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A New Class of Radially Adjustable Stentrievers for Acute Ischemic Stroke: Primary Results of the Multicenter Tiger Trial

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Abstract

Background and Purpose: The Tigertriever is a novel, radially adjustable, fully visible, stentriever that permits the operator to align radial expansion with target vessel diameters. This multicenter trial compared the Tigertriever's effectiveness and safety compared with established stent retrievers.

Methods: Single arm, prospective, multicenter trial comparing the Tigertriever to efficacy and safety performance goals derived from outcomes in six recent pivotal studies evaluating the Solitaire and Trevo stent-retriever devices with a lead-in and a main-study phase. Patients were enrolled if they had acute ischemic stroke with NIHSS≥8 due to large vessel occlusion within 8 hours of onset. The primary efficacy endpoint was successful reperfusion, defined as core laboratory-adjudicated modified Thrombolysis in Cerebral Ischemia (mTICI) score 2b-3 within three passes of the Tigertriever. The primary safety endpoint was a composite of 90-day all-cause mortality and symptomatic intracranial hemorrhage (sICH). Secondary efficacy endpoints included 3-month good clinical outcome (modified Rankin Scale 0-2) and first-pass successful reperfusion.

Results: Between May 2018 and March 2020, 160 patients (43 lead-in, 117 main phase) at 17 centers were enrolled and treated with the Tigertriever. The primary efficacy endpoint was achieved in 84.6% in the main-study phase group compared with the 63.4% performance goal and the 73.4% historical rate (non-inferiority $p<0.0001$; superiority $p<0.01$). The first pass successful reperfusion rate was 57.8%. After all interventions, successful reperfusion (mTICI ≥2b) was achieved in 95.7% and excellent reperfusion (mTICI 2c-3) in 71.8%. The primary safety composite endpoint rate of mortality and sICH was 18.1% compared with the 30.4% performance goal and the 20.4% historical rate (non-inferiority $p=0.004$; superiority $p=0.57$). Good clinical outcome was achieved in 58% at 90 days.

Conclusions: The Tigertriever device was shown to be highly effective and safe compared to Trevo and Solitaire devices to remove thrombus in large vessel occlusive stroke patients eligible for mechanical thrombectomy.

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Abbreviations

ASPECT	Alberta Stroke Program Early CT
BGC	balloon guide catheter
DSMB	data and safety monitoring board
IQR	interquartile range
IV tPA	intravenous tissue plasminogen activator
mRS	modified Rankin Score
mTICI	modified Thrombolysis in Cerebral Ischemia
NIHSS	National Institutes of Health Stroke Scale
PG	performance goal
sICH	symptomatic intracranial hemorrhage

Introduction

Based on convergent evidence from major clinical trials of reperfusion efficacy and improved clinical outcomes, endovascular thrombectomy with stent retrievers has become the standard of care for patients with large vessel occlusion (LVO) ischemic strokes.[1-8] A meta-analysis of five randomized trials demonstrated the number needed to treat with thrombectomy is 1 in 2.6 to improve 3 month global disability outcome by 1 or more levels on the modified Rankin Score (mRS).[9] However, while quite substantial, the benefits conveyed by first-generation stent retrievers are constrained by less than maximal reperfusion rates achieved with these devices. In pooled, individual participant data meta-analyses of the pivotal trials, failure to achieve successful reperfusion (mTICI 2b-3) occurred in 29% of patients and failure to achieve complete reperfusion (mTICI 3) in 67%.[9] Accordingly, developing additional endovascular thrombectomy devices with performance characteristics comparable or better than established stent retrievers is desirable.

The Tigertriever (Rapid Medical) is a novel operator-adjustable stent retriever that affords the interventionalist incremental control over the radial diameter and radial force of the thrombectomy basket. The design is intended to facilitate alignment of the mesh with the anatomy of the occluded vessel and to increase internalization of the thrombus within the device, thereby facilitating retrieval and reducing downstream embolization. (Figure 1A; Supplementary Figure I). The device has had CE mark, the European Union certification indicating conformity with health, safety, and environmental protection, since 2016 and has shown promising signals of efficacy and safety in preliminary case series reported by European centers.[10-12]

The TIGER (Treatment with Intent to Generate Endovascular Reperfusion) trial was a single-arm, multicenter, prospective study assessing the efficacy and safety of the Tiger-21 and Tiger-17 retrievers. The study employed an objective performance criterion, non-inferiority design, comparing efficacy and safety of the Tigertriever with performance goals derived from adjudicated outcomes in six completed prospective trials of two FDA-approved predicate stent retrievers, Solitaire (Medtronic) and Trevo (Stryker).[1-4,13-14]

Methods

Study Design

The data that support the findings of this study are available from the corresponding author on reasonable request and with approval from the TIGER investigators. The primary TIGER study hypothesis was that the Tigertriever device would achieve successful reperfusion performance within 3 attempts would be superior to the performance goal

established using Bayesian meta-analysis of six recent pivotal trials of the Solitaire and Trevo stent-retriever devices - TREVO 2[13], SWIFT[14], MR CLEAN[1], ESCAPE[4], REVASCAT[3] and SWIFT PRIME[2].

The study was overseen by an executive committee, composed of academic investigators, and an independent data and safety monitoring board (DSMB) (Supplementary Table I). The DSMB consisted of an independent stroke neurologist and two independent neurointerventionalists, who did not enroll patients, and a biostatistician. At the level of individual events, the DSMB adjudicated all safety endpoints, including hemorrhages and serious adverse events. At the level of aggregate study data, the DSMB acted in an expert supervisory capacity and monitored subject safety and the conduct of the study. Central readers at a core imaging laboratory assessed qualifying diagnostic catheter angiography to determine location of the target occlusion, and rated reperfusion grades on angiograms obtained after every pass of the Tigertriever device, every pass of rescue therapy, and end of the procedure. The core lab imaging readers also assessed baseline and 24-hour post-procedure CT or MRI scans to verify study entry criteria and determine the presence and type of any post-procedure intracranial hemorrhage. The sponsor, Rapid Medical, and its contracted Contract Research Organization (Genae Americas) were responsible for logistical operations, data management, and monitoring of the trial. The study protocol was approved by the institutional review board or ethics committee at each participating site.

Population and Participating Centers

All patients or their legally authorized representative provided written informed consent before enrollment. Patients aged 18 to 85 years were eligible for the study if they had acute ischemic stroke (AIS) with new moderate-to-severe neurologic deficits, angiographically confirmed occlusion in the intracranial internal carotid, middle cerebral (M1 or M2 segment), basilar, or vertebral artery, and could undergo endovascular therapy (at least one Tigertriever deployment in the target artery) within 8 hours of last known well. Full study entry criteria are shown in the online-only Data Supplement (Supplementary Table II). Key inclusion criteria included: prestroke mRS ≤1; baseline National Institutes of Health Stroke Scale (NIHSS) score 8-29; Alberta Stroke Program Early CT Score 6-10 for CT-qualifying or diffusion restriction volume ≤50 mL for MRI-qualifying anterior circulation cases; ; patient being either: a) eligible for, and received, intravenous tissue plasminogen activator (IV tPA) within 3 hours of symptom onset, or b) ineligible for IV tPA treatment; and anticipated

device deployment within 8 hours of last known well.. Key exclusion criteria included stenosis or occlusion in the deployment site or in a proximal vessel that would prevent device access to the thrombus or require angioplasty or stenting to enable device access to the thrombus. The treatment start inclusion criterion of within 8 hours, rather than also 8-24 hours with advanced imaging selection, was selected as initial trial design discussions and review with the Food and Drug Administration occurred prior to the reporting of results of late window trials. Physicians were trained in the use of the device on a bench vascular model before any procedures were done. In addition, participating sites that had no experience with the Tigertriever device were required to first participate in a lead-in phase before participating in the main-study phase for primary endpoint analysis. During the lead-in phase, up to 4 patients per clinical site were enrolled. The lead-in phase was completed by the site either: 1) achieving two successive successful reperfusions (mTICI 2b or higher), or 2) performing 4 cases. Patients enrolled in the lead-in phase were consented, treated, and followed according to the clinical protocol, in the same manner as the main study patients.

Procedure

Site of arterial access and anesthesia mode were based on operator preference at the enrolling center. The selection of guide catheter type (balloon guide catheter (BGC) vs. non-BGC) and use of an intermediate catheter was also at the discretion of the operator. After placement of the guide catheter in the target vessel, a roadmap was constructed and the microcatheter was navigated across the clot. The Tigertriever was deployed and the amount of expansion of the device was based on vessel diameter and clot length.

Two versions of the Tigertriever device were available: The standard version (Tigertriever) has a net length of 32 mm (unexpanded form) and can expand up to 6 mm diameter, can be delivered through a microcatheter with an internal diameter of 0.021 inches. And a smaller version (Tigertriever 17) has a net length of 23 mm (unexpanded form) and can be delivered through a microcatheter with an internal diameter of 0.017 inches. It can expand up to 3 mm diameter. The device deployment, dwell time, and number of expansions/deflations were based on the instructions for use. The first pass was required to be with the Tigertriever for inclusion in the trial. Up to 3 passes of the Tigertriever were permitted to achieve successful reperfusion (mTICI, 2b-3). For each pass, a new Tigertriever device was used and the total number of passes and devices used were recorded. After three attempts, rescue therapy could be employed by the operator. Rescue therapy could consist of use of another mechanical thrombectomy device, angioplasty, intra-arterial tPA, or intracranial stenting at the discretion of the treating physician. The Tigertriever could not be

used after a rescue attempt and for primary efficacy analysis when revascularization was unsuccessful after Tigertriever attempts it was considered a failure to achieve the endpoint. Imaging with CT or MRI was obtained at 24 hours to assess for intracranial hemorrhage. NIHSS scores were obtained at 24 hours, 48 hours, 4 days (or discharge if sooner) and 90 days; mRS scores were obtained at 4 days (or discharge if sooner), 30 days, and 90 days.

Outcomes

Primary Efficacy Endpoint

The primary efficacy endpoint was successful reperfusion, defined as achieving mTICI 2b-3 within 3 passes with the Tigertriever without use of rescue therapy. All angiograms were interpreted by an experienced neurointerventionalist readers at the independent core imaging laboratory, who assigned scores using the mTICI scale.[15] The core imaging laboratory mTICI ratings were used for assessment of the primary efficacy endpoint.

Primary Safety Endpoint

The primary safety endpoint was defined as the composite of all-cause mortality at 90±14 days and symptomatic intracranial hemorrhage (sICH) within 24 (18-36) hours from the study procedure. sICH was defined as any parenchymal hematoma type 2 hematoma (PH-2), remote intracerebral hemorrhage, subarachnoid hemorrhage or intraventricular hemorrhage that is the predominant cause of an NIHSS deterioration of 4 or more points at 24 hours, as adjudicated by the DSMB (modified Heidelberg Bleeding Classification criteria).[16] The independent core imaging laboratory assessed all 24 hour CT/MR images and radiologically classified hemorrhages as hemorrhagic infarction types 1 or 2, parenchymal hematoma types 1 or 2, remote intracerebral hemorrhage, subarachnoid hemorrhage, and intraventricular hemorrhage.

Secondary EndPoints

Prespecified secondary efficacy endpoints for the study were: 1) good clinical outcome (mRS 0-2 at 90 days; 2) first pass successful reperfusion (mTICI 2b-3); 3) health-related quality of life at 90 days, assessed with the EQ-5D[2,17]; 4) granular level of disability at 90 days, assessed with the Academic Medical Center Linear Disability Score (ALDS).[18,19] Prespecified secondary safety endpoints were: 1) asymptomatic intracranial hemorrhage within 24h (18h-36h) of procedure; 2) neurological deterioration within 24 hours after procedure, defined as a NIHSS increase of 4 points or more; 3) embolization to previously uninvolved vascular territories.

Statistical Analysis

The performance goal for the efficacy primary endpoint was defined as the incidence in the six trials cited below, minus a non-inferiority statistical margin of 10%, the same clinically relevant threshold employed in the registration trials of stent-retrievers, SWIFT and TREVO2,[9, 13] therefore giving a performance goal (PG) of 73.4% - 10% = 63.4%. The pooled incidence was derived from the following six studies: TREVO2, SWIFT[1] MR CLEAN, ESCAPE, REVASCAT and SWIFT PRIME.[1,2,3,4,9,13]. For this efficacy endpoint the primary non-inferiority hypothesis test was performed at an overall two-sided alpha level of 0.05 using exact binomial methods, in which the lower confidence bound on the observed incidence of reperfusion is compared to the PG. If non-inferiority was demonstrated, superiority was then tested in a post-hoc hierarchical manner. The study statistical design is shown graphically in Supplementary Figure IIA.

The PG for safety primary endpoint was defined as the incidence in the six trials cited above, plus a statistical margin of 10%. Thus, the PG was 30.4% (18.2% mortality + 2.2% sICH + 10% non-inferiority statistical margin). For primary safety, the hypothesis test was performed at an overall two-sided alpha level of 0.05 using exact binomial methods, in which the upper confidence bound on the observed incidence of revascularization is compared to the PG.

The primary study population was the main-study phase group. Sensitivity analysis was performed at regulatory request on the combined lead-in/main-study phase population). To evaluate Tigertriever device performance in vessels with of varied size, the study population was divided into two vessel diameter categories, ≥2 mm and <2mm, and performance compared across the groups.

Results

Between May 2018 and March 2020. 1712 patients were preliminarily screened, 183 consented prior to angiography, and 160 met angiographic and device access criteria for full study enrollment. Patients were enrolled at 17 study centers (16 US centers – 159 patients, 1 Israeli center – 1 patient; Supplementary Table I) and included 43 lead-in phase and 117 main-study phase patients. Figure 1B shows the screening, enrollment, treatment, and follow-up flow of the study population.

Patient baseline characteristics are shown for the main-study phase and combined lead-in/main-study phase cohorts in Table 1. (Supplementary Table III shows patient characteristics for the lead-in phase patients alone; Supplementary Tables IV and V compare patient characteristics and outcomes in the current trial with the those of the 6 trials

contributing to the performance goal and the more recent ARISE II trial.) In the main-study phase cohort, patient age was mean 65±15 years, 61.5% were men, and median baseline NIHSS 17 (interquartile range [IQR] 12-21). The median Alberta Stroke Program Early CT (ASPECT) score was 9 (IQR, 8-10). Target occlusion location was in the anterior circulation in 97.4% of patients, with the most common sites the M1 MCA (57.3%) and intracranial ICA (20.5%). Time from last known normal to puncture was 172 minutes [IQR 128-273] and a majority (65.8%) of patients received intravenous t-PA prior to thrombectomy. A BGC was used in 29.9% of the procedures (21.4% BGC alone and8.5% BGC + regional aspiration).

Primary Efficacy EndPoint and Reperfusion Results

In the primary analysis main-study phase population, the Tigertriever achieved the primary endpoint of successful reperfusion (mTICI 2b-3) within 3 passes and without rescue therapy in 99 of 117 patients, 84.6% (95% CI 78.1%-91.2%), compared with the 63.4% performance goal and the 73.4% historical rate (non-inferiority $p<0.0001$; superiority $p<0.01$). (Table 2, Supplementary Figure IIB).

The full distribution of reperfusion outcomes is shown in Figure 2A. The rate of excellent reperfusion (mTICI 2c-3) within 3 passes of the Tigertriever was 63.2% and 71.8% after all interventions. The frequency of first pass excellent reperfusion (mTICI 2c-3) was 41.4% and of first pass substantial reperfusion (mTICI 2b-3) 57.8%. The mean number of passes with the Tigertriever was 1.8±0.9. The rates of reperfusion achieved with each device size (Tigertriever and Tigertriever 17) and in each target artery are reported in Supplementary Results Text I.

Rescue therapy was employed in 33 of 117 (28.2%) main-study phase patients (frequency of other mechanical thrombectomy devices, angioplasty, intra-arterial thrombolysis, and intracranial stenting shown in Supplementary Table VI). In 5, at the interventionalist's discretion, a different device was used prior to reaching 3 passes with Tigertriever. Per protocol, these were counted as failures despite not having not made three attempts with Tigertriever. In 13, the additional devices were used at interventionalist discretion to further improve reperfusion despite mTICI ≥2b having been attained within three passes of the Tigertriever. Per protocol, these were counted as Tigertriever successes in achieving mTICI≥2b Final reperfusion rates after all interventions were: 95.7% mTICI 2b-3; 71.8% mTICI 2c-3; and 41.9% mTICI 3. Median time from arterial puncture to successful reperfusion (mTICI 2b-3) was 24 minutes [IQR 16-38].

Primary efficacy endpoint and additional reperfusion results in lead-in patients did not statistically differ from main-study phase patient results (Supplementary Table VII).

Primary Safety Endpoint

In the primary analysis main-study phase population, the rate for the primary safety composite endpoint of combined sICH and 90-day all-cause mortality was 18.1% (95% CI 11.1%-25.1%, Table 3), compared to the PG of 30.4% and historical rate of 20.4% (noninferiority p=0.004; superiority p=0.57). The primary safety endpoint in lead-in patients did not statistically differ from main-study phase patient results (Supplementary Table VIII).

Secondary Endpoints

Secondary clinical efficacy outcomes are shown in Table 2. In main-study phase patients, good clinical outcome (functional independence, mRS 0-2) was attained by 58.0% (95% CI 48.3%-67.3%), a rate superior to the 43.5% in the pooled comparator trials (p=0.006). The full distribution of disability levels at 90 days is shown in Figure 2B. Health-related quality of life on the EQ-5D at 90 days was median 80 [IQR 70-90] and granular disability level on the ALDS at 90 days was median 93.3 [IQR 57.8-100].

Secondary safety outcomes are shown in Table 3. Neurological deterioration by 4 or more NIHSS points by 24 hours occurred in 7.7% (95% CI 3.6%-14.2%). The rate of embolization to a previously uninvolved new territory was 2.6% (95% CI 0.5%-7.4%), a rate superior to the 7.4 % in the pooled comparator trials (p=0.0403). Asymptomatic intracranial hemorrhage within 24h occurred in 31.0% (95% CI 22.7%-40.3%). (Additional data on radiologic classification of hemorrhages are shown in Supplementary Tables IX, X.)

Secondary clinical efficacy and safety results in lead-in patients did not statistically differ from main-study phase patient results (Supplementary Tables III, IV). All adverse events are shown in Supplementary Table XI.

Tigertriever Performance in Vessels of Different Size

Tigertriever performance in smaller (<2 mm) and larger (≥2 mm) vessels is shown in Table 4. Median vessel diameters were 1.6 mm (IQR 1.5-1.8) for smaller vessels and 2.5 mm (IQR 2.2-3.0) for larger vessels. Rates of both the primary efficacy endpoint (successful reperfusion) and the primary safety endpoint components (sICH at 24h and all-cause mortality at 90d) were comparable in both vessel size groups.

Discussion

In this prospective, multicenter trial, the Tigertriever yielded high rates of reperfusion among acute ischemic stroke patients with large vessel occlusion, with substantial reperfusion achieved in more than 8 of every 10 patients with the Tigertriever alone and more than 9 of every 10 patients after additional interventions. The rate of successful reperfusion surpassed

the pre-defined performance goal against the predicate Trevo and Solitaire devices derived from regulatory registration and additional pivotal trials. The high successful reperfusion rates with the Tigertriever device translated to favorable functional outcomes, with nearly 6 of every 10 patients achieving functional independence at day 90.

Patients enrolled in the TIGER study were similar to the comparator studies in several key features, including age, presenting deficit severity (NIHSS), extent of ischemic injury on initial imaging (ASPECTS), vascular risk factors, rate of pretreatment with t-PA, and frequency of target occlusion in ICA and M1 MCA (Supplementary Table IV). The frequency of M2 MCA occlusions was mildly higher in the present study than several comparator studies but lower than in the most recent comparator investigation, ARISE 2[20]. The greater proportion of M2 occlusions reflects the increasing treatment of more distal vessel occlusions in clinical practice.[21] M2 occlusions have features that make them both more difficult targets for EVT, including distal location, smaller size, reduced accessibility, and less difficult, including smaller thrombus burden. As the frequency of reperfusion of the M2 was similar to other occlusion sites in the present study, the distribution of target occlusions did not affect comparison with prior studies. Patients in this study were treated sooner after onset (last known well to puncture 2h 59m) than in prior studies. in accord with increasing emphasis in national guidelines and national practice on accelerating speed of endovascular thrombectomy .[6-8]

Reperfusion rates were better in the current study than in the comparator studies in a variety of parameters, including first pass reperfusion, mean number of passes, reperfusion after up to three passes before rescue therapy, and final reperfusion after rescue therapy. "First pass effect," defined as achieving mTICI 2c-3 reperfusion with one pass of the stent retriever, is likely to yield better patient outcomes and is a stringent metric to assess device performance.[22] In the current study, a first pass effect was achieved in 41.4% of patients, which compares favorably to the rate of 25% in both the North American Solitaire Acute Stroke (NASA) registry[23] and Trevo acute ischemic stroke (TRACK) registry[24]. In the ARISE II study the first pass effect was seen in 40% of patients[20] which is comparable to the present study. In the current study, successful reperfusion at procedure end, including rescue therapies, was achieved in nearly every patient (96%), a value that elevates cerebral reperfusion success rates to those of cardiac reperfusion procedures.[25,26]

Faster time from puncture to achievement of reperfusion has been associated with improved clinical outcomes.[27] The current study results demonstrate the median procedure

time (from puncture to achievement of mTICI ≥2b) was 25 [IQR 17-43] minutes which compares favorably to the ARISE II study, where the median time was 35 [IQR 24-58] minutes.[20] This time was similar to the contact aspiration first pass thrombectomy time of median 25 min as reported in the COMPASS study, but shorter than the median 35 minutes reported for that trial's stent retriever group.[28] . In experienced, high volume centers performing over 48 thrombectomies annually, the median puncture-to-reperfusion time with the Trevo device was 67 [IQR 42-105] minutes.[29] The reduced procedure times with the Tigertriever may reflect in part the technological advancement of the operator being able to adjust the radial force expansion to interact with the clot in a more productive manner.

The use of a BGC in the proximal vessel of the target occlusion when prior stent retrievers are deployed has been shown to improve the first pass reperfusion effect and clinical outcomes.[30] The proximal flow arrest may prevent distal embolization or non- target distal embolization. The unique design of the Tigertriever allows for more effective internalization of the thrombus into the interstices of the device. As the device is collapsed by the operator, it theoretically limits the chance of distal embolization as the clot is completely entwined in the retriever. The current study had a lower rate of BGC use at 35% in the intention to treat population, in comparison to the ARISE II trial in which this technique was used in 73.6% of patients[20]. Despite the lower use of BGC in this study, there were only 4 patients (2.5%) who had an embolization to a new territory compared to 6.6% in ARISE II and to 7.4% in the pooled data from of MR CLEAN[1], ARISE II[20], REVASCAT[3] and Trevo 2[13].

Clinical outcomes in the present study were favorable. Functional independence (mRS 0-2) at 90 days was achieved in 58% of patients, a rate higher than in the comparator studies. Similarly, health-related quality of life showed a utility value of 0.80, higher than the 0.57 in the MR CLEAN trial.[31] These high rates of good long-term functional outcome likely reflect reduced total brain ischemia time due to high achieved reperfusion rates, early last known well-to-punctures times, and rapid puncture-to-reperfusion times. The faster last known well-to-puncture times versus historical comparator trials likely reflects interval evolution in endovascular workflow and systems of care, while the increased perfusion rates and rapid puncture-to-reperfusion times likely at least in part reflect intrinsic properties of the Tigertriever itself.

Limitations

This study has limitations. The study design was a single-arm trial against objective performance criteria derived from pooled prior studies of predicate devices, rather than a

randomized trial with a contemporaneous control group. This approach constrains precision in delineating how well the Tigertriever compares with any particular comparator device. Reflecting the single-arm design, the central imaging and site clinical outcome evaluators and were not blinded to treatment assignment. However, for imaging the use of a central core laboratory was employed to mitigate any resulting bias. Similarly, for clinical outcomes, the primary efficacy outcome was performed by certified raters using a structured assessment system (the Rankin Focused Assessment) and the congruence of rater assessments of global disability and patient-reported health-related quality of life indicates accurate scoring.

Conclusion

In this prospective, multicenter study with a unique operator-controlled stent retriever, the Tigertriever achieved successful reperfusion within 3 passes in more than 8 of every 10 patients, demonstrating non-inferiority over a performance goal and superiority over actual historical rates derived from trials and prospective studies of established devices. In addition, first pass successful reperfusion was achieved in nearly 6 of every 10 patients and final successful reperfusion in more than 9 of every 10 patients. Rates of embolization to a new territory and sICH were low and rates of good global disability and health-related quality of life outcomes high. Efficacy and safety outcomes were similar in vessels with diameters <2mm and ≥2 mm.

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Dr. Gupta serves as Principal Investigator (PI) for the TIGER study (Rapid Medical), PI for the ASSIST Registry (Stryker Neurovascular), PI for the RECCLAIM II Study (Zoll), CLEAR Study (Vesalio), Clinical Events Committee (CEC) for the MIND Trial (Penumbra), consultant for Cerenovous. Dr Saver discloses consultant or advisory boards from Medtronic, Stryker, Cerenovus, and Rapid Medical; institutional conflict of interest from University of California. The University of California has patent rights in retrieval devices for stroke. Dr. Levy is consultant or advisory board or Ownership interest for Claret Medical, GLG consulting, Guidepoint Global, Imperative Care, Medtronic, StimMed, Misionix, Mosaic, Clarion, Stryker, NeXtGen Biologics, MEDX, Cognition Medical, Endostream Medical, Rapid Medical, Rebound Therapeutics, Three Rivers Medical, and received Honorarium for training from Medtronic and Penumbra. Dr. Zaidat is a consultant for Stryker Neurovascular, Cerenovous, Penumbra, Rapid Medical and Medtronic. He has also received research grants from Penumbra and Stryker Neurovascular. Dr. Yavagal is a consultant for Medtronic, Cerenovous, Rapid Medical, Vascular Dynamics, Poseydon, Neurosave, Neural Analytics and Galaxy Therapeutics. Dr. Liebeskind is a consultant as the imaging core lab for Cerenovous, Genentech, Medtronic, Stryker and Rapid Medical. Dr. Khaldi reports no disclosures. Dr. Gross is a consultant for Medtronic and Microvention. Dr. Lang reports no disclosures. Dr. Naryanan reports no disclosures. Dr. Jankowitz is a consultant for Medtronic and Stryker. Dr. Snyder has reported he is a consultant for Toshiba, Medtronic, EV3, Abbott Vascular, Micrus, Boston Scientific, Codman, Zimmer, Stryker, Vital, Cannon. Significant financial interest in Endo Tex, Micrus, BSC EPI, Access Closure Inc, Cordis, Primus. He is a major stockholder in Boston Scientific, Access Closure Inc, Niagara Gorge Medical. Dr. Siddiqui is a consultant for Amnis Therapeutics, Apellis Pharmaceuticals, Boston Scientific, Canon Medical Systems USA, Inc, Cerebrotech Medical Systems, Inc., Cerenovous, Corindus, Inc., Endostream Medical, Ltd, Imperative Care, Inc., Integra Lifesciences Corp., IRRAS, Medtronic, Microvention, Minnetronix Neuro, Inc., Northwest University-DSMB for HEAT trial, Penumbra, Perflow Medical, Ltd., Q'Apel Medical, Inc., Rapid Medical, Rebound Therapeutics Corp., Serenity Medical, Inc., Silk Road Medical, StimMed, Stryker, Three Rivers Medical, Inc., VasSol, Viz.ai, Inc. W.L. Gore Associates. National PI/Steering Committee for Cerenovous NAPA Trial and ARISE II Trial, Medtronic SWIFT PRIME and SWIFT DIRECT Trials, Microvention FRED Trial and CONFIDENCE Study, MUSC POSITIVE Trial, Penumbra 3D Separator Trial, COMPASS Trial, INVEST Trial. Financial interests in Adona Medical, Amnis Therapeutics, Bend IT Technologies, Ltd., BlinkTBI, Inc., Boston Scientific Corp (for purchase of Claret Medical), Buffalo Technology Partners, Inv., Cardinal Consultants, LLC, Cerebrotech Medical Systems, Inv. Cognition Medical, Endostreamt Medical, Ltd, Imperative Care, Inc, Instylla, Inc, International Medical Distribution Partners, IRRAS, LaunchNY Seed Fund Management, LLC, NeuroRadial Technologies, Inc, Neurovascular Diagnostics, Inc, Perflow Medical, Ltd, Q'Apel, Inc, Radical Catheter Technologies, Inc, Rebound Therapeutics Corp (Purchased 2019 by Integra

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Figure Legends

Figure 1, Tigertriever device and chart of patient flow through study. A) Tigertriever device including external handle for the operator to control the degree of expansion of the stent retriever. Fine wire mesh mounted on a flexible shaft. The design of the wire mesh (magnified view) is optimized to penetrate the clot and encapsulate it during retrieval. B) Patient screening, enrollment, treatment, and follow-up.

Figure 2. Reperfusion and functional outcomes in Main Study Phase of TIGER Trial. A. Reperfusion degree after first pass, after up to 3 Tigertriever passes, and after rescue therapy. B, Distribution of 90-day global disability outcomes on the modified Rankin Scale. mRS was available from 114 patients out of the 117 of the main study group.

Table 1: Patient and procedure characteristics for main-study and combined lead-in/main-study patients.

	TIGER	
	Main-Study (n=117)	All (n=160)
Age, y; mean (SD)	65 (15)	66 (15)
Male sex, n (%)	72 (61.5%)	92 (58%)
Race, n (%)		
White	99 (84.6%)	134 (83.7%)
Black	17 (14.5%)	24 (15%)
Asian	1 (0.85%)	2 (1.25%)
Hispanic ethnicity, n (%)	16 (13.7%)	24 (15%)
NIHSS Score		
Mean (SD)	17.4 (5.6)	17.6 (5.6)
Median (IQR)	17 (12-21)	18 (13-22)
Baseline CT ASPECT score		
Mean (SD)	8.9 (1.1)	8.8 (1.2)
Median (IQR)	9 (8-10)	9 (8-10)
Prestroke mRS, n (%)	(n=117)	(n=156)
0-1	116 (99.2%)	155 (99.4%)
0	93 (79.5%)	127 (81.4%)
1	23 (19.7)	28 (17.8%)
Body mass index, median (IQR)	29.5 (25-35)	30.4 (25.7-36.2)
Medical history, n (%)		
Hypertension	89 (76%)	126 (78.8%)
Diabetes mellitus	36 (30.8%)	52 (32.5%)
Atrial fibrillation	47 (40.2)	60 (37.5%)
Dyslipidemia	57 (48.7%)	81 (50.6%)
Previous MI/CAD	23 (19.7%)	34 (21.3%)
Previous ischemic stroke/transient ischemic attack	16 (13.7%)	20 (12.5%)
Intravenous tPA failure	77 (65.8%)	111 (69.4%)
Proximal occlusion location, n (%)		
M1 middle cerebral artery	67 (57.3%)	87 (54.4%)
M2 middle cerebral artery	23 (19.7%)	37 (23.2%)
Internal carotid artery	24 (20.5%)	31 (19.4%)
Basilar	3 (2.6%)	5 (3.2%)
Occlusion side (left)	48 (41%)	80 (50%)
Last known well to arterial puncture, min; median (IQR)	172 (128.3-273)	179 (127.5-293)
Procedure aspects		
General anesthesia	49 (41.9%)	73 (45.6%)
Balloon guide catheter (BGC) use only	25 (21.4%)	43 (26.9%)
BGC+ Intermediate catheter use	10 (29.9%)	56 (35%)
Intermediate catheter use only	21 (17.9%)	28 (17.5%)

Table 2: Angiographic and clinical efficacy outcomes in main-study and combined lead-in/main-study patients.

	TIGER	
	Main-Study (n=117)	All (n=160)
Primary efficacy endpoint		
Successful reperfusion (mTICI 2b-3) within 3 Tigertriever passes without rescue), n (%)	99 (84.6%) (95% CI 78.1%-91.2%)	130 (81.3%) (95% CI 75.2%-87.3%)
Angiographic outcomes within 3 Tigertriever passes		
Excellent reperfusion (mTICI 2c-3 within 3 Tigertriever passes without rescue), n (%)	74 (63.2%)	94 (58.8%)
0	9 (7.7%)	17 (10.6%)
1	2 (1.7%)	2 (1.3%)
2a	7 (6%)	11 (6.9%)
2b	25 (21.4%)	36 (22.5%)
2c	28 (23.9%)	30 (18.8%)
3	46 (39.3%)	64 (40%)
Other angiographic and procedural outcomes		
Final successful reperfusion (mTICI 2b-3)	112 (95.7%)	150 (93.8%)
Final excellent reperfusion (mTICI 2-3c)	84 (71.8%)	106 (66.3%)
0	3 (2.6%)	4 (2.5%)
1	0	0
2a	2 (1.7%)	6 (3.8%)
2b	28 (23.9%)	44 (27.5%)
2c	35 (29.9%)	38 (23.8%)
3	49 (41.9%)	68 (42.5%)
First-pass successful reperfusion (mTICI 2b-3)*	67/116 (57.8%)	89/158 (56.3%)
First-pass excellent reperfusion (mTICI 2c-3)*	48/116 (41.4%)	66/158 (41.8%)
Use of rescue therapy[#]	33 (28.2%)	51 (31.9%)
Time from puncture to mTICI 2b-3, median (IQR)	24 (16-38) N=103	25 (17-43) N=139
Time from puncture to closure, median (IQR)**	43 (28-72.5)	48 (30-84)
Clinical outcomes		
90-d good outcome (mRS 0–2), n (%) (95% CI)	65/112 (58%) (95% CI 48.33%-67.29%)	86/154 (55.8%) (95% CI 47.63%-63.83%)
EQ-5D at 90 days, median [IQR]	0.80 [0.70-0.90] (N=81)	0.80 [0.68-0.90] (N=112)
ALDS at 90 days, median [IQR} mean (SD)	93.3% [57.8-100] 77.3% (30.2%) (N=83)	93.3% [60.4-100] 78.1% (30.0%) (N=114)

*Angio after first pass was not available from one Lead-in and one Main Study patient.
**Closure time was not available from one Main Study patient.
[#] Stentriever, Aspiration retriever, IA tPA, Angioplasty or stenting.

Table 3: Safety endpoints in main-study and combined lead-in/main-study patients.

	TIGER	
	Main-Study (n=117)	All (n=160)
Primary safety composite endpoint, n (%)		
Symptomatic intracranial hemorrhage within 24h and 90d all-cause mortality*	21 (18.1%) (95% CI 11.1%-25.1%)	31/159* (19.5%) (95% CI 13.3%-25.7%)
Secondary safety endpoints, n (%)		
Symptomatic intracranial hemorrhage within 24h**	2 (1.7%) (95% CI 0.2%-6.03%)	3 (1.9%) (95% CI 0.39%-5.38%)
90d all-cause mortality *	21 (18.1%) (95% CI 11.1%-25.1%)	31/159* (19.5%) (95% CI 13.3%-25.7%)
Asymptomatic intracranial hemorrhage within 24h	36 (31.0%) (95% CI 22.7%-40.29%)	50† (31.4%) (95% CI 24.32%-39.27%)
Neurological deterioration within 24h	9 (7.7%) (95% CI 3.61%-14.21%)	14 (8.8%) (95% CI 4.9%-14.33%)
Embolization to new territory	3 (2.6%) (95% CI 0.53%-7.37%)	4† (2.5%) (95% CI 0.69%-6.31%)

*One patient withdrew consent at the day 4 visit so did not contribute full to 90d mortality assessment.
**All sICH events occurred in cases treated with Tigertriever plus rescue therapy.
†N=159. Reduced sample size due to missing 24 hour CT or final angiogram.

Table 4: Tigertriever performance in vessels of different size among combined lead-in/main study patients.

	Vessel diameter <2mm (N=27)	Vessel diameter ≥2mm (N=133)	P-value
Vessel diameter, mean (SD) (mm)	1.58 (0.29)	2.71 (0.67)	--
Vessel diameter, median (IQR),(range),(mm)	1.6 (IQR 1.5-1.8) (Range 0.7-1.9)	2.5 (IQR 2.2-3) (Range 2.0-6.0)	--
Successful reperfusion (mTICI 2b-3) within 3 Tigertriever passes without rescue), n (%)	23 (85.2%)	107 (80.4%)	0.79
90d all-cause mortality, n (%)	3 (11.1%)	28 (21.0%)	0.29
sICH at 24 hours, n (%)	0 (0%)	3 (2.2%)	1.00

Figure 1A

Figure 1B

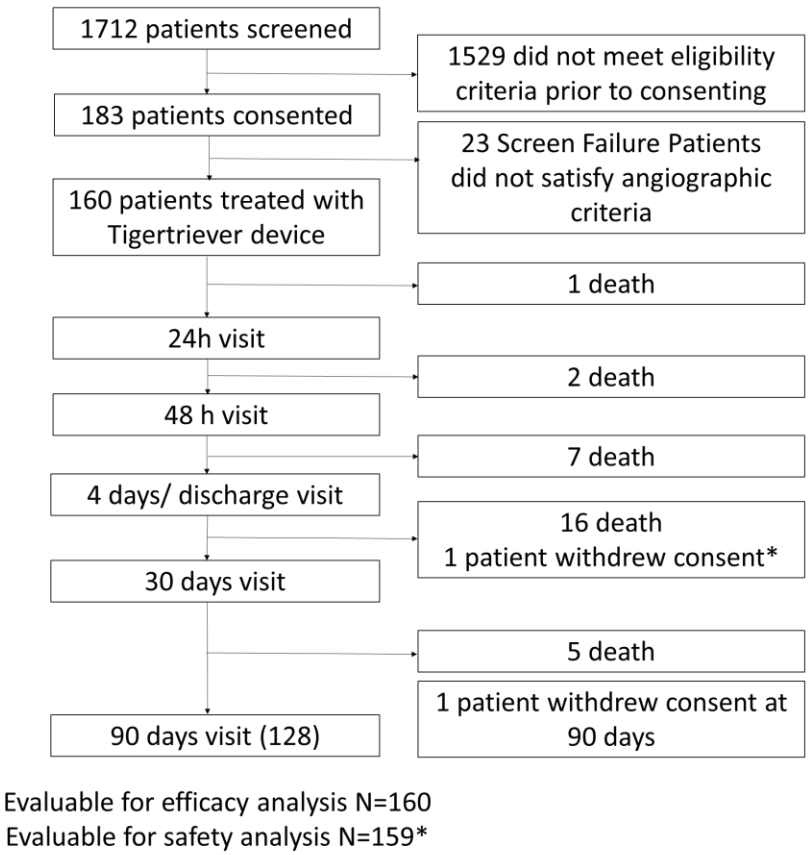

Figure 2

Figure 2A

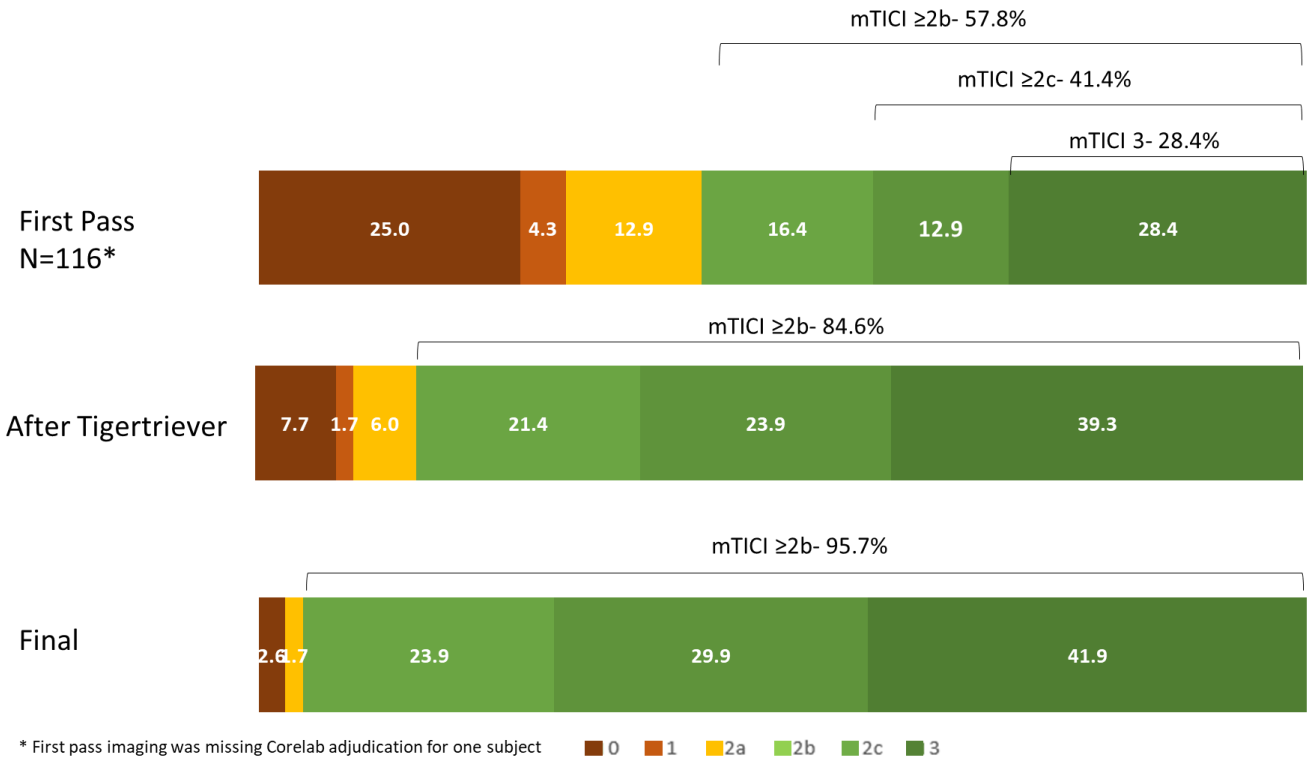

Figure 2B