Periprocedural to 1-year safety and efficacy outcomes with the Pipeline Embolization Device with Shield technology for intracranial aneurysms: A prospective, post-market, multi-center study

SUPPLEMENTAL MATERIAL

SUPPLEMENTAL TABLES

Supplementary Table I. Subject Inclusion/Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
• Subject provided written informed consent; • At least 18 years of age; • Subject already selected for flow diversion therapy as the appropriate treatment; • Parent vessel with diameter 1.5-5.0 mm distal/proximal to the target IA.	• Major surgery including endovascular procedures within the past 30 days; • Target aneurysm located in the basilar artery; • Inappropriate anatomy for endovascular treatment due to severe intracranial vessel tortuosity, stenosis, or a history of intracranial vasospasm not responsive to medical therapy; • Stent in place in the parent artery at the target ICAs location; • Acutely (within 30 days) ruptured aneurysm with a Hunt and Hess grade ≥ 4; • Any known contraindication to PED-Shield as per instructions for use (IFU); • The investigator determined that the health of the subject or the validity of the study outcomes may be compromised by the subject's enrollment; • Pregnant or breastfeeding women or women who wished to become pregnant during the duration of the study; • Enrolled or planning to participate in a potentially confounding drug or device trial during the course of this study, unless pre-approval was obtained from the sponsor (Medtronic Neurovascular); • Legal incapacity or evidence that a subject could not understand the purpose and risks of the study or inability to comply fully with study procedures.

Supplementary Table II. Pre-Procedure Summary of Antiplatelet Therapy

Antiplatelet Therapy	Pre-Procedure [(%) n]		Administered Day of the Procedure (N=195)*	Administered Pre-Procedure (N=195)*
	1 to 6 Days Pre-Procedure (N=195)*	≥7 Days Pre-Procedure (N=195)*		
Aspirin ‡	97 (49.7%)	62 (31.8%)	179 (91.8%)	159 (81.5%)
P2Y12 Inhibitor ‡	112 (57.4%)	62 (31.8%)	190 (97.4%)	174 (89.2%)
Clopidogrel ‡	105 (53.8%)	57 (29.2%)	167 (85.6%)	162 (83.1%)
Prasugrel ‡	4 (2.1%)	4 (2.1%)	12 (6.2%)	8 (4.1%)
Ticagrelor ‡	5 (2.6%)	2 (1%)	10 (5.1%)	7 (3.6%)
Other P2Y12 Inhibitor ‡	3 (1.5%)	0 (0%)	12 (6.2%)	3 (1.5%)
DAPT †	104 (53.3%)	57 (29.2%)	182 (93.3%)	161 (82.6%)
Aspirin + Clopidogrel ‡	96 (49.2%)	54 (27.7%)	160 (82.1%)	150 (76.9%)
Aspirin + Prasugrel ‡	4 (2.1%)	2 (1%)	10 (5.1%)	6 (3.1%)
Aspirin + Ticagrelor ‡	4 (2.1%)	2 (1%)	8 (4.1%)	6 (3.1%)
Aspirin + Other P2Y12 Inhibitor ‡	1 (0.5%)	0 (0%)	9 (4.6%)	1 (0.5%)
Clopidogrel + Other P2Y12 Inhibitor ‡	2 (1%)	0 (0%)	3 (1.5%)	2 (1%)
Aspirin Monotherapy †	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Clopidogrel Monotherapy †	8 (4.1%)	2 (1%)	4 (2.1%)	10 (5.1%)
Prasugrel Monotherapy †	0 (0%)	2 (1%)	2 (1%)	2 (1%)
Ticagrelor Monotherapy †	1 (0.5%)	0 (0%)	2 (1%)	1 (0.5%)
Other P2Y12 Inhibitor Monotherapy †	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Triple Anti Platelet Therapy †	0 (0%)	0 (0%)	0 (0%)	0 (0%)
No Antiplatelet Therapy †	21 (10.8%)		5 (2.6%)	21 (10.8%)

Data are n (%). DAPT=dual anti platelet therapy

†The patient count is mutually exclusive with no other therapy other than the listed therapy.

‡The patient count is independent and only based on the listed therapy.

Supplementary Table III: Procedure Characteristics and Outcomes

Characteristic	Summary (N=204)
Total devices implanted	252
Number of devices implanted per patient	1.1 ± 0.50
Single device	177 (86.8%)
Procedure time (incision to skin closure), min	100.5 ± 92.02
Cumulative fluoroscopy time, min	36.1 ± 27.98
Adjunctive devices	56 (29.8%)
Coiling	38 (18.6%)
Balloon	22 (10.8%)
Complete wall apposition*	190 (93.1%)
Complete neck coverage*	199 (97.5%)
Complete stasis*	22 (10.8%)
Significant stasis*	107 (52.5%)
No disruption of inflow jet*	75 (36.8%)
Complete occlusion*	2 (1.0%)
Residual aneurysm*	202 (99.0%)

Data are n (%) or mean ± standard deviation

*per Imaging Core Lab on day 0 post-procedure

Supplementary Table IV. Adverse Events through 1-year Post-Procedure - ITT

Event	Summary (N=204)
Reported AEs	139
Subjects with AEs	90/204 (44.1%)
Serious (n=41)	36/204 (17.6%)
Non-serious (n=98)	71/204 (34.8%)
Device-related neurological events (n=21)	20/204 (9.8%)
CEC-Adjudicated AEs	155
Subjects with AEs	98/204 (48.0%)
Serious (n=58)	44/204 (21.6%)
Device-related (n=19)	17/204 (8.3%)
Procedure-related (n=40)	33/204 (16.2%)
Non-serious (n=97)	74/204 (36.3%)

Data are n (%).

Supplementary Table V. CEC Adjudicated Neurological Adverse Events of Interest through 1-year Post-Procedure - ITT

Neurological Events of Interest	Peri-Procedure (Day 0)	Acute (Days 1-30)	Delayed (Days 31-365)	Days 0-1-year
Death	0	2 (1.0%)	0	2 (1.0%)
Neurological Death	0	2 (1.0%)	0	2 (1.0%)
Non-Neurological Death	0	0	0	0
Stroke	4 (2.0%)	9 (4.4%)	0	13 (6.4%)
Severity				
Major Stroke	3 (1.5%)	3 (1.5%)	0	6 (2.9%)
Minor Stroke	1 (0.5%)	6 (2.9%)	0	7 (3.4%)
Type				
Ischemic	2 (1.0%)	8 (3.9%)	0	10 (4.9%)
Ischemic with Hemorrhagic Transformation	1 (0.5%)	0	0	1 (0.5%)
Hemorrhagic	1 (0.5%)	1 (0.5%)	0	2 (1.0%)
Location				
Treated Vascular Territory	4 (2.0%)	9 (4.4%)	0	13 (6.4%)
Non-Treated Vascular Territory	0	0	0	0
Intracranial Hemorrhage (ICH)	4 (2.0%)	5 (2.5%)	0	9 (4.4%)
Type				
Intracerebral Hemorrhage	3 (1.5%)	3 (1.5%)	0	6 (2.9%)
Intraparenchymal Hemorrhage (IPH)	3 (1.5%)	3 (1.5%)	0	6 (2.9%)
Intraventricular Hemorrhage (IVH)	0	0	0	0
Subarachnoid Hemorrhage (SAH)	1 (0.5%)	2 (1.0%)	0	3 (1.5%)
Subdural Hematoma (SDH)	0	0	0	0
Epidural Hematoma (EDH)	0	0	0	0
Etiology				
Target Aneurysm Rupture	0	2 (1.0%)	0	2 (1.0%)
Non-Target Aneurysm Rupture	0	0	0	0
Hemorrhagic Transformation of ischemic infarct	1 (0.5%)	0	0	1 (0.5%)
Primary SAH Procedural or Traumatic Complication	3 (1.5%)	0	0	3 (1.5%)
Primary IPH	0	3 (1.5%)	0	3 (1.5%)
Primary IVH	0	0	0	0
Transient Ischemic Attack (TIA)	0	1 (0.5%)	0	1 (0.5%)
Cerebral Infarction	2 (1.0%)	4 (2.0%)	2 (1.0%)	8 (3.9%)
Symptomatic	0	1 (0.5%)	0	1 (0.5%)
Asymptomatic	2 (1.0%)	3 (1.5%)	2 (1.0%)	7 (3.4%)
Neurological Deficit	2 (1.0%)	4 (2.0%)	0	6 (2.9%)
Transient	0	2 (1.0%)	0	2 (1.0%)
Permanent	2 (1.0%)	2 (1.0%)	0	4 (2.0%)
Target Aneurysm Retreatment	0	1 (0.5%)	3 (1.5%)	4 (2.0%)

Data are n (%).

Supplementary Table VI. CEC-Adjudicated Device-Related Serious Adverse Events (SAEs) through 1-Year by Preferred Term and Timing of Event – ITT

MedDRA System Organ Class	MedDRA Preferred Term	Peri-Procedure (Day 0)	Acute (Days 1-30)	Delayed (Days 31-365)	Days 0-1-year
Eye disorders	Retinal artery occlusion	0	1 (0.5%)	0	1 (0.5%)
	Visual impairment	0	1 (0.5%)	0	1 (0.5%)
	Total	0	2 (1.0%)	0	2 (1.0%)
Injury, poisoning and procedural complications	Vascular procedure complication	1 (0.5%)	0	0	1 (0.5%)
	Total	1 (0.5%)	0	0	1 (0.5%)
Nervous system disorders	Cerebral artery embolism	1 (0.5%)	0	0	1 (0.5%)
	Cerebral hemorrhage	0	1 (0.5%)	0	1 (0.5%)
	Cerebral infarction	0	2 (1.0%)	0	2 (1.0%)
	Cerebral microembolism	1 (0.5%)	0	0	1 (0.5%)
	Cerebrovascular accident	0	2 (1.0%)	0	2 (1.0%)
	Hemorrhagic stroke	1 (0.5%)	0	0	1 (0.5%)
	Intracranial mass	1 (0.5%)	0	0	1 (0.5%)
	Ischemic cerebral infarction	0	1 (0.5%)	0	1 (0.5%)
	Ischemic stroke	1 (0.5%)	1 (0.5%)	0	2 (1.0%)
	VIth nerve paralysis	1 (0.5%)	0	0	1 (0.5%)
	Total	6 (2.9%)	7 (3.4%)	0	13 (6.4%)
Surgical and medical procedures	Aneurysm repair	0	0	3 (1.5%)	3 (1.5%)
	Total	0	0	3 (1.5%)	3 (1.5%)
Total		**7**	**9**	**3**	**19**

Data are n (%).

Supplementary Table VII. CEC-Adjudicated Procedure-Related (Possible, Probable and Causal assessment) Serious Adverse Events (SAEs) through 1-Year by Preferred Term and Timing of Event – ITT

MedDRA System Organ Class	MedDRA Preferred Term	Peri-Procedure (Day 0)	Acute (Days 1-30)	Delayed (Days 31-365)	Days 0-1-year
Blood and lymphatic system disorders	Hemorrhagic diathesis	1 (0.5%)	0	0	1 (0.5%)
	Total	1 (0.5%)	0	0	1 (0.5%)
Eye disorders	Retinal artery occlusion	0	1 (0.5%)	0	1 (0.5%)
	Visual impairment	0	1 (0.5%)	0	1 (0.5%)
	Total	0	2 (1.0%)	0	2 (1.0%)
Gastrointestinal disorders	Retroperitoneal hemorrhage	0	1 (0.5%)	0	1 (0.5%)
	Total	0	1 (0.5%)	0	1 (0.5%)
General disorders and administration site conditions	Pyrexia	0	1 (0.5%)	0	1 (0.5%)
	Total	0	1 (0.5%)	0	1 (0.5%)
Infections and infestations	Hematoma infection	0	1 (0.5%)	0	1 (0.5%)
	Infection	0	1 (0.5%)	0	1 (0.5%)
	Staphylococcal sepsis	0	0	1 (0.5%)	1 (0.5%)
	Total	0	2 (1.0%)	1 (0.5%)	3 (1.5%)
Injury, poisoning and procedural complications	Subarachnoid hemorrhage	0	1 (0.5%)	0	1 (0.5%)
	Vascular access site pseudoaneurysm	0	1 (0.5%)	0	1 (0.5%)
	Vascular procedure complication	1 (0.5%)	0	0	1 (0.5%)
	Vascular pseudoaneurysm	0	3 (1.5%)	0	3 (1.5%)
	Total	1 (0.5%)	5 (2.5%)	0	6 (2.9%)
Metabolism and nutrition disorders	Hyponatremia	0	1 (0.5%)	0	1 (0.5%)
	Total	0	1 (0.5%)	0	1 (0.5%)
Nervous system disorders	Cerebral artery embolism	1 (0.5%)	0	0	1 (0.5%)
	Cerebral artery occlusion	1 (0.5%)	0	0	1 (0.5%)
	Cerebral hemorrhage	0	2 (1.0%)	0	2 (1.0%)
	Cerebral infarction	0	1 (0.5%)	0	1 (0.5%)
	Cerebral microembolism	1 (0.5%)	0	0	1 (0.5%)
	Cerebrovascular accident	0	2 (1.0%)	0	2 (1.0%)

MedDRA System Organ Class	MedDRA Preferred Term	Peri-Procedure (Day 0)	Acute (Days 1-30)	Delayed (Days 31-365)	Days 0-1-year
	Cranial nerve palsies multiple	0	1 (0.5%)	0	1 (0.5%)
	Dysaesthesia	0	1 (0.5%)	0	1 (0.5%)
	Hemorrhage intracranial	0	2 (1.0%)	0	2 (1.0%)
	Hemorrhagic stroke	1 (0.5%)	0	0	1 (0.5%)
	Hemorrhagic transformation stroke	1 (0.5%)	0	0	1 (0.5%)
	Ischemic cerebral infarction	0	1 (0.5%)	0	1 (0.5%)
	Ischemic stroke	2 (1.0%)	1 (0.5%)	0	3 (1.5%)
	Ruptured cerebral aneurysm	1 (0.5%)	0	0	1 (0.5%)
	VIth nerve paralysis	1 (0.5%)	0	0	1 (0.5%)
	Total	9 (4.4%)	11 (5.4%)	0	20 (9.8%)
Respiratory, thoracic and mediastinal disorders	Laryngospasm	1 (0.5%)	0	0	1 (0.5%)
	Pulmonary embolism	0	1 (0.5%)	0	1 (0.5%)
	Total	1 (0.5%)	1 (0.5%)	0	2 (1.0%)
Surgical and medical procedures	Aneurysm repair	0	0	1 (0.5%)	1 (0.5%)
	Total	0	0	1 (0.5%)	1 (0.5%)
Vascular disorders	Embolism venous	0	1 (0.5%)	0	1 (0.5%)
	Vasospasm	1 (0.5%)	0	0	1 (0.5%)
	Total	1 (0.5%)	1 (0.5%)	0	2 (1.0%)
Total		**13**	**25**	**2**	**40**

Data are n (%).