Summary of Safety and Clinical Performance (SSCP)

LARIAT® Left Atrial Appendage (LAA) Exclusion System

18 November 2022

REV H

OVERVIEW

This Summary of Safety and Clinical Performance (SSCP) is intended to provide public access to an updated summary of the main aspects of the safety and clinical performance of the device.

The SSCP is not intended to replace the Instructions for Use as the main document to ensure the safe use of the device, nor is it intended to provide diagnostic or therapeutic suggestions to intended users or patients.

INFORMATION INTENDED FOR USERS/ HEALTHCARE PROFESSIONALS

See Section after the page break for device information for patients.

1. Device Identification and General Information

Table 1-1. Device Identification and General Information

Product Name	LARIAT® LAA (Left Atrial Appendage) Exclusion System
Product Group/Family Basic UDI-DI	LARIAT RS LAA Exclusion Device: 0840143900000000000001ZB LARIAT RS LAA Exclusion Device, 50 mm: 0840143900000000000001ZB EndoCATH Balloon Catheter: 0840143900000000000002ZD FindrWIRZ Guide Wire System: 0840143900000000000002ZD SofTIP Guide Cannula: 0840143900000000000002ZD SureCUT Suture Cutter: 0840143900000000000002ZD
Manufacturer Legal Name and Address: Single Registration Number (SRN) (when available)	AtriCure, Inc. 7555 Innovation Way Mason, OH 45040 USA SRN: US-MF-000002974
EU Auth Representative: Single Registration Number (SRN)	AtriCure Europe B.V. De entree 260 1101 EE Amsterdam NL SRN: NL-AR-000000165

Medical Device Scope Expression and Code	CND code(s): LARIAT: P070404 – Left Atrial Appendage Occluders EndoCATH: C0104020103 - Vascular Occlusion Catheters FindrWIRZ: C0499 - Cardiovascular Guidewires - Other SofTIP: C0599 - Cardiovascular Introducer Sheaths - Other SureCUT – V0199 – Cutting Devices, Single Use – Other
Product Classification and Rule (per MDR)	• The LARIAT RS LAA Exclusion Devices are Class III, Rule 8 • The EndoCATH Balloon Catheter is Class III, Rule 6 • The FindrWIRZ Guide Wire System is Class III, Rule 6 • The SofTIP Guide Cannula is Class III, Rule 6 • The SureCUT Suture Cutter is Class III, Rule 6
Year when the first certificate (CE) was issued covering the LARIAT RS Suture Delivery Device	2016 (MDD); see Table 1-2 for MDD certification of all System products
Notified Body Name, Address & Number	BSI Say Building John M. Keynesplein 9 1066 EP Amsterdam NL +31 20 346 0780 CE 2797

Table 1-2. LARIAT LAA Exclusion System Catalog Numbers and Product Names

Catalog #	Product Name	CE Approval Date
LARIAT45	LARIAT RS LAA Exclusion Device	May 2016
LARIAT50	LARIAT RS LAA Exclusion Device, 50 mm	Feb 2019
EndoCATH	EndoCATH Balloon Catheter	July 2010
FindrWIRZ	FindrWIRZ Guide Wire System	April 2009
SofTIP13	SofTIP Guide Cannula	July 2010
SureCUT	SureCUT Suture Cutter	Dec 2009

2. Intended Use of the Device

2.1. Intended Purpose

The LARIAT LAA Exclusion System facilitates delivery and placement of a pre-tied polyester suture for use in cardiac tissue approximation and/or ligation, resulting in exclusion of the Left Atrial Appendage (LAA).

2.2. Indication(s) and target populations

- Indication: The LARIAT LAA Exclusion System is to be used in patients with non-valvular atrial fibrillation for whom LAA closure is warranted.
- Target population: Adults with non-valvular atrial fibrillation who are anatomically eligible for LAA exclusion and who present with the following:
  - Increased risk for thromboembolic events (CHA_2DS_2-VASc ≥ 2) and who are intolerant to or contraindicated for long-term oral anticoagulation therapy

2.3. Contraindications and/ or limitations

DO NOT use the FindrWIRZ guide wires or EndoCATH catheter for crossing chronic total occlusions and/or extreme tortuous anatomy.
DO NOT use the LARIAT LAA Exclusion System devices in coronary or cerebral vasculature.
DO NOT use the LARIAT LAA Exclusion System to ligate/approximant/occlude reproductive structures for contraceptive purposes.
DO NOT introduce the LARIAT RS LAA Exclusion Device through an introducer sheath with a hemostasis valve.

The LARIAT RS LAA Exclusion Device is NOT intended for use in the following conditions:

- Where minimally invasive techniques (e.g., endovascular, percutaneous, transseptal, and sub-xiphoid pericardial accesses) or visualization techniques (e.g., transesophageal echocardiography) are contraindicated;
- Where endovascular devices are contraindicated for use;
- Where exposure to radiation is contraindicated for use (e.g., pregnant and/or breastfeeding women);
- On LAA structures with a diameter exceeding LARIAT RS LAA Exclusion Device snare size (45 mm or 50 mm) and/or that cannot be completely captured or creates excessive tissue overlap at the ligation location;
- If pre-existing condition of local or systemic infection and/or endocarditis or pericarditis is present;
- If pericardial adhesions are suspected and/or observed; and
- If there is thrombus visualized within or near the LAA structure being approximated and/or ligated

3. Device Description

3.1. Description of the device

The LARIAT LAA Exclusion System comprises six devices that are delivered into the body via standard percutaneous pericardial and transseptal access techniques. The system can be divided into four functional categories listed in Table 3-1.

Table 3-1. LARIAT LAA Exclusion System Devices and Functions

Functions	Devices

Access to epicardial LAA Site (Pericardial)	SofTIP Guide Cannula Epicardial 0.035” FindrWIRZ Guide Wire System
Access to endocardial LAA Site (Transseptal)	Endocardial 0.025” FindrWIRZ Guide Wire System EndoCATH Occlusion Balloon Catheter
Suture Delivery and Tightening	LARIAT RS LAA Exclusion Device TenSURE Suture Tightener
Suture Cutting	SureCUT Suture Cutter

The LARIAT RS LAA Exclusion Device is used to remotely deliver a pre-tied suture to the target left atrial appendage (LAA) site. The LARIAT suture was determined to be “MR Safe” per the requirements of standard ASTM F2503-20.

The LARIAT RS LAA Exclusion Device (Figure 1) is a one-piece, single-use suture delivery and deployment device with a pre-tied size “0” polyester suture loop that is pre-loaded on the Delivery Snare. The Lariat shaft has two markers, an integrated snare loop introducer, a snare actuator slide, a suture release tab (Fob), and a guide wire lumen. The Lumen within the LARIAT RS LAA Exclusion Device accommodates the 0.035” FindrWIRZ guide wire. The LARIAT device is available in two different snare sizes (45mm or 50 mm by 20 mm). The Suture is a sterile, braided, non-absorbable, surgical suture, dyed D & C Green No. 6 composed of Poly(ethylene terephthalate). The implantable suture consists of a PTFE coated Polyester Fiber. Suture chemical analysis shows that there are no significant levels of materials or substances that would pose a risk to the patient over the lifetime of the implant. Detailed information on the materials used in the suture are listed below:

Material	Mass (mg)	CAS #
Polyester	14.3 mg	25038-59-9
Polytetrafluoroethylene (PTFE)	1.3 mg	9002-84-0
Titanium Dioxide	0.1 mg	13463-67-7
D&C Green #6 Dye	0.02 mg	128-80-3

Figure 1. LARIAT RS LAA Exclusion Device

The SofTIP Guide Cannula (Figure 2) is used to introduce, guide, and/or place the LARIAT RS LAA Exclusion Device and Epicardial FindrWIRZ within the pericardium. It has a radiopaque marker at the tip, and an orientation marker on the hub.

Figure 2 SofTIP Guide Cannula

The FindrWIRZ Guide Wire System (Figure 3) is a two-component system, 0.025" and a 0.035" steerable guide wires with opposing Magnet Tips and a guide wire introducer. The FindrWIRZ guide wires provide a track to guide the LARIAT RS LAA Exclusion Device Snare over the target LAA tissue.

Figure 3 FindrWIRZ Guide Wire System

The EndoCATH Occlusion Balloon Catheter (Figure 4) has radiopaque Markers at the Balloon's ends to provide fluoroscopic visualization. The proximal end has connections for the balloon lumen and the guide wire lumen. The Balloon is placed at the target LAA site to provide a location marker for the LARIAT RS LAA Exclusion Device Snare closure site.

Figure 4 EndoCATH Occlusion Balloon Catheter

The SureCUT Suture Cutter (Figure 5) cuts the excess LARIAT RS LAA Exclusion Device Suture and detaches it from the LAA. The SureCUT is comprised of a Suture Threader, a Distal Cutting Mechanism, and Plunger Lock, and the Handle/Cutting Actuator.

Figure 5 SureCUT Suture Cutter

3.2. Reference to previous generation(s) or variants if such exist, and a description of the differences

Since market introduction and with gained experience, variations have been made to the device. Most of the changes were made for improving user experience and performance. These variations and reasons for them are listed as follows:

LARIAT RS LAA Exclusion Devices:

- Braid was added to the catheter shaft for additional stiffness and torque response for ease of use.
- 45mm and 50mm snare loop sizes were added to accommodate anatomical structures up to 50mm wide.
- The tip color was changed to the natural Ultem from black Ultem for manufacturing purposes.
- Fob/Tab outer shape and dimension change to accommodate snare release feature.
- A snare release button was incorporated in the handle to release the snare attachment in the tip after deployment and tightening of the suture loop.

SofTIP

- Increased working length to access larger body habitus. Additional working length of the access cannula does not affect the function or compatibility with any of the devices studied.

EndoCATH

- Balloon diameter and length reduced to access more patients.

FindrWIRZ

- The 0.025 wire was shortened, and a polytetrafluoroethylene (PTFE) coating was added for ease of use.

SureCUT

- A molded handle was introduced to reduce cost.

3.3. Description of any accessories which are intended to be used in combination with the device

The TenSURE Suture Tightener (Figure 6) enables the LARIAT RS LAA Exclusion Device Suture to be tightened by the physician. The TenSURE is comprised of a Suture Release Fob Holder and a Force Indicator Mark, red line, to aid in proper tensioning of the Lariat suture.

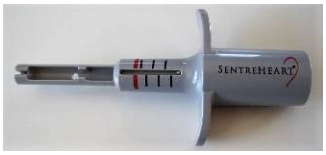

Figure 6 TenSURE Suture Tightener

The TenSURE device is manufactured by AtriCure, Inc. The Basic UDI-DI for TenSURE is 08401439000000000000003ZF.

3.4. Description of any other devices and products that are intended to be used in combination with the device

There are no other devices or products that are intended to be used in combination with these devices.

Other devices, not included with the System, may be used in conjunction with the LARIAT LAA Exclusion System. These may include, but are not limited to, the following:

- Transseptal sheath and guide wire;
- Transseptal needle;
- Step-up introducers (6 F – 16 F);
- 0.035” x 180 cm 3.0 mm J guide wire;
- 0.018” x 130 cm Nitinol Mandrel guide wire;
- 21 G x 4.75” (micropuncture needle);

- 17 G x 6” and/or 17G x 8” Tuohy Needle;
- 18 G x 3.5” Needle;
- Rotating hemostasis valve (Tuohy-Borst);
- 3-way stopcock;
- Torque device compatible with .018” guide wires;
- 60 mL negative pressure syringe;
- 10 mL fixed male syringe;
- 3 mL fixed male syringe; and
- 6 F / 90 cm pigtail catheter.

4. Risks and warnings

4.1. Residual risks and undesirable effects

Potential reactions associated with the use of a LARIAT LAA Exclusion System include, but are not limited to, those listed below:

Table 4-1. Potential Reactions

	Probability within 30 days[a]	
Air embolism	≤5%, 5 or less people in 100	Rare
Allergic reaction to contrast material, anesthesia, heparin[b]	≤5%, 5 or less people in 100	Rare
Arrhythmias	≤5%, 5 or less people in 100	Rare
AV fistula[c]	0.5%; 5 people out of 1000	Extremely rare
Asystole	≤5%, 5 or less people in 100	Rare
Bleeding, possibly requiring transfusion[c]	≤5%, 5 or less people in 100	Rare
Bradycardia (<30 beats/min)	≤5%, 5 or less people in 100	Rare
Cardiac perforation or rupture[c]	≤5%, 5 or less people in 100	Rare
Cardiac tamponade[c]	≤5%, 5 or less people in 100	Rare
Cerebrovascular accident	≤5%, 5 or less people in 100	Rare
Chest pain/discomfort	≤20%, 20 or less people out of 100	More common
Complete or partial heart block	≤5%, 5 or less people in 100	Rare
Congestive heart failure (CHF) (new onset or worsening of existing CHF)	≤5%, 5 or less people in 100	Rare
Coronary artery dissection	≤5%, 5 or less people in 100	Rare
Coronary artery spasm	≤5%, 5 or less people in 100	Rare
Coronary artery thrombosis	≤5%, 5 or less people in 100	Rare
Death	≤5%, 5 or less people in 100	Rare

Device breakage/ Inability to remove	0.5%; 5 people out of 1000	Extremely rare
Diaphragmatic paralysis	≤5%, 5 or less people in 100	Rare
Deep vein thrombosis	≤5%, 5 or less people in 100	Rare
Dyspnea	≤5%, 5 or less people in 100	Rare
Emergency during procedure requiring a change in planned access	≤5%, 5 or less people in 100	Rare
Endocarditis	≤5%, 5 or less people in 100	Rare
Epistaxis	≤5%, 5 or less people in 100	Rare
Extravasation of contrast media	≤5%, 5 or less people in 100	Rare
Gastrointestinal bleeding	0.5%; 5 people out of 1000	Extremely rare
Hematoma[b]	≤5%, 5 or less people in 100	Rare
Hematuria	≤5%, 5 or less people in 100	Rare
Hemothorax[c]	0.5%; 5 people out of 1000	Extremely rare
Hypertrophic scarring or thrombosed veins	≤5%, 5 or less people in 100	Rare
Hypertension[c]	≤5%, 5 or less people in 100	Rare
Hypotension[c]	≤5%, 5 or less people in 100	Rare
Iatrogenic atrial septal defect	≤20%, 20 or less people out of 100	More common
Infection, Sepsis, or Fever[b]	≤5%, 5 or less people in 100	Rare
Ischemia	≤5%, 5 or less people in 100	Rare
Myocardial infarction (MI)	≤5%, 5 or less people in 100	Rare
New arrhythmia other than AF needing treatment (apart from right atrial flutter)	≤5%, 5 or less people in 100	Rare
Newly developed second or third degree AV block requiring permanent pacemaker	≤5%, 5 or less people in 100	Rare
Pain / discomfort	≤20%, 20 or less people out of 100	More common
Pericardial effusion[c]	≤20%, 20 or less people out of 100	More common
Pericarditis[c]	≤20%, 20 or less people out of 100	More common
Pleural effusion[d]	≤5%, 5 or less people in 100	Rare
Pneumothorax[c]	≤5%, 5 or less people in 100	Rare

Prolonged exposure to fluoroscopic radiation	≤5%, 5 or less people in 100	Rare
Pseudo-aneurysm/ aneurysm[b]	0.5%; 5 people out of 1000	Extremely rare
Pulmonary edema	≤5%, 5 or less people in 100	Rare
Pulmonary vein obstruction	≤5%, 5 or less people in 100	Rare
Pulmonary vein stenosis	≤5%, 5 or less people in 100	Rare
Pulseless electrical activity (PEA) arrest	≤5%, 5 or less people in 100	Rare
Reaction to medication/ contrast media	≤5%, 5 or less people in 100	Rare
Renal insufficiency or failure, possibly requiring renal replacement therapy	≤5%, 5 or less people in 100	Rare
Respiratory distress or failure	≤5%, 5 or less people in 100	Rare
Stroke – Ischemic	≤5%, 5 or less people in 100	Rare
Stroke – Hemorrhagic	≤5%, 5 or less people in 100	Rare
Suture dehiscence	≤5%, 5 or less people in 100	Rare
Systemic embolism	≤5%, 5 or less people in 100	Rare
Transesophageal echocardiography (TEE) complications	≤5%, 5 or less people in 100	Rare
Thromboembolism – Cardiac[c]	≤5%, 5 or less people in 100	Rare
Thromboembolism – Non-cerebral	≤5%, 5 or less people in 100	Rare
Thrombosis	≤5%, 5 or less people in 100	Rare
Transient ischemic attack (TIA) or other neurological deficit	≤5%, 5 or less people in 100	Rare
Transseptal complications	≤5%, 5 or less people in 100	Rare
Valvular damage	≤5%, 5 or less people in 100	Rare
Vascular damage	≤5%, 5 or less people in 100	Rare
Vascular access complications[b]	≤5%, 5 or less people in 100	Rare
Vasovagal reactions	≤5%, 5 or less people in 100	Rare
Ventricular fibrillation/ Ventricular tachycardia	≤5%, 5 or less people in 100	Rare
[a]Estimated probability of occurrence based on comprehensive clinical literature search and aMAZE informed consent form [b]Estimated probability of occurrence based on complaints: <0.1%, less than 1 in 1000; improbable		

[c]Estimated probability of occurrence based on complaints: <0.5% and ≥0.1%, between 1 in 200 and 1 in 1,000; remote
[d]Estimated probability of occurrence based on complaints: <1.0% and ≥5%, between 1 and 100 and 1 in 200; Occasional
Note: Data generated from complaints may be underreported.

4.2. Warnings and precautions

WARNINGS

- Carefully read ALL instructions PRIOR to use. Failure to follow these instructions, warnings, and cautions may lead to device damage and/or patient injury. Use of the LARIAT RS System should be restricted to those physicians trained to perform percutaneous procedures (e.g., pericardial and transseptal accesses) and in the proper use of the system
- The LAA is a thin-walled structure. Use caution when accessing the LAA and deploying the suture to avoid perforation or injury to the LAA causing bleeding
- Always use standard visualization techniques (e.g., fluoroscopy and echocardiography) for guidance when moving any device (e.g., advancing, withdrawing, and re-locating) to minimize the risk of injury.
- At no time should any components of the LARIAT LAA Exclusion System or ancillary devices be advanced, withdrawn, torqued or moved when resistance is met without first determining and resolving the cause. Manipulation when resistance is met may lead to perforation of cardiac tissues causing bleeding or embolism.
- At no time should any components of the LARIAT LAA Exclusion System or ancillary devices be placed on or near thrombi or other biologics/materials that may dislodge or may result in embolic events.
- Always use proper care and standard techniques when introducing and maintaining the devices in the body as to not introduce any undesired air or substance into the cardiovascular system (e.g., thorough flushing catheters with isotonic solutions).
- DO NOT place FindrWIRZ guide wires near ferromagnetic materials or instruments during the procedure as this may lead to unexpected movement of the device, resulting in perforation causing altered hemodynamics.
- DO NOT inflate the EndoCATH Balloon beyond maximum inflation volume or with pressure inflation devices as this may lead to balloon rupture causing tissue injury, bleeding or embolism.
- DO NOT place the EndoCATH Balloon in LAAs that are smaller than Balloon dimensions (≤ 20 mm in length and ≤ 15 mm in width) as this may result in trauma to the LAA and bleeding.
- Use only recommended inflation media to inflate the EndoCATH Balloon. DO NOT use air or gaseous media to inflate the Balloon as this may lead to air embolism.
- Care should be exercised in patients with suspected or known allergies or hypersensitivity to nickel, which is present in small quantities in LARIAT RS LAA Exclusion Device, FindrWIRZ, and SureCUT devices.
- FOR SINGLE USE ONLY. DO NOT reuse, reprocess or resterilize. Reuse, reprocessing or resterilization may compromise the structural integrity of the device and/or lead to device failure, which in turn may result in patient injury, illness or death. Reuse, reprocessing or resterilization may also create a risk of contamination of the device and/or cause patient infection or cross-infection, including, but not limited to, the transmission of infectious disease(s) from one patient to another. Contamination of the device may lead to injury, illness or death of the patient.
- Inspect all products prior to use. DO NOT use if the package is opened or damaged. Otherwise, this may lead to infection.
- The FindrWIRZ and SureCUT contain a small fraction of metallic cobalt (CAS# 7440-48-4) alloy between 0.1 and 0.3% wt% of stainless steel.

- Observation of the LARIAT LAA Exclusion System devices using standard visualization techniques (e.g., fluoroscopy, computed tomography (CT), and echocardiography) prior to and during the procedure is essential to patient safety and to ensure optimal placement of the pre-tied suture loop.
- If resistance is met while advancing or moving the LARIAT LAA Exclusion System and/or ancillary devices, DO NOT continue as this may result in unintended tissue trauma. STOP to identify the potential causes and address the causes as appropriate prior to proceeding.
- If risks of dislodging any biologics/materials exist, STOP and DO NOT proceed with the procedure with the LARIAT LAA Exclusion System as this may result in embolism or perforation of cardiac tissues.
- DO NOT use any device that is damaged, its packaging is damaged, or is expired (after the last day of the expiration month). Otherwise, this may lead to infection.
- To avoid bleeding complications exacerbated by heparin infusion, complete pericardial access prior to transseptal access.
- Use conventional pericardial access technique for entering a dry pericardium under fluoroscopic guidance to gain pericardial access on the anterior-lateral aspect of the heart.
- Ensure that the EndoCATH Distal Lumen is well flushed and contain no air prior to introduction into the body to prevent air embolism
- A separation of > 1 cm between the distal end of the EndoCATH catheter and 0.025” FindrWIRZ Magnet Tip should always be maintained while advancing the devices outside of the transseptal sheath to minimize potential cardiac perforation.
- DO NOT place the Balloon into LAAs that are ≤ 20 mm in length and ≤ 15 mm in width (i.e., LAAs that are smaller than the dimensions of the Balloon) as this may result in trauma to the LAA and bleeding.
- DO NOT place the Balloon into LAAs that do not allow for a minimum of 1 cm of exposure of the 0.025” guide wire as this may result in trauma to the LAA and bleeding.
- Prior to inflation, verify that the balloon is positioned clear of any calcified plaque, stents, or any other sharp object/materials. Additionally ensure the balloon is not partially within the transseptal sheath prior to inflation. Either of these may result in balloon rupture resulting in embolism.
- Adhere to the recommended EndoCATH maximum inflation volumes of 1.5 cc. DO NOT inflate beyond 1.5 cc as this may result in balloon rupture causing embolism.
- Do not use a pressure inflation device as it may cause the balloon or catheter to rupture or fragment, or cause damage to vessel wall and/or vessel rupture.
- If resistance is felt while opening and/or closing of the Snare, DO NOT attempt to force the Snare Actuator as this may lead to cardiac injury and bleeding. STOP to identify potential causes and address the causes as appropriate prior to proceeding.
- DO NOT pull the Snare Actuator beyond the stop point of the device as indicated by the “ – “ symbol as this may result in unintended trauma to the LAA.
- DO NOT pull the Snare Actuator beyond the stop point of the device as indicated by the “ – “ symbol as this may result in unintended trauma to the LAA.
- Keep the epicardial 0.035” FindrWIRZ to endocardial 0.025” FindrWIRZ magnet connection steady with no tension on the epicardial 0.035” FindrWIRZ during introduction and advancement of the LARIAT RS LAA Exclusion Device thorough the SofTIP to avoid potential perforation.
- DO NOT excessively bend, rotate, manipulate and/or actuate the Snare while advancing over the targeted tissue structure, as this may lead to premature release of the Suture and or disconnection of the FindrWIRZ magnet system. Overmanipulation during this time can create indirect tension in the FindrWIRZ causing LAA perforation.

- DO NOT twist or rotate the device continuously in one direction at any time to avoid twisting of the Snare and/or Suture and causing injury to the patient. DO NOT rotate the device in excess of 180 degrees.
- If resistance is felt while opening and/or closing of the Snare, DO NOT attempt to force the Snare Actuator as this may lead to cardiac injury and bleeding. STOP to identify potential causes and address the causes as appropriate prior to proceeding.
- If during manipulation, the FindrWIRZ becomes detached, ensure the FindrWIRZ is properly routed through the snare loop. Improper routing of FindrWIRZ through snare loop may lead to false closure, and excessive tissue manipulation potentially causing perforation, lacerations, or bleeding
- If resistance during closure is felt prior to the reaching the closed position, DO NOT attempt to close any further as this may result in intended tissue trauma. Assess whether the closure site has been biased too atrial (i.e. snare actuator does not come back far enough to completely cover the "-" Marker), possibly reposition if needed and Continue to the next step. Continued use during resistance may result in cardiac tissue injury and bleeding.
- If the LARIAT RS LAA Exclusion Device is restrained, release the LARIAT RS LAA Exclusion Device to eliminate any forward force and/or gently retract the LARIAT RS LAA Exclusion Device with the Actuator Slide in the opening position. Failure to do so may result in an entrapped device requiring further medical intervention due to cardiac injury and bleeding. Always ensure the epicardial 0.035" FindrWIRZ is advanced while the LARIAT RS LAA Exlusion Device is retracted, if the magnets are connected.
- Failure to hold the LARIAT RS LAA Exclusion Device stable and in place while deploying and tightening the Suture, could result in failure to deploy the suture, isolate the tissue, and may lead to patient harm
- Avoid any excessive advancement of the LARIAT RS LAA Exclusion Device prior to and during deployment. The LARIAT RS LAA Exclusion Device should naturally curve to the closure site without visible device prolapse to avoid tissue damage.
- The Suture Release Tab must be properly aligned within the grooves of the TenSURE device to avoid tissue damage, and bleeding.
- DO NOT tighten beyond the red mark on the TenSURE device (shown in Figure 5) as this may cause damage to the suture or to the tissue.
- Multiple suture tightenings with TenSURE device at maximum tightening force (red line) may cause damage to the suture or to the tissue.
- Failure to cut the red Suture Release Tab prior to the removal of the LARIAT RS LAA Exclusion Device could result in significant tissue damage or tissue evulsion.
- If resistance is felt during removal of the LARIAT RS LAA Exclusion Device, DO NOT attempt to force removal. Continued use during resistance may result in cardiac tissue injury and bleeding. STOP to identify potential causes and address as appropriate prior to proceeding.
- Verify the Suture Release Tab is removed, the Snare is open, the Suture is fully deployed and the device is free of anatomical constraints or instrument interference. Ensure that the SofTIP cannula is positioned such that it is conducive for LARIAT RS LAA Exclusion Device removal.
- Do not rotate or twist the LARIAT RS LAA Exclusion Device during removal from the ligated tissue as this may result in unintended tissue trauma and bleeding.
- DO NOT over-rotate, torque, or excessively bend the SureCUT device as this may affect the ability of the device to advance and/or cut. Overmanipulation may result in the device being unable to be removed and the need for additional medical intervention.
- Failure to completely actuate the Handle/Cutting Actuator may result in incomplete cutting of the Suture resulting in potentially pulling the suture and lacerating LAA.

- If resistance is felt while withdrawing, DO NOT withdraw further as this may result in unintended tissue trauma. STOP to identify the potential causes and address the causes as appropriate prior to proceeding. Continued withdrawal against resistance may lead to LAA laceration.

PRECAUTIONS/CAUTIONS

- The LARIAT LAA Exclusion System should only be used by trained physicians who perform cardiac interventional procedures.
- Prior to the procedure the physician should review LAA shape and size for suitability of the procedure.
- Attempts to use the LARIAT RS LAA Exclusion Device to ligate LAA structures outside of the size and orientation requirements may result in unsuccessful procedures.
- Use on or before the last day of the expiration month noted on the product packaging.
- DO NOT handle devices by the distal end as it may damage the devices.
- DO NOT handle the device(s) in a manner that may result in damage of the device (e.g., by the distal ends).
- Avoid excessive manipulation (e.g., pinching) of the inflated EndoCATH Balloon as to not damage the Balloon.
- If a safety wire is placed within the pericardial sac, withdraw it back to distal tip of the SofTIP cannula to avoid magnetic interaction.
- DO NOT actuate (open and close) the LARIAT RS LAA Exclusion Device Snare excessively or the pre-tied Suture may prematurely release from the Snare.
- DO NOT pull the red Suture Release Tab (FOB) or the pre-tied Suture may prematurely release from the Snare.
- Before closing and opening the Snare, ensure that the Snare is clear of any other anatomical structure(s) and instrumentation.
- A small amount of slack may need to be advanced into the epicardial 0.035” FindrWIRZ to ensure so that there is no tension on the magnet connection at all times.
- Prior to closing the Snare, ensure non-targeted tissues and instrumentation are free of the closure site.
- Avoid sudden or extreme force during Suture deployment as suture may break.
- While tightening the suture, pull the TenSURE device straight back from LARIAT RS LAA Exclusion Device Handle to avoid damage to the Suture as shown in Figure 5.
- Removal of the open snare loop off of the closure site may be difficult if there is any tissue bunching during the suture tightening. Do not apply excessive force during LARIAT RS LAA Exclusion Device retraction and instead utilize the SofTIP guide cannula position to lift the LARIAT RS LAA Exclusion Device tip off the closure site for confirmation. The device may additionally be slowly opened and closed to release the LARIAT RS LAA Exclusion Device tip from excessively bunched tissue.
- If resistance is felt during removal of the LARIAT RS LAA Exclusion Device, DO NOT attempt to force removal and stop to identify potential causes. Verify the Suture Release Tab is removed, Delivery Snare is open, Suture is fully deployed and device is free of anatomical constraints or instrument interference.
- If removing the LARIAT RS LAA Exclusion Device without having deployed the suture it is recommended to close the Delivery Snare to the “-“ symbol when withdrawing from SofTIP13
- If the epicardial 0.035” FindrWIRZ guide wire and LARIAT RS LAA Exclusion Device Snare are not in the proper configuration, the guide wire may cause excess resistance and potential patient harm during removal through the SofTIP cannula.

- Ensure that if the SofTIP13 is retracted that it still is located within the pericardial space and not pulled back too far.
- Ensure that if the SofTIP13 is retracted that it still is located within the pericardial space and not pulled back too far.
- If the LARIAT RS Suture has NOT been deployed, it is recommended to close the Snare to the " – " symbol when withdrawing the devices from the SofTIP13 cannula.
- Carefully keep the suture from the snare and epicardial 0.035" FindrWIRZ separate during LARIAT RS LAA Exclusion Device removal from the SofTIP13. This will avoid tangling or inadvertent tension placed on the suture attached to the LAA.
- Ensure to separate the suture from the snare and epicardial 0.035" FindrWIRZ as the LARIAT RS LAA Exclusion Device exits the SofTIP13, in effort to ensure no tangling or inadvertent tension is place on the suture as it is still directly attached to the LAA.
- DO NOT remove the red Plunger Lock on the SureCUT Suture Cutter until ready to cut the Suture. Prior removal may result in premature cutting of the Suture.
- Do not continue to advance SureCUT device if resistance in met by either the suture of device during insertion of advancement into the pericardium.
- Cutting of the suture knot may result in incomplete ligation of the LAA
- Confirm that the Handle/Cutting Actuator is released after actuation. Maintaining the Actuator in the cut position may cause continuous tension to the remnant Suture until the Actuator is released.

4.3. Other relevant aspects of safety, including a summary of any field safety corrective action (FSCA; includes field safety notices (FSN)) if applicable

The LARIAT RS LAA Exclusion Devices, EndoCATH Occlusion Balloon Catheter, SofTIP Guide Cannula, SureCUT Suture Cutter, and TenSURE Suture Tightener have not been the subject of any field actions anywhere in the world.

There was one FSCA reported for the FindrWIRZ device, on 30 September 2016, related to guidewire coating delamination. A voluntary worldwide recall was issued via Field Safety Notice. No adverse events were reported related to this defect. The FSCA was reported to the applicable Notified Body. All affected devices in the EU were accounted for and removed.

5. Summary of clinical evaluation and post-market clinical follow-up (PMCF)

This section comprehensively summarises the clinical evaluation results and the clinical data forming the clinical evidence for the confirmation of conformity with relevant general safety and performance requirements, the evaluation of undesirable side-effects and the acceptability of the benefit-risk ratio. It includes a summary of all clinical data, whether favourable, unfavourable, and/or inconclusive.

5.1. Summary of clinical data related to equivalent device, if applicable

The conformity of the LARIAT RS LAA Exclusion Devices (product codes LARIAT45 and LARIAT50) was assessed by the Notified Body on the basis of equivalence. Equivalence has been demonstrated to the LARIAT+ device. LARIAT+ was a previous generation suture delivery device manufactured by SentreHEART (acquired by AtriCure) and CE-marked under MDD. There is no Basic UDI-DI or SSCP available in Eudamed for the LARIAT+ device. The clinical evidence related to the equivalent device LARIAT+ was shown in a multi-centre, observational clinical study summarised in Table 5-1.

Two additional clinical studies included data on the equivalent device LARIAT+ and the subject devices LARIAT RS LAA Exclusion Devices (product codes LARIAT45, LARIAT50). The results of the prospective randomised controlled clinical trial aMAZE and a prospective registry study are summarised in Section 5.2 in Table 5-2 and 5-3.

As shown in Table 5-1, a multi-centre, observational study described use of the LARIAT+ System in 141 patients[1].The authors concluded that their experience with the LARIAT+ System showed that LAA ligation is feasible and that prospective cohorts and longer follow-up are warranted to evaluate safety and effectiveness of thromboembolism prevention.

Table 5-1: Summary of LARIAT+ Multi-Centre European Experience[1]

Identity of the investigation/study	A collective European experience with left atrial appendage suture ligation using the LARIAT+ device Tilz et al. EP Europace 2020.
Identity of the device	LARIAT+ EndoCATH balloon FindrWIRZ TenSURE device SureCUT suture cutter
Intended use of the device in the investigation	LAA closure
Objectives of the study	1) to determine effectiveness of LAA closure with the LARIAT+ device; 2) to assess procedural and 30-day peri-procedural safety; and 3) to obtain initial clinical follow-up.
Study design and duration of follow-up	Multi-centre, observational study; LAA imaging follow-up: 181± 72 days; clinical follow-up: 180± 104 days
Primary and secondary endpoint(s)	See study objectives
Inclusion/exclusion criteria for subject selection	Inclusion: 1) age 18 years or older; 2) non-valvular AF; 3) at least one risk factor of embolic stroke ($CHADS_2$ score of at least 1 or CHA_2DS_2-VASc score of at least 2; 4) ineligible for oral anticoagulation (OAC) therapy (labile international normalised ratio level, non-compliant, contraindicated), or OAC failure (thromboembolism on OAC therapy), or as part of a strategy for LAA exclusion with pulmonary vein isolation (PVI) for symptomatic, antiarrhythmic drug-refractory AF; and 5) a life expectancy >1 year. Exclusion: 1) known history of pericarditis, thoracic radiation, or cardiac surgery; 2) pectus excavatum; 3) recent myocardial infarction within 3 months; 4) prior embolic event within the last 30 days; 5) New York Heart Association (NYHA) functional class IV heart failure symptoms; and 6) left ventricular ejection fraction (LVEF) ≤30%.
Number of enrolled subjects	141
Study population	Age (years): 70.4 ± 12.2 Female patients/total patients: 62/141 (44.0%) Type of AF:

	• Paroxysmal: 67/141 (47.5%) • Persistent: 30/141 (21.3%) • Longstanding persistent: 44/141 (31.2%) Patients with previous stroke/total patients: 13/141 (9.2%) Patients with previous bleeding event/total patients: 30/141 (21.3%) CHA_2DS_2-VASc score: 3 [2; 4] Reason for LAA ligation: • Contraindication/intolerance to OAC: 113/141 (80.1%) Prevention of LAA thrombus formation after LAA electrical isolation: • 23 (16.3%) • Adjunctive to pulmonary vein isolation (PVI): 5 (3.5%)
Summary of study methods	Pericardial access was performed with either a 21-gauge micropuncture needle with or without an 18-gauge telescopic needle approach. Transseptal catheterization and LAA angiography were performed. The endocardial magnet wire and EndoCATH balloon catheter were positioned in the anterior superior LAA. The epicardial magnet was inserted through the epicardial sheath and connected to the endocardial magnet. The LARIAT was advanced through the epicardial sheath over the epicardial magnet wire. The ostium of the LAA was verified with the balloon positioned at the ostium of the LAA, and the snare was closed. The suture was released from the snare and tightened with the TenSure device. The suture was cut with a suture-cutting device. LAA exclusion success was defined as absence of a contrast leak on left atriogram and ≤5mm jet as visualized by color Doppler on TEE. LAA closure was confirmed by TEE at 30-90 days and 6-12 months post-ligation. Incomplete LAA closure defined as color Doppler flow >5 mm. Clinical follow-up was at 1, 3, 12 months post-LAA ligation.
Summary of results	Acute closure: Acute left atrial closure was achieved in 97.9% (138/141) patients, and complete acute closure without leakage was 130/138 (94.2%). Three patients (2.1%) did not undergo deployment due to pericardial adhesion (existing), pericardial access related complication, and multiple posterior LAA lobes. TEE: 103 (74.6%) patients had follow-up TEE at a mean of 181+/-72 days post-ligation. 100/103 (97.1%) of LAAs were closed without leaks >5 mm. 81 (78.6%) cases had no leaks or leaks <2 mm. 19 cases (18.4%) had leaks ≥2 mm and <5 mm. LAA thrombus found on ligated atrial side of LAA stump in 2 patients (1.9%) at 1-3 month TEE; they resolved with OAC and neither had a leak or

	thromboembolic event. Clinical follow-up was available in 111 patients with a mean of 180 +/- 104 days. Two patients (1.8%) had a TIA and 4 and 7 months of follow-up (no LAA leaks were observed). Two patients died, the causes of which were unrelated to the device or procedure (one septic shock and one malignant disease). Serious adverse events within 30 days included (n=4, 2.8%): • Right ventricular perforation with steerable sheath that led to tamponade that resulted in a stroke during surgery • Pneumothorax requiring chest tube • Groin bleed requiring transfusion (pre-existing low hemoglobin values) • Late pericardial effusion >500 cc necessitating drainage Device-related complications (n=2, 1.4%): • 2 cases of LAA perforation with FindrWIRZ that resolved upon completion of the ligation and did not have acute or long-term consequences Minor adverse events (n=19, 13.5%) • 1 pneumothorax with no need for treatment • 1 superficial subxiphoid bleed • 3 pericardial effusions, 2 which required pericardiocentesis) • 1 pseudoaneurysm (conservative management) • 4 pleural effusions (no intervention) • 8 pericarditis >2 days (conservative treatment) 1 arterio-venous fistula (no intervention required)
Study limitations	• Local inclusion criteria used for evaluation of LAA for ligation • Self-reported events • Clinical follow-up may have occurred with referring physician • Two pericardial effusions required intervention but classified as minor per Munich LAA consensus • 74.6% of patients had follow-up TEE available
Any device deficiency or device replacements related to safety or performance during the study	None were reported.

5.2. Summary of clinical data from conducted investigations of the device before the CE-Marking, if applicable

The aMAZE trial (NCT02513797) is a prospective, multicenter, randomized (2:1) controlled study to evaluate the safety and effectiveness of the LARIAT LAA Exclusion System with LARIAT+ and LARIAT RS LAA Exclusion Devices to percutaneously isolate and ligate the LAA from the left atrium as an adjunct to planned pulmonary vein isolation (PVI) catheter ablation in the treatment of subjects with symptomatic persistent or longstanding persistent atrial fibrillation.

The primary results of the aMAZE trial were:

- Primary safety was met with a MAE rate of 3.4% within 30 days, which was below the prespecified safety goal.
- Primary effectiveness did not meet superiority endpoint with Freedom from atrial arrhythmias at 12 months of 64.3% with LARIAT + PVI and 59.9% with PVI alone, a difference of 4.3% (95% Bayesian CI: -4.2, 13.2); Bayesian posterior probability = 0.835; superiority not met
- Technical success of closure was high with 80%, 75%, and 84% of patients showing complete closure (0 mm residual communication) acutely (post-LARIAT-ligation), at 30 days follow-up (post-LARIAT), and at 12-months follow-up (post-PVI).

Table 5-2. aMAZE Clinical Trial[3]

Identity of the investigation/study	aMAZE trial (Presented at American Heart Association Meeting, November 2021)
Identity of the device	• LARIAT+ • LARIAT RS LAA Exclusion Device (product code: LARIAT45) • LARIAT RS LAA Exclusion Device, 50 mm (product code: LARIAT50) • EndoCATH Occlusion Balloon Catheter • SofTIP Guide Cannula • FindrWIRZ Guide Wire System • TenSURE Suture Tightener • SureCUT Suture Cutter
Intended use of the device in the investigation	Percutaneously ligate the LAA as an adjunct to planned pulmonary vein isolation in the treatment of patients with symptomatic persistent or longstanding persistent AF
Objectives of the study	Demonstrate the ability of the LARIAT Suture Delivery System to: • percutaneously isolate and ligate the LAA from the LA as an adjunct to planned PVI catheter ablation in the treatment of subjects with symptomatic persistent or longstanding persistent AF; • demonstrate the adjunctive percutaneous LAA ligation procedure does not result in an unacceptable risk of serious adverse events in the defined subject population; and assess freedom from episodes of AF through 12 months post PVI.
Study design and duration of follow-up	Prospective, multi-center, randomized (2:1) controlled trial with a Bayesian adaptive, superiority design. Follow-up was 12-months.

Primary and secondary endpoint(s)	Primary Effectiveness Endpoint: • Freedom from AF >30 seconds at 12 months post PVI catheter ablation, assessed by 24-hour Holter or symptomatic event monitoring Primary Safety Endpoint: • Composite of device and / or procedure related serious adverse events (SAEs) at 30 days post LARIAT procedure compared against pre-defined performance goal Technical Success: • Closure / degree of residual communication between the LA and LAA assessed immediately post LARIAT procedure (acute), 30 – 45 days post LARIAT and 12 months post PVI catheter ablation.
Inclusion/exclusion criteria for subject selection	Inclusion criteria: Age ≥18 years and ≤80 years; symptomatic persistent or longstanding persistent AF (7 days to <3 years); failed at least 1 Class I/III anti-arrhythmic drug; life expectancy ≥1 year Key exclusion criteria: Prior procedure opening of pericardium or entering pericardial space; prior epicardial or endocardial AF ablation procedure; measured LA diameter >6 cm; documented embolic stroke, TIA, or suspected neurologic event within 3 months prior to planned intervention, currently exhibits class IV heart failure symptoms See https://clinicaltrials.gov/ct2/show/NCT02513797 for all exclusion criteria
Number of enrolled subjects	610
Study population	Age: 66.6±8.12 years Female: 164 (27%) BMI (kg/m2): 31.29±4.55 NYHA Class II-III: 200 (33%) AF Classification: 7 days to <6 months: 465 (79%) ≥6 months to <12 months: 54 (9%) ≥12 months to 3 years: 67 (11%) Left Atrial Volume 137.55±38.85 Hypertension: 506 (83%) Diabetes: 123 (20%)
Summary of study methods	Patients randomized 2:1 to LARIAT + pulmonary vein antral isolation (LARIAT+ PVI) or PVI alone. PVI was performed with an irrigated tip, radiofrequency, contact force, commercially approved catheter. Thirty days after LARIAT ligation, patients had TEE to assess closure and safety events were assessed. Then the patient had PVI. A 90-day blanking period was used. At 12-months post-PVI, effectiveness was assessed and LARIAT closure was again assessed by TEE.

<table>
<tr><td>Summary of results</td><td>
Primary effectiveness:
Freedom from atrial arrhythmias 12 months:
LARIAT+PVI: 64.3%
PVI alone: 59.9%
Difference: 4.3% (95% Bayesian CI: -4.2, 13.2)
Bayesian posterior probability = 0.835; superiority not met

Primary Safety: 30-day major adverse event rate was 3.4% (95% Bayesian CI: 2.0, 5.0)

n=3 (0.8%) serious injury to cardiac/related structure requiring surgical intervention
n=8 (2.2%) bleeding (≥2 packed red blood cells [PRBC]) in post-operative day 1-2; organ structure/injury requiring intervention or fatal
n=1 (0.3%) vascular injury requiring surgical treatment, hospital admission or PRBC

<table>
<tr><th>Technical success of LAA closure – residual communication</th><th>Post-LARIAT ligation</th><th>30-days Post-LARIAT</th><th>12 months Post-PVI</th></tr>
<tr><td>0 mm</td><td>80%</td><td>75%</td><td>84%</td></tr>
<tr><td>≤1 ± 1 mm</td><td>87%</td><td>81%</td><td>85%</td></tr>
<tr><td>≤3 mm</td><td>94%</td><td>89%</td><td>93%</td></tr>
<tr><td>≤5 mm</td><td>99%</td><td>99%</td><td>99%</td></tr>
</table>
</td></tr>
<tr><td>Study limitations</td><td>All U.S. sites.</td></tr>
<tr><td>Any device deficiency or device replacements related to safety or performance during the study</td><td>Four (4) device observations were related to the LARIAT Suture Delivery device: None of the observations resulted in an AE or clinical sequelae. One (1) device observation was related to the SureCUT Suture Cutter: the affected device was replaced and the procedures proceeded as planned. The observation did not result in an AE or clinical sequelae. Two (2) device observations were related to the FindrWIRZ Guidewire: the affected devices were replaced, and the procedures proceeded as planned. One (1) reported procedural observation resulted in an AE that resolved without sequelae. There was no device malfunction reported. The other observation was without clinical sequelae.</td></tr>
</table>

The LARIAT LAA Exclusion System with the LARIAT RS LAA Exclusion Device (product code: LARIAT45) or LARIAT+ devices was used in a prospective, observational, non-randomized study evaluating the feasibility of LAA ligation concomitant with hybrid epicardial-endocardial radiofrequency ablation[4]. This study reported LAA closure acutely and at 1-3 months post-procedure, as well as major adverse events within 30 days. The results are summarized in Table 5-3.

Table 5-3. Summary of LARIAT LAA Exclusion System (LARIAT+/RS) study with subxiphoid hybrid ablation procedure[4]

Identity of the investigation/study	Subxiphoid hybrid epicardial-endocardial atrial fibrillation ablation and LAA ligation: Initial Sub-X Hybrid MAZE Registry Results Ellis et. al., JACC: Clin Electrophysiol 2020. NCT04148625 at clinicaltrials.gov
Identity of the device	• LARIAT RS LAA Exclusion Device (product code: LARIAT45) or LARIAT+ • FindrWIRZ • SofTIP
Intended use of the device in the investigation	Closure of the LAA
Objectives of the study	To report initial safety and efficacy of a new subxiphoid hybrid epicardial-endocardial AF ablation and LAA ligation approach for the treatment of persistent or longstanding persistent AF
Study design and duration of follow-up	Prospective, observational, non-randomized, feasibility
Primary and secondary endpoint(s)	Primary endpoints: 1. Freedom from AF >30 seconds [Time frame: 12 months]; 2. Pre-specified 30-day periprocedural major adverse events on the basis of the Munich LAA consensus document and U.S. Food and Drug Administration approved aMAZE clinical trial
Inclusion/exclusion criteria for subject selection	**Inclusion criteria:** 1) age 18 years or older; 2) history of symptomatic persistent (sustained AF for >7 days), longstanding persistent (>1 year but <3 years), or permanent (>3 years) nonvalvular AF; 3) failure of at least 1 class I or class III antiarrhythmic drug or prior PVI procedure; 4) presence of at least 1 risk factor for embolic stroke ($CHADS_2$ score 1); and 5) life expectancy of at least 1 year. **Exclusion criteria:** 1) history of acute or chronic pericarditis; 2) history of cardiac surgery; 3) pectus excavatum; 4) recent myocardial infarction (within 3 months); 5) prior embolic event within the past 30 days; 6) NYHA functional class IV heart failure symptoms; (7) LVEF <30%; and 8) receipt of thoracic radiation. Additional exclusion criteria on the basis of LAA anatomy obtained using contrast gated computed tomographic angiography included 1) LAA width >45 mm; 2) a superiorly oriented LAA with the LAA apex directed behind the pulmonary artery; 3) a bilobed or multilobed LAA in which lobes were oriented in different planes exceeding 45 mm; and 4) a posteriorly rotated heart.
Number of enrolled subjects	N=33
Study population	Age (yrs): 64 ± 9 Male: 25 (76%) Hypertension: 22 (73%) Diabetes mellitus: 7 (23%)

	CHF/MI: 9 (31%) TIA/stroke: 4 (11%) CHA_2DS_2-VASc score: 2.6 ± 1.6 HAS-BLED score: 1.6±1.2 LVEF (%): 51 ± 10 Left atrial (LA) size (mm): 45 ± 11 Type of AF: Persistent (>7 days): 9 (27%) Persistent (>3 months to 1 yr): 20 (60%) Long-standing persistent (>1 yr): 1 (3%) Permanent (>3 yrs): 3 (9%) Number of prior PVI procedures 1.4 ± 0.7 Number of patients with prior PVI: 9 (39%)
Summary of study methods	Patients received MAZE-like lesion set: PVI, LA posterior wall, ligation of the LAA and a right sided cavotriscuspid isthmus line. LAA ligation was performed with LARIAT; in 20/33 patients, the epicardial guide sheath was through a subxiphoid pericardial window while in the remaining 13, a percutaneous subxiphoid approach was used after epicardial ablation. In two patients, LAA was ligated solely with an epicardial approach with direct visualization of the LAA. Epicardial ablation was performed via a subxiphoid approach to a pericardial window. Endocardial ablation was performed concomitantly in 20 patients and staged in 13 patients. Post-procedurally, patients received colchicine twice a day for 2 weeks and NSAIDs as indicated by pericarditis symptoms. OAC was continued within 2 days of the subxiphoid concomitant procedure or uninterrupted in staged procedures. Clinical follow-up was for 1, 3, 6, and 12 months, after which it was annually or if symptoms occurred.

Summary of results	LAA closure: All 33 patients had acute closure of LAA confirmed by LA Angiography and/or TEE color flow Doppler.
	TEE/CTA were performed 1-3 months after LAA ligation
	• No leaks >5 mm
	• 6 patients (18%) had leaks 1-5 mm (5/6 underwent LAA ligation through pericardial window)
	  ○ Electrical isolation was maintained in 5/6 pts with leaks
	  ○ Four leaks closed with occluder device and one leak closed spontaneously
	Safety events (occurring after LAA ligation and epicardial ablation):
	• No acute periprocedural complications occurred within 7 days.
	• One patient developed acute renal failure that resolved without therapy.
	• Three late adverse events occurred

	between 2-4 weeks. ○ One patient had an incisional hernia that was surgically repaired. ○ Two patients developed pericardial effusions requiring pericardiocentesis with short-term colchicine and NSAIDs.
Study limitations	• Variations within procedural protocol (mainly concomitant vs. staged procedures) • Mixed population of subjects • Lack of long-term continuous monitoring for all patients for rhythm outcomes
Any device deficiency or device replacements related to safety or performance during the study	None were reported.

5.3. Summary of clinical data from other sources, if applicable

The following studies used earlier generations of the LARIAT RS LAA Exclusion Devices. The LARIAT devices for suture delivery used in the studies in this section are not LARIAT+ or the subject devices LARIAT45 and LARIAT50. The identities of the devices is listed as described in the published literature.

Left Atrial Appendage Ligation and Ablation for Persistent AF (LAALA-AF) Registry[5]

A prospective, multi-centre, observational registry study was performed to evaluate the impact of adding the LAA closure system (LARIAT) procedure to conventional AF ablation in patients with persistent AF between Jan 2012 and December 2013. The study also reported LAA closure rates and safety event as shown in Table 5-6.

Table 5-4. LAALA-AF Registry Clinical Summary[5]

Identity of the investigation/study	LAALA-AF Registry Lakkireddy et al. 2016
Identity of the device	LARIAT System
Intended use of the device in the investigation	To exclude the LAA
Objectives of the study	This study was intended to evaluate the impact of adding the left atrial appendage (LAA) closure system (LARIAT) procedure to conventional atrial fibrillation (AF) ablation in patients with persistent AF.
Study design and duration of follow-up	Prospective, multi-center observational study of patients referred for ablation of persistent AF who then received LARIAT followed by ablation or ablation only. Protocol was approved at all institutional IRBs. Patients were enrolled from January 2012 to December 2013. Patients were followed for at least 1 year.
Primary and secondary endpoint(s)	Primary outcome evaluated was freedom from atrial tachycardia (AT) or AF during the first 1 year off anit-arrhythmic drugs (AADs) (after the first 2 months of the post-ablation blanking period).

Inclusion/exclusion criteria for subject selection	Inclusion: 1) age 18 years or older; 2) persistent nonvalvular AF; 3) at least 1 risk factor of embolic stroke (CHADS2≥1); and 4) a life expectancy of at least 1 year. Exclusion: 1) history of cardiac surgery; 2) unfavorable chest anatomy (pectus excavatum); 3) recent myocardial infarction (within 3 months); 4) embolic event within the past 30 days; 5) NYHA functional class IV heart failure symptoms; and 6) history of thoracic radiation. Exclusion criteria based on LAA anatomy included: 1) a LAA width >40 mm; 2) a superiorly oriented LAA with the LAA apex directed behind the pulmonary trunk; 3) bilobed LAA or multilobed LAA in which lobes were oriented in different planes exceeding 40 mm; and 4) a posteriorly rotated heart.
Number of enrolled subjects	156 screened, 18 excluded 69 treated with LARIAT+ PVI ablation; 69 treated with PVI ablation alone
Study population	Adult patients with persistent AF LARIAT group (N=69): Age: 67 ± 10 years Male: 48 (70%) $CHADS_2$: 2.46 ± 1.30 CHA_2DS_2-VASc: 3.68 ± 1.64
Summary of study methods	After excluding 18 patients who were not candidates for LARIAT exclusion, 69 patients underwent LARIAT procedure. Then patients underwent conventional AF ablation procedure (primarily PVI) at least 30 days later. An equal number of age- and sex-matched patients with persistent AF undergoing AF ablation only during the same time frame were used as controls. The LARIAT procedure was performed with the LARIAT LAA Exclusion System. AF ablation in both groups consisted of PVI with additional ablation at operator discretion. Patients seen at 2-, 6-, and 12-months post-procedure for clinical visits.
Summary of results	Treatment failures: 0/69 (0%) for LARIAT ligation Acute closure: Complete: 100% (≤1 mm leak by Doppler) Twenty (20) had a small residual stump (mean 3.1mm). 90-day closure: Complete: (no leak): 62 (90%) Leaks (≤5 mm): 7 (10%) Acute complications with LARIAT procedure: All: 3/69 (5%) • 1 right ventricular puncture (conservatively managed) • 1 pleural effusion (thoracentesis) • 1 groin hematoma (no surgery) Freedom from AF/AT at 1 year off AADs was 65% in LARIAT plus ablation group vs. 39% in ablation only group ([=0.002).

Study limitations	• Non-randomized • Patient characteristics differed between groups • Relatively small study
Any device deficiency or device replacements related to safety or performance during the study	None reported

LARIAT Working Group Multi-Centre Study Clinical Summary[6]
From 2011 to 2015, 18 centres contributed to a registry of epicardial LAA ligation of 712 consecutive patients focusing on complications and leak rates. The results are summarised in Table 5-7. The study described a reduction in acute complications with the use of a micropuncture needle for pericardial access and a reduction in delayed complications with colchicine use. From this study, the investigators concluded the LARIAT procedure had acceptable procedural risks and effectively closed the LAA.

Table 5-5. LARIAT Working Group Multicentre Study[6]

Identity of the investigation/ study	LARIAT Working Group Multicenter Study Lakkireddy et al. 2015
Identity of the device	LARIAT SofTIP FindrWIRZ SureCUT TenSURE device
Intended use of the device in the investigation	LAA closure
Objectives of the study	To delineate the safety and efficacy of LAA closure with the LARIAT device.
Study design and duration of follow-up	Multi-center observational registry study of consecutive patients. Data collection began January 1, 2011 and data collection was completed January 9, 2015.
Primary and secondary endpoint(s)	The primary endpoint was procedural success, defined as successful suture deployment, no leak by intraprocedural transesophageal echocardiography (TEE), and no major complication at discharge (death, cardiac perforation) requiring cardiac surgery, major bleeding requiring transfusion, or stroke). Secondary endpoint: 2–5 mm on follow-up TEE
Inclusion/ exclusion criteria for subject selection	Not specified
Number of enrolled subjects	929 screened, 217 excluded due to unfavorable anatomy 712 treated
Study population	Age: 70.9 ±10.4 years BMI: 30.1 ±7.4 Male: 57.3% Caucasian: 87.0%

<table>
<tr><td></td><td>$CHADS_2$ score: 2.7 ±1.3
CHA_2DS_2-VASc score: 3.9 ±1.8
HAS-BLED: 3.4 ±1.3
Diabetes mellitus: 28.0%
Congestive heart failure: 24.6%
Prior CVA/TIA: 40.2%
Type of AF:
Paroxysmal: 38.4%
Persistent: 31.1%
Longstanding persistent: 30.5%
LVEF: 51.7 ±16.0
LA diameter: 5.6 ±5.9</td></tr>
<tr><td>Summary of study methods</td><td>Participating centers provided information on all patients in whom LAA exclusion with the LARIAT system was attempted. A standardized form was used to collect data. LAA Exclusion was performed with the LARIAT system. In early experience, centers used a large bore Pajunk needle for pericardial access; subsequently many centers used a long micropuncture needle. After the procedure, peri-procedural medications were per operator preference. Following up imaging with TEE was performed 1-3 months based on institutional protocol.</td></tr>
<tr><td>Summary of results</td><td><u>Acute closure</u>: Complete closure: 98.1% (669/682)
Leaks < 2 mm: 1.9% (13/682)
Leaks 2-5 mm: 0%
Leaks > 5 mm: 0%

<u>1-3 month</u>: Complete closure: (448/480)
Leaks 2-5 mm: 6.5% (31/480)
Leaks > 5 mm: 0.2% (1/480)

1-3 month thrombus: 2.5% (12/480) –resolved with OAC

<table>
<tr><th>Acute Complications</th><th>Total (n=712)</th><th>Large bore needle (n=288)</th><th>Micropuncture needle (n=424)</th></tr>
<tr><td>Procedure-related mortality</td><td>1 (0.14%)</td><td>1</td><td>0</td></tr>
<tr><td>Cardiac perforation req. open heart surgery</td><td>10 (1.4%)</td><td>9</td><td>1*</td></tr>
<tr><td>Cardiac perforation without need for surgery</td><td>14 (2.0%)</td><td>11</td><td>3*</td></tr>
<tr><td>Transfusions</td><td>9 (1.3%)</td><td>7</td><td>2*</td></tr>
<tr><td>Perioperative stroke</td><td>0 (0%)</td><td>0</td><td>0</td></tr>
<tr><td>Injury to superior, epigastric, coronary, or internal mammary artery</td><td>4 (0.56%)</td><td>2</td><td>2</td></tr>
<tr><td>Total</td><td>38 (5.3%)</td><td>29</td><td>9*</td></tr>
<tr><td colspan="4">*Significantly fewer in procedures that used micropuncture needle vs. large bore needle</td></tr>
<tr><th>Delayed complications</th><th>Total (n=712)</th><th>No colchicine (n=332)</th><th>Colchicine (n=380)</th></tr>
<tr><td>Severe pericarditis requiring NSAIDs/colchicine</td><td>11 (1.5%)</td><td>9</td><td>2†</td></tr>
<tr><td>Late pericardial effusion</td><td>4 (0.56%)</td><td>4</td><td>0</td></tr>
<tr><td>Late pleural effusion</td><td>19 (2.7%)</td><td>15</td><td>4†</td></tr>
<tr><td>Total</td><td>34 (4.8%)</td><td>28</td><td>7†</td></tr>
<tr><td colspan="4">†Significantly fewer in colchicine group</td></tr>
</table></td></tr>
</table>

Study limitations	• Retrospective data collection • Evolving technique thus acute and long term success definitions may change • Limited pericardial access complications to those requiring post-procedure care
Any device deficiency or device replacements related to safety or performance during the study	None reported

PLACE II

Upon completion of PLACE I, the PLACE II study was initiated to evaluate the safety and the ability of the LARIAT device to completely ligate the LAA during percutaneous stand-alone procedures [7]. PLACE II enrolled subjects from December 2009 to December 2010. The results are summarised in Table 5-8. The authors concluded that LAA closure with the LARIAT device could be performed effectively with acceptably low access complications and periprocedural adverse events in this observational study.

Table 5-6. Summary of PLACE II[8]

Identity of the investigation/study	PLACE II Bartus et. al., 2013
Identity of the device	• LARIAT Suture Delivery Device • FindrWIRZ • EndoCATH • SofTIP • SureCUT • TenSURE Suture Puller
Intended use of the device in the investigation	To ligate soft tissue in humans during surgical and percutaneous procedures.
Objectives of the study	To determine the efficacy and safety of LAA closure via a percutaneous LAA ligation approach.
Study design and duration of follow-up	Single-centre, open-label, non-randomized, non-controlled observational study. One-year follow-up.
Primary and secondary endpoint(s)	Rate of device-related serious adverse events at 30 days; and percent of patients with complete exclusion of the LAA measured with TEE at 90 days and 12 months post-procedure
Inclusion/exclusion criteria for subject selection	Inclusion Criteria: 1) age ≥ 18 years, 2) nonvalvular AF, 3) at least 1 risk factor of embolic stroke ($CHADS_2 \geq 1$), 4) a poor candidate or ineligible for warfarin therapy (e.g., labile international normalized ratio level, noncompliant, contraindicated) and/or a warfarin failure (i.e., transient ischemic attack or stroke

	while on warfarin therapy) and 5) a life expectancy of at least 1 year. Exclusion criteria: 1) history of pericarditis, 2) history of cardiac surgery, 3) pectus excavatum, 4) recent MI within 3 months, 5) prior embolic event within the last 30 days, 6) NYHA IV heart failure symptoms, 7) LVEF < 30% and 8) history of thoracic radiation. Additional exclusion criteria based on LAA anatomy per CT scan included: 1) LAA width > 40 mm, 2) superiorly oriented LAA with the LAA apex directed behind the pulmonary trunk, 3) bilobed LAA or multilobed LAA in which lobes were oriented in different planes exceeding 40 mm, and 4) a posteriorly rotated heart.
Number of enrolled subjects	119 enrolled; 89 treated.
Study population	Adults with AF. Mean age=62 years ± 10 years. Male 57% (n=51); female 43% (n=38).
Summary of study methods	Descriptive statistics.
Summary of results	Eighty-five (96%) of 89 patients underwent successful LAA ligation. Eighty-one of 85 patients had complete closure immediately. Three of 85 patients had a ≤ 2-mm residual LAA leak by TEE color Doppler evaluation. One of 85 patients had a ≤ 3-mm jet by TEE. There were no complications due to the device. There were 3 access-related complications (during pericardial access, n=2; and transseptal catheterization, n=1). Adverse events included severe pericarditis post-operatively (n=2), late pericardial effusion (n=1), unexplained sudden death (n=2), and late strokes thought to be non-embolic (n=2). At 1 month (81 of 85) and 3 months (77 of 81) post-ligation, 95% of the patients had complete LAA closure by TEE. Of the patients undergoing 1-year TEE (n=65), there was 98% complete LAA closure, including the patients with previous leaks.
Study limitations	Limitations: non-randomized, single-center, and use of long-term anticoagulants post procedure, which limit the assessment of post procedure embolic events.
Any device deficiency or device replacements related to safety or performance during the study	None were reported.

Permanent Ligation Approximation Closure Exclusion (PLACE) I [2]
This study was performed prior to CE Marking under MDD in 2009. The first human study, PLACE I, was conducted at John Paul II Hospital, Krakow Poland and enrolled patients to demonstrate the feasibility of the FindrWIRZ, EndoCATH, SofTIP, and SureCUT for use with the LARIAT device to ligate soft tissue in humans during surgical and percutaneous procedures. The authors concluded that catheter-based surgical suture ligation of the LAA is feasible in humans and that this novel catheter approach may be appropriate for patients

with AF who are ineligible for anticoagulation therapy. Further investigation is needed to demonstrate the long-term safety and efficacy of LAA closure. Table 5-2 presents a summary of PLACE I.

Table 5-7. Summary of PLACE I[2]

Identity of the investigation/study	PLACE I Bartus et. al., 2011
Identity of the device	• LARIAT device • FindrWIRZ • EndoCATH • SofTIP • SureCUT
Intended use of the device in the investigation	To ligate soft tissue in humans during surgical and percutaneous procedures.
Objectives of the study	To demonstrate the feasibility of the FindrWIRZ, EndoCATH, SofTIP, and SureCUT for use with the LARIAT device to ligate soft tissue during surgical and percutaneous procedures.
Study design and duration of follow-up	Single-centre, open-label, non-randomized, non-controlled feasibility study. Two-month follow-up.
Primary and secondary endpoint(s)	Primary safety outcome: Rate of device-related serious adverse events (discharge/30 days) Primary efficacy outcomes: Percent of patients with complete exclusion of the LAA measured with TEE (acute/3 months)
Inclusion/exclusion criteria for subject selection	Patients at the study center undergoing either mitral valve replacement (MVR) or catheter ablation for AF with a history of chronic or intermittent AF with at least one risk factor for stroke were identified for LAA closure.
Number of enrolled subjects	13
Study population	Thirteen adult patients undergoing either mitral valve surgery (n=2) or electrophysiological study and radiofrequency catheter ablation for atrial fibrillation (n=11). Mean age = 57 years (range 43-64). Male 62% (n=8); female 38% (n=5).
Summary of study methods	Descriptive statistics
Summary of results	Successful LAA ligation was confirmed in two subjects undergoing mitral valve replacement surgery before enrolling eleven subjects undergoing percutaneous catheter ablation (PCA). Ten of the PCA subjects had complete closure, while the eleventh had their procedure stopped early due to lack of echocardiographic visualization to maneuver the snare over the EndoCATH occlusion balloon. There was one safety event reported, for the inability to remove the LARIAT snare due to the subject's pectus excavatum. The thoracoscopic opening relieved the pericardial pressure and the LARIAT device

	was easily removed from the LAA without further incident and the LAA was successfully ligated.
Study limitations	Limitations include a small sample size, single-center experience, not randomized, and minimal follow-up to assess long-term clinical outcomes.
Any device deficiency or device replacements related to safety or performance during the study	None were reported.

Other published clinical studies describing safety and performance of the LARIAT LAA Exclusion System that were identified through a systematic literature search are summarized in Section 5.4.

5.4. An overall summary of the clinical performance and safety

Safety

The safety objective identified in the LARIAT LAA Exclusion System Clinical Evaluation Plan was a major adverse event (MAE) rate within 30 days of the LARIAT procedure of ≤10% (6% estimated from 2264 patients in literature plus 4% margin) with an upper confidence interval of 11.3%. Major adverse events were defined as major bleeding, pericarditis requiring surgical intervention, pericardial effusion requiring surgical intervention, hemothorax requiring surgical intervention, vascular injury requiring surgical intervention, hospitalization, or blood transfusion, and/or pseudoaneurysm/arteriovenous fistula. Based on a systematic literature review and evaluation of published safety results, the overall MAE rate in more than 2500 patients met the clinical safety objective, with MAE rates in the range of 0-10% in individual studies in more than 2500 patients[1,2,4-6,8-23]. Overall, these published studies suggest the LARIAT LAA Exclusion System is safe for its intended use and meet the clinical safety objective.

Additionally, the aMAZE clinical trial primary safety results found a 3.4% MAE rate within 30 days of the LARIAT procedure in 404 patients who received LARIAT, which met the primary safety objective of the trial[3].

Performance

The clinical performance objectives identified by the Clinical Evaluation Plan were acute closure rate of ≥ 95% and long-term (>45 days-12 months) closure rate of ≥ 91%. Closure was defined as no leak or leak ≤3 ± 2 mm based on state-of-art devices. A leak is defined as residual flow between the LAA and left atrium. The device is intended to be implanted for the rest of the patient's life. Based on a systematic literature review and evaluation of published closure results, the overall closure rates in more than 1900 patients met the clinical performance objective, with acute closure rates in individual studies ranging from 95-100% and long-term closure rates ranging from 91-100%[1,2,4-6,8-12,14-17,19-24]. Small peridevice leaks were reported but the relationship between smaller leaks (≤ 5 mm) and increased thromboembolic events is unknown.

Additionally, the aMAZE clinical trial results found that 99% of patients treated with LARIAT had closure with leaks ≤5mm post-procedure, at 30-days, and 12-months post PVI procedure[3].

The clinical benefit of the LARIAT LAA Exclusion System is reduction in thromboembolic events when used in patients with atrial fibrillation who are intolerant to or contraindicated

for long term oral anticoagulation therapy. A low incidence of thromboembolic events after LARIAT closure was evaluated in several published studies identified in the Clinical Evaluation systematic literature search[1,10,11,14,16,24]. These studies reported a low or reduced thromboembolic event rate compared to that expected for the population based on predictive risk scores for stroke (i.e. CHA_2DS_2-VASc).

Based on the clinical evaluation using LARIAT RS LAA Exclusion Devices (LARIAT45, LARIAT50) or LARIAT+, an equivalent device to LARIAT45/50, it is concluded that the LARIAT LAA Exclusion System is safe and performs as intended, and is in compliance with the General Safety and Performance Requirements. Additional supportive evidence from earlier published studies on previous generation LARIAT devices are supportive of the performance and safety of the System for LAA closure. The known and foreseeable risks have been identified in the risk management file and have been appropriately minimized. The identified risks in the risk management file have been adequately addressed by the body of published clinical data. As demonstrated in the published literature, these risks are acceptable when weighed against the benefits of using the device.

5.5. Ongoing or planned post-market clinical follow-up

The LARIAT LAA Exclusion System is currently the subject of the prospective, multicenter, randomized, controlled aMAZE Trial (ClinicalTrials.gov, Registration No. NCT02513797), which is designed to evaluate the safety and effectiveness of the System to percutaneously isolate and ligate the LAA from the LA as an adjunct to planned pulmonary vein isolation (PVI) catheter ablation for the treatment of symptomatic persistent or long-standing persistent AF. Between 2015 and 2019, 610 patients were enrolled in the aMAZE Trial. All subject data from both stages was included in the primary analysis. Primary results were presented at the 2021 American Heart Association meeting[3] and are summarized in Section 5.1. The aMAZE continued access protocol (aMAZE-CAP) will also serve as PMCF for the LARIAT LAA Exclusion System. All patients enrolled and treated in aMAZE-CAP will be followed for a minimum of 3 years (at 18, 24, and 36 months) after their PVI procedure for assessment of the primary and secondary endpoints (safety and effectiveness), including all adverse events, such as such as death, stroke, system embolic events, and other cardiovascular events reported since the last visit assessment.

6. Possible diagnostic or therapeutic alternatives

Atrial fibrillation (AF) is the most common sustained arrhythmia observed in clinical practice. The LAA specifically has been implicated in both the persistence of AF and the source of thrombus formation, attributed to stasis of blood flow in the appendage itself. The AF population has a higher risk of morbidity and mortality associated with increased incidence of other heart disease (e.g., heart failure, stroke, etc.).[25] Ectopic foci within the pulmonary veins (PVs) are the most active drivers of AF; however other non-PV drivers may contribute. These ectopic non-PV foci contribute more to non-paroxysmal AF (non-PAF) and can be located in the superior vena cava, ligament of Marshall, coronary sinus, crista terminalis, left atrial (LA) posterior wall, or the LAA.[26,27 28]

AF is classified by episode duration and increases in severity as atrial remodeling occurs. This characterization determines the course of therapy and likelihood of success. There are three types of AF treatment: 1) pharmaceutical therapy (antiarrhythmic drugs (AADs) and anticoagulation), 2) surgical treatment, or 3) catheter ablation. The 2012 AHA/ACC/HRS Atrial Fibrillation guidelines provide recommendations for each treatment type. Antiarrhythmic drugs provide modest antiarrhythmic effect and reduce arrhythmia frequency or duration. Guidelines require anticoagulation since AADs are not completely effective. This includes warfarin or new

oral anticoagulants, factor IIa, Xa inhibitors (rivaroxaban, apixaban, and dabigatran). Each anticoagulant has its own benefits and disadvantages.

Pharmaceutical Therapy

Antiarrhythmic Drugs

The primary objectives of AF management are rate control, anticoagulation, and rhythm control for those patients who are symptomatically limited by the arrhythmia. In general, patients who present with early onset AF, particularly those with non-continuous paroxysmal AF, are prescribed AADs for rate and / or rhythm control. The rhythm-control or rate-control treatment approach must be based upon careful consideration of multiple factors for each patient, including degree of symptoms, co-morbidities and probability of successful conversion to normal sinus rhythm. Patients that are symptomatic and refractory to or intolerant of AADs with any form of AF become potential candidates for a surgical Cox maze procedure or ablation therapy (surgical or catheter based).

Anticoagulant Drugs

Atrial fibrillation increases a patient's risk of ischemic (or embolic) stroke 5-fold.[29,30] Warfarin has long been considered the standard of care oral anticoagulant (OAC) for AF patients reporting greater than 50% stroke risk reduction compared to no treatment and greater than 30% stroke risk reduction compared to aspirin (ASA) therapy. However, due to the limitations of warfarin, it is estimated that only 50% of AF patients are treated with the drug, and compliance significantly declines year over year for reasons including, but not limited to, gastrointestinal bleeding, ambulatory risk, inability to cope with the dose adjustments and monitoring required of warfarin.[31,32] Recently, several new oral anticoagulants (NOACs), factor IIa/Xa inhibitors (rivaroxaban, apixaban, and dabigatran) were introduced to address the limitations of warfarin described above. Each was shown to be as least as effective as warfarin in non-valvular AF patients.[33-35] Similarly to warfarin, there remains a population of AF patients who are contraindicated to NOACs.[36-38] Thus, a significant proportion of the AF population remain unprotected and at high risk for stroke and mortality, prompting approximately 30% of patients to choose OAC despite the added risk for future bleeding events.

The benefits of any oral anticoagulant medication must be balanced with the potential for severe hemorrhagic complications.[39-42] Although felt to be an optimal solution for thrombus protection in the majority of cases, numerous studies have demonstrated that anticoagulation substantially reduces, but does not eliminate, the risk of cerebral complications in patients with AF.[43-45] Oral anticoagulation treatment has been established as safe and effective only in those patients with low bleeding risks, high compliance, and no contraindications. The contraindications for these include comorbidities that call for caution in the broad, prescribed use of the drugs in all patient risk strata.

Therefore, for non-valvular AF patients clinically contraindicated to OAC therapy, an optimal, effective pharmacological option is not currently available. These patients remain significantly exposed and therefore present an unmet clinical need for protection against the risk of stroke without the incumbent risk of severe hemorrhagic complications.

Endocardial Implants

Left atrial appendage closure (LAAC) with an implant occluder is a nonpharmacologic option. More recently, percutaneous, device-based LAA closure implanted via endocardial technique (WATCHMAN™, Boston Scientific) was shown to be non-inferior to warfarin in high-risk AF patients (PROTECT-AF; PREVAIL).[46-48] Importantly, the device was found to be superior to warfarin in preventing systemic embolic complications of AF in the subset of patients in whom the device was successfully placed and met predefined transesopheageal echocardiographic (TEE) criteria for successful LAA closure. While this study provides important proof of concept that successful stand-alone, percutaneous LAA

exclusion in high-risk AF patients may derive the same benefit as those receiving OAC, this approach presents potential limitations, including the requirement of a post-implantation anticoagulation therapy for thrombus mitigation as well as acute and long-term post implantation residual leaks or incomplete sealing of the LAA in a substantial number of cases.[46,49] Finally, these patients are left with a permanent, lifelong implant, prompting discussion around the long-term risks and potential non-implant alternatives.

In addition to the WATCHMAN device, other endocardial implants have been developed. The AMPLATZER™ Amulet™ (Abbott) is an LAA occluder that consists of a self-expanding nitinol lobe and disc that are delivered via catheter; the lobe is inside the LAA and the disc seals the opening. It received CE marking in 2013. FDA recently approved an IDE trial (CATALYST) to compare Amulet to NOACs for stroke prevention. Optimal device positioning has been a topic of investigation. There is potential for prolapse of the device into the LAA (increasing risk of tamponade) but device repositioning can also increase risk of cardiac injury. In 87 consecutive patients with angiographic data to confirm final device positioning, 48% of patients had an incomplete seal [50]. There was a trend towards increased device-related major adverse events in the group with incomplete seal and significantly more device-related complications. However, there were no significant differences in long-term outcomes. Another potential complication associated with Amulet is injury to the pulmonary arteries, which was speculated to occur when an oversized device was used [51].

The LAmbre™ device (Lifetech) (“umbrella in the LAA”) is an LAA occlusion device that features U-shaped hooks, is fully repositionable and recapturable, and has a slimmer delivery System compared to WATCHMAN and Amulet. It has been suggested that it is amenable to problematic LAA morphologies [52]. It was CE-marked in 2016. A recent systematic review of 10 studies (403 patients with non-valvular AF) found a mean major complication rate of 2.9%, including pericardial effusion (1.7%), stroke (0.3%), and mortality (0.3%)[71]. With 6-12 months follow-up, leaks > 5 mm were reported in 1%, device-related thrombosis (DRT) in 0.7%, and stroke/transient ischemic attack (TIA) in 1.7%.

Left Atrial Appendage Surgical Isolation

Surgical LAA exclusion has been performed for more than 60 years either during mitral valve surgery and coronary artery bypass grafting (CABG), or as an integral part of the Cox maze procedure for atrial fibrillation.[53-57] The 2006 AHA/ACC/ESC guidelines for treatment of AF, 2014 AHA/ACC/ESC guidelines for management of patients with AF, and the AHA/ACC/ESC guidelines for treatment of valvular heart disease recommend exclusion of the LAA during concomitant procedures as a prophylactic measure to eliminate a primary source of thrombus.[25,58-60] The 2012 ESC Guidelines for AF management also notes that LAA occlusion should be considered in patients with thromboembolic risk and cannot be managed with long-term OAC.[61] With more than 60 years of history, the clinical basis for ligation and exclusion of the LAA has been firmly established.

Left Atrial Appendage Suture Isolation

Braided polyester sutures are often used in cardiovascular surgery where a strong, non-absorbable suture is needed to help permanently repair tissue. Stronger than silk, the polyester suture provides long-lasting support, which is critical in many applications. The application of a lubricous coating, such as PTFE, permits easier knot pushing. In general, the advantages of using braided suture include ease of handling, low memory and increased knot security.[62] The LARIAT RS Suture Delivery System uses a Size-0 braided and PTFE coated polyester suture.

The clinical basis for ligation and exclusion of the LAA is well established in over 60 years of clinical use and as an integral part of the Cox maze procedure for treatment of AF or as a concomitant procedure to cardiac surgery.[58,59,63-66] Over the years, methods of LAA exclusion have included surgical resections, suture ligation, cutting and non-cutting staples, percutaneous implants, and surgical clips. With specific regard to suture ligation of the LAA, closure can be achieved from both the endocardial and epicardial surfaces.

Endocardial suture ligation of the LAA is an extremely invasive procedure requiring the use of cardiopulmonary bypass and invasion of the atrial dome with associated risk of bleeding and injury to the circumflex coronary artery due to its proximity to the LAA. In addition, endocardial suture ligation has been shown to be incomplete in 36% of patients.[67-69] This high rate of incomplete closure is attributed to several factors: the procedure is performed when the heart is in a flaccid state, the access is generally awkward for traditional suturing, and there is no ready method to confirm completeness of closure intra-operatively. The closure result can be adequately assessed only after the heart is re-perfused, after the opportunity to rectify incomplete closure has passed.

Epicardial suture ligation of the LAA can also be performed without opening the LA and without cardiopulmonary bypass. Epicardial suture closure of the LAA is conventionally performed by either directly sewing the appendage closed or by tightening pre-tied suture loops around the base of the LAA. The success of complete epicardial suture closure ranges from 23% to 100%, and is both technique and operator dependent.[57,70-73] Incomplete suture ligation of the LAA does not appear to be a degenerative process (such as due to suture dehiscence), but rather is present immediately after the procedure.[68] Complications rarely arise due to suture closure of the LAA and are generally limited to LAA tearing that occurs either during the suture needle placement or while grasping the LAA as is required in conventional open surgical approaches.[73,74]

Epicardial Clip Exclusion

Another epicardial method to exclude the LAA is with an atraumatic implant applied on the LAA. However, similar to the stapler technique, the clip method creates a non-anatomical linear closure and the need to grasp the LAA, but does allow repositioning of the clip in the event of an undesirable closure site.[75] These implants, designed for the LAA, are placed under direct visualization and typically concomitant with other open cardiac surgical procedures. The clip, once placed on the beating heart, should provide adequate uniform, non-anatomical linear compression to achieve LAA closure.

The AtriClip® device (AtriCure) is the first approved device for surgical LAA exclusion. The AtriClip device is a self-closing, implantable clip made of two parallel titanium rods connected with nitinol hinges covered in a braided polyester lining. The Clip is attached to a disposable guide. The clip may be repositioned if initial placement is inadequate. Early animal studies demonstrated that the clip left a smooth, linear occlusion line without laceration, which did not migrate or damage adjacent structures.[76-78] The animal studies also supported that the LAA tissue, distal to the clip, atrophied (post 30 day follow-up) and was replaced with fibrous tissues. A recent meta-analysis of the safety and efficacy of AtriClip (placed thoracoscopically or during open concomitant surgery) found that in 922 patients, acute closure was 97.8% and there were no peri-procedural device-related adverse events[79].

7. Suggested profile and training for users

Board-certified medical doctors who perform cardiac interventional procedures using AtriCure instrumentation namely Electrophysiologists, Interventional Cardiologists, and Cardiothoracic surgeons. AtriCure offers additional comprehensive education and training on the use of LARIAT LAA Exclusion System and the LAA ligation procedure as per the device instructions for use. This may include didactic review with an experienced operator and optional simulator/cadaver lab

8. Reference to any harmonized standards and Common Specifications applied

Table 8-1. Compliance to standards

Standard	Compliance – Full, Partial, or No	Justification if Partial or No
BS EN ISO 14971:2019+A11:2021 Medical devices - Application of Risk Management to Medical Devices	Full	N/A
BS EN ISO 14155: 2020 Clinical investigation of medical devices for human subjects - Good clinical practice	Full	N/A
BS EN ISO 10993-1:2020 Biological evaluation of medical devices – Part 1: Evaluation and testing	Full	N/A
BS EN ISO 10993-3: 2014 Biological evaluation of medical devices – Part 3: Genotoxicity, Carcinogenicity and Reproductive Toxicity	Full	N/A
BS EN ISO 10993-4: 2017 Biological evaluation of medical devices – Part 4: interactions with Blood	Full	N/A
BS EN ISO 10993-5: 2009 Biological evaluation of medical devices – Part 5: Cytotoxicity	Full	N/A
BS EN ISO 10993-6: 2016 Biological evaluation of medical devices - Part 6: Implantation	Full	N/A
BS EN ISO 10993-7: 2008 Biological evaluation of medical devices –Part 7 EO Residuals	Full	N/A
BS EN ISO 10993-10: 2013 Biological evaluation of medical devices – Part 10: Skin irritation/sensitization	Full	N/A
BS EN ISO 10993-11: 2018 Biological evaluation of medical devices – Part 11: Test for systemic toxicity	Full	N/A
BS EN ISO 10993-12: 2021 Biological evaluation of medical devices – Part 12: Sample Prep	Full	N/A
BS EN ISO 10993-17: 2009 Biological evaluation of medical devices – Establishment of allowable limits for leachable substances	Full	N/A
BS EN ISO 10993-18: 2020 Biological evaluation of medical devices - Chemical characterization	Full	N/A
ISTA 3A: 2018 Performance testing of Shipping Containers and Systems	Full	N/A
BS EN ISO 11135-1:2014:+A1 2019 Sterilization of health-care products -Ethylene Oxide	Full	N/A
AAMI TIR28: 2016 Product adoption and process equivalency for Ethylene Oxide sterilization	Full	N/A
BS EN ISO 11607-1: 2020 Packaging for terminally sterilized medical devices – Part 1: Requirements for materials, sterile barrier Systems, and packaging Systems	Full	N/A
BS EN ISO 11607-2:2020 Packaging for terminally sterilized medical devices – Part 2: Validation requirements for forming, sealing and assembly processes	Full	N/A
AAMI ST72:2019 Bacterial Endotoxins - Test Methods, Routine Monitoring, And Alternatives to Batch Testing	Full	N/A

ASTM F88/F88M-21: 2021 Standard Test Method for Seal Strength of Flexible Barrier Materials	Full	N/A
ASTM F1980-21: 2021 Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices	Full	N/A
ASTM F2096-11: 2019 Detecting Gross Leaks in Packaging – Bubble Test	Full	N/A
ASTM F1929-15: 2015 Standard Test Method for Detecting Seal Leaks in Porous Medical Packaging by Dye Penetration	Full	N/A
BS EN ISO 15223-1: 2021 Medical devices. Symbols to be used with medical device labels, labelling and information to be supplied: General requirements	Full	N/A
BS EN ISO 80369-7: 2021 Small-bore connectors for liquids and gases in healthcare applications - Part 7: Connectors for intravascular or hypodermic applications	Full	N/A
BS EN ISO 80369-20: 2015 Small-bore connectors for liquids and gases in healthcare applications — Part 20: Common test methods	Full	N/A
BS EN ISO 20417:2021: Medical Devices – Information to be supplied by the manufacturer	Full	N/A
BS EN IEC 62366-1: 2015 + A1 2020 Medical devices - Application of usability engineering to medical devices	Full	N/A
EN IEC 63000: 2018 Technical documentation for the assessment for electrical and electronic products for the restriction of hazardous substances	Full	N/A
ASTM F2503-20: 2020 Standard Practice for Marking Medical Devices and Other Items for Safety in the Medical Resonance Environment	Full	N/A
BS EN ISO 10555-1: 2013+A1:2017 Intravascular catheters: Sterile and single-use catheters. General Requirements	Full	N/A
BS EN ISO 11070: 2014+A1:2018 Sterile single-use intravascular introducers, dilators, and guidewires	Full	N/A
EN ISO 14644-1: 2015 Cleanrooms and Associated Controlled Environments – Classification	Full	N/A
EN ISO 14644-2: 2015 Cleanrooms and Associated Controlled Environments – Monitoring	Full	N/A
N/A – not applicable		

9. Revision history

SSCP Revision Number	Date Issued	Change Description	Validated by Notified Body (Yes or No)	Validation Language

A	See CEM-203.A in AtriCure Document Control for official date issued	New Release	No	English
B	See CEM-203.B in AtriCure Document Control for official date issued	Updates to BUDI-DI, CND codes, added two reasons for change (Fob and tip) and reworded last sentence of user training; update to standards	No	English
C	See CEM-203.C in AtriCure Document Control for official date issued	Revision to respond to BSI review. Aligned device descriptions, warnings, cautions with IFU. Added clinical benefits. Added aMAZE data.	No	English

D	See CEM-203.D in AtriCure Document Control for official date issued	Revision to respond to BSI review. Updated suture materials to mass per revised IFU. Updated Intended patient population section. Aligned clinical benefit description to revised IFU, updated references to standard revisions in Section 8.	No	English

E	See CEM-203.E in AtriCure Document Control for official date issued	Listed Basic UDI-DI by individual device; moved TenSURE into sections 3.3 (clinician) and section 3.4 (patient); included Table 8-1 to indicate full/partial/no compliance to standards; removed MDD product codes. Updated residual risks in clinician section to include probability of occurrence (quantitative and qualitative). Revised narratives in sections 5.1 and 5.3 (clinician section). Moved aMAZE data to section 5.2 and PLACE I data to section 5.3. Added details on FSCA to sections 4.3 (clinical section) and 4.4 (patient section). Removed residual risks not relevant to devices.		

F	See CEM-203.F in AtriCure Document Control for official date issued	Clinician section: Aligned clinical benefit wording with IFU. Updated warning on cobalt. Updated SofTIP to SofTIP13 in Cautions per IFU. Moved description of TenSURE to accessories to align with IFU. Clinical and patient sections: Fixed typo in TenSURE Basic UDI-DI	No	English

G	See CEM-203.G in AtriCure Document Control for official date issued	Updated clinician section 5.5 and patient section 5.3 with additional details on aMAZE CAP	No	English

H	See CEM-203 Rev H. in AtriCure Document Control for official date	• **CEM-203.G was validated by BSI. CEM-203. H was revised to indicate "Yes" in Section 9 to denote Notified Body validation and to include translations only. No content changes from Rev G.** • **Changed "The Netherlands" to "NL"**	Yes	English

1. Tilz RR, Fink T, Bartus K, et al. A collective European experience with left atrial appendage suture ligation using the LARIAT+ device. *Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology.* 2020;22(6):924-931.
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A summary of the safety and clinical performance of the device, intended for patients, is given below.

18 November 2022

INFORMATION INTENDED FOR PATIENTS:

This Summary of Safety and Clinical Performance (SSCP) is intended to provide public access to an updated summary of the main aspects of the safety and clinical performance of the device. The information presented below is intended for patients or lay persons. A more extensive summary of its safety and clinical performance prepared for healthcare professionals is found in the first part of this document.

The SSCP is not intended to give general advice on the treatment of a medical condition. Please contact your physician in case you have questions about your medical condition or about the use of the device in your situation. This SSCP is not intended to replace an Implant card or the Instructions For Use to provide information on the safe use of the device.

1. Device Identification and General Information

Product Name:	LARIAT LAA Exclusion System ('LARIAT System')
Product Group/Family Basic UDI-DI	LARIAT RS LAA Exclusion Device: 0840143900000000000001ZB LARIAT RS LAA Exclusion Device, 50 mm: 0840143900000000000001ZB EndoCATH Balloon Catheter: 0840143900000000000002ZD FindrWIRZ Guide Wire System: 0840143900000000000002ZD SofTIP Guide Cannula: 0840143900000000000002ZD SureCUT Suture Cutter: 0840143900000000000002ZD
Manufacturer Legal Name and Address: Single Registration Number (SRN)	AtriCure, Inc. 7555 Innovation Way Mason, OH 45040 USA SRN: US-MF-000002974
Year when the first certificate (CE) was issued covering the device:	2016

2. Intended Use of the Device

2.1. Intended Purpose

The Left Atrial Appendage (LAA) is a small sac about the size of your thumb that hangs off the left atrium of the heart. Blood can collect in the LAA in people with atrial fibrillation. Atrial

fibrillation is an abnormal rhythm in the upper chambers of the heart. This pooled blood may form clots. The clots may be ejected from the LAA into the heart and blood stream, causing strokes, clogged arteries, and loss of life, limb and function. The LARIAT System is used to close off the LAA from the rest of the heart using a loop of suture material. The only part of the LARIAT System that remains in your body after the LAA closure procedure is the suture. This document also explains the possible risks that may happen during the LAA closure procedure. You must discuss your own condition, treatment options and risks with your own doctor.

2.2. Indication(s) and intended patient groups

The intended patient group is people with non-valvular atrial fibrillation who are recommended to have LAA closure with the LARIAT System by their doctor.

2.3. Contraindications

Your doctor will advise you on the best course of treatment. There are certain conditions for which the LARIAT System should not be used. These include but are not limited to:

- You are not a good candidate for minimally invasive procedure on your heart
- You cannot have a polyester suture inserted into your heart
- Your LAA diameter or length is too large
- You have other conditions, such as any kind of infection in/on your body or inflammation of the heart
- You cannot be exposed to radiation (for example, pregnant or breastfeeding)

3. Device Description

3.1. Device description and material/substances in contact with patient tissues

The LARIAT procedure closes off the LAA using a loop of suture material. The suture is a standard non-absorbable Teflon-coated polyester suture. Catheters are used to deliver the suture loop, slip it around the LAA, and tighten it to close off the LAA. A small piece of suture will remain at the base of the LAA on the outside.

The suture is composed of Poly(ethylene terephthalate). It is dyed with D & C Green No. 6. It contains a small amount of titanium dioxide. No materials or substances in the suture have been found at levels that would pose a risk to the patient over the lifetime of the implant.

FindrWIRZ, SureCUT, and LARIAT devices have small amounts of nickel. FindWIRZ and SureCUT have a small fraction of cobalt. Cobalt considered a substance of concern.

3.2. Information about medicinal substances in the device, if any

There are no medicinal substances in the devices.

3.3. Description of how the device is achieving its intended mode of action

The LARIAT LAA closure procedure closes the LAA off non-surgically. A tight loop of a polyester suture is secured around the base of the LAA. Catheters are used to place the suture loop around the LAA base. Then the loop is tightened to permanently close off the LAA.

3.4. Description of accessories, if any

The TenSURE device made by AtriCure, Inc. (TenSURE, Basic-UDI-DI: 08401439000000000000003ZF) is intended to be used with the LARIAT System.

4. Risks and warnings

Contact your doctor if you believe that you are experiencing side-effects from the LARIAT System or LAA closure procedure or if you are concerned about risks. This document does not replace a discussion with or advice from your doctor.

4.1. How potential risks have been controlled or managed

AtriCure has performed rigorous risk assessment and risk management activities for the LARIAT System. These activities are in accordance with AtriCure internal procedures and international standards. The complications that may happen with use of the LARIAT System and LAA closure procedure are believed to be consistent with those for similar devices and procedures. Measures taken by AtriCure to control risks associated with the use of the LARIAT System include:

- The LAA ligation procedure is performed in a fully equipped operating room, catheterization or electrophysiology lab by doctors trained in LAA closure.
- AtriCure offers comprehensive and continuing education and training on the LARIAT System and the LAA closure procedure to provide doctors with the skills and knowledge necessary for using the LARIAT System safely under the normal use conditions.
- AtriCure LARIAT System experts are available to provide support during LARIAT LAA Exclusion System use.
- Use of the LARIAT LAA Exclusion System within the body is carefully performed using standard practices and noninvasive techniques to visualize it. These techniques include fluoroscopy (‘moving x-rays’) or TEE guidance, to reduce the risk of injury.
- The LARIAT System’s instructions are included in every device package and warn the doctor against known potential hazards.

4.2. Remaining risks and undesirable effects

The following risks and undesirable effects have been observed in clinical studies and in ‘real-world’ device use or can potentially occur with this type of procedure. Risks are like other minimally invasive procedures of the heart and vessels.

More Common (may occur in 20 or less people out of 100)

- **Moderate to Serious**
  - Pericardial effusion: an abnormal collection of fluid in the sac that surrounds the heart
- **Moderate**
  - Pericarditis: the pericardium (sac around the heart) may become inflamed. There may be sharp pain or stabbing feelings from the pericarditis. You may feel this when lying down or trying to take a deep breath. Often, pericarditis is treated with anti-inflammatory medicines, such as ibuprofen.
  - Iatrogenic atrial septal defect: this is the development of a hole, formed by medical treatment or procedure, in the wall that separates the top two chambers of the heart (the atria). This hole allows oxygen-rich blood to leak into the oxygen poor chambers of the heart.
- **Mild to Moderate**
  - Pain/discomfort

Rare (may occur in 5 or less people out of 100)

- **Serious and/or Life Threatening**
  - Air embolism: an air bubble that blocks a blood vessel, potentially leading to heart attack, stroke or death

- Asystole: no cardiac electrical activity
- Bradycardia: slow heartbeat (< 30 beats/min)
- Cardiac perforation or rupture: puncture, tear or hole in the heart
- Complete or partial heart block: the electrical signal generated in the atrium of the heart does not travel to the ventricles, so the heart does not pump effectively; may result in death
- Death
- Emergency during the LAA closure procedure requiring a change in approach: your doctor may need to open your chest to complete the procedure or treat a medical emergency
- Pulseless electrical activity (PEA): a heart rhythm is observed on the electrocardiogram that should be producing a pulse, but is not, causing cardiac arrest and death
- Ventricular fibrillation: uncoordinated contraction of the ventricles in the heart, which are the main pumping chambers, so that they quiver rather than contract properly. No blood is pumped; results in death.
- Ventricular tachycardia: rapid heartbeat of the ventricles; they beat so quickly, they cannot properly fill with blood so only a small amount of blood is pumped out of the heart. May cause loss of consciousness and may proceed to ventricular fibrillation and death.

- **Moderate to Serious**
  - Allergic reaction to contrast media, anesthesia, or heparin: a rash or trouble breathing due to iodine dye, anesthesia, or blood thinner
  - Arrhythmias: changes from the normal heartbeat pattern
  - Bleeding – possibly requiring transfusion: blood loss leading to the need to receive blood products intravenously
  - Cardiac tamponade: collection of blood or fluid in the sac around the heart
  - Cerebrovascular accident: stroke – damage to the brain when the blood flow to the brain is slowed or stopped
  - Congestive heart failure (CHF; new worsening of existing CHF): the heart is unable to pump adequate amounts of blood, causing fluid buildup in the lungs and or rest of the body, fatigue, shortness of breath, and death
  - Coronary artery dissection: a tear in one of the arteries that supply blood to the heart, causing blood to flow between the layers of the heart and reducing its ability to pump blood
  - Coronary artery thrombosis: development of a blood clot inside the arteries that supply blood to the heart
  - Endocarditis: inflammation of the innermost layer of the tissue that lines the chambers of the heart
  - Hypertension: high blood pressure, may lead to stroke
  - Hypotension: low blood pressure
  - Infection, sepsis, or fever: a local or body-wide infection or an immune response triggered by an infection
  - Ischemia: decreased blood flow and oxygen delivery to a tissue, may cause tissue death, such as in a heart attack

- Myocardial infarction (MI): heart attack – the death of heart muscle due to ischemia
- Pleural effusion: abnormal collection of fluid in the space that surrounds the lungs
- Pneumothorax: a collection of air in the space between the chest wall and the lung
- Reaction to medication/contrast media
- Renal (kidney) insufficiency or failure, possibly requiring renal replacement therapy: poor function or failure of the kidneys, possibly requiring dialysis or kidney transplant
- Respiratory distress or failure: inability to breathe
- Stroke – Ischemic: damage to the brain caused by a clot or blockage in the artery(ies) that supply the brain with oxygen.
- Stroke – Hemorrhagic: damage to the brain caused by swelling and pressure from a leak or rupture in a weakened blood vessel in the brain
- Systemic embolism: a blockage that usually lodges in the main artery of the lungs
- Thromboembolism – cardiac: an obstruction of a blood vessel in the heart by a blood clot that has become dislodged from another site in the circulation
- Thromboembolism - non-cerebral: an obstruction of a blood vessel (not in the brain) by a blood clot that has become dislodged from another site in the circulation
- Transient ischemic attack (TIA) or other neurological deficit: a passing episode of neurologic dysfunction caused by loss of blood flow without tissue death or other problems with the nerves, spinal cord or brain function
- Transseptal complications: possible complications from transseptal approach include damage to blood vessels, heart valves, and surrounding tissues
- Vascular access complications: complications resulting from the doctor accessing the blood vessels
- Vascular damage: damage to the blood vessels

- **Moderate**
  - Coronary artery spasm: temporary, sudden narrowing of one of the coronary arteries that supply blood to the heart. The spasm slows or stops blood flow through the artery
  - Deep vein thrombosis: blood clot in the veins of the leg causing pain and swelling. In rare cases part of the clot may break off and go to the lungs
  - Dyspnea: shortness of breath
  - Prolonged exposure to fluoroscopic radiation: longer use of procedure x-ray imaging may cause tissue injury, radiation-induced burn, skin injury or hair loss
  - Pulmonary edema: increased fluid in the lungs
  - TEE complications: possible effects from undergoing a TEE include a sore throat and injury to the esophagus and/or surrounding tissues
  - Thrombosis: formation of a blood clot inside a blood vessel
  - Valvular damage: damage to a heart valve
  - Vasovagal reaction: a reflex that causes the heart to slow down and blood to flow to the legs, often causing fainting

    - Vessel spasm: contraction of the blood vessel, often leading to narrowing of the blood vessel and reduced flow of blood and oxygen
- **Mild to Moderate**
    - Epistaxis: nosebleed
    - Extravasation of contrast media: leakage of iodine dye outside of the blood vessel
    - Hematoma: collection of blood outside of a blood vessel; a severe bruise
    - Hematuria: presence of blood in the urine
    - Hypertrophic scarring: a skin condition resembling scarring, most often at the sites of cuts or burns

Extremely Rare (may occur in 5 people out of 1000)

- **Serious and/or Life Threatening**
    - Device failure or breakage: part of the LARIAT System breaks or does not work as expected
    - Inability to remove device: the LARIAT System cannot be removed per the normal procedure and a surgical procedure may be needed to retrieve it
- **Moderate to Serious**
    - Aneurysm: a weakened part of the wall in artery, may allow it to widen abnormally, balloon out, leak, and/or rupture
    - AV fistula: an abnormal duct or passageway between an artery and a vein
    - Gastrointestinal bleeding: bleeding in any part of the digestive tract (stomach, intestines)
    - Hemothorax: a collection of blood in the space between the chest wall and the lung
    - Pseudoaneurysm: a false aneurysm – a hole in an artery allows blood to leak out and collect in the surrounding tissues

4.3. Warnings and precautions

The FindrWIRZ and SureCUT devices contain some stainless steel parts. Stainless steel contains some nickel and small amount of cobalt. The LARIAT devices have a part that contains nitinol. Nitinol contains nickel. You should discuss with your doctor if you have an allergy or sensitivity to nickel. Cobalt is considered a substance of concern.

Other warnings and precautions for your doctor are listed in the Instructions for Use provided in every LARIAT System product package and in LARIAT System training**.**

4.4. Summary of any field safety corrective action, (FSCA) if applicable

There was one FSCA reported for the FindrWIRZ device on 30 September 2016. It was related to guidewire coating delamination. No harmful effects to a patient ('adverse events') were reported related to this defect. The FSCA was reported to the applicable Notified Body. The devices were recalled and removed from Europe.

5. Summary of clinical evaluation and post-market clinical follow-up (PMCF)

5.1. Clinical background of the device

The LARIAT devices received first CE marks between 2010 and 2019. The LARIAT System and earlier device versions have a proven clinical track record of safety and performance. The LARIAT LAA System and previous generation devices have a proven

clinical track record of safety and performance.

5.2. The clinical evidence for the CE-marking

Clinical evidence for LARIAT LAA Exclusion System is based on public data on the current devices and a previous version of the device called LARIAT+. LARIAT+ is equivalent to LARIAT RS. A study (Tilz et. al., EP Europace 2020) from seven European centres used the LARIAT+ System in 141 patients. They found a high success rate of LAA closure after the procedure. They also found a high success rate of LAA closure at 1-3 months after the procedure. The major adverse event rate (specific, serious problems experienced by study patients) was an acceptable rate of 2.8%.

A multi-centre registry study used the LARIAT System with LARIAT RS and LARIAT+ in combination with another procedure, called ablation. The study reported 100% LAA closure after the procedure in 33 patients. At 1-3 months after the procedure, 6 out of 33 patients had small but acceptable leaks in the LAA. No major adverse events occurred within 7 days of the procedure. One major adverse event occurred within 30 days of the LAA closure and ablation procedure. The study is registered at clinicaltrials.gov (NCT04148625) and was published in Ellis et. al., JACC: Clinical Electrophysiology 2020.

The aMAZE trial used the LARIAT System with LARIAT RS and LARIAT+. The LARIAT procedure was followed by ablation. aMAZE found a high rate of successful LAA closure. The major adverse event rate within 30 days was 3.4%. The study is registered at clinicaltrials.gov (NCT02513797).

Additional published clinical evidence from earlier LARIAT devices is also supportive of the satisfactory safety and performance of LAA ligation. The LAA closure rate without severe leaks has been reported to range from 95-100% in patients after the LAA closure procedure across studies. The LAA remained closed without severe leaks in 91-100% of patients at 45 days to 12 months after the procedure across studies. The overall major adverse event rate was acceptable and ranged from 0-10% in individual studies.

5.3. Safety

AtriCure and doctors who are experts in LAA closure have reviewed the clinical data on the safety of the LARIAT System. They have concluded that the LARIAT System is safe and performs appropriately when used properly by trained doctors. AtriCure has identified actual and potential risks for patients who are treated with the LARIAT System. These risks have been reduced as much as possible. AtriCure also has a robust surveillance program that collects information on use of the LARIAT System. This information includes complaints, device recalls, service and repair information, additional ‘real-world’ use in patients, and ongoing clinical studies. The aMAZE trial was one way that AtriCure collected more safety data on the LARIAT System. More safety data, including any unlikely long-term adverse events, will be collected in the aMAZE Continued Access Protocol trial.

6. Possible diagnostic or therapeutic alternatives

When considering alternative treatments, it is recommended to contact your healthcare professional who can take into account your individual situation.

There are other ways to provide LAA closure. Other devices can be placed inside or outside of the heart to close off the LAA. The LAA can also be closed surgically.

7. Suggested training for users

AtriCure provides comprehensive training and continuing education to doctors who use the LARIAT System. All doctors who want to use the LARIAT System will be offered an initial training session before using the LARIAT System.