

## **SUPPLEMENTAL MATERIAL**

### **Outcomes with Endovascular Treatment of patients with M2 segment Middle Cerebral Artery Occlusion in The Late Time Window**

STROBE checklist

Supplemental table I-III

STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation	Page No
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	1
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up  (b) For matched studies, give matching criteria and number of exposed and unexposed	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-5
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	NA
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding  (b) Describe any methods used to examine subgroups and interactions  (c) Explain how missing data were addressed  (d) If applicable, explain how loss to follow-up was addressed  (e) Describe any sensitivity analyses	5

<b>Results</b>				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed  (b) Give reasons for non-participation at each stage  (c) Consider use of a flow diagram		6
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders  (b) Indicate number of participants with missing data for each variable of interest  (c) Summarise follow-up time (eg, average and total amount)		6-7
Outcome data	15*	Report numbers of outcome events or summary measures over time		6-7

**Supplement Table I.** Characteristics of included studies

Study	Italian Registry	Prove-It	ESCAPE/ ESCAPE-NA1	Beaumont Hospital Registry	Acute STroke Registry and Analysis of Lausanne (ASTRAL)	SNUBH	Stroke registry of Turku University Hospital
Type of study	Multicenter cohort	Multicenter cohort	Randomized controlled trial	Monocenter cohort	Monocenter cohort	Multicenter cohort	Monocenter cohort
<i>Population</i>							
Country	Italy	North America, Europe, East Asia	North America, Europe, East Asia	Dublin, Ireland	Lausanne, Switzerland	Korea	Finland
Sample size	139	24	ESCAPE: 18 ESCAPE -NA1(control arm): 74	141	35	18	12
Wake-up vs Witnessed	Available	Available	Available	Available	Available	Available	Available
Inclusion	Onset to imaging>360 minutes	Onset to imaging>360 minutes	Onset to imaging>360 minutes	Onset to imaging>360 minutes	Onset to imaging>360 minutes	Onset to imaging>360 minutes	Onset to imaging>360 minutes
<b>Imaging Criteria Availability</b>							
NCCT ASPECTS	All patients	All patients	All patients	All patients	All patients	All patients	All patients
Collateral assessment modality	sCTA in 87 mCTA in 52	mCTA in all	ESCAPE: all mCTA ESCAPE -NA1: sCTA: 18, mCTA: 56	sCTA in 14 mCTA in 127	sCTA in all	mCTA in all	sCTA in all
Collateral scoring	<u>sCTA</u> : 4-point scale poor (scores, 0–1)	moderate–good collateral grade defined as ≥50% filling of the	ESCAPE: 10-point scale. Moderate–good collateral grade was defined as ≥50% filling	moderate–good collateral grade defined	Graded based on the Tan score.	moderate–good collateral grade defined as ≥50% filling of the MCA	moderate–good collateral grade defined as ≥50% filling of the MCA

	and good (scores, 2–3),  <u>mCTA</u> : 6-point scale poor (grade, 0–3) and good (scores, 4–5)	MCA pial arterial circulation	of the MCA pial arterial circulation  ESCAPE-NA1: good, moderate, or poor	as ≥50% filling of the MCA pial arterial circulation	0=absent; 1=filling <50% of the occluded territory; 2=filling 50%-99% of the occluded territory; 3=filling 100% of the occluded territory; 4=exuberant filling; 5=not applicable (no prox. Occlusion)  Good = Score >1	pial arterial circulation	pial arterial circulation
<b>Occlusion Site</b>	ICA M1 M2 (tandem occlusion specified)	ICA M1 M2 (tandem occlusion specified)	ICA M1 M2 (tandem occlusion specified)	ICA M1 M2 (tandem occlusion specified)	ICA M1 M2 (tandem occlusion specified)	ICA M1 M2 (tandem occlusion specified)	M2 (tandem occlusion specified)
<b>CTP assessment</b>	All patients  Mismatch (Y/N): core ≤50% of hypoperfusion extent or < 33% of the MCA territory according to Turk et al	21	ESCAPE: 18 ESCAPE-NA1: 40	37	29	18	4
<b>Core definition</b>	CBV <2.0 mL/100 g		relative CBF threshold volume, defined as Tmax>12.5	N/A	CBV <2.0 mL/100 g	rCBF <30% compared to the contralateral	N/A

		relative CBF threshold volume, defined as Tmax>12.5				hemisphere (RAPID) rCBV <30% and DT >2 sec (OLEA)	
<b>Penumbra definition</b>	MTT >145% of the contralateral side value	Tmax>9	Tmax>9	N/A	MTT >145% of the contralateral side value	Tmax >6 sec (both RAPID and OLEA)	N/A
<b>Clinical Criteria</b>							
<b>Age</b>	All patients						
<b>Baseline Stroke Severity (NIHSS)</b>	All patients						
<b>Time metrics</b>	Onset to: presentation, to imaging, to puncture, to reperfusion (all)						
<b>Intravenous Alteplase</b>	0 patient	0 patient	ESCAPE: 4 patients ESCAPE-NA1: 10 patients	10 patients	17 patients	0 patient	5 patients
<b>Reperfusion</b>	2b-3 vs not	2b-3 vs not	ESCAPE: mTICI scores ESCAPE-NA1: eTICI scores	eTICI scores	mTICI scores	2b-3 vs not	2b-3 vs not
<b>Outcomes</b>	Symptomatic intracranial hemorrhage (binary) and 90-day mRS scores for all						

1. Prove-IT clinical study (ClinicalTrials.gov Identifier: NCT02184936)
2. ESCAPE randomized controlled trial (ClinicalTrials.gov Identifier: NCT01778335)
3. ESCAPE NA1 randomized controlled trial (ClinicalTrials.gov Identifier: NCT02930018)

**Supplement Table II.** Baseline demographics and outcomes in patients with M2 occlusion stratified by whether they achieved successful reperfusion (eTICI 2b-3).

Characteristic	Final eTICI <2b (n=16)	Final eTICI ≥2b (n=78)	P value
Age, year	76 (69-81)	74 (60-82)	0.58
Female sex	8 (50.0)	43 (55.1)	0.78
<b>Stroke presentation</b>			
Wakeup stroke	5 (33.3)	44 (56.4)	0.16
Baseline NIHSS	18 (9-20)	10 (7-15)	0.05
Tandem cervical occlusion	2 (12.5)	8 (10.3)	0.68
IV Alteplase	3 (18.7)	9 (11.5)	0.42
<b>Time metrics, minutes</b>			
Time from onset to ED door	397 (350-645)	590 (395-738)	0.06
Time from onset to CT scan	450 (398-679)	608 (608-750)	0.09
Time from onset to puncture	530 (445- 787)	720 (514- 900)	0.11
Time from onset to reperfusion	540 (511- 663)	762 (586-968)	<b>0.03</b>
Time from ED door to CT scan	32 (21-40)	26 (15-40)	0.29
Time from CT to puncture	60 (43-118)	75 (36-112)	0.92
Time from ED door to puncture	105 (89-150)	93 (62-131)	0.31
Time from puncture to reperfusion	55 (45-94)	39 (26-60)	<b>0.03</b>
Time from ED door to reperfusion	183 (135-209)	139 (106-185)	0.08
<b>Imaging factors</b>			
ASPECTS	8 (7-9)	10 (8-10)	<b>0.01</b>

ASPECTS: Alberta Stroke Program Early CT Score, CTA: computed tomography angiography, ED: emergency department, ICA: internal carotid artery, MCA: middle cerebral artery, NIHSS: National Institutes of Health Stroke Scale.

Values are expressed as median (interquartile range (IQR)) or n (%).

Significantly results are marked in bold.

**Supplement Table III. Univariable and multivariable logistic regressions for the prediction of functional independence (mRS 0-2) at 90 days in M2 occlusion patients.**

Variable	Univariable analysis		Multivariable analysis	
	Unadjusted OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Age	0.93 (0.89- 0.97)	0.001	0.93 (0.87- 0.99)	0.03
Female sex	1.00 (0.43- 2.38)	0.99	0.80 (0.18- 3.45)	0.77
Baseline NIHSS score	0.88 (0.82- 0.95)	0.003	0.88 (0.83- 0.93)	0.02
Time from onset to reperfusion	0.99 (0.98- 1.00)	0.052	0.99 (0.99- 1.00)	0.01
Final TIC1 2b-3	3.20 (0.97- 10.52)	0.06	2.84 (1.11- 7.29)	0.03

NIHSS: National Institutes of Health Stroke Scale. aOR: adjusted odds ratio. mRS: modified Rankin scale, TIC1: Thrombolysis in cerebral infarction