpatient deaths. Outpatient deaths are only recorded if reported in the electronic medical record. Thus, all-cause mortality rate may be underestimated.
All event rates are censored upon the earliest occurrence of IS recurrence, death, end of data-collection period (29 October 2023), or the end of the study period. Follow-up time does not consider IS recurrence as a censoring criterion.
CI, confidence interval; IS, ischaemic stroke; MI, myocardial infarction; NCIS, non-cardioembolic ischaemic stroke; P-Y, person-year; Q, quartile; SD, standard deviation.

References

1. Feigin VL et al. *Lancet Neurol*. 2024;23:973–1003.
2. Berghout BP et al. *Lancet Reg Health Eur*. 2023;30:100651.
3. World Health Organisation. Data: Japan. Available a: https://data.who.int/countries/392. Accessed 17 Sept, 2025.
4. Li J et al. *Int J Stroke*. 2022;18:657–662.

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Conflicts of interest / disclosures

TH has received honoraria from Bayer, Daiichi Sankyo, and Pfizer. **RM** declares no conflicts of interest. **SO** is an employee of Bayer Yakuhin and may own shares or share options in the company. **CL** is an employee of Aetion Inc and holds share options in the company. **DY** is an employee of Aetion Iberia. **LB** is an employee of Bayer AG and may own shares or share options in the company. **JX** is an employee of Bayer, Inc. and may own shares or share options in the company. **KK** is an employee of Bayer Hispania, S.L.U. and may own shares or share options in the company. **MS** has received research funding and consulted for Bayer, Janssen, BMS, AstraZeneca, Novartis and Alexion.

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