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Present learnings from RCTs in ESUS patients

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Stroke

- More than 10 million strokes per year worldwide
- Second most common cause of death worldwide
- Third most common cause of disability
- About 80% of all strokes are ischemic strokes
- Etiology of ischemic stroke is classified according to TOAST criteria

Etiology of ischemic stroke (according to TOAST)

Large-artery atherosclerosis

Small-vessel occlusion

Cardioembolism

Stroke of determined etiology

Stroke of undetermined etiology (so called “cryptogenic” stroke)

- Two or more causes identified or
- Incomplete diagnostic evaluation
- Negative diagnostic evaluation
- ~ 25 % of all ischemic strokes
- Average recurrent stroke rate of 3-6% per year
- First episode of atrial fibrillation in up to 30% within 3 years

Anticoagulation in non-cardioembolic stroke

... does not provide a benefit in secondary stroke prevention:

WARSS

R

Acetylsalicylic acid (325 mg per day)

Double-blind, Randomisation 1:1
Follow-up 2 years

Warfarin (INR 1.4 - 2.8)

ESPRIT

R

Acetylsalicylic acid (30-325 mg per day)

Double-blind, Randomisation 1:1
Follow-up 4.6 ± 2.2 years

Warfarin (INR 2 - 3)

Embolic Stroke of Undetermined Source

Embolic stroke of undetermined source (ESUS) criteria

- Non-lacunar stroke detected by CT or MRI
- No $\geq 50\%$ stenosis in arteries supplying area of ischaemia
- No major-risk cardioembolic source of embolism (TOAST)
- No other determined cause of stroke

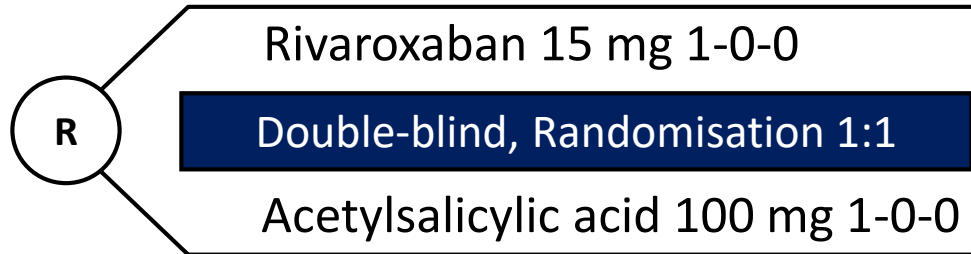
ESUS: Proposed diagnostic assessment

- Brain CT or MRI
- 12-lead ECG & cardiac monitoring for ≥ 24 hours
- (Precordial) echocardiography
- Imaging of extra- & intracranial arteries

Randomized controlled trials in ESUS patients

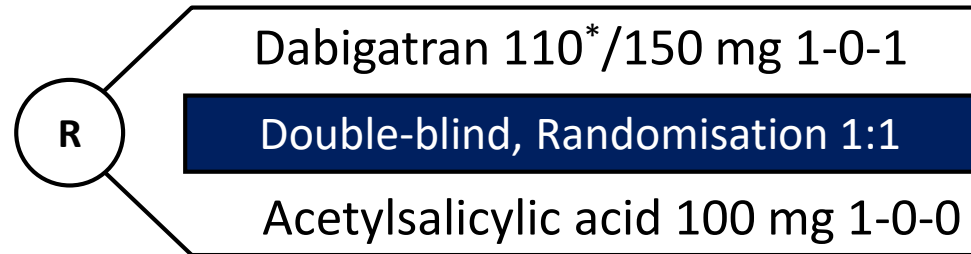
NAVIGATE ESUS

*(early terminated;
published)*



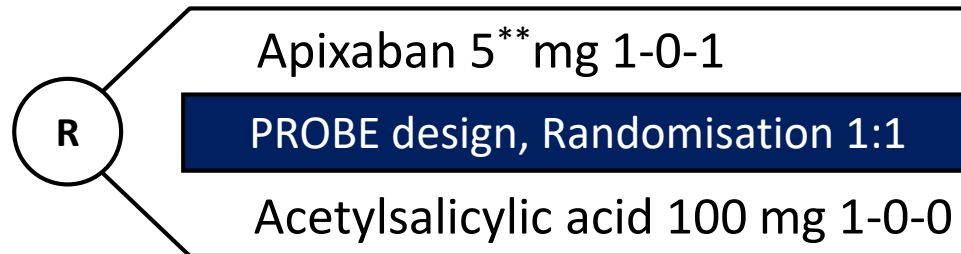
RE-SPECT ESUS

*(presented WSC 2018;
not published)*



ATTICUS

(recruiting)



* ≥ 75 years OR eGFR 30-50 mL/min/1.73 m²; **2.5 mg if GFR 15-30 mL/min/1.73 m² OR 2 of the following criteria: KG \leq 60kg, \geq 80 years, creatinine \geq 1.5 mg/dl
Diener et al. *Int J Stroke*, 2015; Hart et al. *European Stroke Journal* 2016; Geisler et al. *Int J Stroke*, 2016; Hart et al. *NEJM* 2018

Present learnings from ESUS RCTs

- Embolic stroke of undetermined source (ESUS)
 - Definition is defining a *basic* diagnostic standard
 - Secondary stroke prevention: no benefit of rivaroxaban 15 mg OD vs. ASA 100 mg OD in NAVIGATE ESUS
 - Increased bleeding risk of rivaroxaban 15 mg OD vs. ASA 100 mg OD in the NAVIGATE ESUS trial
- Stroke prevention after ESUS: ASA 100 mg OD
- More detailed characterization of ESUS is needed
- Consider ECG monitoring ≥ 72 hours after ESUS