Protocol Synopsis CP13-001
The WEB® Intrasaccular Therapy Study
(WEB-IT)

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1 Study Summary

Protocol:	CP13-001 Rev.3.1
Study Name:	The WEB® Intrasaccular Therapy Study (WEB-IT)
Study Purpose:	To demonstrate the safety and effectiveness of the WEB Aneurysm Embolization System for the treatment of intracranial wide-neck bifurcation aneurysms
Study Device:	The WEB Aneurysm Embolization System
Study Design:	Prospective, single-arm, multicenter, international interventional cohort
Sample Size	Up to 150 treated subjects
Study Population:	Adults (18-75 years of age) with intracranial wide-neck aneurysms located at arterial bifurcations (see eligibility criteria)
Study Duration:	Each subject will participate for at least 5 years. Total study duration will be approximately 6 years.
Primary Endpoints:	The study's **primary effectiveness endpoint** is the proportion of subjects with complete aneurysm occlusion without retreatment, recurrent subarachnoid hemorrhage, without significant parent artery stenosis (>50% stenosis) at one year after treatment. A subject will be considered an effectiveness success upon meeting all of the above criteria. The study's **primary safety endpoint** is the proportion of subjects with death of any nonaccidental cause or any major stroke (defined as an ischemic or hemorrhagic stroke resulting in an increase of 4 points or more on the National Institutes of Health Stroke Scale) within the first 30 days after treatment or major ipsilateral stroke or death due to neurologic cause from day 31 to the 1 year after treatment. A subject will be considered a safety failure upon meeting any of the above criteria. All safety events will be adjudicated by an independent clinical events adjudicator. The **study** will be interpreted as a success if both of the primary effectiveness and primary safety endpoints are met.

Secondary Endpoint:	The study's secondary endpoint is the proportion of subjects with angiographic aneurysmal recurrence defined as aneurysm growth or recanalization at one year after treatment.
Other Endpoints:	Secondary analyses include: • Technical success • IA occlusion status at other time points (6 mo, 2, 5 yrs) • Change in mRS (for unruptured subjects only) • % Aneurysm occlusion • Proportion of IAs with each occlusion category at all angiographic follow-up time points. • Durability of occlusion – defined as "Same", "Better", "Worse" when comparing the 1 year angiographic result with the 6 month angiographic result
Inclusion Criteria	1. Patient must be 18-75 years of age at the time of screening. 2. Patient must have a single ruptured or unruptured IA requiring treatment. If the subject has an additional IA requiring treatment, the additional IA must not require treatment within 60 days of the index procedure. Definition: For the purposes of this study a **ruptured IA** patient is defined as a patient with computed tomography (CT), magnetic resonance imaging (MRI), or lumbar puncture (LP) evidence of subarachnoid hemorrhage attributed to the index aneurysm within the last 60 days. 3. The index IA to be treated must have the following characteristics: a. Saccular in shape b. Located in basilar apex (BA), middle cerebral artery (MCA) bifurcation, internal carotid artery terminus (ICAt), anterior communicating artery complex (ACom) c. Dome-to-Neck (DN) ratio ≥1 d. Diameter of the IA is appropriate for treatment with the WEB Aneurysm Embolization System per device Instructions for Use e. Wide-neck IA with neck size ≥ 4mm or Dome-to-Neck (DN) < 2; 4. Patient has an IA that is appropriate for treatment with WEB without the use of additional implanted devices; 5. If the IA previously ruptured, patient must be neurologically stable with Hunt & Hess Score of I or II. 6. Patient must be able to comply with all aspects of the screening, evaluation, treatment, and the postprocedure follow-up schedule. Patient must sign and date an IRB/EC-approved written informed consent prior to initiation of any study procedures. 7. Patient must sign and date an IRB/EC-approved written informed consent prior to initiation of any study procedures.

Exclusion Criteria	1. Patient has an IA with characteristics unsuitable for endovascular treatment; 2. Microcatheter could not reach patient's index aneurysm to allow necessary access to treat with study device. 3. Patient has vessel characteristics, tortuosity or morphology which could preclude safe access and support during treatment with study device; 4. Patient has vascular disease or other vascular anomaly so as to preclude the necessary access to the aneurysm for use of the study device. 5. Patient has clinical, angiographic or CT evidence of vasospasm, vasculitis, or intracranial tumor (except small meningioma) or any other intracranial vascular malformations on presentation; 6. Patient has conditions placing them at high risk for ischemic stroke or has exhibited ischemic symptoms such as transient ischemic attacks, minor strokes, or stroke-in-evolution within the prior 60 days; 7. Patient has any circulatory, neurovascular, cardiovascular, or neurologic conditions that have resulted in unstable neurological symptoms 8. Patient has mRS $\geq$ 2 prior to presentation or rupture (as applicable); 9. Patient has had an SAH from a nonindex IA or any other intracranial hemorrhage within 90 days; 10. Patient has physical, neurologic or psychiatric conditions which preclude his/her ability to comply with all aspects of the screening, evaluation, treatment, and the postprocedure follow-up schedule; 11. Patient's index IA was previously treated; 12. Patient is taking anticoagulants or has a known blood dyscrasia, coagulopathy, or hemoglobinopathy; 13. Patient is pregnant; 14. Patient has known hypersensitivity, which cannot be medically treated, to any component of the study device, procedural materials, or medications commonly used during the procedure; 15. Patient is concurrently involved in another investigational study or a postmarket study that could affect the safety and effectiveness of IA treatment with the study device or with the study's follow-up schedule; 16. Patient has an acute life-threatening illness other than the neurological disease to be treated in this trial; 17. Patient has a life expectancy of less than 5 years due to other illness or condition (in addition to an intracranial aneurysm).
Study Procedures:	Subjects will be screened for study eligibility after giving informed consent. The WEB embolization procedure will be performed in the digital angiographic suite using standard angiographic techniques.
Schedule of Examinations:	Screening (Day -30 to Day 0) Procedure

	Discharge 30-day follow-up (mRS per office or telephone update) Six month follow-up (office visit and angiographic follow-up) One year follow-up (office visit and angiographic follow-up) Two year and four year follow-up (office visit per standard of care or telephone update) Three year and five year follow-up (office visit and imaging follow-up per standard of care)

Figure 1. Diagram of Study Flow.

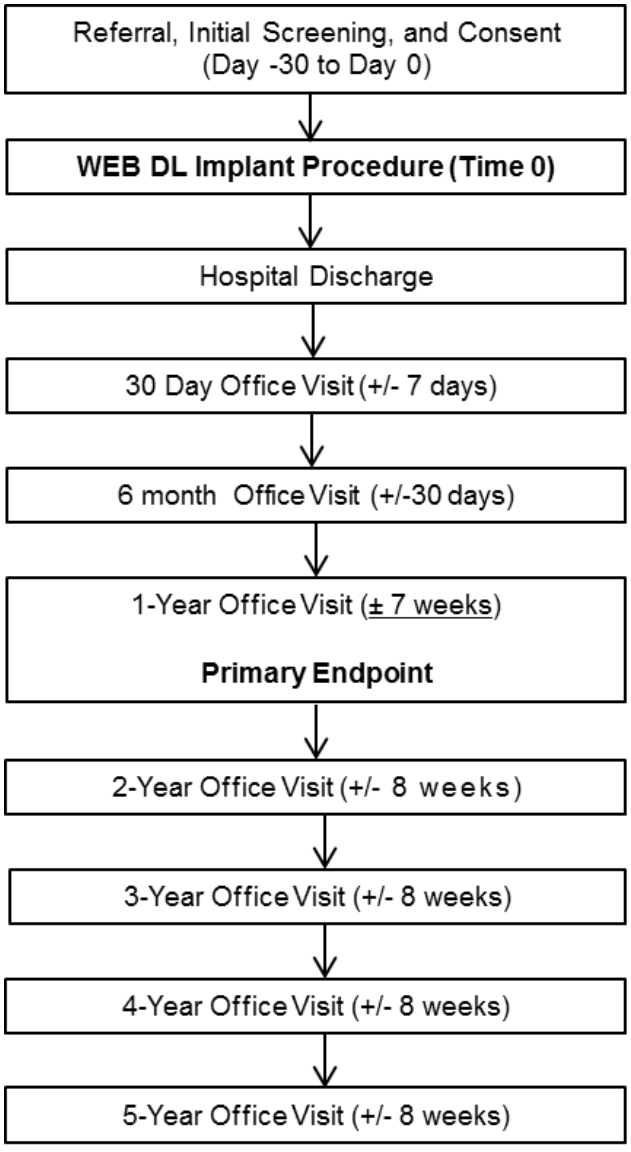

Table 1. Schedule of Assessments.

Parameter	Screening	Procedure	Discharge	30-Day Follow-Up	6-Month Follow-Up	1-Year Follow-Up	2- and 4-Year Follow-Up	3- and 5-year Follow-Up
Health history	X							
Physical examination	X	X	X		X	X		X
Neurological examination	X				X	X		X
Site and subject information	X							
Aneurysm information (size, location, etc.)	X	X						
Rupture status	X							
Hunt and Hess Grade (ruptured aneurysms only)	X							
Microcatheter(s) used		X						
Ancillary devices used (eg, stent, balloon used)		X						
Medications used	X	X	X		X	X		X
Size and lot number of WEB device(s) used		X						
WEB procedure fluoroscopy time		X						
Total procedure fluoroscopy time		X						
3D angiographic imaging	X	X			X	X	Optional	X*
Additional imaging per standard of care							X	X
Occlusion assessments (Core Lab)			X		X	X	Optional	X*
Modified Rankin Scale score	X		X	X	X	X		
NIHSS score	X	As required						
QOL Assessment (EQ-5D)					X			
Additional scales as appropriate		X			X	X	Optional	Optional
Technical events		X						
Adverse events		X	X	X	X	X	X	X
Retreatments /Additional Procedures				X	X	X	X	X
Rebleed (if ruptured)/New bleed			X	X	X	X	X	X
Comments	X	X	X	X	X	X	X	X

* Per local Standard of Care