# A Retrospective Data Collection Evaluating Portal Vein Access Sets For Transjugular Intrahepatic Portosystemic Shunt (TIPS) Procedures

**Short Title:** Achieving Portal Access with Scorpion Post-Approval Study 2 (APASS2)

**Protocol Number:** SCPVA02

**Revision:** B

**Document Date:** 20 September 2024

**Sponsor:** Argon Medical Devices, Inc.
7800 Dallas Pkwy, Suite 200
Plano, Texas 75024

## PROTOCOL REVISION HISTORY

The protocol shall be amended as needed.

| Version | Date | Description of Change | Brief Rationale | eQMS Workflow # |
|---|---|---|---|---|
| A | 13 Mar 2024 | Initial release | N/A | Electronic signature #CP-2024-001 |
| B | 18 Sep 2024 | 1. Update technical success, procedural success, and PVA time definitions<br>2. Update TIPS procedure window start date and enrollment cap wording<br>3. Specify additional datapoints within procedural information and follow up information that will be collected | 1. Clarify primary and secondary endpoint definitions on how the data will be collected<br>2. Site had data prior to March 1, 2022 so TIPS procedure start window was updated to February 1, 2022 plus the enrollment cap was reworded to at least 50 eligible cases<br>3. Clarify what datapoints will be collected in the raw data | CR #05204 |

## SPONSOR APPROVAL PAGE

| | |
|---|---|
| **Protocol Title:** | A Retrospective Study to Assess the Safety and Efficacy of Scorpion for Transjugular Intrahepatic Portosystemic Shunt (TIPS) Procedures |
| **Protocol Number:** | SCPVA02 |
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| **Document Date:** | 20 September 2024 |

**Sponsor's Statement**

This document has been reviewed and approved by the individuals listed below or their authorized representatives.

| DEPARTMENT | NAME / TITLE |
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| **Clinical Affairs** | Danyel Crout Carr<br>Sr. Director, Clinical Affairs |
| **Medical Affairs** | Pete Stibbs<br>VP, Global Medical Affairs |
| **Regulatory Affairs** | Scott Bishop<br>VP, Regulatory Affairs |
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| **Marketing** | Jenson Winkler<br>Product Manager |

*Note: Signature approvals are captured in the Sponsor's eQMS*

## INVESTIGATOR STATEMENT OF COMPLIANCE

| | |
|---|---|
| **Protocol Title:** | A Retrospective Study to Assess the Safety and Efficacy of Scorpion for Transjugular Intrahepatic Portosystemic Shunt (TIPS) Procedures |
| **Protocol Number:** | SCPVA02 |
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**INVESTIGATOR'S STATEMENT**

I have read this protocol and agree to conduct and/or supervise the Study in accordance with this Clinical Investigational Plan, the device Instructions for Use (IFU), and in accordance with accepted Good Clinical Practice principles.

I agree to obtain Institutional Review Board (IRB) approval prior to initiation of the Study and ensure prompt reporting to the IRB of any changes in research activity.

I agree to ensure that all associates, colleagues, and other Study personnel assisting in the conduct of the Study are informed about their obligations in meeting the above commitments.

I agree to maintain adequate and accurate records and to make those records available for inspection to both Argon Medical Devices Inc. and applicable regulatory bodies in accordance with local and national regulations.

My signature below attests that I have read and understood the contents of this Protocol. I hereby confirm and agree to comply with the clinical investigational plan as presented including all statements regarding confidentiality, and according to local legal and regulatory requirements, applicable U.S. Federal Regulations, and International Standards Organization (ISO) Good Clinical Practice (GCP) guidelines.

Investigator Name (print)

Investigator Signature Date (dd/MMM/yyyy)

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## 1. ABBREVIATED TERMS AND DEFINITIONS

| | |
|---|---|
| ADE | Adverse Device Effect |
| AE | Adverse Event |
| CIP | Clinical Investigation Plan |
| $CO_2$ | Carbon Dioxide |
| F | French |
| ga | Gauge |
| HPVG | Hepatic Venous Pressure Gradient |
| HV | Hepatic Vein |
| ICE | Intracardiac Echocardiography |
| ICU | Intensive Care Unit |
| IFU | Instructions for Use |
| IRB | Institutional Review Board |
| ISO | International Standards Organization |
| ISO 14155 | Clinical Investigation of Medical Devices for Human Subjects - Good clinical practice |
| MELD | Model for End-Stage Liver Disease |
| mGy | Milligray |
| mL | Milliliter |
| mm Hg | Millimeters of Mercury |
| MPA | Multipurpose Angiographic |
| PEEK | Polyether Ether Ketone |
| PI | Principal Investigator |
| PTFE | Polytetrafluoroethylene |
| PV | Portal Vein |
| PVA | Portal Vein Access |
| PVPC | Portal Vein Puncture-related Complications |
| SAE | Serious Adverse Event |
| TIPS | Transjugular Intrahepatic Portosystemic Shunt |
| US | United States |

# 2. KEY ROLES AND CONTACT INFORMATION

## 2.1. Sponsor Study Staff Contact Information

| | |
|---|---|
| **Sponsor:**<br>**Sponsor Address:** | Argon Medical Devices Inc.<br>7800 Dallas Pkwy, Suite 200<br>Plano, Texas 75024<br>Phone: 1-800-927-4669 |
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## 2.2. Lead Principal Investigator Contact Information

| | |
|---|---|
| **Lead Principal Investigator:** | Peter J Park, MD |
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## 3. SYNOPSIS

| | |
|---|---|
| **Protocol SCPVA02** | |
| Title | A Retrospective Study to Assess the Safety and Efficacy of Scorpion for Transjugular Intrahepatic Portosystemic Shunt (TIPS) Procedures |
| Short title | **A**chieving **P**ortal **A**ccess with **S**corpion Post-Approval **S**tudy 2 (APASS2) |
| Protocol Number | SCPVA02 |
| **Study Device** | |
| Name | Scorpion® Portal Vein Access Set<br>Scorpion®X Portal Vein Access Set |
| Intended Use | The Scorpion and Scorpion X Portal Vein Access Sets are intended for transjugular liver access in diagnostic and interventional procedures. |
| **Sponsor** | |
| Name | Argon Medical Devices Inc. |
| Contact Details | 7800 Dallas Pkwy, Suite 200<br>Plano, Texas 75024<br>Phone: 1-800-927-4669<br>Fax: 903-677-9396 |
| **Investigational Sites** | |
| Number of Sites | 1 site |
| Location of Sites | United States (US) |
| **Clinical Study Design** | |
| Design | Retrospective, single center, single arm design. |
| Objective | To evaluate the safety and effectiveness of Scorpion Portal Vein Access Kits for TIPS procedures with the goal of creating the parenchymal tract for indicated interventional procedures. Safety, effectiveness, and performance data for the Scorpion Portal Vein Access sets will be collected |
| Hypothesis | No formal statistical hypothesis will be tested |
| Primary Effectiveness Endpoint | Technical success, which is defined as creation of the parenchymal tract between the hepatic vein and an intrahepatic branch of the portal vein confirmed by portogram ($CO_2$/contrast) |
| Primary Safety Endpoint | Major complications associated with the device/procedure, which are defined as complications resulting in an unplanned increase in the level of care, prolonged hospitalization, permanent adverse sequelae, or death |
| Secondary Endpoints | • Procedural success defined as successful delivery of the shunt<br>• Device-Related Complications, in the judgment of the Principal Investigator |

| | |
|---|---|
| Exploratory Endpoints | • Portal vein access (PVA) time defined as the time from hepatic vein access to portal vein access<br>• Procedure duration defined as the interval from the first jugular access for TIPS creation to removal of catheters from the subject<br>• Fluoroscopy Time<br>• Change in Model for End-Stage Liver Disease (MELD) and Child-Pugh score<br>• Radiation dosage measured in Air kerma (mGy)<br>• Contrast volume used<br>• Length of hospital stay and number of ICU days<br>• Change in hepatic venous pressure gradient (HPVG) |
| **Clinical Study Population** | |
| Population | All patients who underwent a TIPS procedure between February 1, 2022, and February 29, 2024 will be considered for enrollment in the study. Procedural data will be collected from patient medical records through hospital discharge.<br><br>Each TIPS procedure that was completed using one of the Scorpion Portal Vein Access Kits will be considered as an individual case. Cases that meet all inclusion criteria and do not meet any exclusion criteria will be considered eligible for enrollment. |
| Inclusion Criteria | 1. Scorpion or Scorpion X kit introduced into the vasculature as the initial device for portal vein access. |
| Exclusion Criteria | 1. TIPS procedure was not initiated and/or no portion of the kit was introduced into the vasculature.<br>2. Inaccessible medical records. |
| **Statistical Analysis** | |
| Statistical Methodology | Patient demographics and performance parameters will be summarized with mean, standard deviation, median, and range for continuous variables and with frequencies and percentages for discrete variables. Sub-group analysis will be conducted when sample size permits. |

# 4. INTRODUCTION

## 4.1. Background

Portal hypertension is high blood pressure in the portal vein located in the abdomen. The portal vein returns blood from the digestive system to the liver for the purpose of cleaning and filtering waste from the blood. This condition is the most frequent cause of hospitalization, variceal bleed, liver transplantation, and death in patients with cirrhosis.[1]

Elevated pressures in the portal venous system will manifest as abdominal ascites, hepatic hydrothorax, hepatorenal syndrome, portal hypertensive gastropathy and gastro-esophageal varices with or without bleeding, which are markers of decompensation and associated with significant morbidity and mortality.

Transjugular intrahepatic portosystemic shunt (TIPS) is a well-established percutaneous modality for decreasing portal hypertension by creating a shunt through the hepatic parenchyma to connect the hepatic vein to the portal vein. Although the major clinical indications for TIPS include refractory variceal hemorrhage and refractory ascites, the full list of TIPS indications includes:[2]

1. Uncontrollable variceal hemorrhage
2. Current or prior variceal hemorrhage that is not amenable to initial or continued endoscopic therapy
3. Prophylaxis against recurrent variceal bleed in high-risk patients
4. Portal hypertensive gastropathy
5. Refractory ascites
6. Hepatic hydrothorax
7. Budd-Chiari syndrome
8. Hepatopulmonary syndrome
9. Hepatorenal syndrome
10. Decompression of portosystemic collaterals prior to abdominal surgical procedures

Overall, the TIPS procedure is one of the most challenging procedures performed by interventional radiologists, and the most difficult and time-consuming step in the procedure is accessing the portal vein. Many techniques for accessing the portal vein have been described in literature and they fall into three broad categories:

- Fluoroscopically guided TIPS creation with the use of landmarks or portography (wedged hepatic vein portography with $CO_2$ umbilical venography)
- Transabdominal ultrasound – guided placement of a portal vein target via transhepatic or transplenic access to facilitate subsequent fluoroscopically guided access
- Transabdominal intravascular ultrasound (IVUS), or intracardiac echocardiography (ICE) guidance[3]

ICE uses a low-frequency, side-firing intravascular transducer and is more commonly used for intracardiac procedures. However, in this application in can be used to depict the central portion of the liver, which permits visualization of the needle and the PV target without the use of fluoroscopy or contrast medium.

Cam et al.[4] reported that ultrasound-guided PV access and percutaneous PV guidewire placement for fluoroscopic targeting during TIPS creation are associated with shorter procedure and fluoroscopic times and potentially decreased complications. Many of the procedure-related complications of TIPS creation, such as arterial injury, biliary injury, and extracapsular puncture may occur during attempted portal vein access. As the number of needle passes for successful PV access increases, so may the potential for puncture-related complications.

Historically, the most performed technique for portal venous access involved wedge hepatic venography with carbon dioxide to visualize the portal vein followed by passing the needle under fluoroscopic guidance. In the last 10 years, imaging guidance options have evolved beyond traditional wedge carbon dioxide portography to include ultrasound-guided options such as transabdominal, intravascular and intracardiac echocardiography to help with visualization and portal vein cannulation. Portal vein access may require multiple needle passes and is considered the riskiest step in TIPS creation with possible incidence of portal vein puncture-related complications (PVPC).[5] Complications result from inadvertent injury to non-target vessels and include damage to the hepatic artery or extrahepatic portal vein, transcapsular puncture and laceration of the liver capsule, all of which can result in life-threatening hemorrhage.[6]

## 4.2. Prior Investigations

The Rosch-Uchida and Colapinto sets manufactured by Cook Medical (Bloomington, Indiana, US) are two different needle sets currently available and most encountered. A recent systematic review of literature showed that the overall incidence of PVPC with the Cook sets was 3.6%.[6] The procedure duration varies in literature due to protocol differences and imaging techniques used. David et al.[7] reported a mean procedure duration of 86.2 minutes using ultrasound guidance. In a study evaluating time to portal vein access, mean time to portal venous access was statistically significant between conventional fluoroscopy at 46 minutes and intravascular US-guided TIPS at 31 minutes.[8]

In a retrospective study of 15 cases with Scorpion X (Needle model), technical success was achieved in 100% of cases with an average of 2.7 passes, and because of the bi-directional needle, no cases required adjustment to the curvature of the needle.[9]

The APASS prospective study had three cases, but the study was early terminated due to slow enrollment accrual. Two cases were Scorpion, while the remaining one was Cook. Procedural success was achieved in 100% of cases.

### 4.3. Study Rationale

The aim of this study is to collect real-world data on safety, effectiveness, and performance of the Scorpion Portal Vein Access Sets in subjects who underwent a TIPS procedure. The study supports post-market surveillance and will serve to provide clinical data for the initial CE Mark application.

Findings from this study will provide valuable clinical evidence to ensure that Argon's standard Portal Vein Access Sets are in line with state of the art and our established acceptance criteria for safety and performance when used as intended.

## 5. DEVICE DESCRIPTION AND INTENDED USE

### 5.1. General Device Description

There are two models of the Scorpion Portal Vein Access Sets: Scorpion and Scorpion X. The Scorpion model has a stylet as the puncture tool and the Scorpion X model has a 17 ga needle as the puncture tool (**Figure 1**).

**A. Scorpion Nitinol Stylet**

**B. Scorpion X Nitinol Needle**

FIGURE 1. SCORPION PUNCTURE TOOL CONFIGURATIONS

In addition to the puncture tool, each Scorpion set contains an MPA catheter, a stiffening cannula, a cannula sheath, and a PEEK catheter (see **Table 1**). The Scorpion® Portal Vein Access Set does not contain medicinal substances, human, or animal tissues or their derivatives, or other biologically active substances.

The Scorpion set is used to gain access to the hepatic vein and guide the puncture tool (stylet or needle) through the liver parenchyma. The puncture tool makes a pathway between the hepatic vein and the portal vein. The choice of stylet or needle is physician preference based on training and the subject case. This will not have an impact on the endpoints of this clinical study and, as such, there is no requirement that the same number of both models is used during the study.

The Scorpion set is compatible with the 10F Flexor® Check-Flo® Introducer Set manufactured by Cook Medical and is typically in use up to four hours.

Table 1. Components of the Scorpion Sets

| Scorpion | Scorpion X | Function / Description |
|---|---|---|
| 0.040" Nitinol Stylet | 17ga Nitinol Needle | The stylet/needle and PEEK catheter assembly is used to navigate the liver parenchyma and make a pathway from the hepatic vein to the portal vein. |
| 5F PEEK Catheter | 6.2F PEEK Catheter | |
| Spacer Clip | Spacer Clip | The spacer clip is placed between the PEEK Catheter and the stylet/needle when assembled to prevent premature puncture prior to proper orientation with the portal vein. |
| 5F MPA Catheter | 5F MPA Catheter | The MPA catheter is used for angiographic procedures to deliver radiopaque media. |
| 14ga Stiffening Cannula | 13ga Stiffening Cannula | The cannula and cannula sheath assembly is used for bi-directional steering through the liver parenchyma into the hepatic vein to orient toward the portal vein. |
| 7F Cannula Sheath | 8F Cannula Sheath | |

MPA = Multipurpose Angiographic

## 5.2. Indications for Use

The Scorpion Portal Vein Access Sets are intended for transjugular liver access in diagnostic and interventional procedures.

## 5.3. Device Identification and Tracking

As commercially available devices, Scorpion® Portal Vein Access Set and Scorpion®X Portal Vein Access Set were obtained by the site through normal commercial procurement methods and stored and accounted for following site-specific policies.

## 5.4. Instructions for Use

The Scorpion sets will be used in accordance with current Instructions for Use (IFU) included in the device packaging. The manufacturer's IFU for each Portal Vein Access Set contains the following information:

- Complete instructions including storage and handling requirements, preparation for use, pre-use checks, precautions to be taken after use, and disposal.
- Complete summary of the necessary training and experience required for use of these devices.
- Complete description of the procedures involved in the use of these devices.

The Scorpion Portal Vein Access Set are identified with part number and lot number.

Table 2. Scorpion Portal Vein Access Kit Part Numbers

| Part Number | Description |
|---|---|
| TPS005 | Scorpion® Portal Vein Access Set |
| TPS006 | Scorpion®X Portal Vein Access Set |

All components of the Scorpion set are supplied sterile and are intended for single use only. The devices must not be re-sterilized.

# 6. RISK ANALYSIS AND RISK ASSESSMENT

## 6.1. Anticipated Benefits

Safe and effective creation of parenchymal tract between the hepatic vein and an intrahepatic branch of the portal vein.

## 6.2. Risks and Foreseeable Adverse Events and Adverse Device Effects

The following foreseeable adverse events, which are captured in the IFU of these commercially available devices, may be considered as potential risks to patients undergoing TIPS procedures with an Argon Portal Vein Access Set:

- Intraperitoneal hemorrhage or hemoperitoneum
- Puncture site hematoma
- Cardiac arrhythmia
- Cardiac tamponade
- Arteriovenous fistula or other arterial injury
- Arterio-biliary fistula or biliary tract injury
- Extrahepatic Organ Injury
- Capsular Perforation
- Needle/catheter/guidewire fracture
- Foreign body retention

There is no additional risk associated with this clinical study since the patient was treated according to standard of care.

# 7. STUDY OBJECTIVE

The objective of this retrospective data collection is to evaluate the safety and effectiveness of Scorpion portal vein access sets during TIPS with the goal of creating the parenchymal tract for indicated interventional procedures.

## 7.1. Outcome Measurements

The data collected will be used to analyze the following outcome measures:

#### 7.1.1. Primary Outcome

a. Technical success defined as creation of the parenchymal tract between the hepatic vein and an intrahepatic branch of the portal vein and confirmed by portogram

#### 7.1.2. Secondary Outcomes

a. Procedural success defined as successful delivery of the shunt
b. Incidence of procedural complications defined as the total occurrence of complications

## 8. STUDY DESIGN

### 8.1. Overview

The planned sample size is to enroll at least 50 eligible cases at a single center in the United States. Clinical data will be retrospectively collected on eligible cases that underwent attempted TIPS procedures with one of Argon's standard Portal Vein Access Set between February 1, 2022 and February 29, 2024.

The participating center will be identified by a site number, and eligible cases will be sequentially assigned a unique 3-digit study identification (ID) number. The ID number will be a combination of the site number followed by a 2-digit number sequentially assigned based on eligibility (e.g. 101, 102, 103).

### 8.2. Eligibility Criteria

#### 8.2.1. Inclusion Criteria

1. Scorpion or Scorpion X kit introduced into the vasculature as the initial device for portal vein access

#### 8.2.2. Exclusion Criteria

1. TIPS procedure was not initiated and/or no portion of the kit was introduced into the vasculature
2. Inaccessible medical records

## 9. STUDY ENDPOINTS

### 9.1. Primary Endpoints

The primary effectiveness endpoint is technical success defined as creation of the parenchymal tract between the hepatic vein and an intrahepatic branch of the portal vein and confirmed by portogram ($CO_2$/contrast).

The primary safety endpoint is a composite of major complications associated with the procedure or study device and defined as complications resulting in an unplanned increase in the level of care, prolonged hospitalization, permanent adverse sequelae, or death.[10]

### 9.2. Secondary and Exploratory Endpoints

The secondary and exploratory endpoints of this clinical study are outlined in **Table 3**.

Table 3. Overview of Secondary and Exploratory Endpoints

| Endpoint | Description / Definition |
|---|---|
| *Secondary Endpoints* | |
| Procedural success | Successful delivery of the shunt |
| Device-related complications | Incidence of complications related to the device as judged by the Principal Investigator |
| *Exploratory Endpoints* | |
| Portal Vein Access (PVA) time | Time (in minutes) from hepatic vein access to portal vein access |
| Procedure duration | Interval (in minutes) from first jugular access for TIPS creation to removal of catheters from subject |
| Fluoroscopy time | Measured in minutes |
| Change in MELD score<br>Change in Child-Pugh score | Change in score from Baseline Characteristics to Follow Up Data |
| Radiation dosage | Measured in air kerma (mGy) |
| Contrast volume used | Measured in mL |
| Length of Hospital Stay | Measured in days |
| Number of ICU days | Measured in days |
| Change in HPVG | Measured in mm Hg |

MELD = Model for End-Stage Liver Disease; ICU = Intensive Care Unit; HPVG = Hepatic Venous Pressure Gradient

## 10. STUDY PROCEDURES

### 10.1. Informed Consent

Since the data for this retrospective review already exists, we request that the IRB waive the consent requirement. Any patient who has previously refused to participate in a study will not have his or her data included in the study. The data will be de-identified and no personal identifying information will be disclosed or compromised.

### 10.2. Patient Selection

Electronic Medical Records (EMR) will be used to identify patients who underwent a TIPS procedure using Scorpion® Portal Vein Access Set or Scorpion®X Portal Vein Access Set with standard techniques from February 1, 2022, through February 29, 2024, by searching for Current Procedural Terminology (CPT) codes 37182 and 37183 within the study period.

Suitable cases identified during the study period will be evaluated for eligibility. Eligible cases will be assigned a sequential 3-digit number as the case ID. Each TIPS procedure attempt will be considered as an individual case with different case ID. The patient log will be retained at the site and filed with the study records at the conclusion of the study.

## 10.3. Data Collection

For eligible cases, clinical data related to the TIPS procedure will be extracted from the medical records and captured into a Data Collection Tool by trained study staff:

Electronic medical records (Epic, Verona, Wisconsin) and the picture archiving and communication system (PACS) database will be reviewed for patient demographic data, applicable TIPS datapoints, and the primary Argon device used for TIPS procedure. Complications will be categorized according to the Society of Interventional Radiology Quality Improvement guidelines.[10]

### 10.3.1. Baseline Information

Demographics including age, sex, height, weight, race, and ethnicity will be captured. BMI will be calculated using the patient's height and weight. Initial indication for TIPS plus MELD and Child-Pugh Score will be collected. Standard-of-Care imaging will be reviewed.

### 10.3.2. Procedural Information

The information of each eligible case that has gone under the TIPS procedure will be captured. Information such as the following will be collected and recorded:

- Procedure date
- Scorpion® Portal Vein Access Set or Scorpion®X Portal Vein Access Set Used
- Jugular access site
- Sheath used
- Imaging used
- Fluoroscopy time
- Radiation dosage measured in Air kerma (mGy)
- Contrast volume used
- Portal vein access (PVA) time
- Hepatic vein used for access
- Portal vein access site
- Pressure gradient measurements: pre- and post-delivery of stent
- Stent used and stent count
- Presence of residual varices
- Procedure duration
- Technical success
- Procedural success
- Length of hospital stay
- Number of ICU days
- AE assessment

#### 10.3.3. Follow up Information

Follow up information will be collected within 30 days post-procedure. Information such as the following will be collected and recorded:

- Follow up visit date
- MELD and Child-Pugh Score
- Patency assessment
- Clinical assessment including status and evaluation for encephalopathy
- Clinical improvement (Yes, No, Unknown)
- AE assessment

Standard-of-Care imaging (e.g. Doppler Ultrasound) will be reviewed for TIPS patency, if available.

## 11. ADVERSE EVENTS, ADVERSE DEVICE EFFECTS, AND DEVICE DEFICIENCIES

### 11.1. Definitions

An adverse event (AE) is defined as any undesirable clinical occurrence or change from the patient's baseline condition, whether it is considered device related or not.

A serious adverse event (SAE) is defined as any untoward/undesirable adverse experience that results in any of the following outcomes:

a) Death
b) A life-threatening illness or injury
c) Inpatient or prolonged hospitalization
d) A permanent impairment of a body structure or a body function
e) Medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function
f) Congenital abnormality or birth defect

An adverse device effect (ADE) is an adverse event that, when in the judgement of the Investigator has a reasonable time sequence associated with use of the device and it is believed that the device directly caused or contributed to the adverse event.

A device deficiency is defined as an inadequacy of the medical device related to its identity, quality, durability, safety or performance, such as malfunction, misuse or use error and inadequate labeling.

### 11.2. Reporting

This investigation is performed using marketed product thus requiring reporting of device-related serious adverse events and deficiencies to the manufacturer via Argon's policy and procedures for complaints and issues handling which is implemented for all products as part of our mandated post market vigilance. Due to the retrospective approach, incidents may have already been reported as part of the hospital's routine.

The collection of adverse events in this study will be limited due to the retrospective nature of the design. Adverse events that will be captured in this study are those believed to be consistent with commercially available TIPS devices. As such, only procedure-related complications will be captured from the medical records and recorded in the study database which may occur at any time during the procedure or within 30 days following the procedure.

Each adverse event will be assessed by the Investigator for severity, seriousness, relationship to the device/procedure, action taken, and outcome. Events will be categorized as defined per Society of Interventional Radiology guidelines.[10]

Table 4. SIR Standards of Practice Committee Classification of Complications by Outcome

| | |
|---|---|
| **Minor Complications** | A. No therapy, no consequence.<br>B. Nominal therapy, no consequence; includes overnight admission for observation only. |
| **Major Complications** | C. Require therapy, minor hospitalization (< 48 hours).<br>D. Require major therapy, unplanned increase in level of care, prolonged hospitalization (> 48 hours).<br>E. Permanent adverse sequelae<br>F. Death |

### 11.3. Procedure-related Complications

Based on state of the art for TIPS procedures and similar devices, the following adverse events may be considered procedure-related complications:

- Hepatic encephalopathy
- Infection/Sepsis
- Liver failure
- Contrast induced nephropathy
- Allergic reaction to contrast utilized intra-procedurally
- Adverse reactions associated with administration of general anesthesia or conscious sedation
- Death

## 12. STATISTICAL CONSIDERATIONS

### 12.1. General

All data processing, analyses, and reporting will be performed by an independent biostatistician who otherwise is not involved in the chart review or data collection. The analysis will be conducted using SAS (PC Version 9.4 or higher).

### 12.2. Sample Size Determination

No formal sample size calculation was performed. All eligible cases will be enrolled in the study. Per preliminary estimation and historical sales report, we anticipate that there will be at least 50 cases for this study at 1 clinical site in the US.

### 12.3. Analysis Population

Due to the nature of this retrospective study, all eligible cases will be analyzed for safety and effectiveness on an 'as-treated' basis.

### 12.4. Statistical Analyses

Unless otherwise specified, for continuous variables, descriptive statistics will include the number of patients/procedures, mean, standard deviation, median, minimum, and maximum values. Categorical variables will be summarized using frequency and percentages. All comparative tests are 2-sided with the confidence level set to 95%.

Given the retrospective nature of this protocol, there may be missing or incomplete data, thus not all may be available for all patients. Unless otherwise stated, missing data will be handled as it is, except for dates that are required for calculating event time, the partial dates will have either '01' or 'Jan' imputed with an exception for dates related to the event where the date closest to the last event (visit date, procedure date, etc.) should be used rather than arbitrary '01' of that month and year.

The analytical unit is TIPS procedure. No formal statistical hypothesis will be tested for this single-arm study.

Sub-group analysis (e.g. by gender, age group, or Portal Vein Access Set type) may be conducted if the sample size in each subgroup is sufficient. Student's t-test will be employed for continuous variables and Pearson's chi-square test for categorical variables.

## 13. QUALITY CONTROL AND QUALITY ASSURANCE

### 13.1. Data Entry and Quality Assurance

Each Investigator or appropriately trained designee shall document the clinical data into the electronic data capture system. Investigators will provide all applicable clinical data and documentation to the sponsor. The data required for this protocol will be collected from patient medical records (Epic Systems, Verona, Wisconsin) and recorded on a Data Collection Tool.

All data and information collected will be considered confidential. All data used in the analysis and summary will be anonymous, and without reference to specific patients. Files will be kept in a locked area with restricted access to authorized personnel or designee, the Investigator, site research staff, and authorized regulatory authorities.

### 13.2. Monitoring

Monitoring may be performed by the Sponsor for clinical quality assurance based on random sampling. During data collection, the Investigator shall permit the monitor to verify the progress of data collection as frequently as necessary.

The Investigator/institution will permit direct access to source data and documents for data-related monitoring and, if applicable, audits, and regulatory inspections to be performed.

### 13.3. Audits

Data may be reviewed by the Sponsor's Quality Assurance Department or an independent designee and/or by Regulatory Authorities. This implies that auditors/inspectors will have the right to inspect the site at any time during and/or after completion of the data collection and will have access to source documents including the patient's file and local standard operation procedures (SOPs). By participating in this data collection, Investigator agrees to this requirement.

### 13.4. Patient Confidentiality

Only de-identified data will be collected in the study database. Personal information will be treated as strictly confidential and will not be made publicly available. For any data transfer, measures will be taken to protect patient data against disclosure to unauthorized third parties. Every precaution will be taken to protect the patient privacy and confidentiality of their personal information. All data used in the analysis and summary will be anonymous, and without reference to specific patients.

### 13.5. Institutional Review Board

The Institutional Review Board (IRB) will review and approve the study protocol, and protocol amendments if applicable. After approval by the IRB, documentation of approval will be sent to Argon Medical and maintained with the study records.

### 13.6. Early Termination of Study

For reasonable cause, either the investigator or the Sponsor, may terminate the investigator's participation in this protocol. In addition, the Sponsor may terminate the Protocol at any time upon immediate notice for any reason.

## 14. DATA MANAGEMENT

### 14.1. Record Retention

The investigator must retain all study records until notified by the Sponsor that they are no longer to be retained. The investigator will also notify the Sponsor in the event he/she relocates, or for any reason desires to dispose of the records.

### 14.2. Publication Policy

Argon Medical Devices recognizes the importance of communication of medical protocol data and encourages the publication of such data in reputable scientific journals and the presentation of such data at scientific seminars and conferences.

Any proposed publication of presentation of the data generated from this study must be provided to Argon Medical Devices for timely review in accordance with the terms of the agreement. Argon Medical Devices shall not, in its scientific publications or promotional material, quote from publications by the investigator without full acknowledgement of the source.

## 15. ETHICAL CONSIDERATIONS

This retrospective clinical study will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and in accordance with applicable laws and regulations including ISO 14155 GCP standard.

The investigator is responsible for obtaining approval of this clinical study from the relevant IRB at his associated institution and is responsible for complying with requirements imposed by their IRB and/or regulatory authority. Furthermore, the investigator will ensure that local regulations concerning data protection are followed.

## 16. REFERENCES

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