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Technique and impact on first pass effect primary results of the ASSIST global registry

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ABSTRACT

Background Patients treated with mechanical thrombectomy (MT) for acute ischemic strokes from large vessel occlusion (LVO) have better outcomes with effective reperfusion. However, it is unknown which technique leads to better technical and clinical success. We aimed to determine which technique yields the most effective first pass reperfusion during MT.

Methods In a prospective, multicenter global registry we enrolled patients treated with operator preferred MT technique at 71 hospitals from January 2019 to January 2022. Three techniques were assessed: SR Classic with stent retriever (SR) and balloon guide catheter (BGC); SR Combination which employed SR with contact aspiration with or without BGC; and direct aspiration (DA) with or without BGC. The primary outcome was achieving an expanded Thrombolysis In Cerebral Infarction (eTICI) score of 2c or 3 on the first pass, with the primary technique as adjudicated by core lab. The primary clinical outcome measure was a 90-day modified Rankin Scale (mRS) score of 0–2.

Results A total of 1492 patients were enrolled. Patients treated with SR Classic or SR Combination were more likely to achieve first pass eTICI 2c or 3 reperfusion (P=0.01). There was no significant difference in mRS 0–2 (P=0.46) or safety endpoints.

Conclusions The use of SR Classic or SR Combination was more likely to achieve first pass eTICI 2c or 3 reperfusion. There were no significant differences in clinical outcomes and safety endpoints.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ The three randomized trials, ASTER, ASTER-2 and COMPASS, were designed to assess if there was a difference in stent retrievers (SRs) to aspiration alone or with combination therapy. The studies included bail outs as part of the primary endpoints, thus making it difficult to ascertain if there is a difference in technical and clinical outcomes with the primary technique.

WHAT THIS STUDY ADDS

⇒ By using first pass reperfusion success as a primary endpoint, the ASSIST Registry is assessing the success of the technique in the hands of operators employing their primary technique in the real world as it segments technical outcomes more effectively as the primary aim of an ideal device or technique.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The current study demonstrates the SR Classic technique leads to a higher rate of first pass effect compared with aspiration techniques. A regression analysis was performed based on patients with a complete dataset. The SR Classic arm demonstrated better 90-day outcomes which allows for future research to confirm this critical finding as it would impact clinical care and technological development.

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INTRODUCTION

The publication of several clinical trials demonstrating superior outcomes for patients receiving mechanical thrombectomy (MT) for acute ischemic strokes (AIS) due to large vessel occlusion (LVO) has dramatically improved outcomes for patients.[1] Unfortunately, only 26.9% of treated patients achieved a modified Rankin Score (mRS) of 0–1 and 46% an mRS of 0–2 at 90-day follow-up in a meta-analysis of five randomized controlled trials.[1] Successful reperfusion is critical to achieving good clinical outcomes, as a higher degree of reperfusion is linked to improved neurological recovery. The expanded Thrombolysis In Cerebral Infarction (eTICI) score segments outcomes based on seven distinct grades.[2] An eTICI 2c or 3 score where >90% of the territory has undergone successful reperfusion is associated with a good 90-day mRS outcome (56.9% and 68.2%, respectively). First pass eTICI 3 score is a potential marker of measuring efficient procedural success,[3] and an excellent tool to compare techniques. There are several MT techniques currently employed to achieve successful reperfusion, but it is unclear whether one is superior in AIS treatment.[4–6]

Current techniques include the use of a stent retriever (SR) with a balloon guide catheter (BGC),[7] a combination of contact aspiration with an SR,[8 9] and direct aspiration (DA) alone.[10] Although each technique is commonly employed, there is limited evidence regarding which is the most effective first line strategy. The ASSIST Registry was designed as a multicenter global study in a real-world scenario to assess which technique will yield the highest rate of first pass eTICI 2c or 3.

METHODS

Study design and participants

The ASSIST Registry is a prospective, global, multicenter registry of anterior circulation AIS patients with an LVO who have undergone treatment with one of the interventional techniques using Stryker Neurovascular devices for the first pass in treating a target occlusion. The protocol allowed for enrollment of 1500 patients at up to 100 clinical sites globally. Seventy-one sites in 11 countries participated in the registry to enroll 1492 patients (online supplemental table 1). The institutional review boards and ethics committees at each site provided written approval of the study before recruitment of subjects into the registry. Each site was required to complete a qualification survey to determine the primary technique employed and ensure operator experience. This study is registered at Clinicaltrials.gov (number NCT03845491). The authors wrote this manuscript according to the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) cohort reporting guidelines.

For inclusion in the registry, patients must have experienced AIS with occlusion in an intracranial anterior circulation vessel. The intended treatment must be one of the pre-defined techniques using Stryker Neurovascular market-released products, the patient or legally authorized representative has signed an informed consent before or within 48 hours post-procedure, and the patient is willing to comply with the protocol follow-up requirements. Patients participating in another device trial or another clinical trial where the study procedure or treatment might confound this study's endpoint were not eligible.

The registry collected data on the following devices (including but not limited to): the AXS Infinity LS Long Sheath, the AXS Infinity LS Plus Long Sheath, the FlowGate[2] and Merci BGC, the AXS Catalyst Distal Access Catheters (DAC), the AXS Vecta Aspiration Catheters, the Trevo Retriever, and the Medela Dominant Flex pump.

On March 29, 2019, protocol amendment AB was approved by the steering committee to increase enrollment in the DA arm to allow for larger bore catheters given contemporaneous advances. Thus, a total of 397 patients were enrolled with AXS Catalyst 7, Vecta 71, and Vecta 74 in the DA arm.

Procedures

After initial clinical and radiographic evaluation, patients deemed candidates for MT had a diagnostic angiogram performed on the target vessel to confirm the site of occlusion. The first technique employed was considered intention to treat with the primary technique. The procedure was completed after either successful reperfusion or an inability to recanalize the occluded cerebral vessel as per standard institutional protocols at each site. Data collected included but were not limited to demographics, pretreatment neurological assessment and radiographic parameters, technique used for each pass, clot location, angiographic imaging of each pass, and eTICI scores after each pass and final pass. Sites were requested to submit all de-identified angiographic data for enrolled subjects. Physicians were instructed to use each device according to the intended use statement and per local regulatory approval. The procedural techniques evaluated were SR Classic, SR Combination, and DA. SR Classic combines a BGC and retrieval with the Trevo Retriever. SR Combination involves using DA, which may include a pump, applied at the clot in conjunction with proximal flow control and an SR. DA involves aspiration through the aspiration catheter, either BGC or long sheath, and may include a pump.

An independent core lab assessed the baseline non-contrast CT imaging as well as the 24 hour post-treatment CT or MRI for the type of hemorrhagic complication if present. Qualifying initial diagnostic angiography of the target vessel was also analyzed for the initial site of occlusion and reperfusion grades after each pass and final pass. The sponsor Stryker Neurovascular was responsible for data management, operations, and monitoring of each site enrolling patients in the registry.

Primary procedural endpoint

The primary procedural outcome was the proportion of patients achieving an eTICI score[2] of 2c or 3 on the first pass with the primary technique as adjudicated by the independent core lab.

Primary clinical endpoint

The primary clinical outcome measure was the proportion of patients achieving a 90-day mRS score of 0–2 which was collected by certified personnel at the centers performing the procedures.

Secondary endpoints

Secondary procedural outcomes included an adjusted analysis of patients achieving successful reperfusion on first pass. Other procedural outcomes included eTICI scores after primary technique used, and the end of the endovascular procedure, time since groin puncture to achieve eTICI scores on first pass, and overall time from groin puncture to achieve eTICI 2c or 3 and final reperfusion. Secondary clinical outcomes included an adjusted analysis for patients achieving a 90-day mRS of 0–2, excellent functional outcome of mRS 0–1 at 90 days, as well as an early response at discharge or post-procedure day 5–7, whichever came first. This was defined as a National Institutes of Health Stroke Scale (NIHSS) drop of ≥10 points from baseline or an NIHSS score of 0 or 1.

Safety endpoints

Safety outcomes included all-cause and stroke related mortality and device and/or procedure related serious adverse events (SAEs) during the study period. Additional outcomes included neurological deterioration at up to 48 hours (defined as an NIHSS increase ≥4 points from baseline), symptomatic intracranial hemorrhage adapted from the European Cooperative Acute Stroke Study (ECASS III),[11] and embolization to new territory as adjudicated by core lab. Adverse events, including SAEs, were collected from the start of the procedure to 90 days (online supplemental Table S2 and Table S3).

Statistical analysis

Sample size considerations for the study were driven around having an adequate number of subjects to compare the rate of 90-day mRS 0–2 between any two technique arms. An overall rate of 50% for 90-day mRS 0–2 was assumed for the study, consistent with that observed in the TREVO Registry and a pooled analysis.[1 12 13] Assuming intra-site correlation of 0.15 and using the normal approximation to the binomial and two-sided

α of 0.05, a sample size of 1500 patients provides 82% power for detecting a 13% difference in the rate of 90-day mRS 0–2 (50% vs 37%) between any two technique arms.

Enrollment caps were instituted per technique to have more uniform subject enrollment and help mitigate the effect between physician and technique. Sites could enroll up to 45 patients in a single technique arm, and with sponsor permission, could enroll more. Enrollment caps per technique were 250 SR Classic, 700 SR Combination, and 550 DA.

All analyses comparing technique arms accounted for clustering within site, with the exception of the Kaplan-Meier analyses. Generalized linear mixed models with a random effect were used for continuous variables, and χ^2 tests adjusted for clustering were used for categorical variables.

Separate logistic regression models were performed for the primary procedural (eTICI 2c or 3 on first pass) and primary clinical (mRS 0–2 at 90 days) outcomes. Variables in the model were selected a priori based on the literature. Technique arm, age, baseline NIHSS, baseline Alberta Stroke Program Early CT Score (ASPECTS), history of atrial fibrillation, clot location, time last known normal to groin puncture, and intravenous tissue plasminogen activator (IV tPA) were candidate variables in the procedural outcome model. Technique arm, age, history of atrial fibrillation, baseline NIHSS, baseline ASPECTS, clot location, eTICI ≥2c on first pass, eTICI ≥2b at end of procedure, anesthesia, blood glucose, IV tPA, and time last known normal to end of procedure were candidate variables in the clinical outcome model. Variables that were significant (P<0.05) in univariate analyses were candidate variables for the multivariable model. The technique arm variable was forced into the model. Backward selection was then carried out until all variables in the model other than the technique arm were significant at P<0.05. Models were adjusted for clustering within sites.

A Kaplan-Meier curve was generated to visualize failure to achieve eTICI 2c or 3 using the primary technique across technique arms, censoring for achievement of eTICI 2c or 3.

P<0.05 was considered statistically significant. All analyses were performed using SAS 9.4 (SAS Institute Inc, Cary, NC).

RESULTS

A total of 1492 patients were enrolled in the study, with 247 (16.6%) patients in the SR Classic arm, 697 (46.7%) patients in the SR Combination arm, and 548 (36.7%) in the DA arm (online supplemental Figure S1). The mean age of the entire population was 70.4±14.3 years, the median NIHSS was 14 (IQR 9–19), and 559 (37.5%) patients received intravenous thrombolytics before thrombectomy. Table 1 and online supplemental Tables S4 and S5 report the baseline demographic and procedural characteristics of patients enrolled in the study. Patients treated with DA alone were younger, more likely to harbor an intracranial internal carotid artery occlusion, presented with a lower baseline ASPECTS, and were more likely to present with a right-side intracranial occlusion.

Primary procedural endpoint

Patients treated with SR Classic or SR Combination had a significantly higher rate of eTICI 2c or 3 after the first pass compared with DA alone (table 2). Operators using the SR Classic technique achieved eTICI 2c or greater first pass reperfusion in 47.2% of patients compared with 45.4% for SR combination and 36.5% for DA (P=0.01).

Primary clinical endpoint

There was no significant difference in 90-day mRS 0–2 among the three techniques (P=0.46) (table 2).

Secondary endpoints

A significantly higher proportion of patients achieved an eTICI 2c or 3 grade with SR Classic or SR Combination compared with DA before bail out or completion of the procedure (table 2). For all techniques, bail out is defined as switching to another technique for treatment of target occlusion, or to a procedural intervention other than treatment of target occlusion to improve eTICI. Bail out rate was 11.3% for SR Classic, 10.7% for SR Combination, and 37.0% for DA. The SR Classic technique achieved eTICI 2c or 3 64.9% of the time, SR Combination 60.9%, and DA 46.4% of procedures (P<0.0001). When assessing rates of eTICI 2c or 3 at the end of the procedure, inclusive of bail outs of the primary technique, there was no significant difference noted. Additionally, there was no significant difference in total procedure time among the techniques, inclusive of bail outs.

A regression analysis was performed to identify predictors of first pass eTICI 2c or 3 reperfusion (n=1249) (table 3). The use of the SR Classic technique compared with DA, higher baseline ASPECTS, and M1 middle cerebral artery occlusion location (compared with internal carotid artery (ICA)) were predictors of first pass success. SR Classic remained a significant predictor of first pass effect after adjusting for potential confounders. When compared with SR Classic, patients treated with SR Combination had similar first pass eTICI 2c or 3 rates while DA had significantly lower rates (adjusted OR 0.65, 95% CI 0.46 to 0.92, P=0.02 compared with SR Classic). An adjusted analysis was performed to identify variables associated with a 90-day mRS of 0–2 (n=927) (table 4). Patients who were treated under 6 hours from last known normal, with a favorable baseline NIHSS, or a higher baseline ASPECTS, had a higher probability of achieving an mRS of 0–2 at 90 days. A favorable eTICI score was also associated with a higher rate of mRS 0–2. Patients with a baseline blood glucose ≥150 mg/dL or age ≥80 years were less likely to achieve a good clinical outcome. SR Classic was a significant predictor of a good outcome after adjusting for confounders; SR Classic had better 90-day outcomes compared with SR Combination (P=0.0006), and marginally better results than DA (P=0.06).

Safety endpoints

There were no significant differences in mortality, embolization to a new territory, or symptomatic hemorrhages among the three techniques (table 5). A total of 209 (14%) patients died within 90 days of their stroke. Embolization to a new territory was uncommon with 11 (0.7%) procedures noting this complication. The overall rate of symptomatic hemorrhages was low with 34 patients (2.3%) suffering this event. Hemorrhage types are outlined in online supplemental Table S6.

Additional analyses

Patients treated with DA had a faster time to achieve eTICI 2c-3 with the first pass compared with both SR arms (19.4±12.6 min DA vs 23.1±13.0 min SR Classic vs 27.4±14.9 min SR Combination, P<0.0001) (table 2). Despite the faster time for a DA pass, the rate of success was significantly less than SRs. SR Combination takes longer for each pass and does not appear to confer improved effectiveness in reperfusion compared with SR Classic.

Table 1 Demographic, clinical and procedural characteristics

	SR Classic	SR Combination	DA	P value†
Age (years), mean (SD)	71.4 (14.3)	71.8 (13.1)	68.1 (15.4)	0.0004
Female, n (%)	121 (49.0)	379 (54.4)	281 (51.3)	0.24
Medical history, n (%)				
Hypertension	166 (67.5)	505 (74.6)	372 (68.6)	0.03
Congestive heart failure	33 (13.5)	99 (15.2)	68 (12.6)	0.50
Atrial fibrillation	93 (38.1)	233 (34.4)	164 (30.4)	0.05
Previous ischemic stroke	33 (13.6)	102 (15.3)	73 (13.8)	0.78
Previous intracerebral hemorrhage	4 (1.6)	14 (2.2)	10 (1.9)	0.87
Diabetes mellitus	50 (20.4)	154 (23.0)	129 (23.8)	0.60
Dyslipidemia	108 (44.1)	309 (47.8)	254 (47.1)	0.75
Current/past smoker	87 (38.2)	243 (41.3)	206 (42.7)	0.65
IV tPA administered, n (%)	79 (32.0)	285 (40.9)	195 (35.6)	0.32
Time last known normal to groin puncture, mean (SD)	7.5 (9.7)	7.5 (8.0)	8.5 (11.8)	0.21
Pre-stroke mRS, n (%)				0.02
0	178 (73.0)	448 (67.3)	390 (75.9)	
1	21 (8.6)	98 (14.7)	64 (12.5)	
2	21 (8.6)	43 (6.5)	30 (5.8)	
3	20 (8.2)	55 (8.3)	23 (4.5)	
4 or 5	4 (1.6)	22 (3.3)	7 (1.4)	
NIHSS score, mean (SD)	15.3 (6.6)	13.6 (6.7)	14.6 (6.2)	0.14
Baseline CT ASPECTS, mean (SD)	7.8 (1.4)	7.7 (1.4)	7.3 (1.5)	0.0002
Procedural characteristics				
Tandem occlusions, n (%)	26 (10.5)	108 (15.5)	78 (14.2)	0.42
General anesthesia, n (%)	69 (27.9)	242 (34.7)	271 (49.5)	0.19
Pre-procedure eTICI (core lab), n (%)				0.91
Grade 0 or 1	230 (93.9)	647 (93.4)	510 (94.1)	
Grade ≥2a	15 (6.1)	46 (6.6)	32 (5.9)	
Right side, n (%)	97 (39.6)	353 (50.9)	285 (52.3)	0.01
Site of occlusion (core lab), n (%)				<0.0001
ICA	38 (15.4)	129 (18.5)	156 (28.5)	
M1	145 (58.7)	341 (48.9)	300 (54.7)	
M2	63 (25.5)	215 (30.8)	90 (16.4)	
Distal vessel occlusion (A1, A2, M3)	1 (0.4)	12 (1.7)	2 (0.4)	
Number of passes to treat target occlusion using primary technique, mean (SD)	1.4 (0.9)	1.5 (0.9)	1.4 (0.8)	0.27
Number of passes to treat target occlusion after primary technique, mean (SD)*	1.5 (1.8)	1.0 (1.4)	1.3 (1.1)	0.19
BGC use	247 (100.0)	354 (50.8)	106 (19.3)	N/A‡
24 hour CT ASPECTS, mean (SD)	6.5 (2.1)	6.1 (2.2)	5.8 (2.3)	0.0013

*Limited to 303 subjects who switched techniques.
†Means and frequencies are reported where the P value is from the generalized linear mixed model or χ^2 test adjusted for clustering.
‡P value cannot be calculated due to 100% cell count.
ASPECTS, Alberta Stroke Program Early CT Score; BGC, balloon-guide catheter; DA, direct aspiration; eTICI, expanded Thrombolysis In Cerebral Infarction; ICA, internal carotid artery; IV tPA, intravenous tissue plasminogen activator; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; SR, stent retriever.

When assessing success rate by primary technique (figure 1), the estimated median time to bail out or failure by primary technique was 50.0 min (95% CI 40.0 to 59.0 min) for SR Classic, 29.0 min (95% CI 27.0 to 31.0 min) for DA, and 55.0 min (95% CI 50.0 to 59.0 min) for SR Combination. In this analysis, to best assess the effectiveness of the primary technique, use of bail out by the operator was considered a failure to achieve reperfusion. Thus, despite each individual DA pass being faster, it was less effective compared with SRs and thus led to a lower chance of successful eTICI 2c or 3 as the primary technique during the procedure.

Patients treated with smaller bore catheters compared with larger bore catheters in the DA arm were compared as part of the expansion of this arm of the study. A total of 548 patients were treated in the DA arm, with 146 (26.9%) treated with a small-bore catheter compared with 397 (73.1%) with larger bore catheters. In a post-hoc analysis, patients treated with the smaller bore catheters were more likely to achieve an mRS of

Table 2 Angiographic and clinical efficacy outcomes

	SR Classic	SR Combination	DA	P value*
Primary clinical endpoint				
90-day mRS 0–2, n (%)	140 (59.1)	351 (52.7)	273 (54.0)	0.46
Secondary clinical endpoints				
90-day mRS 0–1, n (%)	112 (47.3)	264 (39.6)	209 (41.3)	0.17
Early response, n (%)	156 (66.1)	376 (58.2)	294 (58.0)	0.25
Primary procedural outcome (core lab)				
eTICI 2c or greater on first pass for treatment of target occlusion, n (%)	110 (47.2)	309 (45.4)	193 (36.5)	0.01
Secondary procedural outcomes (core lab)				
eTICI 2c or greater after primary technique, n (%)	157 (64.9)	417 (60.9)	248 (46.4)	<0.0001
eTICI 2c or greater at end of procedure, n (%)	171 (69.8)	449 (64.9)	357 (65.6)	0.61
Overall time from groin puncture to first pass efficacy for those who achieved first pass efficacy, mean (SD)	23.1 (13.0)	27.4 (14.9)	19.4 (12.6)	<0.0001
Overall time from groin puncture to final reperfusion (eTICI 2c or 3, mins) for treatment of target occlusion (mins), mean (SD)	29.2 (19.3)	31.3 (17.5)	27.1 (19.2)	0.68
Overall time from groin puncture to end of procedure (mins), mean (SD)	35.5 (24.3)	40.5 (29.4)	33.0 (24.1)	0.54
Overall time from last known normal to eTICI 2c or greater in passes for treatment of target occlusion (hours), mean (SD)	7.7 (9.7)	8.1 (9.0)	8.0 (10.2)	0.94
Overall time from last known well to end of procedure (hours), mean (SD)	8.3 (10.0)	8.2 (8.1)	9.0 (11.9)	0.39

*Means and frequencies are reported where the P value is from the generalized linear mixed model or χ^2 test adjusted for clustering.
DA, direct aspiration; eTICI, expanded Thrombolysis In Cerebral Infarction; mRS, modified Rankin Scale; SR, stent retriever.

Table 3 Regression analysis with eTICI 2c or 3 on first pass as outcome

	Univariate analysis		Multivariable analysis	
	OR (95% CI)	P value	OR (95% CI)	P value
Technique group		0.01		0.02
SR Classic	Reference		Reference	
SR Combination	0.85 (0.59 to 1.22)	0.38	0.91 (0.63 to 1.31)	0.61
Direct aspiration	0.58 (0.40 to 0.85)	0.005	0.65 (0.46 to 0.92)	0.02
Age	1.01 (1.00 to 1.02)	0.02		
Baseline NIHSS	0.99 (0.98 to 1.01)	0.36		
Baseline ASPECTS total score	1.19 (1.10 to 1.29)	<0.0001	1.18 (1.09 to 1.27)	<0.0001
History of atrial fibrillation	1.12 (0.90 to 1.38)	0.30		
Clot location		<0.0001		<0.0001
ICA	Reference		Reference	
M1	2.08 (1.58 to 2.72)	<0.0001	1.93 (1.49 to 2.49)	<0.0001
M2	1.63 (1.17 to 2.26)	0.005	1.28 (0.91 to 1.79)	0.15
Time last known normal to groin puncture		0.07		
<6 hours	Reference			
6–24 hours	0.78 (0.64 to 0.96)	0.02		
>24 hours	0.81 (0.40 to 1.64)	0.55		
IV tPA	1.05 (0.86 to 1.30)	0.61		

Analysis was performed on subjects with non-missing data for all variables in the univariate analysis (n=1249).
ASPECTS, Alberta Stroke Program Early CT Score; eTICI, expanded Thrombolysis In Cerebral Infarction; ICA, internal carotid artery; IV tPA, intravenous tissue plasminogen activator; NIHSS, National Institutes of Health Stroke Scale; SR, stent retriever.

0–2 at 90 days compared with the large bore group (66.2% vs 49.6%, P<0.0001). However, patients in the larger bore group presented with higher NIHSS, lower ASPECTS, and a higher percentage of patients with clots in the ICA. There was no significant difference in first pass eTICI 2c or 3, with the smaller bore group achieving this endpoint 35.2% of the time compared with 37.4% in the larger bore group (P=0.66).

DISCUSSION

The current study demonstrates patients treated with the SR Classic or SR Combination techniques had a higher probability of achieving eTICI 2c or 3 during the first pass compared with DA. Although an individual DA pass was shorter in duration compared with the other two techniques, there was a significantly higher rate of bail out and less successful reperfusion using DA compared with SR. Additionally, patients treated with the SR Combination technique had longer times for each individual pass compared with DA and SR Classic. Patients treated with DA, if successful, achieved faster eTICI 2c or 3 with the first pass, but this rate of success was significantly lower than both SR techniques. Moreover, the efficacy of each successive DA pass does not appear to increase success rates compared with SRs (figure 1). The ASSIST Registry is to our knowledge the largest prospective dataset to assess the impact of technique on first pass reperfusion success based on the proceduralists' preferred primary technique.

The ideal technique would achieve eTICI 3 reperfusion with the first pass, as this has been linked to improved clinical outcomes and reduced complications.[14 15] A meta-analysis demonstrated a 28% rate of first pass effect when analyzing 9082 patients and the analysis did not demonstrate a difference among the three techniques. Care must be taken in interpreting these results as several of the studies were not adjudicated by an independent core lab, which is more stringent than site adjudication.[16] A first pass complete reperfusion was associated with better functional recovery compared with incomplete reperfusion.[15] The current

Table 4 Regression analysis with mRS 0–2 at 90 days as outcome

	Univariate analysis		Multivariable analysis	
	OR (95% CI)	P value	OR (95% CI)	P value
Technique group		0.05		0.002
SR Classic	Reference			
SR Combination	0.73 (0.52 to 1.03)	0.07	0.52 (0.36 to 0.75)	0.0006
Direct aspiration	0.67 (0.46 to 0.96)	0.03	0.63 (0.39 to 1.01)	0.06
Age ≥80 years	0.45 (0.32 to 0.61)	<0.0001	0.29 (0.20 to 0.43)	<0.0001
History of atrial fibrillation	0.70 (0.52 to 0.95)	0.02		
Baseline NIHSS	0.88 (0.86 to 0.90)	<0.0001	0.87 (0.85 to 0.89)	<0.0001
Baseline ASPECTS total score	1.30 (1.18 to 1.44)	<0.0001	1.23 (1.10 to 1.38)	0.0003
Clot location		<0.0001		
ICA	Reference			
M1	1.37 (0.99 to 1.89)	0.06		
M2	2.19 (1.55 to 3.10)	<0.0001		
eTICI 2c or greater on the first pass for treatment of target occlusion	2.03 (1.47 to 2.80)	<0.0001	1.93 (1.31 to 2.84)	0.001
eTICI 2b or greater at end of procedure	4.33 (1.92 to 9.77)	0.0006	4.16 (1.63 to 10.61)	0.004
General anesthesia	1.01 (0.65 to 1.55)	0.98		
Blood glucose ≥150 mg/dL	0.57 (0.41 to 0.80)	0.001	0.56 (0.38 to 0.82)	0.003
Time last known normal to end of procedure		0.0008		0.01
<6 hours	Reference			
6–24 hours	0.64 (0.50 to 0.82)	0.0006	0.66 (0.48 to 0.92)	0.01
>24 hours	0.30 (0.13 to 0.69)	0.005	0.27 (0.10 to 0.72)	0.01
IV tPA	1.57 (1.16 to 2.13)	0.004		

Analysis was limited to subjects with baseline mRS 0–2.
Analysis was performed on subjects with non-missing data for all variables in the univariate analysis (n=927).
ASPECTS, Alberta Stroke Program Early CT Score; eTICI, expanded Thrombolysis In Cerebral Infarction; ICA, internal carotid artery; IV tPA, intravenous tissue plasminogen activator; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; SR, stent retriever.

study demonstrates patients treated with an SR with or without concomitant contact aspiration were more likely to achieve first pass eTICI 2c or 3 reperfusion compared with DA. The ASTER study was designed to assess the superiority of successful revascularization of DA compared with SR alone. The study did not assess first pass reperfusion, but compared the two arms with regards to final successful mTICI 2b or 3 reperfusion. When comparing mTICI 3 by primary technique without bail out, the SR arm achieved this end point in 35.5% of patients compared with 28.7% for DA alone (P=0.16).[5] Although the study was underpowered for assessing this endpoint, the trends noted are consistent with the ASSIST Registry. The second ASTER study assessed whether SR Combination was superior to SR alone with eTICI 2c or 3 at the end of the procedure. There was no significant difference between the two groups inclusive of bail outs, but in secondary analysis the investigators found that patients with combination treatment were significantly more likely to achieve eTICI 2c or 3 with the assigned treatment alone (86.2% vs 72.3%, P<0.001). Moreover, first pass eTICI 2c or 3 trended higher for combination therapy (40.9% vs 33.7%, P=0.12), although the study was not powered to detect a difference.[5] The COMPASS trial was a non-inferiority design to assess if there was a difference between primary aspiration and the use of SR. A large majority of patients in the SR arm were concomitantly treated with an aspiration catheter.[4] There were no significant differences between the two arms with regard to clinical

Table 5 Safety

	SR Classic	SR Combination	DA	P value†
All-cause mortality at 90 days (±14 days), n (%)	28 (11.3)	105 (15.1)	76 (13.9)	0.46
Stroke-related mortality at 90 days (±14 days), n (%)*	19 (7.7)	63 (9.0)	38 (6.9)	0.54
Device and/or procedure related SAEs at 90 days (±14 days), n (%)	16 (6.5)	40 (5.7)	23 (4.2)	0.46
Embolization to new territory during procedure (core lab), n (%)	2 (0.8)	6 (0.9)	3 (0.6)	0.81
Symptomatic ICH up to 48 hours post-procedure, n (%)	5 (2.0)	15 (2.2)	14 (2.6)	0.84
Neurological deterioration (NIHSS ≥4) up to 48 hours post-procedure, n (%)	13 (5.3)	52 (7.5)	47 (8.6)	0.29
Access site complications up to 48 hours post-procedure, n (%)	3 (1.2)	10 (1.4)	2 (0.4)	0.14

*5 subjects died of a new stroke that occurred post-procedure that was not the index stroke.
†Means and frequencies are reported where the P value is from the generalized linear mixed model or χ^2 test adjusted for clustering.
DA, direct aspiration ; ICH, intracranial hemorrhage; NIHSS, National Institutes of Health Stroke Scale; SAEs, serious adverse events; SR, stent retriever.

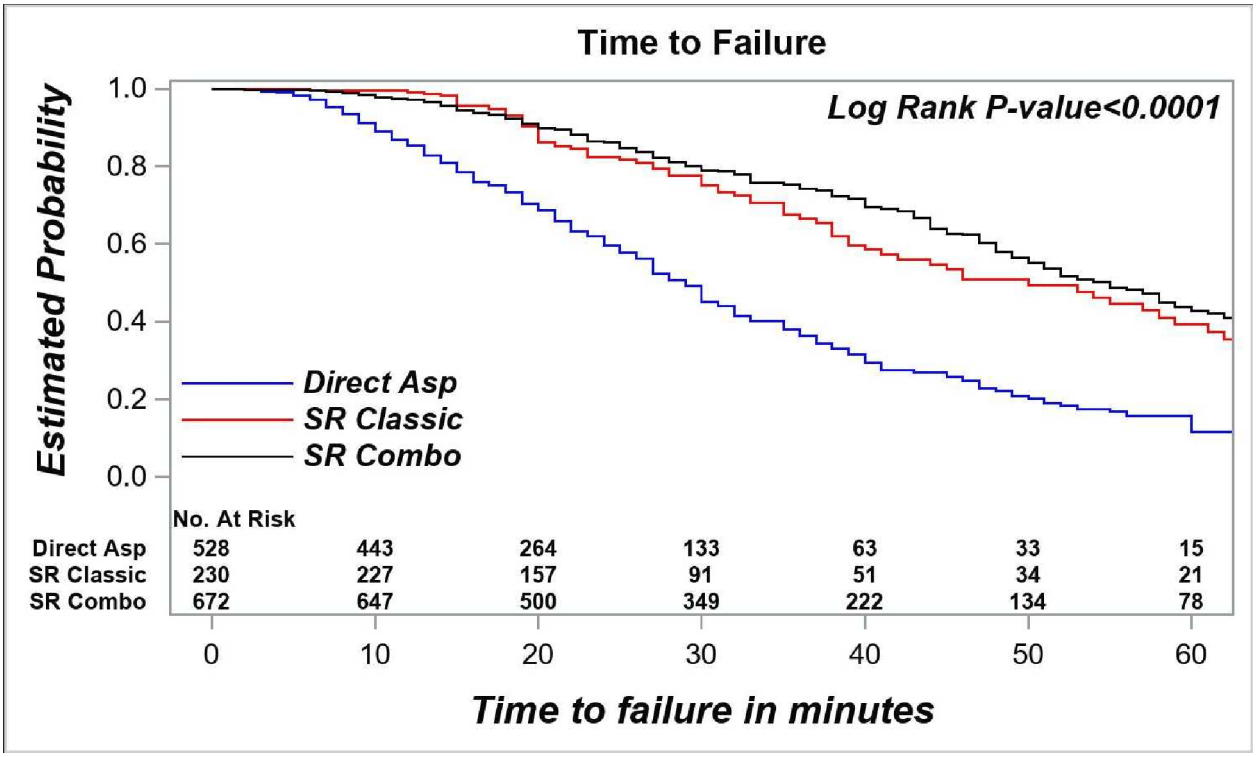

Figure 1 Survival analysis time to failure. Direct Asp, direct aspiration; SR, stent retriever.

outcomes, first pass TICI 2b or greater reperfusion, or final reperfusion grade.

In the ASSIST Registry, the use of BGC was within the range of the ASTER and COMPASS randomized clinical trials.[4 5] It is likely reflective of real-world practice. However, given BGC use may improve outcomes, future studies comparing DA and SR may be warranted with BGC use being mandated in both arms.

There have been advances with larger aspiration catheters to enhance effectiveness. Larger bore catheters provide a higher force on the clot, potentially increasing effectiveness, but have not been proven in core lab adjudicated studies.[17 18] The advent of larger bore 0.088 inch catheters are being tested as potential first line treatment for LVO. Limited reports exist, but a recent report with the TracStar LDP (Imperative Care) demonstrated the catheter can be placed at the target occlusion site 73% of the time.[19] The SUMMIT NZ trial was prospective and core lab adjudicated and reported preliminary results using the 088 HiPoint catheter. In this small study, 17 out of 38 patients (44.7%) achieved eTICI 2c or 3 first pass reperfusion.[20] These results are in the range of what was seen for the SR procedures in the current study. A recent meta-regression analysis demonstrated a higher rate of first pass reperfusion TICI 2b or 3 with increasing diameters of the catheter, but this effect was not seen in binary comparison of 0.071 inch or larger compared with less than 0.071 inch catheters. Moreover, the authors found a higher rate of symptomatic hemorrhages with larger bore catheters.[21] Patients enrolled in the DA arm of the ASSIST Registry did not have a significant difference in first pass reperfusion with larger bore catheters compared with smaller bore catheters.

In unadjusted analysis, there were no differences seen in clinical outcomes among the three techniques. When an adjusted analysis was performed of a complete dataset the patients treated with the SR Classic technique had better clinical outcomes than SR Combination, and a trend was noted for better outcomes than DA. Caution must be taken in interpreting the adjusted analysis as roughly one third of the patients could not be included in the analysis. Nonetheless, the difference does help generate an opportunity for future research to determine if there are clinical outcome differences based on technique.

There are several limitations to the current study. The first is the patients were not randomized, but each site declared their preferred technique during an initial survey phase of the study, allowing for planning of the number of patients anticipated in each arm. Although randomization may be a preferred strategy, the current trial accounted for the technique the operator is most familiar with in their current practice and averts a bias of reduced experience by forcing a technique they may not be accustomed to. Second, centers were highly encouraged to enroll consecutive patients but this did not always occur due to the inability to obtain consent or one of the Stryker devices not being used as first line treatment. Third, some patients or their legally authorized representatives consented retroactively after completion of the procedure. It is possible this created a bias where patients with poor outcomes were not consented, but this would have been consistent across all arms of the study. Fourth, rescue or bail out therapy was allowed during the study and operators may have employed this strategy at various points after their first pass with the primary technique. There was no a priori study protocol for number of passes before failure of a technique, but switching techniques was considered a bail out or failure of the primary technique. Fifth, device technology is constantly evolving, and the current study design did not assess aspiration catheter sizes larger than the Vecta 074 inch catheter. Sixth, the current study assessed the Trevo SR and Catalyst and Vecta aspiration catheters manufactured by Stryker Neurovascular. There may be inherent differences in designs of various current technologies that may yield differing results. Lastly, the analysis for the primary outcomes was based on available data. However, in sensitivity analyses where patients missing outcome data were designated as having poor outcomes, the results did not

change (online supplemental Table S7). Additionally, although a regression analysis could only be performed in patients with complete data, SR Classic may be associated with better clinical outcomes compared with the other two techniques after adjustment. Further investigation is required to confirm this trend.

In conclusion, the ASSIST Registry demonstrates patients treated either with SR Classic or SR Combination are significantly more likely to achieve a first pass eTICI 2c or 3 compared with DA and no significant differences in functional outcomes or safety.

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Contributors RG and MM drafted the initial manuscript and are responsible for the overall content as the guarantors. LLP analyzed the data. All authors were involved and made substantial contributions to the conception or design of the work, or the acquisition, analysis, or interpretation of the data; revising it critically for important intellectual content; final approval of the version published; and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The corresponding author as well as all authors had access to the full dataset and the interpretation and writing of the manuscript was under the discretion of the authors.

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Ethics approval This study involves human participants and was performed in compliance with the World Medical Association's Declaration of Helsinki. This study was approved by Advocate Health and Hospitals 'Western Institutional Review Board Puyallup, WA' 20191803; Buffalo University 'Western Institutional Review Board Puyallup, WA' 20191803; Kaiser Permanente – LA 'Kaiser Permanente Southern California Institutional Review Board Pasadena, CA' 12330; Medical University of South Carolina 'Institutional Review Board for Human Research (IRB) Office of Research Integrity (ORI) Medical University of South Carolina Palmetto Place Office Park Charleston, SC' Pro00089838 Thomas Jefferson University 'Western Institutional Review Board Puyallup, WA' 20191803; U Mass 'Western Institutional Review Board Puyallup, WA' H00020421_2; West Virginia University Hospital 'West Virginia University Office of Humas Research Protections Morgantown, WV' 1908690661; Semmes Murphey Foundation 'University of Tennessee Health Science Center IRB Memphis, TN' 20-07240-XP; Riverside Methodist – OHRI 'Western Institutional Review Board Puyallup, WA' Institution Tracking: 1555244; IRB Tracking: 20191803; UC Irvine 'Western Institutional Review Board Puyallup, WA' Institution Tracking: HS# 2020-5978; IRB Tracking: 20191803;UCLA 'UCLA Office of the Human Protection Research Protection Program Los Angeles, CA' 20-000041-CR-00002; Research Institute, University of Kansas Medical Center 'Western Institutional Review Board Puyallup, WA' Work Order Number: 1-1427195-1; IRB Tracking: 20191803; Valley Baptist Medical Center- Harlingen 'MetroWest Medical Center IRB Framingham, MA' 2021-012 WellStar Health System/ Kennestone Hospital 'Western Institutional Review Board Puyallup, WA' Work Order Number: 1-1427195-1; IRB Tracking: 20191803; St Mary's Medical Center 'Western Institutional Review Board Puyallup, WA' Work Order Number: 1-1547720-1; IRB Tracking: 20191803; Geisinger Medical Center 'Geisinger IRB Danville, PA' 2019-0877; Los Robles Hospital 'Western Institutional Review Board Puyallup, WA' Work Order Number: 1-1203360-1; IRB Tracking: 20191803; Baptist Jacksonville 'Baptist Health IRB Jacksonville, FL' 19-78; Mount Sinai 'Mount Sinai School of Medicine IRB New York, NY' HS#: STUDY-19-00986-CR002 University of S. 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Supplement Tables

Table S1: site of enrollment

Site Name	Role	First Name	Last Name	Patients Enrolled
Hospital Son Espases, Mallorca, ES	Principal Investigator	Salvador	Miralbes	N Total = 154 *SR Classic = 39/154 (25%) SR Combo = 11 Direct Asp = 104
	Sub-Investigator	Marc	Viles	
	Sub-Investigator	Rebeca	Bermejo	
	Sub-Investigator	Ángel	Calleja	
McLaren Health Care, Michigan, USA	Principal Investigator	Bharath	Naravetla	N Total = 151 SR Classic = 27 *SR Combo = 67/151 (44%) Direct Asp = 57
	Sub-Investigator	Aniel	Majjhoo	
	Sub-Investigator	Mahmoud	Rayes	
	Study Coordinator	Onishchuk	Valentyna	
	Study Coordinator	Tanya Mosley	Gardner	
	Study Coordinator	Emily	Paschal	
	Study Coordinator	Stephanie	Bruma	
	Study Coordinator	Marci	Roberts	
Medical University of South Carolina, Charleston, SC, USA	Principal Investigator	Alejandro	Spiotta	N Total = 100 SR Classic = 0 SR Combo = 9 *Direct Asp = 91/100 (91%)
	Sub-Investigator	Jonathan	Lena	
	Sub-Investigator	Kimberly	Kicielinski	
	Sub-Investigator	Sami	Al Kasab	
	Study Coordinator	Emily	Infinger	
	Study Coordinator	Melza	Van Roijen	
	Study Coordinator	Meredith	Robinson	
Klinikum Vest Recklinghausen, Recklinghausen, DE	Principal Investigator	Christian	Loehr	N Total = 69 SR Classic = 0 SR Combo = 25 *Direct Asp = 44/69 (64%)
	Sub-Investigator	Stephan	Bossmann	
	Sub-Investigator	Jan Oliver	Kuhnt	
	Sub-Investigator	Axel	Schaefer	
	Sub-Investigator	Andreea	Cioltan	
	Sub-Investigator	Johanna	Zabel	
	Sub-Investigator	Christian	Dynak	
	Sub-Investigator	Jan Peter	Püttmann	
Uniklinik Heidelberg, Heidelberg, DE	ASSIST Registry Global Principal	Markus	Möhlenbruch	N Total = 69 SR Classic = 0

	Investigator, Steering Committee Member			*SR Combo = 64/69 (93%) Direct Asp = 5
	Sub-Investigator	Christian	Herweh	
	Sub-Investigator	Christian	Ulfert	
	Sub-Investigator	Johannes	Pfaff	
	Sub-Investigator	Alexander	Hubert	
	Sub-Investigator	Alexander	Mohr	
	Sub-Investigator	Leonie	Jestaedt	
	Sub-Investigator	Jessica	Jesser	
	Sub-Investigator	Dominik	Vollherbst	
	Sub-Investigator	Faith	Seker	
	Sub-Investigator	Tim	Hilgenfeld	
	Study Coordinator	Susanne	Bonekamp	
	Study Coordinator	Sabine	Johnson	
	Study Coordinator	Jenny	Frech	
	CT Upload	Lukas	Diebold	
	CT Upload	Gabriele	Neureither	
Hospital Clínico Universitario de Valladolid, Valladolid, ES	Principal Investigator	Mario	Martínez-Galdámez	N Total = 67 *SR Classic = 45/67 (67%) SR Combo = 7 Direct Asp = 15
	Principal Investigator Sub-Investigator	Miguel Arturo	Schüller	
	Sub-Investigator	Jorge	Galván	
	Sub-Investigator	Mercedes	De Lera	
	Sub-Investigator	Carlos	Castañeda	
	Sub-Investigator	Javier	Rodríguez	
Department of Neurology, WellStar Health System, Marietta, Georgia, USA	ASSIST Registry Global Principal Investigator, Steering Committee Member	Rishi	Gupta	N Total = 53 SR Classic = 0 *SR Combo = 51/53 (96%) Direct Asp = 2
	Sub-Investigator	Ahmad	Khaldi	
	Sub-Investigator	William	Humphries	
	Study Coordinator	Stephanie	Rowe	
	Study Coordinator	Lauryn	Taylor	

	Study Coordinator	Martha	Kelly	
Rhode Island Hospital, Providence, Rhode Island, USA	Principal Investigator	Ryan	McTaggart	N Total = 49 SR Classic = 1 SR Combo = 45 *Direct Asp = 3/49 (6%)
	Sub-Investigator	Mahesh	Jayaraman	
	Sub-Investigator	Richard	Haas	
	Sub-Investigator	Radmehr	Torabi	
	Study Coordinator	Wendy	Smith	
	Study Coordinator	Gina	Merola	
	Study Coordinator	Susan	Foley	
Ghent University Hospital, Ghent, BE	Principal Investigator	Luc	Defreyne	N Total = 45 SR Classic = 1 *SR Combo = 42/45 (93%) Direct Asp = 2
	Sub-Investigator	Elisabeth	Dhondt	
	Sub-Investigator	Peter	Vanlangenhove	
	Sub-Investigator	Laurens	Hermie	
	Study Coordinator	Lynn	Huyck	
	Study Coordinator	Lien	Van Cauwenberghe	
Hospital Universitario Central de Asturias-HUCA, Oviedo, ES	Principal Investigator	Pedro	Vega	N Total = 45 *SR Classic = 45/45 (100%) SR Combo = 0 Direct Asp = 0
	Sub-Investigator	Eduardo	Murias	
	Sub-Investigator	Juan	Chaviano	
	Sub-Investigator	Jose Maria	Jimenez	
University Hospital Basel, Basel, CH	Principal Investigator, Steering Committee Member	Marios-Nikos	Psychogios	N Total = 40 SR Classic = 0 *SR Combo = 35/40 (88%) Direct Asp = 5
	Sub-Investigator	Ioannis	Tsogkas	
	Sub-Investigator	Peter	Sporns	
	Sub-Investigator	Kristine	Blackham	
	Study Coordinator	Alex	Brehm	
University Hospital Hradec Kralove, CZ	Principal Investigator, Steering Committee Member	Antonin	Krajina	N Total = 40 *SR Classic = 20/40 (50%) SR Combo = 16 Direct Asp = 4
	Sub-Investigator	Ondrej	Renc	
	Sub-Investigator	Eva	Vitkova	
	Sub-Investigator	Vendelin	Chovanec	
	Sub-Investigator	Jan	Raupach	

	Sub-Investigator	Miroslav	Lojik	
Choonam National University Hospital, KR	Principal Investigator, Steering Committee Member	Woong	Yoon	N Total = 36 *SR Classic = 10/36 (28%) SR Combo = 18 Direct Asp = 8
	Sub-Investigator	Byung Hyun	Baek	
	Study Coordinator	Eugene	Kim	
Bon Secours Mercy Health St. Vincent Medical Center, Toledo, Ohio, USA	Principal Investigator, Steering Committee Member	Osama	Zaidat	N Total = 33 SR Classic = 6 *SR Combo = 17/33 (52%) Direct Asp = 10
	Sub-Investigator	Saif	Bushnaq	
	Sub-Investigator	Bader	Alenzi	
	Sub-Investigator	Nicholas	Liaw	
	Sub-Investigator	Eugene	Lin	
	Sub-Investigator	Varun	Chaubal	
	CRC Manager	Alyssa	Bickley	
	CRC Manager	Ronda	White	
	Research Assistant	India	Bass	
	Study Coordinator	Amy	Krueger	
	Study Coordinator	Cynthia	Upham	
West Virginia University Hospital, USA	Principal Investigator, Steering Committee Member	Ansaar	Rai	N Total = 30 SR Classic = 2 *SR Combo = 26/30 (87%) Direct Asp = 2
	Sub-Investigator	Sohyun	Boo	
	Sub-Investigator	Abdul	Tarabishy	
	Sub-Investigator	Gerard	Deib	
	Nurse Practitioner	Rachel	Gregis	
	Medical Student	Abdul	Alhalak	
	Study Coordinator	Jennifer	Domico	
AOPU G. Martino, IT	Principal Investigator	Antonio	Pitrone	N Total = 30 SR Classic = 0 SR Combo = 13 *Direct Asp = 17/30 (57%)
	Sub-Investigator	Orazio	Buonomo	
	Sub-Investigator	Agostino	Tessitore	
	Sub-Investigator	Nicola	Milazzo	

	Sub-Investigator	Mariano	Velo	
	Sub-Investigator	Antonio	Caragliano	
	Sub-Investigator	Andrea	Calzoni	
	Study Coordinator	Sergio Lucio	Vinci	
The Catholic University of Korea, St. Vincent's Hospital, Suwon, KR	Principal Investigator	Dong Hoon	Lee	N Total = 28 *SR Classic = 10/28 (36%) SR Combo = 15 Direct Asp = 3
	Sub-Investigator	Seung Yoon	Song	
	Sub-Investigator	Ho Jun	Yi	
	Sub-Investigator	Jae Hoon	Sung	
	Study Coordinator	Narae	Kwon	
Ospedale San Martino, Genova, IT	Principal Investigator	Lucio	Castellan	N Total = 25 SR Classic = 0 *SR Combo = 3/25 (12%) Direct Asp = 22
	Sub-Investigator	Laura	Malfatto	
	Sub-Investigator	Nicola	Mavilio	
	Sub-Investigator	Giancarlo	Salsano	
	Sub-Investigator	Bruno	Del Sette	
AO Modena, IT	Principal Investigator	Guido	Bigliardi	N Total = 23 *SR Classic = 1/23 (4%) SR Combo = 21 Direct Asp = 1
	Sub-Investigator	Maria Luisa	Dell'Acqua	
	Sub-Investigator	Laura	Vandelli	
	Sub-Investigator	Giuseppe	Borzì	
	Sub-Investigator	Ludovico	Ciolli	
	Sub-Investigator	Livio	Picchetto	
	Sub-Investigator	Riccardo	Ricceri	
	Sub-Investigator	Francesca	Rosafio	
	Sub-Investigator	Stefano	Vallone	
	Study Coordinator	Stefania	Maffei	
Hospital Clínico San Carlos, ES	Principal Investigator	Luis	López Ibor	N Total = 22 SR Classic = 2 *SR Combo = 18/22 (82%) Direct Asp = 2
	Sub-Investigator	Manuel	Moreu	
	Sub-Investigator	Santiago	Rosati	
	Sub-Investigator	Carlos	Gomez-Escalonilla	
Geisinger Medical Center, Danville, Pennsylvania, USA	Principal Investigator	Clemens	Schirmer	N Total = 21 SR Classic = 0 *SR Combo = 4/21 (19%)
	Sub-Investigator	Itay	Melamed	
	Sub-Investigator	Gregory	Weiner	

	Sub-Investigator	Oded	Goren	Direct Asp = 17
	Sub-Investigator	Christoph	Griessenauer	
	Sub-Investigator	Shamsher	Dalal	
	Nurse	Karissa	Graham	
	Study Coordinator	Katherine	Freedman	
	Study Coordinator	Angela	Whitmire	
	Study Coordinator	Chelsie	Derr	
Mount Sinai Health System, USA	Principal Investigator	Shahram	Majidi	N Total = 18 SR Classic = 0 SR Combo = 5 *Direct Asp = 13/18 (72%)
	Sub-Investigator	Christopher	Kellner	
	Sub-Investigator	Paul	Singh	
	Sub-Investigator	Johanna	Fifi	
	Sub-Investigator	Hazem	Shoirah	
	Sub-Investigator	Reade	DeLeacy	
	Sub-Investigator	Tomoyoshi	Shigematsu	
	Sub-Investigator	Pouria	Moshayedi	
	Sub-Investigator	Krisztina	Moldovan	
	Sub-Investigator	Gregory	Lock	
	Sub-Investigator	Thomas	Oxley	
	Sub-Investigator	Benjamin	Rapoport	
	Sub-Investigator	Jacopo	Scaggiante	
	Sub-Investigator	Mais	Al Kawaz	
	Study Coordinator	Sukaina	Davdani	
	Study Coordinator	Emily	Fiano	
	Study Coordinator	Armand	Harb	
	Study Coordinator	Serina	Deeba	
AZ Sint Jan Brugge Oostende AV, BE	Principal Investigator	Geert	Vanhooren	N Total = 17 *SR Classic = 13/17 (76%) SR Combo = 3 Direct Asp = 1
	Sub-Investigator	Sofie	De Blauwe	
	Sub-Investigator	Olivier	Deryck	
	Sub-Investigator	Bruno	Bergmans	
	Sub-Investigator	Tybault	Hollanders	
	Sub-Investigator	Heleen	Parmentier	
	Sub-Investigator	Ludo	Vanopdenbosch	

	Sub-Investigator	Kristof	Verhoeven	
	Sub-Investigator	Melissa	Cambron	
	Sub-Investigator	Johan	Ghekiere	
	Sub-Investigator	Annelies	Van Dycke	
	Sub-Investigator	Isaline	Demarcin	
	Sub-Investigator	Louise	Adams	
	Sub-Investigator	Robin	Bouttelgier	
	Sub-Investigator	Lisa	Van Doeselaer	
	Sub-Investigator	Charlotte	Vanden Berghe	
	Sub-Investigator	Arne	Hostens	
	Sub-Investigator	Louise	De Temmerman	
	Study Coordinator	Valérie	Schotte	
	Study Coordinator	Heleen	Couckuyt	
	Study Coordinator	Julie	Derous	
Klinikum Rechts Der Isar, Munich, DE	Principal Investigator	Charlotte	Rüther	N Total = 17 SR Classic = 0 *SR Combo = 17/17 (100%) Direct Asp = 0
	Principal Investigator	Monika	Probst	
	Sub-Investigator	Tobias	Boeckh-Behrens	
	Sub-Investigator	Kornelia	Kreiser	
	Sub-Investigator	Christian	Maegerlein	
	Sub-Investigator	Jan	Kirschke	
	Sub-Investigator	Silke	Wunderlich	
	Study Coordinator	Maria	Bauer	
Toronto Western, Toronto, Ontario, CA	Principal Investigator, Steering Committee Member	Timo	Krings	N Total = 15 SR Classic = 1 SR Combo = 12 *Direct Asp = 2/15 (13%)
	Sub-Investigator	Patrick	Nicholson	
	Sub-Investigator	Ronit	Agid	
	Study Coordinator	Alex	Kostynskyy	
Doctors Medical Center, Modesto, CA, USA	Principal Investigator	James	Jaffe	N Total = 15 SR Classic = 0 SR Combo = 0 *Direct Asp = 15/15 (100%)
	Sub-Investigator	Chris	Neal	
	Study Coordinator	Dharati (Dorothy)	Trivedi	

Aurora St. Luke's Medical Center, Milwaukee, Wisconsin, USA	Principal Investigator	Thomas	Wolfe	N Total = 15 SR Classic = 2 SR Combo = 6 *Direct Asp = 7/15 (47%)
	Sub-Investigator	Kessarin	Panichpisal	
	Sub-Investigator	Glen	Pollock	
	Sub-Investigator	Sudeepta	Dandapat	
	Sub-Investigator	Kavit	Shah	
	Nurse Practitioner	Genevieve	Kuchinsky	
	Nurse Practitioner	Samantha	Goedde	
	Nurse Practitioner	Payton	Tepp	
	Study Coordinator	Kristopher	Rowe	
	Study Coordinator	Gary	Dennison	
	Study Coordinator	Batul	Dhariwala	
	Study Coordinator	Kaite	McPolin	
	Image Upload	Tonya	Hollrith	
Indiana University, Bloomington, Indiana, USA	Principal Investigator	Bradley	Bohnstedt	N Total = 15 SR Classic = 0 SR Combo = 2 *Direct Asp = 13/15 (87%)
	Study Coordinator	Marissa	Lowe	
	Study Coordinator	Lauren	Snyder	
CHU Brest, FR	Principal Investigator	Jean-Christophe	Gentric	N Total = 15 SR Classic = 0 *SR Combo = 15/15 (100%) Direct Asp = 0
	Sub-Investigator	Julien	Ognard	
	Sub-Investigator	Lorena	Nico	
	Study Coordinator	Géraldine	Viard	
Hospital 12 de Octubre, Madrid, ES	Principal Investigator	Eduardo	Bárcena	N Total = 15 SR Classic = 0 SR Combo = 6 *Direct Asp = 9/15 (60%)
	Sub-Investigator	Fernando	Ostos	
	Sub-Investigator	Federico	Ballenilla	
	Sub-Investigator	Jorge	Campollo	
	Sub-Investigator	Pedro	Saura	
	Sub-Investigator	Miriam	Fernandez Gomez	
Montefiore Medical Center, Bronx, New York, USA	Principal Investigator	David	Altschul	N Total = 13 SR Classic = 0 *SR Combo = 13/13 (100%) Direct Asp = 0
	Sub-Investigator	Neil	Haranhali	
	Sub-Investigator	Seon-Kyu	Lee	
	Sub-Investigator	Richard	Zampolin	
	Sub-Investigator	Allan	Brook	

	Study Coordinator	Aureliana	Toma	
	Study Coordinator	Lavinia	Williams	
Kaiser Permanente Southern California, Los Angeles, California, USA	Principal Investigator	Lei	Feng	N Total = 11 SR Classic = 4 *SR Combo = 5/11 (45%) Direct Asp = 2
	Sub-Investigator	Kuo	Chao	
	Study Coordinator	Catherine	Lui	
	Study Coordinator	Ashima	Sharma	
	Study Coordinator	Vanessa	Audea	
	Study Coordinator	Nathalie	Sanchez	
	Study Coordinator	Marissa	Barron	
Advocate Hospital, Illinois, USA	Principal Investigator	Demetrius	Lopes	N Total = 11 SR Classic = 0 *SR Combo = 11/11 (100%) Direct Asp = 0
	Sub-Investigator	Joshua	Billingsley	
	Sub-Investigator	Khaled	Asi	
	Clinical Assessor	Kiffon	Keigher	
	Clinical Assessor	Bridget	Cantrell	
	Clinical Assessor	Gina	Barbaglia	
	Clinical Assessor	Eric	Leadley	
	Clinical Assessor	Molly	Baker	
	Clinical Assessor	Abigail	Walters	
	Neurologist	Linda	Jiang	
	Neurologist	Pavan	Murty	
	Neurologist	Arth	Srivastava	
	Study Coordinator	Nicholas	Armijo	
	Study Coordinator	Gina	Littlejohn	
	Study Coordinator	Sherri	Velez	
	Study Coordinator	Nicole	Hannigan	
	Study Coordinator	Kathleen	Hesse	
Dignity Health, Rancho Cordova, California, USA	Principal Investigator	Lucian	Maidan	N Total = 10 SR Classic = 0 *SR Combo = 5/10 (50%) Direct Asp = 5
	Sub-Investigator	Geroge	Luh	
	Study Coordinator	Danielle	Hornbuckle	
	Study Coordinator	Sharon	Bluemel	
Hospital de la Princesa, Madrid, ES	Principal Investigator	Jose Luis	Caniego	N Total = 9 *SR Classic = 9/9 (100%)
	Sub-Investigator	Juan	Vega	

	Sub-Investigator	Rafael	González	SR Combo = 0 Direct Asp = 0
Kaiser Fontana Medical Center, Fontana, California, USA	Principal Investigator	Conrad	Liang	N Total = 9 SR Classic = 3 *SR Combo = 5/9 (56%) Direct Asp = 1
	Sub-Investigator	Mazen	Noufal	
	Sub-Investigator	Valerie	Wyman	
	Study Coordinator	Ashima	Sharma	
	Study Coordinator	Vanessa	Audea	
St. Mary's Medical Center, USA	Principal Investigator	Ali	Malek	N Total = 9 SR Classic = 0 *SR Combo = 8/9 (89%) Direct Asp = 1
	Sub-Investigator	Nils	Mueller-Kronast	
	Sub-Investigator	Dennys	Reyes	
	Neuro Hospitalist	Juan	Ramos	
	Neuro Hospitalist	Muneer	Hassan	
	Neuro Manager	Jennafer	Hallquist	
	APRN	Natasha	Molina	
	APRN	Sandra	Ripper-Brown	
	APRN	Charity	Denson	
	Study Coordinator	Marianne	Torres-Malaga	
Westchester Medical Center, Valhalla, New York, USA	Principal Investigator	Fawaz	Al-Mufti	N Total = 9 SR Classic = 0 *SR Combo = 1/9 (11%) Direct Asp = 8
	Sub-Investigator	Chirag	Ghandhi	
	Sub-Investigator	Justin	Santarelli	
	Sub-Investigator	Gurmeen	Kaur	
	Sub-Investigator	Christeena	Kurian	
	Fellow	Jared	Cooper	
	Fellow	Haris	Kamal	
	Fellow	Katarina	Dakay	
	Physician Assistant	Divya	Viswanathan	
	Study Coordinator	Monique	Carrero-Tagle	
	Study Coordinator	Kevin	Clare	
	Study Coordinator	Bridget	Nolan	
Semmes Murphey Foundation, Memphis, Tennessee, USA	Principal Investigator	Lucas	Elijovich	N Total = 8 SR Classic = 0 *SR Combo = 4/8 (50%)
	Sub-Investigator	Adam	Arthur	
	Sub-Investigator	Daniel	Hoit	

	Sub-Investigator	Violiza	Inoa	Direct Asp = 4
	Sub-Investigator	Christopher	Nickele	
	Sub-Investigator	David	Dornbos	
	Sub-Investigator	Nitin	Goyal	
	Sub-Investigator	Jeremy	Peterson	
	Sub-Investigator	Radmehr	Torabi	
	Sub-Investigator	Daniel	Heiferman	
	Sub-Investigator	Kendrick	Johnson	
	Nurse Practitioner	Stephanie	Wilson	
	Study Coordinator	Amanda	Nolte	
	Study Coordinator	Stephanie	Corder	
	Study Coordinator	Valorie	Horner	
	Study Coordinator	Kamal	Lotay	
Klinikum Dortmund, Dortmund, DE	Principal Investigator	Stefan	Rohde	N Total = 8 SR Classic = 0 SR Combo = 8 *Direct Asp = 0/8 (0%)
	Sub-Investigator	Olaf	Adamczewski	
	Sub-Investigator	Stephan	Schwarz	
	Sub-Investigator	Gernot	Reimann	
	Sub-Investigator	Rachid	El Mouden	
	Sub-Investigator	Ines	Gaedke	
	Study Coordinator	Kristina	Hauptmann	
	Image Upload	Torsten	Döring	
	Image Upload	Bettina	Zoeller	
HUG Geneva, CH	Principal Investigator	Paolo	Machi	N Total = 8 SR Classic = 0 SR Combo = 8 *Direct Asp = 0/8 (0%)
	Sub-Investigator	Gianmarco	Bernava	
	Sub-Investigator	Andrea	Rosi	
	Sub-Investigator	Jeremy	Hofmeister	
	Study Coordinator	Michel	Muster	
	Clinical Research Assistant	Malvina	Destro	
Memorial Healthcare System, Hollywood, Florida, USA	Principal Investigator	Hoang	Duong	N Total = 7 SR Classic = 0 *SR Combo = 6/7 (86%)
	Principal Investigator	Andrey	Lima	
	Principal Investigator	Brijesh	Mehta	

	Research Director	Doris	Alaby	Direct Asp = 1
	RN	Joy	Sessa	
	Financial Manager	Viviane	Kleva	
	Study Coordinator	Erum	Usman	
	Study Coordinator	Pamela	Shaw	
Los Robles Regional Medical Center, Thousand Oaks, California, USA	Principal Investigator	Muhammad	Taqi	N Total = 7 SR Classic = 1 *SR Combo = 6/7 (86%) Direct Asp = 0
	Study Coordinator	Nicole	Mercado	
	Study Coordinator	Anastasia	Vechera	
Valley Baptist Harlingen, Harlingen, Texas, USA	Principal Investigator	Ameer	Hassan	N Total = 7 SR Classic = 0 *SR Combo = 7/7 (100%) Direct Asp = 0
	Sub-Investigator	Wondwossen	Tekle	
	Study Coordinator	Pualani	Smith	
Azienda Ospedaliero-Universitaria di Parma, Parma, IT	Principal Investigator	Roberto	Menozzi	N Total = 6 *SR Classic = 0/6 (0%) SR Combo = 5 Direct Asp = 1
	Sub-Investigator	Enrico	Epifani	
	Sub-Investigator	Andrea	Andreone	
	Sub-Investigator	Matteo	Fantoni	
Azienda Ospedaliera Universitaria le scotte, Siena, IT	Principal Investigator	Ignazio	Vallone	N Total = 6 SR Classic = 0 *SR Combo = 0/6 (0%) Direct Asp = 6
	Sub-Investigator	Sandra	Bracco	
	Sub-Investigator	Paola	Gennari	
Hospital Vall d'Hebron, Barcelona, ES	Principal Investigator	Alejandro	Tomasello	N Total = 6 SR Classic = 0 *SR Combo = 3/6 (50%) Direct Asp = 3
	Sub-Investigator	David	Hernandez	
	Sub-Investigator	Manuel	Requena	
	Sub-Investigator	Carlos	Piñana	
	Sub-Investigator	Marc Ribó	Ribó	
	Study Coordinator	Eila	Rivera	
Centre Hospitalier Universitaire Vaudois, Lusanne, Switzerland	Principal Investigator	Guillaume	Saliou	N Total = 5 SR Classic = 0 SR Combo = 2 *Direct Asp = 3/5 (60%)
	Sub-Investigator	Francesco	Puccinelli	
	Sub-Investigator	Bruno	Bartolini	
	Sub-Investigator	Steven	Hajdu	
	Principal Investigator	Enrico	Cotroneo	N Total = 5 SR Classic = 0
	Sub-Investigator	Andrea	Vallone	

Azienda Ospedaliera San Camillo Forlanini, Rome, IT	Sub-Investigator	Enrico	Pampana	SR Combo = 0 *Direct Asp = 5/5 (100%)
	Sub-Investigator	Sebastiano	Fabiano	
	Sub-Investigator	Luca	Bertaccini	
Buffalo University, Buffalo, New York, USA	Principal Investigator	Elad	Levy	N Total = 5 SR Classic = 0 *SR Combo = 4/5 (80%) Direct Asp = 1
	Sub-Investigator	Adnan	Siddiqui	
	Sub-Investigator	Kenneth	Snyder	
	Sub-Investigator	Jason	Davies	
	Regulatory Specialist	Jennifer	Gay	
	Study Coordinator	Mary	Hartney	
	Study Coordinator	Staci	Smith	
	Study Coordinator	Shelby	Halm	
Thomas Jefferson University, Philadelphia, Pennsylvania, USA	Principal Investigator	Stavropoula	Tjoumakaris	N Total = 5 SR Classic = 0 SR Combo = 2 *Direct Asp = 3/5 (60%)
	Sub-Investigator	Pascal	Jabbour	
	Sub-Investigator	Michael Reid	Gooch	
	Sub-Investigator	Nabeel	Herial	
	Study Coordinator	Viola	Dallas	
	Study Coordinator	Nadirah	Jones	
William Beaumont Hospital, Royal Oak, Michigan, USA	Principal Investigator	Jeffery	Wilseck	N Total = 5 SR Classic = 0 SR Combo = 0 *Direct Asp = 5/5 (100%)
	Sub-Investigator	Chris	Kazmierczak	
	Study Coordinator	Karen	Sherer	
	Study Coordinator	Grace	San Agustin	
	Study Coordinator	Pamela	Sloan	
Allegheny General Hospital, Pittsburgh, Pennsylvania, USA	Principal Investigator	Andrew	Ku	N Total = 4 SR Classic = 0 *SR Combo = 3/4 (75%) Direct Asp = 1
	Sub-Investigator	Jonathan	Pace	
	Regulatory Coordinator	Laurie	Dennis	
	Regulatory Coordinator	Pamela	White	
	Study Coordinator	Mary	Fetter	
	Study Coordinator	Emily	Shank	
Research Institute, University of Kansas	Principal Investigator	Michael	Abraham	N Total = 4 SR Classic = 0
	Sub-Investigator	John	Ernest Madarang	

Medical Center, Kansas City, Kansas, USA	Sub-Investigator	Alan	Reeves	SR Combo = 2 *Direct Asp = 2/4 (50%)
	Study Coordinator	Carissa	Walter	
	Study Coordinator	Angie	Barton	
	Study Coordinator	Gentry	Fowler	
	Study Coordinator	Peyton	Ackerman	
Banner Desert Medical Center, Mesa, Arizona, USA	Principal Investigator	Mohamed	Teleb	N Total = 4 SR Classic = 0 SR Combo = 0 *Direct Asp = 4/4 (100%)
	Sub-Investigator	Joel	Stary	
	Nurse Practitioner	Anna	VerHage	
	Nurse Practitioner	Kirstyn	Andrade Hayes	
	Nurse Practitioner	Megan	Smith	
	Nurse Practitioner	Jennifer	Jones Berry	
	Study Coordinator	Stephanie	Blythe	
	Study Coordinator	Robert	Flynn	
	Regulatory Coordinator	Jenny	Maxon	
	Regulatory Coordinator	Doaa	Abdelmoety	
UC Irvine, Irvine, California, USA	Principal Investigator	Shuichi	Suzuki	N Total = 4 SR Classic = 0 SR Combo = 3 *Direct Asp = 1/4 (25%)
	Sub-Investigator	Kiarash	Golshani	
	Sub-Investigator	Ichiro	Yuki	
	Study Coordinator	Jeein	Kim	
	Study Coordinator	Chris	Nishi	
Hospital Universitario Marqués de Valdecilla, Santander, ES	Principal Investigator	Andrés	González-Mandly	N Total = 4 *SR Classic = 4/4 (100%) SR Combo = 0 Direct Asp = 0
	Sub-Investigator	Alberto	Gil Garcia	
	Sub-Investigator	Enrique	Palacio	
CHU Pellegrin Service de Radiologie et de Neuro-Imagerie, Bordeaux, FR	Principal Investigator	Xavier	Barreau	N Total = 3 SR Classic = 0 SR Combo = 1 *Direct Asp = 2/3 (67%)
	Sub-Investigator	Jérome	Berge	
	Sub-Investigator	Gaultier	Marnat	
	Sub-Investigator	Patrice	Menegon	
	Sub-Investigator	Florent	Gariel	
	Sub-Investigator	Nicolas	Pangon	

	Study Coordinator	Tristan	Kerdraon	
Sparrow Clinical Research Institute, Lansing, Michigan, USA	Principal Investigator	Anmar	Razak	N Total = 3 SR Classic = 0 SR Combo = 1 *Direct Asp = 2/3 (67%)
	Sub-Investigator	Yogesh	Gujrati	
	Sub-Investigator	Muhammad	Saleemi	
	Study Coordinator	Janelle	Dreffs	
	Study Coordinator	Sandra	Mitchell	
	Study Coordinator	Jennifer	Boak	
	Study Coordinator	Lonna	Blaske	
	Regulatory Coordinator	Jacki	Wilson	
Legacy Emanuel Medical Center, Portland, Oregon, USA	Principal Investigator	David	Siker	N Total = 3 SR Classic = 0 *SR Combo = 3/3 (100%) Direct Asp = 0
	Study Coordinator	Karla	Kummer	
	Regulatory Coordinator	Laura	Allen	
Baptist Jacksonville, Jacksonville, Florida, USA	Principal Investigator	Amin	Aghaebrahim	N Total = 3 SR Classic = 0 *SR Combo = 3/3 (100%) Direct Asp = 0
	Sub-Investigator	Ricardo	Hanel	
	Sub-Investigator	Eric	Sauvageau	
	Study Coordinator	Vickie	Melton	
	Study Coordinator	Nancy	Ebreo	
	Study Coordinator	LaNaya	Lewis	
	Study Coordinator	Miranda	Smudzinski	
	Study Coordinator	Gina	Munden	
	Regulatory Coordinator	Carrie	Thornton	
University of S. Florida/Tampa General, Florida, USA	Principal Investigator	Maxim	Mokin	N Total = 3 SR Classic = 0 SR Combo = 0 *Direct Asp = 3/3 (100%)
	Sub-Investigator	Waldo	Guerrero	
	Sub-Investigator	Shail	Thanki	
	Sub-Investigator	Kunal	Vakharia	
	Study Coordinator	Amy	DeNardo	
	Study Coordinator	Jordan	Nickels	
	Regulatory Coordinator	Rachel	Karlnoski	

Stanford, Stanford, California, USA	Principal Investigator	Robert	Dodd	N Total = 3 SR Classic = 0 *SR Combo = 0/3 (0%) Direct Asp = 3
	Sub-Investigator	Nick	Telischak	
	Sub-Investigator	Huy	Do	
	Study Coordinator	Anthony	Bet	
	Sub-Investigator	Jérome	Berge	
	Sub-Investigator	Gaultier	Marnat	
	Sub-Investigator	Patrice	Menegon	
	Sub-Investigator	Florent	Gariel	
	Sub-Investigator	Nicolas	Pangon	
	Study Coordinator	Tristan	Kerdraon	
Klinikum Kassel, Institut für Neuroradiologie, Kassel, DE	Principal Investigator	Ralf	Siekmann	N Total = 2 SR Classic = 0 *SR Combo = 1/2 (50%) Direct Asp = 1
	Sub-Investigator	Kai	Koller	
	Sub-Investigator	Monika	Huegens-Penzel	
	Study Coordinator	Tanja	Reuter	
	Study Coordinator	Frank	Lückert	
Klinikum LMU München, Munich, DE	Principal Investigator	Thomas	Liebig	N Total = 2 SR Classic = 0 SR Combo = 0 *Direct Asp = 2/2 (100%)
	Sub-Investigator	Robert	Forbrig	
	Sub-Investigator	Yigit	Özpeynirci	
	Sub-Investigator	Christoph	Trumm	
	Sub-Investigator	Christian	Brem	
	Study Coordinator	Andrea	Jäger	
University Medical Center, El Paso, Texas, USA	Principal Investigator	Alberto	Maud	N Total = 2 SR Classic = 0 *SR Combo = 2/2 (100%) Direct Asp = 0
	Principal Investigator	Gustavo	Rodriguez	
	Sub-Investigator	Faheem	Sherriff	
	Sub-Investigator	Ofelia	Portillo	
	Study Coordinator	Israel	Alba	
Riverside Methodist – OHRI, Columbus, Ohio, USA	Principal Investigator	Ronald	Budzik	N Total = 2 *SR Classic = 1/2 (50%) SR Combo = 1 Direct Asp = 0
	Sub-Investigator	Nirav	Vora	
	Sub-Investigator	Peter	Pema	
	Sub-Investigator	Abdulnasser	Alhajeri	
	Study Coordinator	Megan	Heckathorne	
	Study Coordinator	Katy	Groezinger	

	Study Coordinator	Heather	Bartelt	
	Regulatory Coordinator	Diane	Goodman	
	Regulatory Coordinator	Laura	Geran	
University of Massachusetts, Worcester, Massachusetts, USA	Principal Investigator	Jasmeet	Singh	N Total = 2 SR Classic = 0 *SR Combo = 0/2 (0%) Direct Asp = 2
	Sub-Investigator	Francesco	Massari	
	Study Coordinator	Noelle	Bodkin	
	Study Coordinator	Baaba	Baiden	
University of Oklahoma Medical Center, Oklahoma, USA	Principal Investigator	Ahmed	Cheema	N Total = 1 SR = 0 SR Classic Combo = 0 *Direct Asp = 1/1 (100%)
	Principal Investigator	Andrew	Bauer	
	Sub-Investigator	Hakeem	Shakir	
	Study Coordinator	April	Vaughan	
	Study Coordinator	Zainab	Al Obaidi	
	Study Coordinator	Blair	Apple	
Imperial College Healthcare NHS Trust Charing Cross Hospital, London, UK	Principal Investigator	Kyriakos	Lobotesis	N Total = 1 SR Classic = 0 SR Combo = 0 *Direct Asp = 1/1 (100%)
	Sub-Investigator	Abhinav	Singh	
	Sub-Investigator	Neil	Rane	
	Sub-Investigator	Dylan	Roi	
	Sub-Investigator	Gavin	Fatania	
	Study Coordinator	Sarah	Cardona	
	Study Coordinator	Tina	Stoycheva	
	Regulatory Coordinator	Lesley	Honeyfield	
CHU Rouen “Charles Nicolle”, Rouen, FR	Principal Investigator	Chrysanthi	Papagiannaki	N Total = 1 SR Classic = 0 *SR Combo = 1/1 (100%) Direct Asp = 0
	Sub-Investigator	Margaux	Lefebvre	
	Study Coordinator	Sebastien	Normant	

Table S2: Sensitivity Analyses

	SR Classic	SR Combination	Direct Aspiration	p-value
Primary Clinical Endpoint 90-day mRS 0-2 vs 3-6				
90-day value, with missing data set to 3-6	140 (56.7)	351 (50.4)	273 (49.8)	0.40
Last observation carried forward (LOCF)	145 (58·7)	361 (52·3)	298 (54·6)	0·41
Primary Procedural Endpoint eTICI 2c or 3 vs <2c on the first pass for treatment of target occlusion				
eTICI with missing data set to <2c [1]	110 (44·5)	309 (44·3)	193(35·2)	0·01

[1] If eTICI at end of first pass for treatment of target occlusion is missing, eTICI is set to <2c to represent a failure.

Table S3: Serious Adverse Events

	SR Classic		SR Combination		Direct Aspiration	
MedDRA System Organ Class/Preferred Term	**Procedure**	**Device [1]**	**Procedure**	**Device [1]**	**Procedure**	**Device [1]**
Any Serious Adverse Event(SAE)	16 (6·5%)	8 (3·2%)	40 (5·7%)	6 (0·9%)	23 (4·2%)	5 (0·9%)
Blood and lymphatic system disorders	0	0	3 (0·4%)	0	1 (0·2%)	0
Gastrointestinal disorders	1 (0·4%)	0	2 (0·3%)	0	0	0
General disorders and administration site conditions	0	0	1 (0·1%)	0	0	0
Injury, poisoning and procedural complications	1 (0·4%)	0	10 (1·4%)	0	1 (0·2%)	0
Nervous system disorders	12 (4·9%)	8 (3·2%)	19 (2·7%)	5 (0·7%)	13 (2·4%)	5 (0·9%)
Product issues	0	0	1 (0·1%)	0	0	0
Renal and urinary disorders	0	0	0	0	3 (0·5%)	0
Respiratory, thoracic and mediastinal disorders	0	0	1 (0·1%)	0	1 (0·2%)	0
Surgical and medical procedures	0	0	1 (0·1%)	0	0	0
Vascular disorders	3 (1·2%)	0	3 (0·4%)	1 (0·1%)	5 (0·9%)	1 (0·2%)

Values reported as n (%) are on a subject level. If a subject has multiple events, they are only counted once within a category.
[1] Only SAEs related to Stryker devices are reported.

Table S4: Non-serious Adverse Events

MedDRA System Organ Class/Preferred Term	SR Classic		SR Combination		Direct Aspiration	
	Procedure	Device [1]	Procedure	Device [1]	Procedure	Device [1]
Any Non-Serious Adverse Event (AE)	24 (9·7%)	3 (1·2%)	44 (6·3%)	11 (1·6%)	25 (4·6%)	5 (0·9%)
Cardiac disorders	1 (0·4%)	0	1 (0·1%)	0	0	0
Ear and labyrinth disorders	0	0	0	0	1 (0·2%)	0
Gastrointestinal disorders	0	0	1 (0·1%)	0	0	0
General disorders and administration site conditions	0	0	1 (0·1%)	0	3 (0·5%)	0
Infections and infestations	0	0	1 (0·1%)	0	0	0
Injury, poisoning and procedural complications	2 (0·8%)	1 (0·4%)	7 (1·0%)	0	5 (0·9%)	0
Nervous system disorders	17 (6·9%)	2 (0·8%)	26 (3·7%)	9 (1·3%)	15 (2·7%)	5 (0·9%)
Psychiatric disorders	0	0	1 (0·1%)	0	0	0
Renal and urinary disorders	0	0	4 (0·6%)	0	0	0
Respiratory, thoracic and mediastinal disorders	0	0	1 (0·1%)	0	1 (0·2%)	0
Vascular disorders	5 (2·0%)	0	6 (0·9%)	2 (0·3%)	1 (0·2%)	0

Note: Values reported as n (%) are on a subject level. If a subject has multiple events, they are only counted once within a category.
[1] Only AEs related to Stryker devices are reported.

Table S5 Device malfunctions (Stryker only)

Device Malfunction/Nonconformity	# Events	# Subjects (n (%))
Any malfunction/nonconformity	41	30 (2·01%)
Damage to device noted (kink, bend, fracture) inside of package/removing from package; device not used	1	1 (3·33%)
Device Sterility Compromised; Device not used	0	0 (0·00%)
Failure to Deliver Device at Intended Location	10	10 (33·33%)
Retriever shaped section will not fully open inside vessel	0	0 (0·00%)
Positioning issues (Difficulty re-sheathing the retriever)	2	2 (6·67%)
Retriever clot integration issue/retracting issue	3	3 (10·00%)
Resistance during advancement	4	4 (13·33%)
Poor visualization of device	0	0 (0·00%)
Device separation or fracture during procedure use	0	0 (0·00%)
Device deformation or collapse during procedure use	2	2 (6·67%)
Device difficult or could not be removed from vasculature	2	2 (6·67%)
Device kink/bend noticed during procedure use	3	3 (10·00%)
Balloon burst or unable to deflate	5	5 (16·67%)
Other	9	9 (30·00%)

Table S6: Race/ethnicity

	SR Classic	SR Combination	Direct Aspiration
Race, n (%) [1]			
Asian	22(20·2)	40(6·7)	14(3·9)
Black/African American	2(1·8)	45(7·6)	55(15·2)
Native Hawaiian/Pacific Islander	0	1(0·2)	1(0·3)
White	84(77·1)	497(83·4)	278(76·6)
Other	1(0·9)	13(2·2)	15(4·1)
Hispanic/Latino, n (%) [2]	5(4·7)	60(10·1)	53(14·8)

[1] 424 patients are missing data on race due to local regulatory requirements
[2] 431 patients are missing data on ethnicity due to local regulatory requirements

Table S7: Baseline Medications

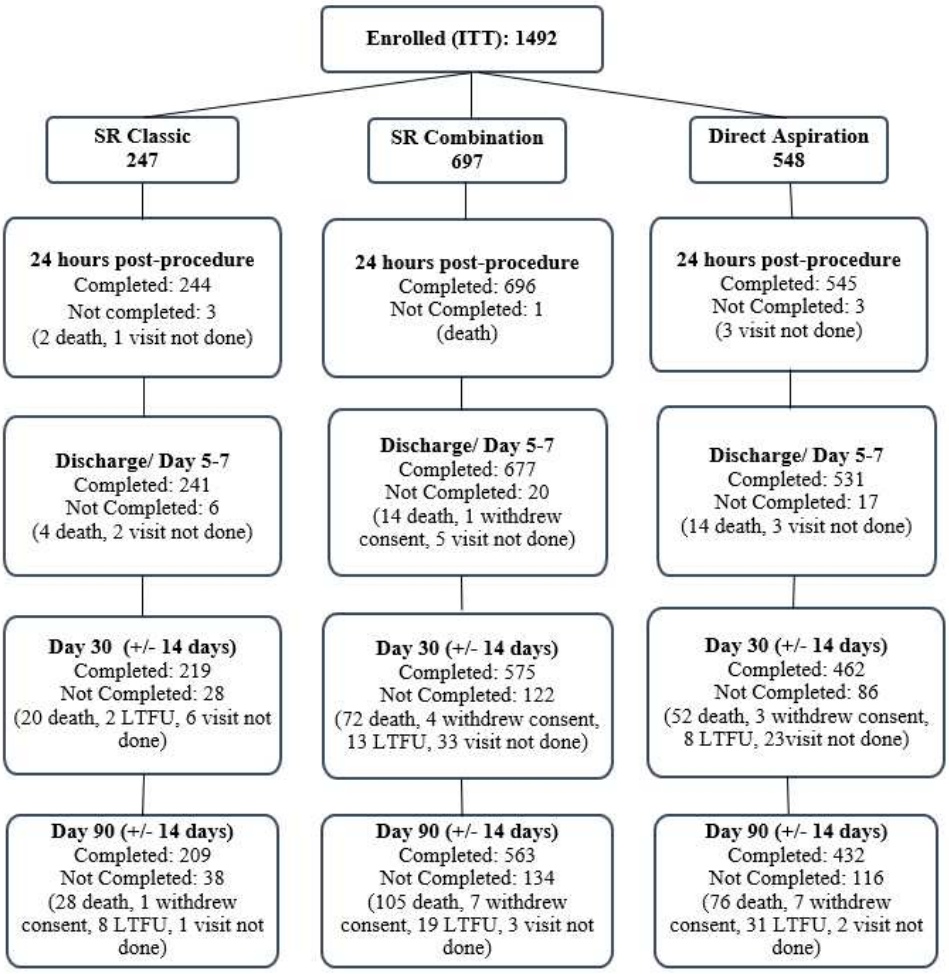
	SR Classic	SR Combination	Direct Aspiration
Taking anti-platelets/anti-coagulants	104 (42·1%)	351 (50·4%)	251 (45·9%)
Aspirin	45 (43·3%)	210 (59·8%)	145 (57·8%)
Dipyridamole (Persantine®)	0	0	0
Aspirin & Dipyridamole (Aggrenox®)	0	3 (0·9%)	0
Clopidogrel (Plavix®)	12 (11·5%)	45 (12·8%)	33 (13·1%)
Cilostazol (Pletal®)	0	0	0
Ticlopidine (Ticlid®)	0	3 (0·9%)	0
Warfarin (Coumadin®)	16 (15·4%)	38 (10·8%)	20 (8·0%)
Direct thrombin Inhibitor	5 (4·8%)	6 (1·7%)	5 (2·0%)
Factor Xa inhibitor	21 (20·2%)	82 (23·4%)	65 (25·9%)
Low molecular weight heparin	9 (8·7%)	17 (4·8%)	10 (4·0%)
Unfractionated Heparin IV	2 (1·9%)	6 (1·7%)	4 (1·6%)
Other anti-platelet/anti-coagulant	15 (14·4%)	11 (3·1%)	16 (6·4%)
Taking IIb/IIa inhibitors	1 (0·4%)	1 (0·1%)	1 (0·2%)
Abciximab (ReoPro®)	0	0	0
Tirofiban (Aggrastat®)	0	1 (100·0%)	1 (100·0%)
Eptifibatide (Integrilin®)	0	0	0
Other IIb/IIIa Inhibitor	1 (100·0%)	0	0
Taking other meds	170 (68·8%)	483 (69·4%)	380 (69·5%)
Statin(s)	100 (58·8%)	274 (56·7%)	213 (56·1%)
Diabetic Medication(s)	38 (22·4%)	106 (21·9%)	98 (25·8%)
Anti-hypertensive Medication(s)	142 (83·5%)	405 (83·9%)	315 (82·9%)
Anti-convulsant Medication(s)	5 (2·9%)	32 (6·6%)	23 (6·1%)

Table S8: Hemorrhage Type (Core Lab Data):

	SR Classic	SR Combination	Direct Aspiration
Any hemorrhage			
Yes	85(35.3%)	262(38·9%)	234(43·5%)
No	156(64.7%)	412(61·1%)	304(56·5%)
Hemorrhage Type			
HI-1	33(38.8%)	116(44·3%)	109(46·6%)
HI-2	22(25.9%)	81(30.9%)	82(35·0%)
PH-1	0	2(0·8%)	0
PH-2	3(3·5%)	11(4·2%)	9(3·8%)
RIH	1(1·2%)	0	0
IVH	0	0	0
Subdural	0	0	0
Epidural	0	0	0
SAH	34(40·0%)	81(30.9%)	53(22·6%)

Subjects can have more than one hemorrhage type.

Figure S1: Flowchart


Enrolled (ITT): 1492
SR Classic 247
SR Combination 697
Direct Aspiration 548
24 hours post-procedure
Completed: 244
Not completed: 3
(2 death, 1 visit not done)
24 hours post-procedure
Completed: 696
Not Completed: 1
(death)
24 hours post-procedure
Completed: 545
Not Completed: 3
(3 visit not done)
Discharge/ Day 5-7
Completed: 241
Not Completed: 6
(4 death, 2 visit not done)
Discharge/ Day 5-7
Completed: 677
Not Completed: 20
(14 death, 1 withdrew consent, 5 visit not done)
Discharge/ Day 5-7
Completed: 531
Not Completed: 17
(14 death, 3 visit not done)
Day 30 (+/- 14 days)
Completed: 219
Not Completed: 28
(20 death, 2 LTFU, 6 visit not done)
Day 30 (+/- 14 days)
Completed: 575
Not Completed: 122
(72 death, 4 withdrew consent, 13 LTFU, 33 visit not done)
Day 30 (+/- 14 days)
Completed: 462
Not Completed: 86
(52 death, 3 withdrew consent, 8 LTFU, 23visit not done)
Day 90 (+/- 14 days)
Completed: 209
Not Completed: 38
(28 death, 1 withdrew consent, 8 LTFU, 1 visit not done)
Day 90 (+/- 14 days)
Completed: 563
Not Completed: 134
(105 death, 7 withdrew consent, 19 LTFU, 3 visit not done)
Day 90 (+/- 14 days)
Completed: 432
Not Completed: 116
(76 death, 7 withdrew consent, 31 LTFU, 2 visit not done)