A Prospective, Multicenter, Randomized Study Evaluating Portal Vein Access Sets During Transjugular Intrahepatic Portosystemic Shunt (TIPS) Procedures

Short Title: Achieving Portal Access with Scorpion Post-Approval Study (APASS)

Protocol Number: SCPVA01
Revision: C
Document Date: 10 May 2023

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

ClinicalTrials.gov Identifier: NCT05765253

PROTOCOL REVISION HISTORY

The protocol shall be amended as needed throughout the clinical study. The amendments to the protocol shall be notified to, or approved by, the IRB and regulatory authorities, as required.

For non-substantial changes [e.g., minor logistical or administrative changes, change of monitor(s), telephone numbers] not affecting the rights, safety and well-being of human subjects or not related to the clinical study objectives or endpoints, a simple notification to the IRB and, where appropriate, regulatory authorities may be sufficient. The version number and date of amendments shall be documented.

Version	Date	Description of Change	Brief Rationale	eQMS Workflow #
A	13 Mar 2023	Initial release	N/A	Electronic signature #CP-2023-001
B	04 Apr 2023	1. Clarify exclusion criteria (#6 & #7) 2. Add/clarify procedure-related data points	1. Only active or uncontrolled hepatic encephalopathy and portal vein thrombosis of the main target portal vein will be excluded. 2. Ensure collection of required procedural data	CR02138
C	10 May 2023	1. Update secondary endpoint “procedure-related complication” to “device-related complication” within Synopsis 2. Remove Duplex Ultrasound as one of the options for Imaging assessment in Section 8.2 3. Add/clarify following Assessments: Randomization, Concomitant Medications, and Study Exit	1. Synopsis was in error and did not match the Section 6.4.3 Table 5 Overview of Secondary and Exploratory Endpoints 2. This was included with CT or MRI Imaging in error and did not match the Section 8.1 Table 6 Schedule of Assessments 3. Ensure Assessment properly noted in Section 8.1 Table 6 Schedule of Assessments	CR02285

SPONSOR APPROVAL PAGE

Protocol Title:	A Prospective, Multicenter, Randomized Study Evaluating Portal Vein Access Sets During Transjugular Intrahepatic Portosystemic Shunt (TIPS) Procedures
Protocol Number:	SCPVA01
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Sponsor's Statement

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

DEPARTMENT	NAME / TITLE
Clinical Affairs	Danyel Crout Carr Director, Clinical Affairs
Medical Affairs	Pete Stibbs VP, Global Medical Affairs
Regulatory Affairs	Scott Bishop Director, Regulatory Affairs
Quality Assurance	Don Kirkland Director of Quality Operations
Marketing	Cheyenne Ware Product Manager

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

PRINCIPAL INVESTIGATOR SIGNATURE PAGE

Protocol Title:	A Prospective, Multicenter, Randomized Study Evaluating Portal Vein Access Sets During Transjugular Intrahepatic Portosystemic Shunt (TIPS) Procedures
Protocol Number:	SCPVA01
Revision:	C
Document Date:	10 May 2023

INVESTIGATOR'S STATEMENT

I have read this protocol and agree to conduct the clinical study in accordance with the design and specific provisions outlined herein. I understand the protocol, and I understand I am solely responsible to ensure the study is conducted in accordance with Good Clinical Practices (GCPs), applicable country regulations, the Declaration of Helsinki, and the signed clinical study agreement with Sponsor. I will conduct this study as outlined therein and will make reasonable effort to complete the study within the period designated by the Sponsor.

I will provide copies of the protocol and all pertinent information to all individuals who will assist in the conduct of this study. I will discuss this material with them to ensure they are fully informed regarding the device and the conduct of the study.

I will fulfill the requirements of my Institutional Review Board (IRB), or other oversight committee, to ensure complete and continual oversight of this clinical study. I will use an Informed Consent Form approved by the Sponsor and my reviewing IRB.

I agree to report all information or data in accordance with the protocol and I agree to report any serious adverse events, device related adverse events, or procedure related adverse events as defined in this protocol to the Sponsor and comply with all adverse event reporting requirements of my reviewing IRB. I agree to permit the Sponsor, its authorized representatives, my reviewing IRB, and any regulatory authority/body access to all records relating to the clinical study.

My signature below attests that I have read and understood this protocol, and its associated amendments or attachments, and will accept respective revisions or amendments provided by the Sponsor.

Principal Investigator Name (print)

Signature Date

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ABBREVIATIONS AND ACRONYMS

ADE	Adverse Device Effect
AE	Adverse Event
CBC	Complete Blood Count
CIP	Clinical Investigation Plan
CFR	Code of Federal Regulations
CMP	Comprehensive Metabolic Panel
CO_2	Carbon Dioxide
COV	Close-out Visit
CRO	Contract Research Organization
CSA	Clinical Study Agreement
CSR	Clinical Study Report
CT	Computed Tomography
CV	Curriculum Vitae
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
EU	European Union
F	French
FDA	Food and Drug Administration
ga	Gauge
HIPAA	Health Insurance Portability and Accountability Act of 1996
HPVG	Hepatic Venous Pressure Gradient
HV	Hepatic Vein
ICE	Intracardiac Echocardiography
ICF	Informed Consent Form
ICU	Intensive Care Unit
IFU	Instructions for Use
INR	International Normalized Ratio
IRB	Institutional Review Board
ISF	Investigator Site File
ISO	International Standards Organization
ISO 14155	Clinical Investigation of Medical Devices for Human Subjects - Good clinical practice
IVUS	Transabdominal Intravascular Ultrasound
LAR	Legally Authorized Representative
MELD	Model for End-Stage Liver Disease
mGy	Milligray
mL	Milliliter
mm Hg	Millimeters of Mercury
MPA	Multipurpose Angiographic
MRI	Magnetic Resonance Imaging
PD	Protocol Deviation

PEEK	Polyether Ether Ketone
PI	Principal Investigator
PT	Prothrombin Time
PTFE	Polytetrafluoroethylene
PV	Portal Vein
PVA	Portal Vein Access
PVPC	Portal Vein Puncture-related Complications
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SIV	Site Initiation Visit
TIPS	Transjugular Intrahepatic Portosystemic Shunt
TMF	Trial Master File
US	United States
USADE	Unanticipated Serious Adverse Device Effect

1. KEY ROLES AND CONTACT INFORMATION

1.1. Sponsor Study Staff Contact Information

Sponsor: **Sponsor Address:**	Argon Medical Devices Inc. 7800 Dallas Pkwy, Suite 200 Plano, Texas 75024 Phone: 1-800-927-4669
Sponsor Contact: **Phone:** **Email:**	Danyel Crout Carr, Director of Clinical Affairs 469-731-1421 Danyel.carr@argonmedical.com
Contract Research Organization (CRO) **CRO Address:**	Avania LLC. 100 Crowley Drive, Suite 210 Marlborough, MA 01752

1.2. Lead Principal Investigator Contact Information

Lead Principal Investigator:	Venkatesh P. Krishnasamy, MD
Institution:	New York Presbyterian – Columbia University Medical Center, Department of Radiology
Telephone:	330-701-6765
Email:	vpk2113@cumc.columbia.edu

1.3. Principal Investigator Contact Information

Each investigational site will have one physician designated as Principal Investigator (PI). Any other physicians involved in the study will be documented and referred to as a Sub-Investigator.

A current list of all investigational sites and Principal Investigators (including their roles, responsibilities, and qualifications) will be maintained separately from the protocol within the Trial Master File (TMF).

2. SYNOPSIS

Protocol SCPVA01	
Title	A Prospective, Multicenter, Randomized Study Evaluating Portal Vein Access Sets During Transjugular Intrahepatic Portosystemic Shunt (TIPS) Procedures
Short title	**A**chieving **P**ortal **A**ccess with **S**corpion Post-Approval **S**tudy (APASS)
Protocol Number	SCPVA01
Investigational Device	
Name	Scorpion® Portal Vein Access Set 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.
Comparator Device	
Manufacturer	Cook Medical Inc.
Name	Rösch-Uchida Transjugular Liver Access Set Ring Transjugular Intrahepatic Access Set
Indication for Use	The Rösch-Uchida Transjugular Liver Access Set and Ring Transjugular Intrahepatic Access Set is intended for transjugular liver access in diagnostic and interventional procedures.
Sponsor	
Name	Argon Medical Devices Inc.
Contact Details	7800 Dallas Pkwy, Suite 200 Plano, Texas 75024 Phone: 1-800-927-4669 Fax: 903-677-9396
Investigational Sites	
Number of Sites	Up to 6 investigational sites
Location of Sites	United States (US)
Clinical Study Design	
Design	This is a prospective, multicenter, randomized, comparative, post-market clinical study
Objective	To evaluate the safety and effectiveness of portal vein access sets during TIPS procedures with the goal of creating the parenchymal tract for indicated interventional procedures. Preliminary safety, effectiveness, and performance data for the Scorpion Portal Vein Access sets will be compared to the Cook Transjugular Liver Access sets.
Hypothesis	No formal statistical hypothesis will be tested
Primary Effectiveness Endpoint	Procedural 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	• Portal vein access (PVA) time defined as the time between initial needle throw to portal vein access confirmed by portogram • Technical success defined as creation of a shunt (stent bridging) between the portal and systemic veins • Number of needle passes • Procedure duration defined as the interval from the first jugular access for TIPS creation to removal of catheters from the subject • Fluoroscopy Time • Device-Related Complications, in the judgment of the Principal Investigator
Exploratory Endpoints	• Change in Model for End-Stage Liver Disease (MELD)/Child-Pugh score • Radiation dosage measured in Air kerma (mGy) • Contrast volume used • Length of hospital stay and number of ICU days • Change in hepatic venous pressure gradient (HPVG)
Arms and Interventions	Two Arms: 1. Procedure with the Scorpion Portal Vein Access Kit 2. Procedure with the Cook Transjugular Liver Access Set Intervention: Subjects will undergo a transjugular intrahepatic portosystemic shunt procedure during which portal vein access will be obtained using the Scorpion (Group 1) or Cook (Group 2) device.
Follow-up Visits	Subjects will be evaluated at: • Screening • TIPS Procedure • Discharge • Day 7 post-procedure • Day 30 post-procedure Evaluation includes the following procedures/assessments: - Medical history - Physical examination - Laboratory values (e.g., complete blood count, comprehensive metabolic panel, prothrombin time, and international normalized ratio) - MELD score - Child-Pugh Score - TIPS Procedure information - Imaging (i.e., ultrasound, computed tomography or magnetic resonance imaging, and echocardiogram) - Adverse events assessment

Total Duration	Estimated enrollment period: Approximately 6 months Study duration for the subject: Approximately 1 month Total study duration: Approximately 7 months
Clinical Study Population	
Population	The study population will consist of subjects undergoing a TIPS procedure for refractory variceal bleeding, refractory ascites and/or hydrothorax. The planned sample size is 60 subjects (30 per group). The planned sample size is empirical, as no formal statistical hypothesis will be tested.
Inclusion Criteria	1. ≥ 18 years of age at the time of the TIPS procedure 2. TIPS procedure initiated for refractory variceal bleeding, refractory ascites and/or hydrothorax 3. Willing and able to provide written informed consent and HIPAA (Health Insurance Portability and Accountability Act) authorization 4. Willing and able to comply with the study procedures and follow up schedule
Exclusion Criteria	1. Known active malignancy 2. MELD score ≥ 18 at time of screening 3. History of polycystic liver disease 4. Active bleeding from any source 5. Pulmonary hypertension, heart failure, severe tricuspid valve dysfunction, right to left cardiopulmonary shunt 6. Chronic, occlusive portal vein thrombosis or complete portal vein thrombosis of the main or target portal vein on prior CT examination 7. Active or uncontrolled hepatic encephalopathy 8. Systemic infection/sepsis 9. Biliary obstruction 10. Uncorrectable coagulopathy 11. Any diminutive or partially thrombosed right portal vein 12. Hepatic vein thrombosis (i.e., no Budd-Chiari syndrome) 13. Known sensitivity to contrast or serious contrast reaction such as anaphylaxis 14. Pregnant women or women who are planning to become pregnant
Statistical Analysis	
Statistical Methodology	Study outcomes will be presented descriptively for each treatment group. In addition, outcomes by baseline demographic and clinical characteristics will be presented. No formal study hypothesis will be tested, however, between-group differences in study endpoints will be assessed with comparative tests, for exploratory purposes.

3. INTRODUCTION

Argon Medical Devices Inc. ("Argon") has developed the Scorpion® Portal Vein Access Set ("Scorpion set") to create a pathway through the liver parenchyma through which an endoprosthesis can be delivered. The objective of this post-market clinical study is to evaluate the safety and effectiveness of Scorpion compared to Cook Transjugular Liver Access Set during transjugular intrahepatic portosystemic shunt procedures. This is a post approval study being conducted in the US and will be used to support initial CE mark approval in the EU.

3.1. 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]

3.2. 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 the paucity of studies available which focus on portal vein access in TIPS interventions, there are few that demonstrate significant differences between the number of needle passes. The data is incomplete because fewer than half of conventional TIPS cases in literature included a recording of the actual number of passes. The Scorpion devices allow for bi-directional positioning of the needle or stylet for precise placement during portal vein puncture.

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]

3.3. 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 undergoing a TIPS procedure. The study supports post-market surveillance and will serve to provide clinical data for the initial CE Mark application. In addition, the study will allow the collection of preliminary clinical performance data compared to competitor devices.

4. STUDY DEVICES

4.1. Investigational Device

4.1.1. Device Manufacturer

Argon Medical Devices Inc. (Plano, Texas, US) is the legal manufacturer of the Scorpion Portal Vein Access Sets. The company address is as follows:

Argon Medical Devices, Inc.
7800 Dallas Parkway, Suite 200
Plano, TX 75024
USA

4.1.2. Regulatory Status and Indications for Use

The Scorpion Portal Vein Access Sets received initial clearance in the US on 15 January 2021 under 510(k) number K202141 and was subsequently modified under 510(k) number K213002. The devices are intended for transjugular liver access in diagnostic and interventional procedures.

In the US, the Scorpion Portal Vein Access Sets are classified as Class II devices. The device common name is catheter introducer per regulation number 21 CFR 870.1340 and product code DYB.

4.1.3. 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

4.1.4. Intended Purpose in the Clinical Study

The Scorpion Portal Vein Access Sets (Scorpion Set) are being used in accordance with the cleared indication for use in this clinical study for transjugular liver access in an interventional procedure.

The intended purpose of the Scorpion set is to create the parenchymal tract between the hepatic vein and an intrahepatic branch of the portal vein during the TIPS procedure in subjects being treated for refractory variceal bleeding, refractory ascites and/or hydrothorax.

4.1.5. Device Instructions for Use

The Scorpion sets will be used in accordance with current Instructions for Use (IFU) included in the device packaging.

The Scorpion Portal Vein Access Kits 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.

4.2. Comparator Device

4.2.1. Device Manufacturer

Cook Medical Inc. is the legal manufacturer of the comparator devices, the Cook Transjugular Liver Access Sets. The company address is as follows:

Cook Medical, Inc.
750 Daniels Way
Bloomington, IN 47404
USA

4.2.2. Regulatory Status and Indications for Use

The Transjugular Liver Access Sets received clearance in the US on 09 March 2018 under 510(k) number K171820. The devices are intended for transjugular liver access in diagnostic and interventional procedures.

In the US, the Transjugular Liver Access Sets are classified as Class II devices. The device common name is catheter introducer per regulation number 21 CFR 870.1340 and product code DYB.

4.2.3. Device Description

The Transjugular Liver Access Sets are comprised of various components that facilitate transjugular access to the liver for the purpose of performing diagnostic and interventional procedures. There are two models of the Transjugular Liver Access Sets: Ring Transjugular Intrahepatic Access Set and the Rösch-Uchida Transjugular Liver Access Set.

Each set includes a core component comprised of a combination of either a stiffening cannula/Teflon catheter or needle stylet/Teflon catheter that facilitates access into the hepatic vasculature and the creation of a pathway into the portal vein. Other components included in some of these sets are a Check-Flo Introducer Set, selective catheters, and wire guides (**Table 3**).

The Ring Transjugular Intrahepatic Access Set's core component is a Colapinto Needle and Catheter Assembly. The Rösch-Uchida Transjugular Liver Access Set's core component is a Stylet and Catheter Assembly that functions coaxially with a stiffening access cannula which provides access and support for the needle stylet/catheter assembly.

TABLE 3. COMPONENTS OF THE TRANSJUGULAR LIVER ACCESS SETS

Ring Transjugular Intrahepatic Access Set	Rösch-Uchida Transjugular Liver Access Set
Ross modified Colapinto Needle	Catheter with 0.038-inch flexible trocar stylet
PTFE Catheter	Stiffening cannula
Flexor® Check-Flo® Introducer Set	PTFE catheter
Dilator	Flexor® Check-Flo® Introducer Set
Torcon® NB Advantage Catheter	Dilator
Van Andel Dilatation Catheter	
Curved Newton Wire Guide	
Amplatz Extra Stiff Wire Guide	

4.2.4. Intended Purpose for the Clinical Study

The Transjugular Liver Access Sets are being used in accordance with the cleared indication for use in this clinical study for transjugular liver access in an interventional procedure.

The intended purpose of the Transjugular Liver Access Set is to create the parenchymal tract between the hepatic vein and the intrahepatic branch of the portal vein during the TIPS procedure in subjects being treated for refractory variceal bleeding, refractory ascites and/or hydrothorax.

4.2.5. Device Instructions for Use

The Transjugular Liver Access Sets will be used in accordance with current Instructions for Use (IFU) included in the device packaging.

Transjugular Liver Access Sets are identified by an order number, reference part number and lot number.

TABLE 4. TRANSJUGULAR LIVER ACCESS SET PART NUMBERS

Order Number	Reference Part Number	Description
G06929	RUPS-100	Rösch-Uchida Transjugular Liver Access Set
G06541	RTPS-100	Ring Transjugular Intrahepatic Access Set (9F Introducer)
G29769	RTPS-100-10.0	Ring Transjugular Intrahepatic Access Set (10F Introducer)

4.3. Required Training and Experience

Investigators participating in this study must be physicians with the appropriate qualifications required to perform a TIPS procedure.[2] At a minimum, Investigators should have performed at least 50 TIPS to demonstrate proficiency with the procedure.

All Investigators must have experience using the Scorpion Portal Vein Access Set and the Cook Transjugular Liver Access Set and be willing to use either set to participate in this study. Given the novelty and recent introduction of the Scorpion sets, Investigators will be required to demonstrate proficiency with the device as part of Argon's certification program.

5. RISK/BENEFIT ANALYSIS

5.1. Potential Clinical Benefits

The study devices facilitate transjugular liver access and portal vein access in TIPS procedures.

The design of the Scorpion set should improve the physician's ability to navigate through the liver parenchyma and reduce the number of attempts necessary to establish access to the portal vein, particularly in diseased livers where irregular anatomy is frequently observed. There are no guaranteed benefits from participation in this study; however, potential clinical benefits may include:

Shorter procedure duration
Shorter fluoroscopic times
Improved navigation control
Reduced needle passes for successful PV access
Decreased puncture-related complications

Information gained from the conduct of this study may be a benefit to physicians and other persons with the same medical condition.

5.2. Risks Associated with Participation in the Clinical Study

This clinical study involves the use and disclosure of health information. It collects only information relevant to the subject's condition and its treatment. Neither the device, nor the procedures and tests conducted, as part of the study are investigational or outside of the standard of care.

The study involves the collection of specific information for research purposes only. Investigators participating in this study are expected to review the indications, contraindications, warnings, precautions, and potential complications described in the IFU. The treating physician is expected to counsel the subject on the risks and benefits specific to the planned treatment and to obtain procedure-related informed consent per institutional policy and procedure.

5.3. Possible Interactions with Concomitant Medical Treatments

Use of additional devices or specific medications is not required as part of this study. If additional devices and/or medications are used per physician discretion in the treatment of a study subject, information on their use will be collected.

5.4. Risk Mitigation

The study is designed to minimize risk through strict selection criteria for investigational sites and Investigators, previous experience with the procedure and devices, and adherence to standard of care with post-procedure evaluations.

Since the study was designed to collect real-world data following use of the portal vein access sets, the risk of providing this health information is believed to be minimal as information directly identifying the subject will not be collected in the study database.

5.5. Benefit-to-Risk Rationale

Any potential risk presented by this clinical study has been minimized and adequate testing, safeguards, and safety monitoring have been incorporated into the clinical study to further minimize and mitigate the risks. Based on the review of all risks, residual risks, and risks resulting from risk mitigation, Argon has determined that the risks to participate are acceptably low. The devices will be used in accordance with their approved indications and standard of care for the subject population is being followed. The potential benefits outweigh the potential risks of using the Scorpion set and participating in this study.

6. DESIGN OF THE CLINICAL STUDY

6.1. Study Objective

The primary objective of this clinical study is to evaluate the safety and effectiveness of portal vein access sets during TIPS with the goal of creating the parenchymal tract for indicated interventional procedures. The study will collect safety and effectiveness data on the Scorpion set which will be compared to data collected on the Cook Transjugular Liver Access Set.

6.2. Study Hypothesis

No formal study hypothesis will be tested, but it is expected that the safety and effectiveness of the Scorpion set are similar to the Cook Transjugular Liver Access Set.

6.3. Study Design

This is a prospective, multicenter, randomized comparative post-market study in the United States (US). The study consists of a one-day intervention in subjects indicated to undergo a TIPS procedure with the aim of collecting real world safety and effectiveness data on the Scorpion set and comparator devices.

The Cook Transjugular Liver Access set was chosen as the comparator device because it is commonly used.

6.4. Study Endpoints

6.4.1. Primary Effectiveness Endpoint

The primary effectiveness endpoint is procedural 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).

Failure to create the parenchymal tract between the hepatic vein and the portal vein with the randomized assignment will be considered a treatment failure. A minimum of 5 needle passes should be attempted before selecting the alternative set.

In the event of a treatment failure, the physician will follow their standard of care procedures and/or use another commercially available product. The patient should be followed in the study through hospital discharge for adverse event monitoring.

6.4.2. Primary Safety Endpoint

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]

6.4.3. Secondary and Exploratory Endpoints

The secondary and exploratory endpoints of this clinical study are outlined in **Table 5**.

TABLE 5. OVERVIEW OF SECONDARY AND EXPLORATORY ENDPOINTS

Endpoint	Description / Definition
Secondary Endpoints	
Portal Vein Access (PVA) time	Time (in minutes) from initial needle throw to portal vein access as confirmed by portogram
Technical success	Creation of a shunt (stent bridging) between the portal and systemic veins
Number of needle passes	Count of needle throws between the hepatic and portal vein to create the parenchymal tract
Procedure duration	Interval (in minutes) from first jugular access for TIPS creation to removal of catheters from subject
Fluoroscopy time	Measured in minutes
Device-related complications	Incidence of complications related to the device as judged by the Principal Investigator
Exploratory Endpoints	

Change in MELD score Change in Child-Pugh score	Change in score from Screening to Day 30
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

6.5. Investigational Sites

The clinical study will be conducted at up to six (6) investigational sites in the US. Sites will have a clinical environment that is representative of the normal conditions of use of the study devices in the target population. The governing Institutional Review Board (IRB) for each participating site will review and approve the protocol, informed consent form, and any other applicable study-related documents prior to enrolling subjects. Additional information on site selection is included in **Section 9.1.**

A site contact list containing contact information for site staff participating in this study will be maintained in the Investigator Site File (ISF) and Trial Master File (TMF).

6.6. Target Enrollment

Approximately 60 subjects (30 per group) indicated to undergo a TIPS procedure who are eligible for the study and agree to participation will be enrolled. Subjects will be enrolled in the study once and have one TIPS procedure.

Each investigational site will be limited to enroll up to 16 subjects.

6.7. Study Duration

The study enrollment period is anticipated to take approximately 6 months. Enrolled subjects are followed for 30 days from the TIPS procedure requiring individual subject participation for approximately 1 month.

Upon completion of all enrolled subjects, study closure, including data analysis and preparation of the clinical study report, is estimated to take up to an additional 6 months.

Total study duration is expected to be approximately 13 months.

7. SUBJECT SELECTION

7.1. Study Population

Subjects undergoing an interventional TIPS procedure for refractory variceal bleeding, refractory ascites, and/or hydrothorax are the target population for this study because cases tend to be non-emergent and scheduled.

The study population represents the intended population for the study devices in terms of age (adult population), sex (both male and female), procedure (transjugular liver access for diagnostic or interventional procedures).

7.2. Inclusion Criteria

Subjects must meet all inclusion criteria listed below to be eligible for enrollment in the study:

1. At least 18 years of age at the time of the TIPS procedure
2. TIPS procedure initiated for refractory variceal bleeding and/or refractory ascites/hydrothorax
3. Willing and able to provide written informed consent and Health Insurance Portability and Accountability Act (HIPAA) authorization, either individually or through a legally authorized representative (LAR)
4. Willing and able to comply with the study procedures and follow up schedule

7.3. Exclusion Criteria

Subjects meeting any of the following exclusion criteria will not be eligible for enrollment in the study:

1. Known active malignancy
2. Model for End-Stage Liver Disease (MELD) score ≥ 18 at time of screening
3. History of polycystic liver disease
4. Active bleeding from any source
5. Pulmonary hypertension, heart failure, severe tricuspid valve dysfunction, right to left cardiopulmonary shunt
6. Chronic, occlusive portal vein thrombosis or complete portal vein thrombosis of the main or target portal vein on prior CT examination
7. Active or uncontrolled hepatic encephalopathy
8. Systemic infection/sepsis
9. Biliary obstruction
10. Uncorrectable coagulopathy
11. Any diminutive or partially thrombosed right portal vein
12. Hepatic vein thrombosis (i.e., no Budd-Chiari syndrome)
13. Known sensitivity to contrast or serious contrast reaction such as anaphylaxis
14. Pregnant women or women who are planning to become pregnant

7.4. Screening

Potential subjects will be identified from non-emergent cases scheduled for a TIPS procedure. All potential subjects will be contacted remotely or in-person by the treating physician (i.e., the PI) or

investigational site staff. During this contact, the PI will verify eligibility of the subject based on the inclusion and exclusion criteria listed in **Sections 7.2** and **7.3**.

Eligibility of potential subjects can be determined from historical laboratory, imaging, and echocardiography results previously taken per standard of care. Labs must have been taken within 30 days prior to the scheduled TIPS procedure. Imaging and echocardiography must have been obtained within 90 days prior to the scheduled TIPS procedure.

Subjects that fail to meet the study screening criteria will be documented as a screen failure on the study screening and enrollment log. Screen failures can be re-screened for study eligibility at the discretion of the Investigator. If a subject is re-screened, a new entry should be recorded on the study screening and enrollment log.

7.5. Informed Consent

Subjects must be fully counseled and informed of their study options, risks, and benefits, and have every opportunity to ask questions about participation in this study. The subject will sign the IRB-approved ICF prior to initiation of the TIPS procedure. For subjects who are unable to provide written consent, consent may be obtained from the subject's legally authorized representative (LAR) per the institution/IRB policies, if allowed.

A copy of the signed statement of informed consent will be provided to the subject and/or LAR.

The PI or qualified designee is responsible for obtaining written informed consent from each subject prior to participation in the clinical study. Should the Investigator delegate the responsibility of conducting the informed consent process to a designee, the Investigator must ensure and document appropriate training of the authorized designee.

If new information regarding the investigational device becomes available and/or changes to the protocol affect a subject's future health and medical care, subjects will be provided with the information and may be asked to sign a revised informed consent form.

The consent process must be documented in the subject's medical record. The original, fully signed consent form will be kept in the site's study file or subject medical record per the institution policy. A fully signed copy must also be provided to the subject and/or LAR.

Subjects that decline participation in the study, do not provide consent, or withdraw consent prior to initiation of the TIPS procedure will be documented as a screen failure on the study screening and enrollment log.

Once the study-specific informed consent form (ICF) is signed, the subject is considered enrolled.

7.6. Subject Identification

Enrolled subjects will be assigned a unique subject identification (ID) number. The subject ID number will be included on all study documentation relating to that subject. If an enrolled subject is withdrawn, the subject ID number will not be re-used in this study.

The investigational site will maintain a study screening and enrollment log linking the assigned study subject ID and the subject's name, alternative identification (e.g., medical record number)

and/or contact information. This log will be maintained only at the investigational site and used during monitoring to assure the correct identity of the subject records used for source document verification.

7.7. Randomization

Randomization will occur after an eligible subject has signed the ICF and prior to initiation of the TIPS procedure. Subjects will be randomly assigned at a 1:1 ratio into one of the two study groups (Scorpion or Cook) via a centralized randomization service.

Once the randomization assignment is received, the physician will determine the model he/she wants to use based on preference, training, and the subject case before beginning the procedure.

7.8. Blinding

This is an open-label study. Blinding is not utilized.

8. STUDY PROCEDURES

8.1. Schedule of Assessments

The procedures and assessments for this study are outlined in the schedule of assessments **(Table 6)**.

Study data will be collected at the following 5 time points: screening, TIPS procedure, hospital discharge, Day 7 follow up, and Day 30 follow up. Subjects will be exited from the study following completion of the Day 30 follow up visit or when they withdraw from the study. More detailed descriptions of the assessments are provided in subsequent sections.

Table 6. Schedule of Assessments

Procedure / Assessment	Screening [1] (Day -90 to Day 0)	TIPS Procedure (Day 0)	Hospital Discharge	Day 7 [7] (± 1 day)	Day 30 (± 7 days)
Informed Consent	X				
Demographic Data	X				
Inclusion/Exclusion Criteria	X				
Medical History	X				
Physical Exam	X		X		X
Labs: CBC, CMP, PT, INR	X[2]		X		X
MELD Score	X		X		X
Child-Pugh Score	X		X		X
Randomization		X[4]			
TIPS procedure		X			
Duplex Ultrasound					X
CT or MRI	X[3]				
Echocardiography	X[3]				
Portogram		X[5]			
AE Assessment		X[6]	X	X	X
Concomitant Medications	X	X	X		X
Study Exit					X[8]

[1] Assessments to be done prior to any study related procedure

[2] Within 30 days prior to the procedure

[3] Preprocedural imaging via standard of care obtained within 90 days prior to the procedure

[4] Randomization must be completed prior to TIPS procedure

[5] At portal vein access and following stent deployment

[6] Adverse Events will be assessed during and after the procedure

[7] Phone call if subject has been discharged, in-person if subject is still in the hospital on Day 7

[8] Study Exit may occur prior to Day 30 as Early Exit

8.2. Screening Assessment (Day -90 to Day 0)

The data captured for the Screening assessment may be gathered over the course of more than one day. However, the data must be obtained within 90 days prior to the TIPS procedure date except as noted below. All data must be documented in the subject's medical record and reported on the appropriate eCRF.

The following activities will be performed for the Screening assessment:

Collection of demographic information

Review of inclusion/exclusion criteria

Collection of clinically significant medical history data, including indications for the procedure

Perform physical examination, including at a minimum:

- Evaluation for hepatic encephalopathy
- Evaluation for presence of ascites

Perform blood draw, if not performed as standard of care within 30 days prior to the procedure, for clinical evaluation of the following labs:

- Complete Blood Count (CBC)
- Comprehensive Metabolic Panel (CMP)
- Prothrombin Time (PT)
- International Normalized Ratio (INR)

Determine MELD Score

Determine Child-Pugh Score

Perform radiologic evaluation to assess hepatic venous patency, portal venous patency, and hepatic arterial patency and excluding potential masses in the liver.

- Computed Tomography (CT) or Magnetic Resonance Imaging (MRI) obtained within 90 days prior to the procedure can be used.

Perform Echocardiography, if not performed as standard of care within 90 days prior to the procedure, to assess cardiopulmonary status

Record Concomitant Medications (only rifaximin, lactulose, and medications which are an anticoagulant, antiplatelet, or diuretic will be recorded)

8.3. TIPS Procedure (Day 0)

The TIPS procedure will be completed in a clinical setting with adequate angiographic equipment and institutional facilities, physiologic monitoring equipment, and support personnel.

Transjugular liver access will be obtained using either the Scorpion set or Cook set per randomization assignment and physician choice of model. The procedure will be performed in accordance with the Scorpion IFU or the Cook IFU. Refer to the current IFU included with the device for techniques and methods for pre-procedure preparation and directions for use. The specific model and treatment details (e.g., access site, access side, stent, etc.) will be determined by the physician based on the condition of the subject.

A minimum of 5 needle passes should be attempted with the initial device assigned through randomization before selecting the alternative manufacturer set. If an alternative manufacturer set is selected, the information will be recorded as part of the study records.

The following procedure data are to be collected and recorded in the subject's medical record or other applicable source documents which will be reported on the appropriate eCRF:

Jugular access site
Number of needle passes
Hepatic vein used for access
Access device used
Portal vein access site
Imaging used
Alternate access sites/techniques used
Sheath used
Stent used, dilated to what size
Pressure gradient measurements: pre- and post-delivery of stent
Presence of residual varices
Adverse events (during and post procedure)
Record Concomitant Medications (only rifaximin, lactulose, and medications which are an anticoagulant, antiplatelet, or diuretic will be recorded)

A portogram must be obtained to confirm creation of the parenchymal tract between the hepatic vein and an intrahepatic branch of the portal vein upon portal vein access and following stent deployment.

8.4. Hospital Discharge

At discharge from the hospital, usually between 1-7 days post TIPS procedure, subjects will be evaluated, and the following activities will be performed:

Physical examination, including at a minimum:
- Evaluation for hepatic encephalopathy
- Evaluation for presence of ascites

Blood draw, for clinical evaluation of the following labs:
- Complete Blood Count (CBC)
- Comprehensive Metabolic Panel (CMP)
- Prothrombin Time (PT)
- International Normalized Ratio (INR)

Determine MELD Score
Determine Child-Pugh Score
Adverse event assessment

Record Concomitant Medications (only rifaximin, lactulose, and medications which are an anticoagulant, antiplatelet, or diuretic will be recorded)

All data must be documented in the subject's medical record and reported on the appropriate eCRF.

8.5. Day 7 (+/- 1 Day) Follow-Up

Adverse events will be assessed seven days (± 1 day) after the TIPS procedure. New adverse events or updates to previously reported adverse events will be documented in the subject's medical record and reported on the appropriate eCRF.

If the subject has been discharged from the hospital, the 7 Day post-procedure follow up will be conducted via phone call with designated study staff.

If the subject remains in the hospital, the 7 Day post-procedure assessment can be done in person by designated study staff.

If the visit window overlaps with hospital discharge, the 7 Day follow up assessment of adverse events should be done as part of hospital discharge.

8.6. Day 30 (+/- 7 days) Follow Up

The 30 Day follow up assessment will be the final study visit and subjects will exit the study after completion of this follow up visit.

Thirty days (± 7 days) after the TIPS procedure, subjects will return to the clinic for a follow up visit during which the following activities will take place:

Physical examination, including at a minimum:
- Evaluation for hepatic encephalopathy
- Evaluation for presence of ascites

Blood draw, for clinical evaluation of the following labs:
- Complete Blood Count (CBC)
- Comprehensive Metabolic Panel (CMP)
- Prothrombin Time (PT)
- International Normalized Ratio (INR)

Determine MELD Score

Determine Child-Pugh Score

Duplex Ultrasound to assess hepatic venous patency, portal venous patency, and shunt status

Adverse event assessment

Record Concomitant Medications (only rifaximin, lactulose, and medications which are an anticoagulant, antiplatelet, or diuretic will be recorded)

8.7. Study Completion

A subject will exit the study after completion of the Day 30 follow up assessments or an event that precludes further participation in the study.

The clinical study will be considered completed when all subjects have exited the study.

8.8. Subject Withdrawal

Subjects have the right to withdraw from the clinical study at any time and for any reason without prejudice to their future medical care by the investigational site staff or institution. If a subject decides to withdraw, all study-specific procedures will be stopped. The data captured for those participants up to the day of withdrawal will be kept in the database, as permitted by national laws and regulations. Whenever possible, the site staff should obtain written documentation from the subject that wishes to withdraw consent for future study activities and contacts. If the site staff is unable to obtain written documentation, all information regarding the subject's withdrawal must be documented in the subject's medical record and reported on the appropriate eCRF.

Withdrawal of a subject from the study may also occur at the discretion of the Principal Investigator or the Sponsor. Reasons for physician and/or Sponsor-directed subject withdrawal include, but are not limited to:

- The subject is not adhering to the study requirements
- Subject enrollment in another study that conflicts with this study's outcomes
- It is in the best interest for the safety or welfare of the subject to be withdrawn

If a subject is amenable at the time of withdrawal, the assessments specified at the final study visit (Day 30) should be collected and documented in the subject's medical record and reported on the appropriate eCRF.

In general, any ongoing or unresolved AEs/SAEs at study end will proceed with standard of care per institution policy.

9. STUDY CONDUCT

9.1. Investigator and Site Selection

9.1.1. Investigator Selection Criteria

The role of the Principal Investigator is to implement and manage the day-to-day conduct of the Study at the investigational site as well as ensure data integrity and the rights, safety and well-being of the subjects involved in the Study. The Principal Investigator is responsible for assuring the Study is conducted according to all protocol requirements and applicable regulations. Refer to **Section 13.3** for more information on Principal Investigator responsibilities.

The following requirements will be evaluated for each Principal Investigator considered for participation in the Study:

- Interest in participating in medical device studies
- Experience conducting clinical studies

- Expertise in performing TIPS procedures
- Availability to oversee study execution
- No conflicts of interest

9.1.2. Site Selection Criteria

The following requirements will be evaluated for each clinical Site considered for participation in the clinical Study:

- Experience of site staff in conducting clinical studies
- Adequate resources (including study coordinator(s), facilities, and administrative support) for the total duration of the study
- Site has the capacity to recruit enough qualified subjects for the study
- Computer with internet access for EDC system (ensuring authorized access in case of firewall)

9.1.3. Investigator Qualifications

A copy of the current medical license and Curriculum Vitae (CV) will be obtained from all Investigators participating in this clinical study as listed on the study delegation log. The CV should be an up to date signed and dated document evidencing any required qualifications and including the Investigator's current position at the investigational site. The signature on the CV must be dated within two years of site activation.

9.2. Site Initiation

Prior to the initiation of this clinical study, each Principal Investigator will approve the protocol by signing the signature page which confirms that the clinical study will be performed in compliance with the current protocol.

A Site Initiation Visit (SIV) will be conducted by the Sponsor or designee in-person or via teleconference to ensure proper training of the investigational site staff participating in the study, including principal Investigators, Sub-Investigators, study coordinators and any other site personnel pivotal to the conduct of the clinical study prior to enrollment of the first study subject. Training will include at least the following: procedures outlined in this protocol, key principles of Good Clinical Practices for Medical Devices (ISO 14155), instructions on completion of the case report forms (eCRF), content of the Investigator Site File, safety reporting, and management of device deficiencies.

Once all required site training and required documentation has been received, reviewed, and approved, the Sponsor or designee will issue written approval of site activation to the Principal Investigator to begin study enrollment.

9.3. Additional Site Staff Activation

Any additional site staff added to the study after the site initiation will receive an individual written approval from the Sponsor or designee once their training and other required documentation have been received, reviewed, and approved.

9.4. Site Staff Training Requirements

Prior to investigational site activation or subsequent involvement in clinical study activities, the Sponsor or designee will provide study training relevant and pertinent to the involvement of the Site staff conducting Study activities.

Study staff training must be documented on a written training record, including at a minimum: the training content, the date of the training, and the trainee's signature.

In the case of non-compliance with the study protocol or other study requirements, study staff may be retrained on pertinent information or documents. Re-training must also be documented on a written training record, including at a minimum: the training content, the date of the training and the trainee's signature.

9.5. Clinical Study Materials and Clinical Study-Specific Equipment

The Sponsor or designee will provide necessary study documentation (e.g., Investigator Site File, eCRF access, Study worksheets, etc.) to the investigational site. The investigational site staff are responsible to acknowledge receipt to the Sponsor or designee after receipt. Computer and internet access is required and is a pre-requisite for site participation.

9.6. Study Device Supply and Accountability

9.6.1. Supply of Devices

The Scorpion Portal Vein Access Kits and the Cook Transjugular Liver Access Sets are marketed products. The devices used in this study will be "off the shelf". No special labeling is required for the devices used in the study. Marketed devices are identified with part and lot numbers included in the device packaging and labeling that will be recorded as part of the study data collection.

9.6.2. Device Storage and Accountability

Devices will be stored according to the requirements described in the current Scorpion set or Cook set IFU. No study-specific device accountability processes are required for this study.

9.6.3. Device Return Procedures

Not applicable. Investigational sites will dispose of used devices in accordance with the labeling and their institution policies.

9.7. Study Closure and Early Termination

9.7.1. Routine Study Closure

When investigational sites are ready to be closed, the Principal Investigator will be notified by the Sponsor or designee. Appropriate notification to IRBs and regulatory authorities, as applicable, will also occur.

A study close-out visit (COV) will be conducted for each site. The purpose of the COV is to collect all outstanding study documents, ensure that the Investigator Site File is accurate and complete, review record retention requirements with the Principal Investigator, and ensure that all applicable requirements are met for the study.

After study closure at the site, the follow up medical care for subjects will continue as per standard of care at the institution.

9.7.2. Early Termination

The Sponsor has the right to terminate the study at any time. Situations that could warrant study termination include, but are not limited to:

- Increased incidence of adverse experiences and/or the severity of such, suggestive of a potential, device-related health hazard
- Insufficient subject enrollment
- Recurrent protocol non-compliance, violations, or deviations
- Inaccurate, incomplete, and/or untimely data recording (>2 business days) on a recurrent basis
- Lack of cooperation with monitoring visits (e.g., failure to adequately prepare for visits, address action items from one visit to the next, or provide access to medical records)

If the Sponsor suspends or terminates the study prematurely, the Sponsor will send a report outlining the circumstances to the IRBs, regulatory authorities as applicable, and all Principal Investigators. Notification of suspension or termination will occur no later than 5 business days after the Sponsor makes the determination. The Principal Investigator should follow subjects per standard of care at the institution.

The Sponsor reserves the right to terminate an Investigator and/or an investigational site for any of the following reasons:

- Repeated failure to secure subject informed consent including protection of personal data prior to enrollment.
- Failure to report safety events in a timely manner.
- Failure to report serious adverse device effects within 24 hours of discovery.
- Repeated protocol deviations.
- Repeated failure to complete case report forms.
- Failure to enroll an adequate number of subjects.

The Principal Investigator may terminate the study at his site at any time. If the Principal Investigator chooses to terminate the study at his site, close out procedures will be arranged on an individual basis after review and consultation by both parties. In terminating the clinical study, the Sponsor and the Principal Investigator will assure that adequate consideration is given to the protection of subjects.

A suspended or terminated Study may not be reinitiated without approval of the reviewing IRBs, and regulatory authority, as applicable.

10. ADVERSE EVENTS, ADVERSE DEVICE EFFECTS AND DEVICE DEFICIENCIES

10.1. Definitions

The definitions and reporting requirements described in this section cover the requirements outlined in ISO 14155:2020.

10.1.1. Adverse Event

An adverse event (AE) is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users, or other persons, whether related to the investigational medical device and whether anticipated or unanticipated.

This definition includes events related to the investigational medical device or the comparator; events related to the procedures involved.

10.1.2. Serious Adverse Event

A serious adverse event (SAE) is an adverse event that leads to any of the following:

a) death
b) serious deterioration in the health of the subject, users or other persons as defined by one or more of the following:
    a. a life-threatening illness or injury, or
    b. a permanent impairment of a body structure or a body function including chronic diseases, or
    c. in-patient or prolonged hospitalization, or
    d. medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function
c) fetal distress, fetal death or a congenital abnormality or birth defect including physical or mental impairment

Planned hospitalization for a pre-existing condition, or a procedure required by the protocol, without serious deterioration in health, is not considered a serious adverse event.

10.1.3. Device Deficiency

A device deficiency is an inadequacy of a medical device with respect to its identity, quality, durability, reliability, usability, safety, or performance.

Device deficiencies include malfunctions, use errors, and inadequacy in the information supplied by the manufacturer including labelling. This definition includes device deficiencies related to the investigational medical device or the comparator.

10.1.4. Serious Health Threat

A serious health threat is a signal from any adverse event or device deficiency that indicates an imminent risk of death or a serious deterioration in the health in subjects, users, or other persons, and that requires prompt remedial action for other subjects, users, or other persons.

This includes events that are of a significant and unexpected nature such that they become alarming as a potential serious health hazard or possibility of multiple deaths occurring at short intervals.

10.1.5. Adverse Device Effect

An adverse device effect (ADE) is an adverse event related to the use of an investigational medical device.

This definition also applies to the comparator medical device and includes:

adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the medical device.

any event resulting from use error or from intentional misuse of the medical device.

10.1.6. Serious Adverse Device Effect

A serious adverse device effect (SADE) is an adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event as defined in **Section 10.1.2**.

10.1.7. Unanticipated Serious Adverse Device Effect

An unanticipated serious adverse device effect (USADE) is a serious adverse device effect which by its nature, incidence, severity, or outcome has not been identified in the current risk assessment.

10.2. Causality

Each adverse event will be classified according to one of four different levels of causality to the study device and/or procedure:

Not related
Possible
Probable
Definite

Not related: relationship to the device, comparator or procedures can be excluded when:

- the event has no temporal relationship with the use of the investigational device or the procedures to application of the investigation device
- the adverse event does not follow a known response pattern to the medical device (if the response pattern is previously known) and is biologically implausible

- the discontinuation of medical device application or the reduction of the level of activation/exposure - when clinically feasible - and reintroduction of its use (or increase of the level of activation/exposure), do not impact on the serious adverse event
- the event involves a body-site or an organ that cannot be affected, the adverse event can be attributed to another cause (e.g., an underlying or concurrent illness/ clinical condition, an effect of another device, drug, treatment, or other risk factors)
- the event does not depend on a false result given by the investigational device used for diagnosis[1], when applicable
- harms to the subject are not clearly due to use error
- the event depends on a false result given by the investigational device used for diagnosis[1], when applicable

Possible: the relationship to the investigational device or comparator or the relationship to the study procedure is weak but cannot be ruled out completely. Alternative causes are also possible (e.g., an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug, or treatment). Cases where relatedness cannot be assessed, or no information has been obtained should also be classified as possible.

Probable: the relationship to the investigational device or comparator or the relationship to the study procedure seems relevant and/or the event cannot reasonably be explained by another cause.

Definite: the adverse event is associated with the investigational device, comparator, or study procedure beyond reasonable doubt when:

- the event is a known side effect of the product category the device belongs to or of similar devices and procedures
- the event has a temporal relationship with investigational device use/application or procedures
- the event involves a body site or organ that
    - the investigational device or procedures are applied to
    - the investigational device or procedures have an effect on
- the adverse event follows a known response pattern to the medical device (if the response pattern is previously known)
- the discontinuation of medical device application (or reduction of the level of activation/exposure) and reintroduction of its use (or increase of the level of activation/exposure), impact on the event (when clinically feasible)
- other possible causes (e.g., an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug, or treatment) have been adequately ruled out
- harm to the subject is due to error in use

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[1] If an investigational device gives an incorrect diagnosis, the subject might, for example, receive an unnecessary treatment and incur all the risks that accompany that treatment, or might be incorrectly diagnosed with a serious disease. In other cases, the subject might not receive an effective treatment (thereby missing out on the benefits that treatment would confer) or might not be diagnosed with the correct disease or condition.

- the event depends on a false result given by the investigational device used for diagnosis[2], when applicable

To establish the relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the serious adverse event.

The Sponsor and the Principal Investigators will distinguish between the serious adverse events related to the study device and those related to a study-specific procedure(s).

An adverse event can be related both to the procedure and the study device. If a causal relationship is established, the adverse event can be classified as an adverse device effect. Complications caused by concomitant treatments not imposed by the protocol are Not related. Similarly, several routine diagnostic or subject management procedures are applied to subjects regardless of the protocol. If routine procedures are not imposed by the protocol, complications caused by them are also considered not related.

In some cases, the event may not be adequately assessed because information is insufficient or contradictory and/or the data cannot be verified or supplemented. The Sponsor and the Principal Investigators will make the maximum effort to define and categorize the event and avoid these situations. Cases where event relatedness cannot be assessed, or no information has been obtained should be classified as “possible”.

10.3. Severity

Adverse events will be classified according to one of three levels of severity. The Investigators will use the following definitions to assess the severity of the adverse event:

Mild: The event does not result in limitation of usual daily activities and/or does not require therapy or only symptomatic therapy is required to treat the injury or illness.

Moderate: The event results in some limitation of usual daily activities and/or requires specific therapy to treat the injury or illness.

Severe: The event interrupts the subject’s usual daily activities, requires specific therapy and/or is incapacitating leading to hospitalization, emergency treatment, life threatening events, or death.

10.4. Anticipated Adverse Events and Adverse Device Effects

Risks associated with the study devices and the related procedure are based on the current state of the art and an objective review of published data.

10.4.1. Anticipated Adverse Events

The following adverse events may occur and are typically associated with the TIPS procedure:

[2] If an investigational device gives an incorrect diagnosis, the patient might, for example, receive an unnecessary treatment and incur all the risks that accompany that treatment, or might be incorrectly diagnosed with a serious disease. In other cases, the patient might not receive an effective treatment (thereby missing out on the benefits that treatment would confer) or might not be diagnosed with the correct disease or condition.

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

10.4.2. Anticipated Adverse Device Effects

Adverse events related to the use of the Scorpion set or Cook Transjugular Liver Access set may include the following:

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

10.5. Reporting Requirements

10.5.1. Site AE Reporting Requirements

Adverse event reporting will start at the time of the TIPS procedure (on Day 0). Adverse events that occur between the signing of the informed consent form and the initiation of the TIPS procedure will not be reported on the eCRF. Underlying diseases are not reported as adverse events unless the condition worsens or re-appears. Adverse event information, including but not limited to the occurrence date, the reported date, procedures, and medications must be recorded in the subject's medical record and reported as part of the study adverse event report. Adverse event information will be collected for all subjects and assessed at every encounter with the subject.

The AE information submitted on the eCRF should include where possible:

Severity of the event
Causality of the event (in relation to the device and/or procedure)
Seriousness of the event
Outcome of the event

Adverse events should be reported by the site on the appropriate eCRF in the EDC system in a timely fashion from discovery by the site.

Serious Adverse Events and Adverse Device Effects must be reported to the Sponsor or designee within 5 working days by the Principal Investigator or designated study staff of discovery.

It is also the responsibility of the Principal Investigator or designee to inform the IRB of adverse events as required per the IRB policies and procedures and, because the study devices are commercially available, Principal Investigators must comply with any institutional user reporting requirements.

10.5.2. Reporting Device Deficiencies

All device deficiencies related to the identity, quality, durability, reliability, safety, or performance of the investigational device shall be documented throughout the clinical study and appropriately managed by the Sponsor. Device deficiencies should be reported by the site by recording them in the EDC within 5 working days of discovery by the site.

It is also the responsibility of the Principal Investigator or designee to inform the IRB of deficiencies, failures, and malfunctions as required per the IRB policies and procedures.

Investigational devices involved in deficiencies, failures, or malfunctions should be retained for return to Argon, where possible. Following the deficiency, failure or malfunction report to Argon, product return information will be provided.

11. STATISTICAL CONSIDERATIONS

11.1. Statistical Design and Methodology

For this post approval study, no formal study hypothesis will be tested. Study outcomes will be presented using descriptive statistics for each treatment group. In addition, outcomes by demographic and clinical characteristics will be presented. For exploratory purposes, between-group differences in study endpoints will be assessed with comparative tests. Statistical analyses will be performed using SAS (SAS Institute, Cary, NC, USA).

11.1.1. Descriptive Results

Unless otherwise specified, for continuous variables, descriptive statistics will include the number of subjects/procedures (N), mean, standard deviation, median, minimum, and maximum values. Categorical variables will be summarized using frequency and percentages.

11.1.2. Exploratory Comparisons

Between-group comparisons will be conducted using Student's t-test for continuous variables and Pearson's Chi-square test for categorical variables. Comparability analysis between two study groups will be first conducted based on demographic and clinical parameters.

Appropriate statistical methods will be employed to explore the correlation and impact of the unbalanced baseline variable, if any, on the study results. When necessary, advanced statistical method such as mixed linear models will be employed to justify the impact.

When sample size permits, the outcomes will be reported for sub-groups such as by gender, age group (≤ 50 years vs > 50 years), type of image used, or operation experience.

11.2. Sample Size

No formal statistical hypothesis is to be tested for this post approval study. The planned sample size is empirical.

11.3. Analysis Sets

11.3.1. Intent-to-Treat Set

The intent-to-treat set will include all procedures/patients with an attempted TIP procedure using a study device regardless it is successful, or an alternative device is needed.

This set will be the base for assessment of technical success rate and overall procedure success rate, as well as overall device safety.

11.3.2. Primary Effectiveness Set

The primary effectiveness set will include procedures/patients who have a successful procedure with only a study device (i.e., no need of an alternative device).

This set will be the base for assessment of cannulation time, fluoroscopy time, procedure duration, as well as other device-specific outcomes.

11.3.3. Safety Population

Safety set will include all procedures/patients defined in the intent-to-treat set.

This set will be the base for the overall study safety assessment.

For study device-specific post-operation safety assessment, only those included in the primary effectiveness set will be used.

Comparability analyses between the two study groups will be conducted on the Intent-to-Treat analysis set.

11.4. Missing Data

Missing data will not be imputed unless otherwise specified.

For categorical variable, if unknown and missing data may be presented as a separate category and the denominator might include unknown and missing category where deems appropriate.

11.5. Interim Analysis

One interim analysis will be conducted when the first 15 cases in each group complete the study procedure. The main purpose of the interim analysis is to more accurately fine tune the study design based on study-specific data. The interim analysis will focus on the impact of the primary imaging techniques on procedural success. If imaging technique is a significant factor, stratified randomization by primary imaging techniques will apply for future included participants. Justification for multiplicity is unnecessary as no formal statistical hypothesis will be tested.

11.6. Statistical Deviations

Any *post hoc* or unplanned analyses not identified in this protocol will be clearly identified in the Clinical Study Report.

11.7. Pooled Data

The proposed study will be conducted in up to 60 participants at up to 6 investigational sites. The final number of participating investigational sites and number of participants treated at each site will be determined by the enrollment status. The number of participants in each study group enrolled by each investigator at each investigational site in this study is expected to be too small to provide valid statistical meaningful conclusions. Therefore, no formal site pooling justification analysis is planned. Data from all sites will be pooled together in analyses.

12. DATA MANAGEMENT

12.1. Data Entry and Collection

An electronic data capture (EDC) system with electronic Case Report Forms (eCRFs) will be used for the purposes of this study. The handling of data from the eCRF will be the responsibility of the Sponsor or designee. Study data will be subject to periodic quality control reviews and checks as documented in the Data Management Plan for this study.

12.2. Data Review and Cleaning

All data in the EDC system will be fully validated using study-specific range and consistency checks and database listings. Queries will be issued to the investigational site via the EDC system and are to be resolved by the Investigator or designee. Data validation will be completed on a regular basis. The entire database will be re-validated to ensure that there are no outstanding data discrepancies prior to database lock. Any changes to the database after database lock will require written approval by the Sponsor.

12.3. Source Data Requirements

The Investigator or designee will perform primary data collection drawn from original documents (printed, optical or electronic document containing source data). Data collected for purposes of the clinical study must not be entered directly into the eCRF before being recorded first in the source documents. All source documentation must be available for review by the study monitor during monitor visits. Source data are defined as all information in original records, certified copies of original records of clinical findings, observations, or other activities in a clinical study, necessary

for the reconstruction and evaluation of the clinical study. This includes source data initially recorded in an electronic format.

The Investigator will ensure the accuracy, completeness, legibility, and timelines of the data reported in eCRF and in all required documentation. Data reported in the eCRF shall be supported by the source documents with any discrepancies being explained. Any corrections made to documents will be done according to Good Documentation Practices. The Principal Investigator must sign the eCRFs to validate that the observations and findings recorded on the eCRFs are complete and accurate. Failure to meet documentation requirements may lead to the disqualification of an Investigator and/or investigational site.

12.4. Subject Confidentiality

Subject confidentiality will be maintained throughout the clinical study in a way that ensures the information can always be tracked back to the source data. For this purpose, a unique subject identification code will be used that allows identification of all data reported for each subject. Data relating to this clinical study might be made available to third parties (i.e., regulatory or IRB inspection) provided the data are treated confidentially and that the subject's privacy is guaranteed.

12.5. Data Protection

Subject confidentiality and privacy are strictly held in trust by the Investigators, their staff, and the Sponsor, their staff, and contractors. Subject confidentiality is extended to cover processing of biological samples (i.e., blood) in addition to the clinical information relating to subjects. Therefore, the protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study, or the data will be released to any unauthorized third party without prior written approval of the Sponsor.

All research activities will be conducted in as private a setting as possible.

The study monitor, other authorized representatives of the Sponsor, representatives of the IRBs, regulatory agencies and/or company supplying study product may inspect all documents and records required to be maintained by the Investigator, including but not limited to, medical records (office, clinic, or hospital) and pharmacy records for the subjects in this study. The investigational site will permit access to such records.

The original consent forms will be kept at the investigational site and a copy will be given to the subject. All study records will be kept in a locked file cabinet and logs linking a subject's name to the study subject ID will be stored separately. Clinical information will not be released without written permission of the subject, except as necessary for monitoring by FDA. The PI must also comply with all applicable privacy regulations (e.g., HIPAA).

12.6. Protocol Amendments and Deviations

12.6.1. Amendments

Investigators may not modify (amend) this study protocol without obtaining prior written approval from the Sponsor, IRB, and applicable regulatory authorities. In the instance where a substantial protocol amendment is initiated by the Sponsor, the amended protocol will not be implemented at the investigational site until documented approval from the IRB has been obtained. The Principal Investigator will acknowledge the amendment by signing the Investigator signature page of the amended protocol. As appropriate, training on the protocol amendment will be provided by the Sponsor or designee.

New findings or the reasons for any amendments to the study protocol that affect the subject's continued participation shall be made available to the participant.

12.6.2. Deviations

A protocol deviation (PD) is the non-adherence to or divergence from any protocol requirements, processes, or procedures. The Principal Investigator and investigational site staff should avoid protocol deviations. Emergency deviations (deviations from the study protocol to protect the life or physical well-being of a subject) are allowed per physician discretion. The use of waivers from the protocol is prohibited.

PD records will be reviewed throughout the conduct of the Study. The Sponsor or designee will address any deviations and work with the Principal Investigator and investigational site staff to determine appropriate corrective and preventative actions. In addition, deviations occurring across investigational sites will be reviewed by the Sponsor on a periodic basis to determine if more global preventive actions may be required.

The Sponsor will determine the effect of the PDs on the scientific soundness of the clinical study and subject safety to determine if additional reports or actions are required. Additional action may include investigational site staff re-training and/or site suspension or termination. The Sponsor will consider terminating or suspending the participation of a particular investigational site or Principal Investigator in the Study if monitoring or auditing identifies serious or repeated deviations.

12.6.3. Reporting

All deviations will be documented in the appropriate eCRF and should be entered soon after the deviation is recognized. Emergency deviations that occur must be reported to the Sponsor or designee within 1 working day and to the IRB per the applicable IRB requirements. Non-emergency deviations that occur must be reported to the Sponsor or designee within 5 working days and to the IRB, if required. Investigators will also adhere to procedures for reporting deviations to the involved IRBs in accordance with their specific reporting policies and procedures.

13. STUDY ADMINISTRATION

13.1. Regulatory Compliance

This clinical study will be performed in accordance with all stipulations of the protocol. The study will be conducted in accordance with the ethical principles that have their origin in the latest version of the Declaration of Helsinki. The clinical study protocol was written in compliance with ISO 14155:2020. Study conduct will comply with 21 CFR Parts 50, 54, 56, 803, and 11 and HIPAA.

The clinical study will not be initiated until approval has been obtained from the governing IRB. Any additional requirements imposed by the IRB will be followed, as appropriate. No deviation from the clinical study protocol will be implemented without the prior written approval of the Sponsor and IRB except when necessary to eliminate an immediate hazard to a subject.

13.2. Sponsor Responsibilities

The Sponsor is responsible for selecting qualified Investigators and providing them with the information they need to conduct the study properly, ensuring appropriate monitoring of the study, ensuring that IRB review and approval are obtained as required and ensuring that any reviewing IRB or regulatory agency is promptly informed of significant new information regarding the study.

Clinical specialists employed by the Sponsor can provide technical assistance to the Investigators and other health care personnel, as needed, during the study which may include device training or addressing questions related to operation of the study device.

13.3. Investigator Responsibilities

The Principal Investigator responsibilities include, but are not limited to, the following:

- Conducting the study in accordance with this protocol, the signed clinical study agreement, and applicable regulations protecting the rights and safety of study subjects
- Ensuring that informed consent is obtained for each study subject in accordance with the protocol
- Ensuring that IRB approval is secured prior to starting the study and ensuring continuing review as required throughout the study
- Ensuring all associates, colleagues, and investigational site staff assisting in the conduct of the study are provided with the required study documentation, informed about their obligations, are adequately qualified and trained, and meet their commitments
- Maintaining adequate and accurate records and ensuring those records are available for inspection at any time
- Ensuring that conducting the study does not give rise to conflict of interest

13.4. Retention of Study Records

The Principal Investigator must maintain adequate records on all aspects of the study, including the following:

IRB approvals
Subject withdrawal information
Subject Informed Consent Forms
Protocol deviations
Electronic Case Report Forms
Study correspondence
Device use
Source documents

The Principal Investigator or investigational site should retain all clinical study data for at least 15 years. The investigational site may also transfer the clinical study records to the Sponsor.

If the Principal Investigator moves, retires, etc., the investigational site must provide the Sponsor with the name and address of the person who will be responsible for the study records or arrange for transfer of the records to the Sponsor.

13.5. Study Funding

The clinical study is funded and sponsored by Argon Medical Devices. Funding provided to the Investigator/investigational site is detailed for each investigational site in their Clinical Study Agreement.

13.6. Clinical Study Agreement

A Clinical Study Agreement (CSA) will be put in place for each investigational site, signed by the appropriate representative of the investigational site and Sponsor prior to initiation of the clinical study at the investigational site. The CSA will be amended as needed during the clinical study.

Each Principal Investigator and Sub-Investigator will provide a signed financial disclosure form to the Sponsor or designee to disclose any financial conflict of interest prior to activation of the Investigator. A new financial disclosure form must be provided promptly if there is a change in previously reported disclosures.

13.7. Subject Compensation

The Sponsor will provide information to subjects regarding the Sponsor’s liability to compensate for any injury sustained due to participation in this clinical study in accordance with local and national guidelines.

Subject compensation for study participation and reimbursement of travel fees for study-specific visits may be provided by the Sponsor if required by local regulations and/or approved by the IRB.

13.8. Insurance

Insurance for the study will be maintained by the Sponsor.

13.9. Publication Policy

13.9.1. Study Registration

This study will be registered in the publicly accessible database, ClinicalTrials.gov. The study information and results will be provided and updated as per the database requirements. Study subjects will be informed of the registration in the study informed consent form.

13.9.2. Clinical Study Report

Results from the clinical study will be summarized in a clinical study report (CSR) following study closure. The final CSR will be compiled and written by the Sponsor or designee and reviewed, approved, and signed off by the Sponsor and the Lead Principal Investigator.

13.9.3. Use of Information and Publications

All information concerning this protocol, the data generated from the protocol, Sponsor operations, and basic scientific data supplied by Sponsor to the Investigator and not previously published, is considered confidential and remains the sole property of Sponsor.

At the conclusion of the study, a multi-center abstract and/or manuscript may be prepared for publication reporting the primary results from the study. Publication of the principal results from any single-site experience within the study is not allowed until the preparation and publication of the multi-center results unless prior approval from the Sponsor is given.

The Sponsor must receive any proposed publication and/or presentation materials in compliance with the Sponsor's publication policy set forth in the Clinical Study Agreement.

13.10. Minimization of Bias

The following activities are intended to reduce the risk of bias:

- Randomized study
- Objective methodology to evaluate endpoints
- Stratified randomization (if applicable after the interim analysis)

Furthermore, potential for bias has been minimized with a well-controlled design, expected conduct under the terms of the approved protocol, use of specific inclusion and exclusion criteria, careful definitions for study procedures and outcomes, and prospectively defined methods of data analysis.

13.11. Potential Confounding Factors

The inclusion and exclusion criteria ensure that possible potential confounding factors (in terms of participant characteristics) are minimized. Potential confounding factors include:

- Active variceal bleeding
- Hepatic tumors
- Polycystic liver disease

Underlying liver failure/ high MELD score
Heart failure/ pulmonary hypertension
Biliary obstruction
Lack of adequate portal vein target or patency

In addition, all Investigators will be trained on the protocol requirements and required safety and efficacy assessments prior to initiation of the study.

13.12. Scientific Robustness

This is a well-designed, multicenter, post approval study that will be conducted by qualified and trained Investigators. Scientific validity and robustness of the study are demonstrated by the study design and using validated and objective statistical methodology to evaluate the primary endpoint. The data that will be generated through this clinical study are therefore considered to be robust and accurately reflect the safety and effectiveness of the Scorpion set.

13.13. Monitoring

The Sponsor will ensure that adequate monitoring at each investigative site is completed. The Principal Investigator and investigative site staff will ensure all study documents and source data are up-to-date and available for review.

The Principal Investigator will permit the Sponsor or designee to inspect all study-related documentation, including case report forms and source documents, at regular intervals throughout conduct of the study. Appropriately trained personnel will conduct monitoring of investigative sites and details of the monitoring activities will be outlined in a separate study-specific monitoring plan.

13.14. Other Aspects of Clinical Quality Assurance

The Sponsor or designee may conduct audits at the investigational sites. Audits may include, but are not limited to, device supply, presence of required documents, the informed consent process, and comparison of CRFs with source documents. The Investigator agrees to participate with Sponsor audits and regulatory inspections.

14. REFERENCES

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