COMPASS

A COMPARISON of DIRECT ASPIRATION vs. STENT RETRIEVER AS A FIRST APPROACH

International Stroke Conference

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Disclosures

Personal

I have received no payments from Penumbra, Inc. and do not serve as a consultant to Penumbra, Inc.

Penumbra has reimbursed me for some travel to scientific meetings for discussion of other trials (THERAPY and INVEST) over past three years, but no honorarium or consulting fees were provided

Consultant: Rebound Medical, EndoStream, Cerebrotech Medical, Viseon, Synchron

Investor: Apama, Viseon, TSP, Vastrax, EndoStream, Synchron, Cerebrotech Medical, Neurvana, NTI, Serenity

Disclosures

Trial

Penumbra, Inc. reviewed and approved the initial grant proposal and funded COMPASS.

Penumbra otherwise played no role in the execution, data collection, data analysis, interpretation, presentation development, or any other part of COMPASS.

Background

Recent trials demonstrated improved patient outcomes with endovascular therapy, as compared to medical therapy, in the treatment of large vessel stroke

The majority of patients in those trials were treated with stent retrievers

Background

Pilot data utilizing an aspiration first pass technique (ADAPT) approach suggest similar functional outcomes with superior technical results, while lowering procedure time and device costs versus traditional stent retriever as a first line (SRFL) approach

J Neurointerv Surg. 2014 May;6(4):260-4. doi: 10.1136/neurintsurg-2014-011125. Epub 2014 Feb 25.
ADAPT FAST study: a direct aspiration first pass technique for acute stroke thrombectomy.
Turk AS[1], Frei D, Fiorella D, Mocco J, Baxter B, Siddiqui A, Spiotta A, Mokin M, Dewan M, Quarfordt S, Battenhouse H, Turner R, Chaudry I.

J Neurointerv Surg. 2014 Apr 1;6(3):231-7. doi: 10.1136/neurintsurg-2013-010713. Epub 2013 Apr 27.
Initial clinical experience with the ADAPT technique: a direct aspiration first pass technique for stroke thrombectomy.
Turk AS[1], Spiotta A, Frei D, Mocco J, Baxter B, Fiorella D, Siddiqui A, Mokin M, Dewan M, Woo H, Turner R, Hawk H, Miranpuri A, Chaudry I.

Objective

To evaluate whether acute ischemic stroke (AIS) patients, treated with ADAPT approach within 6 hours of symptom onset do not have inferior clinical outcomes to those treated with a SRFL approach.

As well as to evaluate whether the ADAPT approach is technically superior, clinically superior, or more cost effective than SRFL approach in the treatment of AIS.

Methods

Study Design

Design	Prospective, randomized, international, multi-center, blinded assessment concurrent controlled trial
Population	Anterior circulation ELVO (ICA to MCA Bifurcation) within 6 hours of onset
Randomization	1:1 ADAPT vs SRFL
Sites	Up to 20
Assessment	Blinded core lab adjudication of imaging Blinded mRS and NIHSS certified clinical assessment

Study Design

Only FDA approved stent retriever or aspiration catheter device.

Physicians were allowed to use their preferred adjunctive techniques (e.g.. BGC, DAC, Solumbra)

Key Inclusion Criteria

1. Age 18 and older
2. NIHSS >= 5 at the time of neuroimaging
3. Presenting or persistent symptoms within 6 hours of when groin puncture can be obtained
4. Neuroimaging demonstrates large vessel proximal occlusion (distal ICA through MCA bifurcation)
5. The operator feels that stroke can be appropriately treatment with traditional endovascular approaches (ADAPT or first-line stent retriever)
6. Pre-event Modified Rankin scale score 0-1
7. Non-contract CT/CTA or MRI/MRA for trial eligibility performed or repeated at treating ADAPT stroke center or outside medical facility within one hour (or as close as possible) of treatment initiation
8. Consenting requirements met according to local IRB

Key Exclusion Criteria

1. Patient is more than 6-hours from symptom onset
2. Rapidly improving neurologic examination
3. Absence of large vessel occlusion on non-invasive imaging
4. Presence of an existing or pre-existing large territory infarction
5. Known or suspected pre-existing (chronic) large vessel occlusion in the symptomatic territory
6. Absent femoral pulses
7. Excessive vascular access tortuosity that will likely result in unstable access platform
8. Pregnancy; if a woman is of child-bearing potential a urine or serum beta HCG test is positive
9. Severe contract allergy or absolute contraindication to iodinated contract that cannot be medically controlled
10. Clinical history, past imaging or clinical judgment suggests that the intracranial occlusion is chronic
11. Patient has a severe or fatal comorbidities that will likely prevent improvement or follow-up or that will render the procedure unlikely to benefit the patient

Head CT or MRI Exclusion Criteria

1. Presence of blood on imaging (subarachnoid hemorrhage (SAH), intracerebral hemorrhage (ICH), etc.)
2. High density lesion consistent with hemorrhage of any degree
3. Significant mass effect with midline shift
4. Core infarct lesion volume >50 cc
5. Angiographic evidence of carotid dissection or tandem cervical occlusion or stenosis requiring treatment
6. Large (more than 1/3 of the middle cerebral artery) regions of clear hypodensity on the baseline CT scan or ASPECTS of <7; sulcal effacement and/or loss of grey-white differentiation alone are not contraindications for treatment

Site selection

Each site submitted their last 20 cases with confirmation of follow up prior to initiation.

At least 5 of those 20 should be with each modality.

PI’s attempted to select sites with consideration of balancing centers’ preferred approach (ADAPT vs SRFL).

Outcomes – Intent to Treat

Primary Efficacy Endpoint:

Functional outcome at 90d as defined by mRS 0-2

Secondary Efficacy Endpoints:

90d outcome assessed over via the overall distribution of mRS (shift)

TICI 2c or greater within 45 minutes of groin puncture

TICI 3 or greater within 45 minutes of groin puncture

Time from groin puncture to TICI 2b or greater (Kaplan-Meyer)

J Neurointerv Surg. 2014 Sep;6(7):511-6. doi: 10.1136/neurintsurg-2013-010726. Epub 2013 Sep 7.
The golden hour of stroke intervention: effect of thrombectomy procedural time in acute ischemic stroke on outcome.
Spiotta AM[1], Vargas J[1], Turner R[1], Chaudry MI[2], Battenhouse H[3], Turk AS[2].

J Neurointerv Surg. 2017 May 2. pii: neurintsurg-2017-013040. doi: 10.1136/neurintsurg-2017-013040. [Epub ahead of print]
The golden 35 min of stroke intervention with ADAPT: effect of thrombectomy procedural time in acute ischemic stroke on outcome.
Alawieh A[1], Pierce AK[2], Vargas J[2], Turk AS[2], Turner RD[2], Chaudry MI[2], Spiotta AM[2].

Outcomes – Intent to Treat

Safety Endpoints:

- All cause mortality at 90 days
- All intracranial hemorrhage within 24 hrs
- Symptomatic ICH within 24hrs (all ICH with NIHSS ≥4 worsening)
- Symptomatic ICH (SITS-MOST criteria)

Cost Endpoint:

- Mean total device costs

Study Management Teams

Data Coordinating Center
Internal Statistic Analysis
Mount Sinai Health System

Core Lab
Jacobs Institute

Coordinating Center
Medical University of SC

Independent External
Statistical Review

BIOSTATISTICAL CONSULTING INC.

Results*

* Just notified from a participating center IRB that one patient may need to be excluded, this is being investigated now, so data may need to be slightly altered and must be considered preliminary/near-complete

Site selection

15 Centers activated

2 additional in-process when enrollment completed

Analysis of 20 submitted cases demonstrated:

6 centers with ≥67% of cases ADAPT

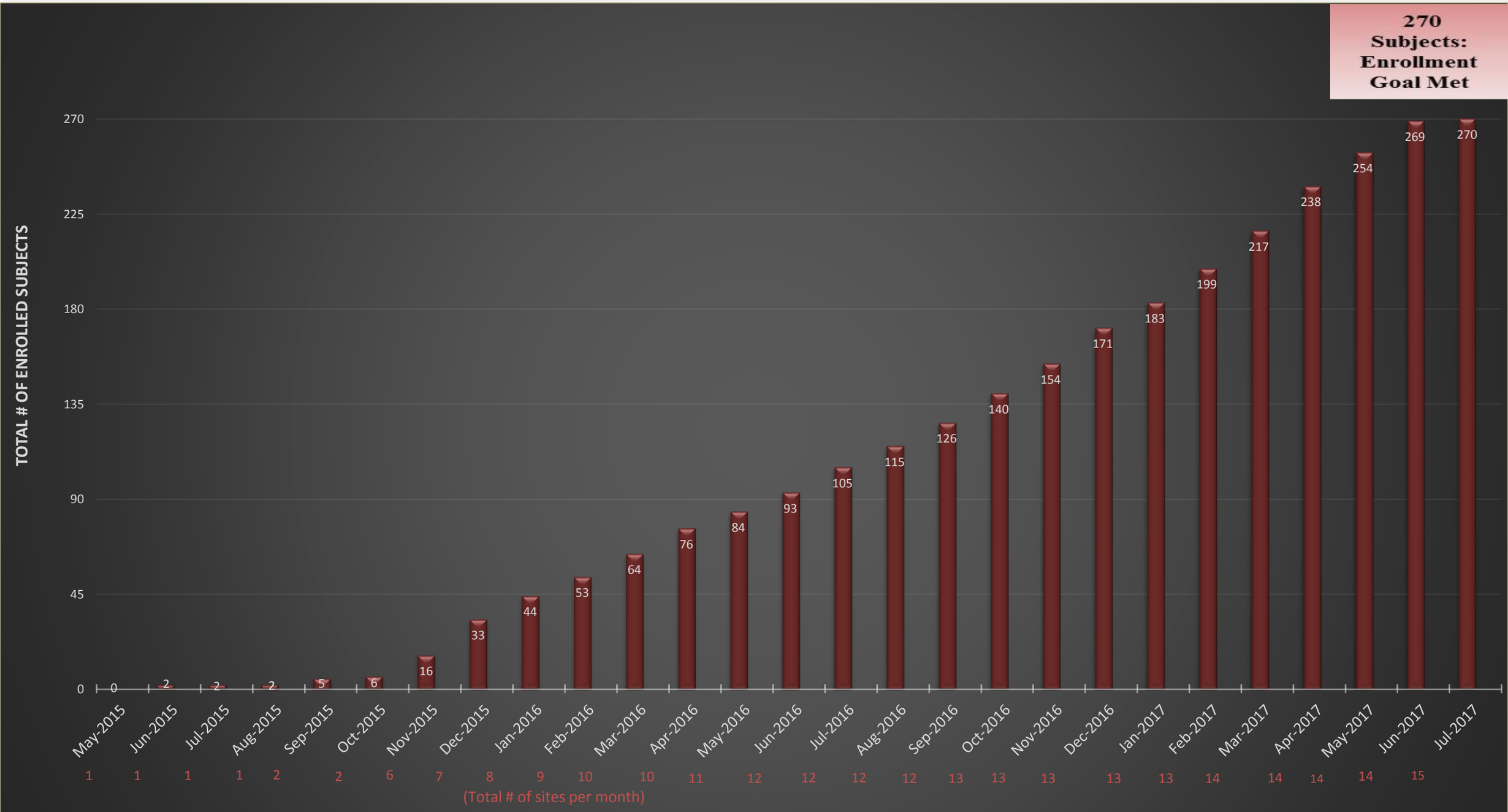
6 centers with ≥67% of cases SRFL

3 centers with mixed technique and no apparent preference

Site selection

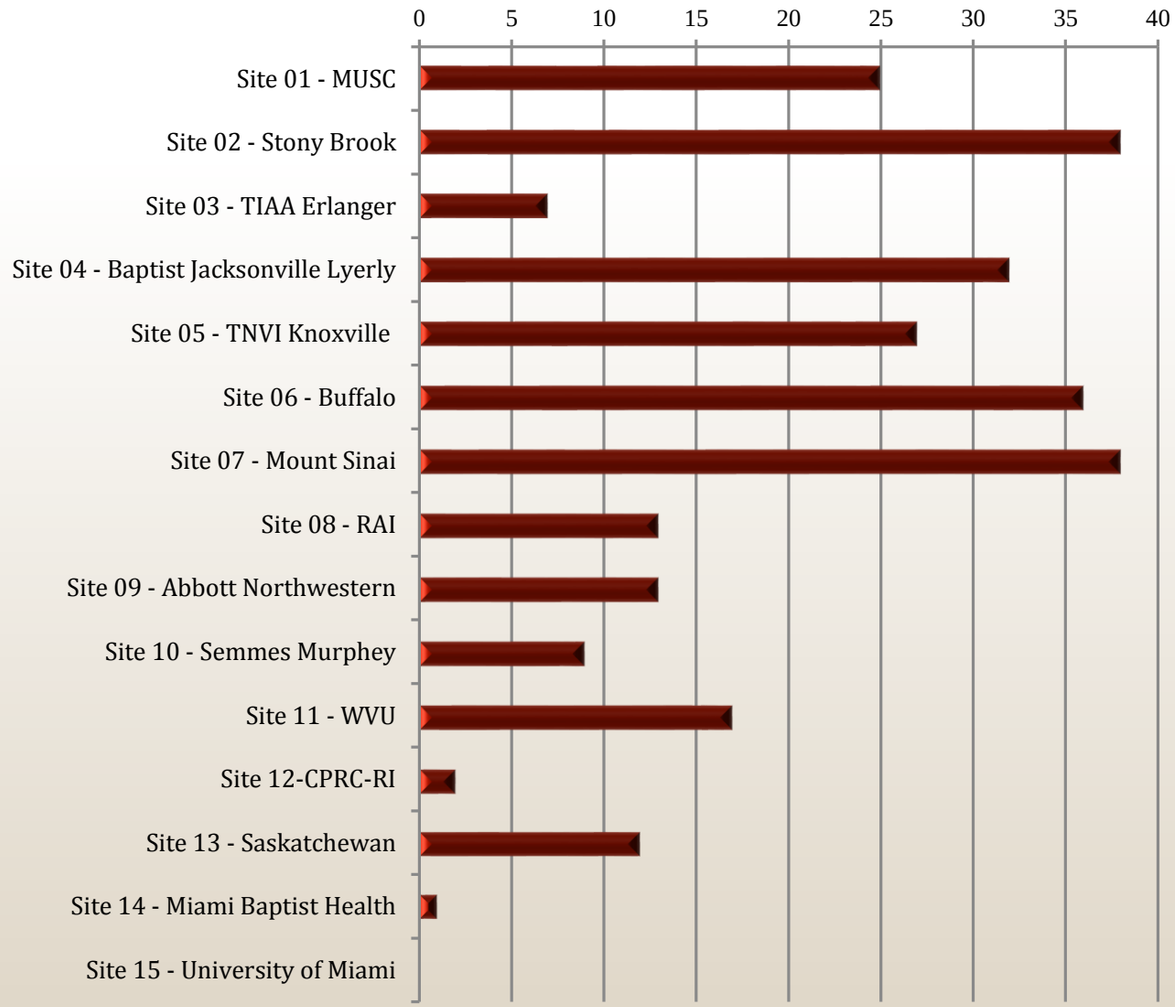
COMPASS

Comparison of Direct Aspiration vs. Stent Retriever as a First Approach



Participating Centers

1. MUSC
2. Stony Brook
3. Erlanger
4. Baptist Jacksonville Lyerly
5. TNVI Knoxville
6. Buffalo
7. Mt. Sinai
8. Swedish (RIA)
9. Abbott NW
10. Semmes Murphey
11. WVU
12. CPMC RI
13. Saskatchewan
14. Miami Baptist Health
15. University of Miami



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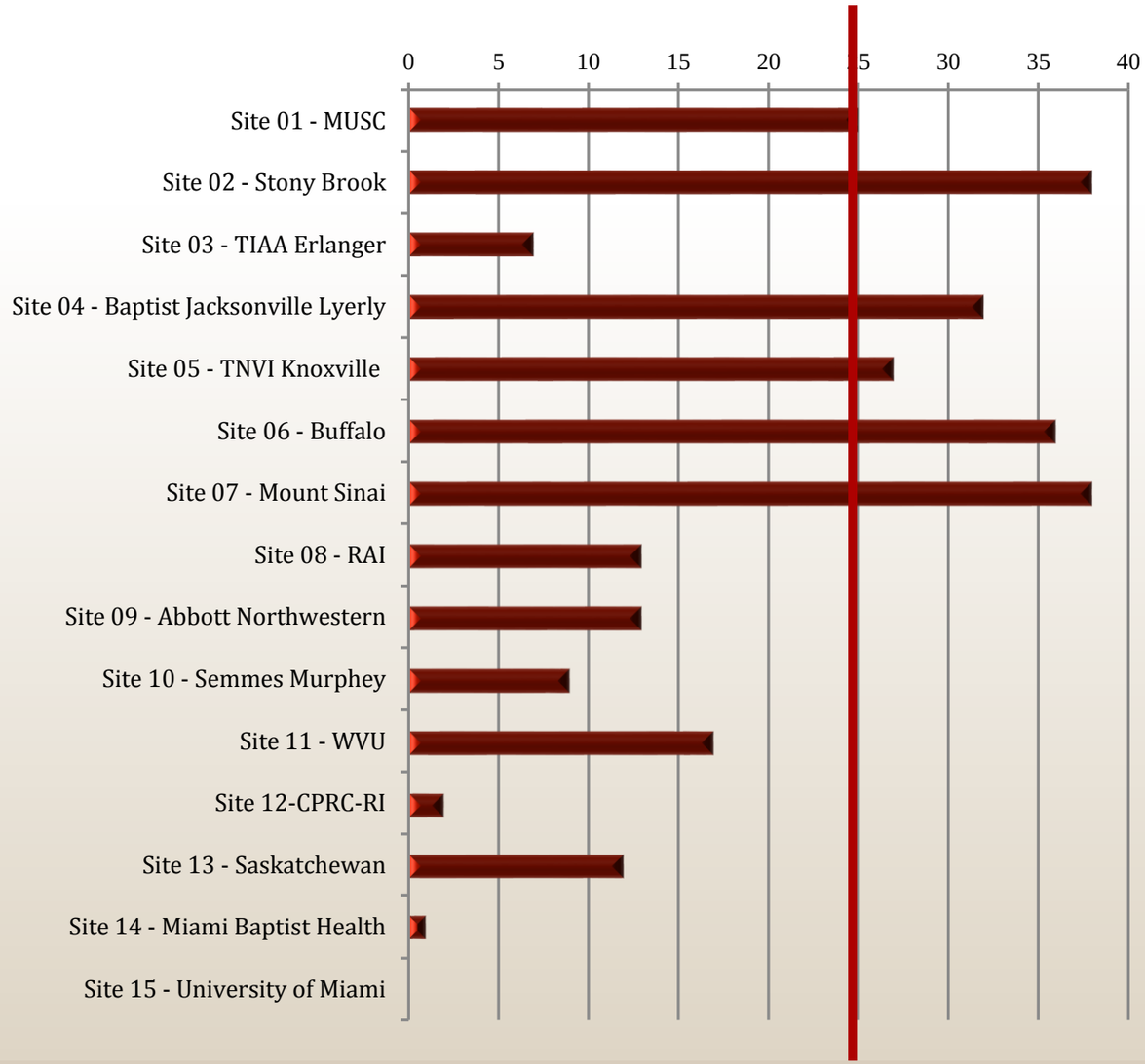
6 centers with ≥25 enrollments



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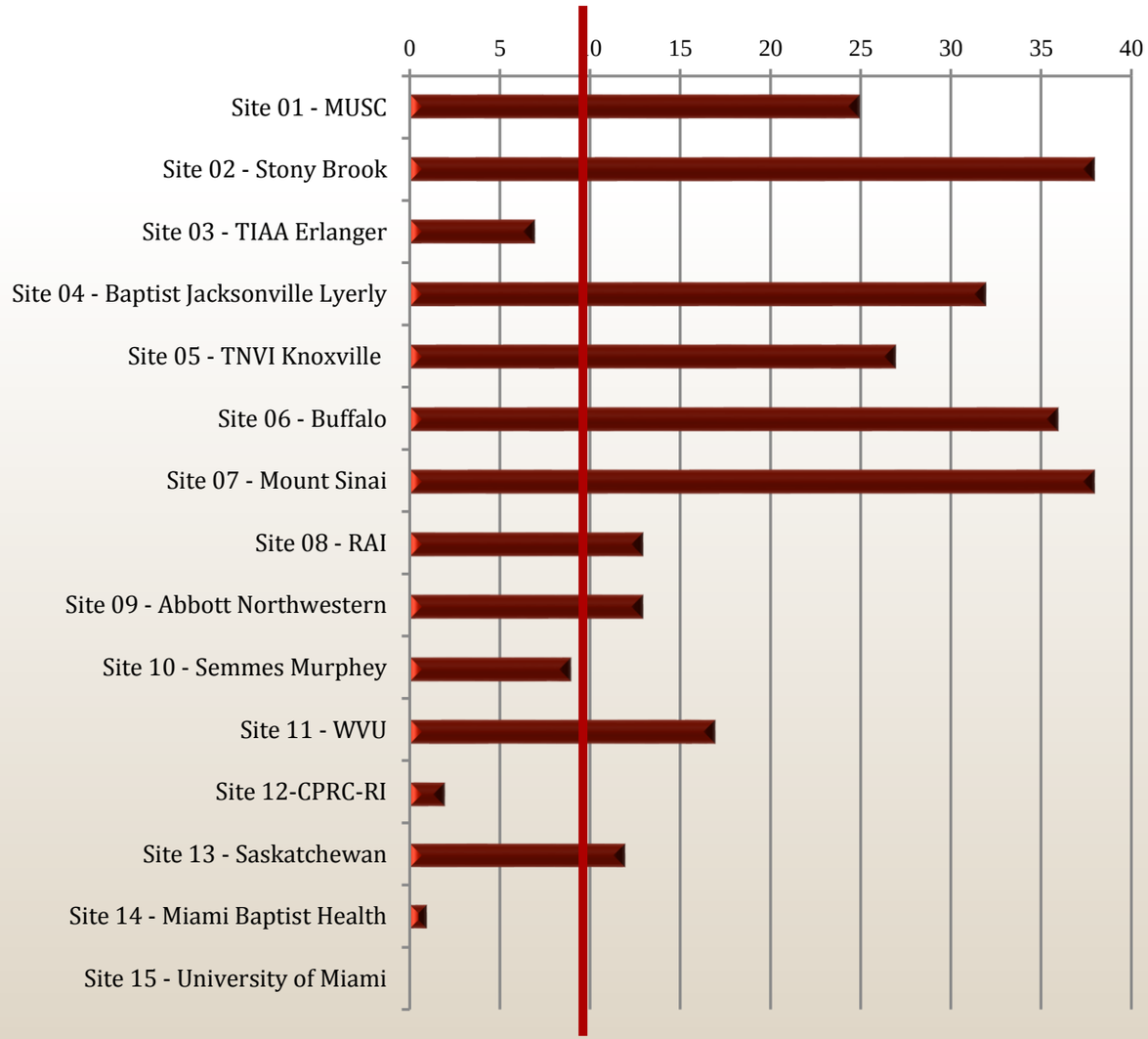
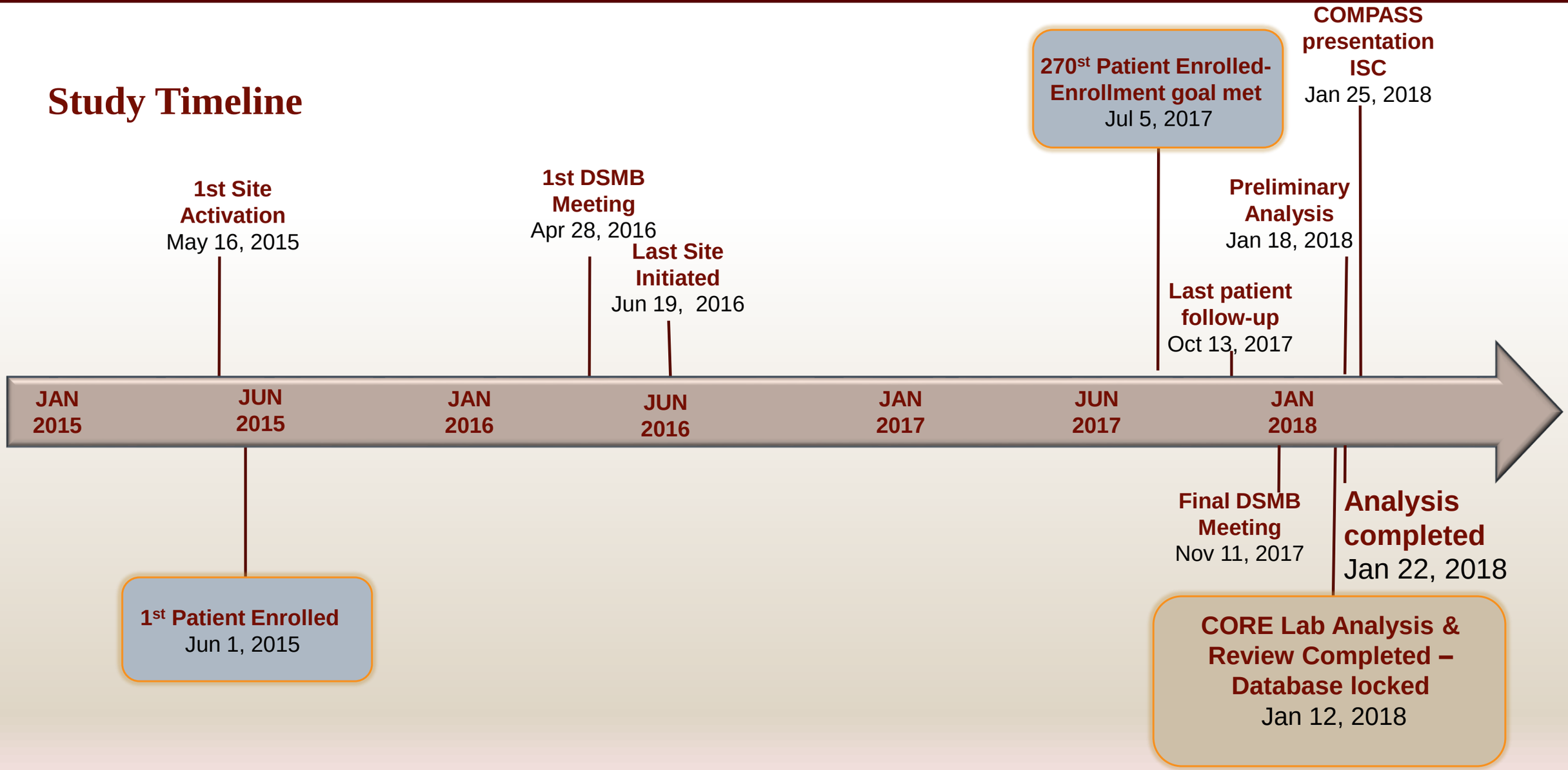
10 centers with >10 enrollments



Study Timeline



270 Subjects Enrolled

Randomization

PPI Analysis

19 Protocol deviations

3 Pre-event mRS>1

5 Cervical occlusion or stenosis requiring treatment

11 M2 clot location

115 Total

3 Loss to follow-up

112 Completed follow-up

Intent to Treat

6 Did not receive ADAPT

2 Spontaneous recanalization

3 Arch/Cervical vessel access failure

1 Physician chose alternative approach (ICAD)

128 ADAPT as randomized

134 Total

3 Loss to follow-up

131 Completed follow-up

Intent to Treat

6 Did not receive SRFL

5 Spontaneous recanalization

1 Physician chose alternative approach (ICAD)

130 SRFL as randomized

136 Total

6 Loss to follow-up

130 Completed follow-up

PPI Analysis

20 Protocol violations

3 Pre-event mRS>1

1 ASPECTS of < 7

3 Cervical occlusion or stenosis requiring treatment

11 M2 clot location

1 M3 clot location

1 Basilar clot location

116 Total

6 Loss to follow-up

110 Completed follow-up

Baseline Characteristics

	ADAPT	SRFL	P value
Age	71.8±13.1	71.1±12.9	0.64
Gender (female)	57.5%	50%	0.23

Baseline Characteristics

	ADAPT	SRFL	P value
Medical History			
Hypertension	68.7 (92/134)	75 (102/136)	0.28
Diabetes	26.9 (36/134)	29.4 (40/136)	0.69
Hyperlipidemia/Hypercholesterolemia1	48.5 (65/134)	46.3 (63/136)	0.81
Atrial Fibrillation	48.5 (65/134)	41.2 (56/136)	0.27
Coronary Artery Disease	23.1 (31/134)	22.1 (30/136)	0.88
Current Smoker	13.4 (18/134)	22.1 (30/136)	0.11
History of Ischemic Stroke	9.0 (12/134)	16.9 (23/136)	0.07
History of Hemorrhagic Stroke	2.2 (3/134)	0.7 (1/136)	0.37
History of TIA	5.2 (7/134)	5.9 (8/136)	1.00
History of untreated intracranial aneurysm(s)	3.0 (4/134)	0 (0/136)	0.06

Baseline Characteristics

	ADAPT	SRFL	OR (95% CI)
Pre-morbid Modified Rankin Score (mRS)			
0	81.3 (109/134)	76.5 (104/136)	
1	16.4 (22/134)	21.3 (29/136)	
2	1.5 (2/134)	0.7 (1/136)	1.33(0.74,2.39)
3	0 (0/134)	1.5 (2/136)	
4	0.7 (1/134)	0 (0/136)	

Baseline Characteristics

	ADAPT	SRFL	P value
Baseline NIHSS(median)	17	17	
Baseline NIHSS (mean)	16.9± 5.8	16.9±6.3	0.99
Systolic Blood Pressure (median)	154	155	
Systolic Blood Pressure (mean)	156.7±28.6	160.9±28.9	0.24
Baseline ASPECTS Score (median)	8	8	
Baseline ASPECTS Score (mean)	8.2±0.7	8.1±0.7	0.45
Laterality			
Left	48.5 (65/134)	45.2 (61/135)*	0.63
Right	51.5 (69/134)	54.8 (74/135)*	

*One Basilar artery occlusion was incorrectly enrolled

Baseline Characteristics

Site of Occlusion	ADAPT	SRFL	P value
MCA			
M1 Proximal	61.2 (82/134)	63.2 (86/136)	0.80
M1 Distal	14.2 (19/134)	11 (15/136)	0.47
M2 Proximal	8.2 (11/134)	8.1 (11/136)	1.00
M3	0 (0/134)	0.7 (1/136)	1.00
ICA			
Supraclinoid ICA(ICA Terminus)	13.4 (18/134)	15.4 (21/136)	0.73
Petrocavernous	0.7 (1/134)	0.7 (1/136)	1.00
Other			
Mid-basilar	0 (0/134)	0.7 (1/136)	1.00
Tandem Cervical-ICA	2.2 (3/134)	0 (0/136)	0.12

Baseline Characteristics

	ADAPT	SRFL	P value
Stenosis requiring treatment	1.5 (2/134)	2.2 (3/136)	1.00
Directly admitted to a comprehensive stroke center	56 (75/134)	57.4 (78/136)	0.90
IV tPA pre-procedure	67.9 (91/134)	69.9 (95/136)	0.79
General Anesthesia %	29.1 (39/134)	30.1 (41/136)	0.89

Procedural Variables

	ADAPT	SRFL	P value
Percent using a Balloon Guide Catheter	33.6 (45/134)	44.8 (61/136	0.06
Percent using a distal access/reperfusion catheter	97.8 (131/134)	86.8 (118/136)	0.001
Percent using at least one SR	20.9 (28/134)	97.8 (133/136)	<0.0001
Percent using >1 SR	6 (8/134)	12.5 (17/136)	0.09
Percent with documeted reporting of using distal aspiration during SR thrombectomy	100 (28/28)	85.3 (110/129)	0.03
Percent achieving ≥TICI 2b with primary modality	83.2 (109/131)*	81.3 (109/134)*	0.75

* Core lab unable to determine when primary modality completed in 3 patients in ADAPT and 2 patients in SRFL

Primary Efficacy Endpoint

Functional outcome at 90d as defined by mRS 0-2

Primary Efficacy Endpoint

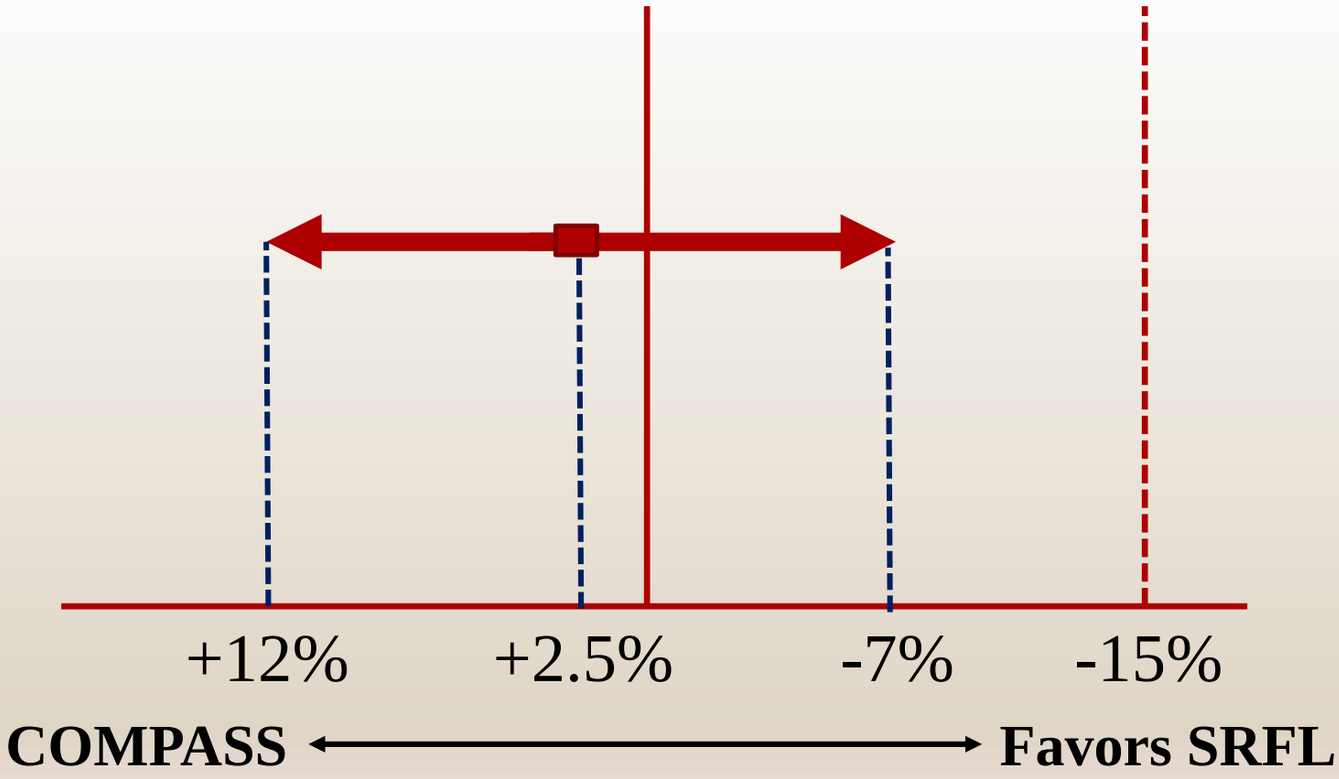
Functional outcome at 90d as defined by mRS 0-2

Cohort	90d mRS 0-2	
SRFL	49%	(41.6, 57.4)
ADAPT	52%	(43.8, 60.3)

ADAPT non-Inferior

p = 0.0014

Primary Efficacy Endpoint



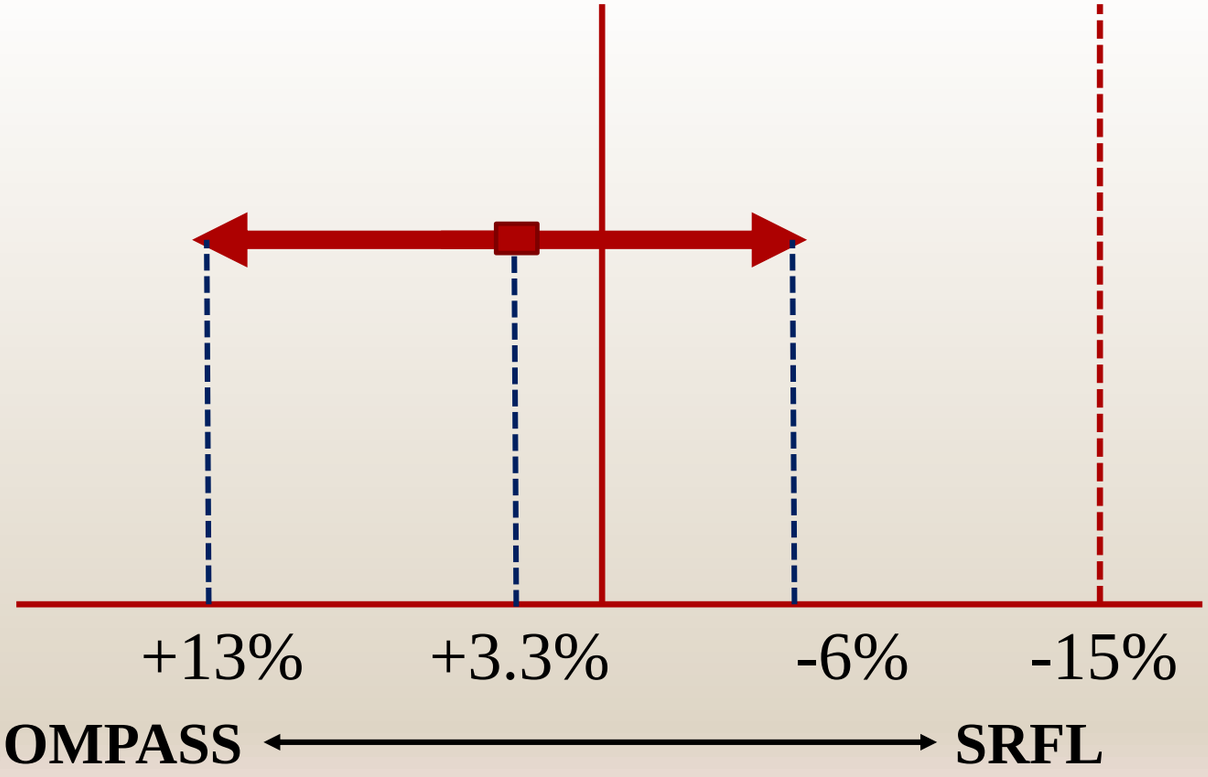
ADAPT non-Inferior

p = 0.0014

Primary Efficacy Endpoint Sensitivity Analysis

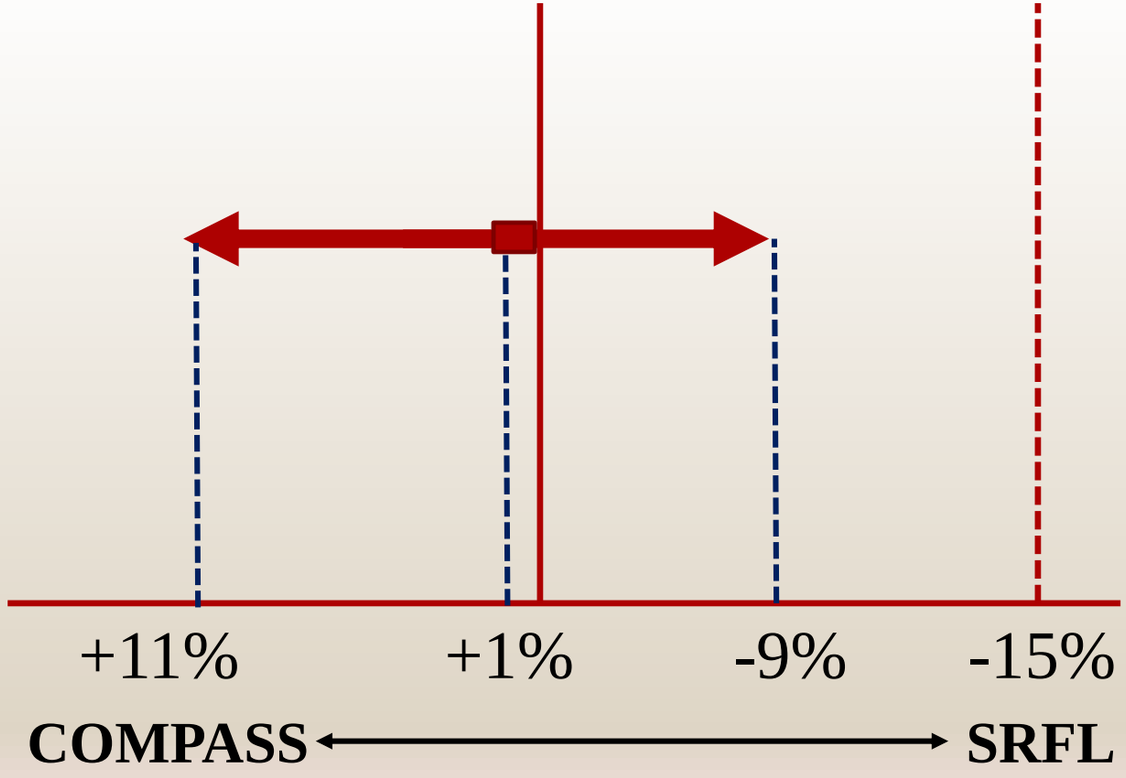
Missing Data as Deaths

ADAPT non-Inferior p = 0.0009



Missing Data Excluded

ADAPT non-Inferior p = 0.0043



Outcomes

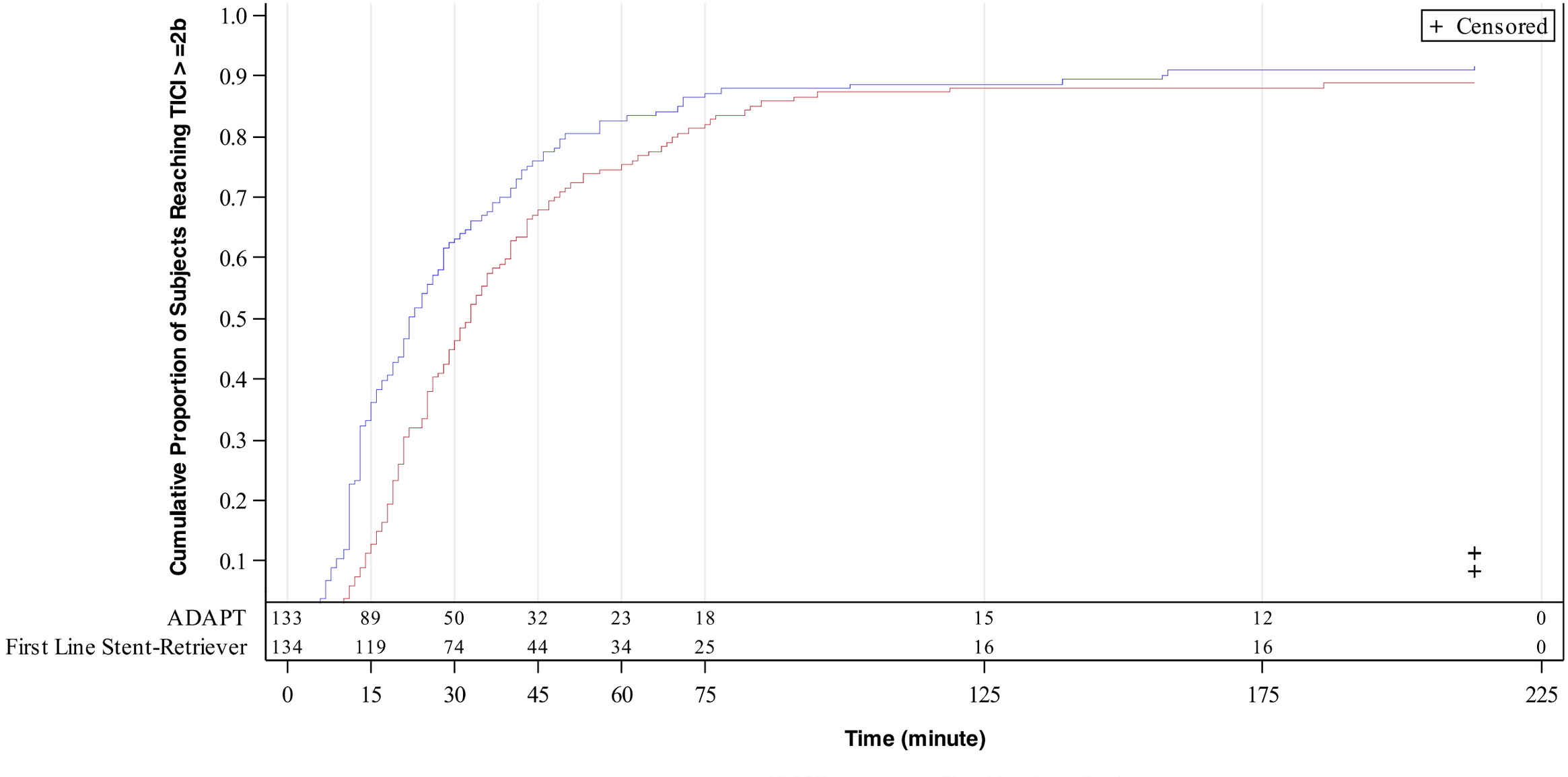
Secondary Efficacy Endpoints:

90d mRS Shift OR (95% CI) = 0.98 (0.64, 1.51)

	ADAPT	SRFL	P value
TICI 2c or greater within 45 minutes	50%	44%	0.2998
TICI 3 or greater within 45 minutes	34%	23%	0.0486
Time to TICI 2b or greater	22 min	33 min	0.0194

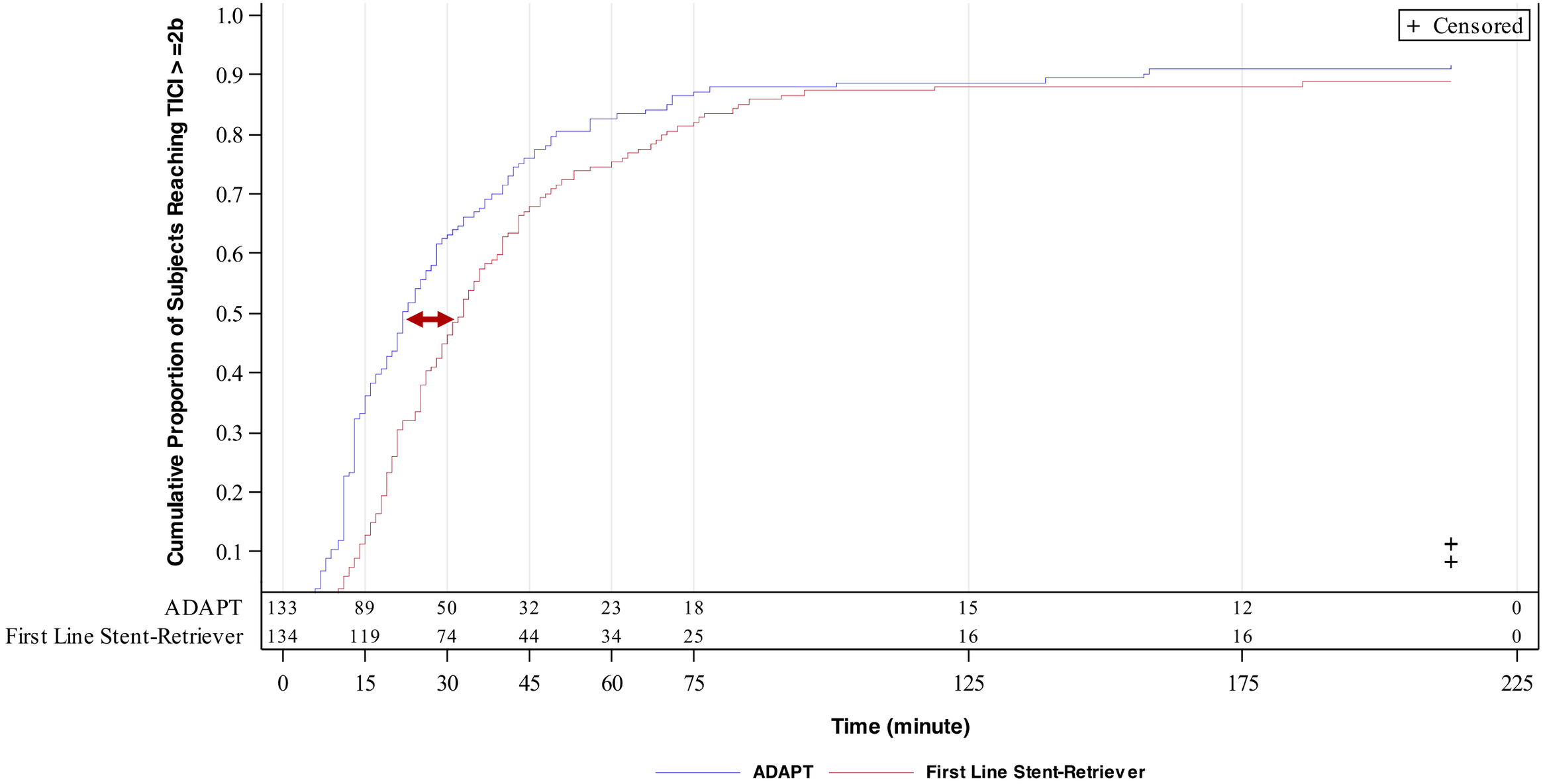
Outcomes

Time from groin puncture to TICI 2b or greater



Outcomes

Time from groin puncture to TICI 2b or greater



Outcomes

Pre-specified secondary outcomes:

TICI 2b at final	91.7% (122/133)*	89% (121/136)	0.2998
TICI 2c at final	56.4% (75/133)*	55.9% (76/136)	0.0486
TICI 3 at final	37.6% (50/133)*	28.7% (39/136)	0.0194

*One case had no imaging available for Core Lab Review, therefore excluded (the site reported TICI 3 outcome)

Safety Endpoints

	ADAPT	SRFL	OR (95% CI)
All cause mortality at 90 days	22%	22%	1.02 (0.57, 1.81)
All intracranial hemorrhage	36%	34%	1.08 (0.65, 1.78)
Symptomatic ICH (all ICH with NIHSS ≥4 worsening)	6.0%	5.9%	1.01 (0.37, 2.77)
Symptomatic ICH (SITS-MOST criteria)	3.0%	3.0%	1.01 (0.25, 4.12)

Cost Endpoint

Ongoing

Discussion

Centers well balanced for preferred technique (ADAPT vs SRFL) and experienced in both techniques

Balloon guide catheter (BGC) use:

- Moderate rate of BGC use in aspiration arm (34%)
- Substantial rate of BGC use in SR arm (45%)

High rate of concomitant distal aspiration used in SR arm (85%)

High rate of aspiration alone success

- Use of ACE68 in COMPASS versus ACE64 in ASTER?
- Use of BGC?
- Aspiration experience?

Conclusion

ADAPT results in non-inferior functional outcomes as compared to a SRFL approach

Time to reperfusion and quality of reperfusion were comparable

Cost data remains pending

Conclusion

There is now Level I evidence that primary Aspiration has non-inferior clinical outcomes as compared to Stent Retrievers in ELVO

Thank You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A COMPARISON of DIRECT ASPIRATION vs. STENT RETRIEVER AS A FIRST APPROACH