PHIL™

Precipitating Hydrophobic Injectable Liquid

Liquid Embolic System

INSTRUCTIONS FOR USE

Humanitarian Device:
Authorized by Federal Law for use in the treatment of intracranial dural arteriovenous fistulas. The effectiveness of this device for this use has not been demonstrated.

Rx Only: Federal (USA) law restricts this device to sale by or on the order of a physician.

MicroVention™ TERUMO

Carefully read all instructions prior to use.

DEVICE DESCRIPTION

The PHIL (Precipitating Hydrophobic Injectable Liquid) Liquid Embolic System is a non-adhesive liquid embolic agent comprised of a co-polymer dissolved in DMSO (dimethyl sulfoxide). A non-ionic iodine component is chemically bonded to the co-polymer to provide a radiopaque element during fluoroscopic visualization during injections. The PHIL Liquid Embolic System consists of a sterile, pre-filled, 1.0 mL syringe of PHIL liquid embolic, a sterile, pre-filled 1.0 mL syringe of DMSO, and a Universal microcatheter adaptor. A Re-PHIL Liquid Embolic System consists of two sterile, pre-filled 1 mL syringes of PHIL liquid embolic and a Universal microcatheter adaptor. A DMSO compatible delivery microcatheter that is indicated for use in the neuro vasculature (Headway™ DUO, Headway™ 17/21 or Scepter™ C/XC/Mini Occlusion Balloon microcatheters) is used to access the embolization target site. The PHIL Liquid Embolic System is available in several product formulations: PHIL 25%, PHIL 30%, and PHIL 35%. PHIL 25% liquid embolic will travel more distally and penetrate deeper into the vascular malformation due to its lower viscosity compared to PHIL 30% or 35% liquid embolic. Final solidification of the PHIL material occurs within three minutes for all product formulations. Other embolic agents, such as coils, may be used adjunctively with the PHIL device.

PRINCIPLE OF OPERATION

The PHIL device is delivered by slow, controlled injection at a target rate of 0.1 mL/min through a microcatheter into the vascular malformation under fluoroscopic control. The DMSO solvent dissipates into the blood, causing the copolymer to precipitate *in situ* into a coherent embolus. The PHIL device immediately forms a skin as the polymeric embolus solidifies from the outside to the inside, while traveling more distally in the vascular lesion.

INDICATIONS FOR USE

The PHIL Liquid Embolic System is indicated for use in the treatment of intracranial dural arteriovenous fistulas (dAVFs).

CONTRAINDICATIONS

The use of the PHIL device is contraindicated when any of the following conditions exist:

- Patient has a severe iodine allergy.
- Optimal microcatheter placement is not possible.
- Provocative testing indicates intolerance to the occlusion procedure.
- Patient has vasospasm that stops blood flow.
- Patients with known hypersensitivity to nickel as the device packaged in glass syringes may contain nickel.

WARNINGS

- Performing embolization to occlude blood vessels is a high-risk procedure. This device should be used only by physicians with neurointerventional training and a thorough knowledge of the vascular pathology to be treated, vascular architecture, angiographic techniques, and super-selective embolization techniques.
- Vascular malformation embolization may influence or change blood flow patterns, thereby subjecting arteries supplying the vascular malformation or the normal surrounding tissues and the perivascular space around the malformation to increased pressure. These conditions could result in hemorrhagic complications.
- If the PHIL device extravasates outside the vascular space, secondary to vessel wall compromise, a sub-acute inflammatory response to the material may occur in the surrounding vascular space which may lead to potential tissue damage.
- There may be some topical hypersensitivity and/or release of histamines from DMSO.
- Do not use the PHIL device in individuals with liver and/or kidney function impairment.

- Therapeutic embolization should not be performed when high blood flow state precludes safe delivery of the embolic agent to prevent non-target embolization.
- The microcatheter tip should be placed as distal as possible and as close to the target vascular lesion as possible to prevent any non-target embolization of normal surrounding tissue or cranial nerves.
- Premature solidification of the PHIL device may occur if the microcatheter or luer hub comes in contact with any solution such as saline, blood or contrast.
- If visualization of the liquid embolic is lost at any time during the procedure, halt the PHIL delivery until adequate visualization is re-established.
- Use only DMSO compatible microcatheters (Headway™ DUO, Headway™ 17/21 or Scepter™ C/XC/Mini Occlusion Balloon Microcatheters) indicated for use in the neuro vasculature. Other microcatheters may not be compatible with DMSO and their use can result in thromboembolic events or other serious adverse events due to microcatheter degradation or breakage.
- Use only the MicroVention pre-filled syringes to inject DMSO and the PHIL device. Other syringes may not be compatible with DMSO.
- Historical animal studies that focused on DMSO have shown that rapid injection into the neurovasculature may lead to vasospasm *or necrosis*. Inject at a target rate of 0.1 mL/min to reduce the risk of this occurrence.
- DMSO contained in the device may interact with other embolic devices, such as polymer coated coils.
- Use at maximum 8 syringes of PHIL liquid embolic in a single treatment.
- In the event of microcatheter occlusion, excessive force may result in microcatheter rupture due to over pressurization causing vessel rupture or non-target embolization.
- DO NOT allow more than **1 cm of the PHIL device** to reflux back over microcatheter tip. Excessive reflux may result in difficult microcatheter removal.
- The long-term effects of an entrapped microcatheter that is left in a patient are unknown, but potentially could include clot formation, infection, or catheter migration.
- Excessive force to remove an entrapped microcatheter may cause adverse effects such as intracranial hemorrhage.
- After using a microcatheter with the PHIL device, do not attempt to clear or inject any material through it. Such attempts may lead to embolus or non-target embolization.
- STOP injection if the PHIL device is not visualized exiting the microcatheter tip. If the microcatheter becomes occluded, over-pressurization and vessel rupture can occur. During injection, continuously verify under fluoroscopy that the PHIL device is exiting the microcatheter tip.
- STOP injection if increased resistance is observed. If increased resistance occurs, determine the cause (e.g., occlusion in microcatheter lumen) and replace the microcatheter if needed. Do not attempt to clear or overcome resistance by applying increased injection pressure, as use of excessive pressure may result in microcatheter or vessel rupture and embolization of non-target area.
- Only use thumb pressure to inject the PHIL device at a target rate of 0.1 mL/min. Using the palm of hand to advance the plunger may result in microcatheter or vessel rupture due to over pressurization in the event of microcatheter occlusion.
- DO NOT interrupt the PHIL device injection for longer than three minutes prior to re-establishing injection. This may cause solidification of the PHIL device within the microcatheter or tip resulting in microcatheter occlusion. Use of excessive pressure to clear the microcatheter may result in microcatheter or vessel rupture and embolization of non-target areas.

PRECAUTIONS

- The safety and probable benefit have not been studied in the following patient populations:
  - Pregnant and nursing women.
  - Pediatric population, this product has only been studied in the adult population.
  - Individuals with feeding pedicle aneurysms not associated with the malformation, or distal feeders to the vascular malformation.
- Safety and probable benefit of the PHIL embolic as a long-term implant has not been established.
- Some data indicates that dimethyl sulfoxide potentiates other concomitantly administered medications.
- A garlic-like taste may be noted by the patient with use of the PHIL device due to the DMSO component. This taste may last several hours. An odor on the breath and skin may be present.
- Inspect product packaging prior to use. Do not use if sterile barrier is open or damaged.

- This device is intended for single use only. Do not reuse, reprocess or re-sterilize. Reuse, reprocessing or re-sterilization may compromise the integrity of the device and/or lead to device failure which, in turn, may result in patient injury, illness, or death. Reuse, reprocessing, or re-sterilization may also create a risk of contamination of the device and/or cause patient infection or cross-infection, including but not limited to, the transmission of infectious disease(s) from one patient to another. Contamination of the device may lead to injury, illness or death of the patient.
- After use, dispose in accordance with hospital, administrative, and/or local government policy.
- Use prior to expiration date.
- Verify that the microcatheters and accessories (see directions for use) used in direct contact with the PHIL polymer are clean and compatible with the material and do not trigger solidification or degrade with contact.
- This device requires the use with fluoroscopy; therefore, operators should take all necessary precautions to limit X-ray radiation doses to patients and themselves by using sufficient shielding, reducing fluoroscopy times, and modifying X-ray technical factors where possible.
- Upon completion of the PHIL device injection, wait three minutes, slightly aspirate the syringe, and then gently pull the microcatheter, to separate it from the PHIL cast. Failure to wait this recommended time to retrieve the microcatheter after injection may result in fragmentation of the PHIL device into non-target vessels.

POTENTIAL COMPLICATIONS

Potential complications include, but are not limited to:

- Hematoma at the puncture site and other access site complications such as fistula, pseudo-aneurysm, pain, tenderness, inflammation, necrosis and granuloma.
- Non-target arterial thrombosis.
- Ischemic events due to embolic migration, vasospasm, thrombosis.
- Hemorrhagic accidents: vascular rupture, perforation.
- Hemodynamic changes induced by the embolization may result in hemorrhagic complications.
- Ischemic or hemorrhagic complications may result in various functional neurological deficits, transient ischemic attack (TIA), stroke, or death.
- Allergic reactions or a sub-acute inflammatory response.
- Device- or procedure-related complications such as arrhythmia, contrast related complications (e.g., burning sensation, nausea, contrast nephropathy), headache, infection, nerve damage or cranial nerve palsy, pulmonary embolism, seizures, thrombocytopenia, visual complications.
- This device uses fluoroscopy, which presents potential risks associated with X-ray exposure. The risks of angiographic and fluoroscopic X-ray radiation doses to the patient include risks such as alopecia, burns ranging in severity from skin reddening to ulcers, cataracts, and delayed neoplasia that increase in probability as procedure time and the number of procedures increase.

See Table 4 below for a listing of all adverse events that occurred in the prospective clinical trial of the PHIL Liquid Embolic System to demonstrate safety and probable benefit.

Magnetic Resonance (MR) SAFETY INFORMATION MR

The PHIL device has been determined to be MR Safe as defined in ASTM F2503-13.

Artifact Information

Magnetic resonance imaging (MRI) testing has demonstrated that the PHIL device is MR Safe and shows no artifacts on MR images in relation to the size and shape of this device. MR Safe at 3 Tesla or less.

CLINICIAN USE INFORMATION

MATERIALS

The PHIL device is not manufactured with natural rubber latex, polyvinylchloride (PVC), or di-2-ethylhexyl phthalate (DEHP).

PACKAGING AND STORAGE

The PHIL syringes and universal adaptor are placed inside separate polycarbonate trays and packaged in a unit carton. The devices will remain sterile unless the package is opened, damaged, or the expiration date has passed. If the sterile packaging is unintentionally opened or damaged, discard the device.

The PHIL syringes and universal adaptor are sterilized by steam sterilization. A small round indicator label has been affixed to the packaging of the PHIL syringe trays and universal adaptor tray. This indicator turns from blue to pink upon exposure to steam sterilization and must be pink in order to use the device. If the indicator is blue, do not use the PHIL embolic device.

Store the PHIL Liquid Embolic System at room temperature in a dry place. Keep away from direct sunlight. If the product freezes due to exposure to colder temperatures, thaw at room temperature before use.

SHELF LIFE

See the product label for the device shelf life. Do not use the device beyond the labeled use by date.

PREPARATION FOR USE

Device and Delivery System Selection

Appropriate selection of the PHIL device is important for patient safety. In order to choose the optimal PHIL device model for any given lesion, examine pre-treatment angiograms for correct and accurate vessel measurements.

TRAINING

Serious, including fatal, consequences could result with the use of the PHIL Liquid Embolic System without adequate training. Contact your MicroVention representative for information on training courses.

HOW SUPPLIED

The PHIL device is provided sterile and non-pyrogenic. The PHIL Liquid Embolic System is available in several product formulations: PHIL 25%, PHIL 30%, and PHIL 35%. With all formulations, care must be taken to identify any normal non-target vessels prior to injection so that the PHIL device does not occlude normal vessels or vascular territories.

- PHIL 25% liquid embolic is recommended when access close to the target lesion cannot be achieved. This formulation is less viscous and can travel distally through the malformation. Care must be taken to control delivery.
- PHIL 30% liquid embolic is recommended when access is distal and at the level of the vascular malformation.
- PHIL 35% liquid embolic is recommended for high flow lesions or has a fistulous component to the malformation.

Final solidification occurs within three minutes for all product formulations.

DIRECTIONS FOR USE

Verify that adequate sedation or general anesthesia is utilized throughout the embolization procedure. Insufficient sedation may result in patient discomfort or movement. Patient movement during embolic agent injection may result in embolization of a non-target vessel.

1. Confirm proper microcatheter placement at the target site with injection of contrast agent using standard angiographic techniques.

   Warning: Use only DMSO compatible microcatheters (Headway™ DUO, Headway™ 17/21 or Scepter™

C/XC/Mini Occlusion Balloon Microcatheters) indicated for use in the neuro vasculature. Other microcatheters may not be compatible with DMSO and their use can result in thromboembolic events or other serious adverse events due to microcatheter degradation or breakage.

2. Completely clear the microcatheter with approximately 10 mL of saline prior to PHIL device delivery.

3. Holding the syringe upwards, inject DMSO using the pre-filled DMSO syringe into the delivery microcatheter in sufficient volume to fill the microcatheter dead space. Refer to delivery microcatheter labeling for dead space volume.

   Warning: Use only the MicroVention pre-filled syringes to inject DMSO and the PHIL device. Other syringes may not be compatible with DMSO.

4. The plunger of the PHIL syringe may stick slightly initially. Pull back slightly on the plunger of the capped PHIL syringe to free up its movement.

5. Remove the cap from the PHIL syringe. Attach the Universal adaptor to the PHIL syringe and purge air.

6. Remove the DMSO syringe from the microcatheter and overfill and wash the luer hub with the balance of the DMSO.

7. Connect the PHIL syringe and adaptor assembly to the microcatheter hub, making sure there is no air in the hub during the connection. Ensure that the hypotube is seated at the bottom most point of the microcatheter hub, and tighten all connections before use.

   Warning: Premature solidification of the PHIL device may occur if the microcatheter luer contacts any solution such as saline, blood or contrast.

8. Begin injecting the PHIL device to displace the DMSO. It is recommended that PHIL be injected at a target rate of 0.1 mL/min.

   Warning: Only use thumb pressure to inject the PHIL device. Using the palm of the hand to advance the plunger may result in microcatheter or vessel rupture due to over pressurization in the event of microcatheter occlusion.

9. Monitor the volume injected to anticipate the first infusion of liquid embolic into the vasculature.

   Warning: Do not allow more than 1 cm of the PHIL device to reflux back over microcatheter tip. Excessive reflux may result in difficult microcatheter removal.

10. After using a microcatheter with the PHIL device, do not attempt to clear or inject any material through it. Such attempts may lead to embolus or embolization of a non-target area.

    Warning: STOP injection if increased resistance is observed. If increased resistance occurs, determine the cause (e.g., occlusion in microcatheter lumen) and replace the microcatheter if needed. Do not attempt to clear or overcome resistance by applying increased injection pressure, as use of excessive pressure may result in microcatheter or vessel rupture and embolization of non-target areas.

    Warning: DO NOT interrupt the PHIL device injection for longer than three minutes prior to re-injection. Solidification of the PHIL device may occur at the microcatheter tip resulting in microcatheter occlusion, and use of excessive pressure to clear the microcatheter may result in microcatheter rupture.

11. Upon completion of the PHIL device injection, wait three minutes, slightly aspirate the syringe, and then gently pull the microcatheter, to separate it from the PHIL cast. Failure to wait this recommended time to retrieve the microcatheter after injection may result in fragmentation of the PHIL device into non-target

vessels.

Difficult microcatheter removal or microcatheter entrapment may be caused by any of the following:

- Angioarchitecture of the vascular lesion, very distal afferent, lengthened, and tortuous feeding pedicle.
- Vasospasm of feeding vessel.
- Reflux of the PHIL device over the distal microcatheter tip/shaft.

Should microcatheter removal become difficult, the following will assist in microcatheter retrieval:

- Carefully pull the microcatheter to assess any resistance to removal.
- If resistance is felt, remove any slack or redundancy in the microcatheter.
- Gently apply traction to the microcatheter (approximately 3-4 cm of stretch to the microcatheter).
- Hold this traction for a few seconds and release. Assess traction on vasculature to minimize risk of vessel rupture or hemorrhage. This should be performed under fluoroscopic control.
- Attempt to apply traction on the microcatheter as well as traction on the guide catheter simultaneously. This should be performed under fluoroscopic control.
- This process can be repeated intermittently until microcatheter is retrieved.

For entrapped microcatheters:

- Under some difficult clinical situations, rather than risk rupturing the malformation and consequent hemorrhagic complications by applying too much traction on an entrapped microcatheter, it may be safer to leave the microcatheter in the vascular system.
- This is accomplished by stretching the microcatheter and cutting the shaft near the entry point of vascular access allowing the microcatheter to remain in the artery.
- If the microcatheter breaks during removal, distal migration or coiling of the microcatheter may occur. Same day surgical resection should be considered to minimize the risk of thrombosis.

SUMMARY OF CLINICAL STUDY

The clinical study, titled, “PHIL dAVF: Study of PHIL Embolic System in the Treatment of Intracranial Dural Arteriovenous Fistulas (dAVF)”, was a prospective, multi-center, single-arm clinical study conducted at 13 centers in the United States (U.S.), with 12 centers that enrolled subjects. The goal of the study was to evaluate the safety and probable benefit of the PHIL Liquid Embolic System for the treatment of intracranial dural arteriovenous fistulas. Subjects were eligible if they were between 22–80 years old with an intracranial dAVF that can be treated by embolization with PHIL without the need for other liquid embolization products. Sixty-four (64) subjects were enrolled and treated between September 2018 and November 2021.

All patients were scheduled to return for follow-up examinations at 30 days (± 14 days), 3 months (-2/+4 weeks), and 6 months (-3/+6 weeks). Sixty-three (63) enrolled subjects completed the 30-day and 3-month visits, and sixty-two (62) subjects completed a 6-month visit. The primary analysis for safety and probable benefit used the Full Analysis Set (FAS) population defined as all enrolled subjects in whom the PHIL device was implanted and had available primary endpoint data at 6 months (N=62). The subject-level data and data analyses presented were all prepared using the FAS population.

The study used an independent Data Safety and Outcomes Monitoring Committee (DSOMC) to monitor the study safety and adjudicate all adverse events that occurred in the study. The study also used an independent core lab which adjudicated angiographic outcomes including target vessel occlusion.

Inclusion Criteria

Subjects in the “PHIL dAVF” clinical study met ALL of the following criteria:

1. Subject is ≥ 22 and ≤ 80 years of age.

2. Subject is willing and capable of complying with all study protocol requirements, including the specified follow-up period.
3. Subject or authorized legal representative signed and dated an Institutional Review Board (IRB)-approved written informed consent prior to initiation of any study procedures.
4. Subject has an intracranial dAVF that can be treated by embolization with PHIL without the need for other liquid embolization products (e.g., Onyx, nBCA).
5. Subject has an intracranial dAVF that is deemed appropriate for embolization with PHIL without significantly increased risk to collateral or adjacent territories.

Exclusion Criteria

Subjects in the "PHIL dAVF" clinical study were excluded if ANY of the following criteria applied:

1. Subject has a modified Rankin Scale (mRS) of > 3 or another neurological deficit not due to stroke that may confound the neurological assessments.
2. Subject has multiple dAVFs to be treated.
3. Subject has dAVF requiring pre-planned treatment with adjunctive treatments (i.e., embolic coils, surgical resection, etc.).
4. Subject presents with an intracranial mass or is currently undergoing radiation therapy for carcinoma or sarcoma of the head or neck region.
5. Subject has known allergies to DMSO, iodine or heparin.
6. Subject has a history of life-threatening allergy to contrast media (unless treatment for allergy is tolerated).
7. Subject is experiencing (or has experienced) an evolving, acute, or recent disabling ischemic stroke, 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 3-month timeframe.
8. Subject has had an acute myocardial infarction within 30 days prior to index procedure.
9. Subject has had or plans to have a major surgical procedure (i.e., intra-abdominal or intrathoracic surgery or any surgery/interventional procedure involving cardiac or vascular system) within 30 days of the index procedure.
10. Subject is currently participating in another clinical study which might interfere with the outcome measurements for this study.
11. Female subject is currently pregnant.
12. Subject has an acute or chronic life-threatening illness other than the neurological disease treated in this study, including but not limited to any malignancy or debilitating autoimmune disease.
13. Subject has existing severe or advanced co-morbid conditions which significantly increase general anesthesia and/or surgical risk, including but not limited to advanced chronic obstructive pulmonary disease (COPD), uncontrolled hypertension/diabetes, congestive heart failure, chronic or acute kidney disease.
14. Subject has evidence of active infection at the time of treatment.
15. Subject has dementia or cognitive or psychiatric problem that prevents the subject from completing required follow-up.
16. Subject has co-morbid conditions that might limit survival to < 24 months.
17. Subject has a history of bleeding diathesis or coagulopathy, international normalized ratio (INR) greater than 1.5, or refused blood transfusions.

Angiographic Exclusion Criteria

18. Subject has severe calcification or vascular tortuosity that might preclude the safe introduction of the sheath, guiding catheter, or access to the lesion with the microcatheter.
19. Subject has a contra-indication to digital subtraction angiography/angiogram (DSA), computed tomography (CT) scan, or MRI/magnetic resonance angiography/angiogram (MRA).
20. Subject has a history of intracranial vasospasm not responsive to medical therapy.
21. Subject has extra-cranial stenosis or parent vessel stenosis > 50% proximal to the target lesion to be treated.

Subject demographics and the baseline characteristics of the target dAVFs are presented in **Table 1** and **Table 2**, respectively.

Table 1. Subject Demographics

Subject Characteristic	**N=62**
Age (years)	
Mean ± SD (Standard Deviation)	56.6 ± 13.31
Range (Min, Max)	31, 78
Sex, n (%)	
Female	19 (30.6%)
Male	43 (69.4%)
Race, n (%)	
Asian	4 (6.5%)
Black or African American	6 (9.7%)
Native Hawaiian or Other Pacific Islander	0 (0.0%)
White	45 (72.6%)
Not Willing to Provide	2 (3.2%)
Unknown	3 (4.8%)
Other	2 (3.2%)
Ethnicity, n (%)	
Hispanic or Latino	6 (9.7%)
Not Hispanic or Latino	53 (85.5%)
Unknown	3 (4.8%)

Table 2. Baseline Characteristics of Target dAVFs

dAVF Characteristic	**N=62, n (%)**
Borden classification	
Type I	23 (37.1%)
Type II	11 (17.7%)
Type III	28 (45.2%)
dAVF location*	
Cavernous sinus and para-cavernous	2 (3.2%)
Foramen magnum	1 (1.6%)
Sigmoid sinus	16 (25.8%)
Superior sagittal sinus	13 (21.0%)
Superior petrosal Sinus	1 (1.6%)
Tentorial	3 (4.8%)
Transverse sinus	25 (40.3%)
Vein of Galen, Straight sinus	1 (1.6%)
Other	12 (19.4%)
dAVF rupture status	
Ruptured	7 (11.3%)
Unruptured	55 (88.7%)
Days between rupture and treatment	
≤ 30 days	4 (6.5%)
> 30 days	3 (4.8%)
Previous treatment	
Previously treated dAVF	9 (14.5%)
Previously untreated dAVF	53 (85.5%)

*A fistula can be reported with multiple locations.

Primary Safety Outcome

The pre-specified primary safety outcome in the PHIL dAVF study was defined as the proportion of subjects with neurological death or ipsilateral stroke within the first 30 days following completion of the first PHIL treatment procedure. Neurologic death was defined as subject death reported as having resulted from a neurologic cause. Stroke was defined as a new focal neurological deficit in a defined vascular distribution of abrupt onset with symptoms persisting for > 24 hours and a neuro-imaging study or other quantitative study that did not indicate a different etiology. This included ischemic and hemorrhagic strokes. The primary safety outcome was evaluated descriptively.

None of the subjects experienced a neurological death or ipsilateral stroke within the first 30 days following completion of the first PHIL treatment procedure as adjudicated by the Data Safety and Outcomes Monitoring Committee, yielding a primary safety outcome event rate of 0% for the FAS population (**Table 3**).

No primary safety outcome events were observed through the 6-month follow-up period.

Table 3. Primary Measured Outcome: Safety, FAS Population

Primary Safety Outcome	**n/N (%)**	**98.75% Exact CI (LCL, UCL)**
Neurological death within 30 days following first PHIL treatment	0/62 (0.00%)	(0.00, 7.86)
Ipsilateral stroke within 30 days following first PHIL treatment	0/62 (0.00%)	(0.00, 7.86)

N = Number of total subjects
CI = Confidence interval
LCL = Lower confidence limit
UCL = Upper confidence limit

Summary of Adverse Events in Clinical Study

A summary of overall adverse events organized by System Organ Class and Preferred Term of the Medical Dictionary for Regulatory Activities (MedDRA) is shown in **Table 4**.

Table 4. All Adverse Events by MedDRA System Organ Class and Preferred Term

System Organ Class **Preferred Term**	**N=62** **# Subjects (%) [# Events]**
Cardiac disorders	1 (1.6%) [1]
Acute myocardial infarction	1 (1.6%) [1]
Ear and labyrinth disorders	3 (4.8%) [4]
Tinnitus	2 (3.2%) [2]
Ear pain	1 (1.6%) [1]
Dysacusis	1 (1.6%) [1]
Eye disorders	4 (6.5%) [4]
Cataract	1 (1.6%) [1]
Visual acuity reduced	1 (1.6%) [1]
Diplopia	1 (1.6%) [1]
Visual impairment	1 (1.6%) [1]
General disorders and administration site conditions	2 (3.2%) [2]
Malaise	1 (1.6%) [1]
Swelling face	1 (1.6%) [1]
Infections and infestations	6 (9.7%) [7]
COVID-19	4 (6.5%) [4]
Pneumonia	1 (1.6%) [1]

System Organ Class Preferred Term	N=62 # Subjects (%) [# Events]
Ear infection	1 (1.6%) [1]
Upper respiratory tract infection	1 (1.6%) [1]
Injury, poisoning and procedural complications	14 (22.6%) [16]
Radiation alopecia	4 (6.5%) [4]
Procedural nausea	2 (3.2%) [2]
Vascular access site pseudoaneurysm	1 (1.6%) [1]
Urinary retention postoperative	1 (1.6%) [1]
Skin laceration	1 (1.6%) [1]
Vascular access site hematoma	1 (1.6%) [1]
Head injury	1 (1.6%) [1]
Thermal burn	1 (1.6%) [1]
Urinary tract procedural complication	1 (1.6%) [1]
Vascular access site pain	1 (1.6%) [2]
Procedural headache	1 (1.6%) [1]
Metabolism and nutrition disorders	1 (1.6%) [1]
Failure to thrive	1 (1.6%) [1]
Musculoskeletal and connective tissue disorders	4 (6.5%) [5]
Arthralgia	2 (3.2%) [2]
Muscle spasms	1 (1.6%) [1]
Arthritis	1 (1.6%) [1]
Neck pain	1 (1.6%) [1]
Nervous system disorders	20 (32.3%) [22]
Headache	7 (11.3%) [7]
Procedural headache	3 (4.8%) [3]
Seizure	2 (3.2%) [2]
Facial paralysis	1 (1.6%) [1]
Ischemic stroke	1 (1.6%) [1]
Cerebral vasoconstriction	1 (1.6%) [1]
Paresthesia	1 (1.6%) [1]
Transient ischemic attack	1 (1.6%) [1]
Dizziness	1 (1.6%) [1]
Facial paresis	1 (1.6%) [1]
Hemiparesis	1 (1.6%) [1]
Papilloedema	1 (1.6%) [1]
Syncope	1 (1.6%) [1]
Psychiatric disorders	1 (1.6%) [1]
Hallucination	1 (1.6%) [1]
Renal and urinary disorders	1 (1.6%) [1]
Acute kidney injury	1 (1.6%) [1]
Respiratory, thoracic and mediastinal disorders	1 (1.6%) [1]
Dyspnoea	1 (1.6%) [1]
Skin and subcutaneous tissue disorders	1 (1.6%) [1]
Chronic spontaneous urticaria	1 (1.6%) [1]
Vascular disorders	2 (3.2%) [2]
Aortic dissection	1 (1.6%) [1]
Hypertension	1 (1.6%) [1]

N=Number of total subjects

The Data Safety and Outcomes Monitoring Committee (DSOMC) reviewed all adverse events and adjudicated adverse events meeting the adjudication criteria set forth by the DSOMC charter. Adjudicated device-related adverse events and procedure-related adverse events are presented in **Table 5** and **Table 6** respectively. Only one adverse event (procedure-related) was considered serious (Failure to Thrive in **Table 6** below).

Table 5. Device-related Adverse Events (DSOMC Adjudicated)

System Organ Class **Preferred Term**	**n/N (%) [# Events]**
Nervous system disorders	1/62 (1.6%) [1]
Facial paralysis	1/62 (1.6%) [1]

N=Number of total subjects

Table 6. Procedure-related Adverse Events (DSOMC Adjudicated)

System Organ Class **Preferred Term**	**N=62** **# Subjects (%) [# Events]**
Eye disorders	2 (3.2%) [2]
Visual impairment	1 (1.6%) [1]
Visual acuity reduced	1 (1.6%) [1]
Injury, poisoning and procedural complications	10 (16.1%) [11]
Radiation alopecia	4 (6.5%) [4]
Procedural nausea	2 (3.2%) [2]
Vascular access site hematoma	1 (1.6%) [1]
Procedural headache	1 (1.6%) [1]
Urinary tract procedural complication	1 (1.6%) [1]
Vascular access site pain	1 (1.6%) [1]
Vascular access site pseudoaneurysm	1 (1.6%) [1]
Metabolism and nutrition disorders	1 (1.6%) [1]
Failure to thrive	1 (1.6%) [1]
Musculoskeletal and connective tissue disorders	1 (1.6%) [1]
Neck pain	1 (1.6%) [1]
Nervous system disorders	5 (8.1%) [6]
Procedural headache	3 (4.8%) [3]
Headache	1 (1.6%) [1]
Paresthesia	1 (1.6%) [1]
Cerebral vasoconstriction	1 (1.6%) [1]
Respiratory, thoracic and mediastinal disorders	1 (1.6%) [1]
Dyspnea	1 (1.6%) [1]

N=Number of total subjects

Probable Benefit

The pre-specified primary probable benefit outcome of the PHIL dAVF study was defined as angiographic occlusion of the pre-specified target vessel intended for treatment at procedure following completion of the first PHIL treatment procedure. Angiographic occlusion of the pre-specified target vessel was defined as complete cessation of flow at the point of embolic agent administration at the target vessel. Angiographic occlusion of the pre-specified target vessel was adjudicated by the Core Lab and the probable benefit results shown are based on all 62 FAS subjects. The complete occlusion (100%) of the dAVF was not evaluated post-operative; therefore, the long-term stability of the PHIL embolization procedure is unknown nor whether patients require further retreatment.

In the FAS population, following completion of the first PHIL treatment, the rate of angiographic occlusion of the

pre-specified target vessel was 96.77% (60/62, LCL 86.28%–UCL 99.81%) for the worst-case analysis and 98.39% (61/62, LCL 88.98%–UCL 99.99%) for the best-case analysis (**Table 7**), as adjudicated by the Core Lab. Best- and worst- case analyses were conducted by considering illegible angiographic imaging as a success and failure, respectively.

Table 7. Primary Measured Outcome: Probable Benefit, FAS Population

Probable Benefit: Angiographic occlusion of the pre-specified target vessel intended for treatment at procedure following completion of the first PHIL treatment procedure	**n/N (%)**	**98.75% Exact CI (LCL, UCL)**
Worst-case analysis*	60/62 (96.77%)	(86.28, 99.81)
Best-case analysis*	61/62 (98.39%)	(88.98, 99.99)

*Worst-case analysis: Illegible angiographic imaging is considered as a failure for probable benefit assessment.
*Best-case analysis: Illegible angiographic imaging is considered as a success for probable benefit assessment.
N=Number of total subjects

Secondary Measured Outcomes

Secondary measured outcomes analyzed on the FAS population are summarized in **Table 8.**

Table 8. Secondary Measured Outcomes, FAS Population

Secondary Measured Outcome	**n/N (%)[+]**
Neurological death or ipsilateral stroke within the first 30 days following completion of all PHIL treatments	0/62 (0.00%)
Angiographic occlusion of the pre-specified target vessel intended for treatment at procedure following completion of **all** PHIL treatment procedures*	60/62 (96.77%)
New onset or worsening of permanent morbidity at 6 months	0/62 (0.00%)
New onset of intracranial hemorrhage at 6 months	0/62 (0.00%)
New onset of cranial nerve palsy at 6 months	1/62 (1.61%)
Clinically significant technical events during the PHIL embolization procedure(s)**	0/62 (0.00%)
Reflux of embolic material	0/62 (0.00%)
Migration of the embolic material	0/62 (0.00%)
Catheter entrapment	0/62 (0.00%)
Catheter damage	0/62 (0.00%)
Vessel dissection	0/62 (0.00%)
Device-related adverse events (AEs) at procedure and ≤ 30 days	1/62 (1.61%)
Device-related mortality at procedure and ≤ 30 days	0/62 (0.00%)
Procedure-related AEs[$]	18/62 (29.03%)
Complications of arterial puncture	2/62 (3.23%)
Contrast-induced nephropathy	0/62 (0.00%)
Radiation-induced injuries	4/62 (6.45%)
Renal and anesthesia-related complications	6/62 (9.68%)
Other^	7/62 (11.29%)
New onset of device/procedure-related neurological deficit or AE, or worsening of a previous neurological complaint, disorder, deficit or AE unresolved at 6-month follow-up even if not associated with a change in mRS	0/62 (0.00%)

[+]Rates represent the rate of subjects with events
*Worst-case analysis occlusion rate reported in the table
[$]22 events occurred in 18 subjects
^Other procedure-related AEs included headaches, non-clinically significant vasospasm, neck soreness and urinary

bleeding.
**Clinically significant technical event is defined as technical event that led to any adverse events.
N=Number of total subjects

Additional Outcomes

The number of PHIL procedures required to treat the fistulas at 6-month follow-up is shown in **Table 9**. The result represents the number of separate PHIL procedures (separated by time) performed in the study.

Table 9. Number of PHIL Procedures Required to Treat the Fistulas, FAS Population

Number of PHIL Procedures	n/N (%)
1	55/62 (88.7%)
2	6/62 (9.7%)
3	1/62 (1.6%)

In addition, information on the adjunctive treatment is summarized in **Table 10**. Throughout the study, adjunctive device was used in eight subjects.

Table 10. Unplanned Adjunctive Treatments, FAS Population

Adjunctive Treatment	n/N (%)
Overall adjunctive treatment	8/62 (12.9%)
Coiling	6/62 (9.7%)
Non-PHIL liquid embolic	2/62 (3.2%)

Lastly, technical events reported in the PHIL dAVF study are summarized in **Table 11**. The three technical events were not associated with any adverse events and were not considered clinically significant by the DSOMC.

Table 11. Technical Events, FAS Population

Technical Event	n/N (%)	Did Event Lead to an AE
Migration of embolic material	2/62 (3.2%)	No
DMSO syringe malfunction	1/62 (1.6%)	No

Conclusion

The PHIL dAVF clinical study demonstrated the safety and probable benefit of the PHIL device for the treatment of dAVFs.

SYMBOLS

	Lot Number
	Catalog Number
	Contents
	Sterilized Using Steam or Dry Heat
	For Prescription Use Only
	Keep Away from Sunlight
	Do Not Reuse
	Consult Instructions for use
	Do not use if package is damaged
	Medical Device
	Unique Device Identifier
	2 PHIL Syringes, 1 Universal Adaptor
	Caution
	Use-by Date
	Manufacturer
	Country and Date of Manufacture
	Keep dry
	MR Safe
	Non-pyrogenic
	Single sterile barrier system
	1 PHIL Syringe, 1 DMSO Syringe, 1 Universal Adaptor

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