PROTOCOL SUMMARY

TITLE:	A Post-Market Study of Transcatheter Perivascular Renal Denervation for the Treatment of Hypertension using the Ablative Solutions Inc. Peregrine System™ Infusion Catheter
SHORT TITLE:	The Peregrine Post-Market Study
PROTOCOL ID:	CR0001
INVESTIGATIONAL PRODUCT:	Peregrine System™ Infusion Catheter
INDICATION:	Hypertension
ClinicalTrials.gov ID:	NCT02570113
PHASE:	Post market clinical follow up study
SPONSOR:	Ablative Solutions, Inc. 6203 San Ignacio Avenue, Suite 110 San Jose, CA 95119, US
COORDINATING INVESTIGATORS:	Prof. Dr. med. Horst Sievert
PROTOCOL VERSION:	Rev K
DATE:	16 April 2018

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INVESTIGATIONAL PRODUCT	
Name of Product	Peregrine System™ Infusion Catheter
CLINICAL CONDITION/INDICATION Hypertension	
Protocol ID	CR0001
Protocol Title	A Post-Market Study of Transcatheter Perivascular Renal Denervation for the Treatment of Hypertension using the Ablative Solutions Inc. Peregrine System™ Infusion Catheter
Short Title	The Peregrine Post-Market Study
Study Phase	Post market clinical follow up study
PLANNED STUDY PERIOD	
Initiation	November 2015
Study Completion	May 2019
Duration	Approximately 3.5 years
STUDY OBJECTIVES AND PURPOSE	
Study Purpose To collect additional safety and performance data pertaining to renal denervation by using dehydrated alcohol as a chemical neurolytic agent delivered into the adventitial/peri-adventitial area of the renal arteries for the purpose of renal denervation, using the Peregrine Catheter, in patients with hypertension.	
Objective The objectives of this post-market study are to collect additional safety and performance data pertaining to renal denervation by using dehydrated alcohol as a chemical neurolytic agent delivered into the adventitial/peri-adventitial area of the renal arteries for the purpose of renal denervation, using the Peregrine Catheter, in patients with hypertension.	
STUDY DESIGN	
Study Type/ Classification/ Discipline	Post market clinical follow up study for safety and performance (ambulatory blood pressure monitoring [ABPM], office blood pressure)
Study Indication Type	Treatment

Study Design	This post-market study is a prospective, single arm, open label, multicenter trial. Up to 60 subjects with hypertension will be treated with 0.6 mL of dehydrated alcohol as the neurolytic agent per renal artery. The data of the first 5 treated subjects in the study (including renal duplex ultrasound) will be assessed at the 1-month follow-up by the Data Safety Monitoring Board (DSMB). If no safety concern arises, treatment with 0.6 mL of alcohol will continue according to the protocol. Contenting subjects will be assessed for eligibility and baseline data collected. Subjects will attend the study site for the day of procedure. Subjects will be discharged from the study site per the physician's judgment. Subjects must be maintained on his/her baseline anti-hypertensive medications at the same doses through the 6 months follow up visit unless the study subject has symptomatic hypotension requiring anti-hypertensive medication reduction. Planned increases in anti-hypertensive medications must be in alignment with JNC-8 and/or European Hypertension Guidelines and with approval from the sponsor. Follow-up visits will be performed at 7 days, 1 month, 3 months, 6 months and 12 months post-procedure.
Study Geography/ Number of Planned Investigational Sites	Europe: up to 10 sites in Europe.
Number of Groups/ Arms/ Cohorts	1 group
Number of Subjects	Up to 60
Planned Duration of Subject Participation	Up to 12 months
INVESTIGATIONAL PRODUCT	
Product	Peregrine System™ Infusion Catheter used to deliver a neurolytic agent (such as dehydrated alcohol) to the perivascular area of the renal arteries to ablate the afferent and efferent sympathetic nerves serving the kidneys **Dose:** 0.6 mL alcohol per treated renal artery. **Mode of administration:** Direct infusion to the perivascular space, during an endovascular procedure
SUBJECT SELECTION Subjects will be enrolled in the study at the time they sign the informed consent form. No study-specific procedures will be performed until after the subject has provided written informed consent.	

Subject Inclusion Criteria

Subjects must meet ALL of the following inclusion criteria to receive the percutaneous procedure:

1. Adult subject, age 18-80, male or female
2. Subject has a target treatment vasculature diameter of ≥4 mm and ≤ 7 mm and length of ≥5 mm
3. Subject has 3 measurements with a mean of office Systolic Blood Pressure of ≥150 mmHg AND office Diastolic Blood Pressure of ≥85 mmHg
4. Subject has a 24-hour mean systolic Ambulatory Blood Pressure Measurement (ABPM) ≥135 mm Hg with ≥70% valid readings (as determined by measurement device)
5. Subject with hypertension is receiving and adhering to a stable medication regimen of at least 3 anti-hypertensive medications of different classes (for at least 4 consecutive weeks), one of which must be a diuretic
6. Subject agrees to have all study procedures performed, to comply with medication regimen and is able and willing to comply with all study follow-up visits
7. Subject has provided written informed consent

Exclusion Criteria

Any subject who meets ANY of the following exclusion criteria will not receive the percutaneous interventional procedure:

1. Subject has a contraindication known for conventional percutaneous interventional procedures such as:
   - intolerance for antiplatelet/anticoagulant therapy
   - known allergy to contrast media
   - bleeding disorders (such as bleeding diathesis, thrombocytopenia and severe anemia)
2. Subject has documented severe untreated obstructive sleep apnea (Apnea Hypopnea Index [AHI] ≥30 per hour)
3. Subjects with nephrotic syndrome
4. Subjects on immunosuppressive medications or immunosuppressive doses of steroids
5. Subject has type 1 diabetes mellitus
6. Subject is pregnant or nursing or planning to become pregnant
7. Subject has an estimated glomerular filtration rate (eGFR) ≤20 mL/min/1.73m^2, based on the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation
8. Subject has imaging-assessed renal artery anatomy abnormalities or variations based on Investigator's evaluation of the screening images [i.e. magnetic resonance angiogram/angiography (MRA)/ computed tomography angiogram/angiography (CTA) examination and/or renal angiography]) meeting one of the following criteria:
   - Renal artery stenosis >60% of the normal diameter segment (diameter stenosis, compared to the angiographically normal proximal or distal segment)

- Any renal artery abnormality or disease that, per the physician assessment, precludes the safe insertion of the guiding catheter (such as but not limited to severe renal artery aneurysm, excessive tortuosity, severe renal artery calcification)
- Previous renal angioplasty associated with stenting or other implants, that, per the physician's assessment, precludes the safe deployment of the Peregrine catheter components in the target treatment segment of the renal artery

9. Subject has a history of nephrectomy, a single kidney or kidney tumor, or urinary tract obstruction (with potential for hydronephrosis)
10. Subject is known to have a non-functioning kidney or unequal renal size (>2 cm difference in renal length between kidneys associated with a chronic kidney disease or a deterioration of the kidney function)
11. Subject has a renal transplant
12. Subject has a history of myocardial infarction, unstable angina pectoris, or stroke/transient ischemic attack (TIA) within the last six months from planned procedure
13. Subject has hemodynamically significant valvular heart disease
14. Subject has heart failure (New York Heart Association [NYHA] III or IV) or has an ejection fraction ≤30%
15. Subject with chronic atrial fibrillation
16. Subjects who are allergic or intolerant of the neurolytic agent (such as dehydrated alcohol)
17. Any contraindication to the imaging as required per the protocol
18. Subject has a life expectancy of <12 months
19. Subject is currently enrolled in other potentially confounding research, i.e., another therapeutic or interventional research trial. Subjects enrolled in observational registries may still be eligible