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WEAVE Trial
Final Results in 152 On-Label Patients

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Background and Purpose—The WEAVE trial (Wingspan Stent System Post Market Surveillance) is a postmarket surveillance trial mandated by the Food and Drug Administration to assess the periprocedural safety of the Wingspan Stent system in the treatment of symptomatic intracranial atherosclerotic disease.

Methods—A total of 152 consecutive patients who met the Food and Drug Administration on-label usage criteria were enrolled at 24 hospitals and underwent angioplasty and stenting with the Wingspan stent. On-label criteria included age 22 to 80 years, symptomatic intracranial atherosclerotic stenosis of 70% to 99%, baseline modified Rankin Scale score ≤3, ≥2 strokes in the vascular territory of the stenotic lesion with at least 1 stroke while on medical therapy, and stenting of the lesion ≥8 days after the last stroke. The primary analysis assessed the periprocedural stroke, bleed, and death rate within 72 hours of the procedure with adjudication by a core study Stroke Neurologist.

Results—The trial was stopped early after interim analysis of 152 consecutive patients demonstrated a lower than expected 2.6% (4/152 patients) periprocedural stroke, bleed, and death rate. This was lower than the 4% periprocedural primary event safety benchmark set for the interim analysis in the study. A total of 97.4% (148/152) patients were event-free at 72 hours, 1.3% (2/152) had nonfatal strokes, and 1.3% (2/152) of patients died.

Conclusions—With experienced interventionalists, and proper patient selection following the on-label usage guidelines, the use of the Wingspan stent for intracranial atherosclerotic disease demonstrated a low periprocedural complication rate and excellent safety profile. This is the largest on-label, multicenter, prospective trial of the Wingspan stent system to date with the lowest reported complication rate.

Clinical Trial Registration—URL: https://www.clinicaltrials.gov. Unique identifier: NCT02034058.

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Key Words: angioplasty ■ antiplatelet therapy ■ atherosclerosis ■ patient selection ■ stents

The Wingspan stent (Stryker, Kalamazoo, MI) is a self-expanding nitinol stent designed for treatment of severe symptomatic intracranial atherosclerotic disease (ICAD) in coordination with use of the Gateway angioplasty balloon. The Wingspan system was cleared by the Food and Drug Administration (FDA) for use under Humanitarian Device Exemption (HDE) in the United States in August 2005, following the initial trial in which 44 patients were stented with the Wingspan stent.[1] The initial enrollment criteria for the trial were patient age 18 to 80 years, with modified Rankin Scale (mRS) score ≤3, with a ≥50% intracranial artery stenosis because of atherosclerotic disease, who presented with a stroke and had recurrent symptoms while on medical therapy, and were >7 days after their stroke. The 72 hours periprocedural stroke and death rate was 2.2%, and the 30-day periprocedural stroke and death rate was 4.5%.

Two subsequent, relatively large multicenter registries were then conducted, using the Wingspan stent system, the National Institutes of Health Wingspan registry,[2] and the US Wingspan registry.[3] Although the intention of these registries was to assess the on-label use of the stent, both studies were designed to enroll consecutive patients at the study institutions and, therefore, enrolled both on-label and off-label stent usage patients. In both studies, the majority of patients enrolled had on-label usage of the stent. However, only 61% of patients in the National Institutes of Health Registry presented with stroke and 58% of patients in the US Wingspan registry. The remainder presented with transient ischemic attack or vertebrobasilar insufficiency. The periprocedural stroke and death rates in these studies were both 6.2%. Concurrently, the most extensive trial evaluating medical therapy for symptomatic ICAD, the WASID (Warfarin-Aspirin Symptomatic

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Intracranial Disease),[4] demonstrated poor patient outcomes in both arms of medical therapy in the trial with stroke, bleed, and death rate of 22.1% in the aspirin group and 21.8% in the warfarin group with a mean follow-up of 1.8 years. In a subgroup analysis of patients with ≥70% intracranial artery stenosis, patients who presented with a transient ischemic attack had a 14% risk for stroke in the stenotic artery territory at 1 year, and patients who presented with stroke had a 23% risk of stroke in the target territory at 1 year.[5] These studies with extremely poor results with medical therapy laid the groundwork for a prospective randomized trial comparing Wingspan stent to medical therapy.

The prospective, randomized SAMMPRIS trial[6] (Stenting and Aggressive Medical Management for the Prevention of Recurrent Stroke in Intracranial Stenosis) evaluated patients in an extended clinical application of the Wingspan stent, beyond its original HDE clearance labeling in an IDE (Investigational Device Exemption) from the FDA. This allowed patients to be stented off-label from the FDA clearance, including stenting patients who had not failed medical therapy, stenting patients who may have presented with transient ischemic attacks only, without history of stroke, and stenting patients earlier than 8 days after their qualifying event. In contradistinction with prior trials, instead of the majority of patients being treated on-label in the study, the majority of patients stented in the SAMMPRIS trial would not have met the original HDE on-label indication.

The stenting arm of SAMMPRIS demonstrated a periprocedural stroke, bleed, and death rate of 14.7%, the highest complication rate of any Wingspan trial before the trial or after. Aggressive medical therapy demonstrated lower stroke, bleed, and death rates compared with stenting in this IDE trial.

The FDA conducted a panel review of the Wingspan stent system in March 2012, including assessment of the data from all of the Wingspan trials and registries and renewed the FDA clearance of the device but with revised on-label criteria. This included raising the minimum degree of stenosis from 50% to 70% and revising the recommended clinical criteria to patients who had 2 strokes in the vascular territory of the stenotic intracranial artery, although no trial has utilized 2 strokes as a criterion for stenting. The original HDE approval trial only required 1 stroke and recurrent symptoms. At the time of the panel review, the FDA also mandated a new 522 postmarket surveillance trial of the Wingspan stent to reassess its safety. The SAMMPRIS trial demonstrated a high periprocedural morbidity and mortality. Therefore, the postmarket surveillance trial was charged with demonstrating specifically the periprocedural safety of the Wingspan stent, not long term efficacy. These events led to the design of the WEAVE trial (Wingspan Stent System Post Market Surveillance), which was a 522 postmarket surveillance study.

Methods

The data that support the findings of this study are available from the corresponding author on reasonable request. The WEAVE trial was an FDA mandated study to evaluate the rate of stroke and death within 72 hours poststenting in patients treated with the Wingspan Stent System according to the Instructions for Use. This was a prospective, single-arm, consecutive enrollment, postmarket surveillance study. All centers enrolling patients received Institutional Review Board approval for the trial, and all patients in the trial were treated according to the HDE approval criteria, so no separate ethics approval was indicated. Written, informed consent was obtained from every patient. All of the patients enrolled in the trial were assessed at 72 hours poststenting either in the hospital by the study Stroke Neurologist or, if the patient had already been discharged home, by telephone interview by a core study Stroke Neurologist. Outcomes of 100% of the patients were adjudicated by study Neurologists.

The original goal of the trial was to enroll 389 on-label patients. Using the Clopper-Pearson exact method, the 72-hour stroke and death rate was projected to be <6.6%, with a 95% CI (0.042–0.097) for the primary analysis group (those patients treated in accordance with the Instructions for Use). After the predetermined interim analysis of the first 100 patients in the trial, there was a lower than expected primary analysis event rate of 3% in the patients stented. Subsequently, Bayesian analysis was used to redefine the safety benchmark for the study at a 4% primary analysis event rate for the first consecutive 150 patients. The trial was stopped early on October 25, 2017, when the second interim data analysis demonstrated that the safety benchmarks had been met. Final study site closure and data audit were completed in September 2018.

In addition to the primary analysis data of stroke or death within 72 hours, the trial also collected data for predetermined secondary analyses. These included prestenting antiplatelet resistance testing (P2Y12, aspirin reactivity unit, or correlate testing), assessment of target lesion proximity to angiographically visible perforator arteries, plaque anatomy, presence of tandem lesions, aortic arch type, proximal tortuosity, cerebral perfusion testing or other assessment of collaterals, intraprocedural blood pressure, and demographic factors. Although the WEAVE trial was designed as an on-label study for primary analysis, the FDA also requested periprocedural data collected on any additional patients stented with the Wingspan stent who did not qualify for on-label use. These off-label patients were enrolled in a separate registry with secondary analysis to be detailed in a subsequent report and were not included in the primary analysis of the study.

The WEAVE trial sought to utilize experienced interventionalists. Although the initial trial design planned to include 50 hospitals as sites for the trial, only 24 centers were felt to meet the Wingspan volume criteria for inclusion and enrolled patients by the time of the interim analysis (see the Appendix for list of participating sites). The mean case volume experience with the Wingspan stent among the participating interventionalists was 37 stents. Interventionalists involved in the trial were encouraged to enroll patients who met the on-label criteria, and patients who were treated off-label were reviewed. A Medical Advisory Committee was organized for the trial to review any clinical complications, device issues, off-label stent use, or patient management issues.

Patients enrolled in the trial in the primary analysis were 22 to 80 years old, with a symptomatic ICAD lesion of 70% to 99% in an artery 2 mm or larger, who had a baseline mRS ≤3, who had experienced 2 strokes, and were stented with Wingspan ≥8 days after their last stroke. The percent stenosis of the target lesion was measured at its most severe stenosis with reference to the normal luminal diameter of the target arterial segment by digital subtraction angiography. Trial sites were advised to adhere to the following stenting guidelines. After the qualifying stroke, the patients were placed on daily aspirin (325 mg), clopidogrel (75 mg), a statin, and blood pressure medication, if indicated. Centers were advised not to bolus patients with clopidogrel but to continue dual antiplatelet medication daily for a minimum of 7 days before stenting. Antiplatelet resistance testing was encouraged, and medication changes were permitted for patients with supratherapeutic P2Y12 results (<80) or subtherapeutic P2Y12 results (>237). For patients who were continuing to have hypoperfusion transient ischemic attacks during the 7 day waiting period, an alpha agonist (midodrine) to increase the blood pressure and volume expander (fludrocortisone) were advocated, as opposed to early stenting.

General anesthesia with close blood pressure monitoring with a radial arterial catheter was recommended during the stenting procedure with goal systolic blood pressure within 20 torr of the patient's

baseline asymptomatic blood pressure to avoid intraprocedural hypotension or hypertension. Femoral access with a 6F or larger sheath and guide catheter was recommended. Heparinization to an activated clotting time of 250 to 300 s was recommended, in addition to pretreatment dual antiplatelet therapy. Use of intraarterial spasmolytic (eg, nitroglycerin) before microcatheterization was encouraged. The guideline for the study was to pass the lesion under roadmap guidance with a microcatheter, use a 300 cm 0.014-inch exchange wire, advance the Gateway balloon over the exchange wire while stabilizing the wire to avoid movement. The study recommendation was to choose the balloon size with nominal diameter at 6 atmospheres to be 80% of the true luminal diameter or ≈60% in lesions directly adjacent to angiographically visible perforators. Underdilation was recommended to avoid arterial dissection, vessel rupture, and snowplow effect of compressed plaque into perforator arteries. Cautious monitoring of the distal exchange wire was recommended during the stent delivery. Poststenting balloon dilation within the stent was discouraged unless the residual stenosis remained ≥50% after stenting. Patients were typically monitored in Neuro Critical Care units for 24 hours postprocedural with blood pressure parameters as above to reduce risk for reperfusion hemorrhage.

Results

Demographic Information

Of the 152 patients stented in the trial who met the on-label indication, 53% were men, and 47% were female. The mean age was 62 years old. Hypercholesterolemia and hypertension were common in the study group, occurring at a rate of 86% and 92%, respectively. A total of 14% of patients were active smokers at the time of their qualifying event, 39% were previous smokers, and 47% had never smoked (Table 1). The mean body mass index for the group was 30.9±7.0 kg^2. The cohort was comprised of 66% of patients who identified as white, 20% black, 8% Hispanic, 3% multiracial, and 3% Asian. The baseline mRS score was 0 in 13% of patients, 1 in 24% of patients, 2 in 34% of patients, and 3 in 29% of patients.

The mean target artery stenosis before the procedure was 83% (range 71%–97%), and the mean stenosis after stenting was 28% (range 0%–84%). A total of 157 arteries were stented in 152 patients. Five patients had tandem stenosis in which both lesions were treated. The target artery distribution was: 25.5% internal carotid artery, 39.5% middle cerebral artery, 20.4% vertebral artery, 14.0% basilar artery, and 0.6% posterior cerebral artery. The median time to stenting from the last stroke was 22 days (range, 8–371).

Periprocedural Data

Efforts were made to avoid hypotension and potential ischemic hypoperfusion. All patients had blood pressure monitoring via an arterial line in the periprocedural period. The periprocedural blood pressure results are listed in Table 2. The mean maximum systolic blood pressure during the stenting procedure was 167 and the minimum 107. The mean balloon inflation pressure was 6 atmospheres, which is the nominal pressure for the Gateway balloon, so over-inflation past the nominal pressure was uncommon (Table 3). Slow balloon inflation was recommended for the procedure, and the mean time to full inflation was 61 s (Table 3). General anesthesia was utilized in 97% of the cases and conscious sedation in the remainder. A single lesion was treated in 97% of cases, and tandem lesions were treated in 3% of the patients.

Table 1. Demographic Factors

Demographic Factors; Primary Analysis Group, N=152	
Age, y	61.89±10.52 (152)
Female	46.7% (71/152)
White	66.4% (101/152)
Black	19.7% (30/152)
Asian	2.6% (4/152)
Hispanic	7.9% (12/152)
Multiracial	3.3% (5/152)
History of hypertension	92.1% (140/152)
History of hyperlipidemia / hypercholesterolemia	86.2% (131/152)
History of diabetes	59.9% (91/152)
Smoking status	
Current smoker	13.8% (21/152)
Previous smoker	38.8% (59/152)
Never smoked	47.4% (72/152)
Body mass index, kg/m^2	30.93±7.03 (152)
Baseline modified Rankin Scale	
0	13.2% (20/152)
1	24.3% (37/152)
2	34.2% (52/152)
3	28.3% (43/152)
4	0.0% (0/152)
5	0.0% (0/152)
No. of qualifying events prior stenting	
<2	0.0% (0/152)
2	79.0% (120/152)
3	17.1% (26/152)
4	3.9% (6/152)

Antiplatelet therapy testing was conducted in 65% of the patients before stenting in the trial. Within this group of patients with laboratory testing, 79% demonstrated therapeutic antiplatelet levels at standard aspirin and clopidogrel dosing, and 21% had either a dose adjustment or new medication prescribed if testing demonstrated subtherapeutic values or antiplatelet therapy drug resistance. The impact of therapeutic values and alternative medication strategies will be detailed in a subsequent report on secondary outcomes in the WEAVE Trial.

Clinical Results

Within the periprocedural time window of 72 hours after the procedure, there were 2 nonfatal strokes and 2 deaths from strokes, for a total of 4 patients with an index event of stroke, bleed, or death of the 152 patients for a 2.6% periprocedural complication rate (Table 4). Of the 2 patients who had nonfatal strokes at the 72-hour assessment, 1 deteriorated to mRS 4 after the procedure with a pontine perforator stroke and the other to mRS 2 with petechial hemorrhage and intraventricular hemorrhage but

Table 2. Periprocedural BP

Maximum systolic BP, mm Hg	
Mean±SD (N)	167.2±29.96 (151)
Median (Q1, Q3)	168.0 (145.0, 189.0)
Range (min, max)	(104.0, 260.0)
Minimum systolic BP, mm Hg	
Mean±SD (N)	106.7±20.38 (151)
Median (Q1, Q3)	105.0 (96.00, 120.0)
Range (min, max)	(38.00, 172.0)

BP indicates blood pressure.

otherwise stable at 72 hours. Therefore, the stroke rate in the trial because of perforator occlusion was 0.7% (1/152). One of the deaths was because of a large reperfusion hemorrhage and the other to a significant periprocedure ischemic stroke, and the patient had subsequent withdrawal of care by the family.

Interventionalist Experience

The mean Wingspan case experience for interventionalists in the WEAVE trial was 37 stents. The interventionalists in the trial who had experience of >50 Wingspan cases before enrolling their first patient in the WEAVE study had a 0% (0/69 stent cases) periprocedural stroke and death index event rate in the on-label cases they enrolled in the trial. Interventionalists with <50 Wingspan cases before the trial had a 4.8% (4/83 stent cases) index event rate in patients enrolled in the trial.

Discussion

The WEAVE trial sought to evaluate the periprocedural safety profile of the Wingspan stent in an on-label application with experienced interventionalists and what were thought to be best practices regarding patient selection, technical aspects of the stenting procedure, and periprocedural medical management. This is the largest on-label trial performed to date of any intracranial stent for the treatment of ICAD with a total of 152 patients. A low periprocedural complication rate of 2.6% was achieved in the trial with outcomes adjudication by core study Stroke Neurologists.

The design of the Wingspan stent has not substantially changed since its introduction into the market in 2005, with the exception of modifications of the radioopaque markers. Therefore, the WEAVE results indicate that the poor clinical results seen in the SAMMPRIS trial were not due primarily to problems with the stent itself, but more likely from a combination of the inexperience of the interventionalists, the poor patient selection, and the underdeveloped standards of practice in intracranial stenting. The selection criteria for the major multicenter Wingspan trials are presented in Table 5. The WEAVE trial results demonstrate that the Wingspan stent is a safe device and can be used by experienced interventionalists to treat patients who meet the on-label indications for usage with a low complication rate, even in a very challenging patient group. The question moving forward is how will this stent, or others, perform in long term efficacy compared with medical therapy alone.

Now that the periprocedural event rate has been reduced, intracranial stents may be evaluated in patients who are refractory to medical therapy for symptomatic ICAD. Challenges such as restenosis or delayed stent thrombosis and their management still need to have paradigms of treatment developed. Patients are typically reimaged at 6 months and a year after stenting for ICAD because studies show this is the most common time period of restenosis. Addressing severe restenosis before the patient presenting with stroke is a treatment paradigm that has yet to be addressed in controlled trials. However, this is clearly a factor which can affect long term results in stents. The SAMMPRIS protocol did not allow

Table 3. Technical Procedural Data

Balloon inflation pressure, atm	
Mean±SD (N)	6.26±2.22 (100)
Median (Q1, Q3)	6.00 (5.50, 8.00)
Range (min, max)	(1.50, 14.00)
Balloon inflation duration, s	
Mean±SD (N)	60.80±74.88 (100)
Median (Q1, Q3)	42.00 (15.00, 60.00)
Range (min, max)	(1.00, 390.0)
Aortic arch type	
I	44.1% (67/152)
II	39.5% (60/152)
III	7.9% (12/152)
Not available	8.6% (13/152)
Total number of lesions planned for treatment	
1	96.7% (147/152)
2	3.3% (5/152)
Type of anesthesia	
General	97.4% (148/152)
Conscious sedation	2.6% (4/152)
Lowest activated clotting time during procedure, s	
Mean±SD (N)	208.2±48.37 (109)
Median (Q1, Q3)	212.0 (169.0, 237.0)
Range (Min, Max)	(105.0, 346.0)
Highest activated clotting time during procedure, s	
Mean±SD (N)	260.4±45.29 (111)
Median (Q1, Q3)	258.0 (236.0, 283.0)
Range (min, max)	(159.0, 400.0)
Percent (%) stenosis baseline	
Mean±SD (N)	83.18±8.26 (157)
Median (Q1, Q3)	82.00 (77.00, 91.00)
Range (Min, Max)	(40.00, 97.00)
Percent (%) stenosis after stent placed	
Mean±SD (N)	28.34±16.90 (160)
Median (Q1, Q3)	27.50 (14.00, 41.00)
Range (min, max)	(0.00, 84.00)

max indicates maximum; and min, minimum.

Table 4. Primary End Point Results

	Primary Analysis Trial / On Label
Enrolled	N=152
Subjects without stroke or death within 72 h	97.4% (148/152)
Subjects with death within 72 h	1.3% (2/152)
Subjects with stroke (without death) within 72 h	1.3% (2/152)
Total percentage of patients with stroke or death within 72 h	2.6% (4/152)

for any delayed follow-up angiography, despite the fact that this was the standard of care at many institutions. These challenges have been met in stenting of other arterial systems, such as cervical carotid stenosis and coronary artery stenosis.

The WEAVE results also indicated that high volume clinical experience with the Wingspan stent was important. This corroborates the findings of the National Institutes of Health registry study,[7] which showed a significantly higher rate of complication rate of low enrollment sites with <10 patients versus higher enrolling sites (P=0.038). Similar studies from China reaffirm that experience of the interventionalist is critical in obtaining low complication rates for intracranial stenting.[8,9] One of the analyses from the SAMMPRIS study by Derdeyn et al[10] concluded that the experience did not account for the poor results in SAMMPRIS. However, this analysis was flawed by Type 2 error in its study evaluation. The number of stents that they used in their analysis to distinguish high volume from low volume centers was 10 stents. In other words, centers that performed <10 Wingspan stents since the stent was approved were considered low volume sites and those that performed ≥11 stents were considered high volume sites. By most interventional study criteria, both of these categories would be considered low volume sites. The median number of Wingspan stents delivered by interventionalists in the SAMMPRIS trial before beginning enrollment was 10 stents. By comparison, the CREST2 Trial (The Carotid Revascularization and Medical Management for Asymptomatic Carotid Stenosis Study) requires evidence of successful performance of 50 carotid stent cases before being approved as an interventionalist in the trial.[11] The mean number of Wingspan stent cases of the WEAVE investigators before enrolling patients in the study was 37 stents, so the WEAVE trial had a more experienced group of interventionalists than those involved in SAMMPRIS. The higher volume stent experience of the interventionalists may account for the significantly improved clinical results in the WEAVE trial compared with SAMMPRIS, in addition to better patient selection and standards of practice.

Regarding the target artery stented, in the HDE trial, only 22% of patients were stented in the middle cerebral artery territory, compared with 41% of patients in the SAMMPRIS trial. The SAMMPRIS trial results demonstrated that the majority of postprocedural ischemic strokes after stenting in the trial were perforator strokes because of occlusion of lenticulostriate perforators related to the procedure. The fact that 40.8% of the patients stented in the WEAVE trial had middle cerebral artery lesions stented and the study still achieved excellent clinical results, demonstrate that the revised treatment paradigms of underdilating middle cerebral artery lesions adjacent to angiographically visible perforators to only 60% to 80% of the true luminal diameter were an effective practice. The periprocedural stroke rate in the SAMMPRIS trial because of perforator occlusion was 5.8%, and in the WEAVE trial, it was 0.7%. Finally, one of the most significant criticisms of the SAMMPRIS trial was that half of the patients in the trial were treated ≤7 days from their qualifying event. The mean time to stenting in the HDE trial was 22 days, but in the SAMMPRIS trial, it was 7 days. In fact, some patients in the SAMMPRIS trial were treated within 24 hours of their stroke. Subgroup analysis from the National Institutes of Health Wingspan registry showed a strong trend towards complications of stroke and death in patients treated <10 days from their qualifying event (P=0.058). The centers with the most experience with stenting of patients with ICAD in China will typically wait ≈3 weeks from the last stroke for intracranial stent treatment.[9] Likewise, the median time to treatment in the WEAVE trial was 22 days, with no patient stented before day 8 poststroke. There is concern that early stenting may have a higher rate of reperfusion hemorrhage because of weakened capillary beds with acute stroke. There is speculation that some patients may have ruptured plaques which are susceptible to early recurrent stroke events. Similarly, there is a high likelihood that patients may not have proper antiplatelet therapeutic effect with early stenting unless the patient is bolused with clopidogrel, which itself may lead to higher hemorrhagic conversion of stroke. Our future subgroup analyses of secondary outcomes in the WEAVE trial and the WEAVE registry will evaluate some of these issues.

The best clinical results in SAMMPRIS with aggressive medical therapy alone for severe symptomatic ICAD demonstrated

Table 5. Comparison of Multicenter Wingspan Trials

Trial	Percent Stenosis	Qualifying Event Stroke	Refractory to Medical Therapy	Median Time to Stent, d	Periprocedural Event Rate
HDE trial[1]	50%–99%	95%	100%	22	4.5%
NIH registry[2]	50%–99%	59%	Not reported	10	6.2%
US registry[3]	50%–99%	61%	75%	Not reported	6.2%
SAMMPRIS[6]	70%–99%	63%	64%	7	14.7%
WEAVE trial	70%–99%	100%	100%	22	2.6%

HDE indicates Humanitarian Device Exemption; NIH, National Institutes of Health; SAMMPRIS, Stenting and Aggressive Medical Management for the Prevention of Recurrent Stroke in Intracranial Stenosis; and WEAVE, Wingspan Stent System Post Market Surveillance.

a 1-year stroke and death rate of 12.2%, so the natural history of this disease is poor. However, in patients with ≥70% stenosis, who presented with a stroke while on medical therapy, the 30-day stroke and death rate for medical therapy was 13.9%, which was not statistically different from the stenting group in SAMMPRIS (*P*=0.5918). The noninferiority in this subgroup of patients was seen, despite the high rate of periprocedural complications. This defined group of patients are high risk of recurrent stroke on even aggressive medical therapy and likely is the group who would most benefit from stenting if the periprocedural complication rate can be maintained at a low level.

The primary limitation of the WEAVE trial is that it was designed as a PMA trial (Post Market Surveillance) to assess periprocedural morbidity only and not long term safety or efficacy. No additional information is provided from this trial on restenosis rates or longer-term stroke and death event rates. Interestingly, the SAMMPRIS trial results demonstrated that the rate of death and disabling stroke beyond 30 days was lower in the stenting group at 2.2% than the medical therapy group at 6.2%, so the worse clinical results for stenting in the SAMMPRIS trial were because of the high periprocedural morbidity and not delayed events.[12] Nevertheless, further studies are needed to show long term efficacy of stenting, now that we have established proper patient selection, periprocedural medical therapy, and best practice interventional techniques to obtain a low periprocedural complication rate.

Conclusions

The WEAVE trial demonstrated periprocedural safety of the Wingspan stent with a 2.6% periprocedural stroke and death rate, which was better than the target of 4% event rate set by the FDA. This was the largest on-label Wingspan stent trial for ICAD with the most homogenous patient population of all the US stenting trials because there was 100% on-label usage for the trial. This trial avoided the type 2 error of the other studies which included a heterogeneous mixture of patients with acute stroke, patients improperly premedicated with aspirin and clopidogrel, and enrolling sites utilizing interventionalists with low clinical experience with the Wingspan. These results provide promise as another treatment option for those patients who are failing medical therapy for high grade intracranial atherosclerotic stenosis. The WEAVE study provides support for consideration of future prospective randomized trials evaluating intracranial stenting for this devastating pathology.

Appendix

WEAVE Trial Sites and Interventionalists

SSM DePaul Medical Center (Richard C. Callison), WellStar Health System (Rishi Gupta), Cedars Sinai Medical Center (Michael J. Alexander), Southern California Permanente Medical Group (Lei Feng), Eden Medical Center (David Bonovich), The Cleveland Clinic (Gabor Toth), Multicare Medical Center (Brian Kott), Capital Health Systems (Erol Veznedaroglu), University Hospital of Cincinnati (Andrew Ringer), Columbia University Medical Center (Philip Meyers), Sentara Norfolk General Hospital (John Agola), Harborview Medical Center (Basavaraj Ghodke), Santa Barbara Cottage Hospital (Alois Zauner), University of Kentucky Medical Center (Abdulnasser Alhajeri, Justin Fraser), Central Baptist Health (Curtis Given II), Morton Plant Hospital (Eric Lopez de Valle), Abington Memorial Hospital (Qaisar Shah), Mount Sinai Medical Center (John Chaloupka), Oregon Health Sciences (Gary Nesbit), Valley Baptist Medical Center – Harlingen (Ameer Hassan), Advocate Health System (Thomas Grobelny), Tennessee Interventional Associates (Blaise Baxter), St. John Medical Center – Providence (Richard Fessler II), Cadence Health Central DuPage (Harish Shownkeen).

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Disclosures

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