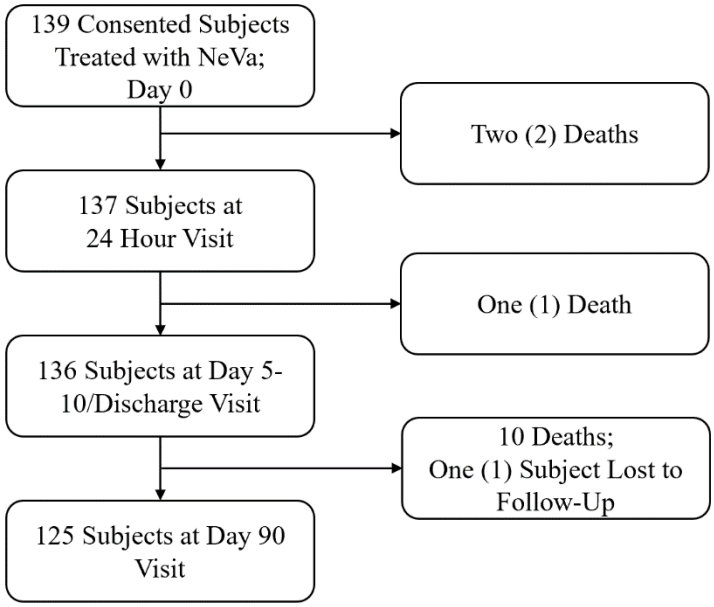
Primary Results from the CLEAR Study of a Novel Stent Retriever with Drop Zone Technology

Supplementary Materials

SUPPLEMENTARY MATERIALS

Supplementary Figure 1. Subject Disposition



Supplementary Table 1. Inclusion/Exclusion Criteria

Inclusion Criteria

Subjects were required to meet all inclusion criteria:

1. Clinical signs and symptoms consistent with the diagnosis of an acute ischemic stroke, and subject belonged to one of the following subgroups:
   1.1. Subject failed IV t-PA therapy
   1.2. Subject was contraindicated for IV t-PA administration
   1.3. IV-tPA administered within 3 hours of symptom onset
2. Age ≥ 18 and < 85 years
3. NIHSS score ≥ 8 and ≤ 25
4. Prestroke mRS score of ≤ 1
5. Intracranial arterial occlusion of the intracranial carotid artery, middle cerebral artery (M1/M2), anterior cerebral artery (ACA), posterior cerebral artery (PCA), basilar artery, or vertebral artery demonstrated with DSA.
6. Thrombectomy procedure initiated within 8 hours of symptom onset with at least one NeVa pass occurring before 8 hours
7. Imaging Inclusion Criteria:
   7.1. Non-Contrast CT Selection (if CT Perfusion or MRI not utilized):
   7.2. ASPECTS 6-10, or CT Perfusion core ≤50 cc , or
   7.3. MRI DWI core ≤50 cc
8. Subject or legal representative was able and willing to give informed consent prior to the intervention.

Exclusion Criteria

Subjects were not eligible for the study if any of the following criteria were present:

1. Pre-existing medical neurological or psychiatric disease that would confound the neurological or functional evaluations, e.g., dementia with prescribed anti-cholinesterase inhibitor (e.g., Aricept)
2. Cardiopulmonary resuscitation, cardiac arrhythmia resulting in hemodynamic instability (hypotension) that was not easily medically correctable, evidence of ongoing myocardial infarction, concern for pre-treatment pulmonary aspiration.
3. Clinical symptoms suggestive of bilateral stroke or stroke in multiple territories
4. Cerebral vasculitis
5. History of severe allergy to contrast medium
6. Known allergy to NeVa materials (nitinol, stainless steel)
7. Suspicion of aortic dissection, septic embolus, or bacterial endocarditis
8. Systemic infection
9. Significant mass effect with midline shift
10. Evidence of intracranial tumor (except small meningioma [≤ 3 cm])
11. Any CT or MRI evidence of acute hemorrhage products on presentation.
12. Inability to deploy NeVa device for at least one pass for any other reason
13. Life expectancy less than 6 months

14. Any other condition that, in the opinion of the investigator, precluded an endovascular procedure or posed a significant hazard to the subject if an endovascular procedure was performed.
15. Females who were pregnant or breastfeeding
16. Known active malignancy
17. Stenosis or occlusion in a proximal vessel requiring treatment or preventing access to thrombus.

Supplementary Table 2. List of CLEAR Study Investigators **{Blinded}**

Trial Principal Investigators	
Steering Committee	
Clinical Events Committee	
Imaging Core Lab	

Country	Site	Name	Role	ITT enrollment	mITT enrollment
			PI	3 (2.2%)	3 (2.8%)
			Sub-I		
			Sub-I		
			PI	5 (3.6%)	5 (4.7%)
			Sub-I		
			PI	2 (1.4%)	1 (0.9%)
			Sub-I		
			PI	1 (0.7%)	1 (0.9%)
			Sub-I		
			Sub-I		
	{Blinded}		PI	4 (2.9%)	4 (3.7%)
			Sub-I		
			Sub-I		
			Sub-I		
			Sub-I		
			Sub-I		
			PI	5 (3.6%)	4 (3.7%)
			PI	13 (9.4%)	12 (11.2%)
			Sub-I		
			Sub-I		
			PI	2 (1.4%)	2 (1.9%)
			Sub-I		
			Sub-I		
			Sub-I		
			Sub-I		
			PI	12 (8.6%)	11 (10.3%)
			Sub-I		
			Sub-I		
			PI	8 (5.8%)	8 (7.5%)
			Sub-I		

			Sub-I		
			Sub-I		
			Sub-I		
			Sub-I		
			Sub-I		
			Sub-I		
			Sub-I		
			Sub-I		
			Sub-I		
	{Blinded}		PI	4 (2.9%)	4 (3.7%)
			Sub-I		
			Sub-I		
			Sub-I		
			PI	3 (2.2%)	3 (2.8%)
			Sub-I		
			Sub-I		
			Sub-I		
			Sub-I		
			Sub-I		
			Sub-I		
			Sub-I		
			Sub-I		
			Sub-I		
			Sub-I		
			Sub-I		
			PI	3 (2.2%)	3 (2.8%)
			PI (former)		
			Sub-I		
			Sub-I		
			Sub-I		
			Sub-I		
			Sub-I		

			Sub-I		
			Sub-I		
			Sub-I		
			Sub-I		
			Sub-I		
			Sub-I		
			Sub-I		
			Sub-I		
			Sub-I		
			Sub-I		
			Sub-I		
	{Blinded}		PI	6 (4.3%)	5 (4.7%)
			Sub-I		
			Sub-I		
			Sub-I		
			PI	7 (5.0%)	6 (5.6%)
			Sub-I		
			PI	1 (0.7%)	1 (0.9%)
			Sub-I		
			Sub-I		
			PI	7 (5.0%)	3 (2.8%)
			Co-investigator		
			Co-investigator		
			Co-investigator		
			PI	5 (3.6%)	3 (3.8%)
			Co-investigator		
			Co-investigator		

			Co-investigator	
			Co-investigator	
			PI	20 (14.4%)	9 (8.4%)
			PI	3 (2.2%)	1 (0.9%)
			Co-investigator		
			Co-investigator		
			Co-investigator		
			Co-investigator		
			Co-investigator		
			Co-investigator		
			Co-investigator		
			Co-investigator		
			PI	6 (4.3%)	1 (0.9%)
			Co-investigator		
			Co-investigator		
			Co-investigator		
			Co-investigator		
			Co-investigator		
			Co-investigator		
			PI	2 (1.4%)	2 (1.9%)

{Blinded}

		Co-investigator		
		Co-investigator		
		PI	8 (5.8%)	6 (5.6%)
		Co-investigator		
	{Blinded}	Co-Investigator		
		PI	3 (2.2%)	3 (2.8%)
		Co-Investigator		
		Co-Investigator		
		Co-Investigator		
		Co-Investigator		
		PI	6 (4.3%)	6 (5.6%)

Supplementary Table 3. Modified Intent to Treat Devices and Device Characteristics

Stent Retriever Model	Retriever Diameter	Retriever Length	Retriever Working Distance	Intended Occlusions for Treatment	Intended Vessel Size Range
NeVa M1S	4.0 mm	35 mm	22 mm	M1, M2 of the MCA, basilar artery, or intracranial vertebral artery	2.0 – 3.5 mm
NeVa T-3S	4.5 mm	42 mm	30 mm	Carotid T occlusions, proximal M1 MCA, basilar or intracranial vertebral	2.0 – 4.5 mm
NeVa 5.5 x 37 mm	5.5 mm	56 mm	37 mm	ICA, basilar or intracranial vertebral	3.5 – 5.5 mm

Supplementary Table 4. Reasons for Exclusion from mITT Population

Reason	Number of Events	Number of Subjects with an Event
Major Protocol Deviations	23	20 (14.4%)
Inclusion/Exclusion criteria not met*	23	20 (14.4%)
Missing eTICI Score	0	0 (0.0%)
Missing Primary Efficacy Assessment	0	0 (0.0%)
Use of non-mITT NeVa Device for the First Pass	12	12 (8.6%)

* Major protocol deviations (PDs) were reported for 20 subjects (14.4%) and involved subjects not meeting eligibility criteria. Note, three subjects did not meet two eligibility criteria.

The following inclusion criteria were not met:

- Signs/symptoms consistent with acute ischemic stroke, and either received IV t-PA within 3 hours of symptom onset, failed IV t-PA or was contraindicated to IV t-PA (n=6)
- Age ≥18 and ≤ 85 years (n=2)
- NIHSS score ≥ 8 and ≤ 25 (n=4)
- Pre-stroke mRS score of ≤ 1 (n=1)
- Able to initiate thrombectomy within 8 hours of TLKW with ≥ one NeVa pass within 8 hours (n=4)
- ASPECTS 6-10, CT perfusion core ≤ 50 cc or MRI DWI core ≤ 50 cc (n=2)

The following exclusion criteria were not met:

- Bilateral stroke or stroke in multiple territories (n=1)
- Active malignancy (n=3)

Supplementary Table 51. Study Procedure Characteristics

Parameter	ITT/Safety (N = 139)	mITT (N = 107)
Side of Lesion		
Left	71 (51.1%)	57 (53.3%)
Right	66 (47.5%)	49 (45.8%)
N/A (Basilar)	2 (1.4%)	1 (0.9%)
Vessel Location of Primary Occlusive Lesion on DSA		
Intracranial ICA	14 (10.1%)	10 (9.3%)
MCA-M1	86 (61.9%)	66 (61.7%)
MCA-M2	37 (26.6%)	30 (28.0%)
Basilar	1 (0.7%)	1 (0.9%)
PCA	1 (0.7%)	0 (0.0%)
Use of General Anesthesia		
Yes	51 (36.7%)	43 (40.2%)
No	88 (63.3%)	64 (59.8%)
Endovascular Procedure Access [1]		
Femoral	133 (95.7%)	103 (96.3%)
Radial	8 (5.8%)	6 (5.6%)
Brachial	0 (0.0%)	0 (0.0%)
Direct Carotid	0 (0.0%)	0 (0.0%)
Significant (>70%) Extra-Cranial Stenosis Proximal to Primary Arterial Occlusive Lesion		
Yes	2 (1.4%)	0 (0.0%)
No	137 (98.6%)	107 (100.0%)
Duration of Procedure (minutes)		
n	139	107

Parameter	ITT/Safety (N = 139)	mITT (N = 107)
Mean (SD)	41.8 (28.7)	41.6 (29.2)
Median	35.0	32.0
Min, Max	2.0, 156.0	2.0, 156.0
Complications (during *any* pass)		
Yes	16 (11.5%)	14 (13.1%)
No	123 (88.5%)	93 (86.9%)
Use of Rescue Therapy/Device		
Yes	5 (3.6%)	4 (3.7%)
No	134 (96.4%)	103 (96.3%)
Use of Heparin or Antiplatelet Medications (during *any* pass)		
Yes	29 (20.9%)	26 (24.3%)
No	110 (79.1%)	81 (75.7%)
Flow Control Strategies (during *any* pass) [1]		
BGC	41 (29.5%)	31 (29.0%)
Local Aspiration	110 (79.1%)	86 (80.4%)
None	9 (6.5%)	7 (6.5%)
Devices Used [2]		
First Pass	139 (100.0%)	107 (100.0%)
NeVa M1S	41/139 (29.5%)	32/107 (29.9%)
NeVa 5.5 x 37 mm	14/139 (10.1%)	11/107 (10.3%)
NeVa T-3S	72/139 (51.8%)	64/107 (59.8%)
NeVa Other	12/139 (8.6%)	0/107 (0.0%)
Other Stent Retriever	0/139 (0.0%)	0/107 (0.0%)
Aspiration Only	0/139 (0.0%)	0/107 (0.0%)
Second Pass	59 (42.4%)	41 (38.3%)

Parameter	ITT/Safety (N = 139)	mITT (N = 107)
NeVa M1S	12/59 (20.3%)	7/41 (17.1%)
NeVa 5.5 x 37 mm	3/59 (5.1%)	2/41 (4.9%)
NeVa T-3S	27/59 (45.8%)	25/41 (61.0%)
NeVa Other	6/59 (10.2%)	0/41 (0.0%)
Other Stent Retriever	8/59 (13.6%)	5/41 (12.2%)
Aspiration Only	2/59 (3.4%)	2/41 (4.9%)
Other: Balloon PTA	1/59 (1.7%)	0/41 (0.0%)
Third Pass	33 (23.7%)	25 (23.4%)
NeVa M1S	7/33 (21.2%)	6/25 (24.0%)
NeVa 5.5 x 37 mm	1/33 (3.0%)	1/25 (4.0%)
NeVa T-3S	11/33 (33.3%)	10/25 (40.0%)
NeVa Other	4/33 (12.1%)	0/25 (0.0%)
Other Stent Retriever	8/33 (24.2%)	6/25 (24.0%)
Aspiration Only	1/33 (3.0%)	1/25 (4.0%)
Other: Self-Expanding Stent	1/33 (3.0%)	1/25 (4.0%)
Fourth Pass	18 (12.9%)	15 (14.0%)
NeVa M1S	3/18 (16.7%)	3/15 (20.0%)
NeVa 5.5 x 37 mm	0/18 (0.0%)	0/15 (0.0%)
NeVa T-3S	2/18 (11.1%)	1/15 (6.7%)
NeVa Other	1/18 (5.6%)	0/15 (0.0%)
Other Stent Retriever	9/18 (50.0%)	8/15 (53.3%)
Aspiration Only	2/18 (11.1%)	2/15 (13.3%)
Other: Microcatheter	1/18 (5.6%)	1/15 (6.7%)
Fifth Pass	9 (6.5%)	7 (6.5%)
NeVa M1S	0/9 (0.0%)	0/7 (0.0%)
NeVa 5.5 x 37 mm	0/9 (0.0%)	0/7 (0.0%)
NeVa T-3S	0/9 (0.0%)	0/7 (0.0%)
NeVa Other	0/9 (0.0%)	0/7 (0.0%)
Other Stent Retriever	8/9 (88.9%)	6/7 (85.7%)

Parameter	ITT/Safety (N = 139)	mITT (N = 107)
Aspiration Only	1/9 (11.1%)	1/7 (14.3%)
Sixth Pass	4 (2.9%)	2 (1.9%)
NeVa M1S	0/4 (0.0%)	0/2 (0.0%)
NeVa 5.5 x 37 mm	0/4 (0.0%)	0/2 (0.0%)
NeVa T-3S	0/4 (0.0%)	0/2 (0.0%)
NeVa Other	0/4 (0.0%)	0/2 (0.0%)
Other Stent Retriever	3/4 (75.0%)	1/2 (50.0%)
Aspiration Only	1/4 (25.0%)	1/2 (50.0%)

[1] Subjects could be counted in more than one category (i.e., multiple options could have been selected for each subject).

[2] Summary of devices used according to data collected in EDC.

Supplementary Table 6. Primary Endpoint Subgroup Analyses in mITT Population

	Core Lab	
Subgroup	**Successful Recanalization [1] n (%) [2]**	**P-value [3]**
Sex		0.042
Male (n = 62)	53 (85.5%)	
Female (n = 45)	44 (97.8%)	
Vessel Location of Primary Occlusive Lesion		0.90
Basilar (n = 1)	1 (100.0%)	
Intracranial ICA (n = 10)	9 (90.0%)	
MCA-M1 (n = 66)	59 (89.4%)	
MCA-M2 (n = 30)	28 (93.3%)	
NeVa Device Model Used at First Pass		0.88
NeVa 5.5 x 37 mm (n = 11)	10 (90.9%)	
NeVa M1S (n = 32)	30 (93.8%)	
NeVa T-3S (n = 64)	57 (89.1%)	
Use of IV Tissue Plasminogen Activator (tPA)		1.00
Yes (n = 59)	53 (89.8%)	
No (n = 48)	44 (91.7%)	
Use of Ancillary Devices (Flow Control Strategies) [4]		0.56
Yes (n = 99)	90 (90.9%)	
No (n = 8)	7 (87.5%)	
Use of Heparin or Antiplatelet Medications [4]		0.22
Yes (n = 23)	19 (82.6%)	
No (n = 84)	78 (92.9%)	

	Core Lab	
Subgroup	**Successful Recanalization [1] n (%) [2]**	**P-value [3]**
Geographic Location		0.50
U.S. (n = 73)	65 (89.0%)	
Non-U.S. (n = 34)	32 (94.1%)	

[1] Result of an eTICI grade ≥ 2b after 3 passes or less without the use of a rescue device.

[2] Number and percentage of subjects who achieved a successful recanalization within each subgroup category.

[3] P-value is from a Fisher's exact test.

[4] During the first 3 passes.

Supplementary Table 7. Overview of CEC Adverse Event Adjudications (ITT/Safety population)

Number of AEs:	Number of Events	Number of Subjects[1] (N=139)
Any Serious AE	25	20 (14.4%)
Serious AE related to procedure[2]	8	8 (5.8%)
Serious AE related to NeVa device[2]	6	6 (4.3%)
Serious AE related to ancillary device[2]	4	4 (2.9%)
Serious AE leading to study discontinuation	13	13 (9.4%)

[1] Subjects reporting more than one serious adverse event are counted only once.

[2] Related events include those reported as 'Possibly Related' and 'Definitely Related'.

Supplementary Table 8. CEC Adjudicated Serious Adverse Events – Relatedness (ITT/Safety population)

Serious Adverse Events	Number of Events	Number of Subjects (N=139)
Number of Events	25	20 (14.4%)
Relation to Procedure		
Definitely not related to procedure	17	16 (11.5%)
Possibly related to procedure	1	1 (0.7%)
Definitely related to procedure	7	7 (5.0%)
Relation to NeVa		
Definitely not related to NeVa	19	17 (12.2%)
Possibly related to NeVa	5	5 (3.6%)
Definitely related to NeVa	1	1 (0.7%)
Relation to Other Device		
Definitely not related to Other Device	0	0 (0.0%)
Possibly related to Other Device	4	4 (2.9%)
Definitely related to Other Device	0	0 (0.0%)

Supplementary Table 9. CEC Adjudicated Adverse Events - Summary (ITT/Safety population)

AE Term	Number of Events	Number of Subjects (N=139)
Access Site Complication requiring surgical repair or blood transfusion	1	1 (0.7%)
Asymptomatic Subarachnoid Hemorrhage ≤ 24 hours	1	1 (0.7%)
COVID-19	1	1 (0.7%)
Cardiac Arrest	4	4 (2.9%)
Cerebral Edema	2	2 (1.4%)
Cerebral and Pulmonary Edema	1	1 (0.7%)
Device Failure (in vivo breakage)	0	0 (0.0%)
Embolization to a new territory	1	1 (0.7%)
Intra-Procedural Mortality	0	0 (0.0%)
Multiorgan Failure	1	1 (0.7%)
Myocardial Infarction	1	1 (0.7%)
New Stroke Post-Discharge	2	2 (1.4%)
Pulmonary Embolism	1	1 (0.7%)
Seizure	1	1 (0.7%)
Sepsis	1	1 (0.7%)
Symptomatic Intraparenchymal Hemorrhage ≤ 24 hours	1	1 (0.7%)
Symptomatic Subarachnoid Hemorrhage ≤ 24 hours	2	2 (1.4%)
Vascular Perforation causing Symptomatic Intraparenchymal Hemorrhage ≤ 24 hours	1	1 (0.7%)
Vasospasm	2	2 (1.4%)
Ventricular Fibrillation	1	1 (0.7%)

Supplementary Table 10. Safety Endpoint ITT and mITT Populations

Measurement	ITT (N=139)	mITT (N=107)
Percent of Subjects deceased at Day 90 and/or experiencing sICH at 24 Hours Post Procedure	17 (12.2%)	10 (9.3%)
95% Confidence Interval	7.8%, 18.7%	5.2%, 16.4%
Percent of Subjects deceased at Day 90	13 (9.4%)	7 (6.5%)
95% Confidence Interval	5.5%, 15.3%	3.2%, 12.9%
Percent of Subjects experiencing sICH at 24 Hours Post Procedure	7 (5.0%)	5 (4.7%)
95% Confidence Interval	2.5%, 10.0%	2.0%, 10.5%
Percent of Subjects with ≥ 4-point increase in NIHSS score at 24-Hours Post-Procedure	7 (5.0%)	6 (5.6%)
95% Confidence Interval	2.5%, 10.0%	2.6%, 11.7%
Percent of Subjects with ≥ 4-point increase in NIHSS score at day 5-10/Discharge	4 (2.9%)	2 (1.9%)
95% Confidence Interval	1.1%, 7.2%	0.5%, 6.6%

Supplementary Table 11. Patient characteristics in CLEAR and comparator device registration trials

	CLEAR mITT (n=107)	TIGER Main Study (n=117)	ARISE II (n=227)	TREVO 2 (n=88)	SWIFT (N=58)
Age, y; mean (SD)	65.1 (13.2)	65 (15)	68 (13)	67 (14)	67 (12)
NIHSS; median (IQR)	16 (12-20)	17 (12-21)	16 (12-19)	19 (14-21)	18 (9-28)
Baseline ASPECTS; median (IQR)	9 (8-10)	9 (8-10)	9 (9-10)	NR	NR
Prestroke mRS 0-1 (%)	100%	99.2%	100% (mRS 0-2)	100%	96% (mRS 0-2)
IV tPA failure (%)	55.1%	65.8%	52.9%	58%	33%
Proximal occlusion location (%)					
ICA	9.3%	20.5%	15.4%	16%	21%
M1 MCA	61.7%	57.3%	55.5%	60%	66%
M2 MCA	28.0%	19.7%	25.1%	16%	10%
Basilar	0.9%	2.6%	4%	8%	2%
Last known well to arterial puncture, min; median (IQR)	181 (131-252)	172 (128.3-273)	214 (155-266)	282 (210-342)	293.5 (85.6)
Procedural aspects (%)					
BGC only	14.4%	21.4%	73.6%	NR	NR
BGC + intermediate catheter	15.1%	8.5%	NR	NR	NR
Intermediate catheter only	64.0%	17.9%	41%	NR	NR

Abbreviations: BGC, balloon guide catheter; ICA, internal carotid artery; M1, main segment; M2, second order branch; MCA, middle cerebral artery; NR, not reported; tPA, tissue plasminogen activator