

Woven EndoBridge (WEB) Intrasaccular Therapy for Treatment of Wide Neck Bifurcation Intracranial Aneurysms

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Sequent Medical

FDA Neurological Devices Panel

Introduction

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WEB-IT Study Met Primary Effectiveness and Safety Endpoints

- Met prespecified primary effectiveness endpoint
- Met prespecified primary safety endpoint
 - No mortality and low morbidity through 12 months

WEB-IT Data Reinforced by 8 Years Experience Outside United States

- Received CE mark in 2010
- Approved and distributed in 44 countries including
 - EU, Brazil, Australia, and Argentina
- More than 6,000 patients
- 5 ongoing WEB studies
 - Results support WEB-IT findings

Original Indication for Use

- The WEB Aneurysm Embolization System is indicated for the embolization of intracranial wide neck bifurcation aneurysms
- The WEB Aneurysm Embolization System is further indicated to embolize intracranial wide neck bifurcation aneurysms, ranging in size from 3 mm to 10 mm in dome diameter, where the neck size is 4 mm or greater or the dome-to-neck ratio is less than 2.

Proposed Indication for Use

- The WEB Aneurysm Embolization System is indicated for the embolization of intracranial wide neck bifurcation aneurysms
- The WEB Aneurysm Embolization System is further indicated to embolize saccular intracranial wide neck bifurcation aneurysms located in the anterior (middle cerebral artery (MCA) bifurcation, internal carotid artery (ICA) terminus, anterior communicating artery (Acomm) complex) and posterior (basilar apex) circulations, ranging in size from 3 mm to 10 mm in dome diameter, where the neck size is 4 mm or greater or the dome-to-neck ratio is less than 2.

Agenda

Unmet Need

Adam Arthur, MD, MPH

Professor, Neurosurgery
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Device Description / MoA

Bill Patterson, PhD

Vice President for Neurovascular Research and Development

WEB-IT Study Design

Adam Arthur, MD, MPH

WEB-IT Study Results

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Training and Post Approval

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Unmet Need for Patients with Wide Neck Bifurcation Aneurysms

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Intracranial Aneurysms (IAs) Can Rupture Without Warning, Cause Significant Morbidity, Mortality

- Subarachnoid hemorrhage (SAH) often devastating
 - ~ 45% of patients who experience SAH die within 30 days^{1,2}
 - ~ 1/2 of survivors have significant neurological disability
- Ruptured aneurysms require strategy to prevent re-bleeding
- Size, location and previous history may increase risk of rupture
 - Associated severity and consequences independent of aneurysm size and location

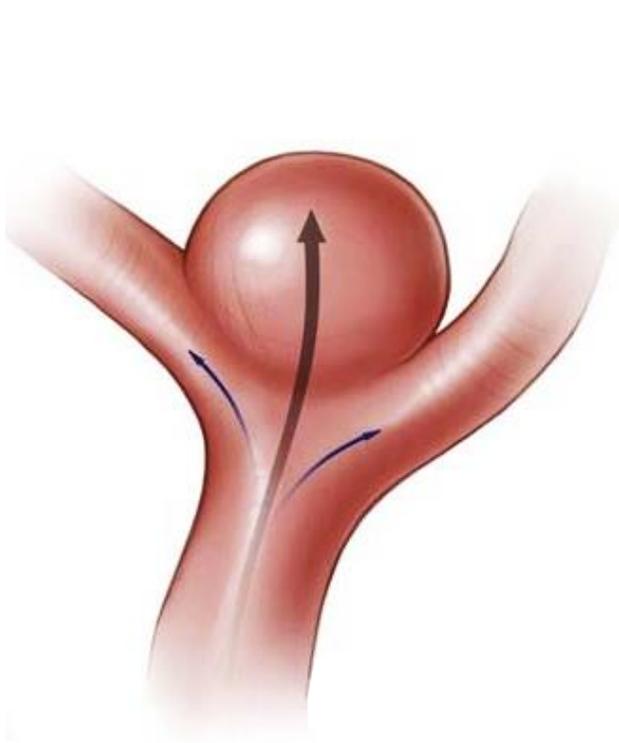
1) Suarez, 2006

2) Broderick, 1993

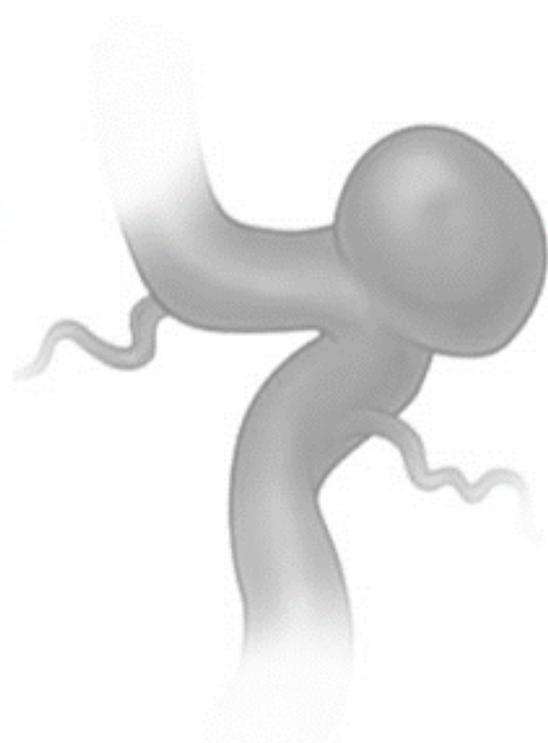
Most IAs Asymptomatic, Affect Significantly More Women Than Men

- Can press on brain or nerves, result in neurological symptoms
 - Headaches, pain behind eye, blurry vision, dizziness
- Typically affect people between 40 and 60 years of age
- Smoking, family history are risk factors

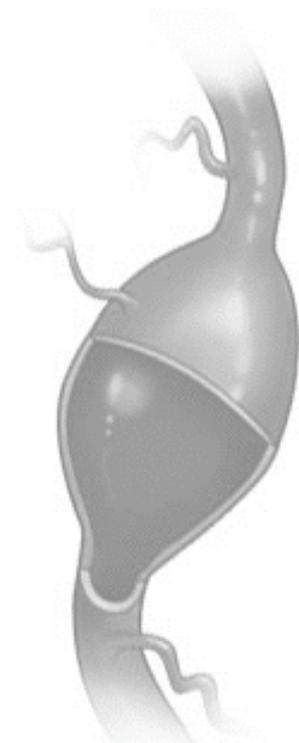
Bifurcation Aneurysms Different from Other Aneurysm Morphologies



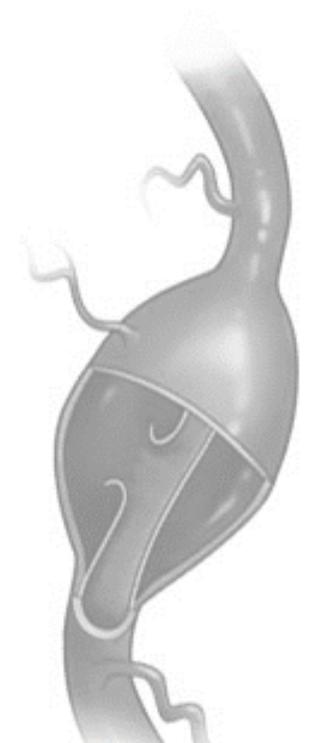
**Saccular
Bifurcation**



**Saccular
Side-Wall**



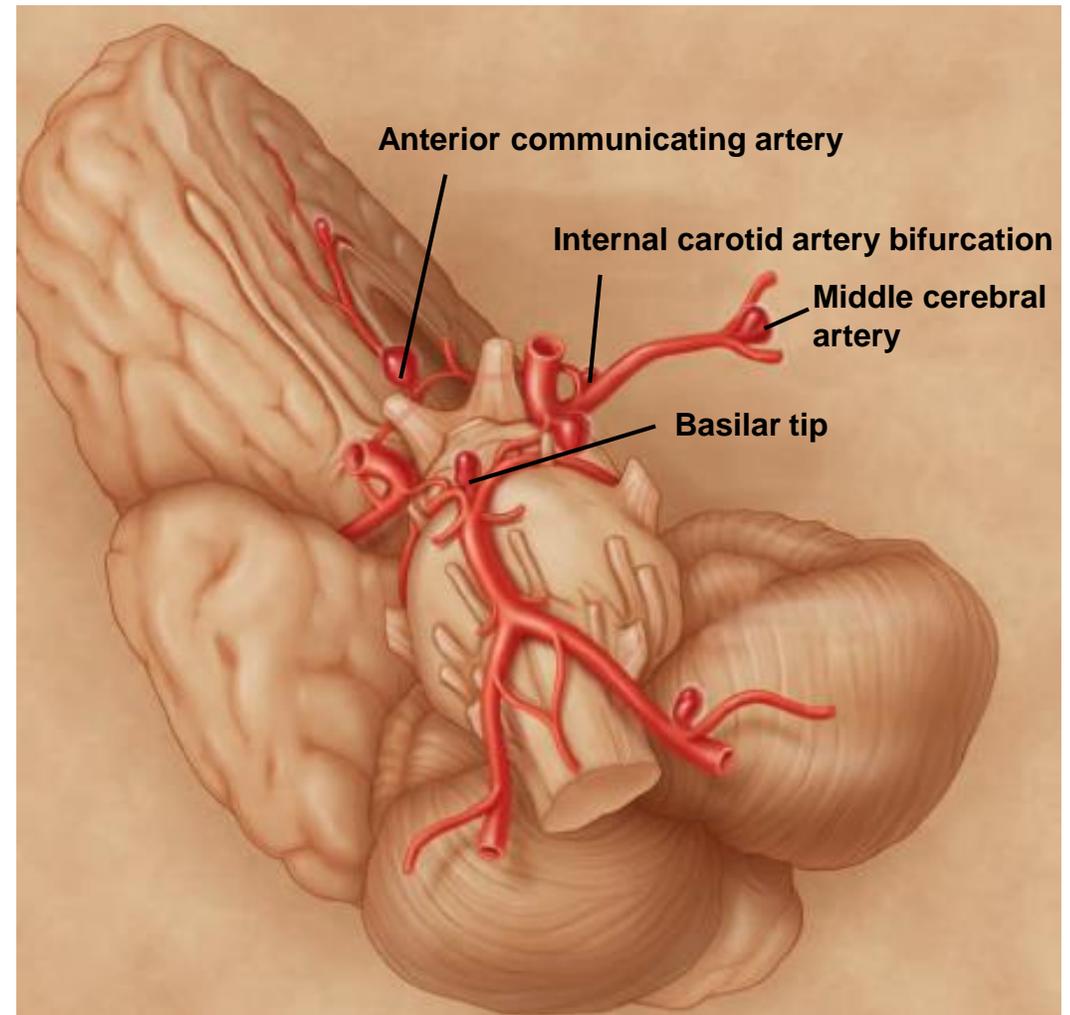
Fusiform



Dissecting

Aneurysms Occur in Many Different Locations

- Common locations
 - Anterior communicating
 - Middle cerebral artery
 - Internal carotid artery
 - Basilar apex
- Treatment challenging if at terminus location and have wide neck
- WNBAs make up about 26-36% of all brain aneurysms¹



Adapted from Brisman et al. *NEJM* 2006

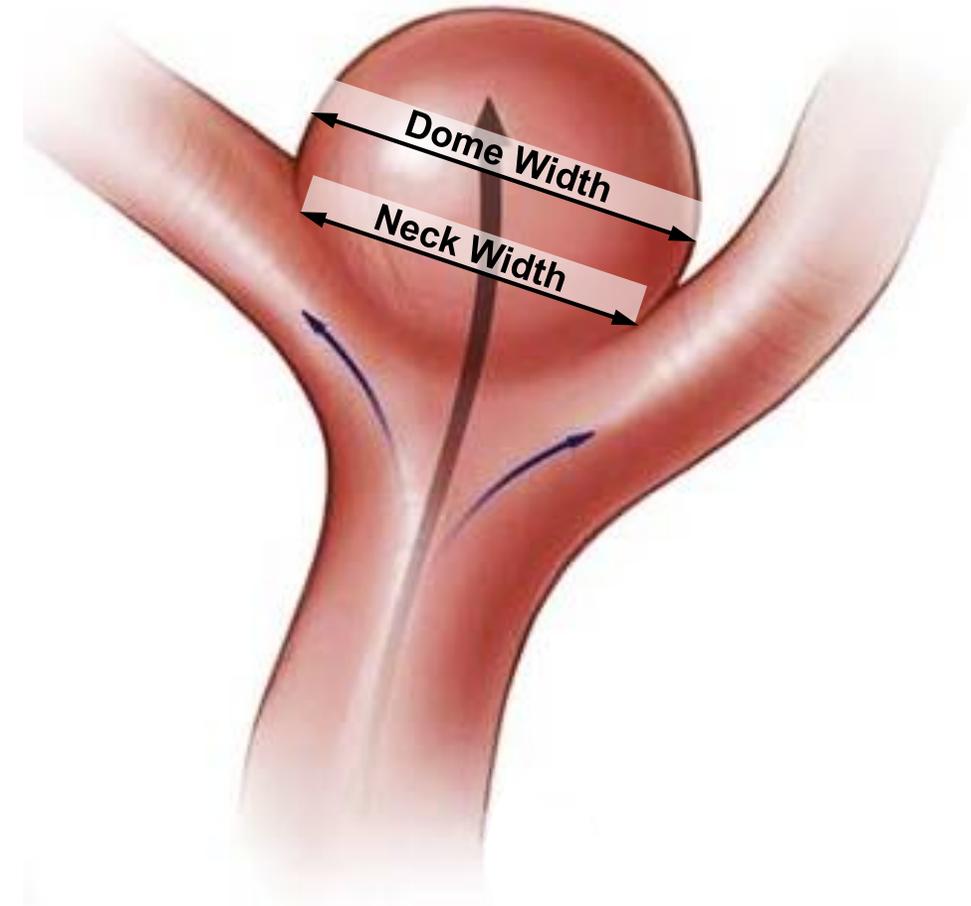
1) Bendok, 2018; De Leacy, 2018; Taschner, 2018; Qui, 2014; McDougall, 2014; Backes, 2014; Mitsos, 2013; Naggara, 2010; Murayama, 2003

Primary Treatment Goal: Prevent Ruptures and Re-Ruptures

- Size, shape, location of WNBAs create unique treatment challenges
- Treatment involves open surgery, or an endovascular procedure frequently requiring adjunctive device

Neck Size and Perforating Arteries are Critical Features That Complicate Treatment Selection

- Wide neck
 - Neck width > 4 mm
 - Dome to neck ratio < 2
- Branching structure of arteries
 - Clipping requires dissecting perforators off aneurysm

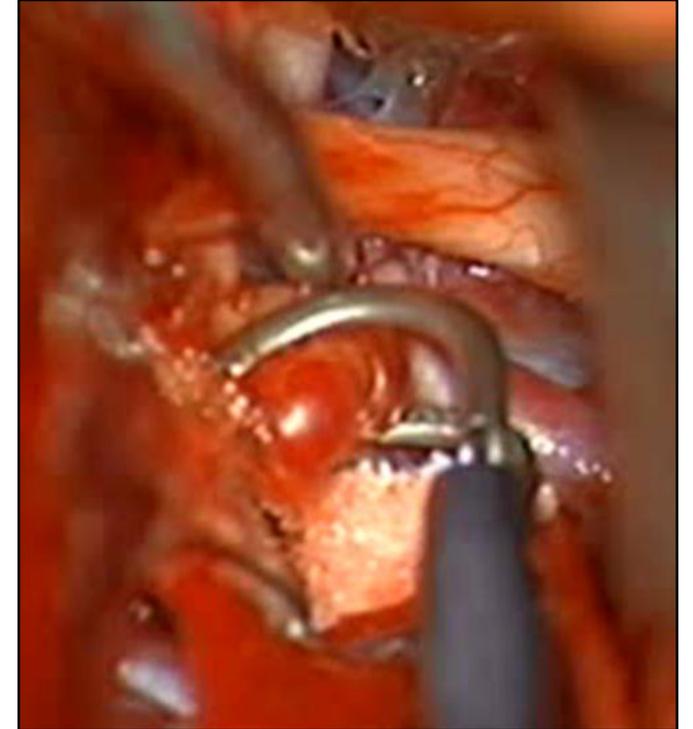


Conservative Management

- Many aneurysms can be managed conservatively
- Patients undergo regularly scheduled imaging
- Some patients need other options
 - Present with ruptured aneurysm
 - Family history, exposure to nicotine
 - History of SAH from another aneurysm

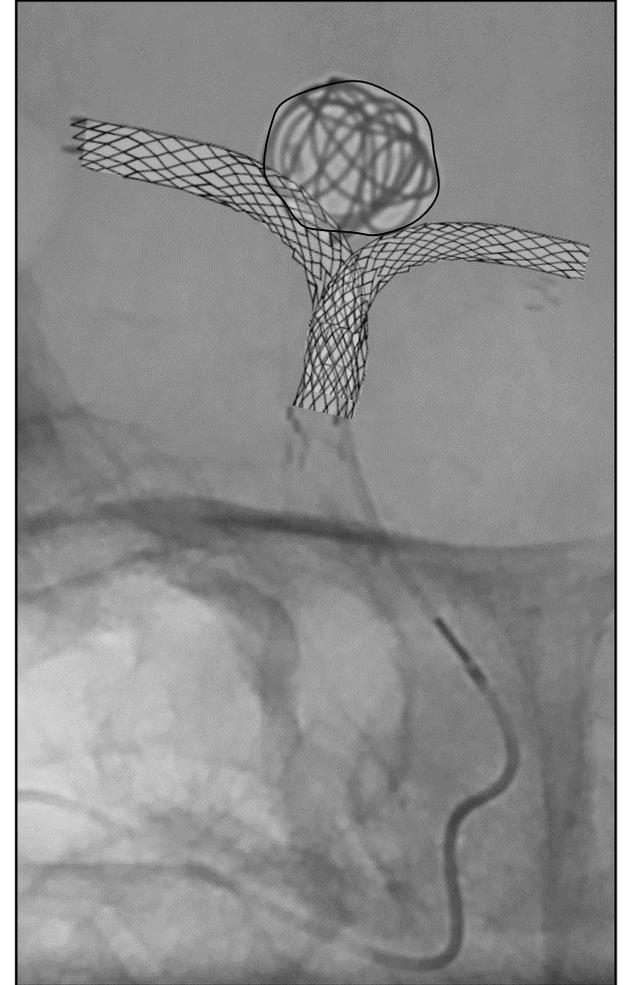
Open Surgical Clipping

- Highest immediate occlusion success, greater invasiveness, higher morbidity and mortality
- If perforator arteries torn, stretched or manipulated, stroke can result
- Rate of safety events 24% to 67%¹
- Not all aneurysms surgically accessible



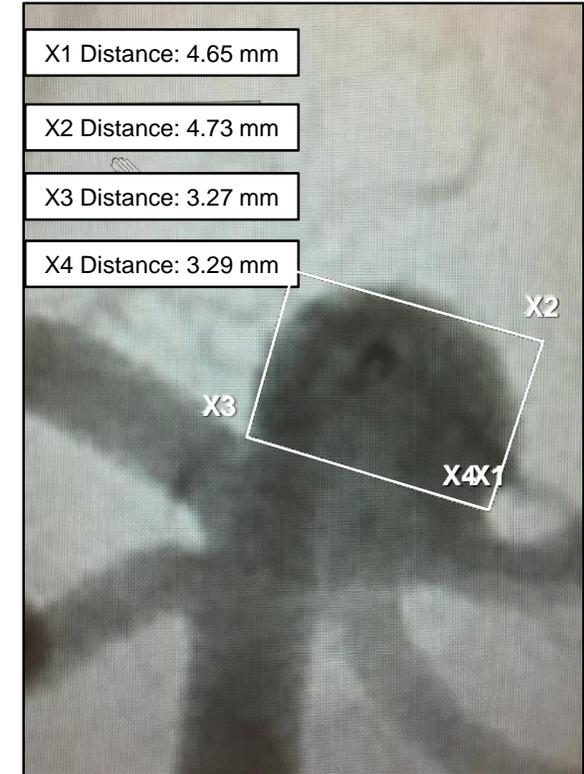
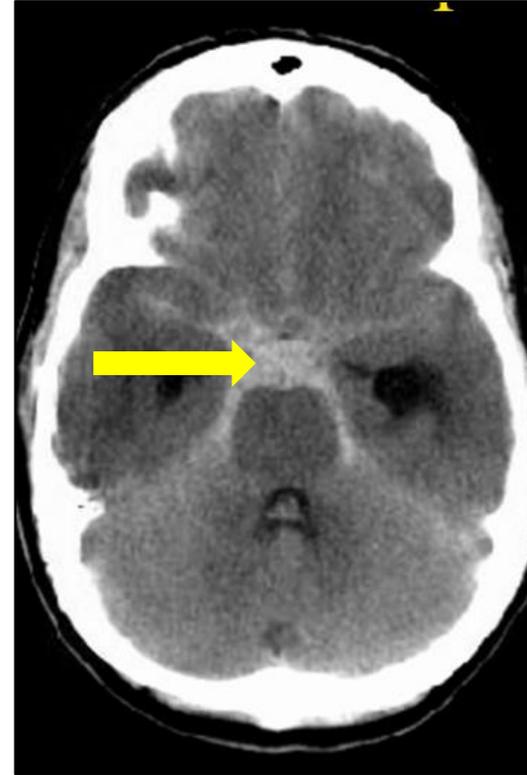
Endovascular Treatments

- Minimally invasive approach – carries less risk, decreases occlusion effectiveness
- Requires:
 - Catheterizing each major branch artery
 - Deploying interlocking stents
 - Deploying coils in aneurysm sac
- Each step adds time and risk
 - Metal struts across opening of brain artery carries risk of blood clot formation, possible stroke
 - Rate of safety events 21% to 40%¹
- Patients treated with antiplatelet therapy for life

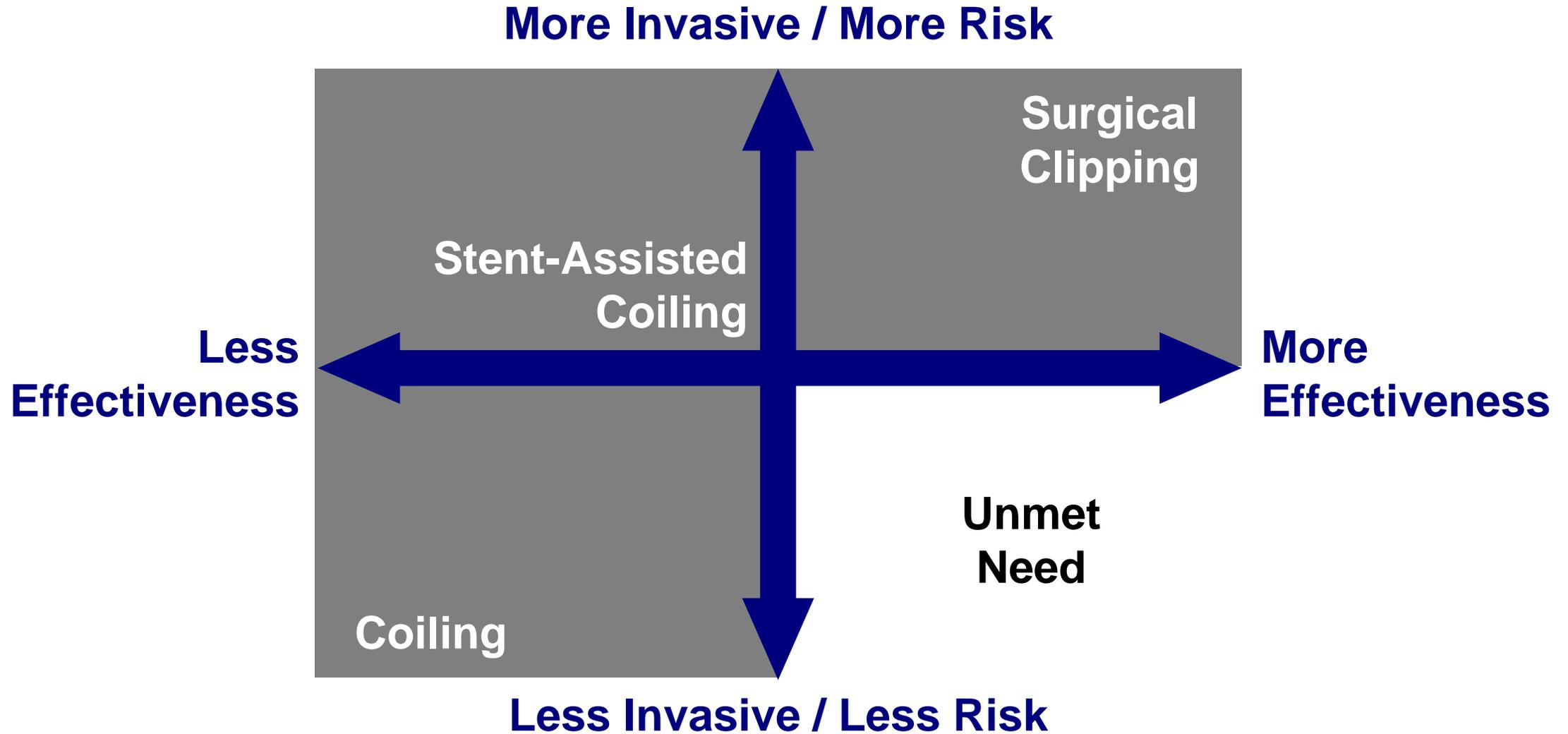


Current Options Present Limitations for Some Patients

- 53-year-old female, SAH, hydrocephalus
- Ruptured WNBA at basilar apex
- Surgical clipping requires
 - Significant drilling at base of skull
 - Extensive dissection to expose neck
 - Clearing perforators away from neck
- Endovascular approach requires
 - 1–2 stents to keep coils from herniating into parent artery
 - Long-term dual antiplatelet therapy



Unmet Need for Minimally Invasive Treatment with Greater Effectiveness and Less Risk in WNBAs



Device Description / MoA

Bill Patterson, PhD

Vice President for Neurovascular Research & Development

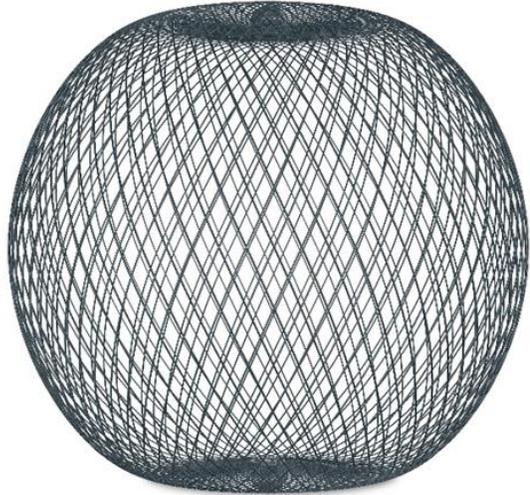
Novel, First-of-a-Kind Device Specifically Designed to Address Challenges of Treating WNBAs

- Braided, intrasaccular implant
- Single device treatment option
- Disrupts flow and promotes clot formation within device leading to aneurysm occlusion
- MoA and implant procedure similar to other endovascular treatment options

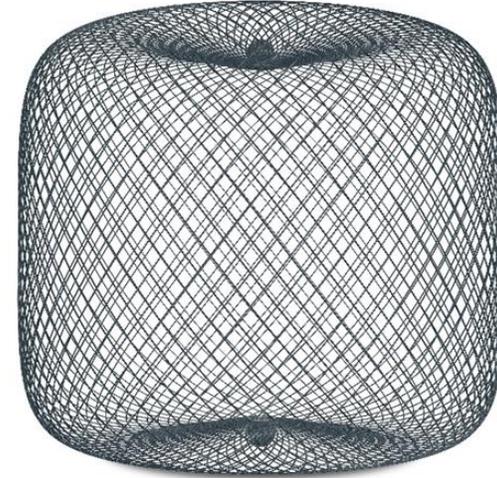
Three Main Components of WEB Aneurysm Embolization System



WEB Shapes and Sizes are Conformable



**WEB Single Layer
Sphere (SLS)**

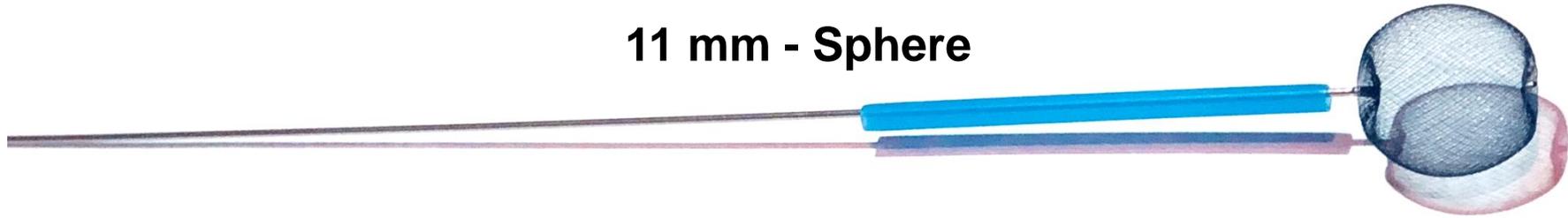


**WEB Single Layer
Barrel (SL)**

- Sizes ranging from 4x3 mm to 11x9 mm
- Braided composite made from nitinol and platinum
 - Highly conformable with fluoroscopic visibility

WEB Demonstration

11 mm - Sphere

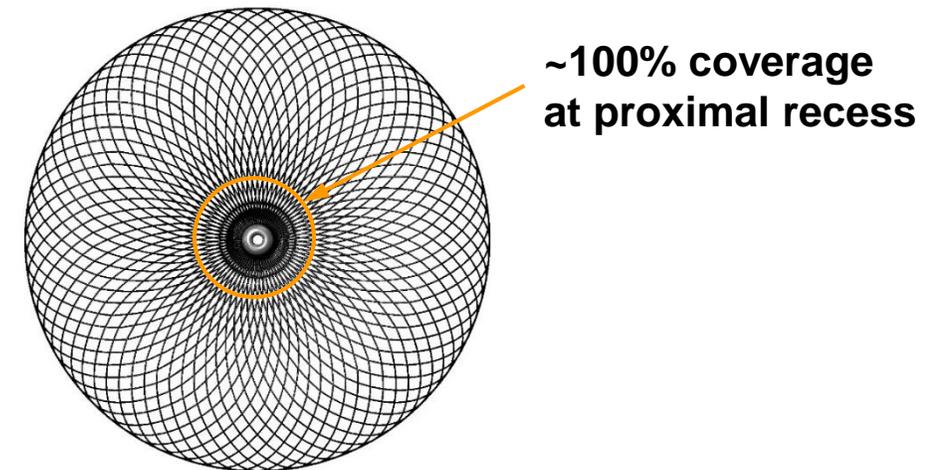
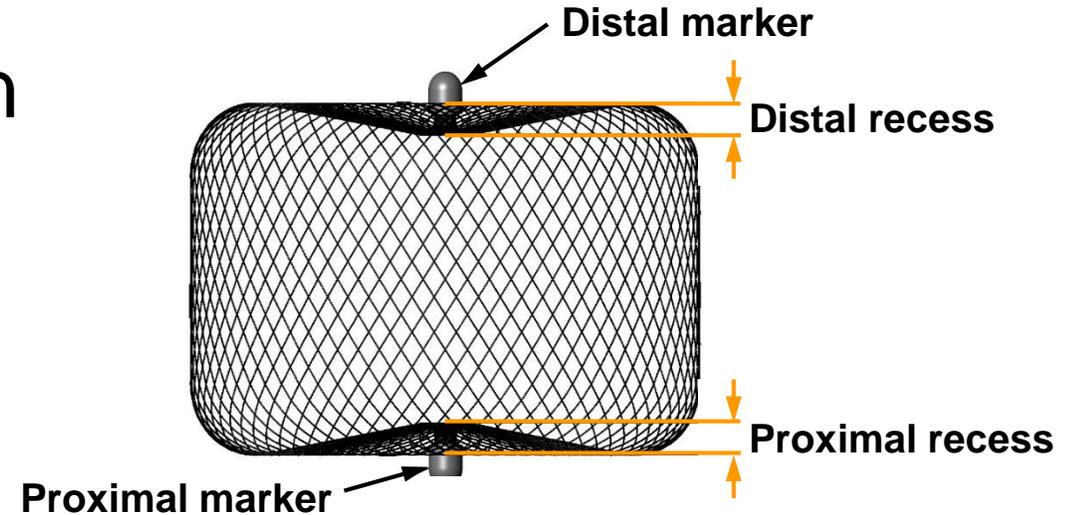


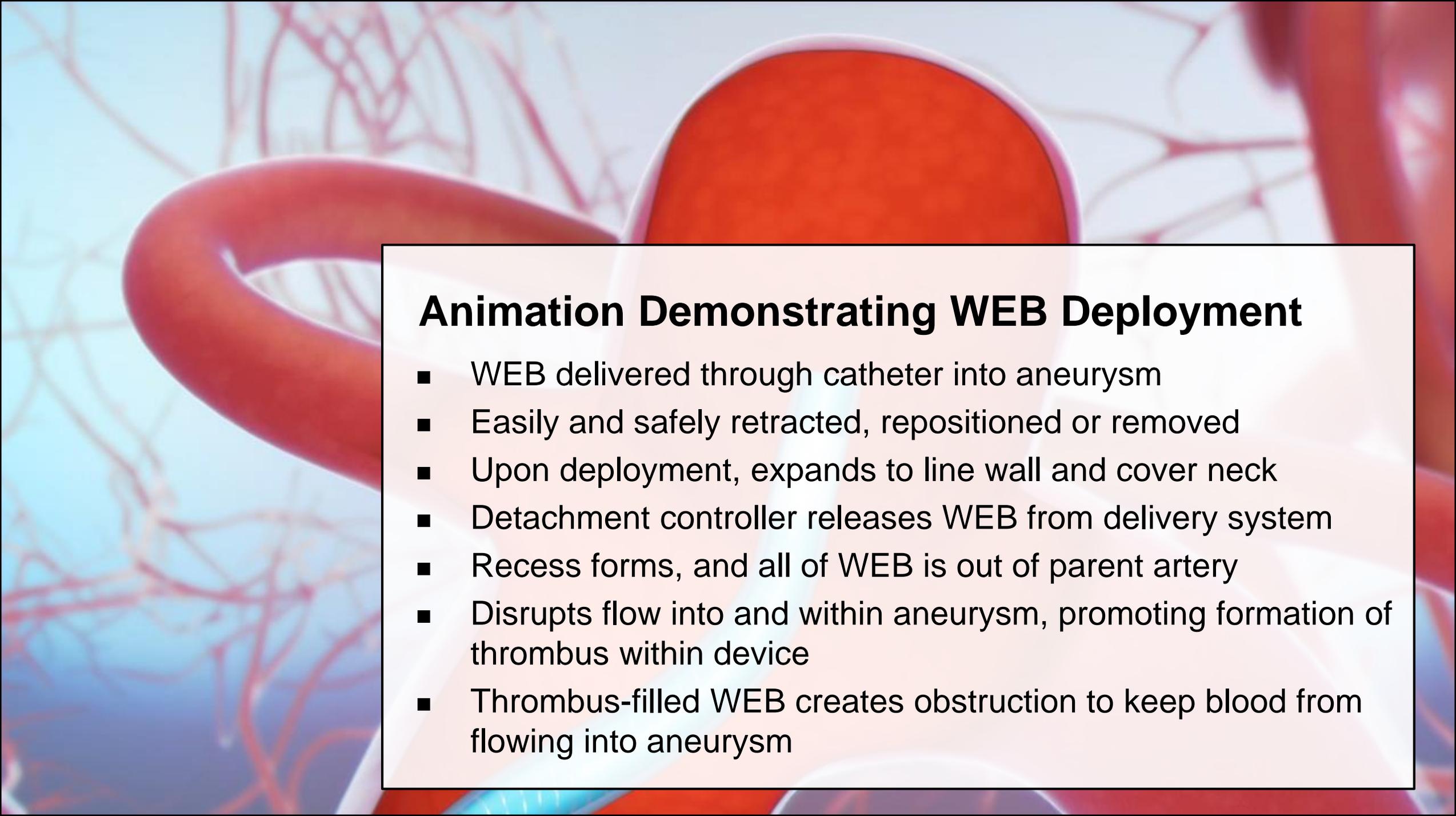
4 x 3 mm - Barrel



WEB's Braided Implant Placed Entirely Within WNBA Sac

- Proximal marker indented design
- Recessed area most densely braided
 - ~100% coverage at proximal recess
- Patients not required to stay on dual antiplatelet medications after procedure



A 3D anatomical illustration of a blood vessel. A large, red, bulbous aneurysm is shown protruding from a parent artery. A red, dome-shaped device, the WEB, is positioned at the neck of the aneurysm. The background shows a network of smaller blood vessels in shades of red and blue.

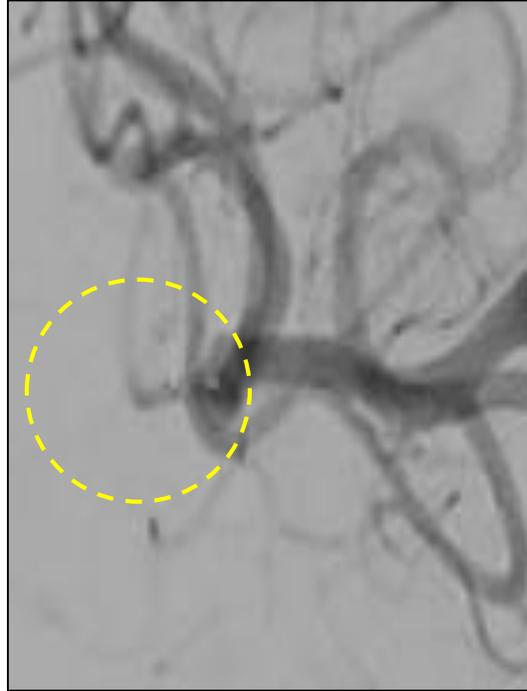
Animation Demonstrating WEB Deployment

- WEB delivered through catheter into aneurysm
- Easily and safely retracted, repositioned or removed
- Upon deployment, expands to line wall and cover neck
- Detachment controller releases WEB from delivery system
- Recess forms, and all of WEB is out of parent artery
- Disrupts flow into and within aneurysm, promoting formation of thrombus within device
- Thrombus-filled WEB creates obstruction to keep blood from flowing into aneurysm

WEB Design New and Unique; Mechanism of Action Well Known



Pre-Procedure



**12-Month Follow-Up
Complete Occlusion**

- WEB obstructs aneurysm's wide neck
- Placement leads to blood flow disruption, isolating weakened aneurysm wall from circulation
- Helps avoid potentially devastating rupture, or re-rupture

Study Design: WEB Intrasaccular Therapy Study (WEB-IT)

Adam Arthur, MD, MPH

WEB-IT First Prospective Clinical Study on WNBAs

- 27 centers
 - 21 US, 6 international
- Sample size: 150 patients
- Single arm study
 - Pre-specified safety and effectiveness endpoints
 - Comprehensive meta-analysis of published literature

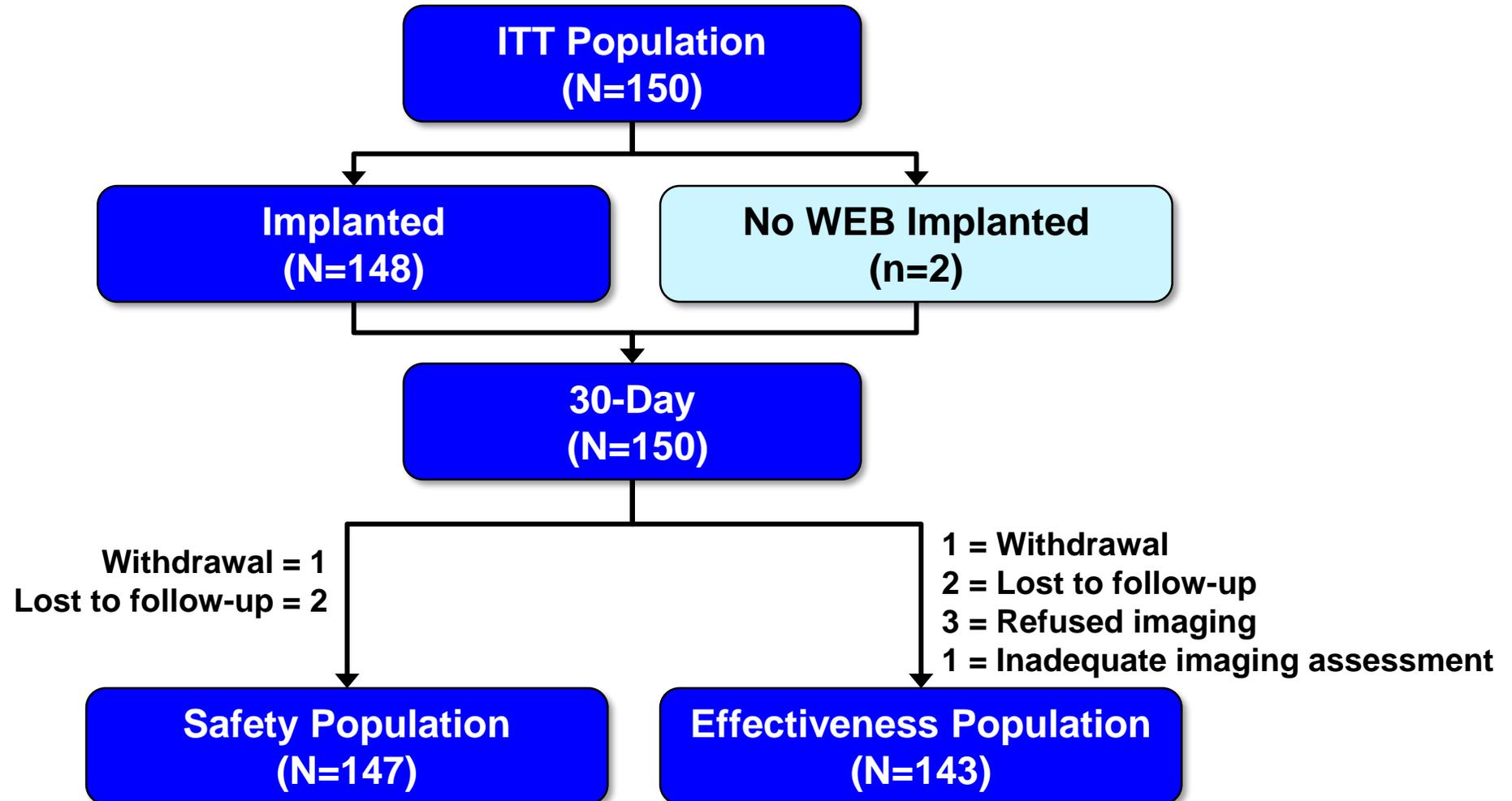
Key Inclusion Criteria

- Patients with aneurysms that required treatment
- Saccular in shape
- Located in basilar apex, middle cerebral artery bifurcation, internal carotid artery terminus, anterior communicating artery complex
- Aneurysm neck ≥ 4 mm or dome-to-neck ratio < 2
- Ruptured or unruptured aneurysm

Key Exclusion Criteria

- Stroke symptoms or any stroke within past 60 days
- mRS ≥ 2 prior to presentation or rupture
- SAH from non-index aneurysm within 90 days
- Previous treatment of index IA

Patient Disposition Through 12-Month Follow-Up



Three Pre-Specified Analysis Populations

	N	Definition
Enrolled, Intent to Treat (ITT)	150	All enrolled patients / device implant attempted
Complete Case (CC)	143	ITT patients with 12 month evaluation
Per Protocol (PP)	143	Complete case patients without protocol deviation

- Complete Case and Per Protocol contain same patients

Independent Study Oversight and Assessments of Both Primary Safety and Effectiveness Endpoints

- Core Lab
 - Adjudicate all angiographic outcomes
- Clinical Events Adjudicator
 - Reviewed all AEs, device failures and site deviations
 - Assessments used in all safety analyses
- Data Monitoring Committee
 - Study oversight and review of all AEs

Primary Safety Endpoint

Time from WEB placement	Death	Stroke
Within 30 days	Any death	Major stroke
Day 31 to 365	Neurologic death	Major ipsilateral stroke

- Major stroke: ischemic or hemorrhagic stroke resulting in increase in NIHSS ≥ 4 points for > 7 days

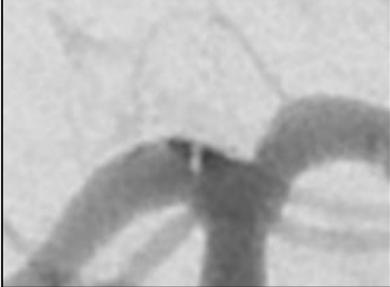
WEB-IT Prespecified Safety Performance Goal

- Prespecified safety endpoint < 20%
 - Aligns with meta-analysis of endovascular and surgical methods
 - Same threshold used in IDE studies for all other PMA-approved aneurysm devices

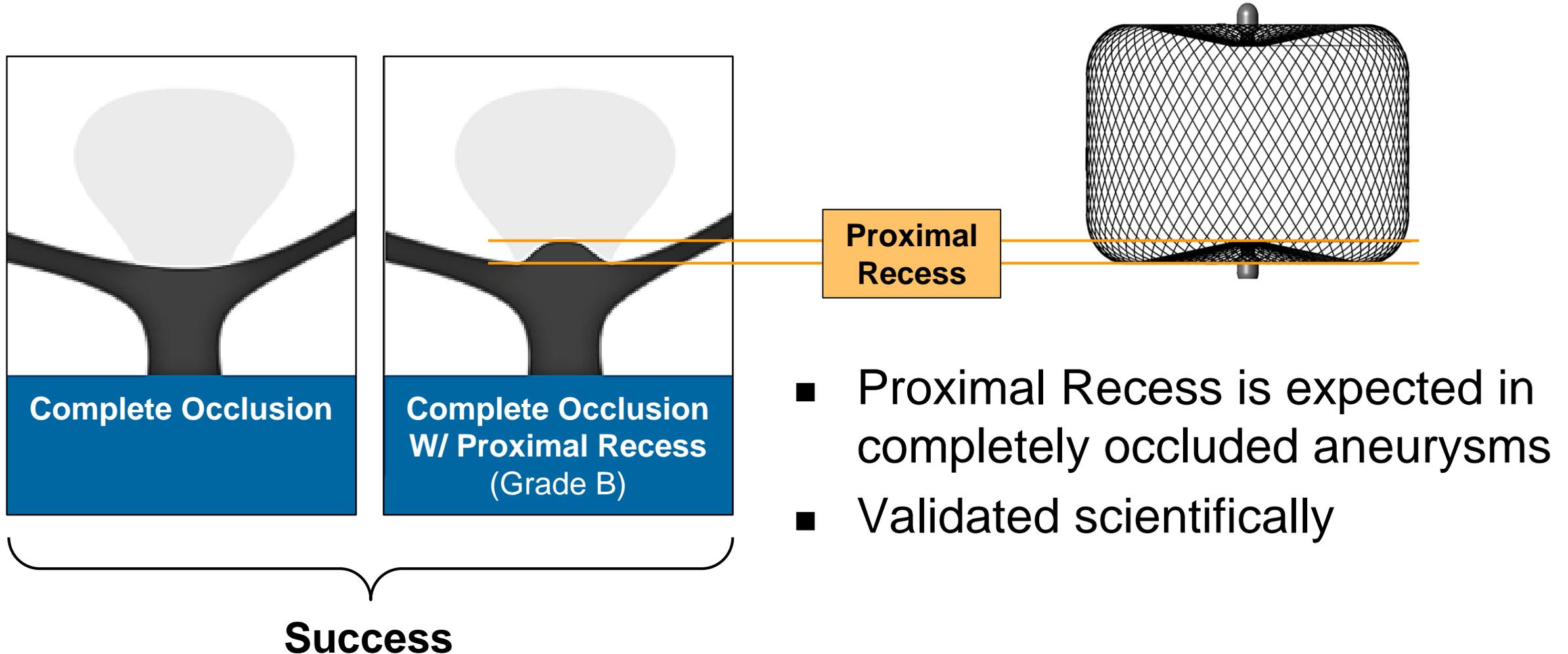
Primary Effectiveness Endpoint

- Pre-specified composite effectiveness endpoint > 35%
 - No retreatment
 - No recurrent subarachnoid hemorrhage
 - No clinically significant stenosis (> 50% stenosis)
 - Complete aneurysm occlusion

WEB Occlusion Scale (WOS) a Modified Raymond Scale to Assess Occlusion Given Novel Design of WEB

Grade	Endpoint	Definition	Schematic	Angiogram
Complete Occlusion	Success	No contrast in contact with IA neck or with wall of IA sac		
Residual Neck	Failure	Some contrast in contact with IA neck but no contrast in contact with wall of IA sac or inside of WEB device		
Residual Aneurysm	Failure	Apparent contrast in contact with IA sac or inside of WEB device		

Complete Occlusion with Proximal Recess Included to Address Unique Design of WEB Device



Prespecified Effectiveness Endpoint from Meta-Analysis of Published Literature of Similar Approved Devices

- Prespecified effectiveness endpoint **> 35%**

Source (Aneurysms N)	Study	Aneurysm Types	Treatment Methods	Complete Occlusion Rate*	95% LCL
WEB IDE (N=1319)	Meta-analysis	Wide Neck & Bifurcation	Surgical / Endovascular	50%	35%
Fiorella, 2017 (N=2794)	Meta-analysis	Wide Neck & Bifurcation	Surgical / Endovascular	46%	39%
De Leacy, 2018 (N=115)	Core Lab Adjudicated	WNBA	Endovascular	31%	22%*

*95% LCL calculated from De Leacy, 2018

WEB-IT Study: Effectiveness and Safety Results

David Fiorella, MD, PhD

Professor of Neurosurgery and Radiology

Director of Cerebrovascular Center

Stony Brook University Medical Center

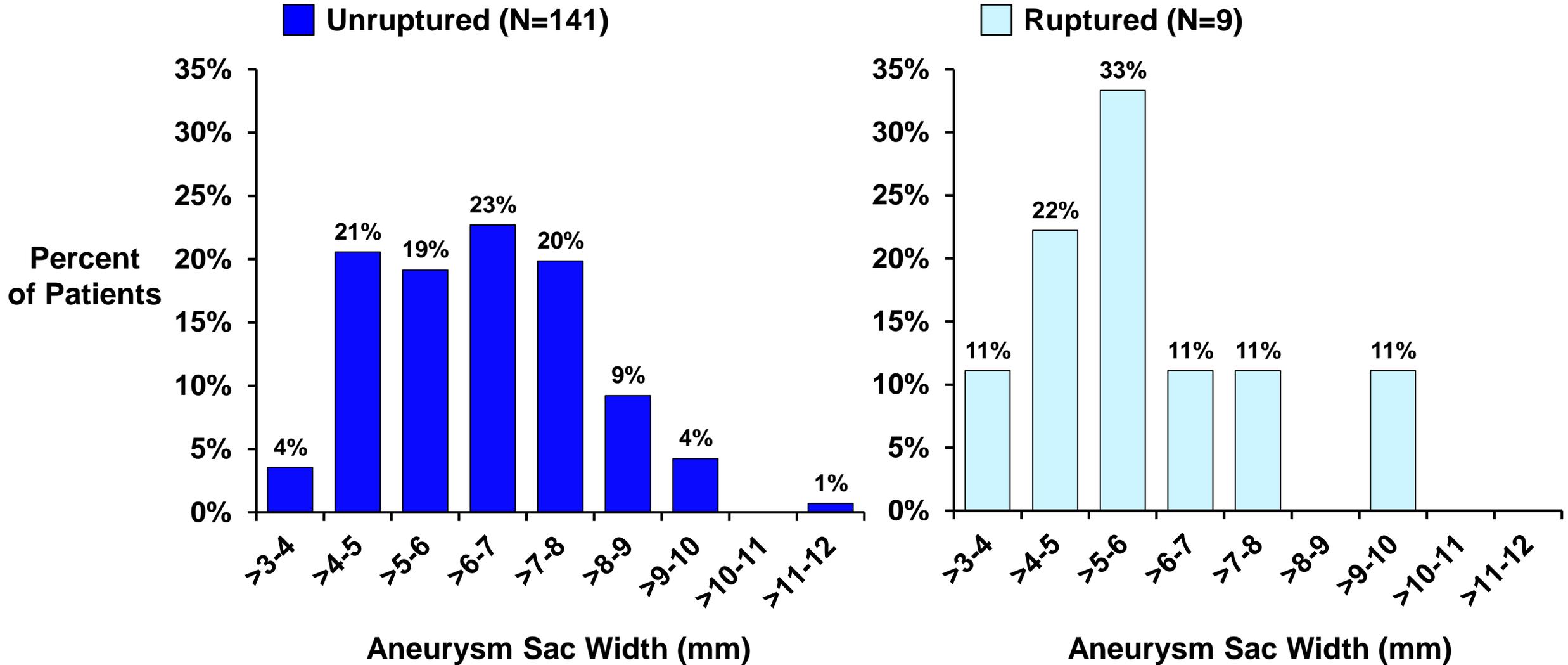
Baseline Demographics Representative of Patient Population Presenting with Intracranial Aneurysms

Variable	ITT Population (N=150)
Age (years), mean	59
Female	73%
Race	
White	85%
Black or African American	12%
Other	3%
Smoking status	
Current smoker	44%
Past smoker	21%

Aneurysm Characteristics

Variable	ITT Population (N=150)
Sac width (mm), mean (SD)	6.4 (1.6)
Neck width (mm), mean (SD)	4.8 (1.1)
Rupture status	
Ruptured	6%
Unruptured	94%
Aneurysm location	
Basilar apex	39%
Middle cerebral artery bifurcation	30%
Anterior communicating artery complex	27%
Internal carotid artery	4%

Enrollment Distribution by Aneurysm Size and Rupture Status (ITT)



WEB Procedure: Short Procedural Time, Low Fluoroscopic Doses

Variable	Mean (SD)
Fluoroscopy time (min)	30.2 (15.7)
Total fluoroscopy (mGy)	2756 (2582.4)

- Technically straightforward and efficient strategy to treat this challenging subtype of cerebral aneurysms

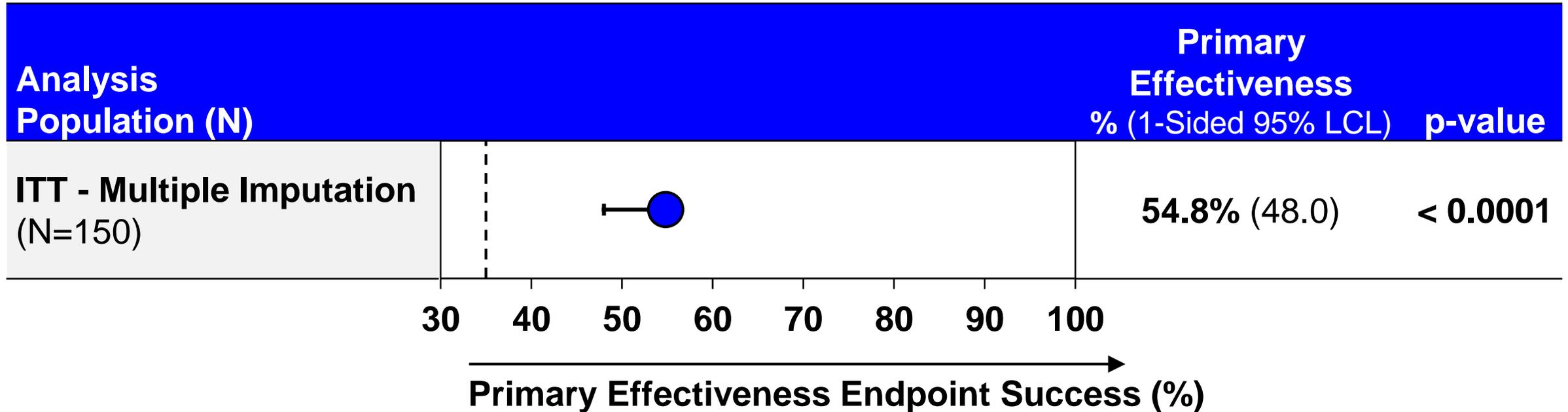
WEB Provides Physicians Ability to Review and Optimize Device Fit Prior to Final Detachment

	WEB Devices	
	%	N
Total WEBs introduced	100%	211
Total WEBs implanted	70%	148
WEBs not implanted	30%	63
Number of attempts		
1	67%	100
2	27%	40
3	6%	9
4	< 1%	1

WEB Successfully Implanted During Index Procedure in 98.7% of Patients

	WEB Devices	
	%	N
Successful delivery of WEB	98.7%	148
Adjunctive device use	4.7%	7
Balloon	3.4%	5
Stent	1.4%	2

54.8% of Patients Met Composite Primary Effectiveness Endpoint (ITT)



- Consistent results in Per Protocol population ($p < 0.0001$)
- In worst case imputation, endpoint met ($p < 0.0001$)

Primary Reasons for Patients Not Meeting Primary Effectiveness Endpoint (CC/PP Population)

	Patients	
	%	N
Total not meeting primary effectiveness outcome	46.2%	66
Residual neck	30.8%	44
Residual aneurysm	10.5%	15
Retreatment within 12 months	2.1%	3
Failure to implant	1.4%	2
Adjunctive device use	1.4%	2

8 patients required retreatment. 5 counted based on pre-retreatment angiogram. 3 without useable 12-month angiogram counted in retreatment category. 1 patient counted as Residual Aneurysm, also had significant parent artery stenosis 12 months following retreatment with stent.

Prespecified Additional Endpoint: 83.2% of Patients Achieved Adequate Occlusion

Complete Case (N=143)	n/N	Percent of Patients (95% CI)
Adequate Occlusion (Complete Occlusion or Residual Neck)	119/143	83.2% (76.1, 88.9)

Secondary Effectiveness: Aneurysmal Recurrence

Complete Case (N=143)	n/N	Percent of Patients (95% CI)
Angiographic Recurrence	18/143	12.6% (7.6, 19.2)

- Occlusion status in patients with recurrence at 12 months
 - 13 with residual neck
 - 5 with residual aneurysm

WEB Allows for Retreatment With All Available Treatment Modalities

- Retreatment after WEB can be easier than retreatment after other endovascular therapies
 - No parent artery implant spanning aneurysm neck
 - Allows for clear visualization of residual filling

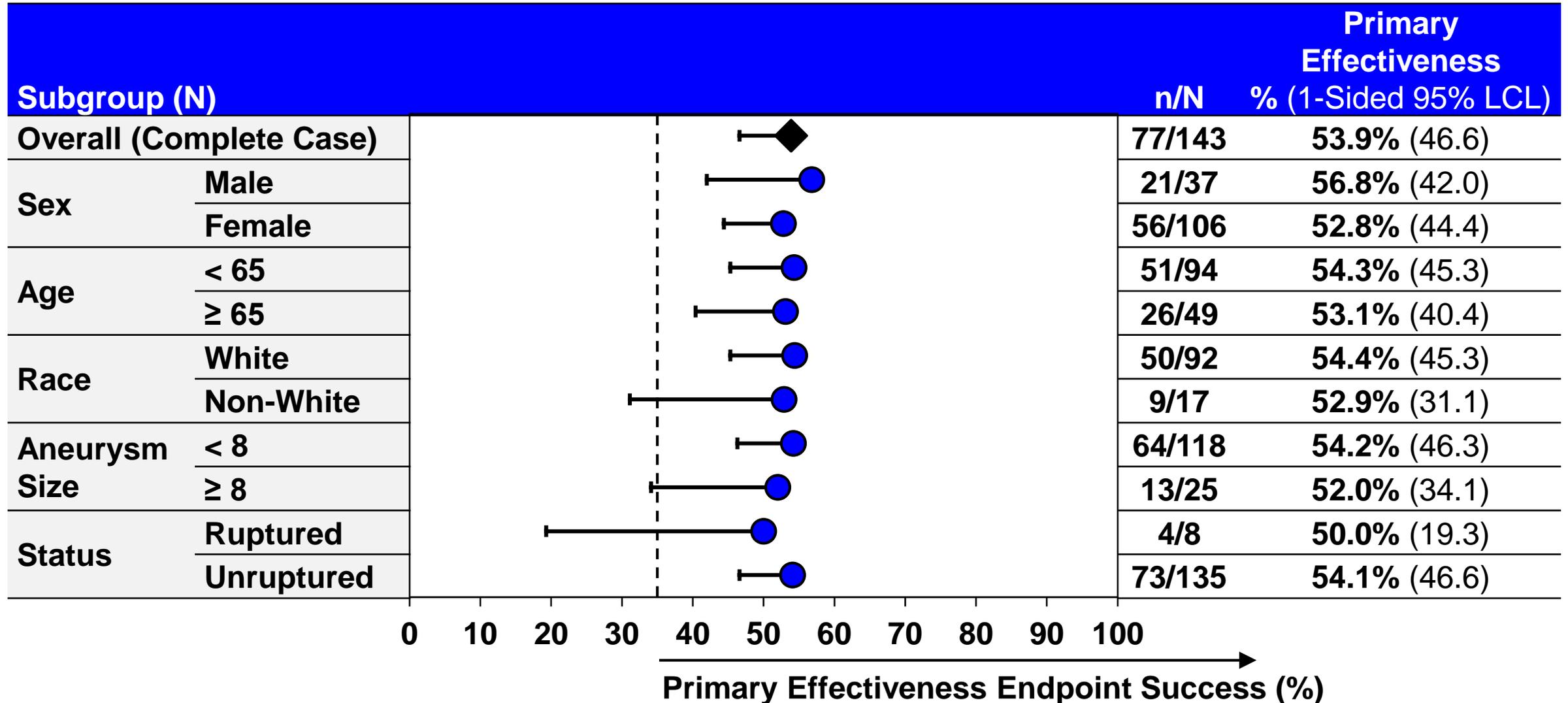
During WEB-IT Retreatments were Technically Successful with Available Endovascular Therapies

- 8 patients had retreatment of target aneurysm up to 12 months
 - All successfully retreated with other endovascular options
 - Coils (n=1)
 - Stent-assisted coiling (n=4)
 - Flow diverter (n=3)
 - All accomplished without mortality or major morbidity

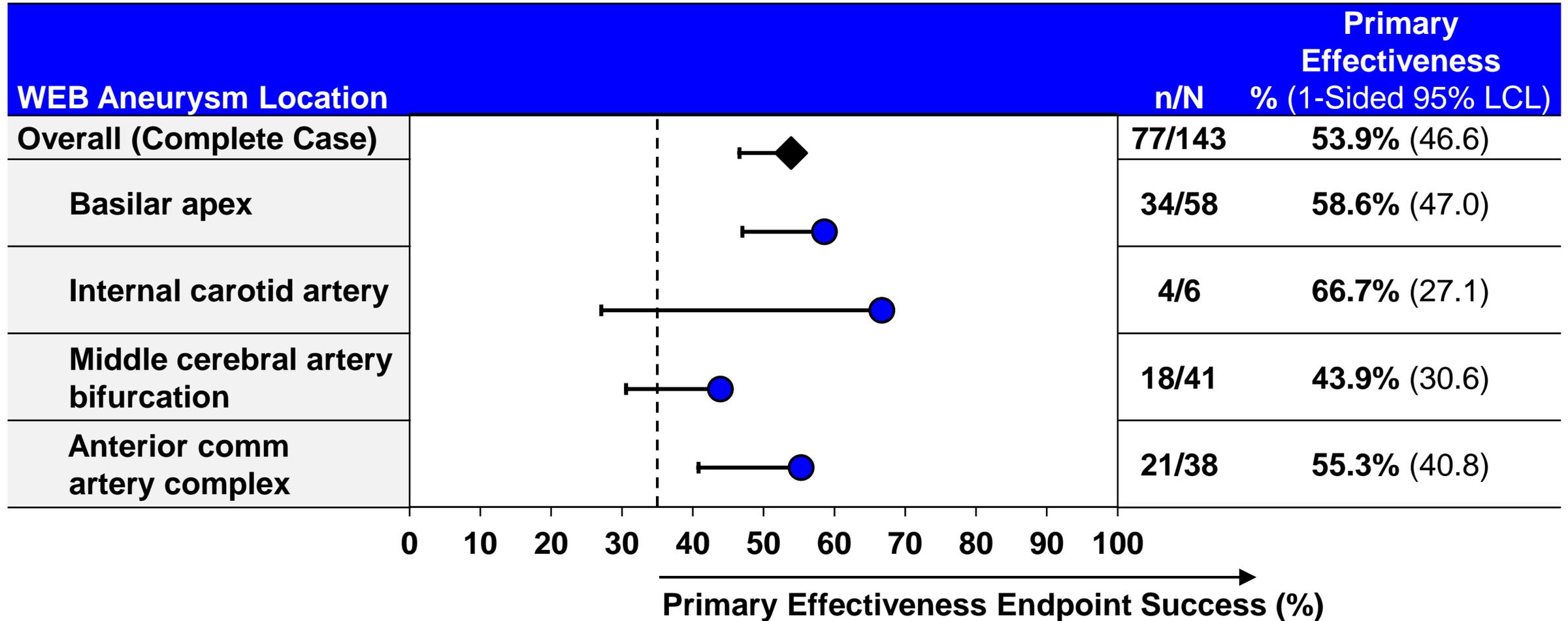
Six Patients Who Failed Effectiveness Endpoint Retreated After 12-Month Angiogram

- 5 retreated successfully without mortality or major morbidity with other endovascular options
- 1 resulted in patient death (Day 625)
 - First flow diverter failed to occlude aneurysm
 - Second retreatment with flow diverter resulted in rupture of parent artery

Primary Effectiveness Results by Baseline Demographics and Aneurysm Characteristics



Primary Effectiveness Results by Aneurysm Location



Safety Results

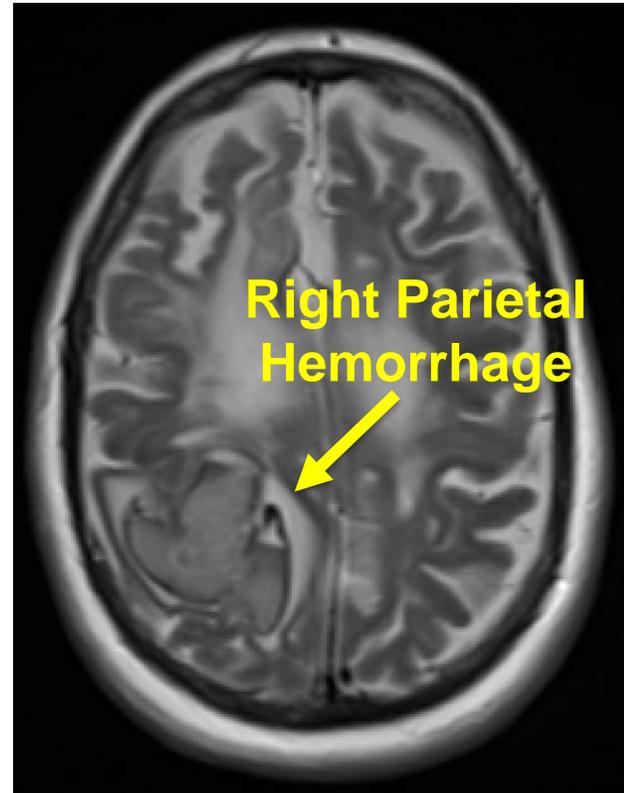
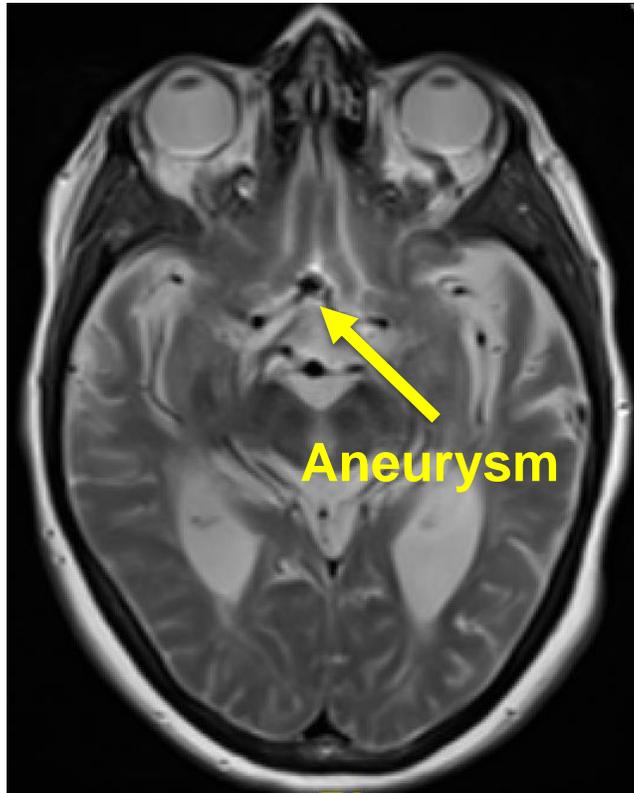
WEB Met Primary Safety Endpoint

	Patients			
	n	%	1-Sided 95% UCL	p-value
Primary safety composite (ITT)	1	0.67%	6.04%	< 0.0001

- No deaths through Day 365 (0/150)
- No major ipsilateral strokes between Day 31 and 365

Primary Safety Endpoint Event (N=1)

Sex	Age	Treatment	Risk Factors	Aneurysm Size	mRS
Female	54	Successful WEB implant	Multiple sclerosis Current smoker	Sac = 7 mm Neck = 4.7 mm	0



Day 22

- Sudden headache, left hemiplegia
- CT demonstrated new right parietal hemorrhage
- Related to index procedure and/or concurrent condition

Month 12

- Residual left hemiplegia (mRS = 4)
- Aneurysm completely occluded, no stenosis of parent artery

Overview of All Adverse Events

	Total Number of Events	Total Patients with Events (N=150)	Percent of Patients with Events
Within 30 days			
Any non-serious AE	135	68	45.3%
Any SAE	27	21	14.0%
Day 31 to 365			
Any non-serious AE	151	65	43.3%
Any SAE	35	21	14.0%

Overview of All SAEs Occurring Within 30 Days

Within 30 Days	Total Number of Events	Total Patients with Events (N=150)	Percent of Patients with Events
Any SAE	27	21	14.0%
Procedure-related	11	10	6.7%
Device-related	1	1	0.7%
Procedure- and device-related	3	3	2.0%
Not related	12	9	6.0%

- No SAEs occurring between Day 31 and 365 related to device or procedure

4 Deaths Reported After Day 365

- Complications from 2nd retreatment attempt with flow diverter of index aneurysm (Day 625)
- Spontaneous thoracic aortic dissection (type A) with complications leading to respiratory failure (Day 589)
- Traumatic brain injury after fall (Day 753)
- Bladder cancer (Day 826)

Additional Endpoint: Change from Baseline in Modified Rankin Score Through 12 Months

Score at Baseline	Score at 12-Month Follow-up Visit						Total
	0	1	2	3	4		
0	108	10	-	-	1	119	
1	14	16	-	1	-	31	
Total	122	26	0	1	1	150*	

 No Change
  Improved
  Worsened

*No 12-month data, 6-month scores used (n=2)

No mRS data at 12 months, as no WEB implanted, 30-day scores used (n=2)

No mRS data after 30 days, 30-day score used (n=3)

No Recurrent Subarachnoid Hemorrhage in Patients with Ruptured Aneurysms at Baseline

- SAEs and AEs in ruptured patients were not different from unruptured WEB-IT cohort
- No indication of increased risk for treatment of ruptured aneurysms with WEB device

CLARYS: Supports the Effectiveness of WEB to Prevent Re-Hemorrhage in Ruptured Aneurysms

Study	Sample Size (N=60)	Time	Recurrent Hemorrhage
CLARYS	60	30 Days	0%
	43	12 Month	0%

- All patients with acute subarachnoid hemorrhage

All Stroke (Serious and Non-Serious AEs)

All Stroke Analysis: Ischemic Events

- 11 minor strokes (10 patients)*
 - 8 strokes resolved without sequelae
 - 3 strokes (2 patients) with minor sequelae
 - mRS = 1 at 12 months

All Stroke Analysis: Neurological Death and All Potential Ischemic Events (Stroke and TIA)

Complete Case (N=147)	Patients N (%)	Device- or Procedure-Related	Outcomes (mRS)
Neurological deaths	0 (0.0%)	N/A	N/A
Ischemic strokes	10 (6.8%)	5	No disabling
Transient ischemic attacks	6 (4.1%)	5	No sequelae
Overall rate	14 (9.5%)	10	N/A

All Stroke Analysis: Hemorrhagic Events

- 1 delayed subarachnoid hemorrhage (Primary Endpoint)
- 2 procedural subarachnoid hemorrhages (1 AE, 1 SAE)
 - Both events asymptomatic, resolved without sequelae
- 1 intracranial hemorrhage
 - Occurred on Day 139
 - Unrelated to device or procedure
 - Resolved without sequelae
 - mRS score unchanged

WEB is Safe and Effective Treatment Option for Patients with Wide Neck Bifurcation Aneurysms

- 54.8% of patients met primary effectiveness endpoint
 - 83.2% achieved adequate occlusion at 12 months
 - Consistent results regardless of baseline demographics, aneurysm characteristics and rupture status
- 99.3% patients free of disabling stroke or death
- Effective, minimally-invasive option for patients with WNBA
- Acceptable safety profile compared to current standard of care

Post-Approval Commitments and Training

Jacques Dion, MD

Vice President Scientific Affairs

> 400 Patients Followed Clinically and Angiographically for Up to 5 Years

Study	Sample Size	Last Patient Enrolled	Case Type	Duration (Years)	Status
WEB-IT	150	Mar 2016	Ruptured & Unruptured	5	30-day safety (published) Effectiveness (publication pending)
WEBCAST	51	Feb 2014	Ruptured & Unruptured	5	12 month safety and efficacy (published)
French Observatory	62	Feb 2014	Ruptured & Unruptured	2	12 month safety and efficacy (published)
WEBCAST 2	55	May 2015	Ruptured & Unruptured	5	12 month safety and efficacy (published)
CLARYS*	60	Sep 2017	Ruptured	1	30-day safety (presented)
WEB-IT China*	43 of 60	Enrolling	Ruptured & Unruptured	1	Enrolling

***DATA NOT REVIEWED BY FDA**

Part 1: Required Centralized New User Training Prior to Independent Use of WEB

- Didactic course work
 - Technical overview
 - Delivery techniques
 - Case planning and patient selection
- Hands-on interaction
 - Imaging best practices
 - Device sizing and preparation
 - Complication management

Part 2: Proctor and Trainer Supported Cases

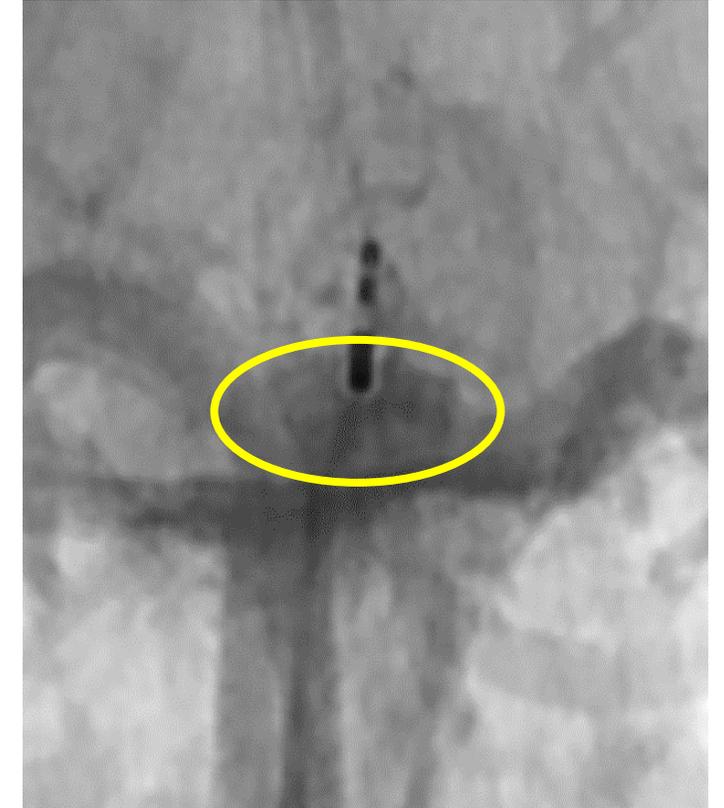
- Proctor supported training cases
 - ≥ 3 cases as primary operator
- Trainer supported cases
 - ≥ 5 cases as primary operator
- Ongoing proctor support for complex cases
- Continued support of new users by company trainers
- WEB only available at hospitals where physician has successfully completed the two-part training

Clinical Perspective

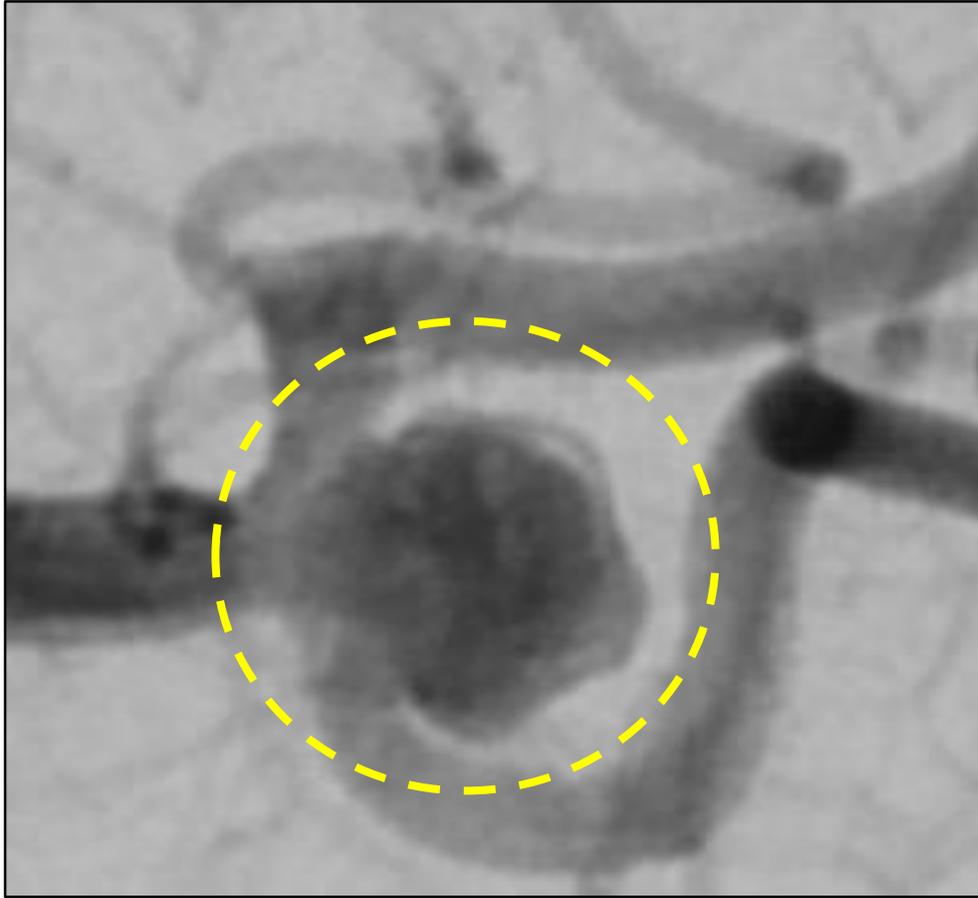
Adam Arthur, MD, MPH

Adequate Occlusion

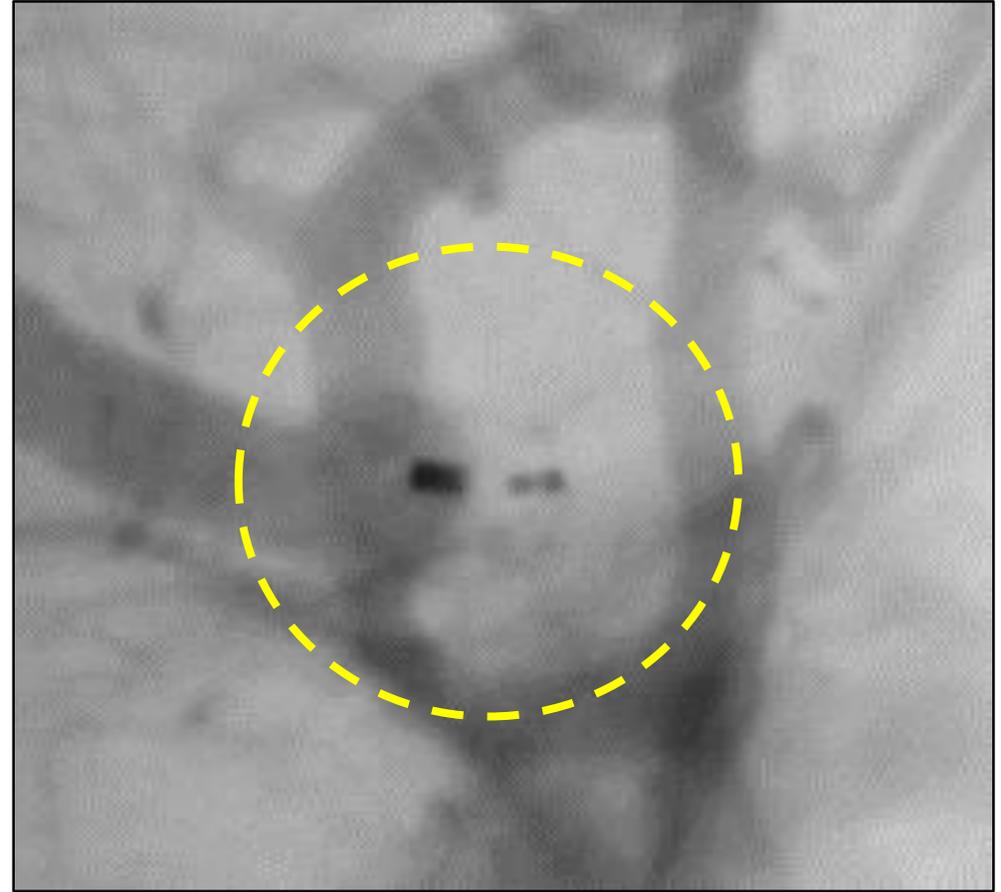
- Primary outcome failure, clinical success
- 53-year-old female, ruptured WNBA at basilar apex
- WEB protected her from re-bleeding
- Cerebral vasospasm, hydrocephalus
- Surgery to place shunt
- 12-month follow-up: small neck remnant
- Lives independently



Middle Cerebral Artery Aneurysm



Pre-Procedure



12-Month Follow-Up

Anterior Communicating Artery Aneurysm



Pre-Procedure

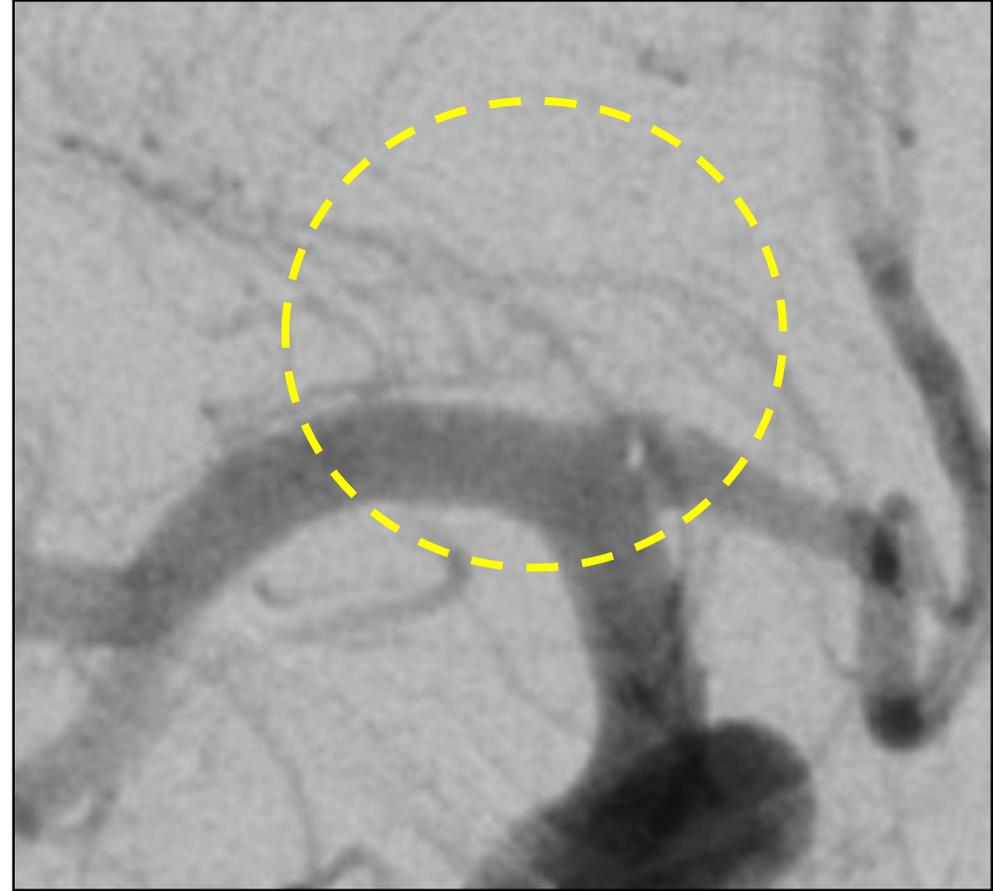


12-Month Follow-Up

Internal Carotid Artery Terminus Aneurysm



Pre-Procedure



12-Month Follow-Up

WEB is Safe and Effective Treatment Option for Patients with WNBAs

Treatment	Study Population	Aneurysms (N)	Complete Occlusion (12 Month)	Morbidity and Mortality (12 Month)
Coiling	MAPS ¹ Wide Neck IAs	N=73	27.1%	1.5%
Stent-Assisted Coiling	MAPS ¹ Wide Neck IAs	N=85	45.7%	7.5%
Endovascular*	BRANCH ² Wide Neck Bifurcation	N=115	30.6%	5.8% Morbidity 1.7% Mortality
WEB	WEB-IT ³ Wide Neck Bifurcation	N=150	54.8%	1.3% Morbidity 0.0% Mortality
WEB	WEB GCP ⁴ Wide Neck Bifurcation	N=169	52.9%	1.3% Morbidity 1.4% Mortality

- No late ruptures in > 768 patient-years of data

Need for WEB as Option for WNBA Patients

Two Populations of Patients



RUPTURED

- Stroke without warning
- Health problems, medications, concerns seen in new light

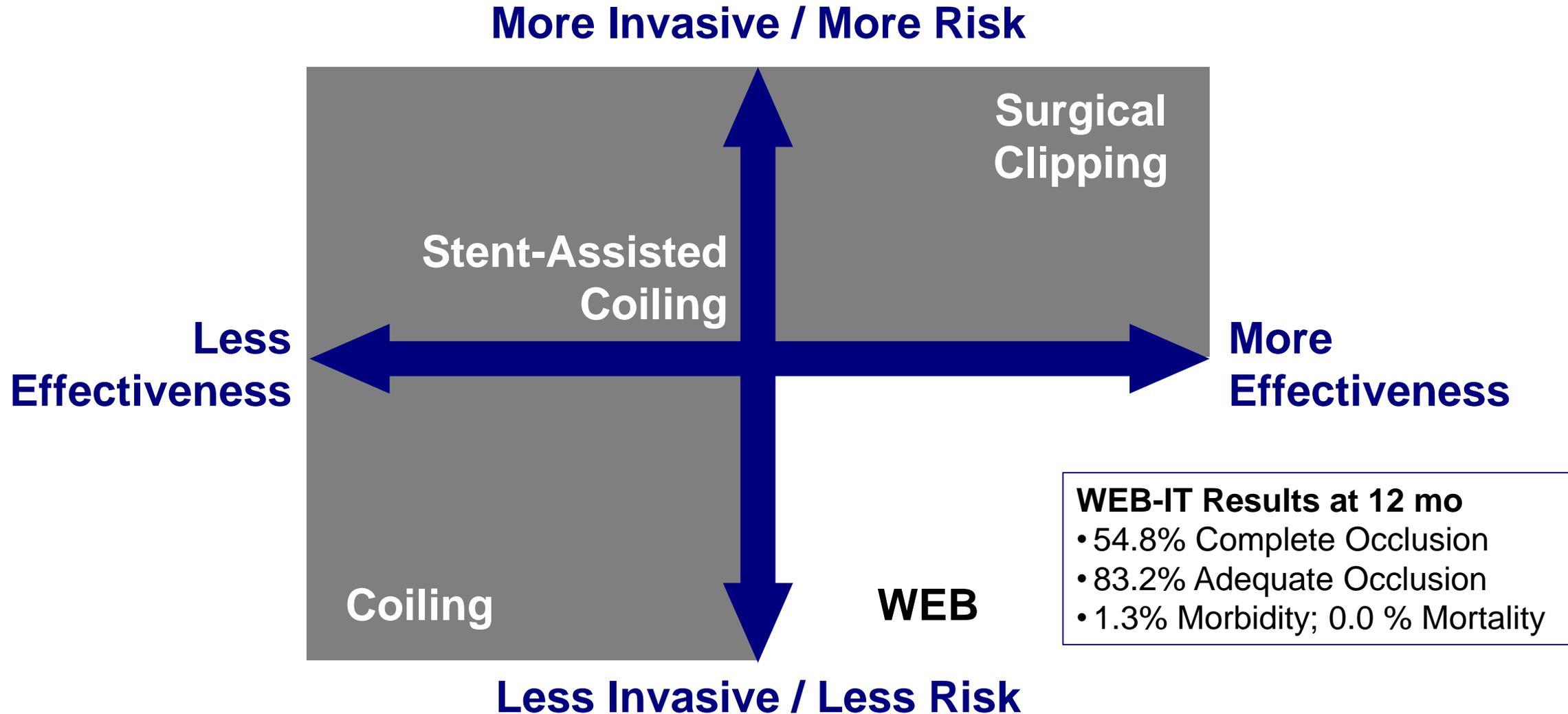


UNRUPTURED At Risk for Rupture

- Incidental finding of aneurysm
- Must understand options and risks
- Consider age, history, health

Treatment options must be tailored
No one treatment is best for all patients
Addition of minimally invasive procedure for WNBA needed

WEB Helps Address Need for Effective, Minimally-Invasive Treatment with Low Risk in WNBAs



Woven EndoBridge (WEB) Intrasaccular Therapy for Treatment of Wide Neck Bifurcation Intracranial Aneurysms

September 27, 2018

Sequent Medical

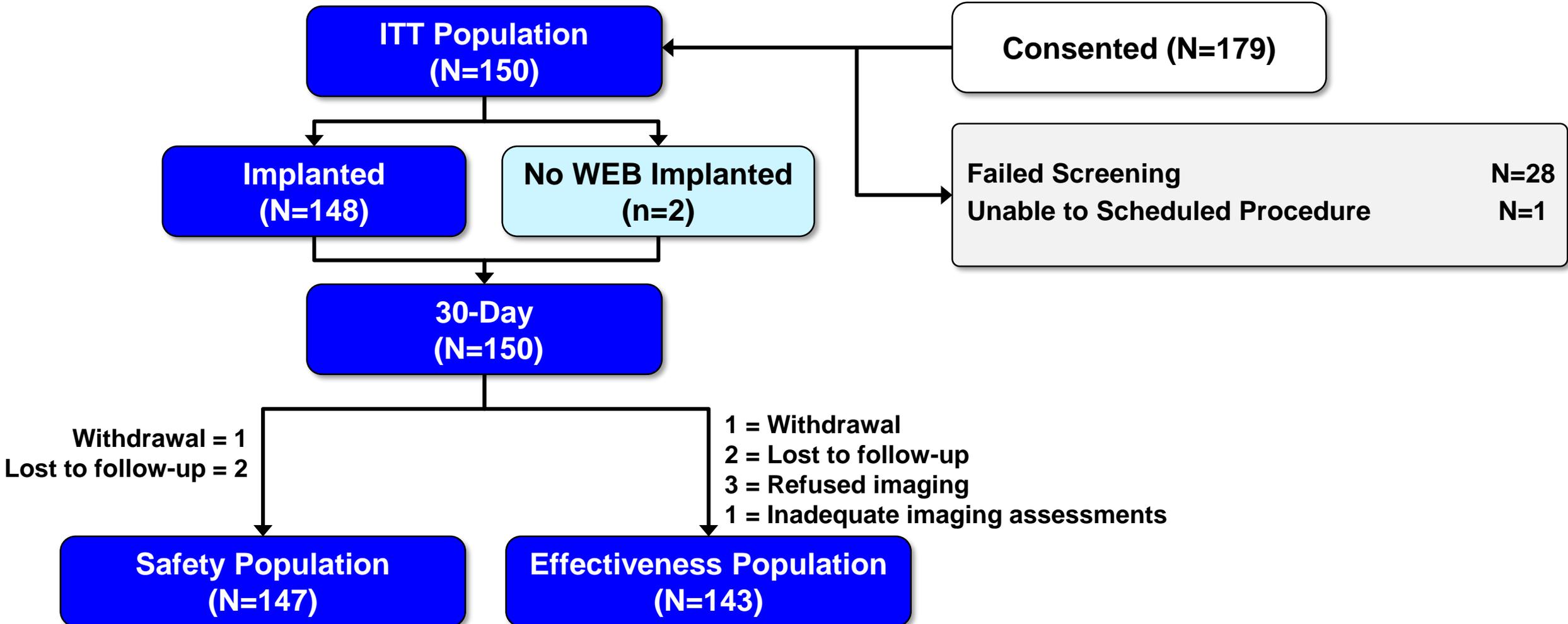
FDA Neurological Devices Panel

BACK-UP SLIDES SHOWN

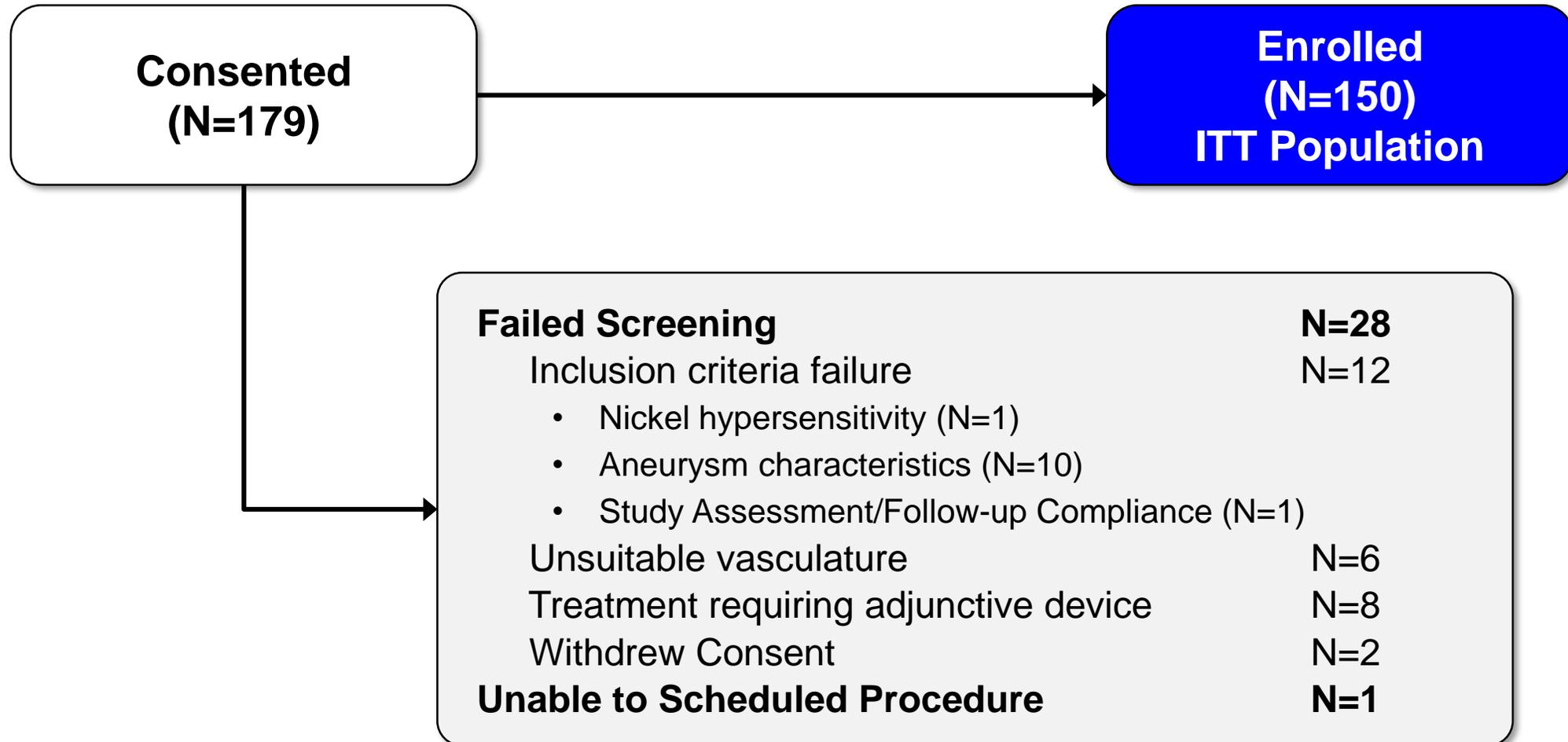
Use of Dual Antiplatelet Therapy in WEB-IT

- 19 of 150 on DAPT at baseline
- 104 of 150 on DAPT at time of procedure
- 47 of 150 remained on DAPT at 30 days
- 16 of 150 remained on DAPT at 6 months
- 10 of 150 remained on DAPT at 12 months

Patient Disposition Through 12-Month Follow-Up



Consented Not Enrolled



Neurological AEs by Anatomic Location

Anatomic Location	Events	Patients (%)	
		n / N	%
ACOM	11	7 / 40	18%
Basilar	9	6 / 59	10%
ICA	2	2 / 6	33%
MCA	11	8 / 45	18%

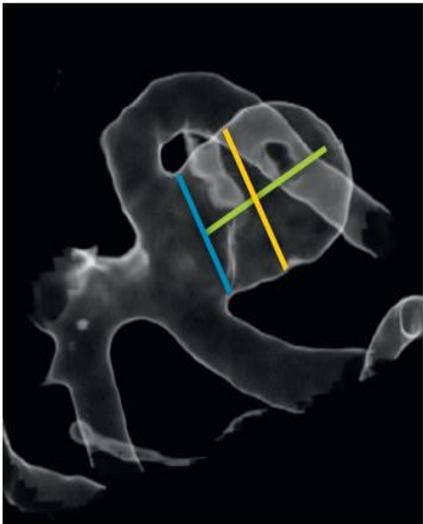
WEB Device Selection – 3 Step Process

Step 1: Measure

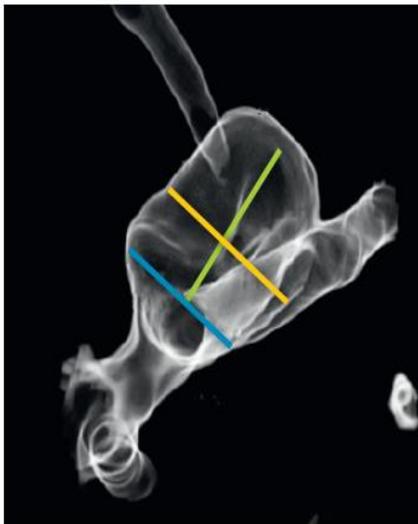


Measure the size (*Width, Height, and Neck*) of the aneurysm in two orthogonal projections.

Projection 1



Projection 2



Step 2: Select



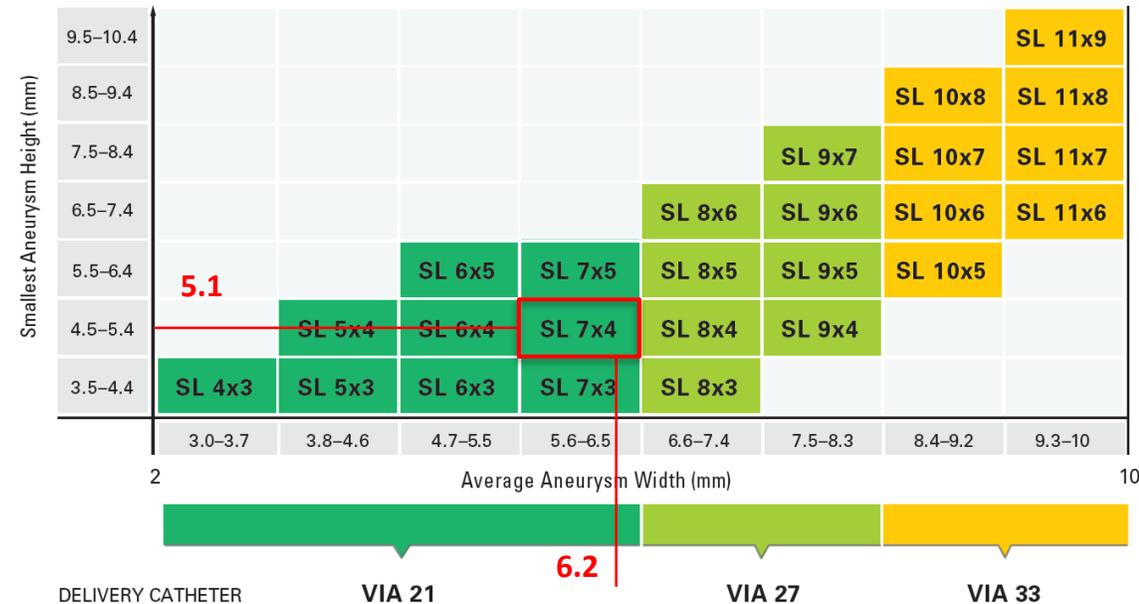
Select the barrel (SL) or sphere (SLS) shape



Step 3: Size



Refer to the corresponding WEB™ Device Selection Table or WEB™ Sizing App to determine the correct WEB™ device size



Small Aneurysm Treatment Risk Factors

- Small Aneurysms $\leq 5\text{mm}$ (n=37)
 - 3 presented with SAH
 - 34 with a single (9) or multiple (25) risk factors including:
 - Symptoms related to target aneurysm (10)
 - Current Smoker (10)
 - History of Intracranial bleeds or strokes (8)
 - Hypertension (19)
 - Family history of aneurysmal rupture (5)
 - Aspect ratio ≥ 1.3 (16)
 - Irregular shape (2)
 - Acom Location (10)

Meta Analysis for the Primary Effectiveness Endpoint

Literature Search	> 30,000
Language = English AND Publication Year = \geq 2000	> 12,000
Any Mention of WBNA	857 (400 wide neck 457 bifurcation)
Prespecified criteria for eligibility aneurysm had to be of same form of WBNA	74
Continual searches maintained on PubMed	105
Remove flow diverters	81
Post IDE Submission Searches	83 articles
References Grouped by Study Design (retrospective vs. prospective)	83 articles + 84 References (3 + MWNA prospective 80 retrospective)
12 month follow-up + MWNA, separated into subgroups	26 articles qualified
Patients	760 anterior 559 posterior
Total Patients	1,319

Most Ruptured Aneurysms Treated Within 36 Hours of Screening

- 6 patients treated within 24 hrs of screening
- 2 patients treated 24-36 hrs of screening
- 1 patient treated > 36 hrs of screening

Subject Reported QOL (EQ-5D)

- Median score of 85 in the 139 subjects
 - 0: Worst health you can imagine
 - 100: Best health you can imagine
- At 6-months:
 - Over 96% of subjects had no problems with self-care
 - 85% had no problems with performing their usual activities
 - 82% had no problems walking about
 - 72% were not anxious or depressed.

Angiography is Preferred Follow Up Imaging Modality for WEB Interior

- Confirmed MR results of Timsit, et al. and Mine, et al.
- Reproduced results from Caroff, et al. showing good visualization of the WEB interior with VasoCT

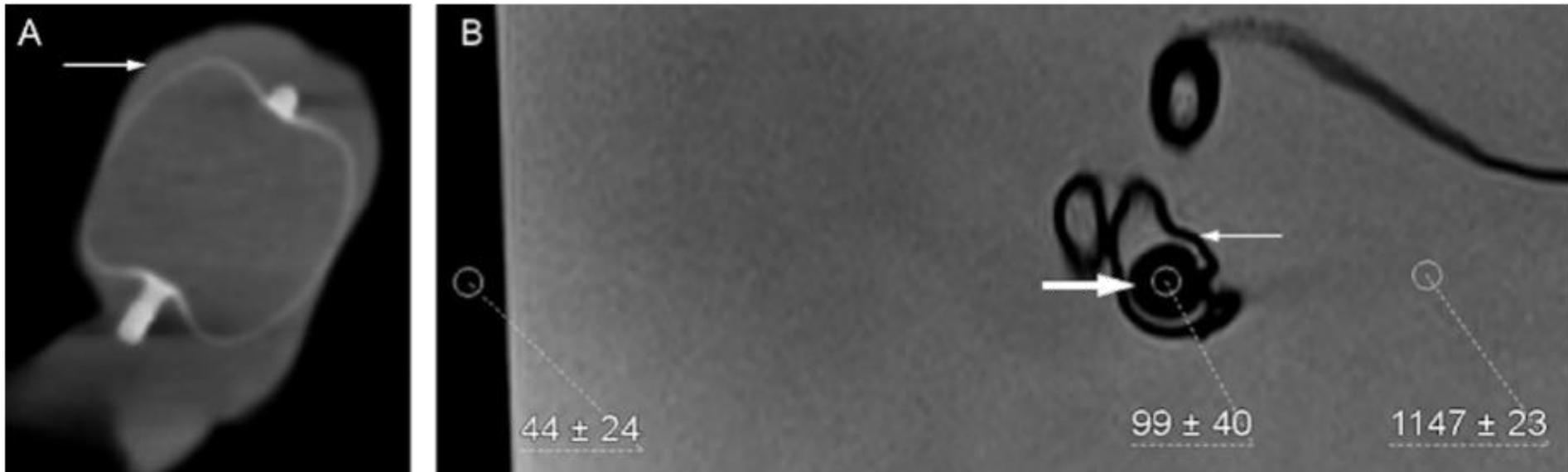
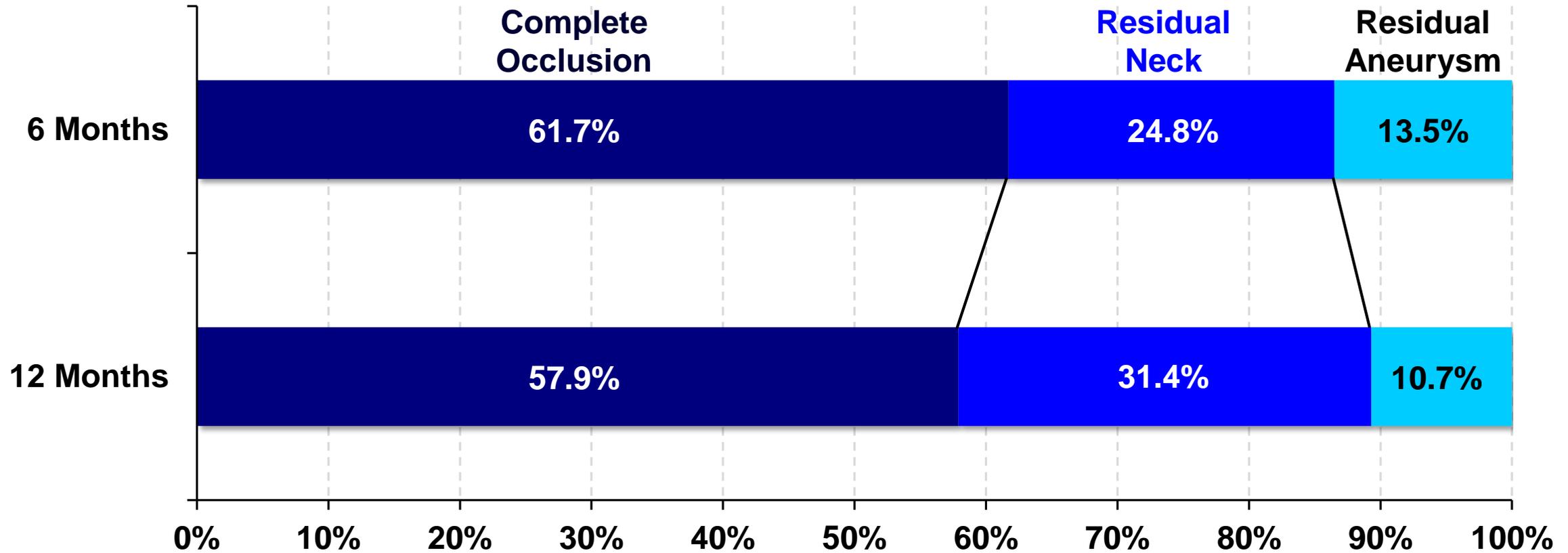


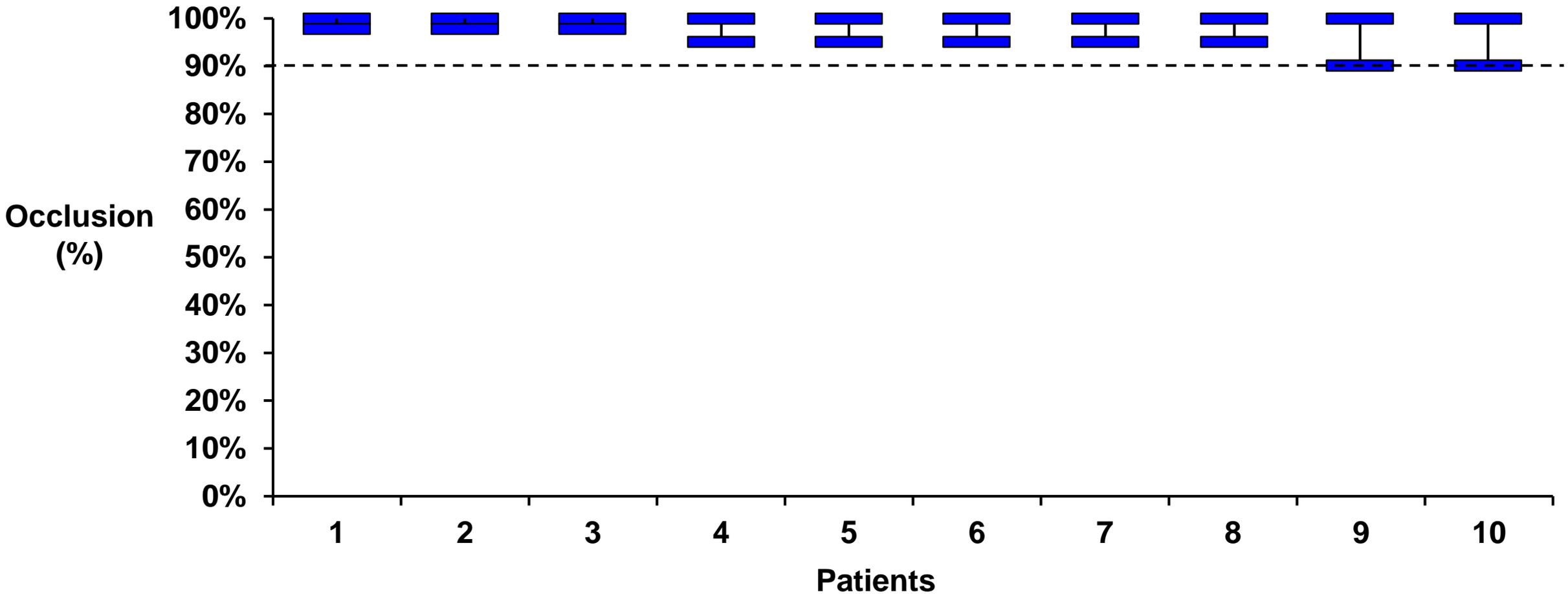
Figure 3

Occlusion at Follow-up Visits



* Completed cases with valid imaging

Percent Occlusion in Patients with Aneurysmal Recurrence (Complete to Adequate Occlusion)



3 GCP Studies: Effectiveness Long Term Data¹

	1Yr (N=153)	2Yr (N=120)	3Yr (N=51)
Complete occlusion	52.9%	50.8%	52.9%
Adequate occlusion	79.1%	80.8%	82.4%

Indications for Use for Recent PMA Approvals for Intracranial Aneurysm Devices

PMA Approvals	Indications for Use	WEB-IT Patients Available for Treatment (N=150)
Pipeline™ Flex	Indicated for the endovascular treatment of adults (22 years of age or older) with large or giant wide-necked intracranial aneurysms (IAs) in the internal carotid artery from the petrous to the superior hypophyseal segments.	N=0
Surpass Flow Diverter	Intended to treat aneurysms with a wide-neck (neck width 4 mm or wider or dome-to-neck ratio less than 2 mm) or fusiform intracranial aneurysms (an elongated, spindle shaped aneurysm involving the entire vessel wall) in the internal carotid artery (which supplies blood to the brain) with a diameter between 2.5 mm and 5.3 mm.	N=0
LVIS	Indicated for use with bare platinum embolic coils for the treatment of unruptured, wide neck (neck \geq 4 mm or dome to neck ratio $<$ 2), intracranial, saccular aneurysms arising from a parent vessel with a diameter \geq 2.5 mm and \leq 4.5 mm	N=40

WEB vs SAC (Recently FDA - Approved LVIS Stent)

- Comparison of primary effectiveness and safety for WEB-IT and LVIS on Patients Meeting WEB-IT Inclusion and Exclusion Criteria

Endpoint	WEB-IT % (LCL)	LVIS % (LCL)
Primary Effectiveness	54.8% (48.0)	62.5% (45.8)
Primary Safety	0.7% (0.02)	7.5% (1.6)

Comparators Derived from Comprehensive Meta-Analysis Available Published Literature on Treatment of WNBAs

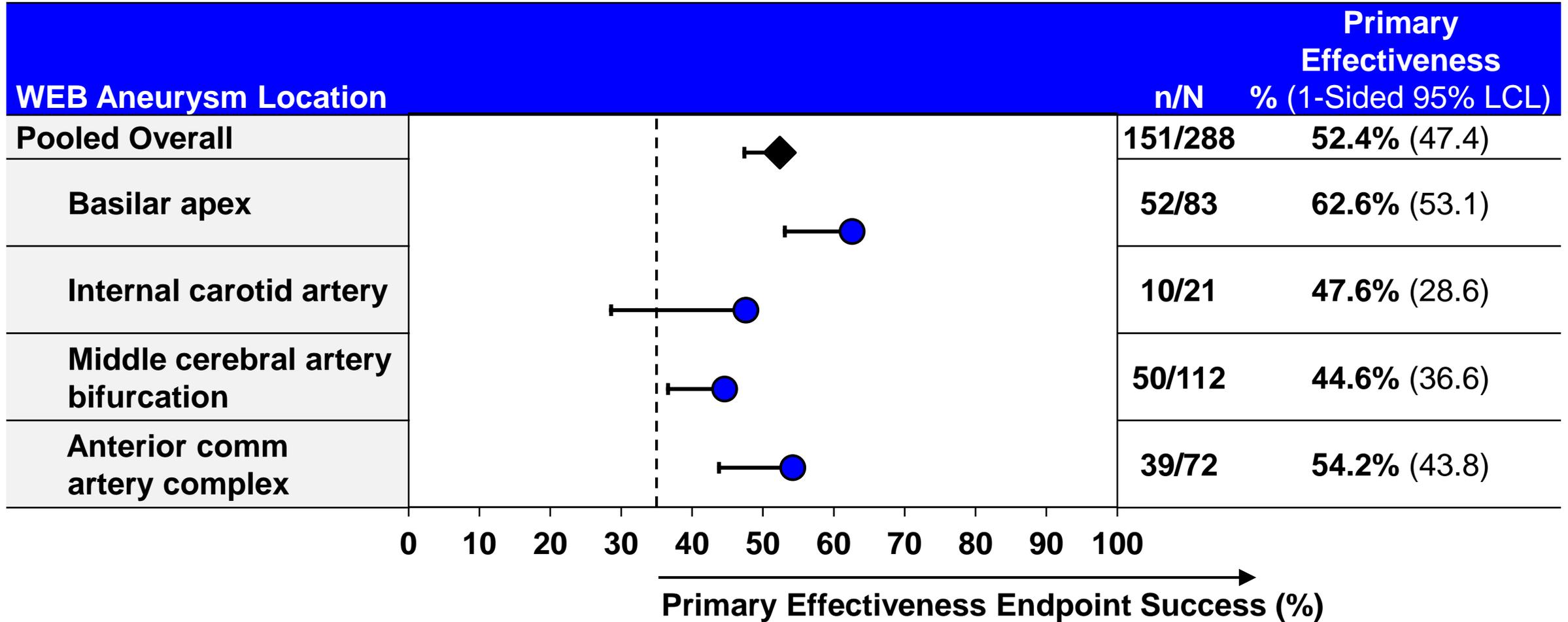
Source (Number of Aneurysms)	Complete Occlusion Rate*	95% LCL	
WEB-IT IDE - October 2014 (N=1,319)	50%	35%**	Comparator
WEB-IT PMA - revalidation 2017 (N= 3,200)	53%	39%**	
SDC #3 - stent assisted coiling only (N=883)	49%	41%**	
OPC - Fiorella et al. 2017 (N=2,794)	46%	39%**	
BRANCH Study 2018 (N=115)	31%	22%***	
WEB-IT 2017 Effectiveness Results (N=150)	55%	48%***	

* Core Lab adjusted meta analysis point estimate or study core lab adjudicated as appropriate

**12% core lab adjustment taken on study-by-study basis

***Actual one-sided 0.05 lower limit

Pooled 3 GCP Studies and WEB-IT: Primary Effectiveness Results by Aneurysm Location



All Stroke Analysis: Ischemic Events by Anatomical Location

Anatomical Location	N	Patients with Ischemic Events (N=10)
Basilar apex	59	2
Internal carotid artery	6	1
Middle cerebral artery bifurcation	45	3
Anterior comm artery complex	40	4

Primary Effectiveness Outcomes by Dual Antiplatelet Therapy Use at 12 Months

At 12 Months	Primary Effectiveness Success	
	n/N	%
Dual Antiplatelet Therapy Use	5/9	55.6%
No Dual Antiplatelet Therapy Use	72/134	53.7%

Increased mRS Scores Primarily Driven by Progression of Comorbidities or Unrelated

- 10 mRS scores increased by 1 point
 - 2 minor ischemic strokes device- or procedure-related
 - 3 minor ischemic strokes unrelated to procedure or device
 - 5 unrelated non-neurological conditions
 - Visual impairment, dizziness, muscle spasms, arthralgia
- **Definition of mRS 1:** No significant disability despite symptoms; able to carry out all usual duties and activities¹

WEB-IT Occlusion Status Shift From 6 to 12 Months

6 Month Occlusion Status	12 Month Occlusion Status		
	Complete Occlusion	Residual Neck	Residual Aneurysm
Complete Occlusion	75 (54.7%)	10 (7.3%)	0 (0.0%)
Residual Neck	5 (3.7%)	28 (20.4%)	2 (1.5%)
Residual Aneurysm	1 (0.7%)	4 (2.9%)	12 (8.8%)

 No Change
  Improved
  Worsened

All Patients with Both 6 and 12 Month Assessments (N=137)

Primary Effectiveness Rate Did Not Vary by Clinician Experience

Clinician Experience (cases)	n/N	Primary Effectiveness Rate (%)	95% CI
1–3	16/29	55.2%	(35.69, 73.55)
4–6	17/41	41.5%	(26.32, 57.89)
> 6	44/73	60.3%	(48.14, 71.55)

WEB Ruptured Aneurysm Experience

Study	Hunt & Hess	Recurrent Hemorrhage (30 days) % (N)	Recurrent Hemorrhage (12-month) % (N)	12-month Complete Occlusion % (N)
WEB-IT (N=9)	I & II	0%	0% (8)	62.5% (8)*
3 GCP (N=14)	I, II & III	0%	0% (13)	69.2% (13)
CLARYS (N=60)	I, II & III	0%	0% (43)**	In progress

* 1 patient stented at implant (primary endpoint failure)

** 43 subjects have had their 12 month follow-up visit, follow-up is still ongoing

Aneurysm Retreated with SAC¹ Within 12 Months

